IRAQI JOURNAL OF MEDICAL SCIENCES

CHAIRMAN OF THE EDITORIAL BOARD
Tariq I. Al-JUBOORI PhD

CONSULTATORY EDITORIAL BOARD
A.M. ABDUL-KAREEM FRCP
Abdul-Hussien M. AL-HADI PhD
Alaa G. HUSSIEN FICMS
Anam R. AL-SALIHI PhD
Faq H. MOHAMMED PhD
Faruk H. AL-JAWAD PhD
Gassan AL-SHAMMA’ PhD
Hikmat A.R. HATAM FRCS
Malka S. AL-SAADI FRCOG
Nashiet A. NASHIET CABP
Tarik I. AL-JEBOORI PhD

CHIEF EDITOR
Khalid ABDULLA FRCP (Lon.), FRCP (Edin.)

EXECUTIVE EDITORIAL BOARD
Aktham Rasheed AL-SALIHI CABS
Aqeel Jabbar AL-BAHADLI FICMS, CABM
Farqad Badir HAMDAN MSc, PhD
Khalid Tariq AL-NAIB MSc, PhD
Shatha Hussain ALI CABP

IRAQI JOURNAL OF MEDICAL SCIENCES is published quarterly by College of Medicine, Al-Nahrain University
All correspondence and subscription information requests should be addressed to:
The Editor of IRAQI JOURNAL OF MEDICAL SCIENCES
P. O. Box 14222, Baghdad, Iraq.
College of Medicine
Baghdad, Iraq
Tel and Fax: 964-1-5224368
E-mail: Iraqi_jms@yahoo.com

All articles published represent the opinions of the authors and do not reflect the policy of IRAQI JOURNAL OF MEDICAL SCIENCES. All rights are reserved to IRAQI JOURNAL OF MEDICAL SCIENCES. No part of the journal may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopying, recording, or via any storage or retrieval system, without written permission from the journal.

© Copyright 2000
Advisory Board

Abdul-Elaah Al-Jawadi (Al-Mosul University)
Akram Jirjies (Al-Mosul University)
Ali Fakhri Al-Zubaidy (Al-Nahrain University)
Amira Shubb'ar (Al-Mustansiriya University)
Amjad Dawood Niazi (Iraqi Board for Medical Specialization)
Dawood Al-Thamiry (Al-Nahrain University)
Dhafir Zuhdi El-Yassin (Baghdad University)
Fawzan Al-Na’ib (Al-Mustansiriya University)
Hasan Ahmad Hasan (Al-Nahrain University)
Hikmat Al-Sha’rbaf (Baghdad University)
Khalid Abdulla (Al-Nahrain University)
Ilham Al-Taie (Al-Mustansiriya University)
Mahmood Hayawi Hamash (Al-Nahrain University)
Najim A. Al-Roznamachi (Iraqi Board for Medical Specialization)
Nazar El-Hasani (Iraqi Board for Medical Specialization)
Nazar Taha Makki (Al-Nahrain University)
Rafi M. Al-Rawi (Al-Nahrain University)
Raja Mustafa (Al-Mustansiriya University)
Raji H. Al-Hadithi (Iraqi Board for Medical Specialization)
Riyadh Al-Azzawi (Al-Mustansiriya University)
Samira Abdul-Hussain (Tikrit University)
Sarkis Krikour Sitrak (Al-Basra University)
Sarmad Al-Fahad (Baghdad University)
Sarmad Khunda (Baghdad University)
Tahir Al-Dabbagh (Al-Mosul University)
Thamir Hamdan (Al-Basra University)
Usama N. Rifat (Iraqi Board for Medical Specialization)
Zakariya Al-Habbal (Al-Mosul University)
Iraqi Journal of Medical Sciences

Aims and Scope

Iraqi Journal of Medical Sciences is published by College of Medicine, Al-Nahrain University. It is a quarterly multidisciplinary medical journal. High quality papers written in English, dealing with aspects of clinical, academic or investigative medicine or research will be welcomed. Emphasis is placed on matters relating to medicine in Iraq in particular and the Middle East in general, though articles are welcomed from anywhere in the world.

Iraqi Journal of Medical Sciences publishes original articles, case reports, and letters to the editor, editorials, investigative medicine, and review articles. They include forensic medicine, history of medicine, medical ethics, and religious aspects of medicine, and other selected topics.
Iraqi Journal of Medical Sciences (Iraqi JMS) is a periodic, peer-reviewed journal published quarterly by College of Medicine, Al-Nahrain University. Iraqi JMS publishes manuscripts in all fields of health and medicine written in English.

**Types of Contributions:** Original articles, review articles, case studies, editorials, medical education, history of medicine, ethics, practical points, medical quiz, conferences, meetings and letters to the Editor.

**Manuscripts:**
- Submission of a manuscript implies that is not being considered for publication anywhere.
- The author should provide a document officially state that the current work was carried out at the site which provides this certification. The document should be signed by the highest authorized member at that location.
- Manuscripts submitted to IJMS are subject to editorial evaluation and revision by two referees.
- The format of IJMS complies with the uniform requirements for manuscripts submitted to Biomedical Journals, published by the International Committee of Medical Journals Editors (ICMJE) (Vancouver, British Colombia, 1979) and its last update in October 2001, available on the web site www.icmje.org.
- Manuscript should be typewritten double spaced on size A4 (29.5x21 cm) paper with wide margins. Page should be numbered consecutively. One original and two photocopies including figures, tables, and photographs should be submitted. Begin each of following sections on separate page in the following sequence: Title page, abstract and keywords, text, acknowledgments, references, tables, and legends for illustration.
- Manuscript and figures will not be returned to the authors whether the editorial decision is to accept, revise or reject.
- Manuscripts must be accompanied by a covering paper signed by all authors that the paper has not been published in and will not be submitted to any other journal if accepted in IJMS.
- The page should contain (a) title of the manuscript, (b) names of each author (first name, middle initial and family name) including highest academic degree, (c) official academic and/or clinical title and affiliation (d) name and address of the institution where the work was done (e) name and address (E-mail if available) of the author to whom correspondence should be sent.

**Abstract:** manuscript should include an abstract of not more than 150 words. Structured abstract typed on a separate sheet and consist of background, objective, method, results, and conclusion. Translation in Arabic to be included:

(خلفية الدراسة، هدف الدراسة، طريقة العمل، النتائج و الاستنتاج).

**Keywords:** three to ten keywords should be provided on the same page as the abstract in Arabic and English. As far as possible, be selected from the National Library of Medicine Medical Subject Headings.

The Arabic abstract should follow the United Medical Dictionary (Council of Arab Ministers of Health/WHO/ Arab Medical Union/ALESCO, 3rd edition).
• Manuscript format: It should be divided into the following parts: introduction, materials and methods, results and discussion.
• References: All references should be listed in consecutive numerical order by English numerical, in the order of citation in the text. Once a reference is cited all subsequent citations should be to the original number.

Examples
• Tables: Each table should be typed on a separate page double-spaced, including all headings, number all tables with English numerals and include a short title. Vertical lines between columns are to be avoided.
• Figures: All figures must be suitable for reproduction without being retouched or redrawn. Figure number, name of senior author, and title of the work should be written lightly on the back with red pencil. Photographs must be supplied as glossy black and white prints. The top of the figures should be indicated clearly.
• Legends: Captions for figures must be typed; double spaced, and must not appear on the figure.

Proof Reading will be done by the secretarial office of the journal. The principal author will receive a copy of the journal. The authors are responsible for accuracy of all statements, data, and references included in the manuscript.
• After the manuscript has been accepted for publication, authors are required to supply the final version of the manuscript on 3.5” IBM-compatible floppy disk in MS word version 6 or later.
• All corresponding to be addressed to the Chief Editor on the address below:

Chief Editor:
Iraqi Journal of Medical Sciences
College of Medicine,
Al-Nahrain University,
P.O. Box 14222,
Tel. 5231521,
Al-Kadhiymia,
Baghdad,
IRAQ.
CONTENTS

LEADING ARTICLE

❖ CARDIAC RESYNCHRONIZATION THERAPY (CRT): A NEW PACING THERAPY FOR CHRONIC HEART FAILURE
   Ammar Al-Hamidi ...........................................................................................................................................1

ARTICLES

❖ ESTABLISHMENT OF REPRODUCIBLE LYMPHOBLASTOID CELL LINES
   Ismail I. Latif, Layla Al-Omar, Nidal Abdul-Muhymen .................................................................3

❖ ALTERATION IN THE LEVEL OF SOME TRACE ELEMENTS IN THE SERA OF PATIENTS WITH KALA AZAR
   Nada M. Al-Basheer, Yahya Y.Z. Farid, Hussein K.A. Hussein, Huda Th. Hatha...............10

❖ SCHOOL ACHIEVEMENT OF DIABETIC ADOLESCENTS: A PRELIMINARY REPORT
   Abdul Hussain M. Al-Hadi, Jawad K.A. Al-Diwan, Eqbal G.A. Ma’ala, Amjad Niazi ..............14

❖ THE ASPARTATE AMINOTRANSFERASE TO ALANINE AMINOTRANSFERASE RATIO AND HCV INFECTION
   Al-Kubaisy W. A., Habib M.A. ..................................................................................................................18

❖ STUDY OF DIFFERENT CLINICAL AND DEMOGRAPHIC CHARACTERS OF PATIENTS WITH THALASSEMIA AND THEIR RELATION TO HEMOGLOBIN, SOME MINERALS AND TRACE ELEMENTS AND ALBUMIN LEVELS IN THEIR BLOOD
   Enas T. Abdul-Karim, Firyal H. Abdul-Jalil, Thabit N. Al-Azawi .........................................................21

❖ ANTIOXIDANT STATUS IN THALASSEMIC PATIENTS
   Subuh S. Al-Mudalal, Raad J. Musa, Najat AL-Duliami ........................................................................38

❖ VASCULARIZATION IN PROSTATIC CARCINOMA
   Faiza A. ALRawi .........................................................................................................................................45

❖ SERUM COPPER AND ZINC LEVELS AND COPPER/ZINC RATIO IN PATIENTS WITH RHEUMATOID ARTHRITIS
   Yahya Y.Z. Farid, Alaa K. Mohammed, Israa S. Mohammed...............................................................49

❖ MOTHER AGE AT MARRIAGE AS A DETERMINANT OF REPRODUCTIVE HEALTH
   Enas T. Abdul-Karim, Abdul-Hussain Al-Hadi .........................................................................................57

❖ THE BIOLOGICAL ROLE OF ZINC, COPPER AND MAGNESIUM DURING THE GROWTH OF EMBRYONIC CHICK LIMB BUDS
   Yahya Y.Z. Farid, Hayder J. Mobarak, May F. Al-Habib .......................................................................63

❖ MALE INFERTILITY AND PHYSIOLOGICAL ROLE OF ZINC
   Ali T. Al-Baldawi, Nazar A. Naji, Aqeel A.A. Al-Ani ............................................................................67
A RANDOMIZED PROSPECTIVE STUDY COMPARING THE EFFECTIVENESS OF MITOMYCIN C AND MITOMYCIN/Scomplex sequential intravesical therapy for superficial bladder cancer
Ahmad A. Al-Azawi, Abdul-Wahab R. Hamad, Mahmood H. Hammash ..........................72

TUBERCULOSIS OF THE BREAST IN SAMARRA CITY
Harith M. Al-Khateeb ........................................................................................................77

EOSINOPHIL COUNT AND RELATION TO CHILDHOOD ASTHMA
Hussam M. Al-Alwany, Falih Salim, Shatha H. Ali ............................................................81

SERUM CALCIUM LEVEL IN PATIENTS WITH TYPE II DIABETES MELLITUS
Baybeen K. Al-Selevany .......................................................................................................84

CONGENITAL HYPOTHYROIDISM IN AL-KADHIYMIA TEACHING HOSPITAL, BAGHDAD-IRAQ
Nasheit A. Nasheit, Husam Al-alwani, Iman S. Mahmoud ..................................................89

RESPIRATORY DYSFUNCTION IN PATIENTS WITH MYASTHENIA GRAVIS
Abdul-Kareem A.M., Sajid I.K. Al-Hussaini ........................................................................93

FEMALE HYPERPROLACTINEMIA: ANALYSIS OF PRESENTATION AND DIAGNOSTIC EVALUATION. IS PITUITARY MAGNETIC RESONANCE IMAGING ALWAYS INDICATED?
Sahar L. Halabia, Ayad Sh. Salih ..........................................................................................99

CASE REPORT

ASSOCIATION OF MULTIPLE NEUROLOGICAL DISEASES IN YOUNG FEMALE
Abdul-Kareem A.M., Hasan A. Al-Hamdani ........................................................................111

NEW THERAPEUTIC MODALITIES ..................................................................................115
Xeloda
Strattera

ARABIC ABSTRACTS
ESTABLISHMENT OF REPRODUCIBLE LYMPHOBLASTOID CELL LINES

Ismail I. Latif MSc PhD, Layla Al-Omar BSc PhD, Nidal Abdul-Muhymen BSc PhD

Abstract
Background: A whole blood culture started with mononuclear cell fraction would contain several different cell types. Nevertheless, the T-lymphocytes can be cultured specifically and will outgrow the others, eventually resulting in highly enriched population.

Objective: The study was conducted as a trial of establishment of lymphocytes cell lines. This series of experiments were done for five selected subjects. The same protocols were applied to all individuals.

Method: One ml of heparinized blood (HB) was cultured in tissue culture flask containing 9 ml stimulation medium. The flask was incubated at 37°C in CO2 incubator for 3 days. Then every three days 1ml of whole blood culture from the flasks was subcultured into other tissue culture flask containing 9 ml stimulation medium, until visible suspension of mononuclear cells intervening agglutinated red blood cells were seen within two weeks of culture.

Results: After the whole blood mononuclear cells cultures were maintained up to two weeks, the mononuclear cells were separated. Twenty four-hour incubation of these separated lymphocytes in stimulation medium, pure rich mononuclear cells were obtained and seen under inverted microscope.

Conclusion: A new method for cultivation of lymphocytes from whole blood was developed for the first time and probably no other reported comparable method conducted elsewhere until now. Pure lymphocytes cultures were established, and maintained cell division. The potentiality of human peripheral lymphocytes themselves to act as precursor has been demonstrated in vitro by the cloning of established lymphoblastoid cell line. Different procedures for generation of T-cell lines were outlined. No feeder cells were needed in our protocol or the addition of IL2.

Key words: lymphocyte culture, cell line, Phytohemagglutinin


Introduction
Advances in the understanding of lymphocyte biology have been accompanied by improvement in the techniques of long-term culturing of human T-lymphocytes[1]. Long-term culturing of human T-lymphocytes can lead to establishment of stable line. These cultures respond to produce a wide range of cytokines. More importantly, T-cell lines can be generated which is antigen responsive.

Many aspects of the T-cell response to antigen have been described using antigen specific cell lines[2,3,4]. Human lymphocytes can be isolated from whole blood by centrifugation using a commercially available high-density medium. This allows a single step gradient separation of blood, which yields the mononuclear cell fraction[5]. A culture started with mononuclear cell fraction would contain several different cell types. Nevertheless, the T-lymphocytes can be cultured specifically and will out grow the others, eventually resulting in highly enriched population. To achieve this, the antigen reactive cells must be first stimulated with antigen followed by expansion of cell
numbers using the T-cell specific growth hormone interleukin 2 (IL2). It should be noted that the absolute frequency of antigen response T-cells is low, being between 0.01% and 0.001%, even when blood known to contain relevant T-cells (i.e. blood from an immune donors) is used. Thus, the majority of the cells in the starting culture will die and only the T-cell activated by antigenic stimulation will survive\[6\].

This stimulation not only selects out the antigen-specific T-cells but result in the cellular expression of the receptor for the IL2\[7\]. When exogenous source of IL2 is now added to the activated T-cells, they will undergo further round of replication. Since T-cells eventually become refractory to the effect of IL2, they must be restimulated for receptor expression\[8\]. A T-cell line can thus be maintained in culture by alternate stimulation with antigen and expansion with IL2\[5\].

Phytohemagglutinin (PHA) activated peripheral CD95+ T-cells are resistant to CD95 mediated apoptosis. After prolonged interleukin-2 treatment, these T-cells become CD95 mediated apoptosis sensitive. In T-cells activated in vitro, up-regulation of bcl-xL, has previously been correlated with general apoptosis resistance\[9\].

Therefore, this study was conducted as a trial of establishment of lymphocytes cell lines from whole blood.

**Materials & Methods**

This series of experiments were done for five selected normal adult subjects, their ages ranged from 15 to 45 years, (four males and one female). The same protocol was applied to all individuals. Two ml of venous blood was collected from each subject and placed in sterile heparinized tube.

One ml of heparinized blood was cultured in tissue culture flask containing 9 ml of stimulation medium (SM) (1 x RPMI 1640, penicillin 100 unit/ml, and streptomycin 100µg/ml, 10mM L-glutamine, 20% fetal bovine serum (FBS), 10mM HEPES, 200µl/ml PHA). The flask was incubated at 37°C in CO\(_2\) incubator. Then every three days 1ml of whole blood culture was subcultured into other tissue culture flask containing 9 ml of SM, until visible suspension of mononuclear cells intervening agglutinated red blood cells were seen within two weeks of culture. Then, the mononuclear cells were separated by the method described by Boyum (1968)\[10\], washed twice with serum free medium (1x RPMI 1640, penicillin 100 unit/ml, and streptomycin 100µg/ml, 10mM L-glutamine 10mM HEPES); counted, assessed for viability, then 1ml of 2 x 10\(^6\) cells were cultured in tissue culture flask containing 9 ml of SM. Another 1 ml of cells was cultured in tissue culture flask containing 9 ml of growth medium (GM) (as stimulation medium without PHA). After 24-hour incubation, cell culture was examined under inverted microscope.

At that time, the cells were counted and assessed for viability. The percent of viable cells were determined at indicated time intervals in both GM and SM, and 2 x 10\(^6\) cells were subcultured in tissue culture flask containing 9 ml of SM or GM, every 72 hour. The lymphocytes culture was maintained continuously by this method.

**Results**

**Preparation of Primary Human Peripheral Blood Mononuclear Cells Culture:**

Heparinized blood was cultured in SM, and subcultured frequently as mentioned in materials and methods. The visible suspensions of mononuclear cells intervening agglutinated red blood cells were seen within the second week of culture (figures 1 a & b).
Establishment of reproducible .... Latif et al

Figure 1a: Photomicrograph Shows Whole Blood Lymphocytes Culture during the first week (X 250)

Figure 1b: Photomicrograph Shows Whole Blood Lymphocytes Culture during the second week (X 250)

Purification and propagation of PBMC culture:
After the whole blood mononuclear cell cultures were maintained up to two weeks, the mononuclear cells were separated as described in materials and methods. Twenty-four hour incubation of these separated lymphocytes in SM, pure rich mononuclear cells were obtained and seen under inverted microscope (figure 2).

Figure 2: Photomicrograph Shows Purified Stimulated Lymphocytes Culture after the second week of whole blood culture (X 250).
Establishment of reproducible …. Latif et al

Iraqi Journal of Medical Sciences

6

Stimulation was indicated by a rapid increase in the number of cells (count were increased 200 fold within two weeks of subculture of the purified lymphocyte) (table 1 & figure 3).

Table 1: Effect of cell proliferation and cell death on viable count over two week’s period, using growth or stimulation medium. The seeding density was 2x10⁶/ml

<table>
<thead>
<tr>
<th>culture media</th>
<th>Number</th>
<th>Absolute Number of viable lymphocyte count /ml (x10⁶)</th>
<th>Zero time</th>
<th>Days after culture initiation</th>
<th>1</th>
<th>3</th>
<th>5</th>
<th>8</th>
<th>11</th>
<th>14</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stimlation medium</td>
<td>Sample1</td>
<td>0.2</td>
<td>2</td>
<td>25</td>
<td>70</td>
<td>125</td>
<td>250</td>
<td>400</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sample2</td>
<td>0.2</td>
<td>1.5</td>
<td>20</td>
<td>50</td>
<td>100</td>
<td>200</td>
<td>350</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sample3</td>
<td>0.2</td>
<td>2.5</td>
<td>30</td>
<td>80</td>
<td>150</td>
<td>300</td>
<td>450</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sample4</td>
<td>0.2</td>
<td>2</td>
<td>22</td>
<td>75</td>
<td>130</td>
<td>260</td>
<td>410</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sample5</td>
<td>0.2</td>
<td>2</td>
<td>18</td>
<td>65</td>
<td>110</td>
<td>220</td>
<td>380</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>0.2</td>
<td>2</td>
<td>23</td>
<td>68</td>
<td>123</td>
<td>246</td>
<td>398</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>0</td>
<td>0.3</td>
<td>4.6</td>
<td>11.5</td>
<td>19.2</td>
<td>38.4</td>
<td>37</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Growth medium</td>
<td>Sample1</td>
<td>0.2</td>
<td>2</td>
<td>25</td>
<td>60</td>
<td>50</td>
<td>31</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sample2</td>
<td>0.2</td>
<td>1.5</td>
<td>20</td>
<td>39</td>
<td>35</td>
<td>26</td>
<td>2.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sample3</td>
<td>0.2</td>
<td>2.5</td>
<td>30</td>
<td>62</td>
<td>52</td>
<td>35</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sample4</td>
<td>0.2</td>
<td>2</td>
<td>22</td>
<td>60</td>
<td>48</td>
<td>25</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sample5</td>
<td>0.2</td>
<td>2</td>
<td>18</td>
<td>58</td>
<td>47</td>
<td>24</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>0.2</td>
<td>2</td>
<td>23</td>
<td>55.8</td>
<td>46.4</td>
<td>28.2</td>
<td>3.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>0</td>
<td>0.1</td>
<td>4.6</td>
<td>9.4</td>
<td>6.6</td>
<td>4.6</td>
<td>0.5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Means cell count (x 10⁶)

Time of maintainance (days)

Figure 3: Effect of cell proliferation and cell death on viable count over two weeks period, using stimulation medium, each point represent the mean of 4 values. The seeding density was 2x10⁶/ml

Many cells became enlarged, and the medium turning yellow 2-3 days after subculture. A clear stimulation event was recognized without the aid of an inverted microscope when the bottom of the tissue culture flask showed a large grayish white central button of cells surrounded by white pinpoint satellitate colonies. Another (2 x 10⁶/ml) of cells from day one culture were cultured in growth medium. A reduction in viable cell
counts after day 5 of culture was observed as shown in table 1 & figure 4.

Figure 4: Effect of cell Proliferation and cell death on viable count over two weeks period, using growth medium. Each point represents the mean of 4 values. The seeding density was 2x 10^6/ml

All the stimulated cells gave lymphoblast characteristics when stained with Giemsa stain, so actually we can apply the lymphoblastoid cell line as indicated from their morphological appearances.

**Discussion**

This work probably to be the first method to be reported for preparation of continuous lymphocytes culture and probably no other reported comparable method conducted elsewhere till know.

**Purification and propagation of PBMC culture:**

Human lymphocytes can be isolated from whole blood by centrifugation using a commercially available high-density medium, which relies on lymphocytes being less dense than erythrocytes and granulocytes. This allows a single step gradient separation of blood, which yields the mononuclear cell fraction\[5\]. Then pure lymphocyte cultures were established, and induced and maintained cell division.

A culture started with mononuclear cell fraction would contain several different cell types. Nevertheless, the T-lymphocytes can be cultured specifically and will out grow the others, eventually resulting in highly enriched population. Beside T-cells, other mononuclear cell types are present in the initial culture. These cells have the capacity to activate T-lymphocyte by processing and presenting antigen to the T-cell receptor (TCR) and provide additional T-cell growth factors\[11,12\].

T-cells can be activated by some mitogens. Most T-cells are stimulated by PHA, a lectin isolated from kidney beans, or by concavalin A extracted from castor bean. These molecules are able to bind to T-cell surface molecules including the T-cell receptors (TCR) complex and CD2, causing them to cluster on cell surface, there by mimicking the clustering caused by antigen presentation. Such mitogens however will activate the T-cells regardless their antigen specificity\[13\].

In this assay, PHA was used as mitogen because their stimulation percentage was higher than that of Con A, as indicated early by the results of our
Establishment of reproducible…. Latif et al

Iraqi Journal of Medical Sciences

study and easy to be manufactured in our laboratory[14].

**Whole Blood Lymphocyte Culture:**
We have developed a new method for isolation and cultivation of lymphocytes from whole blood. Heparinized venous blood drawn from normal individuals was added and incubated in SM and the subculture was regularly maintained. Lymphocytes were isolated when lymphocytes suspension was seen by inverted microscope intervening agglutinated red blood cells (figures 1 a & b).

It has been suggested that a cellular components of erythrocytes in whole blood play an important role for the proliferation of the lymphocytes with no effect on their genetic materials. The use of whole blood greatly simplifies lymphocyte culture. In addition, the use of non-separated blood will retain all blood cells, especially RBC, in natural condition thus allowing metabolic activation of environmental pollutants to take place[15,16].

The potentiality of human peripheral lymphocytes themselves to act as precursor has been demonstrated in vitro by the cloning of established lymphoblastoid cell line[17].

Choi and Bloom in 1970[18] established CKW–1 cell line involved a mixed lymphocyte culture, they used small inoculum of PGLC-33H cells (cell line from infectious mononucleosis patient) as feeder cells. They also used lysates of previously established lines as a second method of lymphocyte cell line establishment.

Different procedures for generation of T-cell lines were outlined[5]. They used Daudi or any lymphoblastoid cell line that are different from that of donor PBMCNs. Antigen specific T-cell lines were established using foreign antigens such as tetanus toxoid or PPD, restimulation with antigen, with the addition of IL2, and treatment of antigen presenting cells were included[5].

None of them used a whole blood culture for establishment of lymphocytes cell lines. No feeder cells were needed in our protocol or the addition of IL2. Phytohemagglutinin-activated peripheral T- cells were found to be resistant to CD95 mediated apoptosis, and after prolonged IL-2 treatment, these T- cells became CD95 mediated apoptosis sensitive[9].

Investigations on resting T-cells, i.e., lymphocytes depleted of macrophages and pre-activated cells were made. When PHA was added to these cells resulted in activation with expression of IL-2R (CD25) but not in proliferation. In contrast, addition of PHA plus sheep RBC, which bind to the CD2 receptors, caused IL-2R expression, IL-2 production, and proliferation[19].

A trial of phenotype of the established cell lines was under work. Great benefits can be obtained from this work: this cell lines can be used for virus propagation for example measles virus, different cytokine production, and for different immunological techniques.

**Monitoring the growth of cultures by direct observation:**
Although the growth of the Lymphoblastoid cell lines was, to a large extend, synchronized by stimulation culture, some cultures will grow faster than the others (as indicated in figure 1). It was only by examining the cells on a routine bases with the inverted microscope that the rapidly growing cultures can be identified and cultured accordingly, or by supplementation of GM. In addition, direct observation was the only way of verifying that the cells are actually growing, on day-to-day basis.

**References**
ALTERATION IN THE LEVEL OF SOME TRACE ELEMENTS IN THE SERA OF PATIENTS WITH KALA AZAR

Nada M. Al-Basheer¹ BSc PhD, Yahya Y.Z. Farid² BSc PhD, Hussein K.A. Hussein³ MSc, Huda Th. Hathal¹ BSc PhD

Abstract

Background: Visceral leishmaniasis (Kala-azar) is an important endemic disease in Iraq (WHO 2000). The disease appears to affect infants and young children mostly under 2 years old. The disease is very dangerous and fatal if it is left without treatment. Trace elements have an important role in the treatment and prognosis of different types of parasitic infection.

Objective: Study the relationship between serum trace elements and the disease which may be used as an indicator of the course of the disease.

Methods: 14 male and 12 female patients (positive IFAT) their age were between 6 months and 15 years were used in this study.

Results: There is a significant increase (p<0.05) in serum Cu and significant decrease in serum Zn of kala-azar patients.

Conclusions: Body reaction against parasite infection is associated with different changes in serum level of trace elements.

Keywords: kala-azar, trace elements, copper, zinc, magnesium, visceral leishmaniasis


Introduction

It has become well established that many trace elements play an essential role in a number of biological processes through their action as activator or inhibitor of enzymatic reaction by competing with other elements and proteins for the binding sites, by influencing the permeability of the cell membrane[1], or through other mechanism[2]. Several biological mechanisms have been proposed to explain how trace elements could reduce the incidence of a number of different cancer and infectious disease[3]. Visceral leishmaniasis is an important endemic disease in Iraq[4,5].

Materials & methods

Twenty-six kala-azar patients were studied depending on their positive IFAT test. The age ranges were between 6 months and 15 years. Twelve patients...
were females and 14 males. Samples were collected from patients attending Al-Kadhimiya teaching hospital. Venous blood samples were collected from patients before administration of any medications. Sera were separated and kept at (-20°C) until used.

**Assay:** 0.1ml of serum diluted to total volume of 1ml using 6% n-butanol solution and analyzed for their copper and zinc contents using atomic absorption spectrophotometer (Shimadzu AA-646) with an. Copper and zinc hallow cathode lamps were used at wavelengths of 324.75 nm and 213.9 nm respectively. The assay for magnesium estimation was carried out by adding 4.9 ml. of (1% lanthanum chloride) solution to 0.1 ml. of serum. These solutions were aspirated directly into air-acetylene flame and the magnesium hallow cathode lamp were used at a wavelength of 285.2 nm.

**Statistical methods:** The results were analyzed statistically, and their values were expressed as (mean ± SED). The level of significance was determined by employing (t) test. Only when the p value was less than 0.05; the difference between two groups considered statistically significant.

**Results & Discussion**

The mean and standard deviation values of serum copper, magnesium, and zinc of healthy controls and patients with kala-azar are presented in Figure 1.

The results showed that there is a significant increase in serum copper in kala-azar patients as compared with healthy controls. This result is due mainly to the body reaction against infection.

Cerruloplasmin which is a copper containing protein is one of the acute phase reactant proteins that increased in inflammation and hence leading to increase serum copper. α-Cerruloplasmin inhibits the oxidant injury of the cells by scavenging the superoxide radicals through dismutation reaction similar to superoxide dismutase enzyme[7] or by reduction the copper ions within the protein[8]. Other workers[9] have proposed that cerruloplasmin acts by converting the reduced iron(Fe^{2+}) to an oxidized form (Fe^{3+}) because it acts as ferroxidase enzyme. Yet, the majority of the antioxidant activity in the serum is dependent on the level of this copper containing protein[10]. There is also other cause explaining the increase of
serum copper in those patients is due to shed copper ions from damaged hepatocells which is the late complication of the disease\[^{11}\]. This fact is confirmed by reports that recorded an elevation in the level of liver enzymes in the sera of kala-azar patients\[^{12}\]. There is a significant decrease at (p<0.05) in serum zinc in kala-azar patients as compared with healthy controls. This may be due to part to the hypoalbuminaemia developed in these patients after a period of incubation of the disease\[^{13}\]. Zinc is transported mainly bound to albumin molecules and the decreased in albumin concentration in serum leads to decrease zinc level in serum. Other reason is associated with the immune changes in kala-azar patients. Those patients have impaired immunity\[^{14}\] and because there are good evidences about the relationship between the zinc level and immunity\[^{15}\]; it can be concluded that the zinc is decreased as the immunity attenuated. These results are in agreement with other previous work regarding serum trace elements levels in cutaneous Leishmaniasis patients\[^{16}\].

Serum magnesium of patients with kala-azar are insignificantly decrease in comparison with healthy controls. Magnesium level is normally kept within narrow limits, which implies close homeostatic control and about 35% of the magnesium in plasma is protein-bound mainly to albumin\[^{17}\]. Hence this decrease is attributed mainly to the hypoalbuminaemia state in kala-azar patients\[^{13}\].

Figure 2 shows the relationship between the serum metals as a function to the sex in kala-azar patients. There is a significant increase in serum copper in male patients as compared with female while there is an inverse correlation in serum zinc between males and females. Serum magnesium is not significantly different in both sexes. There is no simple explanation for these results and more investigations are necessary to predict the sexual variance in the level of the metals.

Figure 3 shows that there is age dependence of serum copper but not zinc or magnesium in kala-azar patients. The patients who were of one-year age. Others had a higher serum copper than patients of more than one year of age. This variation may be related to the rate of development and homeopoiesis between these two groups.
References


SCHOOL ACHIEVEMENT OF DIABETIC ADOLESCENTS: A PRELIMINARY REPORT

Abdul Hussain M. Al-Hadi¹ MBChB MSc PhD, Jawad K.A. Al-Diwan² MBChB MSc, Eqbal G.A. Ma’ala³ BSc MSc PhD, Amjad Niazi⁴ MBChB PhD

Abstract

Background: Adolescents struggle to achieve their identity, independence and to cope with all aspect of life. Diabetes may slow the psychological development of adolescents.

Objective: to through a light on the school achievements of adolescents with type I diabetes mellitus.

Methods: 160 diabetic adolescents were included in this study. Full information including age, sex, age of onset, duration, sport activity and admission to the hospital collected. Multiple regression analysis was used to examine the association between the school achievement and the independent variables.

Results: School achievement was significantly associated with visits to diabetic clinics and sport activity.

Conclusion: Visits to diabetic clinics and sport activity improve the school achievement among diabetic adolescents.

Keyword: Adolescents, diabetes mellitus, school achievements


Introduction

Adolescence period is a transitional period between childhood and adult hood. During this period adolescents struggle to achieve their identity (a major task for this developmental stage), independence and to cope with all aspects of these changes¹,². Chronic illness like type I diabetes mellitus {Insulin Dependent Diabetes Mellitus (IDDM)} has an impact on the achievement of the developmental tasks. Diabetes may slow the psychological development of the adolescents, thus affecting their ability to play and enjoy life, share with others, set limits, identify and make commitments. This study was carried out to through light on the school achievement of the adolescents with type I DM.

Subjects & methods

Adolescents with type 1 DM were enrolled in the study from different diabetic centers (National Diabetic Center at Al-Yarmouk teaching hospital, Diabetic Consultancy Clinic at Al-Kadhimia teaching hospital, Diabetic Consultancy Clinic at Al-Mansour teaching hospital and Diabetic Consultancy Clinic at Ibn Al-Beldy teaching hospital) in Baghdad city. Adolescence period is considered between 12-21 years³,⁴. Each participant was interviewed individually. Questionnaires were checked according to the adolescent’s answers. Full information including age, sex, age of onset, duration, sport activity, school activity and admissions to hospital were collected.

A pilot study was done to examine the adolescent’s understanding of the questions (instrument items) and to obtain preliminary estimates of the time required for each adolescents and to
School achievement of diabetic adolescents …. Al-Hadi et al

School achievement of diabetic adolescents was significantly associated with burden of DM, visits to diabetic clinic and sport activity (p < 0.05).

**Results**

A total of 160 diabetic adolescents with type 1 DM were included in the study. Their age range was 12 – 21 years (15.1± 2.3) and 53.8% of them were females. 51.3% of the adolescents had DM for more than five years. The age of onset was less than six years in 78.2% of them. 76.9% of them reported no history of admission to hospital. None of them was in the secondary school, while 33.1% of them were not able read and wrote, 47.5% were in the primary school and 17.5% were in the intermediate school. 53.8% of the adolescents participated in sport activity (Table 1).

### Table 1: Characteristics of the diabetic adolescents included in the study

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤15 years</td>
<td>98</td>
<td>(61.3)</td>
</tr>
<tr>
<td>&gt;15 years</td>
<td>62</td>
<td>(38.7)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>74</td>
<td>(46.2)</td>
</tr>
<tr>
<td>Female</td>
<td>86</td>
<td>(53.8)</td>
</tr>
<tr>
<td>Duration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤5</td>
<td>78</td>
<td>(48.7)</td>
</tr>
<tr>
<td>&gt;5</td>
<td>82</td>
<td>(51.3)</td>
</tr>
<tr>
<td>Age of Onset</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤6</td>
<td>35</td>
<td>(21.8)</td>
</tr>
<tr>
<td>&gt;6</td>
<td>125</td>
<td>(78.2)</td>
</tr>
<tr>
<td>Hospital admission</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>37</td>
<td>(23.1)</td>
</tr>
<tr>
<td>No</td>
<td>123</td>
<td>(76.9)</td>
</tr>
<tr>
<td>School achievement</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not read and write</td>
<td>3</td>
<td>(1.9)</td>
</tr>
<tr>
<td>Primary</td>
<td>53</td>
<td>(33.1)</td>
</tr>
<tr>
<td>Intermediate</td>
<td>76</td>
<td>(47.5)</td>
</tr>
<tr>
<td>Secondary</td>
<td>28</td>
<td>(17.5)</td>
</tr>
<tr>
<td>Sport activity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>86</td>
<td>(53.8)</td>
</tr>
<tr>
<td>No</td>
<td>74</td>
<td>(46.2)</td>
</tr>
</tbody>
</table>

School achievement was not associated with age, sex, age of onset and duration of DM. These findings are shown in table 2.

### Table 2: Predictors of school achievement among diabetic adolescents

<table>
<thead>
<tr>
<th>P value</th>
<th>R²</th>
<th>Predictors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model I</td>
<td>0.02</td>
<td>NS</td>
</tr>
<tr>
<td>Model II</td>
<td>0.015</td>
<td>NS</td>
</tr>
<tr>
<td>Model III</td>
<td>0.2</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Model IV</td>
<td>0.2</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Model V</td>
<td>0.7</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Model I: Age, sex, and age of onset, Model II: Age, sex, age of onset and duration, Model III: Age, sex, age of onset, duration and burden of DM, Model IV: Age, sex, age of onset, duration, burden of DM and visits to diabetic clinic, Model V: Age, sex, age of onset, duration, burden of DM, visits to diabetic clinic and sport activity.
Discussion
The finding that school achievement are not significantly associated with age, sex and duration of diabetes is inconsistent with the findings of Delamater\textsuperscript{8} and Golden et al\textsuperscript{9}. They reported that patients with early onset of diabetes had shown poorer cognitive performance and associated with subsequent learning disabilities. Larsson et al\textsuperscript{10} reported that patients in poor metabolic control have a lower educational level. The finding that age and duration of diabetes had no effect on school achievement reflects a good metabolic state achieved in the diabetic clinics included in the study.
Visit to diabetic clinics was positively associated with school achievement. Ryan et al\textsuperscript{11} found that children with diabetes missed school twice as much as their peers who do not have diabetes, and the lower school performance was related to the more school absences. Newacheck and Taylor\textsuperscript{12} reported an average of annual bed days was 3.6 day and average school absence was 3.1 day among diabetes. In this study, only 23\% of the diabetic adolescents were admitted to the hospital (diabetic adolescents with bed days). Visits to diabetic clinics may lead to a good metabolic control reflected by reduced hospital admissions and better school performance.
Faro\textsuperscript{13} reported that adolescents are not able to adjust their diabetic regimen to fit their life style. However, better school performance and less bed days found in this study may be attributed to the role of diabetic clinic in monitoring the metabolic control of the diabetic adolescents.
This study shows a positive association between sport activities and school achievement. Campaigene et al\textsuperscript{13} found a significant improvements in the glycaemic control in children after training program. Drash\textsuperscript{14} reported that maintaining high level of physical fitness provide short and long benefit to individual with diabetes including attendance to good control. In conclusion, visits to diabetic clinic and practicing sport improve the school achievement among diabetic adolescents.

References

THE ASPARTATE AMINOTRANSFERASE TO ALANINE AMINOTRANSFERASE RATIO AND HCV INFECTION

Al-Kubaisy W. A. MBchB, PhD1 Habib M.A. MBchB, PhD2

Abstract
Background: Hepatitis C virus (HCV) infection is responsible for the majority of cases of post-transfusion hepatitis. Biochemical analysis of liver enzymes used to estimate the severity of liver injury in HCV infected patients.

Objective: To estimate the aspartate aminotransferase to alanine aminotransferase (AST/ALT) ratio as a non-invasive parameter for assessment of liver injury in HCV infected patients.

Methods: Two groups of subjects were included in this study. 238 thalassemic children from Al-Zahrawi Hospital (172 were seropositive and 66 were seronegative for HCV specific antibody) and 58 pregnant women (32 were seropositive and 26 were seronegative for HCV specific antibody) as a control group. Serum AST and ALT and AST/ALT ratio levels estimated for each subject.

Results: The mean serum AST/ALT ratio levels for anti-HCV seropositive and seronegative thalassemic children were 3.38 ± 4.34 and 2.56 ± 3.09 respectively, while for anti-HCV seropositive and seronegative pregnant women 1.62 ± 1.34 and 0.59 ± 0.42 respectively.

Conclusion: The mean serum AST/ALT ratio is higher among HCV infected subjects than among the non-HCV infected ones.

Keywords: aspartate aminotransferase to alanine aminotransferase ratio, Hepatitis C virus


Introduction
Hepatitis C virus (HCV) now considered as the leading cause of post-transfusion hepatitis worldwide[1]. Chronic transfusion recipient, such as patients with thalassemia major have a high frequency of liver disease[2,3]. HCV is responsible for the majority of cases of post-transfusion hepatitis in such patients[1]. Generally, HCV infection is asymptomatic and most often cases are discovered by chance biochemical analysis when a subject found to have raised liver enzymes[4]. Among routine laboratory tests for liver injury is the measurement of liver enzymes. The AST/ALT ratio used to non-invasively assess the severity of the disease in patients with chronic liver disease[5]. Hence, the aim of this study directed to evaluate the liver function impairment among patients infected with HCV by measurement of AST/ALT ratio.

Materials & methods
A total of 238 outpatients and inpatients thalassemic children were included in this study from Al-Zahrawi hospital from November 1996 to August 1997, of those 172 were seropositive and 66 were seronegative for HCV specific antibody. The control group for this study was 58 pregnant women (26 were seropositive and 32 were seronegative for HCV specific antibody). Serum samples collected from each subject and tested for serum ALT and AST levels using Dinitrophenylhydrozol colorimetric method[6]. The AST/ALT levels estimated. Statistical analysis performed using t test.

1Dept. Community Medicine, 2 Dept. Medical Microbiology, College of Medicine, Al-Nahrain University.
Address correspondence to Dr. Manal Adnan Habib, Email: manalviro@yahoo.com
Received 15th May 2004: Accepted 10th July 2004.
Results
As shown in table 1, the mean serum AST/ALT levels for anti HCV seropositive and seronegative thalassemic patient were 3.38 ± 4.34 and 2.56 ± 3.09 respectively with no significant difference (p>0.05). Regarding the control group (pregnant women), the mean serum AST/ALT levels for anti HCV seropositive and seronegative ones were 1.62 ± 1.34 and 0.59 ± 0.42 respectively with statistical significant difference (p<0.005). A highly significant difference was observed when the mean serum AST/ALT levels for anti HCV seropositive thalassemic patient and pregnant women were compared (p<0.005).

Table 1: The mean serum AST/ALT level ± SD* in among different groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>Number</th>
<th>Mean±SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti HCV seropositive thalassemic patients</td>
<td>172</td>
<td>3.38±4.34</td>
<td>T = 1.407</td>
</tr>
<tr>
<td>Anti HCV seronegative thalassemic patients</td>
<td>66</td>
<td>2.56±3.09</td>
<td>Df= 236 (P &gt; 0.05)</td>
</tr>
<tr>
<td>Anti HCV seropositive Pregnant women</td>
<td>32</td>
<td>1.62±1.34</td>
<td>T = 3.787</td>
</tr>
<tr>
<td>Anti HCV seronegative Pregnant women</td>
<td>26</td>
<td>0.59±0.42</td>
<td>Df = 56 (P &lt; 0.005)</td>
</tr>
<tr>
<td>Anti HCV seropositive thalassemic patients</td>
<td>172</td>
<td>3.34±4.34</td>
<td>T = 4.33</td>
</tr>
<tr>
<td>Anti HCV seropositive Pregnant women</td>
<td>32</td>
<td>1.62±1.34</td>
<td>Df = 202 (P &lt;0.005)</td>
</tr>
<tr>
<td>Anti HCV seronegative thalassemic patients</td>
<td>66</td>
<td>2.56±3.09</td>
<td>T = 5.06</td>
</tr>
<tr>
<td>Anti HCV seronegative Pregnant women</td>
<td>26</td>
<td>0.59±0.42</td>
<td>Df = 90 (P &lt; 0.005)</td>
</tr>
</tbody>
</table>

*SD: Standard deviation

Discussion
Chronic HCV infection is highly prevalent among thalassemic patient[2]. HCV infection is commonly presents as an asymptomatic liver disease, which over years can cause inflammation, fibrosis and eventual cirrhosis in the liver[7]. The challenge lies in identifying those patients. Who will go on to develop fibrosis and subsequent cirrhosis. Assessment of liver injury, therefore, can be important factor in determining both timing and effectiveness of therapy. Measurement of liver enzymes one of the routine laboratory tests for estimation of liver injury.

The serum AST/ALT ratio of more than one indicates progressive liver injury[8] and correlates with both liver histology and clinical evaluation[6]. Moreover, Reedy and coworkers stated that AST/ALT ratio although specific for liver cirrhosis, should not be the sole determinant to identify cirrhosis[9]. In this study the mean serum AST/ALT ratio among anti-HCV seropositive pregnant women was greater than one and showed a significant difference when compared with that of anti-HCV seronegative pregnant women (p<0.005) reflecting liver injury in the former group. However, the mean serum AST/ALT ratio was higher among anti-HCV seropositive thalassemic patient than among the anti-HCV seronegative ones but with no significant difference (p>0.05). A finding that can be explained on the basis that factors other than HCV infection may be involved in damaging the liver, like iron overload and possibly coinfection with other hepatitis viruses, because those patients are chronic blood transfusion recipients[2,3]. Moreover, the mean serum AST/ALT ratio among anti-HCV seropositive thalassemic patients was significantly higher than that among anti-HCV seropositive pregnant women, a finding that support the statement that serum AST/ALT ratio can be used to assess the severity of liver injury[6].

Although the current gold standard for assessing liver injury and fibrosis is the liver biopsy, however, it is assessed with patient discomfort, potential
 complications, and high cost\textsuperscript{10}. Even this invasive measure relies on scoring system that may be limited by sampling error, biopsy size and observe reproducibility\textsuperscript{9}. While measurement of liver enzymes is a non invasive, informative and less costly routine laboratory test. Although ALT level may inflect liver damage, correlation with hepatic fibrosis while elevation in the AST/ALT ratio was observed as patient prognosis for chronic hepatitis to cirrhosis\textsuperscript{12-14}.

References
STUDY OF DIFFERENT CLINICAL AND DEMOGRAPHIC CHARACTERS OF PATIENTS WITH THALASSEMA AND THEIR RELATION TO HEMOGLOBIN, SOME MINERALS AND TRACE ELEMENTS AND ALBUMIN LEVELS IN THEIR BLOOD

Enas T. Abdul-Karim1 MSc PhD, Firyal H. Abdul-Jalil2 BSc PhD, Thabit N. Al-Azawi3 BSc PhD

Abstract
Background: Thalassaemia is considered the most common genetic disorder worldwide. β thalassaemia has emerged as a huge public health problem worldwide. The classic changes of untreated thalassaemia major are now regularly seen only in countries without resources to support long-term transfusion programs.

Objective: To study the different clinical features of patients with anemia attending the center for anemia of Mediterranean origin in Ibn-Albalady Hospital in Baghdad for blood transfusion. To correlate different clinical features with the different demographic characters among the sample patients and with the blood levels of hemoglobin, some trace elements, minerals and albumin.

Methods: Cross-sectional study was conducted in the center for anemia of Mediterranean origin in Ibn-Albalady Hospital, 157 patients were randomly selected using convenient sampling and patients attending the center for blood transfusion. Blood samples were taken from all the studied sample. Tests were done for different serum levels of trace elements, minerals, albumin and hemoglobin.

Results: showed that out of 157 patients studied, there were 112 (71.3%) from Baghdad and 107 (68.2%) from urban areas. The mean age on diagnosis was 1.6 years and that thalassaemia major was found in 121 (77.1%), there were 108 (68.8%) who require blood transfusion between 2-4 weeks, and desferol treatment frequency was >4 times/week in 99 (63.1%) and under nutrition was found in 76 (48.4%) patients.

Conclusion: More centers for thalassaemia are to be established in different areas in our country, with increase efficiency as to include gene frequency. Programs based on carrier screening and counseling of couples at marriage, preconception or early pregnancy to be established. Prenatal diagnosis by mutation analysis on PCR amplified DNA from chorionic villi.

Key word: Mineral, Trace elements, Thalassemia

IRAQI J MED SCI, 2005; VOL. 4 (1): 21-37

Introduction
Thalassaemia is considered the most common genetic disorder worldwide. It occurs in a particularly high frequency in a broad belt extending from the Mediterranean basin through the Middle East, Indian subcontinent, Burma, and South East Asia[1]. The estimated genetic frequencies range from 5% to 10% in some areas[2]. Thalassaemia syndrome is described as a series of genetic disorders of hemoglobin synthesis which have in common a reduce output of the globins chain production, it is inherited as an autonomic recessive basis, that to find heterozygous β thalassaemia in both parents of a child with β thalassaemia major[3]. William et al[4] describes the
distribution of thalassaemia where the gene frequency for the different thalassaemia and structural hemoglobin variants are high. According to him as the social conditions improve in developing countries and childhood mortality due to infection and malnutrition declines, children with thalassaemia who would previously have died early in life are now surviving long enough to require treatment. The reason for high frequency of thalassaemia throughout the tropics, reflect the advantages that carriers are protected from the consequences of infection with Plasmodium falciparum malaria\[5\].

Thalassaemia is classified into α, β, δβ, δ, γ δ β subtypes\[6\]. The severe in effective erythropoiesis results in erythroid marrow expansion to as 30 times the normal level. Both an increase in plasma volume because of shunting through expanded marrow and progressive splenomegaly exacerbate anemia\[7\]. Increased erythropoietin synthesis may stimulate the formation of extramedullary erythropoietic tissue, primarily in the thorax and Para spinal region. Marrow expansion also results in characteristic deformities of the skull and face, as well as osteopenia and focal defects in bone mineralization\[8\].

Marrow hyperplasia leads ultimately to increased iron absorption and progressive deposition of iron in tissues. The marked increase in survival, to the fifth decade of life, patient with well-managed β thalassemia in developed countries represent one of the most dramatic alteration in morbidity and mortality associated with a genetic disease in these countries. Still more than 75 years after the fascinating initial description of peculiar bone changes and other signs and symptoms of the disorder, the β thalassaemia has emerged as a huge public health problem worldwide\[7\]. The classic changes of untreated thalassaemia major are now regularly seen only in countries without resources to support long-term transfusion programs\[9\].

The intention of this study is first, to study the different clinical features of patients with anemia attending the center for anemia of Mediterranean origin in Ibn-Albalady hospital in Baghdad for blood transfusion. Second, to correlate different clinical features with the different demographic characters among the sample patients and thirdly, to correlate the different clinical features with the blood levels of hemoglobin, some of the trace elements and minerals, and albumin.

Subjects & methods
A cross-sectional study was conducted for the period from 1/9 to 1/12/2002 in the center for anemia of Mediterranean origin in Ibn-Albalady Hospital, 157 patients were randomly selected using convenient sampling and patients attending the center for blood transfusion. Well-studied questionnaire form were used to obtain information regarding different socio-demographic characters.

Blood samples for hemoglobin estimation and estimation of various levels of mineral, trace elements and albumin were taken from the entire studied sample. The blood was left at room temperature for 10 minutes for clotting, centrifuged at 3000 rpm for 10 minutes, and then serum was separated and stored at -20°C until used.

Basal metabolic index (BMI) was classified according to the International accepted range of BMI\[10\] as follows: under weight <18.5, normal 18.5-24.9, over weight 25-29.9, obese 30.0-39.9 and extremely obese >40.

Chemicals and reagents
All chemical and standard solutions used in this work were the highest analytical grade, and used without purification.

Measurement of trace elements
Serum trace elements were measured by flame atomic absorption spectrophotometry (Schimadzu AA 646). It is simpler and less tedious to perform than the flameless mode where the metal compound in the flame Hollow cathode lamp made of the same metal to be measured. The lamp was used to generate a wavelength of light specific for the same metal to be analyzed. This light is passing through the flame that contains the free atoms of the metal, which absorb a fraction of the light intensity. The light intensity reached to the recorder is directly proportional to the concentration of the free atoms in the flame, which in turn reflects the original concentration of the metal in the solution.

Dilution of the serum was made by deionized water according to the sensitivity of the atomic absorption spectrophotometer in order to avoid the viscosity and to decrease the interference of the protein in serum. Single element hollow cathode lamps were used as line-radiation sources and were operated at currents or energies recommended by the manufacture. Optimum working conditions are given in Table 1.

<table>
<thead>
<tr>
<th>Element</th>
<th>Wave length (nm)</th>
<th>Slit width (Å)</th>
<th>Air Flow (L/min)</th>
<th>Acetylene Flow (L/min)</th>
<th>Lamp Current (mA)</th>
<th>Burner Height (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zn</td>
<td>213.9</td>
<td>3.8</td>
<td>10</td>
<td>2.4</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Cu</td>
<td>324.7</td>
<td>3.8</td>
<td>10</td>
<td>2.3</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>Fe</td>
<td>248.3</td>
<td>1.9</td>
<td>10</td>
<td>2.7</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Mg</td>
<td>285.2</td>
<td>3.8</td>
<td>10</td>
<td>2.4</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Ca</td>
<td>422.7</td>
<td>3.8</td>
<td>10</td>
<td>2.6</td>
<td>8</td>
<td>10</td>
</tr>
</tbody>
</table>

**Determination of Zinc and Copper**

1000 ppm stock solution was diluted with deionized water to give the following concentrations of the working standard (0.0, 0.4, 0.8, 1.2, 1.6 and 2 ppm) of zinc and copper. Frozen samples were allowed to thaw and come to room temperature then mixed gently.

Samples were diluted 1:10 with 6% butanol as diluents. This method achieved 30% increase in sensitivity compared to use of water only. This effect is due to decrease viscosity and difference in droplet formation and this technique is widely used.

**Determination of Iron**

Serum iron measured using Olson and Hamlin method as follow: Five hundred microliters of 20% trichloroacetic acid were added to 500 microliters of serum and heated at 90°C for 15 minutes, cooled, centrifuged and the iron level in the supernatant determined by flame atomic absorption spectrophotometer at 248.3 nm.

**Determination of total iron binding capacity**

It is the approximate estimate of serum transferrin, 1 ml of serum was added to saturated iron solution mix them, let stand for 20 minutes. Then add 170 mg of magnesium hydroxycarbonate, wait 20 minutes, shaking intermittently, centrifuge for 10 minutes, and pipette 1 ml of supernatant and measure iron, treating it as serum.

**Serum Selenium**

Selenium in serum was measured by atomic absorption (flameless).

**Determination of Magnesium and Calcium**

Samples used for determination of magnesium and calcium were diluted 1:50 with 1% lanthanum chloride solution to exclude the effect of serum.
phosphate\textsuperscript{[15]}. Standard solution of 1000 ppm was diluted with deionized water. Working standards of magnesium were (0,5,10,15,20,25, and 30 µ mol/L). Working standards of calcium were (0,20,40,60,80,100, and 120 µ mol/L).

**Serum Albumin:**
Albumin in serum was measured by Bromocresol Green (BCG) method\textsuperscript{[15]} depending on the procedure of Iraqi Sera and Vaccines Institution kit. The measurement of serum albumin is based on its quantitative binding to the indicator bromocresol green (3,3',5,5',tetrabromo-m- cresolsulphonphthalin). The albumin-BCG-complex absorbs maximally at 578 nm.

**Hemoglobin determination**
The cyanomethaemoglobin using Drabkin test was applied. Five ml of Drabkin solution was added to 0.02 ml whole blood and allow the tube to stand for 10 minutes. The absorbance is measured, against the blank in the photoelectric calorimeter at 540 nm, find the concentration of hemoglobin from the calibration curve with the following working standard of hemoglobin (12 gm \ 100 ml, 10 gm \ 100 ml, 7.5 gm \ 100 ml and 5 gm \ 100 ml) mix volume of standard solution of hemoglobin solution with two volume of Drabkin solution\textsuperscript{[15]}.

**Statistical analysis:**
Frequency tables used statistical tests were done using correlation tests P values < 0.05 were considered significant.

**Results**
The present sample constitutes 157 patients studied randomly from the Thalassaemic Center (center for anemia of Mediterranean origin) in Ibn Al-Balady hospital \Baghdad. Table 2 shows that there were 99 (63.06%) males, and 58 (36.94%) females in the sample, there were 73 (46.5%) patients below the age of 10 years with the mean age 10.8 years, minimal age in years was 0.75 and maximal age 28.0, while there were 88 (56.1%) of patients below the age of one year on diagnosis, and 129 (82.2%) of patients below the age of 3 years on diagnosis, the mean age on diagnosis was 1.6 year mode 0.5, the minimal age in years was 0.08 and the maximal age was 17.

In the sample there were 112 (71.3%) patients from Baghdad, 21 (13.4%) from Diyala, 12 (7.6%) from Wasit, 4 from Karballa, 2 (1.3%) from Najaf and from Anbar, while there was only one patient (0.6%) from Karkuk, Babel and Theekaar governorate. The sample also shows that there were 107 (68.2%) patients from urban and 50 (31.8%) patients from rural areas.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Number</th>
<th>percent</th>
<th>Cumulative percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of patient/year</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10.0</td>
<td>73</td>
<td>46.5</td>
<td>46.5</td>
</tr>
<tr>
<td>10-19.9</td>
<td>67</td>
<td>42.7</td>
<td>89.2</td>
</tr>
<tr>
<td>20-29.9</td>
<td>17</td>
<td>10.8</td>
<td>100.0</td>
</tr>
<tr>
<td>Mean 10.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mode 10.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>STD 10.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimum 0.75</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximum 28.0</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Distribution of the sample (157 patients) according to different variables
Table 2: Continued

<table>
<thead>
<tr>
<th>Age on diagnosis/year</th>
<th>Number</th>
<th>Mean</th>
<th>Mode</th>
<th>STD</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;1.0</td>
<td>88</td>
<td>56.1</td>
<td>56.1</td>
<td>56.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-2.99</td>
<td>41</td>
<td>26.1</td>
<td>26.1</td>
<td>82.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-4.99</td>
<td>14</td>
<td>8.9</td>
<td>8.9</td>
<td>91.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-9.99</td>
<td>11</td>
<td>7.0</td>
<td>7.0</td>
<td>98.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10-19.99</td>
<td>2</td>
<td>1.3</td>
<td>1.3</td>
<td>99.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15-19.99</td>
<td>1</td>
<td>0.6</td>
<td>0.6</td>
<td>100.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sex</th>
<th>Number</th>
<th>percent</th>
<th>Cumulative percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>99</td>
<td>63.1</td>
<td>77.1</td>
</tr>
<tr>
<td>Female</td>
<td>58</td>
<td>36.9</td>
<td>100.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Address</th>
<th>Number</th>
<th>percent</th>
<th>Cumulative percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baghdad</td>
<td>112</td>
<td>71.3</td>
<td>71.3</td>
</tr>
<tr>
<td>Wassait</td>
<td>12</td>
<td>7.6</td>
<td>79.0</td>
</tr>
<tr>
<td>Karkuk</td>
<td>1</td>
<td>0.6</td>
<td>79.6</td>
</tr>
<tr>
<td>Diala</td>
<td>21</td>
<td>13.4</td>
<td>93.0</td>
</tr>
<tr>
<td>Karbala</td>
<td>4</td>
<td>2.5</td>
<td>95.5</td>
</tr>
<tr>
<td>Najaf</td>
<td>1</td>
<td>0.6</td>
<td>96.2</td>
</tr>
<tr>
<td>Salah-Aldeen</td>
<td>2</td>
<td>1.3</td>
<td>97.5</td>
</tr>
<tr>
<td>Anbar</td>
<td>2</td>
<td>1.3</td>
<td>98.7</td>
</tr>
<tr>
<td>Babil</td>
<td>1</td>
<td>1.6</td>
<td>99.4</td>
</tr>
<tr>
<td>Thee-Kaar</td>
<td>1</td>
<td>0.6</td>
<td>100.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Residency</th>
<th>Number</th>
<th>percent</th>
<th>Cumulative percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urban</td>
<td>107</td>
<td>68.2</td>
<td>77.1</td>
</tr>
<tr>
<td>Rural</td>
<td>50</td>
<td>31.8</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Table 3 shows that 121 (77.1%) of patients were suffering from thalassaemia major, 31 (19.7%) from intermedia, and one only from thalassaemia minor, there were also four with Alpha thalassaemia in the sample.

Table 3: The distribution of the sample according to the diagnosis

<table>
<thead>
<tr>
<th>Variables</th>
<th>Number</th>
<th>percent</th>
<th>Cumulative percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thalassaemia Major</td>
<td>121</td>
<td>77.1</td>
<td>77.1</td>
</tr>
<tr>
<td>Intermediate</td>
<td>31</td>
<td>19.7</td>
<td>96.8</td>
</tr>
<tr>
<td>Minor</td>
<td>1</td>
<td>0.6</td>
<td>97.5</td>
</tr>
<tr>
<td>Alpha thalassaemia</td>
<td>4</td>
<td>2.5</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Table 4 demonstrate that the mean hemoglobin level was 8.4 g\ 100 ml among the patients with the mode being 8.0, and the minimal hemoglobin was 5.0 g\ 100 ml and the maximal hemoglobin reading was 11.0 g\ 100ml.

Table 4: Distribution of the sample according to anemia and age groups

<table>
<thead>
<tr>
<th>Age groups/years</th>
<th>Frequency</th>
<th>%</th>
<th>Mean Hb</th>
<th>St.d</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5</td>
<td>26</td>
<td>16.6</td>
<td>9.1</td>
<td>0.84</td>
<td>7.5</td>
<td>10.5</td>
</tr>
<tr>
<td>5-9.99</td>
<td>47</td>
<td>29.9</td>
<td>8.3</td>
<td>1.0</td>
<td>6.0</td>
<td>10.5</td>
</tr>
<tr>
<td>10-19.99</td>
<td>67</td>
<td>42.7</td>
<td>8.2</td>
<td>1.12</td>
<td>5.0</td>
<td>11.5</td>
</tr>
<tr>
<td>20-29.99</td>
<td>17</td>
<td>10.8</td>
<td>8.2</td>
<td>0.91</td>
<td>7.0</td>
<td>10.0</td>
</tr>
<tr>
<td>Total</td>
<td>157</td>
<td>100.0</td>
<td>8.4</td>
<td>1.07</td>
<td>5.0</td>
<td>11.0</td>
</tr>
</tbody>
</table>
Table 5 showed that among the sample group the dominating blood group was group O (51 patients 32.5%), then group B (50 patients 31.8%), while blood group A was found in 42 patients (26.8%), group AB was found in 14 patients (8.9%). Rh factor was mostly positive in 144 patients (91.7%), while it was negative in 13 (8.3%) patients.

Table 5: Distribution of the sample according to their blood group & Rh factors

<table>
<thead>
<tr>
<th>Variables</th>
<th>Number</th>
<th>Percent</th>
<th>Cumulative percent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood groups</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group A</td>
<td>42</td>
<td>26.8</td>
<td>26.8</td>
</tr>
<tr>
<td>Group B</td>
<td>50</td>
<td>31.8</td>
<td>58.6</td>
</tr>
<tr>
<td>Group AB</td>
<td>14</td>
<td>8.9</td>
<td>67.5</td>
</tr>
<tr>
<td>Group O</td>
<td>51</td>
<td>32.5</td>
<td>100.0</td>
</tr>
<tr>
<td>Total</td>
<td>157</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td><strong>Rh factors</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>144</td>
<td>91.7</td>
<td>91.7</td>
</tr>
<tr>
<td>Negative</td>
<td>13</td>
<td>8.3</td>
<td>100.0</td>
</tr>
<tr>
<td>Total</td>
<td>157</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

Table 6 showed that there were 108 (68.8%) of patients who require blood transfusion between 2-4 weeks, 48 (30.6%) of patients require transfusion in > 4 weeks, while only one patient require transfusion in < 2 weeks time. Desferol treatment were taken > 4 times \ week in 99 (63.1%) patients, between 3-4 times \ week in 46 (29.3%) of patients, and < 3 times \ week in 12 (7.6%) patients.

Table 6: Show type and frequency of treatment given to sample group

<table>
<thead>
<tr>
<th>Type of treatment &amp; frequency</th>
<th>Number</th>
<th>Percent</th>
<th>Cumulative percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood transfusion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2 weeks</td>
<td>1</td>
<td>0.6</td>
<td>0.6</td>
</tr>
<tr>
<td>2-4 weeks</td>
<td>108</td>
<td>68.8</td>
<td>69.4</td>
</tr>
<tr>
<td>&gt; 4 weeks</td>
<td>48</td>
<td>30.6</td>
<td>100.0</td>
</tr>
<tr>
<td>Total</td>
<td>157</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>Desferol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 3 times \ week</td>
<td>12</td>
<td>7.6</td>
<td>7.6</td>
</tr>
<tr>
<td>3-4 times \ week</td>
<td>46</td>
<td>29.3</td>
<td>36.9</td>
</tr>
<tr>
<td>&gt; 4 times \ week</td>
<td>99</td>
<td>63.1</td>
<td>100.0</td>
</tr>
<tr>
<td>Total</td>
<td>157</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

Table 7 showed that 76 (48.4 %) of patients were having under nutrition according to the International accepted range of BMI, while 74 patients (47.1 %) were regarded as normal, and only 7 patients (4.5%) were regarded as over weight.

Table 7: Distribution of patients in the sample according to basal metabolic rate (BMI)

<table>
<thead>
<tr>
<th>BMI</th>
<th>Frequency</th>
<th>Percent</th>
<th>Cumulative Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under weight</td>
<td>76</td>
<td>48.4</td>
<td>48.4</td>
</tr>
<tr>
<td>Normal</td>
<td>74</td>
<td>47.1</td>
<td>96.1</td>
</tr>
<tr>
<td>Over weight</td>
<td>7</td>
<td>4.5</td>
<td>100</td>
</tr>
<tr>
<td>Total</td>
<td>157</td>
<td>100</td>
<td>---</td>
</tr>
</tbody>
</table>
Table 8 showed that there were 126 (80.3%) of patients who were pale at time of examination, 93 (59.2%) with jaundice, 95 (60.5%) with frontal bossing, 76 (48.4%) of patients with mongoloid features, 69 (43.9%) with liver enlargement, 78 (49.7%) with spleen enlargement, while there were only 5 (3.2%) with heart failure and 2 (1.3%) with diabetes mellitus.

Table 8: Distribution of patients in the sample according to the presence or absence of some clinical manifestation

<table>
<thead>
<tr>
<th>Variables</th>
<th>Number</th>
<th>Percent</th>
<th>Cumulative percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pale</td>
<td>Yes</td>
<td>126</td>
<td>80.3</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>31</td>
<td>19.7</td>
</tr>
<tr>
<td>Jaundice</td>
<td>Yes</td>
<td>93</td>
<td>59.2</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>64</td>
<td>40.8</td>
</tr>
<tr>
<td>Frontal bossing</td>
<td>Yes</td>
<td>95</td>
<td>60.5</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>62</td>
<td>39.5</td>
</tr>
<tr>
<td>Bronze skin</td>
<td>Yes</td>
<td>84</td>
<td>53.5</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>73</td>
<td>46.5</td>
</tr>
<tr>
<td>Mongoloid features</td>
<td>Yes</td>
<td>76</td>
<td>48.4</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>81</td>
<td>51.6</td>
</tr>
<tr>
<td>Liver enlargement</td>
<td>Yes</td>
<td>69</td>
<td>43.9</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>88</td>
<td>56.1</td>
</tr>
<tr>
<td>Spleen enlargement</td>
<td>Yes</td>
<td>8</td>
<td>49.7</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>59</td>
<td>50.3</td>
</tr>
<tr>
<td>Heart failure</td>
<td>Yes</td>
<td>5</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>152</td>
<td>96.8</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Yes</td>
<td>2</td>
<td>1.3</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>155</td>
<td>98.7</td>
</tr>
</tbody>
</table>

When the relationship between different clinical manifestation was correlated (Table 9a) it was found that, pale skin was correlated with bronze skin, mongoloid features, diabetes mellitus and heart failure. Jaundice was correlated with frontal bossing, bronze skin, mongoloid features and enlarged spleen. Frontal bossing was correlated with jaundice, bronze skin, mongoloid features; enlarge spleen & frequency of treatment with desferol. Bronze skin was correlated with pale skin, jaundice, frontal bossing, mongoloid features, enlarge spleen. Mongoloid features were correlated with pale skin, jaundice, frontal bossing, and bronze skin and enlarge spleen. Enlarge liver was correlated with enlarge spleen and heart failure. Enlarge spleen was correlated with jaundice frontal bossing mongoloid features bronze skin enlarge liver and heart failure.

Table 9a: The association between different manifestations of patients in the sample

<table>
<thead>
<tr>
<th>Variables</th>
<th>Pale</th>
<th>Jaundice</th>
<th>F. Bossing</th>
<th>B. Skin</th>
<th>M. Feature</th>
<th>E. Liver</th>
<th>E. Spleen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pale</td>
<td>------</td>
<td>-0.086</td>
<td>-0.253**</td>
<td>-0.298</td>
<td>-0.157</td>
<td>-0.093</td>
<td></td>
</tr>
<tr>
<td>P. Correlation</td>
<td>-</td>
<td>0.285</td>
<td>0.003</td>
<td>0.157</td>
<td>0.002</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
<td>Significant Number</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td></td>
</tr>
<tr>
<td>Jaundice</td>
<td>-0.086</td>
<td>--------</td>
<td>-0.084</td>
<td>0.003</td>
<td>-0.081</td>
<td>0.093</td>
<td></td>
</tr>
<tr>
<td>P. Correlation</td>
<td></td>
<td>0.285</td>
<td>-0.298</td>
<td>0.312</td>
<td>0.093</td>
<td>0.074</td>
<td></td>
</tr>
<tr>
<td>Significant Number</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td></td>
</tr>
</tbody>
</table>
Table 9a: Continued

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Pale</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P. Correlation</td>
<td>-.229**</td>
<td>-.183**</td>
<td>-.111</td>
<td>-.091</td>
<td>-.055</td>
<td>-.073</td>
<td>-.090</td>
<td>.007</td>
</tr>
<tr>
<td>Significant</td>
<td>.004</td>
<td>.021</td>
<td>.165</td>
<td>.292</td>
<td>.504</td>
<td>.375</td>
<td>.265</td>
<td>.930</td>
</tr>
<tr>
<td>Number</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>136</td>
<td>150</td>
<td>150</td>
<td>156</td>
<td>151</td>
</tr>
<tr>
<td>Jaundice</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P. Correlation</td>
<td>-.021</td>
<td>.150</td>
<td>.078</td>
<td>.111</td>
<td>.060</td>
<td>.088</td>
<td>.070</td>
<td>-.384**</td>
</tr>
<tr>
<td>Significant</td>
<td>.791</td>
<td>.060</td>
<td>.331</td>
<td>.198</td>
<td>.464</td>
<td>.286</td>
<td>.385</td>
<td>.000</td>
</tr>
<tr>
<td>Number</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>136</td>
<td>150</td>
<td>150</td>
<td>156</td>
<td>151</td>
</tr>
</tbody>
</table>

*= Significant at 0.05 level  
** = Significant at 0.01 level

Table 9b showed that diabetes mellitus was found in patients with pale skin & heart failure. Heart failure was found in patients with pale skin; enlarge liver & spleen, diabetes mellitus. Treatment with blood transfusion was correlated with enlarge liver & spleen. Basal metabolic rate (BMI) was correlated with jaundice, frontal bossing, mongoloid features, and enlarge spleen.

Table 9b: The association between different manifestations of patients in the sample
Table 9b: Continued

<table>
<thead>
<tr>
<th>Variables</th>
<th>Cu</th>
<th>Zn</th>
<th>Selenium</th>
<th>Ca</th>
<th>Mg</th>
<th>Albumin</th>
<th>S. iron</th>
<th>TIBC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pale</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P. Correlation</td>
<td>.077</td>
<td>-.046</td>
<td>.093</td>
<td>-.027</td>
<td>.073</td>
<td>.053</td>
<td>-.205*</td>
<td>.250**</td>
</tr>
<tr>
<td>Significant</td>
<td>.336</td>
<td>.370</td>
<td>.244</td>
<td>.740</td>
<td>.367</td>
<td>.506</td>
<td>.013</td>
<td>.002</td>
</tr>
<tr>
<td>Number</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>146</td>
<td>146</td>
</tr>
<tr>
<td>Jaundice</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P. Correlation</td>
<td>-.031</td>
<td>-.077</td>
<td>-.120</td>
<td>.094</td>
<td>-.062</td>
<td>.001</td>
<td>-.125</td>
<td>-.042</td>
</tr>
<tr>
<td>Significant</td>
<td>.701</td>
<td>.336</td>
<td>.135</td>
<td>.242</td>
<td>.443</td>
<td>.513</td>
<td>.133</td>
<td>.612</td>
</tr>
<tr>
<td>Number</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>146</td>
<td>146</td>
</tr>
<tr>
<td>F. Bossing</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P. Correlation</td>
<td>.039</td>
<td>.080</td>
<td>.197*</td>
<td>.042</td>
<td>-.090</td>
<td>.053</td>
<td>-.091</td>
<td>.011</td>
</tr>
<tr>
<td>Significant</td>
<td>.627</td>
<td>.321</td>
<td>.014</td>
<td>.600</td>
<td>.264</td>
<td>.513</td>
<td>.274</td>
<td>.899</td>
</tr>
<tr>
<td>Number</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>146</td>
<td>146</td>
</tr>
</tbody>
</table>

*= Significant at 0.05 level
**= Significant at 0.01 level

Table 9c showed the correlation between different clinical features and blood level of trace elements, minerals and albumin and it showed that serum copper was correlated with enlarge liver. Serum Selenium level in blood was correlated with frontal bossing, bronze skin, mongoloid features. Hemoglobin concentration in blood was correlated with bronze skin. Serum iron & total iron binding capacity (TIBC) were correlated with pale skin only.

Table 9c: The association between different manifestations of patients in the sample
Table 9c: Continued

<table>
<thead>
<tr>
<th>Variables</th>
<th>Bronze skin</th>
<th>M. Feature</th>
<th>Enlarge liver</th>
<th>Enlarge spleen</th>
<th>Diabetes</th>
<th>Heart failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>P. Correlation</td>
<td>.027</td>
<td>.002</td>
<td>-.164*</td>
<td>-.086</td>
<td>.005</td>
<td>.011</td>
</tr>
<tr>
<td>Significant</td>
<td>.740</td>
<td>.978</td>
<td>-.169*</td>
<td>.084</td>
<td>.947</td>
<td>.894</td>
</tr>
<tr>
<td>Number</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
</tr>
</tbody>
</table>

P = Significant at 0.05 level
** = Significant at 0.01 level

Tables 10a and b showed that the age of the patients was correlated with pale skin, jaundice, frontal bossing, bronze skin, mongoloid features, liver and spleen enlargement, frequency of blood transfusion, diabetes mellitus, heart failure, BMI, and hemoglobin level ion blood. Sex of the patients was correlated with bronze skin, hemoglobin level and blood groups. Address, residency, and diagnosis of the disease were not correlated with any of the studying variables. Age on diagnosis was correlated with BMI only.

Table 10a: The occurrence of different clinical manifestation in the sample of patients in association with different variables

<table>
<thead>
<tr>
<th>Variables</th>
<th>Pale</th>
<th>Jaundice</th>
<th>F. Bossing</th>
<th>B. Skin</th>
<th>M. Feature</th>
<th>E. Liver</th>
<th>E. Spleen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P. Correlation</td>
<td>.160*</td>
<td>-.234**</td>
<td>-.208**</td>
<td>-.233**</td>
<td>-.251**</td>
<td>-.306**</td>
<td>-.507**</td>
</tr>
<tr>
<td>Significant</td>
<td>.045</td>
<td>.003</td>
<td>-.009</td>
<td>.003</td>
<td>.002</td>
<td>.000</td>
<td>.000</td>
</tr>
<tr>
<td>Number</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P. Correlation</td>
<td>-.081</td>
<td>.090</td>
<td>.084</td>
<td>.239**</td>
<td>.081</td>
<td>.093</td>
<td>.074</td>
</tr>
<tr>
<td>Significant</td>
<td>.331</td>
<td>.262</td>
<td>.298</td>
<td>.003</td>
<td>.312</td>
<td>.248</td>
<td>.355</td>
</tr>
<tr>
<td>Number</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
</tr>
<tr>
<td>Address</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P. Correlation</td>
<td>.011</td>
<td>-.085</td>
<td>.010</td>
<td>.112</td>
<td>.045</td>
<td>.029</td>
<td>-.021</td>
</tr>
<tr>
<td>Significant</td>
<td>.895</td>
<td>.291</td>
<td>.903</td>
<td>.161</td>
<td>.572</td>
<td>.718</td>
<td>.790</td>
</tr>
<tr>
<td>Number</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
</tr>
</tbody>
</table>
Table 10a: Continued

<table>
<thead>
<tr>
<th>Variables</th>
<th>Freq. Blood</th>
<th>Freq. desferol</th>
<th>DM</th>
<th>Heart failure</th>
<th>BMI</th>
<th>Hb</th>
<th>Blood group</th>
<th>Rh factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.65*</td>
<td>0.14</td>
<td>-0.06</td>
<td>0.06</td>
<td>-0.12</td>
<td>-0.31</td>
<td>0.04</td>
<td>-0.09</td>
</tr>
<tr>
<td>Significant</td>
<td>0.86</td>
<td>0.45</td>
<td>0.469</td>
<td>0.701</td>
<td>0.903</td>
<td>0.671</td>
<td>0.251</td>
<td>0.269</td>
</tr>
<tr>
<td>Number</td>
<td>157</td>
<td>136</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>156</td>
<td>150</td>
<td>150</td>
</tr>
<tr>
<td>Sex</td>
<td>-0.03</td>
<td>-0.61</td>
<td>0.44</td>
<td>-0.32</td>
<td>-0.02</td>
<td>-0.058</td>
<td>-0.073</td>
<td>-0.211</td>
</tr>
<tr>
<td>Significant</td>
<td>0.71</td>
<td>0.636</td>
<td>0.582</td>
<td>0.693</td>
<td>0.984</td>
<td>0.469</td>
<td>0.375</td>
<td>0.801</td>
</tr>
<tr>
<td>Number</td>
<td>157</td>
<td>136</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>156</td>
<td>150</td>
<td>150</td>
</tr>
<tr>
<td>Residency</td>
<td>-0.15</td>
<td>-0.42</td>
<td>0.245</td>
<td>-0.02</td>
<td>-0.015</td>
<td>-0.029</td>
<td>-0.049</td>
<td>-0.053</td>
</tr>
<tr>
<td>Significant</td>
<td>0.19</td>
<td>0.815</td>
<td>0.574</td>
<td>0.369</td>
<td>0.850</td>
<td>0.720</td>
<td>0.550</td>
<td>0.523</td>
</tr>
<tr>
<td>Number</td>
<td>157</td>
<td>136</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>156</td>
<td>150</td>
<td>150</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>0.14</td>
<td>-0.033</td>
<td>-0.408</td>
<td>0.163</td>
<td>-0.067</td>
<td>-0.146</td>
<td>-0.189</td>
<td>-0.089</td>
</tr>
<tr>
<td>Significant</td>
<td>0.96</td>
<td>0.666</td>
<td>0.217</td>
<td>0.553</td>
<td>0.047</td>
<td>0.413</td>
<td>0.078</td>
<td>0.286</td>
</tr>
<tr>
<td>Number</td>
<td>154</td>
<td>133</td>
<td>154</td>
<td>157</td>
<td>157</td>
<td>153</td>
<td>147</td>
<td>147</td>
</tr>
</tbody>
</table>

*= Significant at 0.05 level
**= Significant at 0.01 level

Table 10b: The occurrence of different clinical manifestation in the sample of patients in association with different variables

Table 10c showed that only age on diagnosis and frequency of desferol treatment were correlated with serum level of magnesium, while there were no significant correlation between other variables studied with serum level of mineral, trace element and albumin level in blood.
and and Selenium reasons were diagnosed before the age (Significant at 77.1% and 88 of patients in the sample (107 patients from rural areas 0.05 121 S. Iron 129 the prevalence of the level therapy. Deilla. Ca Albumin iya and The blood levels of different trace element in patients in association with different Zn Wassiet 21 Cu the other hand level (patients living in Baghdad. The name of the center was changed recently to Center of anemia of Mediterranean Region, for this r Thalassaemic Centre in Ibn Al-Balady hospital in Baghdad; this center is the only center for thalassaemia in Baghdad. The name of the center was changed recently to Center of anemia of Mediterranean Region, for this reasons we can see that patients included in this sample were from ten governorate, but mostly from Baghdad 121(77.1%), and then from Diyala 21(13.4%), Wassiet12 (7.6%). This could be explained by the fact that patients living in Baghdad and Dilla can more easily come to the center for blood transfusion and treatment and that doctors in these areas are more aware about this condition, so the diagnosis and treatment are more available to patients. On the other hand, patients living in far areas probably will not have the chance for early diagnosis and treatment and die from the disease in early age, or it is very difficult for their families to come to the center in proper time for blood transfusion and therapy. In addition, the prevalence of the disease might be higher in these areas than in other areas in our country, the same observation could be applied to the distribution of the sample according to the residency of patients as the number of patient were 107 (68.2%) from urban areas while they were 50 (31.8%) patients from rural areas. The finding that more than half of the patients 88 (56.1%) were diagnosed before the age of one year and 129 (82.2%) were diagnosed before the age of three years, this agree with the fact that 77.1% of patients in the sample were suffering from thalassaemia major, most of those patients usually developed severe anemia early in their life[17].

**Table 10C:** The blood levels of different trace element in patients in association with different variables

<table>
<thead>
<tr>
<th>Variables</th>
<th>Cu</th>
<th>Zn</th>
<th>Selenium</th>
<th>Ca</th>
<th>Mg</th>
<th>Albumin</th>
<th>S. Iron</th>
<th>TIBC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P. Correlation</td>
<td>.017</td>
<td>-.076</td>
<td>.052</td>
<td>-.084</td>
<td>.090</td>
<td>.034</td>
<td>.126</td>
<td>.073</td>
</tr>
<tr>
<td>Significant</td>
<td>.834</td>
<td>.342</td>
<td>.521</td>
<td>.297</td>
<td>.263</td>
<td>.677</td>
<td>.130</td>
<td>.379</td>
</tr>
<tr>
<td>Number</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>146</td>
<td>146</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P. Correlation</td>
<td>-.001</td>
<td>.097</td>
<td>-.030</td>
<td>-.156</td>
<td>.020</td>
<td>-.063</td>
<td>-.120</td>
<td>-.126</td>
</tr>
<tr>
<td>Significant</td>
<td>.994</td>
<td>.226</td>
<td>.708</td>
<td>.052</td>
<td>.808</td>
<td>.432</td>
<td>.150</td>
<td>.129</td>
</tr>
<tr>
<td>Number</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>146</td>
<td>146</td>
</tr>
<tr>
<td>Address</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P. Correlation</td>
<td>-.043</td>
<td>-.043</td>
<td>.007</td>
<td>-.001</td>
<td>-.016</td>
<td>-.117</td>
<td>-.039</td>
<td>-.112</td>
</tr>
<tr>
<td>Significant</td>
<td>.592</td>
<td>.592</td>
<td>.926</td>
<td>.989</td>
<td>.840</td>
<td>.146</td>
<td>.643</td>
<td>.180</td>
</tr>
<tr>
<td>Number</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>146</td>
<td>146</td>
</tr>
<tr>
<td>Residency</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P. Correlation</td>
<td>.072</td>
<td>-.063</td>
<td>-.037</td>
<td>-.099</td>
<td>-.135</td>
<td>-.140</td>
<td>.078</td>
<td>.060</td>
</tr>
<tr>
<td>Significant</td>
<td>.370</td>
<td>.436</td>
<td>.642</td>
<td>.215</td>
<td>.092</td>
<td>.081</td>
<td>.349</td>
<td>.473</td>
</tr>
<tr>
<td>Number</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>146</td>
<td>146</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P. Correlation</td>
<td>-.037</td>
<td>.065</td>
<td>.063</td>
<td>.030</td>
<td>-.038</td>
<td>-.061</td>
<td>.051</td>
<td>.053</td>
</tr>
<tr>
<td>Significant</td>
<td>.645</td>
<td>.416</td>
<td>.435</td>
<td>.711</td>
<td>.634</td>
<td>.444</td>
<td>.541</td>
<td>.522</td>
</tr>
<tr>
<td>Number</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>157</td>
<td>146</td>
<td>146</td>
</tr>
<tr>
<td>Age on diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P. Correlation</td>
<td>-.004</td>
<td>-.062</td>
<td>-.095</td>
<td>-.055</td>
<td>.161*</td>
<td>-.072</td>
<td>.076</td>
<td>.072</td>
</tr>
<tr>
<td>Significant</td>
<td>.957</td>
<td>.448</td>
<td>.242</td>
<td>.501</td>
<td>.046</td>
<td>.375</td>
<td>.364</td>
<td>.393</td>
</tr>
<tr>
<td>Number</td>
<td>154</td>
<td>154</td>
<td>154</td>
<td>154</td>
<td>154</td>
<td>144</td>
<td>144</td>
<td>144</td>
</tr>
</tbody>
</table>

* = Significant at 0.05 level
** = Significant at 0.01 level

**Discussion**
The present sample was taken from the Thalassaemic Centre in Ibn-Al-Balady hospital in Baghdad; this center is the only center for thalassaemia in Baghdad. The name of the center was changed recently to Center of anemia of Mediterranean Region, for this reasons we can see that patients included in this sample were from ten governorate, but mostly from Baghdad 121(77.1%), and then from Diyala 21(13.4%), Wassiet 12 (7.6%). This could be explained by the fact that patients living in Baghdad and Deilla can more easily come to the center for blood transfusion and treatment and that doctors in these areas are more aware about this condition, so the diagnosis and treatment are more available to patients. On the other hand, patients living in far areas probably will not have the chance for early diagnosis life.
The patients age were mostly <10.0 years (73 patients 46.5%), and there was no patient above the age of 30 years, these finding can be explained by the fact that most of the patients included in the sample were those suffering from thalassaemia major with shorter life period, in a study done by Zurlo et al [18], they found that the over all survival from birth for patients born in 1970-74 was 97.4% at 10 years and 94.4% at 15 years, the most common cause of death was heart disease, followed by infection, liver disease and malignancy. Modell [19] showed that patients who adhere fully to treatment usually complete their education, work, and find a partner, and are expected to live at least until their mid- forties.

In the past decade, treatment of patients with beta-thalassemia has changed considerably, with advances in red cell transfusion and the introduction of iron chelation therapy. This progress has greatly increased the probability for a thalassemic child to reach adult age with a good quality of life [20]. Currently all newborns in the United States are screened for hemoglobinopathies, if a newborn screen returns with large amounts of fetal hemoglobin, alpha hemoglobin, or hemoglobin E, further investigation for thalassemia takes place [21].

In the present sample male patients 99 (63.1%) constituted higher number than females 58 (36.9%), this could be explained by the fact that people especially in developing countries are more concern about their male children than female children.

Treatment of patients with thalassemia major has improved dramatically during the past 40 years; however, the status of these patients remains poorly characterized [22].

The mean Hb. level in the present sample was 8.4 g/dl with the minimal reading of 5.0 g/dl and maximum of 11.0 g/dl, this result is expected since those blood samples were taken from patients who were coming for blood transfusion and accordingly their Hb. level were expected to be low, when the Hb. level was correlated with the clinical manifestation, it was found that it correlated significantly with bronze skin only, while pale looking was correlated with bronze skin, mongoloid feature, diabetes mellitus, heart failure which signified severe complication of thalassemia, and again the patients examined were in the majority suffering from thalassemia major.

Blood group O was the dominating blood group among the sample of patients then comes blood group B, A, AB. The National blood transfusion centre in Baghdad (1988-1993) recorded that blood group O shows the highest percentage (31%) among people attending the blood bank for giving blood then comes group A, B, AB (personal contact), the higher prevalence of blood group B in the thalassemic patients than group A could be due to chance only, or possibly that people with blood group B are more prone to develop thalassemia, a suggestion which need to be studied in a wider and more generalized form, since we could not find a reference which touch this particular point (blood group difference in thalassemic patient and general population).

As for treatment with blood transfusion, it was found that most of the patients (108 68.8%) where having blood transfusion between 2-4 weeks and desferol treatment > 4 times \ week (99 patients 63.1%), which indicate reasonable treatment program, this does not coincide with the severity of clinical manifestation found among the patients, which could be explained by the fact that those patients probably need more aggressive treatment than the one planned for them, on the other hand regular blood transfusion will inevitably lead to multi-organ...
Thalassemia, mineral and trace element …. Abdul-Karim et al

Hemosiderosis and are attended by risks of blood-born infections\textsuperscript{23}. In the present sample the BMI showed that around half of the patients were underweight and only 7 patients were overweight, which means that a good number of patient were suffering from growth retardation, this finding coincide with the finding that large proportion of patients were suffering from thalassemia major with symptomatic manifestation of the disease, and probably those patients are in need of more aggressive treatment than the present one.

The clinical picture of inadequately treated $\beta$ thalassaemia is characterized by anemia, splenomegaly, bone changes, and being prone to infection\textsuperscript{24}, the severity of the disease is extremely variable, and those so called major forms of the illness reflect the severe end of a spectrum that stretches from less severe anemias, which do not require transfusion, through intermediate forms of $\beta$ thalassaemia to the completely symptom less conditions that are identified only by chance\textsuperscript{25}.

Clinically patient in the present sample showed high proportion of clinical manifestation of severe thalassaemia, for example, there were 126 (80.3\%) of patients who were pale (the mean hemoglobin level was 8.4 g/100ml), 93 (59.2\%) of them were with jaundice, 84 (53.5\%) with bronze skin.

One of an important issue to be considered during follow up of patient with thalassaemia is bone abnormalities characterized by bone marrow expansion of the medullary cavity, and osteopenia with cortical thicking and trabecular coursing\textsuperscript{26}, in the present sample, it was found that 95 (60.5\%) of patients had frontal bossing, and 76 (48.4\%) had mongoloid features (complication of bone marrow expansion).

Hepatospleenomegaly had been mention in many articles\textsuperscript{19,24,27-29} especially in those patients suffering from severe form of thalassaemia due to hypertrophy of ineffective bone marrow, in the present sample we find that 69 (43.9\%) of patients suffers from liver enlargement, and 78 (49.7\%) suffer from enlarge spleen.

There were 5 (3.2\%) patients with heart failure in the sample group, it is well Known fact that if excess iron derived from transfusion is not removed patients die in the second or third decade from iron loading of the myocardium\textsuperscript{30,31}. In a study done by Ferrara et al\textsuperscript{32} 2004, they found that patients with thalassemia major in the study sample showed marked reduction in contractile state and milder LV than in thalassemia intermedia. It is important to notice that classic changes of untreated thalassaemia major are now regularly seen only in countries without resources to support long-term transfusion programs\textsuperscript{9}.

The striking increases in survival in patients with $\beta$ thalassemia over the last decade have focused attention on abnormal endocrine function, for example diabetes mellitus was observed in 5\% of adults which is due to exhaustion of beta cell and reduce circulating insulin concentration\textsuperscript{33,34}, in the present sample only 2 (1.3\%) of patients were having diabetes mellitus, this could explain by the fact that most of the patients in this sample are of younger age with severe clinical symptom of thalassemia major, which makes the possibility of detecting diabetes mellitus among them less likely than those who are with better treatment programs and older in age.

Growth retardation in early childhood is a consequence of severe anemia. It can be prevented (although not corrected) by an aggressive blood transfusion program\textsuperscript{35}. Even in children optimally transfused, however, the preadolescent
growth spurt is delayed and curtailed, so that full potential stature is rarely realized\(^3\). Growth failure occurs as a result of low somatomedin activity, because the liver synthesizes somatomedin, hemosiderosis has been held responsible for preadolescent growth failure\(^3\). Filosa\(^3\) concluded that puberty positively influences the bone mineral density only at the start of puberty, while subsequently, the degree of osteoporosis is the expression of widespread and chronic systemic damage due to the hematological phenotype. In the present sample, it was found that 48.4\% of patients suffer from under weight, which means that about half of the patients their BMI level were below the normal, this result is expected since 77.1\% of patients suffer from thalassemia major and a good percentage of them show different clinical manifestation of thalassemia, also age on diagnosis of the patient was found to be correlated with BMI, which is an expected finding.

Again, the finding of significant correlation between age of patient with most of the clinical feature of thalassemia, type of treatment applied and diabetis mellitus was expected one, while sex was correlated with bronze skin, Hb level, and blood groups only probably because 63.1\% of patients were males, and parents of thalassemic children do care about their male children more than the female ones, so different clinical features were correlated less frequently with the sex of the patients. The finding that the address, residency and diagnosis of the disease were not correlated with any of the studied variables could be due to the fact that the sample size is not big enough to show differences and most of the patients were from urban areas, the same things could be said for the finding that age on diagnosis and treatment with desferol were correlated with magnesium level in the blood, while other variables were not correlated with any of the trace elements, minerals, or albumin level in the patient blood.

**Recommendation**
1. It is very important that more centers for thalassemia are to be established in different areas in our country, with increase efficiency as to include gene frequency
2. To established programs based on carrier screening and counseling of couples at marriage, preconception or early pregnancy, which can be done by simple hematological analysis. These programs are operating in several Mediterranean at risk population, and are very effective, as indicated by increasing knowledge on thalassemia and its prevention by the target population and by the marked decline of the incidence of thalassemia major.
3. Prenatal diagnosis by mutation analysis on PCR amplified DNA from chorionic villi Molecular diagnosis of homozygotes and identification of carrier of beta thalassemia may lead to improved clinical management of patients with the disorder and prevention of the birth of affected homozygotes.

**References**
35. Logothetis, J.: Body growth in Cooley’s anemia (homozygous beta-thalassemia) with a crrelative study as to other aspects of the illness in 138 cases. Pediatrics, 1972; 50: 92.
ANTIOXIDANT STATUS IN THALASSEMIC PATIENTS

Subuh S. AL-Mudalal1 MSc FICMS, Raad J. Musa1 MSc FICMS, Najat AL-Duliami2 MSc PhD

Abstract

Background: Increased membrane lipid peroxidation in patients with thalassemia has been reported suggesting that superoxide radicals generated in excess following auto-oxidation of isolated hemoglobin chains is an important contributor to the hemolytic process.

Objective: This study was undertaken to evaluate the extent of lipid peroxidation and antioxidant status of patients with beta-thalassemia in comparison to healthy people.

Methods: Red cell superoxide dismutase (SOD) activity and red cell catalase activity were measured in the biochemistry department for the period from January 2003 to October 2003. 76 patients with beta-thalassemia, 14 patients with beta-thalassemia minor and 19 healthy controls were studied.

Results: Erythrocytes of patients with beta-thalassemia major had significantly higher SOD than control (p<0.0004). Red cell catalase activity of thalassemia minor patients was significantly higher than that of the control (p<0.05). In thalassemic patients, the more anemic patients have significantly higher SOD activity, but this correlation was not present between anaemic patients & catalase activity.

Conclusion: Red cell superoxide dismutase activity was greatly increased in homozygous beta-thalassemia, and inversely correlated with severity of anemia.

Keyword: SOD, Catalase, Thalassemia.

IRAQI J MED SCI, 2005; Vol. 4 (1): 38-44

Introduction

Auto-oxidation of biomembranes is considered to be the primary factor involved in cellular senescence and breakdown1,2. An increased production of highly activated forms of oxygen released during the oxidation of hemoglobin to methemoglobin in thalassemic red blood cells (RBC)3-8 has stimulated much interest in superoxide dismutase (SOD) and cellular antioxidant for the control of such deleterious radical reactions. The aim of this study was to evaluate the extent of lipid peroxidation and antioxidant status of patients with beta-thalassemia in comparison to healthy people. Also to find any correlations between the level of these antioxidants with the appropriate time of transfusion.

Patients & Methods

During the period of ten months from January 2003 to October 2003, 109 subjects were included in this study; 76 patients with beta-thalassemia major, 14 patients with beta-thalassemia minor were taken from hematology center of Ibn-Balady Hospital, and 19 healthy controls were taken from laboratory healthy staff in Al-Kadhimiya Teaching Hospital. Venous blood was collected from patients before blood transfusion and then hematological studies were done including; red cell count, white cell count, mean corpuscular volume and haematocrit were determined in a coulter counter,MS9. Haemoglobin concentrations were measured on a haemoglobinometer. Haemoglobin types and quantitation of different types...

1Dept. pathology 2Dept. Chemistry & Biochemistry, College of Medicine, Al-Nahrain University
Address Correspondence to Dr. Subuh S. Al-Mudalal
Received 20th November 2004: Accepted 14th March 2005.
were identified by variant haemoglobin testing system.

Enzyme assay: the method for SOD measurements is based on the ability of the enzyme to inhibit the reduction of nitroblue tetrazolium by superoxide radical, which is generated by the reaction of photoreduced riboflavin and oxygen\[^9\]. The method for measuring catalase activity is based on the ability of catalase to decompose hydrogen peroxide\[^10\]. Units of the enzyme assays were reported as mg/g Hb, mg/ml red blood cells.

**Statistical Analysis**

All values are given as mean ± SD (standard deviation). The differences were assessed by unpaired student t-test. P< 0.05 was considered to be statistically significant. The correlation probability and correlation coefficient (R) of any two variables was computed by an AMSTRAD PCW 8256 computer using the AMSTAT computer program.

**Results**

The mean SOD of erythrocytes of thalassemia major patients was 1478.4 IU/ml, SD (standard deviations) = 346.79, SE (standard error) = 48.09, range: (1012.07-2556.82). The mean SOD of erythrocytes of thalassemia minor patients was 1189.0 IU/ml, SD (standard deviations) = 212.84, SE (standard error) = 56.88, range: (871.51-1568.72). The mean SOD of erythrocytes of healthy controls was 1261.7 IU/ml, SD (standard deviations) = 165.81, SE (standard error) = 40.22, range: (984.58-1547.19).

The mean Catalase of erythrocytes of thalassemia major patients was 5.0 mg/ml, SD (standard deviations) = 1.63, SE (standard error) = 0.23, range: (1.35-8.56). The mean Catalase of erythrocytes of thalassemia minor patients was 6.0 mg/ml, SD (standard deviations) = 1.78, SE (standard error) = 0.48, range: (3.35-10.08). The mean Catalase of erythrocytes of healthy controls was 5.3 mg/ml, SD (standard deviations) = 1.63, SE (standard error) = 0.39, range: (3.58-8.71). Figures 1 and 2 show the mean values of SOD and Catalase activities.

![Figure 1: Bar Chart showing mean values of SOD for thalassemia major, thalassemia minor and control subjects](image-url)
Antioxidant Status . . . Al-Mudalal et al

Figure 2: Bar chart showing mean values of catalase for thalassemia major, thalassemia minor and control subjects

Erythrocytes from thalassemia major have significantly higher SOD than control (p<0.0004), also erythrocytes of thalassemia minor had a higher SOD than that of the control but statistically was not significant (p= 0.3138), while erythrocytes of thalassemia major patients had a higher SOD than that of thalassemia minor patients but statistically was not significant (p= 0.36817).

Red cell catalase activity of thalassemia minor patients was significantly higher than that of the controls (p<0.05), also was higher than that of thalassemia major patients but statistically was not significant (p= 0.1234).

In thalassemic patients, the more anaemic patients had significantly higher SOD activity (Figure-3), but this correlation was not present between anaemic patients and Catalase activity (Figure-4).

Figure 3: there is negative correlation between hemoglobin (G/dl) and SOD of erythrocytes in thalassemia major patients
Antioxidant Status …. Al-Mudalal et al

Figure 4: there is no correlation between hemoglobin (G/dl) and catalase of erythrocytes in thalassemia major patients

There was no significant correlation between SOD activity, Catalase activity and the last time of blood transfusion (Figures 5 and 6).

Figure 5: there is no correlation between SOD of thalassemia major patients with the last time of transfusion

Figure 6: there is no correlation between Catalase of thalassemia major patients with the last time of transfusion
Discussion
In beta-thalassemic red blood cells (RBC), increased precipitation of alpha chain associated with increased oxidation of heme iron has been cited as the principal mechanism for generating activated species of molecular oxygen \[3-6\], conceivably, these activated forms of oxygen can be formed during transport of oxygen through the membrane as well as within the cell. In this context, the role of small molecules endowed with antioxidant activity would be more effective in protecting membrane lipids from undergoing free radical chain reactions. In contrast, SOD, being effective in the dismuta
tion of superoxide anion in the cell, may be not accessible to the lipid matrix of the membrane due to its size and charged groups. Consequently, the effective radical scavenging action of SOD within the membrane would be markedly diminished \[11\]. Measurements of the specific activity of SOD in thalassemic RBC show a higher percent inhibition of cytochrome c per milligram of protein as compared with normal individuals. The increase of SOD specific activity found in RBC of thalassemic patients may be associated with increased production of superoxide anion. An induction of SOD was demonstrated in experiments on oxygen toxicity \[12-14\].

The results of this study concerning the increased specific activity of SOD in thalassemic RBC donot agree with reports from other laboratories \[15\] which have observed no differences in the level of SOD in normal and thalassemic RBC. Conceivably, the different assay methods employed in such comparison might explain the discrepancy, these methods describes by Nishikimi \[22\] and by Misra \[23\], both methods are based on inhibition by the enzyme of color development by chromogenic substance reacting with \(\text{O}_2^-\). In the method of Nishikimi, Nitro Blue Titrazolume aqueous solution giving blue formazan which can be monitored at 560nm. In the method of Misra; epinephrine at pH 10.2 acts both as the source of \(\text{O}_2^-\) and as the detecting system giving adrenochrome which can be monitored at 480nm. The interesting observation that emerges from this work is that high SOD activities found in thalassemic RBC apparently do not protect them from increased rate of autohemolysis, and polyamines might be more effective in protecting biomembranes against the deleterious effect of free radicals.

The findings of this study indicate that patients with more sever disease, beta thalassemia major, having a greater excess of alpha globin chain, also have higher activities of SOD but lower catalase activity than the milder genotype, beta thalassemia minor. Increased red cell SOD values in thalassemic patients have previously been explained as a reaction to, or compensation for the increased production of superoxide radicals, the amount of which is related to excess globin chain \[16,19\]. This study showed significantly lower red cell catalase activity ( although higher than normal subjects) , in patients with the more severe form of the disease expressed both as per g Hb and per ml red blood cells and that was similar to other study \[21\] . A possible explanation for lower red cell catalase activity found in the more severe genotype of beta thalassemia is that the greater amount of hydrogen peroxide might produce direct toxic damage to catalase \[17,18\], the concentration of this is considerably reduced in conditions of high oxidative stress \[20\].

The increase of erythrocyte superoxide dismutase activities is most likely due to abnormalities specific to thalassemic red cells rather than an increased number of younger red cells for...
reticulocytes and nucleated red blood cells did not affect the enzyme activity. Patients with beta-thalassemia major disease with lower haemoglobin concentration had significantly higher superoxide dismutase activities 16. In all 76 subject with beta-thalassemia major, haemoglobin concentrations and superoxide dismutase activities were inversely correlated (r=−0.60) (p<0.001). This indicates that the amounts of superoxide generated in red cells may, at least partly, determine severity of disease; the increased superoxide dismutase activity in thalassemia is a response to superoxide generated in greater amounts because of accumulation of excessive globin chains and iron in the red cells.

**Conclusion**

1. Red cell superoxide dismutase activity was greatly increased in homozygous beta-thalassemia.
2. Lower red cell catalase activity was found in the more severe genotype of beta-thalassemia.
3. The more anaemic patients had significantly higher SOD activity.

**References**


VASCULARIZATION IN PROSTATIC CARCINOMA

Faiza A. Al-Rawi MBChB MSc FICPath.

Abstract

Background: Angiogenesis means the creation of new blood vessels, a critical natural process that occurs in the body both in health and in disease.

Objective: Quantitative assessment of tumor vascularization in different grades of prostatic tumors.

Methods: 23 paraffin blocks of prostatic biopsies (8 cases of benign prostatic hyperplasia and 15 cases of prostatic carcinoma equally distributed in well, moderately and poorly differentiated (Gleason's grade 2, 3 and 4&5 respectively). Processed routinely and stained with hematoxylin and eosin, elastica Van Gieson, and Masson Trichrome stain. The vascular surface density (VSD), the microvessels number (NVES), and the maximum microvessels number (NVES-MAX) was assessed by means of stereology, and the results were related to grade of tumor differentiation.

Results: NVES and NVES-MAX showed a significant increase with rising tumor grade ranging from 16.1 in BPH to 109.0 microvessels/mm² in poorly differentiated (grade 4&5) tumors. Discrimination of different tumor grades was more accurate with NVES-MAX. The VSD was significantly higher in low-grade tumors compared with BPH, whereas there was continuous decrease from low grade (11.6 mm⁻¹) to high-grade tumor areas (5.1 mm⁻¹).

Conclusions: The present study shows a correlation between tumor grade and vascularization.

Key words: Prostate cancer, angiogenesis, vascularization.


Introduction

Rapid cellular proliferation in malignant tumors requires nutritional support guaranteed by a sufficient vascular bed and unrestricted growth of tumors is dependent upon angiogenesis[1,2]. Recent studies have clarified the molecular basis of tumor neovascularization, a process mediated by several growth factors[3]. Angiogenic activity first appears in a subset of hyperplastic tissue before the onset of tumor formation[4,5]. Hyperplasia per se does not obligate angiogenesis. Rather, a few hyperplastic tissues become angiogenic correlates closely with subsequent tumor incidence[4,6]. The vessels surface in a tumor is a putative target of tumor cell adhesion and invasion, and consequence local and systemic spread[5-8]. On light microscopic level, the process of tumor angiogenesis results in an increase number of vessels within the tumor tissue, and areas of maximum vascularization, called hot spots[9,10].

Materials & Methods

This study comprises of 23 paraffin blocks of prostatic biopsies (8 cases of benign prostatic hyperplasia and 15 cases of prostatic carcinoma equally distributed in well, moderately and poorly differentiated (Gleason’s grade 2, 3 and 4 or 5 respectively). Fixed in 10% buffered formalin processed routinely and stained with hematoxylin and eosin, elastica Van Gieson, and Masson Trichrome stain.

Stereological measurements: Areas of unequivocal tumor tissue were marked on the cover slide. Within the tumor 10 areas were randomly chosen for

Dept. Pathology, College of Medicine, Al-Nahrain University
Received 8th May 2004: Accepted 29th November 2004.
assessment of the vascular surface density (VSD), microvessel number (NVES), and Maximum Microvessel number (NVES-MAX)\(^5\).

**VSD:** The vascular surface density and the stromal volume portion were assessed by means of stereology at a \(x160\) microscopic magnification\(^6\). An ocular square lattice (periplan \(x10\), leitz Wetzlar, Germany) with 121 points composed of 11 horizontal and 11 vertical test lines with line length (Lg=2.6875Mm) was superimposed on the test fields to be measured, and the number of intersections (Ia) between the test lines and labeled vessels walls was counted (Figure 1). VSD was assessed according to (Barth et al 1996)\(^5\).

\[
VSD = \frac{E \cdot I_a^{2}}{LR \cdot Vv (STR)}
\]

**Microvessel number (NVES):** In the same procedure step, the number of vessel (N) within the measuring field was counted and the number of vessels per mm2 stroma (NVES) was computed according to

\[
NVES = \frac{N}{Vv (STR)}
\]

**Maximum Microvessel number (NVES-MAX)\(^5\):**

To simulate hot-spot measurements, maximum microvessels counts were computed from the arithmetic mean of microvessel counts in the tumor areas that yielded the 30% highest values.

**Statistical analysis:** Differences between study groups were performed by the analysis of variance procedure; \(P< .05\) was defined to be a statistically significant value.

**Results**

In low-grade tumor, the vessels formed well-branched network of small capillary vessels, whereas in the intermediate and high-grade tumor the vascular bed was mainly composed of plump less branched vessels (Figures 2 and 3). In BPH, the average number of the vessels (NVES) and (NVES-MAX) was found to be 15.4+1.12 mm\(^{-2}\) and 16.1 mm\(^{-2}\) respectively.

In prostatic carcinoma, NVES and NVES-MAX increased significantly with rising tumor grade. However, no statistically significant difference could be confirmed between moderately (G3) and poorly differentiated (G4&5) carcinoma (Table 1). Assessment of the VSD yielded completely different results. In well-differentiated tumors, the VSD reached value significantly higher compared with BPH (11.6 Vs 5.2). While in moderately and poorly differentiated carcinoma, significantly lower values compared with well-differentiated tumors were obtained, and not significantly different from that of BPH (Table 1).
Vascularization in prostatic carcinoma …. Al-Rawi F.A.

Figure 2: Morphology of low-grade prostatic carcinoma (G2). In this area the NVES is 58, the VSD is 16.3mm\(^{-1}\) (Trichrome stain)

Figure 3: Morphology of high-grade prostatic carcinoma (G4). In this area the NVES is 110, the VSD is 7.3mm\(^{-1}\) (Trichrome stain)

Table 1: Vessel Parameters in Different Prostatic carcinoma grades

<table>
<thead>
<tr>
<th>Method</th>
<th>BPH</th>
<th>Well differentiated carcinoma (G2)</th>
<th>Moderately differentiated carcinoma (G3)</th>
<th>Poorly differentiated carcinoma (G4&amp;5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VSD(mm(^{-1}))</td>
<td>5.2±0.2</td>
<td>11.6±1.3</td>
<td>9.2±3.1</td>
<td>5.1±0.6</td>
</tr>
<tr>
<td>NVES(mm(^{-2}))</td>
<td>15.4±1.1</td>
<td>52.7±23.6</td>
<td>75.7±22.6</td>
<td>105.0±0.4</td>
</tr>
<tr>
<td>NVES-MAX(mm(^{-2}))</td>
<td>16.1±2</td>
<td>69.8±21.1</td>
<td>97.5±19.6</td>
<td>109.0±0.4</td>
</tr>
</tbody>
</table>

P values < 0.5.

Discussion
The present study shows a correlation between tumor grade and vascularization. In low grade lesions (G1) the microvessel number increased with increasing tumor grade and data concerning the maximum microvessel number correspond well to those already published\(^{5,7-11}\). In contrast to counts of vessel profiles per area, the assessment of VSD showed no significant correlation to tumor grade. This behavior of the vascular surface density is not specific for prostate cancer and also has been reported in renal cell carcinoma\(^{5,9}\). In contrast to the microvessel number, the VSD concerns the physiological status of the vasculature as it quantifies the vascular surface available for substrate diffusion\(^{4,5}\).

In normal tissue and low-grade tumors, the microvessel are well branched and show a high surface/vessel ratio, whereas the microvessel in high grade lesions are plump and non-branched, disclosing a low surface/vessel ratio\(^{5,11}\). Although in high-grade lesions the vascular surface is decreased, the vascular bed serves its function to supply the tumor tissue\(^{5,8}\). Possible explanations are an increased permeability of the vessel wall and changes of the tumoral vascular bed, which compensates the reduced vascular surface\(^{8}\).

Counts of microvessel profiles per area unit tissue section provide a significant parameter for the prediction of tumor grade, whereas the VSD primarily reflects the vascular geometry and is only weakly related to the tumor grade. Nevertheless, both methods provide valuable information in studies concerning tumor angiogenesis.

References
SERUM COPPER AND ZINC LEVELS AND COPPER/ZINC RATIO IN PATIENTS WITH RHEUMATOID ARTHRITIS

Yahya Y.Z. Farid1 BSc PhD, Alaa K. Mohammed2 BSc PhD, Israa S. Mohammed2 BSc

Abstract
Background: Trace elements particularly copper and zinc have a great role in a number of biological processes, therefore estimation of these metals in serum of Rheumatoid Arthritis (RA) patients may ameliorate the understanding of trends in the relationship between the serum copper and zinc levels and activity of disease.

Objective: To determine the serum copper and zinc levels and its relation with the degree of disease activity and compare with a normal group.

Methods: The investigation was carried out on forty-three healthy (25 females, 18 males) and fifty-four (37 females, 17 males) sick adults. The patients were subdivided according to the activity of the disease (Tentative EULAR Criteria) in to two groups. Of them 29 patients (21 female, 8 male) had low disease activity [age range 32-65 years] and twenty-five patients (16 female, 9 male) had high disease activity [age range 22-52 years]. They were compared with 43 healthy control [age range 19-64 years]. Serum copper and zinc were determined by using the atomic absorption spectrophotometry.

Results: Serum copper level and copper/zinc ratio in patients with RA in both groups were significantly increased than the control group. In addition the serum zinc level in patients with low activity RA was significantly decreased and more in high activity disease.

Conclusions: As a result, the alteration of copper and zinc levels in the sera patients with RA can related to degree of disease activity and enable to shed more light on the role of trace elements in both physiological and pathological states.

Key words: Rheumatoid Arthritis, copper, zinc, and serum.


Introduction
Metal ions have a great variety of functions in biochemistry. They serve as catalyst in active center of enzymes, as factors stabilizing the structure of the enzymes or as a counter ion to provide electro neutrality. Metal ions in human serum have various functions. They act as the physiologically active part of enzymes (copper in coeruloplasmin) or they are bound to proteins in order to be stored (iron in ferritin) or transported (iron in transferrin)[1]. The trace elements copper and zinc have a significant role in antioxidant protection and immunity. They are constituents in antioxidative enzymes, zinc and copper in cytoplasmic superoxide dismutase[2] and copper in ceruloplasmin[3], which is an important antioxidant in serum[4]. Zinc is important in the maintenance of proper immune response[5,6]. In inflammatory conditions, such as rheumatoid arthritis (RA), there are alterations in blood and serum concentrations of these micronutrients. Serum zinc was found to be reduced and serum copper increased in adult rheumatoid arthritis and these variations appeared to be associated with the immune inflammatory rheumatoid
Serum Cu, Zn levels in RA patients …. Farid et al

Neidermeier and Griggs\(^7\) reported low serum zinc values in patient with RA. Similar observations have been reported by other researchers\(^8,9,10\). Moreover, both in humans\(^11\) and in animals\(^12\) zinc preparations have been shown to be anti-inflammatory and antiarthritic agents. In contrast, Alegree, et al\(^13\) reported normal serum zinc values in patient with RA. Low serum zinc and zinc deficiency in patients with RA could be the results of zinc deficient diet, therapeutic regimens, shift of zinc from plasma to other body compartments, and/or increased urinary zinc excretion.

Our purpose was to elucidate the alteration of copper and zinc concentration in sera patient with RA and to evaluate the relation between the levels of copper and zinc with various degrees of disease activity compared with a normal control group.

**Materials and Methods**

**Chemicals:** Standard solution for copper and zinc of 1000 µg/ml concentration (Atomic absorption grade) were obtained from Aldrich chemical company LTD. All solutions were prepared from analytical grade chemical and distilled deionized water was used throughout.

**Apparatus:** Serum copper and zinc were measured with a shimadzu- flame atomic absorption model AA-646. Single elements hallow cathode lamps were used as line-radiation sources for individual elements and were operated at current recommended by the manufacturer and the manual of the atomic absorption spectrometer.

**Preparation of standard working solutions:** On the day of determination, the working solutions were prepared by sequential dilution (i.e. standard 1000 µg/ml was diluted to 10 µg/ml from which the lower concentration of working solution were prepared sequentially) to obtain the following concentration of the working standard (0.4, 0.8, 1.2, 1.6 and 2.0 µg/ml) of copper and zinc.

Frozen sample were allowed to thaw and come to room temperature then mixed gently. Sample were diluted 1:10 with (6%) butanol as diluents, this method achieved 30% increases in sensitivity compared to use of water only\(^14\).

**Patient’s selection and sample collection:**

**Subjects:** The clinical part of this study was completed between April and August 2004 in the Rheumatology Outpatient Clinic in Baghdad Teaching Hospital-Medicine City. The study population consisted of ninety-seven healthy and sick adults. Fifty-four (37 female, 17 male) from the Rheumatology Out patients’ clinic were diagnosed as having RA according to the Rheumatoid Arthritis Disease Activity Index (RADA) for epidemiological research\(^15\). Forty-three healthy persons made up the control group (Group 1). Age range of the control group was 19 to 64 (mean 44.3 ± 4.2); male/female ratio was 0.72.

The patients with RA were divided into 2 groups after evaluation of their disease activity by the Tentative EULAR Criteria\(^16\). [Number of tender joints: maximum 28; number of swollen joints; maximum 28; pain score: 0 (no pain) to 10 (very sever pain), erythrocyte sedimentation and morning stiffness of at least 30 min duration]. Twenty-nine patients (21 female, 8 male) with less than 14 swollen joints and one hour morning stiffness were considered to have low activity of the disease; these patients made up Group 2 and 3. Another twenty-five patients (16 female, 9 male) presenting a higher number of swollen joints and more prolonged morning stiffness, were considered to have a high degree of inflammation and were defined as Group 4 and 5. Characteristics of the
groups 2, 3, 4 and 5 are presented in tables 1 and 2.

Table 1: Characteristics of the Rheumatoid Arthritis Groups (2) and (3) low activity

<table>
<thead>
<tr>
<th>Data</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>No. of patients</td>
<td>8.0</td>
<td>21.0</td>
</tr>
<tr>
<td>Age range (years)</td>
<td>32-65</td>
<td>19-16</td>
</tr>
<tr>
<td>Age (years)</td>
<td>55.30±1.90</td>
<td>48.8±2.30</td>
</tr>
<tr>
<td>Duration of disease (years)</td>
<td>6.90±1.10</td>
<td>5.90±1.20</td>
</tr>
<tr>
<td>Morning stiffness (hours)</td>
<td>0.70±0.20</td>
<td>1.10±0.30</td>
</tr>
<tr>
<td>No. of tender joints</td>
<td>15.20±3.0</td>
<td>16.20±2.30</td>
</tr>
<tr>
<td>No. of swollen joints</td>
<td>6.10±1.20</td>
<td>8.90±2.0</td>
</tr>
<tr>
<td>ESR (mm/h)</td>
<td>36.0±8.0</td>
<td>34.0±2.0</td>
</tr>
<tr>
<td>+ve rheumatoid factor</td>
<td>5/8</td>
<td>17/21</td>
</tr>
</tbody>
</table>

Table 2: Characteristics of the Rheumatoid Arthritis Groups (4) and (5) high activity

<table>
<thead>
<tr>
<th>Data</th>
<th>Group (4)</th>
<th>Group (5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>No. Of patients</td>
<td>9.0</td>
<td>16.0</td>
</tr>
<tr>
<td>Age range (years)</td>
<td>22-52</td>
<td>19-58</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>45.6±7.9</td>
<td>43.8±4.8</td>
</tr>
<tr>
<td>Duration of disease (years)</td>
<td>5.2±1.2</td>
<td>6.6±2.3</td>
</tr>
<tr>
<td>Morning stiffness (hours)</td>
<td>3.4±1.1</td>
<td>3.3±0.3</td>
</tr>
<tr>
<td>No. of tender joints</td>
<td>18.9±2.3</td>
<td>24.0±0.8</td>
</tr>
<tr>
<td>No. of swollen joints</td>
<td>15.1±3.5</td>
<td>14.2±2.5</td>
</tr>
<tr>
<td>ESR (mm/h)</td>
<td>65.0±5.0</td>
<td>78.0±5.0</td>
</tr>
<tr>
<td>+ve rheumatoid factor</td>
<td>9/9</td>
<td>16/16</td>
</tr>
</tbody>
</table>

Serum preparation:
Avenues blood samples were drawn by utilizing disposable needle and plastic syringes from each patient and control. The blood was allowed at room temperature for 10 minutes for clotting; centrifuged at 3000 rpm for 10 min, then serum was separated and stored at (-20°C) until analysis.

Accuracy and Precision:
The accuracy and precision of the method were checked. Table 3, shows the relative standard deviation and relative error percent for five replicate results obtained for lowest and highest concentration range of each individual constituent.

Table 3: Accuracy and precision of copper and zinc analysis.

<table>
<thead>
<tr>
<th>Cu added µmol/l</th>
<th>Cu found µmol/l</th>
<th>Relative Standard Deviation %</th>
<th>Relative Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>9.6</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1.40</td>
<td>11.31,11.21</td>
<td>1.0</td>
<td>1.36</td>
</tr>
<tr>
<td>3.50</td>
<td>13.10,13.12,13.12,13.15,13.18</td>
<td>0.24</td>
<td>0.24</td>
</tr>
<tr>
<td>5.65</td>
<td>15.20,15.25,15.31,15.15,15.12</td>
<td>0.50</td>
<td>0.32</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Zn added µmol/l</th>
<th>Zn found µmol/l</th>
<th>Relative Standard Deviation %</th>
<th>Relative Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>5.44</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2.50</td>
<td>7.85,7.92</td>
<td>0.61</td>
<td>0.47</td>
</tr>
<tr>
<td>5.0</td>
<td>10.60,10.51,10.31,10.45,10.51</td>
<td>1.01</td>
<td>0.34</td>
</tr>
<tr>
<td>7.20</td>
<td>12.52,12.62,12.56,12.55,12.60</td>
<td>0.27</td>
<td>0.58</td>
</tr>
</tbody>
</table>

Results and discussion
The current study provides data on copper and zinc levels in Rheumatoid Arthritis sera patients and compared with those of normal subjects. As different degree of inflammation may specifically possess different characteristics of the disease and different levels of these elements, separate calculation were made for each test.

Normal subjects:
Serum total copper and zinc were detected in normal subjects. The normal values for copper and zinc in female
was (18.60±1.24) and (15.07±0.66) µmol/l while they were (15.87±2.1) and (14.07±0.85) µmol/l in male respectively, the results show little differences between females and males for both copper and zinc, so that the total means for both sexes was (17.23±0.91) and (14.57±0.21) µmol/l respectively, as show in table 4.

Table 4: The serum copper, zinc levels of the patients with RA and control

<table>
<thead>
<tr>
<th>Cases</th>
<th>Serum Cu</th>
<th>Serum Zn</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD µmol/l</td>
<td>Mean ± SD µmol/l</td>
</tr>
<tr>
<td>RA with low activity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female (21)</td>
<td>21.39±3.31*</td>
<td>8.36±0.79*</td>
</tr>
<tr>
<td>Male (8)</td>
<td>19.69±2.31*</td>
<td>8.07±1.03*</td>
</tr>
<tr>
<td>RA with high activity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female (16)</td>
<td>32.25±6.12*</td>
<td>5.33±0.92*</td>
</tr>
<tr>
<td>Male (9)</td>
<td>29.40±4.46*</td>
<td>4.62±0.98*</td>
</tr>
<tr>
<td>Total (54)</td>
<td>25.68±1.22*</td>
<td>6.66±1.23*</td>
</tr>
<tr>
<td>Normal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female (25)</td>
<td>18.60±1.40</td>
<td>15.07±0.66</td>
</tr>
<tr>
<td>Male (18)</td>
<td>15.87±2.0</td>
<td>14.57±0.85</td>
</tr>
<tr>
<td>Total (43)</td>
<td>17.23±0.1</td>
<td>14.57±0.21</td>
</tr>
</tbody>
</table>

* = P <0.001

Rheumatoid Arthritis (AR) patients:
The results of sera samples from patients suffered from (RA) compared to these of normal subjects, were generally characterized by increase and decrease levels of copper and zinc respectively. Serum copper level for patients and normal are shown in table 4. In general the copper concentration in 54 (Fifty-four) patients sera samples was found to be 25.68±1.22 µmol/l, while the corresponding level in 43 (Forty-three) healthy subject was 17.23±1.80 µmol/l. This increase of 49% in copper level was statistically significant (P< 0.001).

As different degree of inflammation may specifically possess different activity of the disease lead to different concentration of copper, separate calculation were made for each characteristics of the disease test. Both in the normal donors and in the various groups of patient, these were significant difference between values obtained for male and female; therefore they were grouped independent. The mean serum copper levels were found to be 21.39±3.11µmol/l and 19.69±2.31 µmol/l for female and male respectively with low activity patient; and 32.25±6.12 µmol/l, 29.40±4.46 µmol/l for serum female and male with active disease. The magnitude of the increase in the value varied between 24% for female and 14% for male patients with low activity. In contrast, the magnitude of the increase in serum copper level varied between 87% for female and 70% for male patient with active disease.

Figure 1 shows a histogram of the distribution of the serum copper levels in the normal donors and in the (RA) patients grouped according to the activation and severity of disease.

![Figure 1: Serum copper level in normal and in patients with RA](image)

The mean level of the serum copper in the total groups of (RA) patients was significantly elevated compared to the levels of the normal donors; nevertheless, only 4 of 21 (20%) and 4
of 8 (50%) for female and male patients with low activity disease have serum copper levels higher than 2SD (standard deviation) above the mean for normal donors. Of these all cases of proven active (RA) had copper serum levels higher than 2SD above the mean for normal donors. All cases of proven active (RA) had copper serum levels higher than 2SD above the mean for normal donors.

The most pronounced changes were found in the levels of serum zinc (Table 4). The mean zinc level in 54 normal controls was found to be 14.57±0.21 µmol/l, while the mean zinc in all the patients with (RA) was 6.66±1.23 µmol/l, this 56% decrease in the zinc level was statistically significant (P<0.001). The results show no significant differences between values obtained for female and male. The decrease in the zinc serum level was more pronounced when the patients were grouped according to the high activity of the disease, the magnitude of the decrease in the value varied between 63% for female and 68% for male with active disease.

Table 5 shows the results obtained for serum copper, serum zinc levels and Cu/Zn ratios of the patients with RA and the controls.

Table 5: The mean serum copper, serum zinc levels and copper/zinc ratios of the patients and normal.

<table>
<thead>
<tr>
<th>Cases</th>
<th>Serum Cu µmol/l</th>
<th>Serum Zn µmol/l</th>
<th>Cu/Zn µmol/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA with low activity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>female (21)</td>
<td>21.39±3.31</td>
<td>8.63±0.79</td>
<td>2.47±0.52</td>
</tr>
<tr>
<td>male (8)</td>
<td>19.69±2.31</td>
<td>8.07±1.01</td>
<td>2.43±0.24</td>
</tr>
<tr>
<td>RA with high Activity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>female (16)</td>
<td>32.25±6.12</td>
<td>5.33±0.92</td>
<td>6.05±0.66</td>
</tr>
<tr>
<td>male (9)</td>
<td>29.40±4.46</td>
<td>4.62±0.98</td>
<td>6.36±0.41</td>
</tr>
<tr>
<td>Total (54)</td>
<td>25.68±1.22</td>
<td>6.66±1.23</td>
<td>3.93±0.43</td>
</tr>
<tr>
<td>Normal (43)</td>
<td>17.23±1.80</td>
<td>14.57±0.21</td>
<td>1.17±0.29</td>
</tr>
</tbody>
</table>

It was found a highly significant differences (P <0.001) between the copper/zinc ratio for the control group and that for the patients group, this differences is the result of both higher values for copper and lower values for zinc in serum from the patients group as compared with normal persons. In all cases of proven active disease, the Cu/Zn ratio was significantly higher as compared to low activity patients group. Copper and zinc are very effective in DNA and RNA synthesis and cell division. These elements are required for the activation of enzymes such as timidin Kinase, RNA-polymerase and DNA-polymerase. Zinc also play an important role in the catabolism of RNA by regulating RNase activity. These two metals prevent the formation of free radicals capable of mutation with the antioxidant effect [6,17,18].

One approach to the assessment the role of copper and zinc in inflammatory conditions, such as (RA), analogous to that used for other nutrients, is measurement of copper and zinc in the serum or plasma over time because they are co-factors of important enzymes involved in collagen and bone metabolism [19] and immune system function [20]. Results studies have demonstrated that both copper and zinc alterations can be explained by the active inflammatory process and that serum trace elements are measures of disease activity.

Our studies show elevated level of copper in serum of (RA) groups and decrease level of zinc in serum patients with low activity and a more decreased level in high (RA) disease activity. Change in serum zinc and copper levels observed in RA patients led some investigators to hypothesis that a marginal deficiency in zinc and copper might contribute to the development of RA and to the progression of the disease itself.

One of hypothesis of decrease zinc and increase of copper in sera of acute or chronic inflammatory processes cause an accumulation of copper and zinc in many body compartments and in the inflamed ares, supporting the hypothesis that the development of inflammation induces an increased body requirement of copper and zinc.
containing proteins and enzymes such as metallothioneins, ceruloplasmin and Cu-Zn-superoxide dismutase\(^\text{[7,18,21]}\). Our results in both RA groups confirm those of studies that observed low plasma or serum zinc in patients with RA\(^\text{[22,23,24]}\), and the results also show that serum copper and zinc levels are correlate to severity of disease. Low serum and plasma zinc could be regarded as a secondary phenomenon arising from the hypoalbuminemia observed in patients with RA\(^\text{[25]}\). Levels of both zinc and albumin were found to be decreased by about 12% in plasma and correlated significantly with each other in patients with RA\(^\text{[7]}\).

However, it seems that the decrease in serum zinc is independent of the reduction in circulating albumin\(^\text{[7]}\). This hypothesis is supported by data showing that only 1.10-2.6% serum albumin in humans’ functions in zinc transport and that zinc occupies less than 0.2% of the total zinc binding capacity of the protein\(^\text{[26]}\). Other investigators attribute zinc deficiency in patients with RA to inadequate nutrition\(^\text{[27]}\).

One of the hypothesis proposed to explain the decreased in plasma or serum zinc is due to redistribution of zinc in the organism, including in particular accumulation of the metal in the liver\(^\text{[28]}\). In contrast, Alegre et al\(^\text{[13]}\) reported normal serum zinc values in patients with RA, the weakness of that study was the lack of measurement of serum levels in a control group. Michaelsson and Ljunghall\(^\text{[29]}\) reported decreased zinc concentrations in the serum and epidermis of men with dermatitis herpetiformis, which is considered an autoimmune disease. Svenson et al\(^\text{[10,30]}\) examined zinc concentration in peripheral blood cells; erythrocytes, granulocytes and platelets. Therefore, at this stage of research, it seems that zinc malabsorption is not a specific defect of RA, but rather is common to other inflammatory connective tissue diseases.

Since zinc may act as a stabilizer of various biological membranes by interacting with the extrinsic macromolecule components of the membrane mainly the enzymes and/or directly with the intrinsic structure of the plasma membrane, therefore the low zinc level will affect the membrane stability as well\(^\text{[31]}\).

Zinc deficiency results in blunted cellular immunity, measured by in vitro lymphocyte response to mitogens and delayed cutaneous hypersensitivity testing\(^\text{[32]}\). In addition, neutrophil chemotaxis is slowed; natural killer cell function is reduced\(^\text{[33,34]}\). It is possible that zinc deficiency may perpetuate disease in patients with RA through immunocompromised cellular mechanisms. This hypothesis calls for a prospective double blind study of the effect of zinc administration on clinical manifestations and cellular immunological functions of patients with RA.

The model involvement of increase in serum copper particularly serum cupro-enzyme and ceruloplasmin which was observed in various specific and non specific pathological condition and was attributed in biological damage caused by superoxide, a radical found in all living tissues, according to this model, superoxide radical or other reducing agents, such as ascorbate, reduced the copper complexes to the cuprous state. In turn, these complexes react with hydrogen peroxidase to form hydroxyl radicals that damage proteins, RNA and most important DNA. Repetitive formation of OH radicals at a specific location-where the copper ions are found is probably the mechanism of this process. These radicals may cause double strand break in the cellular DNA that are not repairable by cellular mechanisms\(^\text{[35]}\).
References
Abstract:
Background: Early pregnancy and unplanned childbirth may have far-reaching physical, psychological and social consequences for adolescent girls and her offspring. Therefore, public health issues of concern because of the growing cultural and social sensitivity and controversy over reproductive health issues.

Aim of the study: Studying mother age at marriage in association with different socioeconomic characters in the family, which might affect reproductive health of mothers.

Subject & methods: A cross-sectional study conducted taking data obtained from 800 randomly selected healthy mothers, during their visits to five primary health centers, which selected randomly from different areas in Baghdad city; this done during the period from June- November 1994. Information from the mothers obtained using well-studied questionnaire form.

Results: Significant relationship between mother's age at marriage and maternal education, birth interval, father age at marriage, number of pregnancies, under 5 years children in the family, crowding index, degree of consanguinity (P <0.001). Significant relationship found with father occupation, under 5 years death in the family (P <0.01). No significant relationship with number of abortion and type of family (P > 0.05) found.

Conclusion: Maternal age at marriage is an important determinant of reproductive health of women when it studied with different socioeconomic variables.

Emphasis should be made on young people to have better access to health information schools, and the medical profession needs to work together both to provide information and to help young females to develop confidence to use available information sources.

Key words: reproductive health

Introduction
National family planning programs have been an important instrument in accelerating global fertility decline and in restricting ultimate world population to a level probably below ten billion. They begin to come into being after 1950 and probably go out of existence in most of the world 'regions by 2050[1]. The 1994 International Conference on Population and Development held in Cairo has generated wide spread commitment to changing family planning programs from categorical and medically focused service organizations to reproductive health initiatives that embrace wide range of social and human services[2]. Teenage pregnancy has reached epidemic proportions in the United States with 1 million pregnancies and more than 500000 live births occurring each year among women under the age of 20[3]. Early pregnancy and unplanned childbirth may have far-reaching physical, psychological, and social consequences for adolescent girls and her offspring and are therefore public health issues of concern[4]. Reproductive health-seeking behavior, source of advice, and access to care issues studied among a sample of clinic-based homeless adolescent women in USA,
and it found that adolescent women are among the most vulnerable homeless population in the United States. Homeless youth rarely invited to participate in research aimed at improving their access to appropriate health care, also the culture in which they live and the personal experience of being homeless are often not addressed\(^5\).

A family planning program can be deemed successful if an individual is able to avoid having an unintended pregnancy (or is able to have a wanted child) within the stipulated period and if she experiences no severe reproductive health problems in the process\(^6\).

Because of the growing cultural and social sensitivity and controversy over reproductive health issues, we aimed at studying mother age at marriage in association with different socioeconomic characters in the family, and its effect as a risk factor on reproductive health of the mothers.

**Subjects & methods**

A cross-sectional study was conducted taking data obtained from 800 randomly selected healthy mothers, during their visits to primary health centers for different reasons, five primary health centers were selected randomly from different areas in Baghdad city, and about 100-150 mothers were included from each center making a total of 800 mothers, which done during the period from June-November 1994.

Information from the mothers obtained and filled by the researcher only, using well studied and preceded questionnaire form, which include information regarding different socioeconomic characters that might be affected by mothers’ age at marriage.

**Statistical analysis:**

Frequency tables used, statistical tests done using Chi-square. P values <0.05 were considered significant.

### Table 1: Distribution of the sample by mother’s age at marriage and occupation

<table>
<thead>
<tr>
<th>Variables</th>
<th>&lt; 20 years</th>
<th></th>
<th>&gt; 20 years</th>
<th></th>
<th>Total</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Frequency</td>
<td>Percent</td>
<td>Frequency</td>
<td>Percent</td>
<td>Frequency</td>
<td>Percent</td>
</tr>
<tr>
<td>Age at marriage</td>
<td>441</td>
<td>55.1</td>
<td>359</td>
<td>44.9</td>
<td>800</td>
<td>100</td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>House wife</td>
<td>431</td>
<td>53.8</td>
<td>311</td>
<td>38.9</td>
<td>742</td>
<td>92.7</td>
</tr>
<tr>
<td>Employed</td>
<td>10</td>
<td>1.3</td>
<td>48</td>
<td>6.0</td>
<td>58</td>
<td>7.3</td>
</tr>
</tbody>
</table>
Table 2: Distribution of different variables in association with mother age at marriage in the studied sample

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mother’s age at marriage</th>
<th>Significant</th>
<th>&lt; 20 years</th>
<th>&gt; 20 years</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Frequency</td>
<td>Percent</td>
<td>Frequency</td>
<td>Percent</td>
<td>Frequency</td>
</tr>
<tr>
<td>Mothers education</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Illiterate</td>
<td>52</td>
<td>6.5</td>
<td>41</td>
<td>5.1</td>
<td>93</td>
</tr>
<tr>
<td>Read &amp; write</td>
<td>106</td>
<td>13.3</td>
<td>44</td>
<td>5.5</td>
<td>150</td>
</tr>
<tr>
<td>Primary school</td>
<td>196</td>
<td>245</td>
<td>112</td>
<td>14.0</td>
<td>308</td>
</tr>
<tr>
<td>Intermediate school</td>
<td>67</td>
<td>8.4</td>
<td>45</td>
<td>5.6</td>
<td>112</td>
</tr>
<tr>
<td>Preparatory School</td>
<td>18</td>
<td>2.3</td>
<td>57</td>
<td>7.1</td>
<td>75</td>
</tr>
<tr>
<td>Diploma/University</td>
<td>2</td>
<td>0.2</td>
<td>60</td>
<td>7.5</td>
<td>62</td>
</tr>
<tr>
<td>Total</td>
<td>441</td>
<td>55.1</td>
<td>359</td>
<td>44.9</td>
<td>800</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Birth interval</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 -11.99 months</td>
<td>112</td>
<td>14.0</td>
<td>145</td>
<td>18.1</td>
<td>257</td>
</tr>
<tr>
<td>12-17.99 months</td>
<td>73</td>
<td>9.1</td>
<td>59</td>
<td>7.4</td>
<td>132</td>
</tr>
<tr>
<td>18-23.99 months</td>
<td>41</td>
<td>5.1</td>
<td>25</td>
<td>3.1</td>
<td>66</td>
</tr>
<tr>
<td>24-35.99 months</td>
<td>81</td>
<td>10.1</td>
<td>53</td>
<td>6.6</td>
<td>134</td>
</tr>
<tr>
<td>36+ months</td>
<td>134</td>
<td>16.8</td>
<td>77</td>
<td>9.7</td>
<td>211</td>
</tr>
<tr>
<td>Total</td>
<td>441</td>
<td>55.1</td>
<td>359</td>
<td>44.9</td>
<td>800</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Father age at marriage</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 20 years</td>
<td>69</td>
<td>8.6</td>
<td>11</td>
<td>1.4</td>
<td>80</td>
</tr>
<tr>
<td>&gt; 20 years</td>
<td>372</td>
<td>46.5</td>
<td>348</td>
<td>43.5</td>
<td>720</td>
</tr>
<tr>
<td>Total</td>
<td>441</td>
<td>55.1</td>
<td>359</td>
<td>44.9</td>
<td>800</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of pregnancies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-2</td>
<td>90</td>
<td>11.2</td>
<td>139</td>
<td>17.4</td>
<td>220</td>
</tr>
<tr>
<td>3-4</td>
<td>157</td>
<td>19.6</td>
<td>116</td>
<td>14.5</td>
<td>273</td>
</tr>
<tr>
<td>5 +</td>
<td>194</td>
<td>24.3</td>
<td>104</td>
<td>13.0</td>
<td>307</td>
</tr>
<tr>
<td>Total</td>
<td>441</td>
<td>55.1</td>
<td>359</td>
<td>44.9</td>
<td>800</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Under 5 years children in the family</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-2</td>
<td>147</td>
<td>18.4</td>
<td>188</td>
<td>23.5</td>
<td>335</td>
</tr>
<tr>
<td>3-4</td>
<td>180</td>
<td>22.5</td>
<td>117</td>
<td>14.6</td>
<td>297</td>
</tr>
<tr>
<td>5 +</td>
<td>114</td>
<td>14.2</td>
<td>54</td>
<td>6.8</td>
<td>168</td>
</tr>
<tr>
<td>Total</td>
<td>441</td>
<td>55.1</td>
<td>359</td>
<td>44.9</td>
<td>800</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crowding index</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2</td>
<td>57</td>
<td>7.1</td>
<td>88</td>
<td>11.1</td>
<td>145</td>
</tr>
<tr>
<td>2-5</td>
<td>310</td>
<td>38.8</td>
<td>220</td>
<td>27.4</td>
<td>530</td>
</tr>
<tr>
<td>&gt;5</td>
<td>74</td>
<td>9.2</td>
<td>51</td>
<td>6.4</td>
<td>125</td>
</tr>
<tr>
<td>Total</td>
<td>441</td>
<td>55.1</td>
<td>359</td>
<td>44.9</td>
<td>800</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Degree of consanguinity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First degree</td>
<td>227</td>
<td>28.4</td>
<td>127</td>
<td>15.9</td>
<td>354</td>
</tr>
<tr>
<td>Second degree</td>
<td>23</td>
<td>2.8</td>
<td>24</td>
<td>3.0</td>
<td>47</td>
</tr>
<tr>
<td>Third degree</td>
<td>53</td>
<td>6.6</td>
<td>25</td>
<td>3.1</td>
<td>78</td>
</tr>
<tr>
<td>No relation</td>
<td>138</td>
<td>17.3</td>
<td>183</td>
<td>22.9</td>
<td>321</td>
</tr>
<tr>
<td>Total</td>
<td>441</td>
<td>55.1</td>
<td>359</td>
<td>44.9</td>
<td>800</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Father occupation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Student</td>
<td>4</td>
<td>0.5</td>
<td>1</td>
<td>0.1</td>
<td>5</td>
</tr>
<tr>
<td>Employed/self employed</td>
<td>377</td>
<td>47.2</td>
<td>334</td>
<td>41.8</td>
<td>711</td>
</tr>
<tr>
<td>Others</td>
<td>60</td>
<td>7.4</td>
<td>24</td>
<td>3.0</td>
<td>84</td>
</tr>
<tr>
<td>Total</td>
<td>441</td>
<td>55.1</td>
<td>359</td>
<td>44.9</td>
<td>800</td>
</tr>
</tbody>
</table>
Table 2: Continued

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mother’s age at marriage</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; 20 years</td>
<td>&gt; 20 years</td>
</tr>
<tr>
<td></td>
<td>Frequency</td>
<td>Percent</td>
</tr>
<tr>
<td>Under 5 years death of children in the family</td>
<td>60.0</td>
<td>7.5</td>
</tr>
<tr>
<td>Yes</td>
<td>381</td>
<td>47.6</td>
</tr>
<tr>
<td>No</td>
<td>441</td>
<td>55.1</td>
</tr>
<tr>
<td>Total</td>
<td>841</td>
<td>100</td>
</tr>
<tr>
<td>Number of abortion</td>
<td>288</td>
<td>36.0</td>
</tr>
<tr>
<td>No abortion</td>
<td>122</td>
<td>15.2</td>
</tr>
<tr>
<td>1-3</td>
<td>31</td>
<td>3.9</td>
</tr>
<tr>
<td>4+</td>
<td>441</td>
<td>55.1</td>
</tr>
<tr>
<td>Type of family</td>
<td>325</td>
<td>40.6</td>
</tr>
<tr>
<td>Extended</td>
<td>116</td>
<td>14.5</td>
</tr>
<tr>
<td>Nuclear</td>
<td>441</td>
<td>55.1</td>
</tr>
<tr>
<td>Total</td>
<td>841</td>
<td>100</td>
</tr>
</tbody>
</table>

Results
Table 1 shows that more than half of mothers (55.1%) were married before the age of 20 years, and that 92.7% of mothers were housewives in the studied sample. There were significant relationship between mother’s age at marriage and maternal education, birth interval, father age at marriage, number of pregnancies, under 5 years children in the family, crowding index, degree of consanguinity ($\chi^2=201.1, 27.7, 29.74, 27.1, 31.8, 19.1, 27.5$ respectively $P < 0.001$), also there were significant relationship with father occupation, under 5 years death in the family ($\chi^2=11.54, 10.16$ respectively $P < 0.01$), while there were no significant relationship between mother age at marriage and number of abortion, and type of family($\chi^2=1.28$, $4.84$ respectively $P > 0.05$).

Discussion
This study was done on mothers from whom data were taken in the year 1994, since that time, many changes have occurred in our country which might have great effect on the Iraqi families especially the reproductive health of mothers, the results presented in this article might be useful for future similar studies to show changes in behavior and reproductive health of mothers during the last 10 years. The end of the twentieth century is an appropriate half way mark at which to evaluate the twentieth-century National family planning programs, and to assess what changes in them needed for twenty-first century[1].

A reproductive health approach recognizes that the foundation of women’s health are laid in childhood and adolescence, and are influenced by factors such as education, nutrition, social roles and social status, cultural practice, and the socioeconomic environment[7].

In the present sample, data taken from 800 women; of them, 441 (55.1%) women were married at the age less than 20 years, which means that more than half of women in the sample were adolescent at time of their marriage. According to Sedlecki 2001[8], the reproductive health of adolescent girls is endangered by their sexual behavior, poor acceptance of healthy life styles,
lack of responsibility in sexual relationship, and high prevalence rates of unintended pregnancy and sexually transmitted diseases. Another fact found that 742 (92.7%) of women were housewives.

The finding that there was a significant association between maternal age at marriage and mother education coincide with the finding of other studies. Heck K 2002 concluded that public health insurance coverage is critical to ensure adequate health care access and utilization among children of less educated mothers, regardless of family structure.

Significant association was found in this study between mother age at marriage and birth interval (P < 0.001), which coincide with other studies. Modin 2002 also came to important conclusion that childhood social condition that linked to birth order position seem to have had consequences for their individuals health and survival that extended over the whole life-course.

Under 5s death in the family was significantly associated with maternal age at marriage in this study (P < 0.01), this result coincide with other studies.

Number of abortion was not significantly associated with mother age at marriage (P > 0.05), this result does not coincide with the result obtained by Yassin 2000, and he found that the incidence of abortion was significantly associated with gravidity, consanguinity, and mother occupation, while recurrent abortion was associated with mothers’ age at marriage, consanguinity, and mother occupation.

Also in the present study significant association was found with father age at marriage, degree of consanguinity, number of pregnancies and children, crowding index (P <0.001), father occupation (P <0.01), while there was no significant association with the type of family (P > 0.05). Those results possibly reflect the effect of socioeconomic conditions on maternal age at marriage as a determinant of reproductive health of mothers in the family in the studied sample, in which a good proportion of the women were of low education, housewives, married at a young age, and usually lived with their relative and having a higher number of pregnancies and children; with possibly little knowledge about their reproductive health.

**Conclusion**

Maternal age at marriage is an important determinant of reproductive health of women when it studied with different socioeconomic variables. Special attention should be paid to adolescent sexual and reproductive health services, these should include contraceptive counseling in order to prevent pregnancy at a young age, also emphasis should be made on young people to have better access to health information schools, and the medical profession need to work together both to provide information and to help young females to develop confidence to use available information services.

**References**

THE BIOLOGICAL ROLE OF ZINC, COPPER AND MAGNESIUM DURING THE GROWTH OF EMBRYONIC CHICK LIMB BUDS

Yahya Y.Z. Farid¹ BSc PhD, Hayder J. Mobarak² MSc PhD, May F. Al-Habib³ MSc PhD

Abstract
Background: The limbs bud development is induced by the apical ectodermal ridge. The trace elements were found to have important role in biological growth of tissues such as tumor tissues.

Objectives: This study was done to reveal the possible biological role of trace elements as zinc, copper, and magnesium in the limb development induced by the apical ectodermal ridge.

Methods: Chick embryos of Hamburger and Hamilton stages 20-26 were used. Trace elements were measured in limb buds with and without apical ectodermal thickening.

Results and discussion: The decrease in zinc concentration found in limb buds tissues having no apical ridge suggested a relationship between this trace element and the inductive effect produced by the apical ectoderm for limb buds formation. The detectable concentration of copper only in buds having no apical ridge was correlated with the embryonic organization of the limb buds. The lower magnesium concentration in the limb buds was considered as a criterion for the metabolism accompanies the functioning apical ectoderm during the embryogenesis of the limb buds.

Conclusions: Trace elements may have a significant role in the embryonic process of budding.

Keywords: Limb buds, trace elements, zinc, copper, magnesium, development.

IRAQI J MED SCI, 2005; VOL. 4 (1): 63-66

Introduction
Embryonic development of the limb bud is induced by thickening of the ectoderm at the apex of the bud[1,2]. The limb primordium starts to develop at stage 16 of Hamburger and Hamilton (H&H) corresponding to about 50-60 hours of incubation. It appears as inconspicuous condensation of the mesoderm at the wing level of the chick embryo, followed by formation of the primordia of the leg bud. The toe plate becomes distinct at stage 24 H&H (at about 4.5⁵th day of incubation) prior to the digital plate that develops a stage later. Faint grooves appear in the toe and the digital plates during the 5⁵th day of development (stages 25 &26 H&H). The differentiation of the wing and leg buds exhibit many resemblances, both have apical ectodermal thickened at earlier embryonic periods[3,4]. The centers of codifications appear in the condensed mesenchyme of limb bud at about the end of sixth day of incubation[5].

The biochemical aspects of induction in embryonic development were not investigated meticulously. In this study, a trial has been carried out to reveal the possible biological role of trace elements as zinc, copper, and magnesium in early embryonic development of limb buds induced by the apical ectodermal ridge. Influence of trace elements in body metabolism and their physiological importance have motivated their accurate quantitative

¹Dept. Chemistry & Biochemistry ²Dept. Human Anatomy ³Dept. Human Anatomy-Section of Histology & Embryology, College of Medicine, Al-Nahrain University
Address correspondence to Prof. Yahya Y.Z. Farid.
Received 31st July 2004: Accepted 28th March 2005.
determination in biological tissues\textsuperscript{[6]}. In chick embryos growth of the limb bud and its parts (including the apical ectodermal ridge) were investigated during the period between the onset of its formation (Hamburger and Hamilton's stage 17) and the stage of nerve fiber in growth (H&H stage 22)\textsuperscript{[7]}.

**Materials & methods**

Fertilized chick eggs of Euribrild Lohman and Faobro type were incubated at 38°C in a humid environment. Embryos of Hamburger and Hamilton stages 20-26 were used corresponding to the incubation period of 3-5 days\textsuperscript{[3]}. Sixty embryos were used in this study. Forty five embryos of stages 20-22 having the apical ectodermal thickening were classified as group (A), fifteen embryos of stages 23-26 with no apical ectodermal thickening were classified as group (B). Limb buds of embryos group (A) were excised and collected in a container with 0.5 ml of normal saline in three sets each set containing the buds of fifteen embryos. Similar procedure was done for the limb buds of group (B) embryos, in each of the three sets of containers limb buds of five embryos were collected.

At first the container were weighed empty, then they were weighed with 0.5 normal saline and lastly we weighed the container and normal saline plus the tissue added. The final weight of the tissue was obtained by abstracting the weight of container plus normal saline from the total weight (Table 1).

Each set of the specimens of limb buds in each groups (group A and B) were mixed with 0.5 ml of normal saline, homogenized by homogenizer for few minutes, and centrifuged. Then after, a known amount of segmentate was treated as following:

**1. determination of Zinc and Copper:**

One hundred ug/ml stock solution was diluted with de-ionized water to give the following concentrations of the working standard (0.0, 0.4, 0.8, 1.2, 1.6, and 2 One hundred ug/ml) of Zinc and Copper. Samples were diluted 1:10 with 6% butanol as diluents. This method achieved 30% increase in sensitivity compared with the used of water only\textsuperscript{[8]}. This effect is due to a decrease in viscosity and difference in droplet formation. This technique is more widely used\textsuperscript{[9]}.

**2. determination of Magnesium:**

The samples used for determination of magnesium were diluted 1:50 with 1% lanthanum chloride solution to exclude the effect of segmentate phosphorous\textsuperscript{[10]}. Standard solution of 1000 ppm was diluted with de-ionized water. Working standards of Magnesium were (0, 5, 10, 15, 20, 25, and 30 One hundred ug/ml).

### Table 1: Method of weighing limb buds with AER

<table>
<thead>
<tr>
<th>Wt. for empty container (gm)</th>
<th>Wt. of the container with normal saline (gm)</th>
<th>Wt. of the container with normal saline + the tissue (gm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.8962</td>
<td>1.4182</td>
<td>1.4533</td>
</tr>
<tr>
<td>0.8913</td>
<td>1.4171</td>
<td>1.4529</td>
</tr>
<tr>
<td>0.8906</td>
<td>1.4167</td>
<td>1.4599</td>
</tr>
</tbody>
</table>

### Table 2: Method of weighing limb buds with AER

<table>
<thead>
<tr>
<th>Wt. for empty container (gm)</th>
<th>Wt. of the container with normal saline (gm)</th>
<th>Wt. of the container with normal saline + the tissue (gm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.7404</td>
<td>1.2586</td>
<td>1.2780</td>
</tr>
<tr>
<td>0.7511</td>
<td>1.2776</td>
<td>1.2974</td>
</tr>
<tr>
<td>0.7415</td>
<td>1.2685</td>
<td>1.2877</td>
</tr>
</tbody>
</table>

### Table 3: Mean concentrations of the trace elements

<table>
<thead>
<tr>
<th>Trace element</th>
<th>Group (A) mean concentration (mg/gm)</th>
<th>Group (B) mean concentration (mg/gm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnesium</td>
<td>0.002</td>
<td>0.037</td>
</tr>
<tr>
<td>Zinc</td>
<td>0.007</td>
<td>0.005</td>
</tr>
<tr>
<td>Copper</td>
<td>0</td>
<td>0.006</td>
</tr>
</tbody>
</table>
Results and Discussion

Embryonic stages included in-group (A) embryos have well developed ectodermal thickening at the apices of their limb buds\cite{7}. Embryos of group (B) have toe and digital plates in their limb buds\cite{4}. The mean values of the trace elements concentrations measured in this study are shown in table 1.

Embryonic tissue of the limb bud of group (B) shows higher magnesium and lower zinc concentration compared to that of group (A). Buds of group (B) only demonstrate detectable tissue concentration of copper.

It was concluded that many trace elements in tumor tissues exert direct or indirect action that accelerate growth of tumors\cite{11}. Trace elements measured in this study may have a role to accelerate the growth of the limb buds.

Experimental studies showed evidence for special function of the ectodermal apical ridge in limb morphogenesis indicating chemical messengers. Striking and distinctive characteristics of the mesoderm close to the apical ectodermal ridge were found providing possibilities for the understanding of the function of the apical ridge in limb morphogenesis\cite{12}.

The higher concentration of the zinc was linked with rapidly growing tumor tissues in many studies; such elevated concentration was suggested to be a sign of increased cellular activities\cite{13,14}. The higher concentration of zinc in limb bud tissues of group (A) having the apical ridge may signify the biological role of this element in motivation of limb development. The decrease of zinc concentration in limb buds of group (B) having no apical ridge may suggest a relationship between this trace element and the inductive effect produced by the apical ectoderm for limb bud formation. Lower zinc concentration of group (B) bud tissues may be a sign of a reduced inductive influence.

The detectable concentration of copper in limb buds of group (B) may indicate the beginning of embryonic organization. It was suggested that concentration of tissue copper is lowered during the metabolic changes of biological stress\cite{15}. Accordingly, the low and undetectable concentration of copper in buds of group (A) may be correlated with the metabolic stressful events accompany the induction of the apical ectoderm for the early rapid growth and budding of limbs. Extirpation studies of the apical ectodermal ridge reveal its essential task during the critical early stages of limb bud formation; no limb was formed if the apical ectoderm is removed\cite{16}.

The above interpretation of the copper concentration in limb tissue may be applied to explain the higher magnesium concentration measured in limb buds of group (B) compared to that of group (A). Lower magnesium concentration in buds of group (A) may be a criterion for the metabolism accompanies the functioning apical ectoderm during the embryogenesis of the limb buds.

Budding is an embryological phenomenon observed in many embryonic regions. The concentration of trace elements should be more thoroughly investigated to establish a judgment for the significance of the biological role of trace elements in this embryological process.

References


MALE INFERTILITY AND PHYSIOLOGICAL ROLE OF ZINC

Ali T. Al-Baldawi¹ MBChB FICMS (Chemical Pathology), Nazar A. Naji² BSc PhD, Aqeel A.A. Al-Ani² BSc MSc

Abstract

Background: Male infertility is the inability to conceive a baby in the absence of female causes. Most causes reflect an abnormal sperm count or quality. Zinc is a component of semen and plays an important role in the process of reproduction and sexual maturation.

Objectives: To assess the relationship between concentration of zinc in serum, seminal plasma and semen quality among infertile and fertile men to clarify the possible impact of zinc in male reproductive system.

Methods: Fifty-eight male (infertile group) partners who were undergoing investigation for infertility and thirty-seven men (fertile group) whose wife were pregnant and have normal sexual life studied as a control group. Seminal fluid analysis, reproductive hormones (luteinizing hormone, follicular stimulating hormone and testosterone) were analyzed by using radioimmunoassay method (RIA) while serum and seminal plasma zinc concentration were determined by using colorimetric methods.

Results: All semen properties (count, motility and morphology) for the infertile group were lower than for the fertile group. No significant differences were found in the levels of L.H. and F.S.H. between the two groups while testosterone levels were significantly lower in the infertile men group than in the fertile group (p<0.005).

It was also found that the mean level of serum and seminal plasma zinc concentration were significantly lower in the infertile group compared to the fertile group (p<0.0001). No correlation was found between the concentrations of zinc in serum and seminal plasma in both groups. A lack of correlation was also found between zinc concentrations in serum and seminal plasma with semen properties.

Conclusion: The study revealed the importance of zinc in fertility through its direct and its indirect effects on spermatogenesis.

Keywords: Male infertility, Zinc, semen, spermatogenesis


Introduction

Many recent studies have indicated an increasing prevalence of various abnormalities of the reproductive system in human males[1]. Male infertility is as the inability to conceive a baby after 1 year of unprotected sex in the absence of female causes. Most causes of male infertility reflect an abnormal sperm count or quality. Although it only takes one sperm to fertilize an egg, in an average ejaculate a man will eject nearly 200 million sperm. However, because of the natural barriers in the female reproductive tract only about 40 sperm will ever reach the vicinity of an egg.

There is a strong correlation between the number of sperm in an ejaculate and fertility. In about 90% of the cases of a low sperm count, the reason is deficient sperm production. Unfortunately, in about 90% of cases, the cause for the decreased sperm formation cannot be identified. Other causes of male infertility may include ductal obstruction, ejaculatory dysfunctions, and infections or disorders of the accessory glands[2].

Prostate gland is the largest accessory gland of the male reproductive tract and there is a good deal of research being conducted on the prostate. Yet it

¹Dept. Pathology-Section of Forensic Medicine, College of Medicine ²Dept. Chemistry, College of Science, Al-Nahrain University
Address correspondence to Dr. Ali T. Al-Baldawi
Received 14th April 2004: Accepted 29th November 2004
Male Infertility … Al-Baldawi et al

remains one of the least understood structures in the body. One area of study concentrates on the major function of the gland, the production and the secretion of minerals that play an important role in prostate and the reproductive system functions.

Zinc is a component of semen and it is thought that at least 1 mg of zinc is excreted by an ejaculum. Zinc plays an important role in the processes of fertility, reproduction and sexual maturation[^3]. At a biochemical level, zinc's primary role as a component of zinc metalloenzymes, many enzymes of the cell nucleus involved with genetic information transfer and cellular replication are metalloenzymes of zinc. Zinc also participates in RNA metabolism, prostatic fluid and ocular tissues contain the highest levels of zinc in the body[^4].

The present study aimed at clarification of the interrelationship of serum and semen zinc levels, in both men with a history of infertility and men with no history of infertility. Also, investigate the possible role of seminal zinc in the regulation of human spermatozoa functions.

**Subjects & Methods**

**Subject selection:**

Iraqi men in the age range of 20 to 50 years with no apparent chronic or acute disease were selected for the study, 37 men of known fertility and 58 infertile men were studied.

The infertile men were unable to be fathers of children for at least 1 year; their wives were considered fertile based on extensive gynecologic evaluations. At the first interview for the infertile men, a complete history was obtained, especially with respect to any history of sexual dysfunction. Physical examination was performed to exclude patients with chromosomal abnormalities. None of the subjects were on drug treatment or on especial diet and none of the subjects used vitamin supplements.

**Procedures:**

1. **Semen collection:** semen analysis were performed on three separate specimens for each subject, samples were collected after 2-3 days of sexual abstinence by masturbation into polyethylene containers.

2. **Serum collection:** Blood was drawn into sterile, disposable plastic syringes. After allowing 30 minutes, for blood clotting, the serum was separated from blood cells by centrifugation at 900 g for 5 minutes at room temperature. The serum was decanted and stored in a metal-free polypropylene tube at -20°C until required.

3. **Seminal plasma collection:** The semen was put into plain tube and after one hour the seminal plasma was separated by centrifugation at 3000 rpm at room temperature for 10 minutes. The seminal plasma was decanted and stored in a metal-free polypropylene tube at -20 °C until required.

4. **Hormonal Assay:** Basic endocrine measurements includes serum LH and FSH will testosterone by radioimmunoassay method (RIA)[^5] from (CIS Bio International, groups ORIS, B.P. 32-91192. GIF-SUR-Yvette Cedex-France).

5. **Zinc analysis:** Zinc analysis was done by Jenway 6100 spectrophotometer (model 6100 serial No. 3000; frequency 50/60 Hz, UK. England) according to the methods described by Shibata, S., who said pyridylazo compounds of phenol derivatives are sensitive chromogenic reagents for the analysis of zinc and many other metals[^6].

An aliquot of 50μL of serum was mixed with 1ml of the reagent and 10μL of seminal plasma was mixed with 1ml of the same reagent. All tubes were mixed and incubated for 10min at 25°C. Then measured against blank at 560nm using (Cat. No. 0033, Giesse Diagnostics, C.F. 03084750581, P. IVAO
Male Infertility …Al-Baldawi et al


Statistical Analysis
The results are presented as (mean ± standard deviation) for better comparison with relevant data in literature.
The results within the groups were also presented, as ranges, and the significance of the differences between the groups were calculated using student’s t-test two-tailed.

Table 1: Parameters of semen quality, reproductive hormones, and Zinc concentrations in fertile and infertile men groups

<table>
<thead>
<tr>
<th>Item</th>
<th>Fertile men group (n=37)</th>
<th>Infertile men group (n=58)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean±SD</td>
<td>Range</td>
<td>Mean±SD</td>
</tr>
<tr>
<td>Count (60-150x10^6/ml)</td>
<td>96.6±28.3</td>
<td>57-154</td>
<td>31.28±30.0</td>
</tr>
<tr>
<td>Motility (&gt;60%)</td>
<td>75.1±11.7</td>
<td>55-95</td>
<td>15.0±12.3</td>
</tr>
<tr>
<td>Morphology (&gt;70%)</td>
<td>84.3±5.5</td>
<td>70-90</td>
<td>56.9±31.8</td>
</tr>
<tr>
<td>LH (1-5mlu/ml)</td>
<td>3.5±1.0</td>
<td>1.5-5.0</td>
<td>4.7±3.9</td>
</tr>
<tr>
<td>FSH (1-9mlu/ml)</td>
<td>6.0±1.7</td>
<td>2.8-9.8</td>
<td>6.4±6.0</td>
</tr>
<tr>
<td>Testosterone (8.2-34.6nmol/L)</td>
<td>22.5±4.5</td>
<td>15.8-33.0</td>
<td>18.0±8.2</td>
</tr>
<tr>
<td>Serum Zn (70-120µg/dl)</td>
<td>118.7±16.8</td>
<td>90.6-162</td>
<td>97.5±26.9</td>
</tr>
<tr>
<td>Seminal plasma Zn (1.2-3.9nmol/L)</td>
<td>3.1±0.4</td>
<td>2.5-3.8</td>
<td>2.1±0.6</td>
</tr>
</tbody>
</table>

The parameters of semen quality were significantly lower in the infertile men group than in the fertile men group (P<0.0001). No significant differences were found in the mean concentrations of LH and FSH in serum, when fertile men group was compared with infertile men group, but the mean serum testosterone concentration was significantly lower in the infertile men group than in the fertile men group (P<0.005).
The results revealed that serum zinc levels in infertile men group were lower than in the fertile men group (P<0.0001). In addition, seminal plasma zinc levels were lower in the infertile men group than in the fertile men group (P<0.0001).

From table 2, there was no significant correlation between serum zinc and the parameters of semen quality in both groups. Moreover, no significant correlation between semen zinc and the parameters of semen quality in both groups.

Table 2: Values of simple correlation coefficient (r) between Zinc concentration and parameters of semen quality for both groups

<table>
<thead>
<tr>
<th>Item</th>
<th>Serum Zn</th>
<th>Seminal Plasma Zn</th>
<th>Serum Zn</th>
<th>Seminal Plasma Zn</th>
</tr>
</thead>
<tbody>
<tr>
<td>Count</td>
<td>-0.096</td>
<td>0.056</td>
<td>-0.006</td>
<td>-0.041</td>
</tr>
<tr>
<td>Motility</td>
<td>-0.285</td>
<td>0.12</td>
<td>-0.025</td>
<td>-0.187</td>
</tr>
<tr>
<td>Morphology</td>
<td>-0.071</td>
<td>-0.368</td>
<td>-0.179</td>
<td>0.099</td>
</tr>
</tbody>
</table>
No correlation was found between semen zinc and serum zinc level in the fertile men group \((r=0.075)\) nor in the infertile men group \((r=0.120)\).

**Discussion**

Our data are in agreement with those of Bonde et al.\(^7\), who reported that not sperm concentration but sperm quality determines fertilizing capacity of spermatozoa. Although, the most cases of male infertility are nonendocrine in origin. However, routine evaluation of hormonal parameter is not warranted unless sperm density is extremely low or there is clinical suspicion of an endocrinopathy. A scrotal varicocele is the most common causative finding in infertile men\(^8\). To explain the abnormalities in spermatogenesis with varicocele, the most point have been proposed was the abnormal blood flow can interfere with testosterone production, which in turn can interfere with sperm production and this in agreement with our results that about 25% of infertile men had varicocele.

We did not find any difference in the our data and in those previously published in the literature for that the serum zinc and semen zinc levels were significantly lower in infertile patients than fertile males\(^9\), in contrast to other reports, that unable to find a significant difference in serum and semen zinc levels between fertile and infertile men\(^{10,11}\).

The lack of correlation between zinc concentration and semen quality found in our study suggests that biochemical complexity of seminal fluid attempts to perform such simple correlations between seminal plasma component and andrological parameters are likely to produce inconsistent results. These effects include no significant correlation between the total amount of zinc per ejaculate and sperm quality\(^{12}\) with no statistically significant correlation between zinc concentration and the motile sperm concentration\(^{13}\).

However, our results are in contrast to other studies that showed zinc-related decrease in human semen quality\(^{14,15}\). Most previous results of colorimetric methods and the present method found that the results obtained using the proposed method were not statistically different from those obtained by atomic absorption spectrophotometry\(^{16,17}\).

The high level of zinc found in semen is due primarily to the secretions of the prostate gland and reflects prostatic stores. Serum zinc may be a reasonable indicator of zinc status. The lack of correlation between serum zinc and semen zinc found in our study suggests that mild zinc deficiency may lower serum zinc while the larger prostate zinc stores remain unaffected. However, we obtained 25% had varicocele, which are enlargement of the internal spermatic veins that drain the testes.

The significant decrease of the zinc in seminal plasma of varicocele men were significantly lower than in the normal subjects .This decrease indicated an impairment of the prostatic function or secretion due to decreases the availability of oxygen and nutrient required for sperm live.

Citrate is part of the circular chain of cellular respiration, known as the Krebs’s cycle. The Krebs’s cycle is the process in which a sequence of enzymatic reactions involving the metabolism of carbon chains of sugars, fatty acids, and amino acids to yield carbon dioxide, water, and high-energy phosphate bonds. The Krebs’s cycle provides a major source of adenosine triphosphate energy and produce molecules that are starting point for a number of vital metabolic pathways for the cell, citrate that been chelated with zinc and their evidence that zinc is...
required for oxygen consumption by sperm. Varicocele decreases the concentration of zinc and decreases the availability of oxygen for live sperm. Further studies to elucidate the significance of zinc and other factors presents in seminal plasma in different types of causes of male infertility for the functional properties of human spermatozoa appear to be of importance since such studies may give hints to new ways of regulating male fertility.

References
A RANDOMIZED PROSPECTIVE STUDY COMPARING THE EFFECTIVENESS OF MITOMYCIN C AND MITOMYCIN/S2 COMPLEX SEQUENTIAL INTRAVESICAL THERAPY FOR SUPERFICIAL BLADDER CANCER

Ahmad A. Al-Azawi1 FICMS, Abdul-Wahab R. Hamad2 BSc MSc PhD, Mahmood H. Hammash3 BSc, PhD

Abstract
Objective: Comparison of two protocols regarding efficacy and toxicity of intravesical mitomycin C versus mitomycin C and S2 complex sequential therapy for superficial transitional carcinoma of urinary bladder.

Methods: A prospective, randomized parallel two lines of treatment groups. Seventy-three patients were evaluated after transurethral resection of superficial bladder cancer with median follow-up of 26 months. In group A, 37 patients received intravesical mitomycin C 30mg on day1 weekly for 6 week and monthly for 12 month, while group B (36 patient) received in addition to mitomycin C, intravesical S2 complex 3ml on day 2. Statistical analysis performed by Kaplan-Meier methods.

Result: After follow-up of 26 months, 46% of patient given mitomycin C were disease free compared to 70% for that of group B patient who received mitomycin C and S2 complex, with no significant difference in incidence of the adverse effects.

Conclusion: The results show that intensive intravesical instillation of sequential mitomycin C and S2 complex; were highly effective in eradication and/or prophylaxis of superficial transitional bladder cancer.

Key word: Transurethral resection; bacillus Calmitte-Guerin; complete response; mitomycin C, carcinoma in situ


Introduction
Bladder cancer is the third most prevalent malignant disease among male patients and the tenth among female patients in the United States[1]. Superficial transitional type constitutes 75-80 percent of bladder cancer and 30-60% recur within 6-18 month after transurethral resection[2]. Transurethral resection can effectively control the primary tumor, confirm the superficial nature of the disease, provide cytological and histological tumor, characteristics of prognostic significance; and allows for assessment of extent of mucosal involvement by tumor[1,2]. Tumor recurrence and progression related to stage, grade, number, and size, duration of the disease, positive or negative cytology and aneuploidy[1,3].

There is increasing interest in intravesical instillation of cytotoxic agent or immunotherapy bacillus Calmitte-Guerin (BCG) and become common practice after TUR to cure or prevent recurrence of superficial transitional cell bladder cancer (cis; Ta and Tb) in more than 45% of cases[3-5]. Intravesical trials divided into 2 major categories
1. Therapeutic, designed to treat established disease and
2. Prophylactic/adjuvant, designed to prevent recurrence in patients at high risk for tumor recurrence and progression[1,6]. The most effective intravesical therapy is mitomycin C (can achieve complete
A randomized prospective study…. Al-Azawi et al

response in 48%) and BCG (60%) after the basic therapy with TUR[5,8]. After TUR, those patients with: transitional cell stage T1 papillary tumor, multifical stage Ta (grade 1-III), multifocal and/or symptomatic carcinoma in situ (CIS) and persistent positive urine cytology, are require adjuvant intravesical therapy[1,8].

In the present paper, a clinical study of efficacy of therapeutic of cytotoxic and immunotherapy in patient with superficial transitional bladder cancer after TUR and were analyzed for incidence of recurrence, time-free progression according to Japanese Urological Association[7]. We tried in this study to evaluate, investigate the effectiveness and the adverse effects of MMC in comparison with the immunotherpeutic agent S2 complex in intravesical local therapy of superficial bladder cancer. MMC selected in our study because of its proved efficacy[8]. S2 complex (has been developed at Medical Research Center at the Iraqi Medical College), it is a low molecular weight synthetic organs-metalic complex[9]. The high effectiveness of BCG as immunotherapeutic agent encouraged us to use S2 complex on it base because S2 complex is a potent immunostimulator and seem to have antitumor activity[9-11].

**Patients and methods**

Our study included 75 patients with grade 1-III superficial transitional cell bladder (cis, Ta-T1) who had been registered, treated (and then followed-up between 2001-2003 in Al-Kadhymia Teaching Hospital with intravesical installation mitomycin C and S2 complex, 2 weeks post TUR. We randomized the patients in two groups: Group A (38 patients) received therapeutic MMC installation (30mg/30ml/1hour) on day 1 weekly for 6 week & then prophylactic regimen, monthly for 12 month. Group B (37 patient) had been receiving additional S2 complex (3ml, diluted in 30ml normal saline/1hour) on day 2 after each of the eighteen MMC installations. The response assessed after induction therapy (6 weeks) and after maintenance doses (12 months), complete response defined as no residual carcinoma cystoscopically and negative urine cytological finding, follow-up ranged from 16 to 26 months with median of 18 months.

Statistical analysis was done for recurrence-free rate (disease free-rate), performed by Kaplan-Meier method for both disease group and were tested with the log rank test.

**Results**

Patient and tumor characteristics:

Seventy-five patients were entered the study between June 2001 to November 2003 with patient and tumor characteristics were equally distributed between 2 arms. Two patients had been lost during the study; one died because of myocardial infarction and the other refused to continue after the second dose. Table 1 Shows 33 patients had grad-II tumor; male to female ratio 7.1:1 and the age range 21-75 years.
Table 1: Clinicopathological profile of 73 patients with superficial bladder cancer

<table>
<thead>
<tr>
<th>Criteria's of the study group</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>64</td>
<td>87.6</td>
</tr>
<tr>
<td>Women</td>
<td>9</td>
<td>12.4</td>
</tr>
<tr>
<td>Age ≤ 30</td>
<td>12</td>
<td>16</td>
</tr>
<tr>
<td>≥ 50</td>
<td>54</td>
<td>74</td>
</tr>
<tr>
<td>Stage TA</td>
<td>51</td>
<td>70</td>
</tr>
<tr>
<td>T1</td>
<td>16</td>
<td>22</td>
</tr>
<tr>
<td>cis</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Grade GI</td>
<td>33</td>
<td>45</td>
</tr>
<tr>
<td>GII</td>
<td>27</td>
<td>37</td>
</tr>
<tr>
<td>GIII</td>
<td>13</td>
<td>18</td>
</tr>
<tr>
<td>Multicentricity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Solitary</td>
<td>49</td>
<td>67</td>
</tr>
<tr>
<td>Multiple</td>
<td>15</td>
<td>21</td>
</tr>
<tr>
<td>Unknown</td>
<td>9</td>
<td>12</td>
</tr>
</tbody>
</table>

The efficacy of treatment and the time to first recurrence recorded in both groups showed more effective treatment system in the group B who treated with MMC and $S_2$ complex especially for those with TA and grade-III, (Table 2 and figure 2).

Table 2: Overall results of the study, according to stage and grade of the cancer

<table>
<thead>
<tr>
<th>Result</th>
<th>MMC Group</th>
<th>MMC+S₂ Complex group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrence of tumor</td>
<td>No (%)</td>
<td>No (%)</td>
</tr>
<tr>
<td>Stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cis</td>
<td>1(3)</td>
<td>0(3)</td>
</tr>
<tr>
<td>T1</td>
<td>4(10)</td>
<td>3(6)</td>
</tr>
<tr>
<td>TA</td>
<td>15(24)</td>
<td>8(27)</td>
</tr>
<tr>
<td>Grade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GI</td>
<td>8(20)</td>
<td>2(13)</td>
</tr>
<tr>
<td>GII</td>
<td>7(11)</td>
<td>6(16)</td>
</tr>
<tr>
<td>GIII</td>
<td>5(6)</td>
<td>3(7)</td>
</tr>
</tbody>
</table>

Figure 1: Kaplan Meier curves for time recurrence of patient with papillary tumor cis, pTa, pT1; grade 1 to 3 transitional cell cancer free of tumor after TUR% and adjuvant MMC group and MMC-S₂ group.
Figure 2 shows higher percent of patients in group A were remain in remission state after 26 months of follow-up, two patient end with cystectomy and pulmonary metastases in group A while another 3 patients end with total cystectomy and with radiotherapy in group B.

![Graph showing percentage of patients in remission at the end of the study.](image)

**Figure 2: Percentage of patient in remission at the end of the study.**

The number and severity of adverse effects were recorded during instillation period are listed in table 3. Mild drug induced cystitis equally reported in both groups.

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Number</td>
</tr>
<tr>
<td>Bladder irritation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>Moderate</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Severe</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Microscopical hematoria</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Systemic allergy (mild)</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

**Table 3: Toxicity**

**Discussion**

Administration of adjuvant intravesical chemotherapy after TUR of superficial transitional cell cancer of the urinary bladder (cis: Ta: T1) has become a common practice and confirmed to be effective in reduction of the short and intermediate term incidence of recurrence[12,13]. Intravesical MMC and doxorubicin sequential therapy seemed to be more effective in eradicating carcinoma in situ than single therapy with MMC or doxorubicin and equally affective as BCG[8,15,17]. Topical BCG therapy is now widely accepted as a choice of treatment on base of immunomodulating effect, although systemic adverse and even fatal reaction may occur[7,14,15].

According to those data about the effectiveness of the combination therapy and immunotherapy: The evaluation of sequential MMC and S₂ complex therapy, confirm clearly the efficacy and safety of this regimen in induction (eradication) and maintenance ( prophylactic) treatment of transitional cell carcinoma of bladder after TUR, than if those of MMC or BCG is used singly[6,16,17].

Seventy-six clinical studies reviewed, reporting intravesical therapy within last 20 years; their results rate of the net
benefit: thioptepa (8-27%), doxorubicin (12-23%), MMC (13-35%); MMC and doxorubicin sequential therapy (60-65%)\(^1\,^2\,^4\), and in comparison to the overall response of MMC and S\(_2\) sequential therapy (70%) and can reduce significantly the number of tumor recurrence within 2 years\(^1\,^13\).

In addition, S\(_2\) complex is economically available with minimal local and systemic side effect if compared to that of BCG and the majority of patient can tolerate this treatment schedule\(^7\).

Future efforts have to teach us how to select patient for instillation therapy as surprisingly, when patients were separated according to the presence or absence of ABH antigen on the tumor, the more aggressive ABH-negative tumor were found to recur less frequently than ABH positive tumor\(^14\,^15\). Many questions remain unanswered in relation to scheme of instillation, when the ideal time to start treatment? What is the optimal duration of treatment? When is the ideal interval between two instillations? Those entire questions must be included in longer duration study to evaluate another schedule and real effect of the promising agent S\(_2\) complex\(^6\).

References

Abstract

Background: Tuberculosis of udder is not a rare disease in animals especially cows but it is rare in human female breast and extremely rare in male breast.

Objectives: Looking for involvement of women breast with tuberculosis.

Methods: From the 1st of July 1992 to the 1st of July 2002, 15 female patients, all in reproductive age were studied for their breast problems under the suspicion of tuberculosis, 14 cases appeared to be tuberculosis diagnosed by FNA cytology and biopsy and treated by anti TB drugs therapeutic trial.

Results: Treatment with anti-tuberculoc drugs cured 14 cases.

Conclusion: The tuberculosis of human breast is not very rare disease and should keep in mind when breast infection, ulcers, sinuses and inflammatory masses are not responding to traditional drugs. Tuberculosis of the breast responds very well to anti-tuberculoc drugs and cure completely.

Keywords: Breast, tuberculosis, anti-tuberculoc drugs

INTRODUCTION

Tuberculosis (TB) is an old and nasty disease, it was common all over the world but it starts to disappear after the discovery of the anti-tuberculoc drugs, yet, in the last two decades a flare up in the disease all over the world is noted and reported[1].

Tuberculosis can affect creatures other than human being especially the cows and mainly it affects its udder, the milk production apparatus which cause infection of the milk by TB bacilli which can infect the human if it is consumed without proper sterilization[2,3].

Tuberculosis can affect any system in the body, and many centers reported that human female breast can be involved by the disease usually unilateral and rarely bilateral and there are reported cases in India of male breast TB[4].

Hippocrates named tuberculous lesions “phthis” from the Greek word meaning, “to decay”. Sir Astley Cooper was the first one who described a case of breast tuberculosis in 1829 and called it “scrofulous swelling of the bosom”[5]. In 1944, Klossner reported 50 cases of tuberculosis of the breast in women, out of 75,000 with lung involvement. Later on, in 1952, McKeown an Wilkinson described two forms of breast tuberculosis, the primary in which breast infection is the only manifestation of the disease and the secondary one in which the patient had already tuberculosis diagnosed elsewhere[6,7].

PATIENTS & METHODS

Fifteen female patients of ages 21 years-46 years, all were married and had breast-fed their children collected along 10 years from July 1, 1992 to July 1, 2002.

The right breast affected in six cases, both breasts affected in one case, and the left breast affected in eight cases including the single case of granulomatus mastitis.
The patients presented as slowly developing breast problem, pain, swelling, and tenderness. In four patients, (26.6%) there was a nipple discharge, pus or serosanguinous in nature. 6 patients (40 %) had local redness and indurations, 3 patients (20%) had a mildly tender mass, freely mobile and not very well marginated. 2 patients (13.3%) had diffuse indurations of a localized sector of the breast.

Ten patients (66.6 %) underwent surgical drainage to their breast lesions but the drainage opening did not heal and changed to chronic ulcer with dark, undermined edges with thin watery discharge. These 10 patients subjected to fine needle aspiration (FNA) cytology, which revealed some acute and mainly chronic inflammatory cells with giant cells of Langhans type.

The rest, five cases underwent open surgical biopsy for their breast lesions, which showed a picture of chronic inflammatory changes with giant Langhans cell also. One case (6.6%) the biopsy showed a picture of granulomatous mastitis.

Nine patients had small palpable mobile lymph nodes in the same side axilla, but no one had a chest or lung problem. Because of no response of these cases to treatment by traditional antibiotics and the lesions, persist for more than 1-2 months, Anti TB drugs therapeutic trial given with a very good response within 2-3 weeks in 14 cases.

The anti TB drugs used are INH tablets 100 mg three times daily, ethambutol tablets 500mg three times daily, refampicin capsules 300mg twice per day for two months then stopping ethambutol and continue on the others for 6-9 months.

**Results**

The single case, which did not respond to anti TB drugs, was the case of granulomatus mastitis, which responded moderately to steroids. All tuberculous patients have cured and the affected breasts became normal in shape, size, texture and consistency. All the ten patients who had ulceration of the skin of the breast developed a small scar with a faint white yellowish discoloration at the site of the ulcer after its healing.

One patient developed cholestatic jaundice 2 weeks after starting refampicin capsules due to hepatic toxicity. Thus, the treatment stopped for 3 weeks until the patients condition improved. Again, anti TB regimen started with substituting refampicin by streptomycin injections one gm. i.m daily for 2 months. INH and ethambutol tablets then stopped for other 4 months. One year after, the patient developed swelling and induration with pain at the same site of the previous lesion. FNA cytology revealed epithelioid cells with Langhans giant cells. So the case regarded as recurrence and new course of anti TB regime started, INH, ethambutol, streptomycin, and pyrazinamid for 2 months. The streptomycin stopped and we continued with the other three drugs for other 4 months.

Including the recurrent case, eight patients became pregnant and breast-fed their babies after delivery with no problems.

The treatment and cure of the 14 patients whose diagnosis depends on the clinical picture, FNA cytology and biopsy suggestion because it is very difficult to reveal the TB bacilli in the examined samples and cultures, and it is the same policy followed in other countries, India and North Korea.

**Discussion**

Today, TB remains as a major public health problem in the world. According to the WHO, 10 million new cases of active TB occur each year worldwide[8]. HIV infection, chronic diseases, malignancy, transplantation and other
immunosuppressive conditions, aging, and resistant strains lead to increase of TB patients. In these groups, tuberculosis may present atypically and sometimes with predominant extra-pulmonary manifestations that result in delays in diagnosis and treatment. Tuberculosis of the breast is a rare disease. It is uncommon even in countries where the incidence of pulmonary and extra-pulmonary tuberculosis is high. Primary form is an infection of the breast through abrasions or through the openings of ducts in the nipple. Secondary form is the result of reverse lymph flow in the axillary lymph nodes or it may be due to direct spread of the infection from intra-thoracic foci. Routes of infection include hematogenous spread, lymphatic spread from intra-thoracic foci or from intra-abdominal foci, and by direct extension from adjacent tissues or via abrasions of the skin. According to clinical, radiological and pathological appearance of the disease, there are three types of breast tuberculosis:

1. Nodular tuberculosis characterized by a well circumscribed, slowly growing, painless mass. Often the mass, getting larger, infiltrates the skin. At this point, the tumor becomes painful, causing ulceration, and discharge from one or more sinus tracts. This course makes differentiation from carcinoma very difficult.

2. Diffuse type or disseminated tuberculous mastitis characterized by multiple foci, which may lead to sinus formation. The overlying skin thickened and painful ulcers may develop. Axillary lymph nodes frequently infiltrated.

3. Sclerosing type, were excessive fibrosis is the dominant feature. It is slow growing, and suppuration is rare. Clinically there is a hard, painless lump with nipple retraction. Clinical examination usually fails to differentiate carcinoma from tuberculosis. FNA cytology has proved to be very useful for diagnosis of breast tuberculosis and reflects the histopathological lesion very accurately. Treatment with standard anti tuberculous drugs has proved to be very successful and avoids unnecessary mutilating surgery.

**Conclusion**

The TB of the breast in human female is not a very rare disease neither in our country nor in other countries so the disease should be kept under suspicion in treating breast lesions. The response to treatment with standard anti tuberculous drugs is very good and the cure rate is high. Because it is difficult to reveal the TB bacilli in the specimens from the lesion, the policy of anti TB drugs therapeutic trial should be followed in the treatment.

**References**

Breast T.B. in Samarra City …. Al-Khateeb H.M.


EOSINOPHIL COUNT AND RELATION TO CHILDHOOD ASTHMA

Hussam M. Al-Alwany¹ DCH CABP, Falih Salim² FIBMS, Shatha H. Ali¹ CABP

Abstract
Background: Asthma is a diffuse obstructive lung disease with hyperreactivity of the airways to variety of stimuli. The prevalence and severity of the disease are steadily increasing. In addition to broncho-constriction and viscid secretions, inflammation is an important pathophysiological factor, eosinophil play important role in this inflammation. Eosinophil peripheral blood count in Asthmatic patient is our concern in this study.

Objective: Study the relationship of eosinophil peripheral blood count and Asthma.

Methods: A total number of 55 asthmatic children subjected to a prospective study regarding the severity of asthma, which assessed by clinical examination and spirometry and for each patient a sample of blood, were collected and eosinophil count was calculated.

Results: 35 of a total 55 asthmatic patient found to have moderate to sever asthma of this category 82.8% (29 patients) were having high eosinophil count >400 / mm³ while 17.2% ( 6 patient) of less eosinophil peripheral count < 400 / mm³. The other 20 patients were mild to moderate severity, of these 80% (16 patients) were of low eosinophil count < 400 and 20% (four patients were of high eosinophil count).

Conclusion: There is an increase in eosinophil peripheral blood count in Asthmatics and the more the severe the attack, the more the eosinophil count.

Key words: Asthma, Eosinophil, Severity

IRAQI J MED SCI, 2005; VOL. 4 (1): 81-83

Introduction
Asthma is a leading cause of chronic illness in childhood and responsible for a significant proportion of school days lost because of chronic illness. Asthma can lead to severe psychosocial disturbance in the family¹. Asthma is a condition characterized by variation of intrathoracic airway obstruction, which occur spontaneously, or because of treatment. Asthma in fact is an umbrella term rather like hypertension both are clinically important syndromes brought about by several different mechanisms. The prevalence and severity are steadily increasing in most industrialized nations, presumably as a result of environment change². Asthma defined as a diffuse obstructive lung disease with hyperreactivity of the airways to a variety of stimuli and a high degree of reversibility either of the obstructive process, which may occur spontaneously, or because of treatment. In addition to broncho-constriction and viscid secretions, inflammation is an important pathophysiological factor; it involves eosinophil monocytes and other immune mediators³. The eosinophil is a minor species of granulocyte comprising 1-4% of total peripheral blood WBC (normal range 0.04-0.44 x 10³/L). The eosinophil is the densest leukocyte in the peripheral blood but can also exist as hypodense form common in the blood of patients with asthma or dermatitis. Eosinophils have less phagocytic and bactericidal activity than neutrophils but have an important role in mediating hypersensitivity reactions, bronchial asthma and skin inflammation⁴.

¹ Dept. Pediatrics ² Dept. Pathology, College of Medicine, Al-Nahrain University
Address correspondence to Dr. Hussam M. Al-Alwany.
Received 25th September 2004: Accepted 6th December 2004.
Eosinophil, predominantly provide protection against parasites aided by T-Helper lymphocyte\(^4\). The intention of the study is to find the relation between eosinophil count in the peripheral blood of patients with asthma and severity of their disease.

**Patients and Methods**
A total number of 55 asthmatic children subjected to a prospective study regarding the severity of their asthma, which assessed by clinical criteria (mild, moderate and severe) and supported by spirometry measurement of FEV1 taken by portable spirometer in out patient clinic.

From each patient venous blood collected into dik-EDTA tube, and 20-millimeter blood mixed with 400 mm of glacial acetic acid, improved Neubaur chamber used to calculate the total leukocyte count, a blood film was prepared using leishman’s stain and the differential WBC count found\(^5\). The absolute Eosinophil count calculated according to the formula\(^6\).

\[
\text{Absolute eosinophil count} = \text{differential eosinophil count} \times \text{total WBC/100}
\]

**Results**
There was 35 cases with moderate-sever asthma (63.6%), divided into 29 (82.8%) with \(>400/\text{mm}^3\) and 6 (17.2%) \(<400/\text{mm}^3\) and 20 cases were mild-moderate asthma (36.4%), divided into 16 (80%) \(<400\) and 4 (20%) \(>400\), the difference between the two groups was statistically significant using chi-square.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Respiratory arrest imminent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Talking in alertness</td>
<td>Sentences, may be agitated</td>
<td>Phrases, usually agitated</td>
<td>Words, usually agitated</td>
<td>Drowsy or confuse</td>
</tr>
<tr>
<td>Respiratory rate</td>
<td>Increased</td>
<td>Increased</td>
<td>Mark increase</td>
<td>Paradoxical</td>
</tr>
<tr>
<td>Accessory muscle</td>
<td>Usually not</td>
<td>Usually</td>
<td>Usually</td>
<td>Paradoxical thoraco-abdominal movement</td>
</tr>
<tr>
<td>Wheeze</td>
<td>Moderate, often only end expiratory</td>
<td>Loud</td>
<td>Usually Loud</td>
<td>Absence of wheeze</td>
</tr>
<tr>
<td>Pulse / min</td>
<td>(&lt;100)</td>
<td>100-200</td>
<td>(&gt;120)</td>
<td>Bradycardia</td>
</tr>
<tr>
<td>PEF</td>
<td>over 80%</td>
<td>60-80%</td>
<td>(&lt;60)%</td>
<td></td>
</tr>
</tbody>
</table>

**Discussion**
Many studies suggest the relation of eosinophils to allergy and hyper reactive airway diseases. The increase in the percentage of moderate-severe asthmatic children may be because the mild case did not reach the center and treated as out patients. The following are examples of some international studies about asthma and eosinophil: Tonnel and colleagues in their study\(^7\) showed the relation of neutrophils and eosinophil increase in asthma in blood and sputum\(^6\). Lemiere and colleagues\(^8\) discover the increase in eosinophil in peripheral blood with the more exposure to trigger factors (which support this study\(^\). Yamada and colleagues said that the high eosinophil count. And Eotaxin (protein secreted in the lung of asthmatic which is a chemo attractant for eosinophil) the more unstable asthma\(^9\). They found that about 75% of patients were of high eosinophil count. Also Lilly CM and Colleagues showed that the more unstable acute attack of asthma the more high eotaxin and eosinophil count\(^8,10\). However good relationship of eosinophil to asthma
Eosinophil count and asthma.

Alwani et al.

Iraqi Journal of Medical Sciences

Eosinophil can increase by many allergic conditions and parasitic infestation, which can bias the study and this, can be overcome by selection of defined asthmatic by proper history and clinical finding and spirometry.

Conclusion
The increase in eosinophil count in asthmatic patients is correlate with the severity of attack, the more severe the high blood eosinophil

Recommendations
1. Eosinophil count could be used to assess asthmatic severity.
2. Correlation of clinical and lab finding (eosinophil count) give the best assessment by decrease the range of error in the assessment.

References
SERUM CALCIUM LEVEL IN PATIENTS WITH TYPE II DIABETES MELLITUS

Baybeen K. Al-Selevany PhD

ABSTRACT

Background: Evidence for a disturbance of mineral metabolism in diabetes has accumulated since the eighties of the last decade. Calcium ion shown to play an important role in the biosynthesis, storage, release and activity of insulin, in addition, to glucose tolerance in human beings.

Objective: To examine if serum calcium level (SCaL) is influenced in patients with type II diabetes mellitus (type 2 DM).

Methods: The study comprised one hundred twenty subjects of both sexes. Sixty patients of newly diagnosed type 2 DM with a mean±SD age of 47.6±11.6 years and 60 healthy controls with a mean age±SD of 35.2±14.3 years. Main outcome measures (SCaL) and serum glucose level (SGL) in fasting blood samples.

Results: Serum calcium level and SGL were significantly higher in newly diagnosed type 2 DM as compared to healthy non-diabetic controls. Furthermore, there was no correlation between SCaL and hyperglycemia in diabetic patients.

Conclusion: Hypercalcemia may be a result of other factors in diabetes mellitus rather than hyperglycemia.

Key words: Type 2 diabetes mellitus, calcium, glucose, hypercalcemia, hyperglycemia.

IRAQI J MED SCI, 2005; VOL. 4 (1): 84-88

Introduction

Approximately 97% of people who have diabetes mellitus have type II diabetes mellitus (DM)\(^1\). Evidence for a disturbance of mineral metabolism in diabetes has accumulated since the eighties of the last decade\(^2\). Extracellular calcium provides calcium for maintenance of intracellular calcium ion, bone mineralization, renal function, hormone secretion, and a second messenger affecting enzyme activity\(^3\). Calcium ion shown to play an important role in the biosynthesis, storage, release and activity of insulin. In addition to, glucose tolerance in human beings\(^3-7\). Pancreatic β-cells of the islets of Langerhans are rich in Ca\(^{2+}\)\(^8\). The role of Ca as a mediator of insulin action was originally proposed by Clausen et al\(^8\) and Kissebah et al in the mid seventies\(^9\). Although some investigators failed to observed a relationship between Ca and insulin action\(^10-11\) diverse aspects of insulin action have been demonstrated to be dependent upon extracellular and cytoplasmic Ca\(^{2+}\)\(^12-15\). Several studies among diabetics of both types I and II have demonstrated abnormalities in Ca\(^{2+}\) metabolism\(^16-18\). Also, type II DM results in altered cellular Ca\(^{2+}\) regulation and transport\(^19\). Homeostasis of Ca\(^{2+}\) is disturbed in animal models with diabetes mellitus; nevertheless the effects of DM on Ca\(^{2+}\) metabolism in human are controversial. Although some authors have found no significant alterations, apart from excessive urinary loss of Ca\(^{2+}\)\(^20\), increased Ca\(^{2+}\) absorption has been reported following oral Ca\(^{2+}\) loading in type I diabetics\(^21\) and slightly higher levels of serum calcium have been found in type II DM patients than in normal subjects\(^2, 5, 22\).
The aim of the present study was to examine serum calcium level in newly diagnosed type II diabetics attending Al-Waffa Diabetic Clinic in Mosul.

Patients & Methods
Sixty patients with newly diagnosed type II DM of both sexes with a mean±SD age of 47.6±11.6 years who were attending Al-Wafa Diabetic Clinic in Mosul during the period from September 2002-February 2003, and sixty non-diabetic healthy controls with a mean±SD age of 35.2±14.3 years, were included in this study. No participants were taking any mineral supplements or medication, during the period of the study.

The median and range of the ScaL and SGL in controls and type II diabetics presented in the table. The proportion of patients who had hypercalcemia was 81.7%.

Table 1: Median and range for the ScaL and SGL in healthy controls and type 2 diabetics

<table>
<thead>
<tr>
<th>Parameters (mmol / L)</th>
<th>Controls n = 60</th>
<th>Type II diabetics n = 60</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>median range</td>
<td>median range</td>
</tr>
<tr>
<td>ScaL</td>
<td>2.22 1.64 - 2.71</td>
<td>3.08 2.21– 4.01</td>
</tr>
<tr>
<td>SGL</td>
<td>4.96 3.47 – 6.87</td>
<td>11.84 3.37 – 21.85</td>
</tr>
</tbody>
</table>

Venous blood samples were taken between 8 and 10 a.m. after overnight fast and collected into an acid-rinsed metal-free covered glass test tube and allowed to clot for 1-2 hours at room temperature. After centrifugation, the serum removed. Glucose measurement performed immediately, while serum for estimation of calcium level was stored at -20 °C in other metal free plastic test tubes for further analysis.

Serum glucose concentration was measured by spectrophotometric enzymatic end point method. Serum calcium level analyzed by dye colorimetric method, which uses O-cresolphthalein complexone (CPC). In alkaline solution, CPC forms a red chromophore with Ca$^{2+}$.

The kit purchased for estimation of ScaL and SGL was from Biocon Co. (Germany). Z-test and Pearson’s correlation coefficient (r) used for the analysis of the data. The accepted level of significance was at P < 0.05.

Results
Serum calcium and serum glucose levels were significantly higher in type II diabetics (P< 0.001) compared with those in healthy controls (Table 2 and Figure 1).

Table 2: Mean±SD for ScaL in type II diabetics compared to the healthy non-diabetic controls (data presented as mean±SD)

<table>
<thead>
<tr>
<th>Variables (mmol/L)</th>
<th>Control (n = 60)</th>
<th>Type II diabetics (n = 60)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ScaL</td>
<td>2.17±0.27</td>
<td>3.11±0.45**</td>
</tr>
<tr>
<td>SGL</td>
<td>5.17±0.85</td>
<td>12.62±4.33**</td>
</tr>
</tbody>
</table>

** Significantly different from the respective control value, p<0.001
Figure 1: Comparison between mean values of SCaL and SGL in control subjects and type 2 diabetics.

There was no significant correlation between SGL and SCaL ($r = -0.03$, $p > 0.05$) in type 2 diabetics, or in healthy controls ($r = -0.091$, $p > 0.05$).

**Discussion**

The exact manner by which defective glucose homeostasis interferes with mineral metabolism remains unsettled\[2\]. A series of reports suggest the existence of altered Ca metabolism in diabetes mellitus\[16-18, 25\]. Hypercalcemia has been reported by several another to be present in type II diabetics\[2,5,22,26\] which is in agreement with the observation in the present study, but in contrast with the report of others\[27-31\].

Hypercalcemia occurs because of an increased flux of Ca$^{2+}$ into the extracellular fluid compartment from the skeleton, intestine, or kidney\[23\].

The assumed hypercalcemia in this study may be due to dehydration; this is expected in the newly diagnosed diabetics with severe hyperglycemia\[32\]. Bone mineral loss is another abnormality that recognized as a feature of the diabetic patients. This suggests that hypercalcemia may be as a result of calcium loss from bone\[33\].

Hypercalcemia in diabetic patients is speculated to be partly attributed to the low level of serum albumin\[5,26\]. Normally about 47% of Ca$^{2+}$ in the plasma combined with plasma proteins\[34\].

The tendency of hypercalcemia observed in diabetic patients could be also due to the decreasing renal tubular reabsorption\[2,5\], and increasing intestinal absorption of calcium\[24\]. Such inhibition of tubular reabsorption could be caused by hyperglycemia per se\[35-36\] or by some other direct action of abnormal glucose homeostasis on the renal tubules. The definitive mechanism is still unknown.

Many interactions occur between Ca$^{2+}$ and insulin metabolism. Calcium ion shown to be associated with the conversion of pro-insulin into insulin or
glucose tolerance in human beings and numerous laboratory animals\textsuperscript{[3-5,7]}. This suggests that hypercalcemia may be a result of insulin resistance\textsuperscript{[3, 6]}. The other probable causes of hypercalcemia may include primary hyperparathyroidism which is a common disorder resulting from increased secretion of parathyroid hormone from parathyroid adenomas, carcinomas or hyperplasia. Parathyroid hyperplasia may be associated with other inherited endocrine disorders (multiple endocrine neoplasia 1 and IIa). Multiple endocrine neoplasia; type I (MENI) which also called werner's syndrome, this disorder includes tumor or hyperplasia of parathyroid, pituitary, and non-β cells of pancreas. Hypercalcemia secondary to malignancy is relatively common and occurs in 10 to 20 of patients with cancer. The degree of hypercalcemia is worse with malignant disease (often greater than 3.5mmol/L) than with hyperparathyroidism (serum calcium less than 3.5 mmol/L\textsuperscript{[37,38]}. 

References
CONGENITAL HYPOTHYROIDISM IN AL-KADHIYMIA TEACHING HOSPITAL, BAGHDAD-IRAQ

Nasheit A. Nasheit1 CABP, Husam Al-alwani1 CBAP, Iman S. Mahmoud2

Abstract

Background: Congenital hypothyroidism is one of the most encountered endocrine diseases in childhood and the importance of this diagnosis is because early and adequate treatment prevents developmental retardation and other squeal of the condition.

Objective: Looking for the congenital hyperthyroidism in Iraqi children.

Methods: A retrospective study involved 40 children who were attended Pediatric Endocrine and diabetic Clinic for children in Al-Kadhiyimia Teaching Hospital, College of Medicine, Al-Nahrain University Baghdad, Iraq, over period from Jan 1993-Jan 2003.

Results: Of the 40 patients, 24 were female and 16 male. Female to male ratio 1.5:1. A history of parental consanguinity was positive in 36(80%) of the patients and 25(62.5%) had family history of hypothyroidism, and 24(60%) of the patients were from urban area 16(40%) from rural area west to Baghdad. Ten children (25%) detected in first month of life, 15(37.5%) in first 3 months and 25(62.5%) within the first 6 months. Seven patients had aplasia of thyroid gland, five had ectopia, and 8 had thyroid in normal position. Developmental assessment performed on all patients, also clinical manifestation in 20 patients diagnosed before 6 months of life.

Conclusion: Although we do not know much about the overall prevalence of congenital hypothyroidism in Iraq, the first observation to make is that it is not a rare disease in this country. A genetic explanation suggested by the involvement of multiple siblings and the high rate of consanguinity in this population.

Key Words: Congenital hypothyroidism, Retrospective


Introduction

Congenital hypothyroidism (CH) results from deficient production of thyroid hormone or defect in thyroid hormone receptor activity. Congenital causes of hypothyroidism may be sporadic or familial, goitrous or non-goitrous. In many cases the deficiency of the thyroid hormone is sever and symptoms develop in early weeks of life, in others lesser degree of deficiency occur or manifestations may be delayed for months.1 Early treatment of CH particularly within first 3 months of life usually results in normal psychomotor development since the mass neonatal thyroid screening programmes have been introduced in many industrialized countries aiming at prevention of mental retardation by early diagnosis of CH and prompt thyroid replacement therapy2,3. However, in most of the developing countries the diagnosis of CH still based on clinical grounds. This may results in a delay in the diagnosis and the initiation of thyroid replacement therapy with consequent mental retardation.

1 Dept. Pediatrics, College of Medicine Al-Nahrain University 2 Central Arab Child Hospital

Address correspondence to Dr. Nasheit A. Nasheit e-mail: naazna2003@yahoo.com
Received 5th December 2004: Accepted 14th February 2005.
Patients & Methods
This retrospective study included children who were attended Pediatric Endocrine and Diabetes Clinic in Al-Kadhimiya Teaching Hospital, Baghdad-Iraq, over period of 10 years from Jan. 1993-Jan. 2003. They were clinically diagnosed as having CH. Data recorded includes sex, age, residency, parental consanguinity, family history of thyroid disease, pregnancy history, place of birth, postnatal follow up, clinical manifestation, age at diagnosis and treatment, and assessment of mental development by Stanford-Binet scale.

Diagnosis of CH was confirmed by thyroid function tests (T4, T3, TSH and TC99M thyroid scan), the values considered according to the age (some investigation performed out side Iraq Perchlorate discharge test). Skeletal maturity was assessed by X-ray of the knee for infants and other joints for older children. Thyroid function tests made by radioimmunoassay methods using commercially available kits.

Results
Forty Patients with CH, Twenty-four (60%) from urban area and 16(40%) from rural area west to Baghdad. The female to male (24/16) ratio was 1.5:1.

A history of parental consanguinity was positive in 36(80%) of the patients and 25(62.5%) had family history of thyroid disease. In seven families, multiple siblings affected and in none of the patients was maternal history of ingestion of any medication during pregnancy. Eleven children (27.5%) were detected in first month of life, at age from 1-3 months 6 (15%) and at age 4-6 months 5(12.5%), at age 7-12 months 3(705%), and nine (22.5%) at age from1-3 years and six (15%) were diagnosed after age of 3 years (Table 1).

TC-99M thyroid scan was performed for 20 patients, seven had no thyroid gland (aplasia), five had ectopia and 8 had thyroid gland in normal position (Table 1). The mean period of follow up was 2.1 year (range 6 months- 5.5 year).

Development assessment performed on all patients: Ten (25%) had moderately severe mental retardation (IQ more than 50), Sixteen children (40%) achieved normal psychomotor development and 14 patients (35%) had mild mental retardation (IQ 50-75; Table-1).

<table>
<thead>
<tr>
<th>Age of diagnosis</th>
<th>No.</th>
<th>%</th>
<th>Development outcome</th>
<th>Findings on (TC-99M)scan of the thyroid gland</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Normal</td>
<td>Mild mental retardation (IQ 50-75)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 1 month</td>
<td>11</td>
<td>27.5</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>1-3 months</td>
<td>6</td>
<td>15</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>4-6 months</td>
<td>5</td>
<td>12.5</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>7-12 months</td>
<td>3</td>
<td>7.5</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>1-3 years</td>
<td>9</td>
<td>22.5</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>&gt;3 years</td>
<td>6</td>
<td>15</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>40</td>
<td>100</td>
<td>21</td>
<td>(52.5%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 1: Ages at diagnosis, Sex and the development outcome
The clinical manifestation in 20 patients with congenital hypothyroidism diagnosed before 6 months (Table-2).

Table 2: Clinical manifestation in 22 patients with congenital hypothyroidism diagnosed before the age of 6 months

<table>
<thead>
<tr>
<th>Manifestations</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coarse faces</td>
<td>18</td>
<td>81.8</td>
</tr>
<tr>
<td>Delayed bone maturation</td>
<td>16</td>
<td>72.7</td>
</tr>
<tr>
<td>Constipation</td>
<td>15</td>
<td>68.2</td>
</tr>
<tr>
<td>Neonatal Jaundice</td>
<td>12</td>
<td>54.5</td>
</tr>
<tr>
<td>Umbilical hernia</td>
<td>11</td>
<td>50</td>
</tr>
<tr>
<td>Hoarse cry</td>
<td>8</td>
<td>36.3</td>
</tr>
<tr>
<td>Large anterior fontanel</td>
<td>8</td>
<td>36.3</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>6</td>
<td>27.2</td>
</tr>
<tr>
<td>Macroglossia</td>
<td>6</td>
<td>27.2</td>
</tr>
<tr>
<td>Skin mottling</td>
<td>3</td>
<td>13.6</td>
</tr>
</tbody>
</table>

Discussion
Neonatal screening programmes for congenital hypothyroidism have revealed a variable incidence. In Iraq the incidence is not known, but in USA and other countries (1/2500) [1,4,5]. Although we do not know much about the overall prevalence of CH in Iraq, the first observation to be made is that this is not a rare disease in this country. Congenital hypothyroidism can be due to absent or hypo-plastic gland 35%, an ectopic gland 43%, or in born error of metabolism of thyroid hormone 22% 6, while in our series the percentage of ectopic gland is 20%, aplasia is 50% and normal position 30%. Determination of the cause of CH has genetic, epidemiological and prognostic importance [7,8]. The overall sex distributions showed the same pattern of female predominance reported elsewhere [1,9,10], while there was even sex distribution in infants with thyroid aplasia or ectopia presented in the first 6 months of life, similar to the experience of Daoud et al [9]. The most frequent initial clinical manifestation in 22 patients presented in the first months of life was coarse facial features, constipation, prolonged neonatal jaundice, umbilical hernia and delayed skeletal maturation (Table-2) which is similar to those reported by Smith [6,12], while in older age group the main reason for referral was psychomotor retardation, constipation and short stature. Though many of these features are rather non-specific, it is important to notice that most of the hypothyroid infants had several of these features at a time. Forty-two percent of our patients detected in the first 3 months (62.5%) in the first year. These results are similar to those reported by others [11,12].

Children with thyroid gland aplasia or ectopia might present early in life. Nine out of eleven of our patients with either thyroid aplasia or ectopia presented within the first 6 months of life. Among 21 children who achieved normal mental and motor development, Thirteen received thyroid replacement therapy within the first 6 months of life, and seven of the eight patients with moderately severe mental retardation were diagnosed and received therapy after the age of 1 year(Table-1). This demonstrates the favorable effect of early treatment, which has been confirmed by recent prospective studies in children with CH detected by neonatal thyroid screening [13].

Conclusion
These results demonstrate that CH is not uncommon disease, which is probably due to high rate of consanguinity among our population, and many thyroid investigation if needed are necessary to identify the cause of CH, which has genetic, epidemiology and prognostic importance.


**Recommendation**

Because of the sequelae of untreated CH are so severe and because the benefits of early treatment have been well-documented eight or national screening programme should keep in consideration the characteristic of neonatal practice in Iraq to achieve the maximum diagnostic benefits. General practitioners and pediatricians should be aware of this disease and treat such patients early enough to minimize the unwanted sequelae.

**References**


RESPIRATORY DYSFUNCTION IN PATIENTS WITH MYASTHENIA GRAVIS

Abdul-Kareem A.M.¹ FRCP, Sajid I.K. Al-Hussaini² FICMS

Abstract
Background: Myasthenia Gravis, a neuromuscular disorder causing skeletal muscle weakness involving respiratory muscles which sometimes sever enough to need assisted respiration. Approximately 30% of patients with MG develop some degree of respiratory weakness, myasthenic crisis most often precipitated by systemic infection (40%), thymoma (30%) and aspiration pneumonitis (10%).

Objectives: To evaluate respiratory function status with MG and to determine the triggering factors for respiratory dysfunction and effect of thymectomy.

Method: 50 consecutive cases of MG, 33 females and 17 males with an age range between 16–60 years old, 29 of them underwent thymectomy. The study was done throughout the period October 1999 to June 2001 in Al-Kadhiymia Teaching Hospital.

Results: 46% of patients show respiratory muscles involvement. 47.82% of cases show respiratory involvement in the first 4 years. 68.9% of thymectomized patients show no respiratory muscles involvement while 66.7% of non-thymectomized show respiratory muscles involvement. Infection is the highest triggering factor (39%).

Conclusion: Respiratory dysfunction seems to develop in the first 4 years of the disease course. The incidence of respiratory dysfunction is less frequent in thymectomized patients. Infection is the main triggering factor.

Keywords: Myasthenia Gravis, Neuromuscular, Thymectomy, Respiratory failure


Introduction
Myasthenia Gravis (MG) is a neuromuscular disorder characterized by fluctuating weakness and easy fatigability of the skeletal muscles that resolves with rest. It is an autoimmune disorder of neuromuscular transmission in which antibodies of IgG class reduce the functional status of acetylcholine receptors at the neuromuscular junction.

Myasthenic crisis defined as a marked clinical worsening of myasthenic weakness of the intercostals and diaphragmatic muscles leading to respiratory failure that requires intubations and mechanical ventilation. Approximately 30% of all patients with MG develop some degree of respiratory weakness. 15-20% will experience at least one crisis; one third of the patients who survive their first crisis will later experience a second one.

Myasthenic crisis tends to occur early in the course of the disease. The median interval from onset of the myasthenia gravis to the first crisis is 8 months with almost 75% of cases occurring within

1¹ Section of Neurology-Dept. Medicine, College of Medicine, Al-Nahrain University
2² Al-Numan General Hospital, Adhamiyah, Baghdad, Iraq

Address correspondence to Dr. Abdul-Kareem A.M. Al-Sheikhly, E-mail a_mutaleb@yahoo.uk.com, POBox 70041, Kademeyiah Baghdad, Iraq.

Received 16th June 2004: Accepted 14th March 2005
the first 2 years of the disease onset and rarely a respiratory distress is the first manifestation of myasthenia gravis[2-4,6]. Patients are often asymptomatic from the respiratory symptoms point of view in the early stages but as weakness progresses (VC< 30 ml/kg) atelectasis, reduced lung compliance, ventilation perfusion mismatch and hypoxia develop[4]. Respiratory crisis is mediated through two mechanisms of equal importance, respiratory muscles weakness and oropharyngeal weakness which leads to aspiration, infection and inability to clear airway passages[4,5]. Myasthenic crisis is most often precipitated by infection (40%), thymoma (30%), aspiration pneumonitis (10%), change of medications (8%) and spontaneous exacerbation (no risk factor) (30%). Myasthenic crisis can be avoided in many patients through immunosupression and thymectomy[4]. Pulmonary function tests (PFT) provide objective standardized measurements for assessing the presence and severity of respiratory dysfunction. The most common measurements of lung function through pulmonary function test are the ventilatory capacities (FVC, FEV1, and VC)[7,8].

In MG the respiratory muscles involvement results in restrictive pattern of defect on PFTs[4,6-8]. The best, simplest and most reliable way to evaluate respiratory functions in patients with MG is frequent measurement of VC[9,10]. Normal VC value is 60-70 ml/kg, Patients below these values should be monitored and treated aggressively. Vital capacity of 15ml/kg (~ 1 litter) is generally considered the level of which intubations is needed[4,6-8,10].

Aims of the study
1. To evaluate respiratory function depending on PFTs (VC) to recognize the cases where respiratory muscles are involved.
2. The relationship between respiratory dysfunction in patient with MG with onset of clinical presentation of respiratory dysfunction, thymectomy and the aggravating factors.

Patients & Methods
A prospective cohort clinical study; evaluation of fifty patients with MG, 33 females and 17 males with an age range between 16-60 years, 29 of them underwent thymectomy; throughout the period from October 1999 to June 2001 at Al-Kadihymia Teaching Hospital. The diagnosis of MG is secured through clinical, tensilon test and neurophysiological assessments. Other investigations that were needed for the study, PFTs, TFT, CT scan or MRI of the chest, Chest X-ray, X-ray of the sinuses, CBP and ESR, vasculitic screening tests and other basic hematological tests.

In this study, patients were classified according to their vital capacity into three groups: first, those patients with absent pulmonary function abnormality (VC > 80%), no ventilatory complaint. Second, those patients with mild to moderate impairment in pulmonary function test (V.C. 60-80%) of its predicted value, (V.C. 15-30 ml/kg), in which patients tend to have a low tidal volume and breath faster than healthy persons (RR 25-30 / minute). Third, those patients with severe pulmonary function tests impairment (VC <60%) of its predicted value, (VC <15 ml/kg), with RR >35/minute clinically[4,6,7,11, 12].
Results

Table 1: Percentage of Respiratory muscles involvement in M.G. patients depending on vital capacity

<table>
<thead>
<tr>
<th>All patients with M.G.</th>
<th>VC&gt; 80% Absent</th>
<th>VC 60-80% Mild -Moderate</th>
<th>VC &lt;60% Sever</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Without respiratory muscles involvement</td>
<td>27</td>
<td>0</td>
<td>0</td>
<td>27 (54%)</td>
</tr>
<tr>
<td>With respiratory muscles involvement</td>
<td>0</td>
<td>16 (32%)</td>
<td>7 (14%)</td>
<td>23 (46%)</td>
</tr>
</tbody>
</table>

Percentage of patient without respiratory muscles involvement =54%
Percentage of patient with respiratory muscles involvement = 46%

Table 2: Time of onset of respiratory muscles involvement in relation to the time of onset of the disease

<table>
<thead>
<tr>
<th>MG patients with respiratory muscles involvement</th>
<th>Presenting (respiratory failure)</th>
<th>1-2 years</th>
<th>3-4 years</th>
<th>&gt;5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>23</td>
<td>2 (8.7%)</td>
<td>11 (47.82%)</td>
<td>8 (34.78%)</td>
<td>2 (8.7%)</td>
</tr>
</tbody>
</table>

The onset of respiratory muscles involvement in relation to the time of onset of the disease is more frequent in the first four years and rare after five years or as a presenting clinical feature (R.F.).

Table 3: Respiratory muscles involvement in relation to thymectomy

<table>
<thead>
<tr>
<th>All patients with M.G.</th>
<th>Thymectomized</th>
<th>Non thymectomized</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>(%)</td>
<td>No.</td>
<td>(%)</td>
</tr>
<tr>
<td>Without respiratory muscles involvement</td>
<td>20 (68.9 %)</td>
<td>7 (33.3 %)</td>
<td>27</td>
</tr>
<tr>
<td>With respiratory muscles involvement</td>
<td>9 (31.1%)</td>
<td>14 (66.7%)</td>
<td>23</td>
</tr>
</tbody>
</table>

Total 29 | 21 | 50

Most M.G. patients with respiratory muscles involvement were not thymectomized, while most patients without respiratory muscles involvement were thymectomized.

Table 4: Respiratory muscles involvement in relation to aggravating factors

<table>
<thead>
<tr>
<th>All patients with respiratory muscles involvement</th>
<th>No.</th>
<th>Infection</th>
<th>Pregnancy</th>
<th>Surgery and stress</th>
<th>Drugs</th>
<th>Exercise</th>
<th>Mixed</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>UR</td>
<td>LR</td>
<td>Others</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>6</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Moderate</td>
<td>10</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>4**</td>
</tr>
<tr>
<td>Severe</td>
<td>7</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>2***</td>
</tr>
<tr>
<td>Total</td>
<td>23</td>
<td>5</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>6</td>
</tr>
</tbody>
</table>

Total 23 | 9 | 3 | 1 | 1 | 1 | 3 | 6 | 23

*Steroid induced, ** Infection & exercise, *** Infection & surgery.
Infection > Exercise & Pregnancy > Drugs, stress & surgery.

Discussion

In this study, 46% of the cases showed respiratory muscles involvement (respiratory dysfunction) which is more in contrast with other studies: Younger (1997) 16%[13], Thomas et al (1997) 30%[14], Fink (1993) 30%[15], Michael et al (1981) 16%[16].
This higher percentage of involvement in this study is due to, firstly delay in diagnosis and treatment of the disease itself, which leads to a more progression of the disease pathology and thus possibility of involvement of respiratory muscles, and secondly frequent infections in our patients, which is one of the main aggravating factors for myasthenic crisis.

This study shows that the onset of respiratory muscles involvement is more frequent at the first two years in the course of illness (47.82%), and less frequent at the (3-4) years of the course (34.78%) and rare to occur after 5 years of the disease course (8.7%) or as a presenting feature (acute respiratory failure) (8.7%) which agree with other studies\[14, 17\].

This high incidence of respiratory dysfunction in the first four years of the disease course is due to many factors which include: firstly the progression of the disease is more in the first three years, secondly most of the patients are not thymectomized at that time, and if they underwent thymectomy they may not get the full benefit of that operation early.

While low incidence of respiratory dysfunction after five years of the disease course is that, rarely the disease progress after five years and most cases are stabilized and in stationary state, and most patients are diagnosed and treated properly and were thymectomized and had the full benefit of it.

The present study shows that most patients with respiratory muscles involvement (66.7%) are not thymectomized, while most patients without respiratory muscles involvement (68.9%) were thymectomized which means that thymectomy is one of the protective measures against the development of respiratory dysfunction which agree with study done by Stephan (1997)\[4\] who said that thymectomy is a protective measure to avoid myasthenic crisis. In addition, this is in agreement with other studies about benefit of thymectomy in achieving remission\[18, 19, 20, 21, 22, 23\].

In addition, this study shows that infection is the main frequent aggravating factor for respiratory muscles involvement that includes upper respiratory tract infections, urinary tract infections and other infections for milder cases. URTI and LRTI like sinusitis and pneumonia are the main aggravating factors for moderate and severe cases. Some patients have mixed types of aggravating factors like infection, pregnancy and exercise.

Pregnancy (1\textsuperscript{st} and 2\textsuperscript{nd} trimester) was less frequent precipitating factor while drug induced, stress and surgery were the least frequent precipitating factors for respiratory dysfunction which agree with other studies\[1, 3, 14, 16, 24-27\].

The pregnancy plays an important rule in the aggravation of myasthenic weakness and inducing myasthenic crisis especially in the first and second trimesters which is due to, frequent emesis during pregnancy which interferes with absorption of oral medications as drug treatment of myasthenia gravis. It also leads to hypokalemia which can aggravate myasthenic weakness, and the large uterus elevates the maternal diaphragm resulting in relative hypoventilation of the lower portions of the lungs, and lastly, expanded plasma volume and increased renal clearance may require that AchE medications be adjusted during pregnancy\[28\].

**Conclusions**

1. The vital capacity as a part of PFTs is a simple test that can give a reliable idea about respiratory muscles involvement in patients with myasthenia gravis.

2. The respiratory dysfunction seems to develop early in the first years of the
course of the illness, while it is less frequent after five years of the course of the illness and rarely as a presenting feature (acute respiratory failure).

3. The incidence of respiratory dysfunction is less frequent in thymectomized patients compared to non thymectomized patients.

4. Infection is the main aggravating factor for the development of respiratory dysfunction followed by pregnancy, exercise, surgery and stress factors in sequence.

**Recommendations**

1. Patients with moderate or severe respiratory dysfunction should be kept under monitoring in RCU with frequent vital capacity assessment.

2. MG should be considered as differential diagnosis in patient with acute respiratory failure.

3. Thymectomy should be done as early as possible as one of the protective measures to prevent the occurrence of respiratory dysfunction.

4. Search and treatment of infection is essential as immunocompromised patients to prevent myasthenic crisis.

**References**


FEMALE HYPERPROLACTINEMIA: ANALYSIS OF PRESENTATION AND DIAGNOSTIC EVALUATION. IS PITUITARY MAGNETIC RESONANCE IMAGING ALWAYS INDICATED?

Sahar L. Halabia¹ CABOG, Ayad Sh. Salih² DMRD

Abstract
Background: Hyperprolactinemia (HPRL) is the most common endocrine disorder of the hypothalamic-pituitary-ovarian axis. The most important and common cause is pituitary tumor.

Objectives: 1. Analysis of the presenting features. 2. Role of MRI in the diagnostic evaluation of HPRL. 3. MRI measurements and correlation between MRI findings and serum prolactin concentration (PRL) in Iraqi women. 4. Literature review and work-up for HPRL.

Method: clinical assessment, basal PRL and pituitary and cranium MRI performed in a case-series study for 82 Iraqi HPRL female patients attending gynecologic clinic after excluding secondary HPRL.

Results: sub-fertility, galactorrhoea and menstrual irregularities were the commonest features. MRI abnormalities found in 41.46% of the patients. 88.24% were pituitary abnormalities. Their PRL was significantly higher than those with idiopathic HPRL (p=0.03). Right pituitary adenomas were more common than the left. The pituitary gland occupied 81.73% of the sella turcica in case of pituitary hyperplasia. There was no significant correlation between adenoma size and PRL (p=0.077), while there was significant positive correlation between pituitary and sella areas in those with normal MRI (p=0.007) as well as those with pituitary hyperplasia (p=0.04).

Conclusion: PRL of 18.5ng/ml considered as the cut-off value to perform high-resolution pituitary and cranium MRI. Primary pituitary hyperplasia may carry a risk of parasellar extension during pregnancy. There is positive correlation between pituitary and sella turcica sizes. MRI considered as the gold-standard imaging method for the pituitary while sella X-ray should be abandoned.

Key words: Hyperprolactinemia, Pituitary adenoma, Pituitary hyperplasia, MR imaging, MR measurement, Iraqi


Introduction
Hyperprolactinemia (HPRL) is the most common endocrine disorder of the hypothalamic-pituitary-ovarian axis, occurring mostly in women, with a prevalence of 0.4-0.5% in unselected normal adult population to as high as 9-17% in women with reproductive disorders[1,2]. Hyperprolactinemia defined as serum prolactin (PRL) level above the normal range. This is considered as > 19 ng/ml[3], > 20-25 ng/ml[4,5] or > 30ng/ml[6]. There is great deal of variability between laboratories in their analytic methods and ranges of normal. Unselected autopsy studies had shown pituitary tumors in 1.5-26.7%. Magnetic resonance imaging (MRI) signs of pituitary tumor found in 10% of normal population. However, clinically significant pituitary tumors affect the health of 8.2-20/100000 people[2, 3, 6-8]. The causes of HPRL fall into five categories:

---

¹ Dept. Obstetric & Gynecology, College of Medicine, Al-Nahrain University ² Dept. Radiology, Al-Kadhimiya Teaching Hospital, Baghdad, Iraq.
Correspondence: Dr. Sahar Halabia, c/o Basil Ghazala P.O.Box 3290 Saadoon Baghdad Iraq.
e-mail: ghazalahalabia@yahoo.com
Received 14th April 2004: Accepted 29th November 2004.
First: Pituitary causes classified to:
Tumors secreting intact hormones that result in clinical syndromes of hormones hypersecretion. These tumors may secrete either pure hormones as PRL (termed prolactinoma which constitute 40% of pituitary tumors), growth hormone (GH), adrenocorticotrophic hormone (ACTH) or thyroid stimulating hormone (TSH) or may be mixed which express more than one hormone; Non-functioning tumors (non-secreting adenoma NSA) form 25-39% of pituitary tumors. They do not cause clinical syndromes of hormone hypersecretion but indeed produce either silent glycoprotein hormones or their subunits. They may present with functional HPRL. The cause of pituitary tumors is unknown and is not inheritable\[8\]; Pituitary hyperplasia i.e. global pituitary enlargement which is either primary or secondary to puberty, pregnancy, primary hypothyroidism with secondary HPRL, hypothalamic tumors as GH releasing hormone-secreting tumors or mental depression\[3\]. Pituitary incidentoloma represented 12% of pituitary tumors. It means incidentally discovered pituitary mass during imaging performed to evaluate conditions not linked to pituitary disease\[3,7,9\].

Second: Non-pituitary sellar and parasella lesions with functional HPRL:
Structural lesions as empty sella, intrasellar cyst, tumours as craniopharangioma, germinoma, meningioma, chordoma, astrocytoma, lymphoma, metastatic tumors, glioma and vascular abnormalities as aneurysm; Non-structural lesions as sarcoidosis, cranial irradiation, stalk resection, lymphocytic hypophysitis\[1,3,4,10\].

Third: Secondary HPRL to renal impairment, liver cirrhosis, primary hypothyroidism, lesions in dermatomes T 3-5 & mammary line, spinal cord tumors, seizures, ectopic PRL production by malignant lesion as bronchogenic carcinoma and PRL-enhancing drugs\[1,10,11\].

Fourth: Physiological HPRL in response to stress, sleep, food intake, sexual activity and nipple stimulation as well as in pregnancy and lactation. PRL is secreted in pulses every 20 minutes with a diurnal rhythm\[1,4,10,12\].

Fifth: Lastly idiopathic HPRL in 32.8-61%, when no underlying cause is found\[4,13,14\].

The commonest features of HPRL are menstrual irregularity, galactorrhoea, infertility, pregnancy loss, loss of libido, acne and hirsutism, headaches and osteopenia. It is important to consider HPRL and pituitary adenoma in an expanded range of clinical situations. Baird's in his recent study\[15\] adds other troublesome complaints as physical and mental fatigue, mood disorder, sleep problem, unexplained pain, emotional behavior dysfunction and decline in sexual function. HPRL alters the pattern of hypothalamic catecholamines and so suppresses pulsatile secretion of gonadotrophin releasing hormone thus blocking follicular stimulating (FSH) and leutinizing hormones (LH) by blunted or no response to estradiol. In addition, PRL inhibits gonadotrophin effect at ovarian level. There is hypoestrogenism and chronic hyperandrogenism\[2,10\]. The increased mean intracellular pressure (MISP) contributes to the development of headaches even in those with microadenomas\[16\]. However, our understanding of HPRL has improved greatly since the availability of finer diagnostic imaging. MRI now regarded as the pituitary imaging method of choice that provides the most detailed information and
suggests pathological diagnosis, tumor vascularity and invasiveness to surroundings. It can be used during pregnancy and can be repeated. It has no ionizing radiation like computed tomogram (CT) which also provides less precise information\(^6\), although tissue calcifications are better detected by CT\(^17\). Nevertheless, even MRI may have pitfalls i.e. false-positive results due to normal anatomic variations or imaging artifacts\(^7\). For pituitary and cranium, imaging the trend now is to use the high resolution MRI with dynamic contrast enhancement\(^3,17\).

The primary treatment of prolactinomas whether micro- or macro-adenomas and for idiopathic HPRL is medical therapy when indicated, while surgery is the first treatment for the non-PRL secreting and non-secreting pituitary adenoma as well as for the sellar and parasellar tumors\(^3,4\).

Differentiation between prolactinomas and the other tumors is possible by immunohistochemistry study of the specimen after surgery. Since few prolactinoma patients are now submitted to surgery, dynamic tests of PRL in HPRL patients are useful in suggesting a pathological diagnosis of pituitary adenomas.

Dopamine antagonists domperidone\(^17\), metoclopramide or perphenazine\(^2\) stimulation tests give blunted PRL response in prolactinoma i.e. PRL 30/PRL 0<3 in comparison to PRL response of ≥3 in functional HPRL secondary to the other tumors. The blunted PRL increment of less than 30% after thyrotropin releasing hormone (TRH) stimulation test is typical of macroprolactinoma and excludes other pituitary adenoma, but the cut-off not yet established for microadenoma\(^3\).

In prolactinoma when dopamine agonists are used as bromocriptine suppression test there is decrease of serum PRL by 70%\(^18\).

Macroprolactin, a PRL aggregate with high molecular weight 150-170 Kda is active in vitro but has no or low biological activity in vivo. It is indistinguishable from the low molecular active PRL by routine assay but by special tests as chromatography and others\(^7,18,20\). Macroprolactinemia is present in 8-46% of HPRL. It found that 78-78.9% of those with macroprolactinemia had normal MRI\(^6,20\) while the others have pituitary lesions. Because MRI is expensive some studies\(^17,21\) suggest the dynamic tests of PRL and macroprolactin assay in HPRL to be done first and then to select those who need the MRI. While others studies\(^2,4,6,19,20\) concluded that pituitary imaging is necessary in the diagnostic evaluation of HPRL.

The aims of the study of female:
1. Analysis of the presenting features.
2. Role of MRI in diagnosing the cause of HPRL with comparison to X-ray of pituitary fossa.
3. MRI measurements and correlation between MRI findings and PRL in Iraqi women.
4. Literature review and work-up for HPRL

**Methods**

This case-series study included 172 consecutive Iraqi women with PRL concentration higher than 14ng/ml, who were non-pregnant, non-lactating and not on hormonal contraception attending Al-Kadmyia Teaching Hospital and private gynecologic and infertility clinics during the period from 1 June 2001 through the fifteenth of March 2003. For all of them a second basal PRL assay in standardized conditions was performed. A fasting morning specimen drawn after suspending any sexual activity and nipple stimulation for at least four days. In spontaneously menstruating women, the sample drawn on the second or third day of the cycle. While in amenorrheic women,
pregnancy excluded by clinical assessment and pregnancy test before sampling. These measures were to reduce potential confounding physiological factors. During medical history and examination, we looked for: PRL enhancing drugs, mammary line skin lesion or irritation at dermatomes T3-T5, features of renal, liver and thyroid dysfunction. For all the 120 patients with persistent HPRL, screening with blood urea, serum thyroxine and TSH performed. Fifty-two women (30.23%) were found to have transient HPRL with the basal PRL ≤14ng/ml while the first PRL concentration mean was 16.67±1.38 (range 14.2-24ng/ml). Twenty-six patients (15.12%) were found to have possible secondary HPRL including: 14 (8.14%) with pharmacological HPRL using amitriptyline HCL, alaphametyldopa, digoxin, cortisteroid, danazol, diphenhydramine or cimetidine; 11 (6.39%) had mammary line skin lesion or irritation (one herpes zoster, 3 breast pruritus and 7 used local methods for breast hair removal); one with high blood urea (70 mg/dl). None had chronic liver disease or primary hypothyroidism. Those 26 patients with secondary HPRL with PRL concentration mean 19.2±2.01 range 14.5-29.3 ng/ml not presented in this study. Another 12 patients (6.98%) excluded from the study because they did not attend for the MRI. The remaining 82 women (47.67%) were the study group with HPRL (basal PRL>14ng/ml) who did not have any of the above factors and for whom pituitary and cranium MRI was performed. For the first thirteen patients lateral view X-ray of the pituitary fossa in addition to the MRI performed during the era when the MRI newly introduced to practice in this hospital. Then sella X-ray abandoned. For the study group, detailed history and examination performed regarding symptoms possibility related to HPRL as menstrual irregularity, galactorrhea, breast pain, sub-fertility with ovulatory factor, abortion, acne and hirsutism, dyspareunia and loss of libido. Also features of mass affect including headaches, visual symptoms, cranial neuropathies as third and sixth nerve palsy and cerebrospinal fluid (CSF) rhinorrhea.

Clinical features of excess or deficiency of GH, ACTH and TSH looked for. Full ophthalmologic examination including visual field campimetry using Goldmann perimetry was requested for 50 patients desiring pregnancy as a base line, also for 5 patients with symptoms of mass effect and 5 with pituitary macroadenoma on MRI for whom neurosurgical opinion was also requested. Enquiry about previous brain trauma, postpartum hemorrhage and birth asphyxia made for those found to have empty sella on MRI.

Prolactin assay: PRL measured by immunoradiometric assay (IRMA, reference value for adult females 3.6-14 ng/ml; ImmunoTech, Bechman Coulter Company) with a sensitivity of 0.5 ng/ml, intra-assay and inter-assay variation were ≤2.8 and ≤ 8% respectively.

High Resolution Dynamic Contrast MRI Examination: MRI study was performed on 1.5 Tesla superconductive system (philsips Gyroscan NTCS) with the use of dedicated phase array head coil. The used protocol included whole brain scan as survey by using T2 Turbo-spin-echo (Tse) axial and then dedicated scanning of: 1-The pituitary gland: Coronal and Sagittal planes T1 weighted Se, repetition time (TR) 625, echo time (TE) 13, slice thickness (SL) 1.5mm, 256x256 matrix, field of view(FOV) 180mm, number of excitation (NEX) 4 and intersection gap 0.3mm. 2-Coronial T2 weighted Tse, TR 6772, TE 150, SL 2mm, matrix...
256x256, FOV 200 and NEX 4. Dynamic contrast study on T1 coronal study after administration of 0.1 mmol/kg body weight gadolinium diethylene triamine pentaacetic acid (Gd-DTPA) intravenously.

**MRI Assessment:** Sella turcica: size, antero-posterior (AP) diameter and height (HT) on sagittal view, the U-shaped configuration, walls and borders. Pituitary: position in the sella, the bean shaped configuration, superior border, size, AP diameter and HT on sagittal views, pituitary homogenisity before and after contrast enhancement, any circumscribed hypo- or hyper-intense area and dynamic sequence for any time differential in the enhancement of different pituitary areas.

Infundibulum (pituitary stalk): position and size. Optic chiasma: position, size and symmetry. Suprasella CSF spaces: symmetry and constriction. Cavernous sinus: symmetry, size and infiltration. Internal carotid arteries: symmetry, size, narrowing or expansion. Neurocranium: temporal lobe, hypothalamus and floor of third ventricle. Sphenoid sinus: margins especially the roof and pneumatization. Diagnosis of pituitary adenoma and hyperplasia and the SIPAP classification as a grading system for extension was according to the imaging characteristics demonstrated in Ref. 3, 11, 22.23. In this study pituitary hyperplasia was diagnosed when both pituitary sagittal diameters AP and HT were >10mm and >8mm respectively with generalized pituitary heterogeneity with or without enhancement.

**Statistical Analysis**
Analysis of data was with the personal computer Microsoft Excel program. Results presented as frequencies. Mean and standard error of the mean (M±SEM) was calculated. Student *t*-test and ANOVA used as tests of significance taking *p*≤0.05 as significant value. Degree of association assessed by correlation coefficient *r* and linear regression analysis. Sensitivity, specificity and accuracy were calculated using the contingency two-by-two table.

**Results**
The results of the study group i.e. the 82 patients with HPRL who consulted the gynecologic clinics, for whom pituitary and cranium MRI was performed were presented.

**Patients’ characteristics:** The results presented as M±SEM and (Min-Max). Age (year) =31.37±0.96 (16-52); weight (kg) =69.93±1.78 (45-105); 10 (17.5%) were obese with BMI>30kg/m²; 12 (15%) were unmarried; gravidity mean 1.42±0.25 (0-8); parity mean 0.93 (0-7); number of abortions mean 1.74±0.31 (1-6); primary sub-fertility duration (year) 4.83±1.01 (0.9-24); secondary sub-fertility duration (year) 4.82±0.92 (1-16).

**Clinical features:** The 82 patients had one or more of the features presented in Table 1. Their mean PRL was 39.64±2.47 (16.6-168).
Female hyperprolactinemia & pituitary MRI …. Halabia & Salih

Table 1: Frequencies of clinical features and PRL concentrations of the 82 HPRL patients

<table>
<thead>
<tr>
<th>Features</th>
<th>Total 82 patients*</th>
<th>PRL ng/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>%</td>
</tr>
<tr>
<td>Sub-fertility§</td>
<td>50 (43)</td>
<td>71.43 (61.43)</td>
</tr>
<tr>
<td>1ry</td>
<td>32 (27)</td>
<td>45.71 (38.57)</td>
</tr>
<tr>
<td>2ndary</td>
<td>18 (16)</td>
<td>25.71 (22.86)</td>
</tr>
<tr>
<td>Galactorrhea</td>
<td>38 (4)</td>
<td>46.34 (4.88)</td>
</tr>
<tr>
<td>Menstrual abnormality</td>
<td>31 (19)</td>
<td>37.8 (23.17)</td>
</tr>
<tr>
<td>Abortion§</td>
<td>19 (2)</td>
<td>27.14 (2.85)</td>
</tr>
<tr>
<td>Hirsutism/Acne</td>
<td>14 (3)</td>
<td>17.07 (3.66)</td>
</tr>
<tr>
<td>Breast pain</td>
<td>9 (3)</td>
<td>10.98 (3.66)</td>
</tr>
<tr>
<td>Headache</td>
<td>3 (0)</td>
<td>3.66 (0)</td>
</tr>
<tr>
<td>Visual symptoms</td>
<td>2 (0)</td>
<td>2.44 (0)</td>
</tr>
<tr>
<td>Dyspareunia/loss of libido</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*within parenthesis are the patients presenting symptoms
§the denominator was 70 instead of 82 because the 12 unmarried patients were not included

Coexisting conditions: Some of the HPRL patients had also polycystic ovary syndrome (PCOS), uterine leiomyoma (LM) or goiter. Their results presented in Table 2. Of the 11 PCOS patients, only one had MRI abnormality. The remaining 10 with normal MRI had PRL concentration of 36.29±3.58, which compared with the PRL of 35.08±2.62 of the 38 patients who had neither PCOS nor MRI abnormality. Two tail student t-test revealed no significant difference (t=0.27 df=20 p=0.79). Of the 10 LM patients with HPRL 4 had MRI abnormalities. The remaining six LM patients with normal MRI had PRL concentration of 30.12±4.06, which compared with the 36.05±2.37ng/ml of the 42 patients with neither LM nor MRI abnormality. t-test revealed no significant difference (t=1.26 df=9 P=0.24). The two patients with HPRL and goiter were found to have neither hyper- nor hypo-thyroidism.

Table 2: Frequencies of coexisting conditions and PRL concentration in the 82 HPRL patients

<table>
<thead>
<tr>
<th>Condition</th>
<th>Total 82 patients</th>
<th>PRL ng/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>%</td>
</tr>
<tr>
<td>Polycystic ovary syndrome</td>
<td>11</td>
<td>13.41</td>
</tr>
<tr>
<td>Uterin leiomyoma</td>
<td>10</td>
<td>12.2</td>
</tr>
<tr>
<td>goitre</td>
<td>2</td>
<td>2.44</td>
</tr>
</tbody>
</table>

Pituitary MRI Characteristics: MRI findings and their correlation to prolactinemia values presented in Table 3 and Table 4. Of the 48 normal MRI i.e.idiopathic HPRL patients 2 (4.2%) had normal variations: one with left local asymmetry of the pituitary gland and the other with left sided pituitary stalk. Another two had incidental findings in the form of nasopharangeal polyp in one and left sphenoid sinus mucocele in the other. Three (10%) of the 30 patients with MRI abnormality showed convexity or bulge of the upper pituitary margin. In 2 (8.4%) MRI with pituitary adenoma the adenoma areas 99mm², 276mm² were larger than their sella areas 90 mm², 258mm² respectively with suprasellar extension grade 1 according to SIPAP classification but no pressure on optic chiasma. One MRI with pituitary microadenoma showed shift of the lower pituitary stalk. The mean pituitary area, mean sella area and their percentage ratio calculated for the 48 women with normal pituitary MRI and for the 5 women with pituitary hyperplasia. Results revealed
69.79±3.32 mm², 107.15±4.83 mm² and 65.13% vs. 139.75±38.8 mm², 171±38.9 mm² and 81.73% respectively. Only one patient with macroadenoma had restricted visual field and treated medically under the supervision of the neurosurgeon. Opened cranial surgery done with removal of the meningioma and the cerebellar cyst. The latter revealed heamangioblastoma tumor.

Table 3: Pituitary and cranium MRI findings in the 82 HPRL patients

<table>
<thead>
<tr>
<th>MRI findings</th>
<th>Total 82 patients</th>
<th>PRL ng/ml</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>%</td>
<td>mean±SEM</td>
</tr>
<tr>
<td>Normal*</td>
<td>48</td>
<td>58.54</td>
<td>35.3±±2.19</td>
</tr>
<tr>
<td>Abnormal</td>
<td>34</td>
<td>41.46</td>
<td>45.4±±4.87</td>
</tr>
<tr>
<td>Pituitary abnormality§</td>
<td>30</td>
<td>36.59</td>
<td>46.3±±5.28</td>
</tr>
<tr>
<td>Microadenoma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>11</td>
<td></td>
<td>45.5±±7.09</td>
</tr>
<tr>
<td>Left</td>
<td>9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Macroadenoma</td>
<td>5</td>
<td>6.59</td>
<td>57.7±±13.68</td>
</tr>
<tr>
<td>Right</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperplasia</td>
<td>5</td>
<td>4.88</td>
<td>38.3±±4.68</td>
</tr>
<tr>
<td>Non-pituitary brain abnormality</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meningioma</td>
<td>1</td>
<td></td>
<td>26.3</td>
</tr>
<tr>
<td>Cerebellar cyst</td>
<td>1</td>
<td></td>
<td>21.7</td>
</tr>
<tr>
<td>Empty sella§</td>
<td>2</td>
<td></td>
<td>53.4</td>
</tr>
</tbody>
</table>

* Those HPRL patients with normal MRI considered to have idiopathic HPRL
§ Microadenoma means: its largest diameter < 10 mm while macroadenoma ≥ 10 mm
☆ One empty sella associates microadenoma

Table 4: Pituitary gland, pituitary adenoma and sella measurements of the 82 HPRL patients

<table>
<thead>
<tr>
<th>MRI findings</th>
<th>M±SEM</th>
<th>Min-Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal pituitary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AP(mm)</td>
<td>10.5±±0.31</td>
<td>8-16</td>
</tr>
<tr>
<td>HT(mm)</td>
<td>6.6±±0.29</td>
<td>4-10</td>
</tr>
<tr>
<td>AREA(mm²)</td>
<td>69.7±±3.32</td>
<td>32-105</td>
</tr>
<tr>
<td>Microadenoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AP(mm)</td>
<td>5.4±±0.54</td>
<td>2.2-9.7</td>
</tr>
<tr>
<td>HT(mm)</td>
<td>4.3±±0.45</td>
<td>1.2-8.8</td>
</tr>
<tr>
<td>AREA(mm²)</td>
<td>27.1±±5.11</td>
<td>4.2-77.44</td>
</tr>
<tr>
<td>Macroadenoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AP(mm)</td>
<td>16.2±±2.19</td>
<td>11-23</td>
</tr>
<tr>
<td>HT(mm)</td>
<td>8.5±±1.10</td>
<td>5.1-12</td>
</tr>
<tr>
<td>AREA(mm²)</td>
<td>146.1±±38.2</td>
<td>62.22-276</td>
</tr>
<tr>
<td>Hyperplasia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AP(mm)</td>
<td>12±±1.08</td>
<td>9-14</td>
</tr>
<tr>
<td>HT(mm)</td>
<td>11.2±±2.29</td>
<td>8-18</td>
</tr>
<tr>
<td>AREA(mm²)</td>
<td>139.7±±38.8</td>
<td>81-252</td>
</tr>
<tr>
<td>Sella</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AP(mm)</td>
<td>119±±0.25</td>
<td>9-16</td>
</tr>
<tr>
<td>HT(mm)</td>
<td>9.3±±0.3</td>
<td>6-18</td>
</tr>
<tr>
<td>AREA(mm²)</td>
<td>113.2±±5.32</td>
<td>54-270</td>
</tr>
</tbody>
</table>

AP=antero-posterior diameter  HT=height

Correlation Study: These presented in Table 5 and Figure 1.

Pituitary and cranium MRI vs. sella turcica X-ray: Of the 13 patients who had sella X-ray in addition to the MRI, six X-rays showed abnormal findings in the form of calcifications, ballooning or doubling of the floor, erosion of the floor or clinoid process. Calculation from the 2*2 Table 6 revealed 12.5% sensitivity of the sella X-ray, 16.67% specificity and the overall accuracy of only 15.71%.
Table 5: correlation between pituitary and cranium findings and other parameters

<table>
<thead>
<tr>
<th>MRI findings</th>
<th>Variables</th>
<th>Statistical tests</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Independent(X)</td>
<td>Dependent(Y)</td>
</tr>
<tr>
<td>Pituitary adenoma</td>
<td>Adenoma area(mm²)</td>
<td>PRL(ng/ml)</td>
</tr>
<tr>
<td>Pituitary hyperplasia</td>
<td>Pituitary area(mm²)</td>
<td>PRL(ng/ml)</td>
</tr>
<tr>
<td>Normal pituitary</td>
<td>Pituitary area(mm²)</td>
<td>PRL(ng/ml)</td>
</tr>
<tr>
<td>Pituitary adenoma</td>
<td>Age(year)</td>
<td>Adenoma area(mm²)</td>
</tr>
<tr>
<td>Normal pituitary</td>
<td>Age(year)</td>
<td>Pituitary area(mm²)</td>
</tr>
<tr>
<td>Normal pituitary</td>
<td>Gravidity</td>
<td>Pituitary area(mm²)</td>
</tr>
<tr>
<td>Normal pituitary</td>
<td>Parity</td>
<td>Pituitary area(mm²)</td>
</tr>
<tr>
<td>Pituitary hyperplasia</td>
<td>Sella area(mm²)</td>
<td>Pituitary area(mm²)</td>
</tr>
<tr>
<td>Normal pituitary</td>
<td>Sella area(mm²)</td>
<td>Pituitary area(mm²)</td>
</tr>
</tbody>
</table>

r=correlation coefficient  p=significant value  n=sample size

* In 15 HPRL patients with normal pituitary MRI, the pituitary diameters not measured. The gravidity and parity not mentioned in three of them.

Discussion

with NSAs. Patients lost weight during PRL lowering therapy. In addition, he found that recent weight gain is an indication to measure serum PRL as it may be the presenting symptom of HPRL. In Dublin’s study drug-
LH as well as PRL. Therefore, the central basal hypothalamic deficiency of dopaminergic activity leads to the increased LH/FSH ratio and PRL in PCOS HPRL patient.

PRL produced by human endometrium, myometrium and uterine leiomyoma. Insulin-like growth factor and others mediate this production. Proliferative phase leiomyomas contain elevated levels of PRL in vivo and synthesize PRL in vitro. Could leiomyoma be the source of the high PRL in patients with idiopathic HPRL? The answer may be “NO” as we found no significant difference in PRL level in those with idiopathic HPRL whether they had leiomyoma or not (p=0.24).

PRL is two folds higher in tumoral HPRL than secondary HPRL. This also proved in our study, the mean PRL in MRI abnormality group was 45.45 ± 4.87 ng/ml (Table 3) vs. 19.2±2.01 in those with secondary HPRL. Table 3 showed the significantly higher PRL level in those with pituitary and brain MRI abnormality than those with idiopathic HPRL (P=0.03). This is consistent with Dr. Reba findings. As PRL of 18.5ng/ml was the minimal value for those HPRL with pituitary and brain lesions (Table 3), this figure may be suggested to be considered as the cutoff value at or above it MRI is indicated. In Ref 3 a patient with pituitary adenoma had even a PRL level of 18ng/ml. The mean PRL level in those with pituitary lesions was 46.35±5.28 in our study while in other studies it was 61±16.6, 62±13 and 79.9±63.6.

The results of Table 3 can be compared with Cano et al. study of MRI findings in HPRL which were: pituitary adenoma in 40.6%, questionable nodule in 4.7%, homogenous gland (i.e. pituitary hyperplasia) in 12.5%, 9.4% empty sella and 32.8% normal pituitary gland while Hauche et al study revealed 6.2% pituitary macroadenoma, 32.8% microadenoma and 61% normal induced, HPRL is found in 16% vs. 8.14% in our study which may be explained by the more common use of neuroleptic drugs in developed countries.

The prevalence of HPRL varies according to patient selection and presenting symptom. Our study included patients attending gynecologic clinic: subfertility was the commonest clinical feature followed by galactorrhoea and menstrual abnormality (Table 1) while in other studies menstrual abnormalities was the commonest followed by galactorrhoea then subfertility but these studies include male and female patients presenting to endocrine centers. We should stress that not all HPRL women have galactorrhoea; it ranges between 40.5-67.4%.[3,10,14] Only 25% of those with galactorrhoea have HPRL. It was found that 20-30% of those with menstrual abnormality had HPRL vs. only 10% of those regularly menstruating. Thirty percent of patients with infertility have HPRL. There was no significant difference (P=0.14) in PRL concentration between the different clinical features of HPRL (Table 1). PRL level indeed correlates with the severity of the symptoms rather than the type of the symptom.

The association between polycystic ovary syndrome (PCOS) and HPRL remains controversial. In one study HPRL was found in 17% of PCOS patients. PCOS found in 13% of the study group (Table 2). There was no significant difference in PRL level in those with idiopathic HPRL whether they had PCOS or not (P=0.79). It seems that these two conditions may coexist and they have independent origin. However, Dr. Luciano explained the relationship between PCOS and HPRL: First, the high oestrone of PCOS stimulates PRL; second, dopamine inhibits the release of...
response to treatment on follow-up MRI[22].

It seems that women with HPRL present to the gynecologist early. In this study, no one with pituitary adenoma had suprasellar significant extension, invasion or compression as manifested by MRI, full ophthalmologic and neurological examination. Because of the vague presenting features of HPRL in men, they tend to present late with larger prolactinomas and at older age than women[8]. If we assume that microadenoma increases in size with time to change to macroadenoma then we should find increasing adenoma size with increasing women age but this was not found (r=0.2, p=0.35) Table 5. This is supported by the fact that microadenomas tend to remain the same size[18] and in less than 5% the tumor enlarges slowly; while macroadenomas are already established at time of presentation and in 25% significant tumor growth occurs during follow-up[1,9,12,18]. Adverse pregnancy outcome occurs in <5% in macroadenoma as compared to 40% in macroadenoma patients[5]. In those with normal pituitary MRI no correlation (r=0.3, p=0.09) between age and pituitary size was demonstrated in women of reproductive age; while pituitary size is larger in pubertal girls and smaller in postmenopausal women[23].

In women with normal MRI no correlation was found between pituitary area and previous gravidity (r=0.15, p=0.44) or parity (r=0.01, p=0.96) (Table 5). Although there is, 2% and 5% increase in height and width of pituitary gland respectively 2-6 months postpartum as compared to non-pregnant control but the difference is not statistically significant[60]. Post-pregnancy PRL returns to pre-pregnancy level in HPRL women yet it is significantly lower in parous than pituitary .It seems that right pituitary adenomas are more common than left. It was 15 vs. 10 in our study, and twice as frequent in the right as left in Gspones et al study[3].

The relation between PRL level and adenoma size not settled yet. We found no significant difference (P=0.57) in PRL concentration between those with micro- and macroadenoma (Table 3). In addition, there was no correlation between PRL concentration and each of adenoma area(r=0.06 P=0.77) and normal MRI pituitary area(r=0.28 P=0.11) (Table 5). In Arafah et al study[16] PRL levels correlated positively with the MISP but the tumor size did not correlate with MISP or PRL level. While in other studies there is relatively linear relationship between degree of PRL elevation and the size of “True Prolactinoma”[4,13]. Indeed, PRL level correlates positively with the vascular density in prolactinoma. MRI can diagnose pituitary adenoma and its size but not its type. Not all adenomas are secretary and not all secretary adenomas are “True Prolactinomas”. In those with non-PRL, producing mass there is usually large mass and mild functional HPRL[4], which is explained by secondary interruption of the normal PRL inhibiting dopamine traveling via the portal blood vessels down the pituitary stalk due to either compression by the mass or due to increased MISP, which impairs portal blood flow[16].

In women of childbearing age the normal pituitary MRI sagittal diameters are: AP 8-10 (< 10 mm) HT 3.5-8 (2-6 mm) Ref 23 and 29 respectively. The normal sella turcica MRI sagittal diameters are: AP 11-16 mm and HT 8-10 mm[23]. These are comparable to our results in table 4. Variation in different populations is possible. Indeed for each patient more than one diameter basic measures of the pituitary adenoma is necessary to diagnose growth and
ng/ml\textsuperscript{[3]} and >100 ng/ml\textsuperscript{[2]} are 100% diagnostic of "True macroadenoma". Third: If milder HPRL of ≤85 ng/ml is associated with MRI pituitary mass, further dynamic tests of PRL are required to differentiate prolactinomas, which treated primarily medically from other pituitary and brain tumors, which require surgery. Dynamic tests alone do not differentiate tumor induced functional HPRL from idiopathic HPRL. Therefore, they cannot replace MRI.

Fourth: 21.1-22% of those with macroprolactinemia have prolactinomas, usually microprolactinomas\textsuperscript{[6,20]}. Therefore, MRI still indicated to diagnose them with follow-up of their mass effect. However, there is no need to treat those who have macroprolactinemia as they do not have clinical features of HPRL.

References
8. Pituitary Disorders Education and Support-Pituitary disorders-Prolactinoma. Online nulliparous normoprolactinemic women\textsuperscript{[5]}. There were no previous reports on pituitary size and its correlation with sella turcica size. We found the correlation to be highly significant between pituitary area and sella area in normal pituitary MRI cases ($r=0.46$, $p=0.007$) and significant in pituitary hyperplasia ($r=0.96$, $p=0.04$) (Table 5, Figure 1). According to our results, the pituitary area occupied 65.13% of the sella turcica in those with normal pituitary vs. 81.73% in those with primary pituitary hyperplasia. As the pituitary doubles its size during pregnancy\textsuperscript{[1]} and increases by 120% in the third day postpartum\textsuperscript{[31]}, we may suggest that primary pituitary hyperplasia to be another indication for pre-pregnancy dopamine agonist therapy in order to shrink the pituitary size in a manner similar to the management of macroadenoma. No sufficient information regarding primary pituitary hyperplasia found in all the literatures reviewed in this study. Simple sella turcica x-ray should be abandoned as a test for the pituitary because of its low sensitivity, specificity and accuracy (Table 6). Interpretation of sella X-ray is vague and incorrect\textsuperscript{[11,12]}.

From the results of this study and from reviewing literatures the following work-up suggested in the diagnostic evaluation of female HPRL:

First: whenever clinical features of HPRL are present, basal PRL should be measured and secondary HPRL should be diagnosed before treating the symptoms in order not to miss serious diseases and pituitary or brain tumors.

Second: Then if the basal PRL is > 18.5 ng/ml (as suggested from our study), MRI is indicated in order to differentiate pituitary macro- and microadenoma, pituitary hyperplasia or other brain tumors. MRI diagnosis of pituitary macroadenoma and PRL of > 85

ASSOCIATION OF MULTIPLE NEUROLOGICAL DISEASES IN YOUNG FEMALE: CASE REPORT

Abdul-Kareem A.M. FRCP, Hasan A. Al-Hamdani FICMS

Abstract
A 20-year-old female was diagnosed as a case of epilepsy since 1995. The patient was diagnosed as a case of myasthenia gravis in April 2002. Since 1999, her complaint became more announcing over two years. Until April 2002, when the patient consulted a neurologist, she was diagnosed as case of Myasthenia gravis.

The patient diagnosed as a case of multiple sclerosis then after. The key to the clinical criteria for the diagnosis was lesions disseminated in space and in time. This case may represent an association of multiple neurological diseases of dysimmune reaction.

Key words: Multiple Sclerosis, Myasthenia and epilepsy


Introduction
Myasthenia gravis (MG) is not rare, has a prevalence of at least one in 7500. It affects individuals in all age groups, but peaks of incidence occur in women in their twenties and thirties and in men in their fifties and sixties. Overall, women are affected more frequently than men, in a ratio of approximately 3:2[1]. The neuromuscular abnormalities in MG are brought about by an autoimmune response mediated by specific anti-acetylcholine receptor (anti-AChR) antibodies. The anti-AChR antibodies reduce the number of available AChRs at the neuromuscular junctions[2]. Multiple sclerosis affects approximately 350,000 Americans and 1.1 million individuals worldwide. The prevalence of MG is probably not affected by geographic variation on the other hand the prevalence of multiple sclerosis has been shown to vary with geographic latitudes[1].

Using the definition of epilepsy as two or more unprovoked seizures, the incidence of epilepsy is approximately 0.3 to 0.5% in different populations throughout the world, and the prevalence of epilepsy has been estimated at 5 to 10 persons per 1000. Because seizures are common, this clinical problem is encountered frequently during medical practice in a variety of settings[3]. Although epileptic seizures are uncommon in multiple sclerosis, they are more prevalent than in the general population, which may support an etiological relationship. Gurtubay reported two patients where the epileptic seizures formed part of the first episode of their illness[4].

The Case:
A 20-year-old female was diagnosed as a case of epilepsy since 1995. The seizures were uncontrolled. The seizures were generalized tonic clonic in nature without focal symtomatology. Tongue biting and incontinence accompanied the seizures, which were followed by confusion for as long as thirty minutes. She was maintained on 300mg of Carbamazepine twice daily
Distribution of neurological diseases … Abdul-Kareem & Al-Hamdani

with poor compliance and variable response.
The patient diagnosed as a case of myasthenia gravis in April 2002. Since 1999, increased in severity over two years, the patient started to have diplopia, drooping of upper eyelids, difficulty in chewing and swallowing, nasal regurgitation, inability of combing her hair and difficulty in climbing stairs. Facial weakness produces a “snarling” expression when the patient attempts to smile. Speech has a nasal timbre. The examination reveals limb weakness is often proximal and asymmetric. This weakness, by exertion with diurnal variation. Deep tendon reflexes were preserved. Until April 2002, when the patient consulted a neurologist, and was diagnosed as case of MG. The diagnosis was confirmed by neostigmine test and electroneurophysiological study. She was kept on pyridostigmine, with good improvement. She was advised for thymectomy but her family refused.
The patient was admitted to our hospital on June 2002 because of impairment of her balance, clumsiness of the hands, and a feeling of weakness and tiredness in the legs. She was admitted to the hospital on October 2002 because of an acute onset left sided weakness. Over the course of a few days, her left arm and leg became weak and her left leg become numb. She then noticed that her walking went unsteady. Her symptoms progressively worsened up to the time of her admission to hospital. The examination revealed normal fundi, bilateral facial palsy, of an upper motor neuron type more on the right. All the tendon reflexes were hyperactive and were unequal, being more active on the left side than the right and Babinski sign bilaterally. The superficial abdominal reflexes could not be elicited. Finger nose test revealed intention tremor. The patient was unable to walk steadily along a straight line. Vibration sense was impaired bilaterally over the malleoli and joint sense was impaired in the toes. The remainder of the physical examination disclosed no abnormal findings.
The patient’s birth and development were normal. She did not have a history of encephalitis or febrile convolution. She is unmarried and because of her condition is unemployed. There is family history of MG. Her sister was diagnosed as a case of MG.
Visual evoked potential showed prolonged P100 latencies in both eyes, but well preserved waveform. Connective tissue screen normal. Thyroid function test was normal. Brain MRI was normal.
The patient diagnosed as a case of Multiple sclerosis. The key to the clinical criteria for the diagnosis was lesions disseminated in space and in time. She received pulses therapy of methyl prednisolone with Good improvement.

Discussion
This case may represent an association of multiple neurological diseases of dysimmune reaction. The present case may be an example of multiple medical disorders characterized by immune dysregulation and represents the association of MG, multiple sclerosis and epilepsy.
Current evidence indicates that multiple sclerosis is an autoimmune disease that develops in a genetically susceptible individuals who have resided in certain permissive environments. Multiple sclerosis and MG occasionally are found in association with other diseases but rarely in association with each other. Both diseases are immunogenic in origin, and their association is probably not coincidental.
There have been numerous case reports of the concurrence of MG and multiple sclerosis. At least 28 cases of MG in combination with multiple
sclerosis have been described in the literature. Margolis and Graves in 1945 described a 43-year-old white female with an 18-year history of transient neurologic signs and symptoms felt to be manifestations of multiple sclerosis fleeting ocular palsies develop that never completely cleared, and she noted worsening of her ocular symptoms with fatigue. She responded to neostigmine with clearing of her ptosis and of much of the ocular palsy..

Multiple sclerosis may be present in the MG patient as described by Kean and Hoyt. Patten and associates have described three patients, with an overlap syndrome or both multiple sclerosis and myasthenia gravis. Aita and co-workers described 4 cases of unusual combination of MG and multiple sclerosis.

Certainly, these interesting patients with their unusual combination of diseases raise more questions than they answer.

There have been numerous case reports of the concurrence of MG and multiple sclerosis, again suggesting a common autoimmune basis, but the statistical association is not certain.

The finding of autoimmune system activation in patients with a seizure disorder has lead to the suggestion that immune mechanisms may play a role in the pathogenesis of some forms of epilepsy. Although epileptic seizures are uncommon in multiple sclerosis they are more prevalent than in the general population, which supports an etiological relationship. Similarly, in a considerable proportion of patients with multiple sclerosis and epileptic seizures, alterations in magnetic resonance and electroencephalologic studies that can be correlated with the clinical features of epilepsy were observed. There is great variability with regard to the type of seizure, point at which this occurs during the course of the disease, degree of recurrence and other aspects.

In 1977, Pechadre et al reported that children with epilepsy who were treated with intramuscular injections of immunoglobulin for recurrent upper respiratory tract infections had a decrease in the frequency and severity of their seizures. This has been supported by several reports. The suggestion of Masson, may explain how the immune dysregulation affect the nervous system to develop these conditions, by that acquired ionic channel dysfunction resulting from autoimmune aggression. Channelopathies are responsible for muscular diseases certain forms of Mendel's law hereditary epilepsy.

It probably plays a part in the clinical, and particularly the sensitive expression (paresthesia and pain) of certain central nervous system affections, such as multiple sclerosis.

References
10. Masson, C.: Ion channel abnormalities 
    (“channelopathies”) in neurologic diseases. 
المجلة العراقية للعلوم الطبية
قائمة المحتويات

المقالات

- استحدث طريقة منتجة لخطوط الزرع النسيجي للخلايا المفاوية
- إسحاق إبراهيم طهيف، ليلي شبيب العمر، نهاد عبد الهيمن
- التغييرات في مستوى العناصر الحمضية في مصل مرضى الثديية الاحشائية
- د. البشير، حبيبي زي زي، حسن كاظم عبد الحسين، هدي ظاهر
- اداء المراهقين المصابين بداء السكري في المدارس: تقرير أولي
- عبد الحسين مهدي الياباني، جواد كاظم البیدان، امیر غاني معاة، امیر نايري
- نسبة الابتسامات في النمشنبطات إلى الانتين النمشنبطات 
- التهاب الكبد الفيروسي 
- وقار عبد الفهد الكبيسي، م살ا عبد الحسين
- دراسة مختلف الأعراض المرضية والديموغرافية لمرضي التلالسما وعائلتها مع الهيموجلوبين، بعض المعادن
- والعناصر الشحيحة في مرضى سرطان الدم الحاد
- ايناس طالب عبد الكريم، فریان حسن عبد الجليل، نتیج نعوان المعاوض
- دراسة بعض العوامل الديموغرافية والتشخيصية المحوّرة في مرضى سرطان الدم الحاد
- علاء كريم محمود، سعيد بوجی خوری، نوری عبد الرؤف زیدی
- تولیة الانفصال المومیة في أورام غدة البروستات
- فائزة عفتن الرأوي
- مستويات النخاس والزینك ونسبة النخاس/الزینك في مصل مرضى الانفصال الرئوی
- بحیبی حیبی زی فیی، علاء كرم محمود، سالم محمود
- عمر الأند الزواج كمؤشر للصحة الأنجابیة
- ايناس طالب عبد الكريم، عبد الحسين مهدي الياباني
- الدور الأدیاعي للنخاس، المقصد، والمنهموم خلال فترة نمامة الأطراف في اجنة النجاح
- بحیبی حیبی زی فیی، حیدر جودا مبارک، عیسی فاضل مجید
- عدم الخصوبة في الذكور والدرو الوظیفی للخارصین
- علي مثنی البلداوي، تزار أحمد طه، عیسی عبد الامیر العیان
- دراسة عشوائية مستقلة تتأثر علاج مایتوسماسین می مع مایتوسماسین می بالمقارنة مع مایتوسماسین می 1 مركب
- محمد العزاوی، عبد الله رضوی، حمید حمید حمید
- تدریم الثدي في مدينة سامراء
- حارث محاضر الخطيب

المجلة العراقية للعلوم الطبية 2005، المجلد 4، العدد 1
تعداد خلايا الأيسينوفيل وعلاقته بالربو لدى الأطفال

حسام محي الطولاني، فالح سالم سرحان، خدي حسن علي

مستوى الـKالمسبوم في مصل دم مرضى السكري من النمط ٢

بيبي خورشيد السيفاني

نقص الفحص الـجليقي الخلقي لدى الأطفال الذين يراجعون عـيادة الغدد الصماء و السكري لدى الأطفال في مستشفى الكاظمية التعليمي.

نشأت عزيز نشأت، حسام الطولاني

اختلال وظيفة التنفس لدى مرضى الوهن العقلي الوأبل

عبد العلّم عبد الكريم، ساجد إبراهيم الحسيني

فرط برووكتين الدم في النساء: دراسة تحليلية للملامح السريرية وتشخيصية

الإسباب: هل يتوجب إجراء التصوير بالرنين المغناطيسي دائمًا؟

سحر لويس خليلة

مزالة لعدد من الأمراض العصبية لفتاة صغيرة السن: حالة مسجلة

عبد العلّم عبد الكريم، حسن عزيز الحمamy

النجمة العراقية للعلوم الطبية ٢٠٠٥ م، المجلد ٤، العدد ١
استحداث طريقة منتجة لخطوط الزراعة النسيجي للخلايا اللمفاوية

اسماعيل إبراهيم لطيف، ليلى شهيب العمر، نضال عبد المهنيم

الخلاصة

خليفة الدراسة: إن استئناف الخلايا الوراثية النواة من محتويات الدم الكامل يؤدي إلى احتواء على الأنواع المختلفة من الخلايا. مع ذلك، فإن الخلايا المقاومة نوع (T) يمكن أن تنمو وتنمو في نموها على الأنواع الأخرى من الخلايا لمنتجة في النهاية وسط غني بها.

هذة الدراسة: اجريت دراسة لإجراء محاولة لإبتكار طريقة جديدة لانتهاج وعزل خلايا الخلايا المقاومة في مكونات الدم الكامل. سلسلة التجارب هذه تم اجراءها على الأشخاص الذين أن الطريقة المستخدمة هي نفسها أجريت على جميع الحالات.

طريقة العمل: تم زرع 1 مل من الدم الكامل المضاف له مادة الهيبرلين إلى قارة الزراع النسيجي والتي تحتوي على 9 مل من الوسط الزراعي المحلى للخلايا. تم حضانته في حاضنة ثانية أوكسيد الكرسي تحت درجة حرارة 37 درجة مئوية لمدة ثلاثة أيام. اخذ 1 مل من هذا الزرع النسيجي وجزء ثاني من قارة أخرى تحتوي على 9 مل من الوسط الزراعي المحلى لخلايا. كربت هذه العملية كل ثلاثة أيام لحين تكون عائل من الخلايا الوراثية النواة تتخلل كرات الدم المتجحلة وخلايا اسعوديين.

النتائج: تم العثور على خلايا وحيدة النواة وبصورة نفية والتي تم ملاحظتها بواسطة الكرسکوب. وذلك بعد فترة اسبوعين من المحافظة عليها. وبعد فصلها عن مكونات الدم الأخرى بعد فترة حضانة 24 ساعة والتي تم فصلها بواسطة الوسط الزراعي المحلى لنمو.

الاستنتاج: تم ابتكار طريقة جديدة لعزل وتكييف الخلايا المقاومة من محتويات الدم الكامل عيناً كما أتم التطرق إلى هذا الاكتشاف سابقاً. وقد تم ملاحظة امكانية عمل الخلايا المقاومة نفسها كعامة بادئة في الزواج بواسطة استناد هذه الخلايا، وذلك تم الخطأ إلى مختلف الطرق لتكوين خطوط من الخلايا المقاومة نوع (T) في هذه الدراسة لم يتم استخدام خلايا مساندة أو إضافة (IL2).

مقتفي الكلمات: زرع الخلايا المقاومة، خط الخلايا، قايموكولونين.

قسم الأحياء المجهرية (كلية الطب- جامعة الهرير).

الملخصات العربية للعلوم الطبية ٢٠٠٥، المجلد ٤، العدد ١، ص ٩-٣٣
المملصات العربية

التغييرات في مستوى العناصر الضئيلة في مصعول مرضى اللشمائية الاحتشانية

ندي البشیر، يحيى يحيى زكي فريد، حسين كاظم عبد الحسين، هدى ظاهر هدى

الخليفة

خلالة الدراسة: يعتبر مرض اللشمائية الاحتشانية من الأمراض المستوطنة في العراق وحسب أخبار أخصائيات منظمة الصحة العالمية (WHO 2000) وهو يصيب الأطفال دون سن الستين، وتعتبر العناصر الضئيلة دوراً في العلاج والتشخيص للأنواع المختلفة من الأمراض الطفيلية، وربما تكون كدليل مهم في متابعة المرض والاستجابة للعلاج.

هدف الدراسة: دراسة مستوى العناصر الضئيلة في مصعول المصابين بمرض اللشمائية الاحتشانية، وأيضا العلاقة بين الإصابة بالمريض ليكون مستوى تلك تم جمع 26 العناصر كدليل يتم من خلاله التعرف على الأصلية بالمرض ومتابعه بعد العلاج.

طريقة العمل: عينة من المرضى من الذكور والإناث الذين تراوحتم مابين 2-3 أشهر، ثم تم تحديد العناصر الضئيلة التي لها علاقة بالناحة كالثناوس الخارجي والمغنيسيوم، حيث تم قياس مستوياتهم في مصعول المريض مقارنة مع الأصحاء باستخدام مطيافية الاتصال الذهري.

النتائج: اوضحت النتائج وجود زيادة في مستوى النحاس في مصعول المريض مقارنة بالاصحاء في حين كان هناك نقصان في مستوى كلا من الخارجي والمغنيسيوم عند المصابين مقارنة بالاصحاء.

الاستنتاج: تعكس النتائج التغييرات الكيميائية الحياتية المصاحبة للمرض نتيجة لتفاعل الحاضر ما بين الطلبية والخلايا المناعية المهاجمة لها.

مفتاح الكلمات: الحمي السوداء، العناصر الضئيلة، النحاس، الزئبق، المغنيسيوم، اللشمائية الاحتشانية.

مركز البحث الطبي (جامعة النهرين)
قسم الكيمياء، الكويت (كلية الطب، جامعة النهرين)
قسم الكيمياء، الكويت (كلية الطب، جامعة كربلاء)

المجلة العراقية للعلوم الطبية 2005، المجلد 4، العدد 1، ص 13-10
الملخصات العربية

اداء المراهقين المصابين بداء السكري في المدارس: تقرير أولي

عبد الحسين مهدي الهادي١، جواد كاظم الديوان٢، اقبال غامض معلمة٣، امجد نيازي٣

الخلاصة
خلفية الدراسة: يسعى المراهقون الى تكوين الذات والاستقلالية وتحمل كل تحديات الحياة وداء السكر في فترة المرحلة يؤدي الى تعثر النمو النفسي وتناثر قابلية المراهق على مواجهة تحديات الحياة ومنها اداء في المدرسة.

هدف الدراسة: توضيح اداء المصاب بداء السكر في المدارس.

طريقة العمل: تم جمع معلومات (العمر، الجنس، فترة المرض، النشاط الرياضي، النشاط الدراسة ومرحلة الدراسة) عن 120 مراهقا بداء السكر. تم استخدام تحليل الانحدار المتعدد لدراسة الارتباط بين الاداء في المدرسة والعوامل الأخرى.

النتائج: ظهرت علاقة إحصائية ذات قيمة معنوية بين اداء المراهق في المدرسة وعدد الزيارات لعيادة السكر ومارسه الرياضة.

الاستنتاج: عدد الزيارات لعيادة السكر ومارسه الرياضة تحسن اداء المراهق المصاب بداء السكر في المدرسة.

مفتاح الكلمات: المراهقين، داء السكر، الانتصارات المدرسية

١ قسم طب المجتمع (كلية الطب، جامعة النجاح)
٢ قسم طب المجتمع (كلية الطب، جامعة الآبار)
٣ كلية التمريض (جامعة بغداد)
٤ الهيئة العراقية للاختصاصات الطبية

المجلة العراقية للعلوم الطبية ٢٠٠٥ م، المجلد ٤، العدد ١، ص ١٧-١٤
الخلاصة

خلفية البحث: أن التهاب الكبد الفيروسي ج هو السبب لغالبية حالات التهاب الكبد التي تتبع نقل الدم. إن التحاليل الكيميائية لانزيمات الكبد تستخدم لتحديد مدى تلف الكبد عند المصابين بالتهاب الكبد الفيروسي ج.

هدف البحث: تقدر نسبة الإسبارتات امينوتراكسيز إلى الألانين امينوتراكسيز (AST/ALT) كطريقة غير مؤذية لتقدير مدى تلف الكبد عند المصابين بالتهاب الكبد الفيروسي ج.

طريقة العمل: تضمنت الدراسة مجموعتين: المجموعة الأولى تضمنت 238 نسمة من مرضى الالتهاب البصري في مستشفى الزهراءي (منهم 172 لديهم إسبرتة للأسس tanto مع AAMG) والمجموعة الأخرى تضمنت 86 نسمة من مرضى الالتهاب البصري في مستشفى الزهراءي (منهم 66 لديهم إسبرتة للأسس tanto مع AAMG).

النتائج: أظهرت النتائج أن معدل نسبة أنبوب الدم البصري في المرضى الذين لديهم إسبرتة للأسس tanto مع AAMG. عند المرضى الذين لديهم إسبرتة للأسس tanto مع AAMG. عند المرضى الذين لديهم إسبرتة للأسس tanto مع AAMG. عند المرضى الذين لديهم إسبرتة للأسس tanto مع AAMG. عند المرضى الذين لديهم إسبرتة للأسس tanto مع AAMG.

الاستنتاج: إن معدل نسبة أنبوب الدم البصري في المرضى الذين لديهم إسبرتة للأسس tanto مع AAMG. عند المرضى الذين لديهم إسبرتة للأسس tanto مع AAMG. عند المرضى الذين لديهم إسبرتة للأسس tanto مع AAMG. عند المرضى الذين لديهم إسبرتة للأسس tanto مع AAMG.

مفتاح الكلمات: نسبة الإسبارتات امينوتراكسيز إلى الألانين امينوتراكسيز، التهاب الكبد الفيروسي ج.
دراسة مختبر الأعراض المرضية والديموغرافية لمرضى التلامسية وعلاقاتها مع الهيموگلوبين،
بعض المعادن والعناصر الشحمية في دم المرضي

إيناس طالب عبد الكريم، فریال حسن عبد الجليل، ثابت نعمان العزاوي

الخلاصة:

الفحصية للدراسة: تعتبر التلامسية من أكثر الأمراض الوراثية انتشاراً في العالم و هي موجودة بنسبة عالية في الحزام الممتل من حوض البحر الأبيض المتوسط و الذي يمر خلال منطقة الشرق الأوسط في أسيما إلى مناطق شبه القارة الهندية و بورما و جنوب شرق آسيا. لاتزال بيئة ثالاسيميا تظهر كمشكلة صحية عامة في العالم أجمع. كما أن أعراض المرض المتعلقة بعدم أخطار العلاج الخاص بالمرض لا تزال موجودة في البلدان التي تلتقي إلى المصادر الأساسية التي تدعم برامجه أطعمة الدم للفترات طويلة.

هدف الدراسة: دراسة مختبر الأعراض الموجودة عند المرضي الصابين بفقر دم البحر الأبيض المتوسط و الذين يراجعون مركز فقر الدم لحوض البحر الأبيض المتوسط في مستشفى أين البلدي لأجل إعطائهم الدم. دراسة مدى العلاقة بين مختبر الأعراض الموجودة عند المرضي مع مختلف الصفات الديموغرافية لهذا المرض. دراسة مستوى العلاقة بين الأعراض الموجودة عند المرضي و مستوى الهيموغلوبين بعض المعادن و العناصر الشحمية و الألبيون في دم المرضي.

طريقة العمل: أجريت دراسة عرضية مقطعية للفترة ما بين 09/2022 إلى 12/2021 في مركز التلامسية (فقر دم حوض البحر الأبيض المتوسط) في مستشفى أين البلدي في بغداد. حيث اختبر 157 مريض بصورة عشوائية عند مراجعتهم المركز لفقر الدم استعملت استعارة مروية بشكل جيد تُلاح الأعراض المختبرة أخذ نموذج دم من كل مرض و حفظ بعد فصله في درجة حرارة 200 درجة مئوية لحين الاستعمال. أجريت الفحوصات الخاصة بالهيموغلوبين و المعادن باستعمال الطراقة المعتمدة لكل مادة.

النتائج: أظهرت النتائج أن من بين 157 مريض تم تнстру دراستهم كان هناك 121 (112/2%) من سكان مدينة بغداد و 107 (15/2%) من مناطق حضرية. كما أن معدل العمر عند التشخيص كان سن 15 سنة و كانت التلامسية الشديدة تشكل نسبة 77/2% من المرضى (32/6%) كان هناك 108 مريض (48/8%) يدرجون في فئة بين 24 - 4 أسابيع و أخذ بالدفصول لأكثر من 4 مرات بالأسبوع عند 99 مريض (32/1%). كما كان هناك 78 مريض (48/4%) يعانون من سوء التغذية. و捔خت وجد مختبر العلامات المرضية بنسبة عالية على المرضي مراجعين للمركز و قد أجري تحليل العلاقة بين مختلف هذه الأعراض و كذلك بينها و بين نسبة الرصاص و السلييوم. الحديد المجموع الكلي لقابلية الحديد الرابطة و الهيموغلوبين في الدم و كما وجد أن هناك علاقة بين العمر و الجنس مع مختلف العلامات المرضية عند المرضي.
المجلة العراقية للعلوم الطبية ٢٠٠٥ م، المجلد ٤، العدد ١، ص ٣٧٢١-٣٧٤٤

المجلة العراقية للعلوم الطبية

الاستنتاج: من الضروري جداً تهيئة مراكز عدة في مختلف أرجاء العراق وزيادة كفافتها المختبرية لتشمل أجراء تحليل تكاثر الجينات الخاص بهذا المرض. وضع برامج مرتكزة على أجراء الاختبارات لحاملي المرض، الاستشارة الطبية للمرأة في الزواج وقبل الحمل وفي بداية الحمل. التشخيص المخبرى للمرض أثناء الحمل باستخدام DNA PCR وفحص الأم الخواض من الجنين.

مفتاح الكلمات: المعدن، العادات الطبية، العادات السريرية، مرضى الفيما.
الملخصات العربية

العوامل المضادة لكسادة الكريات في مرضى الثلاسيميا

صبح سالم المنثل، هراج موسى، نجا عبد الرزاق

الخلاصة:

خلفية الدراسة: إن زيادة كسادة شحوم الكريات في مرضى الثلاسيميا يؤدي إلى انتظام انزيمات السوبر أوكسايد بكميات كبيرة، وهذا هو سبب تحلل كريات الدم الحمراء في مرضى الثلاسيميا.

هدف الدراسة: أجريت هذه الدراسة لغرض حالة كسادة شحوم الكريات الحمراء في مرضى الثلاسيميا وكذلك قياس العوامل المضادة لكسادة الخلية.

العمليات: أجري فحص انزيمات السوبر أوكسايد والكاتاليزات لستة وسبعون مريضاً للثلاسيميا الثقيلة وابتعة عشر مريضاً للثلاسيميا الثقيلة وتعسة عشر اصحاء.

النتائج: وجدت دراسة الثلاسيميا الثقيلة لديهم انزيم السوبر أوكسايد نسبة أعلى (وهم من ناحية إحصائية) من الأصحاء، بينما في الر能看到 الثقيلة والكاثاليزات لديهم انزيم الكاثاليز نسبة أعلى (وهم من ناحية إحصائية) من الأصحاء وكذلك اظهرت النتائج بأنه كلاً قلت نسبة الهيموغلوتين عند مرضى الثلاسيميا الثقيلة كلاً ازدادت نسبة انزيم السوبر أوكسايد.

الاستنتاج: انزيم السوبر أوكسايد يكون أكثر في مرضى الثلاسيميا الثقيلة وتتناسب كميته بشكل عكسي كلاً قلت نسبة الهيموغلوتين.

المفتاح الكلمات: ثلاسيميا، سوبر أوكسايد، كاتاليز

قسم علم الأمراض (كلية الطب-جامعة النهرين) قسم الكيمياء، و الكيمياء الحيوية (كلية الطب-جامعة النهرين)
تولد الأوعية الدموية في أورام عدسة البروستات
فانزية عفتان الراوي

الخلاصة

خلفية الدراسة: تولد الأوعية الدموية يعني تكوين أوعية دموية جديدة، عملية طبيعية حرجة تحدث في الجسم في النزلة الصحية والمرضية.

الهدف من الدراسة: التقييم العددي للأوعية الدموية في أورام عدسة البروستات ومقارنتها مع درجة الورم.

طريقة العمل: 33 حالة مصورة من نماذج عدسة البروستات (8 تضخم عدسة البروستات الحميد و15 عدسة أورام غديه مقصودة بالتناوب بين ذات تؤثر جيداً، متوسط وضعيف). صممت مثلها مقارنة ببعضها م琵طود وابوضين، صبغة فان كيزي وماشون ترايكروم. أحصيت عدد الأوعية الدموية وكثافتها حسب معدلات رياضية، وقررنت النتائج مع درجة تأثير الورم.

النتائج: أردت عدد الأوعية الدموية والحد الأعلى لها مع زيادة درجة الخبث وتراوح من 19.1 في التضخم الحميد إلى 20.0 في الأورام الخبيثة ذات التأثير ضعيف.

الاستنتاج: أظهرت الدراسة علاقة ذات تأثير بين درجة الورم ونسبة الأوعية الدموية.

مفتاح الكلمات: تولد الأوعية الدموية، أورام عدسة البروستات.

قسم علم الأمراض (كلية الطب-جامعة النهرين)
مستويات النحاس والزنك ونسبة النحاس/الزنك في مصل مرضى التهاب المفاصل الرثوي

الخلاصة

الهدف

الطريقة العملية: تضمنت 97 شخصاً مقصدين إلى ارتفاع وخصوم مريضاً (37 إثاث، 17 ذكور) يعانون من مرض التهاب المفاصل الرثوي و 49 مقصدين إلى مرشح مريضاً (21 إثاث، 8 ذكور) بعمر يتراوح بين (32-57 سنة) و لديهم فعالية قليلة للمرض و 45 مريضاً (16 إثاث، 9 ذكور) بعمر يتراوح بين (29-61 سنة) و لديهم فعالية مرتفعة للمرض و مقارنة النتائج مع 43 شخص سليم بعمر يتراوح بين (19-61 سنة). تم تقييم مستوي النحاس والزنك في مصل المرضى بتحليلية مطيافية الاتصالات التي.

التقديم: مستوى النحاس في مصل الدم وكذلك نسبة النحاس/الزنك تزداد بصورة ملحوظة في كل المجموعتين قيد الدراسة مقارنة بمستواها في مصل الأصحاء. إضافة إلى انخفاض ملحوظ في مستوى الزنك في مصل المرضى ذو الفعالية القليلة و بصورة أكبر عند المرضى ذو الفعالية العالية للمرض.

الاستنتاج: إن التغير في مستوى النحاس والزنك في مصل المرضى المصابين بالتهاب المفاصل الرثوي له علاقة بفاغية و درجة المرض مع تسلسل الضوء على أهمية دور العناصر في الحالات المرضية و الفسيولوجية.

مفتاح الكلمات: التهاب المفاصل الرثوي، النحاس، الزنك، المصل
الملخصات العربية

عمر الأم عند الزواج كمؤشر للصحة الأنجابية

إيناس طالب عبد الكريم، عبد الحسين الهادي

الخلاصة

هدف الدراسة: هو تحديد عمر المرأة عند الزواج وعلاقته بالحالة العنيفية وبيئية و مدى تأثيرها على الصحة الأنجابية عند الأمهات.

طريقة العمل: أجريت دراسة مقطعية عريضة حيث أخذت المعلومات بطريقة عشوائية من 800 أم بحالة صحية جيدة و من خلال زيارتهم إلى حضور مرشد صحية من مدينة بغداد و خلال الفترة من حزيران إلى شهر تموز لعام 1994. تم اخذ المعلومات من الأمهات من خلال استمارات مدونة بشكل جيد.

النتائج: أظهرت النتائج أن هناك علاقة ذات غمزة إحصائي بين عمر المرأة عند الزواج و عدد من المؤثرات مثل المستوى التعليمي للمرأة، الفترة بين الحمل الأول والثاني، عمر الأب عند الزواج، عدد مرات الحمل وعدد الأطفال دون سن الخامسة في الأسرة، درجة الكثافة الأسرية، درجة القدرة بين الوالدين (P<0.001)، وكذلك كان هناك علاقة ذات غمزة إحصائي مع عمل الزوج، وعدد وفيات الأطفال دون سن الخامسة (P<0.01). بينما لم تكن هناك علاقة ذات غمزة إحصائي مع نوع العائلة وعدد مرات الإسقاط عند الأم (P>0.05).

الاستنتاج: إن عمر الأم عند الزواج يعتبر عامل مهم في الصحة الإنجابية للمرأة عندما درست مع مختلف العوامل الاجتماعية وبيئية مما يؤكد على ضرورة أن يكون هناك إقبال من الشباب على المعلومات الصحية، وثلك العاملين في مجالات الصحة يجب أن يعملوا على توفير المعلومات الضرورية، التي تساعد النساء الصغيرات في العمر لكي تكون لديهم الثقة في استخدام مصادر المعلومات المثلى لهم.

مفتاح الكلمات: عمر الأم، الصحة الإنجابية.

قسم طب المجتمع (كلية الطب-جامعة النيرو)

المجلة العراقية للعلوم الطبية ٢٠٠٥م، المجلد ٤، العدد ١، ص ٦٢-٥٧
المجلة العراقية للعلوم الطبية

الملخصات العربية

الدور الإحيائي للنحاس، القصدير و المغنيسيوم خلال فترة نماء براهم الأطراف في أجنة الدجاج

هيحيى بحبي زكي فريد، حيدر جواد مبارك، مي فاضل ماجدة

الخلاصة

خلفية الدراسة: ان نماء براهم الأطراف يستحث بالحافة الظهيرة للأدبيم الظهير. وجد ان لعناصر الزهيدة دور مهم في نماء الإحيائي للانسجة كما في أنسجة الأورام.

هدف الدراسة: أجريت هذه الدراسة للكشف عن الدور الإحيائي المحتمل لعناصر الزهيدة مثل الزنكي، النحاس، والمغنيسيوم في نماء الأطراف المستحث بالحافة الظهيرة للأدبيم الظهير.

طريقة العمل: استعملت أجنة الدجاج في مراحل هامبرك و هاملتن 26-20. تم قياس العناصر الزهيدة في براهم الأطراف المحتوية وغير المحتوية على الشحنة اليوتي للأدبيم الظهير.

النتائج: وجد ان انخفاض تركيز الزنكي في أنسجة براهم الأطراف التي لا تمتلك الحافة الظهيرة للأدبيم الظهير يشير إلى العلاقة بين هذا العنصر الزهيد و الفعل الحات لهذه الحافة في تكون الأطراف. ربط تركيز النحاس المكتشف فقط في البراعم التي لا تمتلك الحافة الظهيرة بالتنظيم الجنيني لبراعم الأطراف. ان اختلاف تركيز المغنيسيوم في براهم الأطراف اعتبر كشفا للأدبيم الظهيرة في التنوك الجنيني لبراعم الأطراف.

الاستنتاج: ان العناصر الزهيدة قد تتناول دور هام في عملية التبرع الجنينية.

مفتاح الكلمات: براهم الطرف، العناصر الزهيدة، الزنكي، النحاس، المغنيسيوم، النمو

قسم الكيمياء والكيمياء الحياتية (كلية الطب-جامعة النهرين)
قسم التشريح البشري (كلية الطب-جامعة النهرين)
فرع الأنسجة والأجنة - قسم التشريح البشري (كلية الطب-جامعة النهرين)

المجلة العراقية للعلوم الطبية

٢٠٠٥ م، المجلد 4، العدد ١، ص ٦٦-٦٣
الملخصات العربية

عدم الخصوبة في الذكور و الدور الوظيفي للخارصين

علي تقي البلداوي، أحمد ناجي، عقيل عبد الأمير العاني

الخلاصة:

خلفية الدراسة: عدم الخصوبة في الذكور تعرف بأنها عدم التأقلم على إنتاج طف لحى غياب السبب عند الأناث. تمكن معظم أسبابها في اختلاف النسب الطبيعية للحى. وبعد الخدراءين إحدى مكونات السائل المنو الهامة له من دورين رئيسيين في عملية الخصوبة والانجاب.

هدف الدراسة: يهدف البحث إلى دراسة العلاقة بين تراكيز الخدراءين في مصل الدم و مصل السائل المنو و جودة السائل المنو بين الرجال غير الخدراءين والخارصين.

طريقة العمل: اجري البحث على ثمانين و خمسون ذكرًا متوسطًا (مجموعة غير الخدراءين ) حيث تم اختصاصهم لاستقصاء أسباب عدم الخصوبة و سبعة وثلاثون ذكرًا متوسطًا (مجموعة الخدراءين ) لهم زيجات حالية درسوا كمجموعة سيطرة. تم إجراء تحليل السائل المنو و الهرمونات النووية للمجموعتين كما و اجري قياس نسبة تراكيز الخدراءين في مصل الدم و مصل السائل المنو باستخدام تحليل مقياس شدة اللونية.

النتائج: أظهرت الدراسة أن جميع خواص السائل المنو (العدد، الحركة، الهيئة الخارجية) للرجال غير الخدراءين أقل مما هو عليه الحال عند الرجال الخدراءين. باستثناء، هورمون الشحم الخصوبي كانت بقية الهرمونات النووية (هورمون البرودة، الهورمون المتب كجر)، للرجال غير الخدراءين ليست مختلفة مما عليه الحال عند الرجال الخدراءين. كما وجدت معدلات تراكيز الخدراءين في مصل الدم و السائل المنو أقل في الرجال غير الخدراءين إذا ما قورنت مع الرجال الخدراءين. كما أظهرت الدراسة عدم وجود علاقة بين تراكيز الخدراءين في مصل الدم مع تراكيزه في مصل السائل المنو في كل المجموعتين.

الاستنتاج: أظهرت الدراسة في ضوء النتائج التي تم التوصل إليها إلى أن الخدراءين يسهم في الخصوبة من خلال التأثير المباشر وغير المباشر على عملية الانطفاط.

مفتاح الكلمات: عدم الخصوبة، الخدراءين، السائل المنو، عملية الانطفاط.

مراجع:
\footnote{فرع الطب العلوي قسم علم الأمراض كلية الطب-جامعة الهرم.
قسم الكيمياء (كلية العلوم-جامعة الهرم).}

المجلة العراقية للعلوم الطبية ٢٠٠٥، المجلد ٤، العدد ١، ص٧١-٦٧
دراسة عشوائية مستقبيلة لتأثير علاج مايتومايسين سي مع مايتومايسين سي بالمقارنة مع مايتومايسين سي/مركب S2. متعاقب لغسل المثانة في سرطان المثانة السطحي

أحمد العزاوي، عبدالوهاب رفوقي جمال، محمود حياوي حماش

الخلاصة

خلفية الدراسة: يأتي سرطان المثانة بالترتيب الثالث في الذكور والمرتبة العاشرة في الأنان في الولايات المتحدة الأمريكية. في اححابين كبيرة بعد استئصالات تمت علاجات كيميائية في غسل المثانة.

هدف الدراسة: هو مقارنة بين قصرين لدراسة التأثير والفعالية والسمية لعلاج غسل المثانة بعقار مايتومايسين سي مقابل من علاج مايتومايسين سي ومركب S2 تعايقبا لسرطان المثانة السطحي.

طريقة العمل: دراسة عشوائية مستقبلية لمجموعتين من المرضى المصابين بسرطان المثانة السطحي (73 و73). بعد الاستئصال تؤثر المثانة عبر الأحليل مع متابعتهم لمدة 22 شهرا. المجموعة الأولى (A): استعملوا علاج مايتومايسين سي (غسل المثانة) 30 مل في اليوم الأول و 6 مساعي يوميا لعدة 22 شهرا. المجموعة الثانية (B): استعملوا علاج مايتومايسين سي ومركب S2 تعايقبا.

النتائج: بعد متابعة لعدة 22 شهرا، 45% من المرضى في المجموعة (A) كانوا خاليين من الرضي مقارنة مع 70% للمرضي في المجموعة (B).

الاستنتاج: النتائج بينت أن علاج غسل المثانة بعقار مايتومايسين سي مع مركب S2 تعايقبا كانت فاعلا جدا في انتها، و/أو الوقاية من سرطان المثانة السطحي.

مفتاح الكلمات: مايتومايسين سي، س2، غسل المثانة، سرطان المثانة السطحي

قسم الفيزياء (كلية الطب-جامعة النهرين)
قسم الكيمياء والكيمياء الحيوية (كلية الطب-جامعة النهرين)
فرع الأنسجة والأنبج-قسم التشريح البشري (كلية الطب-جامعة النهرين)

المجلة العراقية للعلوم الطبية 2005، المجلد 4، العدد 1، ص 26-72
تدرن الثدي في مدينة سامراء

خلاصه

خلفية الدراسة: إن تدرن الثدي ليس نادرًا في ضرع الحيوانات و خاصة الأبقار و لكنه أقل إصابة لدى المرأة و عادة لدى واحده و اندرون ذلك إصابة الثدي معًا و حتى لدى الرجل يمكن إصابته.

هدف الدراسة: البحث عن نسبة إصابة ثدي المرأة بالتدرن.


النتائج: تم شفاء 14 حالة من 15 إصابة بالتدرن الثدي باستخدام إيزونيازيد، ايثامبيوتول، و ريفادين لمدة شهرين ثم الاقترار على دوائيين منها لمدة 9 شهور.

الاستنتاج: إن تدرن الثدي عند المرأة يجب أن يكون في الحساب عند وجود قرة أو عقدة التهابية أو ندور أو عدة نواسر في الثدي لا تستجيب للعلاج التقليدي و لكنها تستجيب للأدوية المضادة للتدرن و يمكن شفاها تمامًا و لصعوبة عزل عصبات السل من الأنسجة يمكن اعتماد طريقة الاستجابة السريرية للعلاج التجريبي في التشخيص.

مفتاح الكلمات: الثدي، التدرين، أدوية مضادة للتدرين.

قسم الجراحة (كلية الطب-جامعة تكريت)

المجلة العراقية للعلوم الطبية 2005 م، المجلد 4، العدد 1، ص 80-77
تعداد خلايا الايزينوفيل و علاقته بالربو لدى الأطفال

حسام محي العلواني، فالح سلم سرحان

الخلاصة

خلفية الدراسة: الربو القصبي هو عبارة عن انسداد في المجاري التنفسية ينتج عن محفزات مختلفة. لقد شهد المرض زيادة في نسبة الأصابات وشدتها في الأونة الأخيرة. في مرض الربو هناك تضيق في المجاري الهوائية مع افرازات كثيفة إضافة إلى الالتهاب الذي يلعب دورًا مهمًا و هنا تحلبا الايزينوفيل دور مهم.

هدف الدراسة: هو دراسة العلاقة بين مرض الربو و تعداد خلايا الايزينوفيل في عينة الدم.

طريقة العمل: تضمنت الدراسة 55 طفل مصاب بالربو القصبي، و درست شدة الربو لديهم عن طريق العلامات السريرية، و جهاز فحص وظائف الرئة، و اخذت عينة دم وريدي من كل مريض لتقياس عدد خلايا الايزينوفيل.

النتائج: بينت النتائج ان 35 مريض كان مصاباً بنوبة متوسطة إلى شديدة، و كانت نسبة 82.8% منهم لديهم تعداد خلايا الايزينوفيل عالي (أكثر من 400 10^{-6} / مم3) بينما 17.2% كان تعداد الخلايا أقل من 400. العشرون مريض الباقين كانوا من ذوات الشدة البسيطة إلى المتوسطة و كان 80% منهم لديهم نسبة خلايا الايزينوفيل أقل من 400 و 20% نسبة عالية من الخلايا.

الاستنتاج: هناك زيادة في نسبة خلايا الايزينوفيل في دم مرضى الربو، و تزداد هذه النسبة مع زيادة شدة الربو.

مفتاح الكلمات: الربو القصبي، خلايا الايزينوفيل، شدة المرض.

قسم طب الأطفال (كلية الطب-جامعة النهرين)
قسم علم الأمراض (كلية الطب-جامعة النهرين)
المملوكتات العربية

مستوى الكالسيوم في مصل دم مرضى السكري من النمط 2

بيبين خورشيد السليفاني

الخلاصة

خلفية الدراسة: يعتبر الكالسيوم من العناصر الهامة في التصنيع الأحيائي، خزن، افراز، و حيوية الأنسولين.

هدف الدراسة: لمعرفة مستوى الكالسيوم في مصل الدم لدى مرضى السكري من النمط 2.

طريقة العمل: تمت الدراسة في عيادة الوقاية لداء السكري في الموصل لل فترة من تموز 2012 - شباط 2013 وقد شملت 120 شخساً من كلا الجنسين. ستون مريضاً من المصابين بدءاً السكري من النمط 2 و كلاً السكري من النمط 2 الذين حددت اعمارهم 11.6±47.6 سنة و 60 شخساً أصحاء كجيمية سيطرة معدل (± الانحراف القياسي) أعمارهم 14.3±5 سنة. تم قياس تركيز الكالسيوم والكولوكوز في مصل الدم.

النتائج: أظهرت النتائج ارتفاعاً ذا معنى في مستوى الكالسيوم والكولوكوز في مرضى داء السكري من النمط 2 السكري من النمط 2 في مرضى داء السكري.

الاستنتاج: زيادة الكالسيوم في مصل دم مرضى داء السكري من النمط 2 قد يعزى إلى عوامل أخرى و ليس زيادة الكولوكوز.

مفتاح الكلمات: داء السكري من النمط 2، الكالسيوم، الكولوكوز، فرط الكالسيوم، فرط الكولوكوز.

قسم الفلسفة (كلية الطب-جامعة الموصل)

المجلة العراقية للعلوم الطبية

٠٠٢٥ م، المجلد ٤، العدد ١، ص ٨٨-٨٤
الملخصات العربية

نقص الغدة الدرقي الخفقي لدى الأطفال الذين يراجعون عيادة الغدد الصماء و السكري لدى الأطفال في مستشفى الكاظمية التعليمي

نشاط عزيز نشأت، حسام العلواني، ايمان محمود

الخلاصة

خلاصة الدراسة: نقص الغدة الدرقي الخفقي يعتبر من أكثر أمراض الغدد الصماء الشائعة لدى الأطفال، و التشخيص المبكر له هامة و ذلك لمنع حدوث تخلف عقلي وبدني في حالة اعتداءعلاج مبكر.

هدف الدراسة: البحث عن نسبة الأطفال المصابين ب نقص الغدة الدرقي الخفقي في العراق.


النتائج: 24 من الأطفال كانوا من البنات و 16 ذكر و نسبة الأبناء للذكور 1 : 1.1. زواج الأقارب موجب في 36 (80%) من المرضى، (24.5%) لديهم مرض الغدد الدرقية في عوائلهم و (24.1%) من المناطق الريفية غرب بغداد. عشرة اطفال (25%) اكتشفوا في الشهر الأول من اعصارهم (15% في الأشهر الثلاثة الأولى و 25% في الأشهر الثلاثة الأولى) هم سبعة مرضى لديهم ضمور خفقي و خمسة لديهم انتباذ في الغدة و قد تم تقدير التطور الذهني لدى هؤلاء الأطفال و كذلك الأعراض و العلامات.

الاستنتاج: على الرغم من عدم معرفتنا بسبب الأطفال المصابين بالعراق إلا أنه هناك اللاحظ الأولية أنه ليس نادر حدوث و الأسباب الجينية ترجع و ذلك يوجد عدة اقتصاد مصايد و النسبة عالية للنزاع بين الأقارب في العراق. انس نقص الغدة الدرقية الولادي مرض ليس نادر الحصول و نقص برنامج وظيفي شاملي الفحص حديثي الولادة لتشخيص نقص الغدة الدرقية مبكرا.

مفتاح الكلمات: نقص الغدة الدرقية الخفقي، مراجعة.

قسم طب الأطفال (كلية الطب، جامعة النهرين) مستشفى الأطفال المركزي، بغداد، العراق

المجلة العراقية للعلوم الطبية 2005، المجلد 4، العدد 1، ص 96-89
الملخصات العربية

اختلال وظيفة التنفس لدى مرضى الوهن العظلي الوبيل

عبد المطلب عبد الكريم، ساجد إبراهيم الحسيني

الخلاصة

خلفية الدراسة: فإن العيادات الوبيل مرش مناعي ذاتي بسبب عضلات الجسم الهيكلي و من ضمنها عضلات التنفس والتي يمكن أن تؤدي إلى عجز التنفس والاحتياج للتنفس الأصطناعي في الحالات الشديدة.

هدف الدراسة: تقييم وظائف الرئة ورئتين الاحتيال محافظة حالات الشمول بالأختلال. تبيان العلاقة بين اختلال وظائف الرئة و العوامل المهيجة لذلك الاختلال. تبيان فائدة رفع الغدة الزيتية للتقليل من اختلال وظائف الرئة.

طريقة العمل: تم إجراء دراسة سريرية تقديرية لـ (205) حالة من مرضى وغن العيادات الوبيل، 36 حالة أنثى و 171 حالة من الذكور. وكانت أعمارهم تتراوح بين 12-60 سنة. 29 حالة من هؤلاء المرضى خضعوا لعملية رفع الغدة الزيتية. تمت الدراسة في الفترة بين شرين الأول عام 1999 و,DB شهر شريان عام 2001 في مستشفى الكاظمي التعليمي-بغداد-العراق.

النتائج: 42 من المرضى لديهم اختلال في عضلات التنفس اعتداعاً على فحص وظائف الرئة و بالنائرات السد الشمالي. 42.8من هذه الحالات كانت خلال السنين الأربعة الأولى من الخطر السريري. 89.6من المرضى الذين خضعوا لعملية رفع الغدة الزيتية لم يصابوا بختال وظائف التنفس. الأعراضات الخفيفة هي من أكثر العوامل المهيجة للاختلال (39%).

الأستنتاج: أن اختلال وظيفة التنفس لدى مرضى وقن العيادات ليست نادرة. إن رفع الغدة الزيتية مبكرًا ذو فائدة ملموسة لمنع حدوث اختلال وظيفة التنفس وخصوصاً في السنوات الأولى من الخطر السريري.

مفتاح الكلمات: وقن العيادات الوبيل، الصفيحة العصبية العضليه، رفع الغدة الزيتية، اختلال التنفس.

فرع الجملة المصرية-قسم الطب (كلية الطب-جامعة النهرين)

مستشفى النهرين العام-بغداد-العراق

المجلة العراقية للعلوم الطبية 2005م، المجلد 4، العدد 1، ص 98-93
الملخصات العربية

فرط برولوكتامين الدم في النساء: دراسة تحليلية للملامح السريرية و التشخيصية للأسباب

سحر لوبس حلبية

الخلاصة

الخلاقية الدلاس: فرط برولوكتامين الدم هو الأكثر شيوعاً في اضطرابات الغدد الصماء لمحور الوطاء-النخامية-المبيض. حيث تعتبر اورام النخامية من أهم الأسباب وأكثرها شيوعا.

هدف الدراسة: تحليل الملامح السريرية. دور التصوير بالرنين المغناطيسي في التقييم التشخيصي لحالات فرط البرولوكتامين. اجراء قياسات بالبرولوكتامين والمهرمون مع بيان العلاقة بين نتائج الرنين و نسبة برولوكتامين الدم في النساء، العدريات، مراجعة المصاديق و اقتراح طريقة اجراءات التloffيتش لحالات فرط البرولوكتامين في مهرمون.

طريقة العمل: اجري التقييم السريري والقياس الأساسي لتركيز البرولوكتامين بعمل الدم وكذلك فحص النخامية و القحف بالرنين المغناطيسي في دراسة تعقبية لـ 82 امرأة عرقتية مصابة بفرط البرولوكتامين عند مراجعتهن لعيادة الأمراض النسائية بعد استبعاد حالات فرط البرولوكتامين الثانوية.

النتائج: لقد وجد أن حالات نقص الخصوبة وثر الحليب و عدم انتظام الدورة الشهرية هي الملامح الشائعة، وقد ظهر البرولوكتامين خلايا ضد 24.7% من المرضى، وكان 87% منها نسباً للنخامية، والتي تنتج عنها ارتفاع تركيز البرولوكتامين بالدم بصورة معينة أكثر من الحالات المجهولة السبب 0.03. كما وجد أن مترجم النخامية في المرة الأولى أكثر من اليسرى. تحتل النخامية 31.3% من سادية السرطان الشرقي في حالة فرط النخامية. ثم تظهر النتائج وجود علاقة محددة بين جسم الدم و مستوي البرولوكتامين في الدم، ولكن توجد علاقة إيجابية معينة بين ساحتي النخامية والسرطان الشرقي في كل حالة فرط النخامية 0.04 و كذلك حالة الرنين المغناطيسي طبيعي P=0.07.

الاستنتاج: يمكن اعتبار تركيز برولوكتامين الدم بقياس 18.5/100/ملي/ملي/ملي/مزاجي لإجراء الرنين المغناطيسي الشاملة للنخامية و القحف. في انتظام النخامية قد يحدث خطورة الانتظار خارج السرطان، هناك علاقة محددة بين جسم الدم و السرطان الشرقي. ممكن اعتبار الرنين المغناطيسي هو العدري المذهل كمحاولة لصور النخامية بينما التوفر الشعاعي للسرطان الشرقي قد ينطوي استعمالاً.

مفتاح الكلمات: فرط برولوكتامين الدم، غلوم النخامية، فرط تشخيص النخامية، التصوير بالرنين المغناطيسي، قياسات بالبرولوكتامين المغناطيسي، عدريات.

قسم النسيان والوفيات (كلية الطب-جامعة النهرية)

المجلة العراقية للعلوم الطبية 2005، المجلد 4، العدد 1، ص 110-99
الملخصات العربية
تقرير حالة

مزامنة لعدد من الأمراض العصبية لفتاة صغيرة السن: حالة مسجلة

عبد المطلب عبد الكريم، حسن عزيز الحمداني

الخلاصة

الحالة لفتاة تبلغ من العمر عشرون عاماً، سُجِّلَت إصابتها بمرض الصرع سنة 1999 و كان نوع الصرع، صرع أكبر بدون علامات بورية في تياس 1999، تقول، كانت قاسية في اللحاء، وقد بدأت الراية تدعم من علامات تزداد شدة بشكل مستمر ممتثلة بالإدوار، هطول الإفراط، صعوبة في التعب، البلع و صعوبة في صعود السلم و تشتيت شعر الرأس. العلامات كانت أكثر وضوحاً عند النساء. وقد أثبت وجود الراية بواسطة الفحص الكهروهيلوجي و بواسطة ملاحظة الاستجابة لفقار

اليستوستيكلين وريدياً. وقد وصف العلاج بواسطة عقار اليستوستيكلين عن طريق الفم و أظهرت الراية تحسن ملحوظ.

في كل الانتهاء إلى المستشفى بعد ظهور أعراض جديدة مختلفة عن السابق متصلة بإدوار التوازن و صعوبة القيام بالأعمال الدقيقة بواسطة اليد و صعوبة في الاتصال. أدخلت الراية مرة أخرى إلى المستشفى في تشريح الأول نتيجة حصول شلل في الجوهر العصبي.

أظهر الفحص السريني وجود شلل في العصب السريني تطور جهتي من الأعضاء غير الوعرة في جسم المر차 مع خدر في نفس المنطقة. العلاجات كانت تزداد شدة أثناء تواجها في المستشفى.

الاستنتاج: هذه الحالة قد تمثل مزامنة لعدة أمراض عصبية كالأورام متصلة بالإدوار المناعي.

فرع طب الجملة العصبية-قسم الطب (كلية الطب-جامعة النهرين)
المجلة العراقية للعلوم الطبية

رئيسي هيئة التحرير
طارق إبراهيم الجبوري

هيئة التحرير الإستشارية
نعته شديد الصالحي
غسان الشمع
فاتن حسين محسن
فاروق حسين الجوات
ملكه سلمان السعدي
نشأت عزيز نشأت

هيئة التحرير التنفيذية
خالد د. عيسى
رئيسي هيئة التحرير
مهدي ر. محمد
محمود علي
حامد طارق
عبد الحسن مهدي الهادي
عبد المطلب عبد الكريم

تعنون الماسلات إلى المجلة العراقية للعلوم الطبية، صندوق بريد 14222 بغداد، العراق. تلقيون وفاكس (076) 1-24368.

المجلد الرابع، العدد الأول، 1424 هـ، 2005 م
الهيئة الاستشارية

اسماء نهاد رفعت (الهيئة العراقية للأختصاصات الطبية)
أكرم جرجيس (جامعة الموصل)
أهلاام الطائي (الجامعة المستنصرية)
امجد داوود ينادي (الهيئة العراقية للأختصاصات الطبية)
أميرة شبير (الجامعة المستنصرية)
ثامر أحمد حمدان (جامعة البصرة)
حسن أحمد حسين (جامعة النهرين)
حكيم الشعرف (جامعة بغداد)
خالد عبد الله (جامعة النهرين)
داود الثامر (جامعة النهرين)
راجي الحديثي (الهيئة العراقية للأختصاصات الطبية)
رافع الراوي (جامعة النهرين)
رجاء مصطفى (الجامعة المستنصرية)
رياض العزاوي (جامعة المستنصرية)
زكريا الحبال (جامعة الموصل)
سركيس كريكور ستراك (جامعة البصرة)
سرمد الفهد (جامعة بغداد)
سرمد خوندة (جامعة بغداد)
سميرة عبد الحسين (جامعة تكريت)
طاهر الدباغ (جامعة الموصل)
ظافر زهدي الياسين (جامعة بغداد)
عبد الا له الجوادي (جامعة الموصل)
علي فخري الزيبيدي (جامعة النهرين)
فوزان النائب (الجامعة المستنصرية)
محمد حياوي حماس (جامعة النهرين)
نجم الدين الروزنامي (الهيئة العراقية للأختصاصات الطبية)
نزار طه مكي (جامعة النهرين)
نزار الحسني (الهيئة العراقية للاختصاصات الطبية)
CARDIAC RESYNCHRONIZATION THERAPY (CRT): A NEW PACING THERAPY FOR CHRONIC HEART FAILURE

Ammar Al-Hamdi FRCP

It has almost become a cliché to say that chronic heart failure (CHF) is a major health problem all over the world\[1\]. It constitutes 1-3% of the population and 10% in the elderly, and about 5% of all medical admissions\[1\]. CHF combines a high prevalence with a terrible burden of symptoms and morbidity, all of these contributing to a huge societal and health care costs\[1,2\]. To compound the problem, patients with CHF lives only a short time, though CHF predominantly afflicts the elderly, it is still a cause of significant premature loss of life and affecting children, young and middle age group\[3\].

Cardiac fibrosis has been proposed to alter cardiac performance, namely diastolic function, in fact accumulation of collagen fibers within the myocardium is mainly responsible for in an increase in intrinsic myocardial stiffness that may alter left ventricular diastolic properties and the pattern of left ventricular filling. In addition, fibrosis may affect the conduction system of the heart including left bundle branch block (LBBB) or right bundle branch block (RBBB) and AV conduction delay, which cause biventricular dyssynchrony\[4\]. Cardiac contraction normally occurs in a spatially and temporally uniform manner, so that all portions of the wall contract synchronously. Biventricular dysynchrony, which occurs in CHF with intraventricular conduction delay especially in LBBB, is disadvantageous to the heart causing:

1. Inefficient ejection.
2. Abnormal regional loading which alters function and arrhythmogeneity
3. Abnormal mitral valve function causing mitral regurgitation\[4\].

Resynchronization by means of left or biventricular pacing has been found to improve the timing of regional contraction, enhance chamber systolic function and reduces mitral regurgitation with end result of 40% increase in cardiac output\[5\]. Biventricular pacing allows significant hemodynamic improvement in most patients with chronic CHF and intraventricular conduction delay, especially LBBB. Growing experiments indicate that the pacing site and the optimization of atrioventricular / intraventricular delay (PR interval optimization) seem to be crucial to obtain short and long term improvement of LV function\[5\].

Cardiac resynchronization therapy (CRT) has been recently proposed as a supplementary treatment of drug refractory CHF\[6\]. This new therapy aims to improve quality of life and exercise capacity in patients selected as the basis of a dilated cardiomyopathy and cardiac a synchrony. In this particular heart failure population,
the expected benefits depend on careful placement of the pacing leads, particularly that responsible for left ventricular (LV) pacing.

In practice, the optimal LV lead placement associated with the best hemodynamic improvement is often
varies from one patient to another due to the variable coronary sinus anatomy. The LV lead is placed in the lateral vein of the LV. Prior to the implant, echocardiography and more precisely tissue Doppler imaging investigations, may be helpful to identify the ideal LV pacing site, based on the late activated segmental contraction, which in most of the cases turns out to be the midlateral wall.[5,7]

Complications observed during LV lead implantation remain low, consisting mainly of phrenic nerve stimulation and coronary sinus perforation in < 1% and should further decrease with the use of new instrumentation dedicated to the procedure.[6]

Three randomized trials (PATH-CHF,[6] MUSTIC and MIRACLE) have reported similar short, mid and long-term improvement of functional class, exercise capacity and quality of life of patients with CHF chronically paced with CRT. The significant symptomatic benefits have also been confirmed in a large European registry, the COTAK registry, including more than 1000 patients followed up to 6 months after CRT.[8]

The indications for CRT are:
1. Advanced heart failure (NYHA class III-IV).
2. Right BBB or left BBB
3. Low ejection fraction with or without mitral regurgitation refractory to medical therapy.

In the Cardiology Unit, Al-Kadhimiya Teaching Hospital CRT is available now moreover, we have implicated 30 CRT over the last 12 months. The results up till now are encouraging; more patients are waiting for implantation of the device.

References
7. Stellbrirle, A.A.: The pacing therapies for congestive heart failure (PATH-CHF) study rational, design and endpoints of a proposed randomized multicenter study. Am J cardiol, 1999; 83 (suppl. 5B): 130D-5D.
Xeloda: Targeted Therapy in Colo-Rectal cancers

Introduction
For the last 50 years, the Fluopyrimidines (the 5-Flourouracil) was the standard chemotherapy in the treatment of colo-rectal cancers. F-Flourouracil was given in different doses and different ways to increase its efficacy and decreases its toxicity. If 5-flourouracil administered as intravenous bolus it will be effective but its efficacy is limited because the plasma concentration of the drug rapidly fall below the cytotoxic threshold due to rapid degradation of the drug. Continuous intravenous infusion or protracted infusion with folinic acid is superior to intravenous bolus regarding survival benefit. This method of treatment requires good medical, nursing, pharmacy staff, and it is associated with a lot of complication. Thus, there is real need to find oral drug, which mimic the efficacy of intravenous infusion method without associated side effects.

Capecitabin
Capecitabin “Xeloda” is the first new oral drug of the class Fluopyrimidines. It offers the following advantages:
1. It is capable of mimic continuous intravenous infusion of 5-Flourouracil.
2. Providing convenient method of treatment i.e., oral method.
3. Tumor selective activation:
   a. improve efficacy
   b. reducing side effects

Mechanism of action
Xeloda taken by mouth and absorbed by the stomach unchanged. In the liver, it is cleaved to 5-deoxy-5-Flurocytidin and 5-deoxy-5-Flourouridin. Inside the tumor, these compounds cleaved to active 5-Flourouracil by the effect of enzyme called “Thymidine phosphorylase” which is present in high concentration inside the tumor cells and in low concentration inside the normal tissue. By this way, we expose the tumor cells to high concentration of cytotoxic drug with low concentration inside the normal healthy tissues.

Dosage
It is given in 1250 mg twice daily for 14 days, one-week rest and the cycle repeated every three weeks

Side effects
The side effects usually mild include mild nausea and vomiting, mild diarrhea, hand-foot syndrome and mild myelotoxicity.

References
1. 11th European Cancer Conference (ECCO), Lisbon, Portugal, 2001.
2. 27th European Society of Medical Oncology, Nice, France, 2002.

Khudhair Al-Rawaqe, DMRD
Associate Professor of Oncology, College of Medicine, Baghdad University.
**Strattera: Non-Stimulant Drug for Attention Deficit Hyperactivity Disorder (ADHD)**

**European Congress of Neurosciences (Schizophrenia & Bipolar Disorders), Germany-Berlin, 8-10 April 2005**

**About ADHD**
Attention deficit hyperactivity disorder (ADHD) is chronic and impairing disorder affects 3-7% of school-age children and manifest itself in levels of attention, concentration, activity, distractibility, and impulsivity that are inappropriate to the child’s age[1]. In addition, 60% of children with the disorder carry their symptoms into adulthood[2]. Experts estimate 4% of adults in the United States, more than 8 million people, have ADHD[3,4].

**About Strattera**
Strattera, (atmoxetine HCl) regarded as the first therapy option for ADHD. It is a selective norepinephrine reuptake inhibitor, works differently than other FDA-approved treatments for the disorder, all of which are stimulant.

It is not known precisely how Strattera reduces ADHD symptoms, but scientists believe it works by blocking os slowing reabsorption of norepinephrine, a chemical in the brain considered important in regulating tension, impulsivity and activity levels. This keeps more norepinephrine at work in the spaces between neurons in the brain. Improved efficiency in norepinephrine system is associated with improvement in symptoms of ADHD.

It is the only medication indicated specifically for the treatment of ADHD in children, adolescents and adults. Strattera provides full-day symptoms control without insomnia in most children and adolescents. The American Academy of Child and Adolescent Psychiatry (AACAP) states that decision to place Strattera as a first-line therapy option will have positive impact on the lives of many patients and their families who struggle with this disorder.

**Special precautions**
Strattera should not be taken at the same time as, or within two weeks of taking, a monoamino oxidase inhibitor, or by patients with narrow angle glaucoma. Patients with a history of high or low blood pressure, increased heart rate, or any heart or blood vessel disease should tell their doctor before taking Strattera. Strattera has not been tested in children less than six years of age or in geriatric patients. Some children may lose weight when starting treatment with Strattera. As with all ADHD medications, growth should be monitored during treatment.

**Side effects**
The most common side effects in children and adolescents in medical studies were upset stomach, decreased appetite, nausea and vomiting, dizziness.

The U.S. Food and Drug Administration approved Strattera on November 26, 2002, for the treatment of ADHD in children, adolescents and adults.

**References**

Mohammed Al-Kureishi MSc (Neurosychaitry)