VOLUME 8 ISSUE 2 DECEMBER 2014

University of Duhok
College of Medicine

Duhok Medical Journal

The Official Journal of Duhok College of Medicine

ISSN: 2071 - 7326

Photo on the cover page

Gali Sherana - Deralok District - Duhok

The journal is also available at the college website (Online ISSN 2071-7334)

http://www.uod.ac/en/dmj

VOLUME 8 ISSUE 2 DECEMBER 2014

University of Duhok
College of Medicine

Duhok Medical Journal

The Official Journal of Duhok College of Medicine

Duhok University Press ISSN: 2071 - 7326

This page is left intentionally

Duhok Med J

EDITORIAL BOARD

Submission of Manuscript:

Manuscripts should be submitted to:
The Editor,
Duhok Medical Journal,
Duhok College of Medicine,
Post address: Nakhoshkhana Road 9, 1014, AM, Duhok, Iraq.
Telephone No.: 00964-62-7224268 EXT 115
E-mail: dmj@uod.ac
Electronic submission of articles is also accepted

Duhok Med J

ADVISORY BOARD

This page is left intentionally

Duhok Med J

INSTRUCTIONS FOR AUTHORS

Aims and Scope Duhok Medical Journal is a peer reviewed journal issued bi – annually by Duhok College of Medicine. Scientific and clinical researches are the main issues. The journal also publishes short articles, letters to editors, review articles and case reports.

General The Duhok Medical Journal is a signatory journal to the uniform requirement for manuscripts submitted to biomedical journals, February 2006 [updated 2009] (http://www.icmje.org).

To present your original work for consideration three manuscript copies written in English together with Kurdish and Arabic abstracts should be submitted to the editor. All authors are required to provide the manuscript on a CD labeled with the name and title of the paper.

Preparation of the manuscript The manuscript should be typed double spaced as normal text on one side of the paper in single column format, font size 14 pt, paper type A4, 1″ margin at each side and each of the following sections should begin on a new page in the following sequence:

1- **Title page**; should include the following: title, font size 16 pt, each author's full name, academic degree(s), scientific title (if available), institutional affiliation, full contact information including emails. If there are more than one author, article should include author to whom correspondence should be addressed including the scientific title (if available), institution affiliation, address, email, telephone.

2- **Structured abstract**; of no more than 250 words including background and objectives, methods, results, and conclusions.
3 – 10 keywords or phrases should be put at the end of each abstract (Printed in bold font; size12 pt).

3- **Body of the text**; structured in an IMRAD style;
(Introduction, Methods, Results and Discussion).

4- **Acknowledgment** (if any.)

5- **References.**

6- **Tables with legends**.

7- **Illustrations with legends**.

8- **Structured Kurdish abstract including title in Kurdish.**

پێشەکی و ئارمانج، ڕێکێن ڤەکولینێ، ئەنجام، دەرئەنجام

9- **Structured Arabic abstract including title in Arabic.**

خلفية و اهداف البحث، طرق البحث، النتائج، الاستنتاجات

Tables Each table must be typed on separate page and should follow the reference list. All the tables must be numbered consecutively in the order of their first citation in the text. Supply a brief title for each on top and place explanatory matter in foot notes not in the heading (if needed). Tables should be simple and not duplicated in the text. Percentages are included with numbers in the same cells but in brackets.

Illustrations Graphs, line drawing, photographs, printed x rays and other illustrations are accepted only if they add to the evidence of the text. They should be of a high quality and suitable for reproduction. They should be numbered consecutively according to the order in which they have been first cited in the text. Supply a brief title beneath each illustration. Graphs should have white background; should be colored and non 3-dimensional figure; and should have labels for X and Y axis.

Numbers and Units Measurements of length, height, weight and volume should be reported in metric units. Temperature in degrees Celsius, blood pressure should be expressed in mmHg and all hematologic and clinical chemistry measurements in SI units.

Abbreviations should be defined on first use and then applied consistently throughout the article. Avoid abbreviations in the title and abstract.

References should be numbered both in text and in the list of references in the order in which they appear in the text. The punctuation of the Vancouver style should be followed; if the original reference is not verified by the author, it should be given in the list of references followed by (cited by) and the paper it was referring to. The titles of journals should be abbreviated according to the style used in Index Medicus. This can be obtained from website (http://www.nlm.nih.gov/). The author is responsible for the accuracy of references. The following are examples of the three most common types of citations:
The article citation: if six authors or fewer list all; if seven or more authors list the first six and then add "et al":
1- Nuwayhid IA, Yamout B, Azar G, Kambris MA. Narghile (hubble bubble) smoking, low birth weight, and other pregnancy outcomes. Am J Epidemiol. 1998;148(4):375-83.
Book citation, noting chapter and authors:
2- Arevalo JA, Nesbitt TS. Medical problems during pregnancy. In: Taylor RB, editor. Family medicine: principles and practice. 6th ed. New York: Springer – Verlag; 2003. p. 109-16.
Electronic source:
3- Garfinkel PE, Lin E, Goering P. Should amenorrhoea be necessary for the diagnosis of anorexia nervosa? Br J Psych [Internet]. 1996 [cited 1999 Aug 17];168(4):500-6. Available from: URL:http://biomed.niss.ac.uk

Authorship and consent form All authors must give signed consent (Form No.1- Submission Form), which should accompany the manuscript. The letter should say "this manuscript is an unpublished work, which is not under consideration elsewhere in the record. Authors are requested to state an approximate estimate of their contribution in the study, sign the form and send it with the manuscript.
Authors must declare if they have any competing interests in the study and to specify any funds given to conduct the study.

Ethical considerations When experiments on humans are being reported the whole work in the manuscript should conform to the ethical standards of the responsible committee on human experimentation.

Submission of manuscript

Manuscripts should be submitted to:
The Editor,
Duhok Medical Journal,
Duhok College of Medicine,
Post address: Nakhoshkhana Road 9, 1014, AM, Duhok, Iraq.
Telephone no.: 00964-62-7224268 EXT 115
E-mail: dmj@uod.ac
Electronic submission of articles is also accepted

N.B.

* Accepted manuscripts may be altered by the editorial board of Duhok Medical Journal to conform to details of the journal publication style.

** The Editorial Board of Duhok Medical Journal accepts no responsibility for statement made by authors in articles published by the journal.

Duhok Med J

CONTENTS

This page is left intentionally

CRISIS INTERVENTION PROGRAM FOR CHILDREN AND ADOLESCENTS (CIPCA) TO PREVENT POSTTRAUMATIC PSYCHOPATHOLOGY, PRELIMINARY REPORT

ABDULBAGHI AHMAD, MBChB, SBCAP, PhD*

Submitted 1 December 2014; accepted 31 December 2014

ABSTRACT

Background and objectives Despite devastating psychopathology after childhood trauma, no evidence-based prevention has been identified. After the Islamic State (IS) war in Iraq and Syria, a group intervention program is provided to the internally displaced and refugee children, in attempt to prevent posttraumatic psychopathology, and to identify children who need special care.

Methods A Crisis Intervention Program for Children and Adolescents is developed by the author. Three instruments (Crisis Expression Guidelines, Crisis Screening Instrument, and Modified Family Map) are delivered through Training of Trainers (ToT) to help the displaced and refugee children (6-11 and 12-18 years) within a one-hour group session (10-30 children) express thoughts and emotions related to the war crises, and to screen for further care.

Results In a pilot project, 37 professionals working with children applied to the ToT course، and 300 IDP teachers completed training to provide CIPCA to the Internally Displaced People (IDP) and refugee children in the temporary camps in the region. In a pilot project, 315 children received the CIPCA, and a further 67500 school children are waiting for the intervention when the schools start in the IDP camps. Screening revealed 15.2% of the participating children need individual assessment.

Conclusion CIPCA is applicable as a cost and time effective crisis intervention to IDP and refugee children of IS war. Further expansion of the program is planned. Follow-up will evaluate the preventive effect of CIPCA.

Duhok Med J 2014;8(2): 1-11.

Keywords: Posttraumatic, Psychopathology, Prevention

Research has revealed a wide range of long-lasting mental and behavioral sequelae in children following disasters.[1] Increasing research is available on the preconditions for child mental health and optimal development in traumatic conditions. Less is known on how to translate the findings into effective interventions to help traumatized children.[2] Lack of social support and recognition by the environment is one of the most consistent risk factors for posttraumatic stress disorder (PTSD) in children and adolescents.[3] Practical and theory-informated research on strategies to protect children and youth victims of disasters, war and terrorism, and promote their resilience is considered a global priority.[4] Disaster experiences have found exchanging of information among the people in the disaster stricken areas helps to reduce the psychological damage to children, aiding in their recovery.[5] Systematic screening is suggested for

* *Associate Professor, Senior Consultant in Child and Adolescent Psychiatry*
Uppsala University, Uppsala – Sweden
IACAPAP Ambassador, Founder of Child Mental Health & Investor of Metin Health House
Duhok, Kurdistan Region – Iraq Telephone: 0046702212155, e-mail:abdulbaghi.ahmad@neuro.uu.se

psychological problems in children exposed to disasters. An integrated approach using psycho-socio-educational and clinical interventions is expected to be effective[1]. Group interventions have been found to be effective to promote catharsis, support, and a sense of identification with the group.[6] However, different types of intervention have led to different conclusions.[7,8] While subjective reports of systematic preventive interventions were effective in decreasing PTSD and depressive symptoms among children traumatized due to armed conflict, the more objective results of a meta-analysis concluded that substantial additional work needs to be done in developing effective preventive interventions and treatments for children traumatized by exposure to war and violence.[2]

Children of Kurdistan

During the 1990s, researches showed trauma-related psychopathology among children and adolescents for the first time in Kurdistan. However, it also revealed protective factors related to family systems and survival strategies 9-11. The Islamic State in Iraq and Syria (ISIS) started its war in Iraq on 9 June 2014 when the city of Mosul, in the province of Nineva, in northern Iraq was occupied. The majority of the population, consisting mainly of Christians, fled north to the Kurdistan Region of Iraq (KRI). Later on, the ISIS march continued to the east leading to a further mass exodus; this time of mainly Sunni Muslim Arabs, from central Iraq to the KRI. In 3 August 2014, ISIS attacked the Yezidi-dominated area of Shingal near the border with Syria. Yezidis are Kurds who retain their old religion from Zoroastrian times. ISIS gave them three options; either to convert to Islam, to pay the fee "Cizye", or execution. The result was a panic mass-escape among the strictly traditional Yezidi society moving towards the KRI. Those who could not flee were subjected to brutal violence at ISIS hands, with mass executions of men, abduction of women and children who were subjected to rape or traded into sex slavery. The mass escapes ended up finally in the Duhok governorate in the KRI, bordering Nineva to the south, Syria to the west, and Turkey to the north. In 19 September 2014, the Kurdish city of Kobane in Syria was attacked by the ISIS army. Most of the civil population left the city escaping from the intensive war between the defending forces and the attacking ISIS army. After crossing the two borders of Turkey and Iraq, more than 200000 refugees from Kobane settled in different refugee camps in the three governorates of Duhok, Erbil and Sulaymani in the KRI, under the UNHCR management.

The aim of study is to test the applicability of a time and cost effective group intervention program on IDP and refugee children of ISIS war in Kurdistan, in an attempt to prevent posttraumatic psychopathology, and to identify at an early stage, children who need special care.

METHODS

Target population: One month after their mass escape from the ISIS sudden occupation of Shingal, the responsible

authorities and NGOs in Duhok reported that 700,000 Yezidi IDPs were living in the temporary camps inside and around the city of Duhok when a psychosocial team from Sweden came to the Metin Health House (MHH) in Duhok to provide crisis intervention to the displaced and refugee children and adolescents in the region. At the same time, 200,000 Kurdish refugees from Syrian were reported living under the management of the UNHCR in the camps of Gwelan in Duhok, and Qushtepe in Erbil governorates in the KRI.

Visiting these camps, the psychosocial teams from the MHH found the refugee families were living in well-guarded camps under the UNHCR management, while the IDPs were living in temporary camps, empty houses, such as schools, uncompleted buildings, uninhabited houses or in parks and in forests, protecting themselves from the heat of the sun which sometimes exceeded 40ºC. Common for all families, they had lost members either in ISIS captivity, or being killed or not found. Many young men had returned to participate in the war against ISIS. While adults were preoccupied with their traumatic experiences and worries, children often ended up outside adult care and attention without school or structured activities. Searching for loved ones was ongoing. Rumors of mass executions, sex slavery, mass rapes, and horror scenario spread about ISIS terror and violence were widespread. Extended families of three generations reunited when they found each other. The hierarchical social system began to re-establish itself as a protective survival strategy. No outbreaks of diseases had been reported. While the conditions for the escaped IDPs were far from stable, the situation for the refugees seemed reasonably under control.

The MHH, where the Swedish psychosocial team was stationed in the city of Duhok, which is a private clinic for prevention and treatment of child mental health problem that has been established in the city of Duhok in collaboration with the local authorities. It was among the first non-governmental organizations (NGO) that provided psychosocial support to the IDPs in the region when the ISIS war started in Nineva and then in Shingal and Kobane. Daily, psychosocial teams from the MHH visited the scattered IDP stations in and around the city of Duhok, providing support and counseling to the families, adults and children.

Crisis Intervention Program for Children and Adolescents (CIPCA): has been developed by the author to provide, through Training of Trainers (ToT), a cost and time effective one-hour group session of structured crisis intervention to groups of 10-30 children (6-11 years) or adolescents (12-18 years).

The trainees are professional working with children. They receive training in a two-week ToT course. Each course consisted of 10 hours theory and 20 hours practical training. After completing the course, the trained professional was provided with a certificate qualifying for 1.5 European Credit Transfer and Accumulation System (ECTS) high school credits. Every group session is led by two trained professionals, one acting as group leader and the other is co-leader. The group leader follows the

Crisis Expression Guidelines to support participating children and adolescents to verbalize and express thoughts and emotions related to their crises. This stepwise semi-structured interview is based on several well-known theories, such as catharsis[6], debriefing[7], group therapy[8], cognitive paradigm[12], systemic theory[13], attachment theory[14], salutogenesis[15], and posttraumatic growth.[16] (Figure 1)

In order to help children speak, ask them to tell their experiences of the disaster, starting by the following question:
Who wants to tell us about an experience during the disaster?
-In turn, each child should be given time to tell her/his story.
-Help to find out and reinforcing positive thoughts and feelings.
-In each story, help the child to describe the event as a clear situation, using step-by-step the following questions:
1- What happened? Did somebody die or get wounded? (who, how many?).
2- When did it happen? (recently or long ago, day or night, for how long period..etc).
3- Where did it happen? (at home or outdoors, in building or outside, near or distant..etc).
4- Who was there? (alone, few or many, familiar or strangers..etc).
5- How did it happen? (encourage spontaneous telling without forcing or disrupting).
6- What did you think? (Personalize, differentiate thoughts from feelings).
7- What did you feel? (Support expressing feelings, give time and comfort).
8- What did you do? (Behavior, action, participation, avoidance, reaction…etc).
9- What do you think the cause of the event was?
10- What do you think the future will be like?

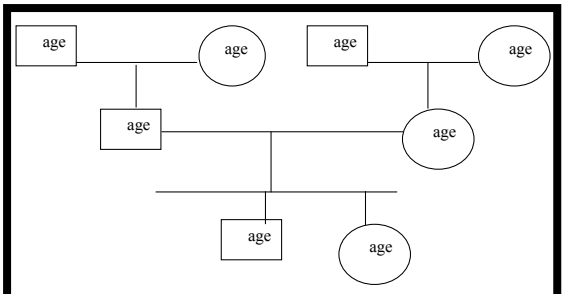
Figure 1. Crisis Expression Guidelines

A trained co-leader simultaneously uses the Crisis Screening Instrument (Figure 2) to identify children showing any sign or symptom of psychological distress that is qualifying to further individual assessment. This instrument is derived from two widely used screening questionnaires with satisfactory validity and reliability in Kurdistan society.[17-18]

Those children who are showing one or more of the following symptoms/signs must be offered further individual intervention, write down their names and contacts:
1-Not responding to the questions/refuse to participate
2-Seems mostly absent/ daydreaming/sleeping
3- Hypersensitive to stimuli/startle
4- Crying/depressed
5- Wetting him/herself
6- Stuttering/ not speaking
7- Hyperactive
8- Aggressive
9- Sulking
10- Fainting
11- Any somatic complaint
12- Any unusual behavior

Figure 2. Crisis Screening Instrument

Children showing positive screening were referred for individual assessment to be performed by a trained expert in using a Modified Family Map (Figure 3) to identify risk and protecting factors in three generations in addition to examination of psychiatric status for planning of adequate management.[19]



Female ○ Male □

B	Birth Country
MA	Changed address within the country, date and duration
MW	Moving from to countries, date
R	Residence type (Asylum, PUT and Citiziship) country, date and duration
SH	School (Nr of years) Homeland
WH	Works (Types of works) Homeland
D	Death, date, age, reason
CD	Chronic Disease, types, age and duration
SD	Serious Disease, types, age and duration
Med	Current medication
O	Operations, age and duration
Ab	Abuse, types, age and duration
H	Handicap, type, age and duration
C	Criminlity, type, age and duration
Ad	Adoption, date
Disp	Displaced, date
Abs	Absence, date
W	War experience (Exposed, witnessed or heard), date
V	Violence, (Exposed, witnessed or heard), date
M	Marriage, date
/	Separation, date
//	Divorce, date
H	House/Apartment, Own or Rent
F	Farm
P	Properties
L	Language mostly speaking hom

Figure 3. The Modified Family Map

RESULTS

In a pilot project, a total of 37 professionals working with children completed a course of Training of Trainers (ToT) to provide CIPCA to the displaced and refugee children and adolescents in the temporary camps in the Duhok region (Table 1).

Table 1. Gender distribution of the professional completed training of trainers

	Female No. (%)	Male No. (%)	Total
Total	**21 (56.8)**	**16 (43.2)**	**37**
Country			
Iraq	**15 (50.0)**	**15 (50.0)**	**30**
Turkey	**0**	**1 (100)**	**1**
Sweden	**6 (100)**	**0**	**6**
Ethnicity			
Kurd	**19 (57.6)**	**14 (42.4)**	**33**
Arab	**2 (50.0)**	**2 (50.0)**	**4**
Religion			
Muslim	**21 (60)**	**14 (40)**	**35**
Yezidi	**0**	**1 (100)**	**1**
Christian	**0**	**1 (100)**	**1**
Training station			
Duhok (main health house)	**17 (56.7)**	**13 (43.3)**	**30**
Erbil (Swedish specialist hospital)	**2 (50.0)**	**2 (50.0)**	**4**
Sweden (Mental health Ahmad AB)	**2 (100)**	**0**	**2**
Turkey (online, Skype, e-mail)	**0**	**1 (100)**	**1**

Every 2 trained professionals performed training of 30 IDP teachers inside the camps, one acting as a leader and the other as co-leader in each group of teachers. Totally, 300 teachers received the training in 5 IDP camps in Duhok province. They are ready to offer crisis intervention to the school children according to CIPCA, when the schools start in the IDP camps.

During the pilot project, 315 school aged children in the displaced and refugee

camps received one-hour group sessions of crisis intervention (Table 2).

Table 2. Gender distribution of the participating children in CIPCA (N=315)

	Girls No. (%)	Boys No. (%)	Total
Total	**141 (44.8)**	**174 (55.2)**	**315**
Age (years)			
6-11	**57 (50.9)**	**55 (49.1)**	**112**
12-18	**84 (41.4)**	**119 (58.6)**	**203**
Country			
Iraq	**114 (41.9)**	**158 (58.1)**	**272**
Syria	**27 (62.8)**	**16 (37.2)**	**43**

The children's groups (6-11 years) usually contained 4 – 10 children per session, while teenage groups (12-18 years) were larger (10-30 adolescents per session). Every session ran for 45-60 minutes. Girls were as keen to participate as boys, although parents usually interrupted and argued against the participation of girls. However, parents mostly respected the wish of their children who often competed for a place in each session. In one camp, the competition became fierce; the gathering masses of children required interference from the adult IDPs who sometime were near to using violence to separate the struggling children. Special arrangements for play and free activities were offered by the accompanied members of the psychosocial team to calm down the situation and to move away children from the tent where the session was going on. In total, 5 IDP stations were visited by the trainees in Duhok region and two camps in Erbil.

Only 48 (15.2 %) of the participating children and adolescents (25 girls and 23 boys) showed a need for individual assessment after the crisis intervention screening (Table 3). They were referred to the governmental health system for further management. The most common symptom was Crying/depressed (4.8%) while no one reported Hyperactivity.

Table 3. Gender distribution of the participating children in CIPCA pilot project (N=315)

	Girls No.	Boys No.	Total
1- Not responding questions / refuse to participate	**2**	**4**	**6**
2- Seems mostly absent/daydreaming/sleeping	**2**	**1**	**3**
3- Hypersensitive of stimuli/startle	**2**	**2**	**4**
4- Crying/ depressed	**12**	**3**	**15**
5- Wetting him/ herself	**0**	**2**	**2**
6- Stuttering/ not speaking	**1**	**1**	**2**
7- Hyperactive	**0**	**0**	**0**
8- Aggressive	**1**	**1**	**2**
9- Sulking	**2**	**1**	**3**
10- Fainting	**4**	**3**	**7**
11- Any somatic complaint	**1**	**2**	**3**
12- Any unusual behavior	**0**	**6**	**6**
Reporting at least one of the above	**25**	**23**	**48**

DISCUSSION

About one month after the mass escape from the ISIS military attack, 315 displaced and refugee children and adolescents received one-hour group session of crisis intervention according to the (CIPCA) through trained professionals from the two-week ToT course. The CIPCA, mainly based on structured cognitive emotional expression, proved to be time and cost effective crisis intervention. It was suitably applicable to separate groups of displaced and refugee children (6-11 years), and adolescents (12-18 years). Different professionals such as

physicians, psychologists, social workers, teachers and other professionals working with children and adolescents were shown to be suitable trainees through the two-week ToT course, consisting of 10 hours theory lectures and 20 hours practical training. During the ToT course, the trainees applied the crisis intervention model to the separated target groups of displaced and refugee children and adolescents as a practical training under daily supervision, even before completing the course. Permission to train other professionals was restricted to those who completed all 30 hours of theory and practice that qualified for a trainer certificate.

Children groups (6-11 years) showed a better intervention effect in small groups, not exceeding 10 participants per group, while it was possible to have up to 30 adolescents (12-18 years) in each group. This might be a cultural effect, as small children are usually considered as "properties" belonging to the parents in collective societies in Kurdistan, as in the case of the Yezidi communities, while adolescents are considered as full adults[10]. Cultural aspects were obvious also in the adults' response to CIPCA. With full respect and courtesy, all parents in the displaced and refugee camps showed agreement and verbal consent to the trainees providing crisis intervention for their children, even if some doubt was shown at the beginning concerning the girls' participation. Involving the parents in the process of collecting the groups increased the parents' confidence. Children, on the other hand, were enthusiastic to participate regardless of gender. On the contrary, it was difficult to select the groups due to severe competition among the adolescents to participate in the group session, a matter leading in some instances to overcrowding and manifested disappointment among those children who did not have the opportunity to participate. Conducting the CIPCA in school settings, as it is planned in the currently WHO supported project, might solve some of these problems which is in line with previous research[20].

In this preliminary report, the CIPCA seems to be well tolerated by the participating children and adolescents. The majority of the participants in each group session showed active involvement and genuine commitment. Although no complications appeared during the group sessions, it is worth emphasizing the importance of providing adequate information and obtaining consent both from the participating children and their parents or caregivers in order to maintain ethical codes and avoid any unpleasant surprises.

This preliminary report of our project shows the feasibility of the CIPCA for the IDP and refugee children and adolescents. However, much remains to be proved regarding its effectiveness as a preventive method for posttraumatic psychopathology. This is going to be elaborated in the coming follow-ups of our research.

Only 15,2 % of participating children showed the need for further individual assessment from our screening. This is probably explained by the protective effect

of the authoritative extended family system and inherited survivor strategies among this highly exposed religious and ethnical group. Still, appropriate plans have to be arranged for detecting and treating any emerging psychopathology, especially when the current health care system in the region is not adequate to prioritize this group of young people due to the ongoing war situation. Searching for external sources of financial support is essential.

REFERNCES

1. Kar N. Psychological impact of disasters on children: review of assessment and interventions. World J Pediatr. 2009;5(1):5-11.
2. Peltonen K, Punamäki RL. Preventive interventions among children exposed to trauma of armed conflict: a literature review. Aggress Behav. 2010;36(2):95-116.
3. Olff M, Koch SB, Nawijn L, Frijling JL, Van Zuiden M, Veltman DJ. Social support, oxytocin, and PTSD. Eur J Psychotraumatol. 2014; 9;5.
4. Masten AS, Narayan AJ. Child development in the context of disaster, war, and terrorism: pathways of risk and resilience. Annu Rev Psychol. 2012;63:227-57.
5. Takada S. Post-Traumatic Stress Disorders and mental health care (lessons learned from the Hanshin-Awaji Earthquake, Kobe, 1995). Brain Dev. 2013;35(3):214-9.
6. Austin LS, Godleski LS.Therapeutic approaches for survivors of disaster. Psychiatr Clin North Am. 1999; 22(4):897-910.
7. Rose S, Bisson J, Churchill R. Psychological debriefing for preventing post-traumatic stress disorder (PTSD). Cochrane Database Syst Rev. 2002;(2):CD000560.
8. Pfefferbaum B, Newman E & Nelson SD. Mental health interventions for children exposed to disasters and terrorism. J Child Adolesc Psychopharmacol. 2014; 24(1): 24-31.
9. Ahmad A, Mohamad K. The socioemotional development of orphans in orphanages and traditional foster care in Iraqi Kurdistan. Child Abuse Neglect 1996;20(12):1164-73.
10. Ahmad A, Mohammad H, Ameen N. A 26-month follow-up of posttraumatic stress symptoms in children after Mass-Escape Tragedy in Iraqi Kurdistan. Norm J Psychiat 1998; 52(5):357-66.
11. Ahmad A, Sofi M. A, Sundelin-Wahlsten V, von Knorring A-L. Posttraumatic stress disorder in children after the military operation "Anfal" in Iraqi Kurdistan. European Journal of Child and Adolescent Psychiatry. 2000,9:235-243.
12. Buckley TC, Blanchard EB, Neill WT. Information processing and PTSD: a review of the empirical literature. Clin Psychol Rev. 2000;20(8):1041-65.
13. Lecic-Tosevski D, Draganic-Gajic S, Pejovic-Milovancevic M, Popovic-Deusic S, Christodoulou N, Botbol M. Child is father of the man: child abuse and development of future psychopathology. Psychiatriki. 2014; 25 (3): 185-91.

14. Levy KN. Introduction: attachment theory and psychotherapy. J Clin Psychol. 2013;69 (11): 1133-5.
15. Benz C, Bull T, Mittelmark M, Vaandrager L. Culture in salutogenesis: the scholarship of Aaron Antonovsky.Glob Health Prom ot. 2014; 21 (4): 16-23.
16. Sattler DN, Boyd B, Kirsch J. Trauma-exposed firefighters: relationships among posttraumatic growth, posttraumatic stress, resource availability, coping and critical incident stress debriefing experience. Stress Health. 2014; 30(5): 356-65.
17. Ahmad A, Qahar J, Siddiq A, Majeed A, Rasheed J, Jabar F et al., Reporting questionnaire for Children as a screening instrument for child mental health problems in Iraqi Kurdistan. Transcultural Psychiatry. 2007; 44(1): 5-26.
18. Ahmad A, Sundelin Wahlsten V, Sofi MA, Qahar JA, von Knorring A-L. Reliability and validity of a child specific cross-cultural instrument for assessing posttraumatic stress disorder. European Journal of Child and Adolescent Psychiatry. 2000, 9:285-94.
19. Ahmad A., Mohamad K. The socioemotional development of orphans in orphanages and traditional foster care in Iraqi Kurdistan. Child Abuse Neglect. 1996;20(12):1164-73.
20. Schultz JH, Langballe , Raundalen M. Explaining the unexplainable: designing a national strategy on classroom communication concerning the 22 July terror attack in Norway. Eur J Psychotraumatol. 2014; 2:5.

پوخته

بەرنامەیەکێ دەستکاریا قەیرانان بو زاروک و گەنجان، راپورتا دەستپێکرنێ

پێشەکی و ئارمانج: نەبۆنا ئامویرەک جەرباندی بو پاراستنێ ژ نەساخیێن دەرونی پشتی قەیرانان بو ئەگەرا پەیداکرنا ڤی پروگرامێ د ڤێ نڤیسیدا.
رێکێن ڤەکولینێ: نڤیسەری پروگرامێ دەستکاریا قەیرانان بو زاروک و گەنجان ئامادەکر کو دوو رێڤەبەرێن فیرکری پێشکێشی ١٠-٣٠ زاروکان بکەن ب کوم د یەک دەمژمێردا قەیرانا خو دلدەرێژ بکەن.
ئەنجام: ب رییا فیرکرنا فیرکەران، ٣٧ بسپورێن د گەل زاروکان کار دکەن هاتن فیرکرن و ٣١٥ زاروکێن ئاوارە دناڤ کەمپاندا دلدەرێژکرنا ب کوم بو هاتە کرن. رێخراوا ساخلەمیا ناڤنەتەوەی پشتگیریا بەرفرەهکرنا بەرنامەی کر و درێیا فیرکرنا ٣٠٠ ماموستایێن ئاوارە ل ناڤ کەمپێن دهوک دا ٦٧٥٠٠ زاروکێن قوتابخانا د دلدەرێژکرنا ب کوم دگەل بهێت کرن.
دەرئەنجام: سەرهاتیا مە نیشا دا کو ئەڤ بەرنامە ئامویرەکێ گونجایە ژلایێ دەم و بهای ڤە بو دلدەرێژکرنا زاروک و گەنجان پشتی قەیرانان.

الخلاصة

برنامج تداخل الأزمات للأطفال والشباب، تقرير أولى

خلفية وأهداف البحث: نظراً لعدم وجود تداخل وقائى مبرهن ضد الإصابة بالأمراض النفسية بعد الكوارث تم إختراع التداخل الجماعى فى هذا البحث.

طرق البحث: تم تطوير برنامج تداخل الأزمات للأطفال والشباب من قبل المؤلف. يعرض البرنامج على ١٠-٣٠ طفل فى جلسات جماعية للتنفيس النفسى فى ساعة واحدة بمساعدة دليلين مدربين خلال دورة تدريب المدربين.

النتائج: تم تقديم البرنامج ل ٣١٥ طفل من قبل ٣٧ حرفيين تم تدريبهم فى بيت متين الصحى فى دهوك. بعد ذلك ساعدت منظمة الصحة العالية فى دهوك على توسيع البرنامج لتغطى ٦٧٥٠٠ طالب فى معسكرات النازحين، خلال تدريب ٣٠٠ معلم نازح .

الإستنتاجات: أثبتت التجربة ملائمة التداخل كوسيلة فعالة زمناً وسعراً لتقديم التنفيس النبسى للأطفال والشباب بعد الأزمات. يتم قياس فعالية البرناج بعد متابعة مبرمجة.

SEASON OF BIRTH EFFECTS ON KURDISH AUTISTIC CHILDREN

TWANA A. RAHIM MBChB, FIBMSPsych *

Submitted 2 Nov. 2014; accepted 31 Dec. 2014

ABSTRACT

Background and objectives Influence of season of birth has been predictable for different neuropsychiatric disorders including Autistic disorders. The objectives of the study is to examine the association between months as well as season of birth and the risk of Autistic Disorder.

Methods The sample recruited all Kurdish autistic children (359) in Hawler who were diagnosed by Kurdistan Autism Committee from 2009 due to the end of 2012. The researcher collected necessary data throughout the four-year period of the study.

Results Although January birth rates outnumbered the rest months, the study found no significant correlation between particular season of birth and the risk of Autistic Disorder. However, Kurdish autistic children's birth rates were significantly more during colder half of a given year.

Conclusion Findings of current report do not support the notion of seasonal pattern of birth in Autistic Disorder.

Duhok Med J 2014;8(2): 12-19.

Keywords: Autism, Seasonality, Risk Factors

Since the first description of a group of 11 children with similar exceptional odd behaviors by Leo Kanner, and his introduction of the first category of 'early infantile autism at 1943[1], Autism received increasingly attentions by scientific researchers and politicians alike.

American Psychiatric Association (APA), in it's text revised of the fourth edition of Diagnostic and Statistical Manual of Mental Disorders fourth (DSM-IV-TR), described autism in an individual category named Pervasive Developmental Disorders (PDD). PDD comprise: Autistic Disorder (AD), which is the commonest kind, Rett's Disorder, Childhood Disintegrative Disorder, Asperger's Disorder, and PDD not otherwise specified[2].

Despite the countless efforts to understand the underlying origin of this disabling condition, the exact etiological factors are precisely not clear yet[3]. However, several hypotheses are forwarded to explain this neurodevelopmental disorder including: biological factors like genetic abnormalities[4-6], associated medical conditions[7], as well as psychological factors like 'theory of mind.[8]

Impact of season of birth has been documented on different neuropsychiatric disorders, for which winter birth and schizophrenia is not the only debate. During last decades, researchers, worldwide, addressed similar question in

* *Assistant Professor of Psychiatry, Department of Medicine, School of Medicine, Faculty of Medical Sciences, University of Sulaimani, Sulaimani, Kurdistan region, Iraq*
Tel: +964 (0) 771 924 4549 Email: rahim.twana@gmail.com

relation to autism. However, findings were non-concluding. For instance, March births were reported in several studies[9-14]. While August births were also reported by some as well as other reports.[10,11] On the other hand, another study recorded October peak.[15]

Apart from individual months, researchers, also, attempted to find a correlation between seasons of birth and autism. Bolton et al concluded winter peak[15], while Konstantareas et al and Hebert et al came back with spring.[16,17]

Notwithstanding, several studies suggested neither significant seasonal nor monthly patterns of birth rates of children with autistic disorder.[12,13,18,19]

Present study aimed to reflect the correlation of birth date among Kurdish autistic children. Depending on literatures review, the author hypothesized that autism birth rate would be more represented in a particular season.

METHODS

Author recruited entire autistic children who did visit the Kurdistan Autism Committee (KAC) in Hawler governorate from 2009 to the end of 2012 for the purpose of assessment.

For the current analysis, the only inclusion criterion was children with Autistic Disorder (AD) type of PDD. Other categories, however, were ruled out. The reason behind excluding Rett's Disorder, Childhood Disintegrative Disorder, Asperger's Disorder, and PPD not otherwise specified was, principally, because the committee, KAC,' diagnoses were not certainly unquestionable.

For the purpose of diagnosis, the committee relies on Diagnostic and Statistical Manual (DSM-IV-TR) criteria for PDDs[2] as well as Mini International Neuropsychiatric Interview (MINI-KID-PARENT-6)[20-23].

MINI-KID-PARENT-6 is a semi-structured interview designed for the diagnosis of mental disorders among children and adolescents. It covers almost all psychiatric disorders, over 23 modules, in this age-frame group. This interview kit is principally intended to interview the child and parents together. Nevertheless; should the child be unable to understand or respond to questions, then parents are interviewed instead.

The last module, Module X, is designed for PDD. This module entails four key questions addressing the parents. The questions are, essentially, targeting social comprehension, stereotypic rituals, and peculiarity in behaviors. There are three answer-options: NO, UNSURE, and YES. For the purpose of definite diagnosis, the answers to all questions should be YES[20-23].

Since the emergence of KAC, the author obtained both the official and ethical approvals from Ministry of Health (MoH) and Hawler Medical University for recruiting autistic children who were diagnosed by the committee for the purpose of the study, acknowledging anonymity of each individual and family.

To address the questions of the study, the author obtained the day, month, and year of birth of each patient, in addition to gender of patients, age of mother at birth as well as the type of PDD.

Descriptive analyses as well as significance testing of differences at p value ≤ 0.05 were applied by adopting SPSS-21.

RESULTS

During the four-year period of the study (2009-2012), 369 patients with PDD were registered by KAC. Among them, 359 were diagnosed as Autistic Disorder (AD) and recruited in the current analyses. Among the remaining excluded 10 children, four were diagnosed as Rett's Syndrome, three as Childhood Disintegrative Disorder, one as Asperger's Syndrome, and two as Autistic Disorder Not Otherwise Specified.

For the remaining autistic sample, majority were male as shown in table 1.

Table 1. Description of the sample

Total		**359**
Gender N (%)	**Male**	**286 (79.7)**
	Female	**73 (20.3)**
Age of Mothers at Birth (M (SD))		**28.03 (6.415)**

Figure 1 illustrates that there was a statistically significant difference regarding month of birth among autistic children, when approximately 13% of autistic children were born at January, while, May, stood for the least common month of birth at below 5%.

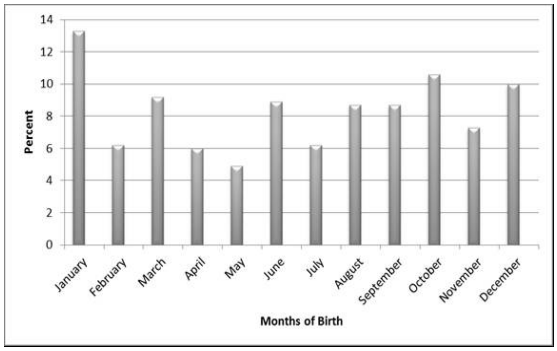


Figure 1. Months of birth of autistic patients
X2 =25.77, df= 11, p < 0.01

Although there were no significant differences among the four seasons of birth (Fig-2), significantly more autistic children were born in 'cold' than 'warm' weathers (55 vs 45 percent respectively) (Fig-3).

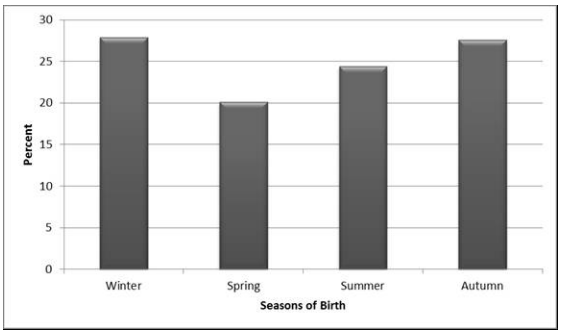


Figure 2. Seasons of birth of autistic patients
X2 = 5.334, df= 3, p > 0.05

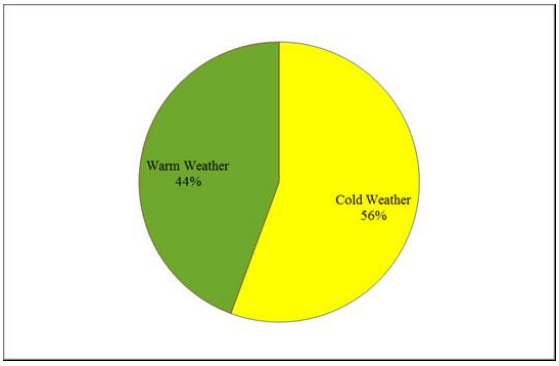


Figure 3. Weather of birth of autistic patients
X2 = 4.237, df= 1, p < 0.05

DISCUSSION

The author assessed the entire autistic children who were diagnosed by KAC during its first four years of founding. 359 children were found to suffer from AD. There was a relative increase in January birth dates (around 13%). On the other hand, while winter and autumn were the most, and spring the least common seasons of birth, the study couldn't contribute significant particular seasonality of birth among autistic children.

As referred earlier in this paper, studies elsewhere returned back with different findings, with birth rates peaked at March,[9-14] April, May, and June,[24]

August,[10,11] or October.[15] The confusion extended further to the season of birth when winter birth rate was highest in a study[13], and spring in others.[16,17,24] Such a mixed evidence of seasonality pattern of autistic birth rates might be returned back to several limitations in the previous studies as well as the current investigation. Stevens et al pointed out difficulties in defining autism in different studies as well as reliance on possible inaccurate statistical analyses.[13] These pitfalls, possibly, coupled by disagreement on seasons' definition.[19] For instance the significance of findings may depend on whether December is assigned to winter[15] or autumn.[24]

Meanwhile, several other studies pointed out to the myth of seasonality in autistics' birth rates.[18,19,25] Kolevzon et al concluded absence of any season of birth effect in autism, and they suggested that any future similar attempts have to be exercised with caution.[19]

In an attempt to test the difference between cold and warm climates, both autumn and winter births were aggregated under a new category named 'cold weather, while spring and summer births were allocated to 'warm weather'. When the difference between birth rates of both weathers was assessed, the study reported significant higher birth rate of autistic children during the 'cold weather'. Although there are no identical analyses in previous literatures, but such a 'cold weather' peak in autistic birth pattern may come parallel to previous findings where March or October birth rates outnumbered the rest of year. However, such a finding, possibly limited by the variability of weather across different months in different planet's zones.

Overall, the study concludes no evidence for seasonal pattern of birth among Kurdish autistic children. However, their birth rates were significantly more during the colder half of years. Based on current and previous investigations, and since the concept of seasonality may vary accordingly, current report suggests the future analyses to focus more on temperature dimensionality rather than chasing particular month or season of birth among autistic children.

As a final point, several limitations have faced the current project. The most outstanding one was the lack of 'control' which came about, unwillingly, due to lack of proper documentation of birth rates in the study region. This limitation turned out the study, more or less, descriptive. Nonetheless, current observation may serve as a proper snapshot for future, more conclusive, relevant analyses.

Also, lack of analogous studies in our region halted present critical comparison with findings from similar climates.

CONFLICTS OF INTEREST

None

ACKNOWLEDGEMENT

Acknowledgment are due to Kurdistan Autism Committee for its generous cooperation in collecting necessary data.

REFERENCES

1. Kanner L. Autistic disturbances of affective contact. Nerv Child 1943; 2:217–50. Reprinted in 1968. Acta Paedopsychiatr. 35(4):100–36.

2. American Psychiatric Association: diagnostic and statistical manual of mental disorders. Washington, DC: American Psychiatric Association, 2000.
3. Volkmar FR, Lord C, Bailey A, Schultz RT, Klin A. Autism and pervasive developmental disorders. J Child Psychol Psychiatry 2004; 45:135-70.
4. Rutter ML, MacDonald H, LeCouteur A, Harrington R, Bolton P, Bailey A. Genetic factors in child psychiatric disorder-II Empirical findings. J Child Psychol Psychiatry. 1990; 31:39-83.
5. Rutter ML, Bailey A, Bolton P, Le Couteur A. Autism: syndrome definition and possible genetic mechanisms. In: Plomin R, McClearn GE, eds. Nature, nurture and psychology. Washington DC American Psychiatric Association; 1993. p 269-84.
6. Bailey A, Le Couteur A, Gottesman I, Bolton P, Simonoff E, Yuzda E, Rutter M. Autism as a strongly genetic disorder: evidence from a British twin study. Psychol Med. 1995; 25:63-77.
7. Rutter ML, Bailey A, Bolton P, LeCouteur A. Autism and known medical conditions: myth and substance. J Child Psychol Psychiatry. 1994; 35: 311-22.
8. Baron-Cohen S, Tager-Flusberg H, Cohen DJ. Understanding other minds: perspectives from developmental cognitive neuroscience. 2nd ed, UK Oxford University Press; 2000.
9. Atlas JA. Birth seasonality in developmentally disabled children. Psychol Rep. 1989; 64: 1213-4.
10. Bartlik BD. Monthly variation in births of autistic children in North Carolina. J Am Med Wom Assoc. 1981; 35: 363-8.
11. Barak Y, Ring A, Sulkes J, Gabbay U, Elizur A. Season of birth and autistic disorder in Israel. Am J Psychiatry 1995; 152: 798-800.
12. Gillberg C. Do children with autism have March birthdays? Acta Psychiatr Scand. 1990; 82: 152-6.
13. Stevens MC, Fein D, Waterhouse LH. Season of birth effects in autism. J Clin Exp Neuropsychol. 2000; 22: 399-407.
14. Mouridsen SE, Nielsen S, Rich B, Isager T. Season of birth in infantile autism and other types of childhood psychoses. Child Psychiatry Hum Dev. 1994; 25: 31-43.
15. Bolton P, Pickles A, Harrington R, Macdonald H, Rutter M. Season of birth: issues, approaches and findings for autism. J Child Psychol Psychiatry. 1992; 33 (3): 509-30.
16. Konstantareas M, Hauser P, Lennox C, Homatidis S. Season of birth in infantile autism. Child Psychiatry Hum. Dev. 1986; 17(1): 53-65.
17. Hebert KJ, Miller LL, Joinson CJ. Association of autistic spectrum disorder with season of birth and conception in a UK cohort. Autism Res. 2010; 3(4): 185-90.
18. Landau EC, Cicchetti DV, Klin A, Volkmar FR. Season of birth in

autism: a fiction revisited. J Autism Dev Disord. 1999; 29(5): 385-93.

19. Kolevzon A, Weiser M, Gross R, Lubin G, Knobler HY, Schmeidler J, et al. Effects of season of birth on autism spectrum disorders: fact or fiction? Am J Psychiatry. 2006; 163: 1288-90.
20. Sheehan DV, Lecrubier Y, Harnett-Sheehan K, Amorim P, Janavs J, Weiller E, et al. The Mini International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview. J Clin Psychiatry. 1998; 59(Suppl 20):22-33.
21. Sheehan DV, Lecrubier Y, Harnett-Sheehan K, Janavs J, Weiller E, Bonara LI, et al. Reliability and validity of the MINI International Neuropsychiatric Interview (M.I.N.I.): according to the SCID-P. Eur Psychiatry. 1997; 12: 232-241.
22. Lecrubier Y, Sheehan D, Weiller E, Amorim P, Bonora I, Sheehan K, et al. The MINI International Neuropsychiatric Interview (M.I.N.I.) A short diagnostic structured interview: reliability and validity according to the CIDI. Eur Psychiatry. 1997; 12: 224-231.
23. Amorim P, Lecrubier Y, Weiller E, Hergueta T, Sheehan D. DSM-III-R Psychotic disorders: procedural validity of the Mini International Neuropsychiatric Interview (M.I.N.I.). Concordance and causes for discordance with the CIDI. Eur Psychiatry. 1998; 13: 26-34.
24. Tanoue Y, Oda S, Asano F, Kawashima K. Epidemiology of infantile autism in southern Ibaraki, Japan: differences in prevalence in birth cohorts. J Autism Dev Disord. 1988; 18: 183-6.
25. Yeates-Frederikx MHM, Nijman H, Logher E, Merckelbach HLGJ. Birth patterns in mentally retarded autistic patients. J Autism Dev Disord. 2000; 30: 257-62.

پوختە

کاریگەیەکانی وەرزی لەدایکبوون لە سەر منداڵانی ئۆتیزمی کورد

پێشەکی و ئارمانج: کاریگەری وەرزی لە دایکبوون پێشبینی کراوە لە چەندین نەخۆشیەکانی مێشک و دەمار، لە نێواندانیا تێکچوونەکانی ئۆتیزم. بەم توێژینەوەیە هەولی دا دەریخات کە مانگ و وەرزی لە دایک بوون کاریگەری دەبێت لەسەر ئەگەری تووشبوون بە ئۆتیزم.

ڕێکێن ڤەکولینێ: هەموو ئە و منداڵانەی لەلایەن لیژنەی دەست نیشانکردنی ئۆتیزم لە کوردستان کە ژمارەکەیان (٣٥٩) منداڵی تووشبوو بوون کۆکرانەوە لەنێوان ساڵانی ٢٠٠٩ و ٢٠١٢ دا. هەموو ئەو زانیاریانەی پێویست بوو کۆکرایەوە بە درێژایی چوار ساڵی توێژینەوەکە.

ئەنجام: هەرجەندە منداڵانی ئۆتیزم زیاتر لەدایکبووی مانگی یەکەمی ساڵەکان بوون، ئەم توێژینەوەیە دەریخست کە مانگی لەدایکبوون کاریگەری نییە لەسەر ئەگەری تووشبوون بە ئۆتیزم. بەڵام، ئەم توێژینەوەیە دەریخست کە منداڵانی ئۆتیزم بە شێوەیەکی بەرچاو لەوەرزە ساردەکاندا لەدایک بوون.

دەرئەنجام: ئەم توێژینەوەیە دەری خست کە وەرزی لە دایکبوون کاریگەری نییە لەسەف مەترسی تووشبوون بە ئۆتیزم.

الخلاصة

تأثيرات موسم الولادة على الأطفال الكرد المصابين بالتوحد

خلفية وأهداف البحث: من الممكن التنبؤ بتأثيرات موسم الولادة على نسب ظهور مختلف الاضطرابات العصبية و النفسية. من جملة هذه الاضطرابات، اضطرابات التوحد لدى الاطفال هو دراسة العلاقة بين مختلف الأشهر وكذلك موسم الولادة مع خطر ظهور اضطرابات التوحد.

طرق البحث: شملت العينة جميع الأطفال الكرد المصابين بالتوحد والبالغ عددهم (٣٥٩) في مدينة اربيل و الذين تم تشخيصهم من قبل لجنة تشخيص التوحد في المدينة و في الفترة الممتدة بين عام ٢٠٠٩ لغاية نهاية عام ٢٠١٢. لقد قام الباحث بجمع البيانات اللازمة طيلة فترة الدراسة البالغة أربع سنوات.

النتائج: على الرغم من أن معدلات الولادة في شهر كانون الثاني قد فاقت نظيراتها في بقية الأشهر، أثبتت الدراسة عدم وجود ترابط مهم بين أي موسم معين من الولادة مع خطرظهور اضطرابات التوحد. ومع ذلك، لقد كانت معدلات ولادة الأطفال الكرد المصابين بالتوحد أكثر بشكل ملحوظ خلال النصف الاكثر برودة من السنة.

الاستنتاج: نتائج التقرير الحالي لا تدعم مفهوم التأثير النمطي لموسم الولادة وانعكاسه على ظهور اضطرابات التوحد في تلك المواليد.

A STUDY OF BLOOD CHOLESTEROL AND RELATED RISK FACTORS IN PRIMARY SCHOOL CHILDREN OF DUHOK GOVERNORATE, KURDISTAN REGION, IRAQ

HIVI M. MAHMOUD, MSc*
SHERWAN F. SALIH, FIBMS**
DHIA J. AL-TIMIMI, M.Phil, PhD***

Submitted 4 Nov 2014; accepted 31 Dec 2014

ABSTRACT

Objective: To determine blood cholesterol levels and related risk factors of hypercholesterolemia in a sample of primary school children from Duhok governorate.
Methods: A cross sectional- study of 1136 primary school children (572 males, 564 females) aged 6-10 years; from December 2013 to May 2014 was conducted. A structured questionnaire was used to get information relating to animal fat intake, social status; and family history of diabetes mellitus, hypertension and hypercholesterolemia. The children were examined for height, weight, blood cholesterol levels and the body mass index (BMI) were calculated. Hypercholesterolemia defined according to the American Academy of Pediatrics (AAP) guidelines. A cutoff point of < 170 mg/dl of total cholesterol used to classify children as on desirable level, borderline 170-199 mg/dl and high > 200 mg/dl.
Results: The mean blood cholesterol was 154.4±35.8 mg/dl with a range of 76-278 mg/dl. Desirable, borderline and high blood cholesterol levels were defined in 745(65.6%), 286(25.2%) and 105(9.2%) children, respectively. Of 1136 children, 50(4.4%) were overweight; mean blood cholesterol in overweight was 181.2 mg/dl compared to 153.8 mg/dl in not overweight children (P < 0.01). Mean blood cholesterol levels were not significantly different by age, gender, positive family history of children for diabetes mellitus, hypertension and hypercholesterolemia, animal fat intake/week and social status. Odds ratio of having high blood cholesterol levels in overweight children compared to not overweight children was 2.14 (95%Cl 1.21-3.78).
Conclusions: A borderline or abnormal blood cholesterol level screened by the American Academy of Pediatrics guidelines (AAP) values defined in one third of primary school children. Overweight was the major risk factor for elevated blood cholesterol in primary school children from Duhok governorate.

Duhok Med J 2014;8(2): 20-29.

Keywords: Blood Cholesterol, Pediatric hypercholesterolemia

Adults are not the only people affected by high cholesterol; children also may have high levels of cholesterol, which can cause health problems when the child gets older. Too much cholesterol leads to the build-up of plaque on the walls of the arteries, which supply blood to the heart and other organs. Completing evidence shows the atherosclerotic process (buildup of fatty plaque in arteries) begins in childhood and progresses slowly into adulthood later in life, it often leads to coronary heart disease.[1] Children from families with coronary heart disease or if a

*Assistant Lecturer, Department of Clinical Biochemistry, College of Medicine, University of Duhok
** Lecturer, Department of Clinical Biochemistry, College of Medicine, University of Duhok
*** Professor, Department of Clinical Biochemistry, College of Medicine, University of Duhok
Corresponding author: Prof. Dhia J. Al-Timimi. Email: altmimidj@yahoo.com. Mobile: +9647504228908

parent of the child has high cholesterol are often tested for lipids to identify those who needs to take steps to prevent the risk of atherosclerotic disease.[2] In July 2008, the American Academy of pediatrics (AAP) made new recommendations for cholesterol screening in children. Screening advised for kids with a family history of high cholesterol or blood fats, or a family history of premature heart disease (age 55or younger for men, age 65 or younger for women). Screening is also recommended for kids who are overweight (at or above the 85th percentile), and who have other risk factors such as smoking, diabetes, or high blood pressure.[3] Later on, the AAP released a new practice guideline for "cardiovascular health". The AAP no longer recommends routine cholesterol testing in preschool age children, as was recommended back in 2008, this recommendation is replaced by universal lipid profile screening at age 9-11 years and then again at age 12-17 years, even in the absence of high-risk factors.[4] Thus, special emphasis directed toward screening of hypercholesterolemia of children aged 8 years and older. In Iraq, there have been no recorded attempts to study the prevalence and risk factors of pediatric hypercholesterolemia and data on serum cholesterol levels of Iraqi children are limited[5]. This study therefore aimed to establish baseline data on blood cholesterol levels and related risk factors of hypercholesterolemia in primary school children from Duhok governorate.

METHODS

Across sectional study carried out during the period from December 2013 to May 2014. One thousand and one hundred thirty six primary school children, aged 6-10.2 years (572 males and 564 females) enrolled in the study. A stratified random sampling method used to select a representative sample of children from thirteen different primary schools in different areas of Duhok governorate, Kurdistan region, Iraq. Children with acute illnesses, a history of chronic liver or renal disease, thyroid dysfunction and those who were taking medication that altered cholesterol metabolism were excluded from the study. Informed consent with questionnaire obtained from all children provided by their parents. The Board of postgraduate committee of the Duhok University-medical branch approved the study protocol. All children completed a pre-tested questionnaire, which included anthropometric data and family history of diabetes; hypertension and hyperlipidemia. Body Mass Index (BMI) was calculated for each child. For analysis, the height and weight measurement for each child was used to calculate the (BMI) as a weight in kilograms (kg) divided by height in meter squared (m^2). Children were divided according to growth chart and BMI were plotted on chart and divided into two groups not overweight(less than 95th percentile), and overweight (more than 95th percentile)[6] .Animal fat intake /week recorded for each child. Crowding index (CI) based on number of household dividing by number of rooms in the house calculated.

American Academy of pediatrics reference values adopted for classification of children hypercholesterolemia. A cutoff

point of < 170 mg/dl of total cholesterol used to classify children as on desirable level, borderline 170-199 mg/dl and high > 200 mg/dl[3].

A finger prick was used to obtain blood for total cholesterol analysis using a portable cholesterol analyzer (biochemical systems international BSI, S.r.I. vai G. Ferranis 220-52100 Arezzo-Italia). About 5ml of blood samples withdrawn by venepuncture, using VACUTAINER from the antecubital vein and transfer into BD Vacutainer System CAT- plain tubes for those students having serum cholesterol levels of 170mg/dl or more by portable device analyzer. The sera then collected in a plain tube labeled numerically for later analysis in emergency Duhok teaching hospital using Biolis 24i auto analyzer. Inter- assay precision of portable cholesterol method was determined, mean of 30 pooled serum sample =182.2 mg/d ± SD = 4.4 mg/dl. Coefficients of variation = 2.9%. All data analyzed using the Statistical Package for Social Science SPSS version 18.0; paired student t- test used to assess differences in serum analyte among groups. Categorical variables compared by Chi-square test. Level of statistical significance (P value) was set at < 0.05.

RESULTS

The general characteristics of the primary school children described in Table 1. The mean age was 8.02±1.29 years with a range of 6 to 10.2 years. The mean blood cholesterol was 154.4±35.8 mg/dl with a range of 76-278mg/dl. Desirable, borderline and high blood cholesterol levels were defined in 745 (65.6%), 286 (25.2%) and 105 (9.2%) children, respectively. Blood cholesterol levels and number of children with respect to age has shown in Table 2. Blood cholesterol levels were not significant difference by age using cutoff value 8 years (p >0.05). The overall prevalence of borderline or abnormal blood cholesterol (>170mg/dl) was 34.4%; 36.6% in children at age of 6 years and 25.5% in children at age of 10 years (p<0.01). The mean±SD of blood cholesterol levels with respect to categoric variables has shown in Table 3. No significant deference detected in blood cholesterol between male and female children. Blood cholesterol levels were significantly higher in overweight children than in children who were not overweight (p <0.01).Children with positive family history of diabetes mellitus (DM), hypertension and hypercholesterolemia had higher mean blood cholesterol levels than those with negative family history, but the difference was not statistically significant. Children with high social status also had higher mean blood cholesterol levels than those with low social status. Odds ratio of having high blood cholesterol levels in overweight children compared to not overweight children was 2.14 (95%Cl 1.21-3.78). Odds ratio of having high cholesterol levels were not significant differences by other categoric variables such as age group using cutoff value 8 years, gender ,family history of DM, hypertension and hypercholesterolemia (Table 4). None of the children found with clinical manifestation of primary hypercholesterolemia.

Table 1. Children characteristics (n=1136)

Parameters	
Age (years)*	**8.02±1.29**
Male sex [n (%)]	572(50.3)
BMI (kg/m^2)*	16.0±2.3
Prevalence of overweight [n (%)]	**50(4.4)**
Blood cholesterol level (mg/dl)*	154.4±35.8
Prevalence of blood cholesterol	
Desirable <170 mg/dl [n (%)]	745(65.6)
Borderline 170-199mg/dl [n(%)]	286(25.2)
High >200mg/dl [n(%)]	105(9.2)
Prevalence of positive family history	
DM [n(%)]	64(5.6)
Hypertension [n (%)]	173(15.2)
Hypercholesterolemia [n (%)]	141(11.4)

* mean±SD

Table 2. Blood Cholesterol levels in children according to age

		Blood cholesterol leves (mg/dl)			
			Desirable <170	**Bodrerline 170-199**	**High => 200**
Age (Yrs)	**n**	**mean±SD**	**n(%)**	**n(%)**	**n(%)**
6	**161**	**155.90±33.4***	**102(63.4)**	**35(21.7)**	**24(14.9)****
7	**244**	**153.5±37.1**	**163(66.8)**	**58(23.8)**	**23(9.4)**
8	**226**	**155.94±29.9**	**131(58.0)**	**71(31.4)**	**24(10.6)**
9	**313**	**153.30±39.1**	**206(65.8)**	**82(26.2)**	**25(8.0)**
10	**192**	**153.61±31.8**	**143(74.5)**	**40(20.8)**	**9(4.7)**

*Not significant, $p>0.05$, ** Children at age 6 years Vs at 10 years, $p<0.01$

Table 3. Blood cholesterol levels in children according to categoric variables

Variables	**Blood Cholesterol levels (mg/dl)**		
	n	***mean±SD**	***p*-value**
Age (Yrs)			
<8.0	405	154.4±35.6	0.92
≥8.0	731	154.1±34.4	
Sex			
Males	572	154.3±27.4	0.90
Females	564	155.2±31.2	
BMI (kg/m^2)			
Not overweight <95th %	1086	153.4± 37.7	<0.01*
Overweight ≥95th %	50	181.2±34.2	
Family history			
DM			
Negative	1072	153.7±41.3	0.27
Positive	64	165.1±28.1	
Hypertension			
Negative	963	152.8±39.2	0.13
Positive	173	166.9±32.6	
Hypercholesterolemia			
Negative	995	153.8±29.9	0.09
Positive	141	171.7±27.6	

Variables		Blood Cholesterol levels (mg/dl)	
	n	*mean±SD	*p*-value
Animal fat intake/Week			
<3.0	364	152.7±33,6	0.08
≥3.0	772	155,2±37.4	
Social status			
Low (CI >3.3)	397	150.7± 31.1	0.07
High (CI<2.1)	739	160.0 ±36.5	

***overweight versus not overweight, $p<0.01$**

Table 4. Numbers of children with desirable and abnormal blood cholesterol levels according to categoric variables

Variables		Blood Cholesterol levels (mg/dl)			
	n	<170 n(%)	≥170 n(%)	Odds ratio	(95% CI)
Age (Yrs)					
<8.0	405	265(65.4)	140(34.6)	1.0	0.76-1.27
≥8.0	731	480(65.7)	251(34.3)		
Sex					
Males	572	375(65.6)	197(34.4)	0.99	0.78-1.27
Females	564	370(65.6)	194(34.4)		
BMI (kg/m^2)					
<95th %	1086	721(66.4)	365(33.6)	2.14	1.21-3.78
≥95th %	50	24(48.0)	26(52.0)		
Family history					
DM					
positive	64	43(67.2)	21(32.8)	1.07	0.63-1.8
Negative	1072	702(65.5)	370(34.5)		
Hypertension					
Positive	173	102(59.0)	71(41.0)	0.71	0.51-0.99
Negative	963	643(66.8)	320(33.2)		
Hypercholesterolemia					
positive	141	87(61.7)	54(38.3)	0.82	0.57-1.19
Negative	995	658(66.1)	337(33.9)		
Animal fat intake/Week					
<3.0	364	243 (66.7)	121 (33.3)	1.08	0.83-1.40
≥3.0	772	502 (65.1)	270 (34.9)		
Social status					
Low (CI >3.3)	397	275 (69.3)	122 (30.7)	1.29	0.99-1.67
High (CI<2.1)	739	470 (63.6)	269 (36.4)		

DISCUSSION

This study determined the levels of blood cholesterol and the risk factors for abnormal blood cholesterol levels in primary school children from Duhok governorate. The main findings of the present study were that one third of children screened by AAP guidelines had borderline or abnormal cholesterol levels and overweight in children increases the odds of having hypercholesterolemia risk factors. Several studies have shown that the prevalence of elevated serum total cholesterol of >200mg/dl varies from 1.2-3%.[7,8] The present study demonstrated an abnormal cholesterol levels in 9.2% of

children. The current abnormal cholesterol levels in primary school children are worth mentioning. The prevalence is markedly higher than values of school- children in western countries.[9] Several factors have a positive impact on blood cholesterol level, particularly in childhood of these, overweight and obesity are the factors that cause the most marked positive effects on blood cholesterol levels. There was a trend towards cholesterol-overweight association. Children with overweight (as was assessed by BMI-95th %) had higher mean blood cholesterol levels and a higher prevalence of elevated blood cholesterol as compared to children that were not overweight. This observation reflects the additive effect of increase body weight on blood cholesterol levels, which is consistent with previous studies[10]. Although the proportion of overweight was lower than that reported in some Arab countries,[11,12] but the risk of abnormal cholesterol was higher in overweight children compared to children that were not overweight (52.0% Vs 33.6%). It was difficult to find a high prevalence of abnormal blood cholesterol levels among the studied children; since elevated cholesterol has been associated with many etiological factors, such as genetic, socioeconomic status, sedentary life style and lack of physical activities with increasing body weight. All these are at increasing rate in our population; it is therefore, we could attribute the high prevalence of abnormal cholesterol to genetic and body weight variations. Our results were in agreement with some reports on ethnic groups, especially on Arabic and Turkish population that had a high prevalence of abnormal cholesterol.[13,14] However, no firm conclusion can be draw about risk factors leading to high prevalence of abnormal blood cholesterol levels in our population, but still permissible to speculate that family history of hypercholesterolemia and high body weight are major effective factors. The proportions of family history of hypercholesterolemia among children in our study are similar to or higher than that previously reported in offspring and other first-degree relatives of patients with metabolic disease.[15] Since the prevalence of abnormal blood cholesterol levels among children with positive family of hypercholesterolemia compared with negative family history as evident from our study showed no significant difference, early detection and weight reduction could reduce the significant atherosclerosis risk in these children. However, there is still a controversy whether the children with primary hypercholesterolemia benefited from weight reduction, although, none of the children studied, had primary hypercholesterolemia.

A new study of over 12,000 children finds that about a third of them have borderline or "abnormal" cholesterol levels.[16] The results of the current study showed 34.4% of children had borderline or abnormal blood cholesterol levels, this observation of high prevalence of abnormal blood cholesterol does support the high risk in the population studied. This encourages us to implant the preventive efforts at young ages. Preventive efforts are very important in

reducing blood cholesterol levels, as secondary prevention of hypercholesterolemia will result in primary prevention for coronary artery disease. It is well known in the preventive health that Knowledge, Attitude and Practice (KAP) are formed early in life, although knowledge can be changed easily, attitude and practice are much harder to change especially with age. Therefore, we have to target the youth, as attitudes and practices are easier to change and changes are more effective.[17] Modification of risk factors beginning in childhood and young adulthood can lead to restoration to normal or improvement in measures of subclinical atherosclerosis, both in those with genetic dyslipidemias and those with dyslipidemia secondary to obesity. Further studies are needed in larger sample size to investigate the effectiveness of control program for lowering blood cholesterol levels among Duhok children. The present study was limited by its some variables were dependent on history taking and this carries an inherent risk of bias. Despite this limitation, our descriptive study, interpreted with suitable caution, can offer some useful insight to complement the data from the forthcoming studies using follow up.

A borderline or abnormal blood cholesterol level screened by the American Academy of Pediatrics guidelines (AAP) values defined in one third of primary school children. Overweight was the major risk factor for elevated blood cholesterol in primary school children from Duhok governorate. We need a comprehensive program that includes dietary education and weight reduction to improve the cholesterol level of the Duhok governorate children.

ACKNOWLEDGEMENT

we acknowledge the support of the staff of Duhok primary schools who provided the facilities for the interviews and the records.

REFERRENCES

1. McCrindle BWI, Kwiterovich PO, McBride PE, Daniels SR, Kavey RE.Guidelines for Screening in children and adolescents: Bringing evidence to the debate. Pediatrics 2012 ;130(2): 353-6.
2. Makedou A, Kourti M, Makedou K, Lazaridou S, Varlamis G. Lipid profile of children with a family history of coronary heart disease or hyperlipidemia: 9-year experience of an outpatient clinic for the prevention of cardiovascular diseases. angiology 2005; 56: 391-5.
3. Daniels SR, Greer FR. Lipid screening and cardiovascular health in children. Pediatrics 2008; 122(1):198-208.
4. Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents. pediatrics 2011; 128 (5): S213-56.
5. Mula-Abed W-A, Chilmeran SK. Prevalence of dyslipidemia in the Iraqi population. Saudi Medical Journal 2007; 28 (12): 1868-74.
6. Flegal KM, Ogden CL, Wei R, Kuczmarski RL, Johnson CL.Weight-for-stature compared with body mass index-for-age growth charts for the united states from the centers for

disease control and prevention. Am J Clin Nutr 2002; 75: 761-6.
7. Rerksuppaphol S, Rerksuppaphol L Prevalence of dyslipidemia in Thai schoolchildren. J Med Assoc Thai 2011; 94(6):710-5.
8. Fesharakinia A, Zarban A, Sharifzadeh GR. Profiles and Prevalence of dyslipidemia in school children in south Khorasan Province, eastern Iran. Arch Iranian Med 2008; 11 (6): 598-601.
9. Couch SC, Cross AT, Kida K, Ros E, Plaza I, Shea S, Deckelbaum R. Rapid westernization of children's blood cholesterol in 3 countries, evidence for nutrient-gene interactions. Am J Clin Nutr 2000; 72(5): 1266s-74s.
10. Lobstein T, Baur L, Uauy R. Obesity in children and young people: a crisis in public health. Obes Rev 2004; 5(1):4–104.
11. Rizk NM, Yousef M. Association of lipid profile and waist circumference as cardiovascular risk factors for overweight and obesity among school children in Qatar. Diabetes Metab Syndr Obes 2012; 5: 425–32.
12. El-hazmi M,Warsy A. A comparative study on prevalence of overweight and obesity in different provinces of Saudi Arabia. J Trop pediatr 2002;48: 172-7.
13. Al-Haddad FH, Little BB, AbdulGafoor AG. Childhood obesity in United Arab Emirates school children: a notional study. Ann Hum Biol 2005,32:72-9.
14. Uçar B, Kiliç Z, Dinleyici EC, Colak O, Güneş E. Serum lipid profiles including non-high density lipoprotein cholesterol levels in Turkish school-children. Anadolu Kardiyol Derg 2007;7(4):415-20.
15. Al-Timimi DJ, Mustefa AH. Prevalence of metabolically obese normal weight individuals among first degree relatives of patients with type 2 diabetes mellitus. JABHS 2012; 13(3): 2-8.
16. Pharma and healthcare. Cholesterol levels too high In most children, Study Finds 2014. Avialable at http://www.forbes.com.
17. Vaidya A, Aryal UR, Krettek A. Cardiovascular health knowledge, attitude and practice/behaviour in an urbanising community of Nepal: a population-based cross-sectional study from Jhaukhel-Duwakot Health Demographic Surveillance Site. BMJ Open 2013; 3(10): 1136.

پوختە

ڤەکۆلینا کولیستیرولی دناڤ خوینیدا دگەل هوکارین مەترسیێ بێن گرێدای پێڤە لدەف زاروکێن قوناغا بنەرەتی ل پارێزگەها دهوکێ، هەرێما کوردستانێ – عێراق

پێشەکی و ئارمانج: ژبو دەستنیشانکرنا ئاستێن کولیستیرولی دناڤ خوینیدا دگەل هوکارین مەترسیێ بێن گرێدای پێڤە لدەف زاروکێن قوناغا بنەرەتی ل پارێزگەها دهوکێ.

ریکێن ڤەکولینێ: ڤەکولینەکا cross sectional هاتە وەرگرتن کو پیکهاتبو ژ ١١٣٦ قوتابیێن قوناغا بنەرەتی (٥٧٢ نێر، ٥٦٤ مێ) ژێرێ ٦–١٠ سالی، دماوێ دناڤبەرا کانونا ئێکێ سالا ٢٠١٣ بو ئەیارا سالا ٢٠١٤. بیاننامەك هاتە بکار ئینان بو خرڤەکرنا پێزانینا لسەر بکارئینانا دوهنێ گیانەوەرا، بارێ جڤاکی، و هەبونا بلندبونا فشارا خوینێ و نەخوشیا شەکرێ و بلندبونا کولیستیرولێ دناڤ مالێ دا. و هەروەسا (Body Mass Index) هاتە هەژمارتن بو هەر کەسەکی. بلندبونا کولیستیرولێ دناڤ خوینێدا هاتە سنورکرن لدیف رێنمایێن ئەکادیمیا ئەمریکی بو پزیشکیا بچویکا. ١٧٠ mg/dl هاتە بکارئینان وەکو ئاستەکێ باش بو کولیستیرولێ دناڤ خوینێدا، ١٧٠ mg/dl –١٩٩ لسەر لێڤێ و پتر ژ ٢٠٠ mg/dl هاتە هەژمارتن بلند.

ئەنجام: تێکرایێ قیمەتی یێ کولیستیرولی دناڤ خوینێدا 154.4±35.8 mg/dl دگەل مەدایەکی ژ 76-278 mg/dl. ئاستێن کولیستیرولی بێن باش و ئەوێن لسەر لێڤێ و بلند هاتنە پێناسەکرن لدەف ,745(65.6%) 286(25.2%) ئو 105(9.2%) زاروکان، لدیف ئێك. ژ 1136 زاروکان (4.4٪) 50 ژوان کێشا وان یا زێدەبوو: تێکرایێ قیمەتی یێ کولیستیرولێ دناڤ خوینێدا 181.2 mg/dl بەرامبەر 153.8 mg/dl لدەف وان زاروکێن کێشا وان نەیا زێدە ($P < 0.01$). تێکرایێ قیمەتی یێ کولیستیرولی دناڤ خوینێدا نەیێ جیاوازبوو برەنگەکێ بەرجاف سەبارەت تەمەنی، رەگەزی، هەبونا ئێشێن شەکرێ یان بلندبونا فشارا خوینێ یان بلندبونا ئاستێ کولیستیرولی دناف خوینێدا دناف بنەمالێ دا، ئان وەرگرتنا دونێ گیانەوەرا یان بارێ جڤاکی. رێژەیا Odds بو بلندبونا ئاستێ کولیستیرولی دناف خوینیدا لدەف وان زاروکێن کێشا وان یا زێدە بەرامبەر وان یێن کێشاوان نەیا زیدە 2.14 (95%Cl 1.21-3.78).

دەرئەنجام: بلندبونا کولیستیرولی دناف خوینێدا یان نە دروستیا وی ئەوا هاتیە خاندن لدیف رێنمایێن ئەکادیمیا ئەمریکی بو پزیشکیا بچویکا هاتە پێناسەکرن لدەف پشکەکێ ژ سێ پشکا ژ زاروکێن قوناغا بنەرەتی. بلندبونا کێشا لەشێ مرۆڤی هوکارێ مەترسیێ یێ سەرەکی بوو بو بلندبونا کولیستیرولی دناف خوینێدا لدەف زاروکێن قوناغا بنەرەتی ل پاریزگەها دهوکێ.

الخلاصة

دراسة الكوليسترول في الدم مع عوامل الخطورة المرتبطة بها في اطفال المرحلة الابتدائية في محافظة دهوك، إقليم كردستان، العراق

خلفية البحث والأهداف: لتحديد مستويات الكوليسترول في الدم مع عوامل الخطورة المرتبطة بأرتفاع الكوليسترول في عينة من اطفال المرحلة الابتدائية في محافظة دهوك.

طرق البحث: أخذت الدراسة مقطعية، حيث تألفت من 1136 طالب من طلاب المرحلة الابتدائية (572 ذكر، 564 إناث) من عمر 6–١٠ سنوات؛ من الفترة ما بين كانون الاول 2013 لغاية أيار2014. استعمل اسيبيان منظم لجمع معلومات تتعلق بأخذ الدهون الحيوانيه, الحالة الاجتماعية, و تأريخ العائلة متضمنا ارتفاع ظغط الدم, مرض السكر, وأرتفاع الكويستيرول في الدم. تم فحص طول الاطفال, اوزانهم, مستوى الكوليستيرول وكذلك تم قياس مؤشر كتلة الجسم (BMI). تم تحديد أرتفاع الكوليستيرول في الدم حسب قيم ارشادات الاكاديمية الامريكية للأطفال. تم استعمال نقطة الفصل اقل من 170 mg/dl كمستوى مرغوب فيه للكوليستيرول في الدم, على الحواف 170–199 mg/dl واعتبارها عالي اذا كان يساوي أو أكثر من 200 mg/dl.

النتائج: معدل القيمة لمستوى الكوليستيرول في الدم كان 154.4±35.8 mg/dl مع مدى يتراوح من 76–278 mg/dl. مستويات الكوليستيرول المرغوبة, والتي على الحواف والعالية عرفت في 286(25.2%), 745(65.6%) و 105(9.2%)طفل، على التوالي. من 1136 طفل, 50(4.4%) كانوا زائدي الوزن; معدل القيمة لمستوى الكوليستيرول في الدم كان 181.2 mg/dl مقارنة ب 153.8mg/dl في الاطفال الذين هم ليسوا زائدي الوزن ($P < 0.01$). معدل القيمة لمستوى الكوليستيرول في الدم لم يكن يختلف بشكل ملحوظ بالعمر, الجنس, ايجابية وجود مرض السكر في العائلة او ارتفاع ضغط الدم او ارتفاع الكوليستيرول في الدم او أخذ الدهون الحيوانيه والحالة الاجتماعية. نسبة ال odds لوجود ارتفاع الكوليستيرول في الدم في الاطفال زائدي الوزن مقارنة بالذين هم ليسوا زائدي الوزن كان 1.21– 95%CI 2.14 3.78

الاستنتاج: ارتفاع الكوليستيرول في الدم او شذوذه والتي تم مسحها من قبل قيم ارشادات الاكاديمية الامريكية للأطفال عرفت في ثلث اطفال المرحلة الابتدائية. زيادة الاوزن كان عامل الخطورة الاساسي لزيادة الكوليستيرول في الدم لدى اطفال المرحلة الابتدائية في محافظة دهوك.

EFFECT OF ZINC SUPPLEMENTATION ON PERIODONTAL STATUS

SUZAN M. SALIH (MSc)*
HASHIM D. MOUSA (Ph.D)**
DHIA J. AL-TIMIMI (MPhil, PhD)***

Submitted 2 Dec 2014; accepted 31 Dec 2014

ABSTRACT

Background and objectives A link between the occurrence of periodontitis and zinc deficiency has been suggested. The aim of this study was to evaluate the effect of zinc supplementation on periodontal status in patients with type 2 diabetes mellitus.

Methods Three hundred diabetic patients with chronic periodontitis (age range 45-65 years old) were selected. The patients divided into three groups as I :zinc supplement; II: scaling and polishing; III: zinc plus scaling and polishing. At initial visit, the blood samples of all patients collected and analyzed for serum zinc and glucose. Periodontal status of the patients based on clinical attachment loss and probing pocket depth score was determined. The patients in group I and group III were assigned to receive 50 mg elemental zinc three times a day for six months period. Periodontal status reassessed after intervention following the same procedure.

Results At initial, there were no significant differences in any parameter between the three groups. At the end of the 6 months period, the mean values of clinical attachment loss and probing pocket depth scores were significantly lower among group III as compared to group II ($P<0.01$). The percentage of change in clinical attachment loss and probing pocket depth were significantly higher in the group III as compared to group II ($p<0.05$).

Conclusion Zinc supplement for vulnerable population to low zinc status such as type 2 diabetes mellitus patients decreases the chance of the occurrence of severe periodontitis.

Duhok Med J 2014;8(2): 30-37.

Keywords: Zinc, Periodontitis, Diabetes mellitus

Periodontitis is a multifactorial disease caused by gram-negative anaerobic bacteria, with systemic and environmental factors. Periodontitis, if untreated, leads to loss of alveolar bone and supporting tissues of the teeth, so a proper intervention is required from stage to stage in order to retain the teeth in the oral cavity in functional state for long period[1]. Patients with type 2 diabetes mellitus (T2DM) are at a higher risk for periodontitis[2,3,4], and screening of patients with diabetes and periodontitis that may threaten longevity and the quality of life is necessary[5].

Zinc(Zn) is an essential trace element to all forms of life because of its fundamental role in gene expression, cell development of cell[6]. It has been reported that the altered metabolism of zinc would lead to some diabetic complications such as periodontitis[7,8]. In rate, the improve effect of oral supplementation of zinc has been determined in rat; oral and periodontal

* *Assistant lecturer, Department of Clinical Biochemistry , Department of Periodontology, Faculty of Medical Sciences, University of Duhok, Kurdistan Region, Iraq.*
** *lecturer Department of Clinical Biochemistry , Department of Periodontology, Faculty of Medical Sciences, University of Duhok, Kurdistan Region, Iraq.*
*** *Professor of clinical Biochemistry Department of Clinical Biochemistry, Faculty of Medical Sciences, University of Duhok, Kurdistan Region, Iraq.*
Corresponding author: Prof. Dhia J. Al-Timimi. Email: altmimidj@yahoo.com. Mobile: +9647504228908

health in rat was better in oral zinc supplementation than in zinc deficiency[9]. In the light of these findings; considering that link between zinc and periodontitis may have a role in the improvement of periodontal tissues in T 2 DM; we aimed to evaluate the effect of zinc supplementation on periodontal status in patients with T2 DM.

METHODS

Study population

A total of 300 T2 DM patients with periodontal disease were included in the study.

The patients were divided into three groups consisting of 100 participants in each group as follows: Zinc supplement (group I); scaling and polishing (group II); and zinc plus scaling and polishing (group III).Their age ranged from 45-65 years. All patients were selected from the outpatients attending Diabetes Health Center, Duhok, Kurdistan Region, Iraq. Patients interviewed and informed about the nature of the study and then verbal consent was obtained from each subject. The study protocol was approved by the ethical Committee of the General Directorate of Health in Duhok.

Study protocol

The participants underwent two visits, at base line and after 6 months of taking oral zinc supplementation and periodontal treatment. A protocol for zinc supplementation involved zinc sulphate cap 220 mg three time daily which is equivalent to 50mg elemental zinc (150mg /day) for six months period. The first group were given zinc only, the second group involved periodontal treatment (scaling and polishing) without zinc therapy, and the third group were given zinc as a complementary to their conventional treatment, scaling and polishing. After 6 months, blood samples were collected from 199 patients only. Of these, 51 in (group I), 83 in (group II) and 65 in (group III). The remainder, 101 did not complete the study because some of them not taken zinc supplement regularly, while others were missed for follow up.

CLINICAL EXAMINATION

The oral examination was done by calibrated periodontal probe (Williams probe) at 4 sites mesiobuccal, distobuccal, midbuccal and midlingual. This included clinical attachment loss(CAL) and probing pocket depth (PPD). The CAL was assessed by measuring the distance from cement-enamel junction (CEJ) to base of the probing pocket depth in millimeters. The PPD was assessed from gingival margin to base of the pocket[10].

DATA COLLECTION

A pre-tested questionnaire was done to obtain information, on age, gender, and duration of the disease. The participants were asked to fast overnight for at least 12 hours. At the morning venous blood samples were collected for serum glucose and zinc measurements. Serum glucose and Zinc levels were determined by using (Giesse Diagnostica-Italy) kits in clinical chemistry analyzer Kinza 240.

STATISTICAL ANALYSIS

Data were collected and analyzed using SPSS version 19.0 for windows (SPSS, Chicago; Illinois, USA). Quantitative data were analyzed by using independent sample t- test.

RESULTS

The base line characteristics of the patients have been described in Table 1. The mean of age, serum glucose and serum zinc concentrations were not significantly different between the three groups. The clinical attachment loss and probing pocket depth was also not significantly differing.

At the end of the 6 months period, the mean values of clinical attachment loss and probing pocket depth were significantly lower among group III as compared to group II ($P<0.05$, $P<0.01$ respectively). Patients in Group III had also lower mean values of clinical attachment loss and probing pocket depth as compared to group I ($p<0.01$), as shown in Table 2.

On using percentage of change, the result showed significant higher values in group III with respect to clinical attachment loss and probing pocket depth as compared to Group II ($p<0.05$). Similarly, group I had a high percentage of changes as compared to group II (Table 3).

Table 1 . Clinical and anthropometric characteristics of the subjects studied

Parameter	Group I n=100	Group II n=100	Group III n=100	P* value
Age(years)	51.0 ± 6.0	52 ± 6.0	51.0 ± 7.0	0.927
Male sex [(n %)]	26 (51)	43(51.8)	36 (55.4)	0.71
Fasting blood glucose (mg /dl)	221.7 ± 59.9	221.9 ± 67.1	222.4 ± 49.1	0.999
Serum zinc(mg /dl)	61.2 ± 4.5	62.3 ± 5.4	60.4 ± 4.7	0.540
Probing Pocket Depth (mm)	5.9 ± 0.9	5.4 ± 1.0	5.7 ± 1.2	0.145
Clinical Attachment Loss (mm)	4.0 ± 1.0	3.4 ± 1.1	3.6 ± 1.2	0.158

* One way ANOVA

Table 2. Comparison of Blood glucose, Serum zinc level, clinical attachment loss, probing pocket depth in(Zinc, Scaling and Polishing), (Zinc), (Scaling and Polishing) groups at the end of the study

group	n	Fasting blood glucose	Serum zinc	Clinical attachment loss **	Probing pocket depth *
Group I	51	181.5 ± 53	85.6 ± 8.3	3.6 ± 1.0	5.3 ± 1.1
Group II	83	210.3± 68.7	61.8 ± 4.4	3.2 ± 1.1	5.1 ± 1.1
Group III	65	180.7± 36.2	82.3± 7.3	3.0 ± 1.1	4.8 ± 1.1

Group III Vs group II , Clinical attachment loss p < 0.05, Probing pocket depth p <0.01
Group III Vs group I , Clinical attachment loss <0.01 , Probing pocket depth p < 0.01

Table 3. Baseline and 6 months comparison of fasting blood glucose, serum zinc level, clinical attachment loss and probing pocket depth in groups

Groups	Fasting blood glucose		Serum zinc level		Probing pocket depth		Clinical attachment loss	
	Change of mean	% of change	Change of mean	% of change	Change of mean	% of change	Change of mean	% of change
Group I	40.1	18.2*	-24.5	28.6*	0.54	10.1*	0.38	9.6*
Group II	11.5	5	-0.5	0.8	0.18	3.5	0.20	5.8
Group III	41.7	18.7**	-21.9	26.6**	0.80	14.2**	0.58	15.9**

*** Group I Vs. group II, P < 0.05 for all parameters**
**** Group I Vs. group III, P < 0.05 for all parameters**

DISCUSSION

Accumulating evidence suggests that zinc may be associated with increase chance of decreasing severity of periodontitis and improvement of glycemic status in type 2 diabetes patients. Although there have been several studies investigating the role of zinc in DM patients with periodontitis, there are few published data on zinc supplementation in our population[11]. Thus, a large group of diabetes mellitus patient may be at increased risk for developing zinc deficiency, which in turn, may lead to periodontitis, a finding previously reported by (Biju *et al.*,)[12]. It is noteworthy that 100% appears at risk for mild-moderate zinc deficiency, serum zinc level<70 ug/dl; a cutoff value stated by others (Al-Timimi *et al.*,)[13] and an improvement in biochemical zinc status during supplementation support the existence of low zinc status in those patients. Because zinc may play a role in the pathophysiology of this condition, our finding that T2 DM patients with periodontitis have lower concentrations of serum zinc of potential concern. It has been shown that serum zinc level were lower in diabetic patients with periodontitis when compared to healthy individuals with periodontitis[12].

The lower concentrations of serum zinc among those with diabetes may have resulted from lower intake, excessive loss or inherited disturbances in its metabolism. In our study, the patients with non-surgical periodontal therapy plus oral zinc supplementation had a higher percentage of change of clinical attachment loss and probing pocket depth as compared to the other therapy groups. Several potential mechanisms has been suggested, zinc might protect cells against oxidative damage by inhibition the production of reactive oxygen species (ROS). Zinc may also play different role in mitochondria, because it prevent H2O2-induce apoptosis of cells through regulation of B-cell lymphoma -2/ Bax protein ratio[14].

There is clear evidence that diabetes have increased prevalence and severity of periodontitis and that individual with periodontitis have an increased prevalence of diabetes[11]. Indeed, unstable periodontitis may have the potential to worsen glycemic control in diabetes .Taylor et al showed that in the pima Indian population of Arizona individuals with severe periodontitis had up to 13 times greater risk of worsening glycemic control after 2 years, depending on age[15].

Interventional studies, in which glycemic control was assessed in participant with preexisting periodontitis and diabetes before and after a course of periodontal therapy, provide insight into this relationship. Randomized controlled trials have demonstrated significant improvement to glycemic control in type1[16] and type two diabetes[17,18] following non-surgical periodontal therapy. Several other studies failed to support this including randomized controlled trials investigation type 1[19,20] and type 2 diabetes[21]. However, our data show that individuals on zinc supplementation had higher percentages of change in fasting blood glucose than those without supplementation. Moreover, our data show that individual's periodontal health and glycemic control was better in group III than in group Iand II, so a combination of zinc supplementation with non-surgical periodontal therapy appears to have a significant effect.

Zinc supplement for vulnerable population to low zinc status such as patients with T 2 DM decreases the chance of the occurrence of severe periodontitis. Therefore we recommended the routine screening of zinc status in patients with T2DM. Zinc supplementation may be an effective dental health intervention means, to improve the periodontal status of the population.

ACKNOWLEDGMENT

We acknowledge the support of the staff of Diabetes Health Center, Duhok, Kurdistan Region, Iraq; who provided the facilities for conducting interviews.

REFERENCES

1. Morimoto-Yamashita Y, Ito T, Kawahara K, Kikuchi K, Tatsuyama-Nagayama S, Kawakami-Morizono Y, et al.. Periodontal disease and type 2 diabetes mellitus: Is the HMGB1-RAGE axis the missing link?. Med Hypotheses . 2012;79:452-5.
2. Anjani Kumar P, Vijaykumar S, Chandra A, Kopal G Association between diabetes mellitus and periodontal status in north Indian adults. Eur J Gen Dent . 2013;2:58-1.
3. Rajhans NS, Kohad RM, Chaudhari VG, Mhaske NHA clinical study of the relationship between diabetes mellitus and periodontal disease. J Indian Soc Periodontol. 2011;15:388-92.
4. Tomat AL, Costa MA, Girgulsky LC, Veiras L, Weisstaub A R,Inserra F, et al..Zinc deficiency during growth: Influence on renal function and morphology. Life Sciences. 2007; 80: 1292–1302.
5. Judith J, Wolfram K, Lothar R, .Zinc and diabetes – clinical links and molecular mechanisms. J. Nutr Biochem. 2009; 20:399-417
6. 6.Uckardes Y, Tekcicek M, Ozmert EN, et al. The effect of systemic zinc supplementation on oral health in low socioeconomic level children .Turk J Pediatr. 2009;51:424-8.
7. Seyed Ali, Maryam Seyedmajidi, Aliiakbar et al.. Effect of zinc-deficient diet on oral tissues and periodontal indices in Rats. IntJ Mol Cell Med. 2014.Vol 3, No2

8. Neema S, Rajesh S, Lalit K, Balaji M, Aditi M, Meetu J. Gingival crevicular blood.: As a non-invasive screening tool for diabetes mellitus in dental clinics. J Indian Soc Periodontol. 2013 Jul-Aug; 17(4): 472–477.
9. Orbak R, Kara C,Ozbek E,Tezel A, Demir T..Effect of zinc deficieny on oral and periodontal diseases in rats. J Periodont Res. 2007; 138-143.
10. Loe, H, Brown LJ. Early–onset periodontitis in the United States of America.J Periodontal. 1991;62:608-616.
11. Al-Timimi DJ, Salih SM .Periodontal status in patients with metabolic syndrome. Duhok Med J. 2012; 6(3): 117-127.
12. Thomas B, Ramitha SK, Kumari MBA. Comparative evaluation of micronutrient status in the serum of diabetes mellitus patients and healthy individuals with periodontitis. Indian Society Periodontology. 2010; vol. 14 (1): 46-49.
13. Al-Timimi DJ, Al-Sharbatti SS, Al-Najjar F .Zinc deficiency among a healthy population in Baghdad, Iraq .Saudi Med J.2005 ;Vol.26(11): 1777-1781.
14. Viktorinova A,Toserova E, KrizkoM, Durackova Z. Altered metabolism of copper, zinc and magnesium is associated with increased levels of glycated hemoglobin in patients with diabetes mellitus. Metabolism. 2009; 58: 1477-1482.
15. Taylor GW, Burt BA, Becker MP, GencoRJ, Shlossman M,Knowler WC, et al. Sever periodontitis and risk for poor glycemic control in patients with non-insulin-depended diabetes mellitus .J Periodontol. 1996 ; 67: 1085-93.
16. Skleric U,Schara R, Medvesscek M, Hanlon A, Doherty F, Lessem J. Periodontal treatment by Arestin and its effects on glycemic control in type diabetes patients. J Acad Periodontal. 2004; 6:160-5
17. Kiran M, Arpak N, Unsal E, Erdogan MF. The effect of improvement of periodontal health on metabolic control in type two diabetes mellitus .J Clin Periodontol. 2005; 32: 266-72.
18. Rodrigues DC, Taba MJ, Noves AB, Souza SL, Grisi. Effect of non-surgical periodontal therapy on glycemic control in patients with type 2 Diabetes mellitus. J Periodontol. 2003; 74:1361-7
19. Aldridge JP, Lester V, Watts TL, CollinsA, Viberti G, Wilson RF. Single-blind studies of the effect of improvement periodontal health on metabolic control in type 1 diabetes mellitus. J Clin Periodontol. 1995; 22: 271-5.
20. Tervonen T, Lamminsalo S, Hiltunen L, Raunio T, Knuuttila M. Resolution of periodontal inflammation does not guarantee improved glycemic control in type 1 diabetic subjects. J Clin Periodontol. 2009; 36: 51-7.
21. Jones JA, Miller DR, Wehler CJ, Rich SE, Krall-Kaye EA, McCoyLC et al. Does periodontal care improve glycemic control? The Department of Veterans Affairs Dental Diabetes Study. J Clin Periodontol. 2007; 34: 46-52.

پوختە

کارتێکرنا دانا زنکی ل سەر رەوشا پدیێ

پیشە کی و ئارمانج: فاکتە رێ رییس و گروپێن خوینێ هاتە خواندن پشێوە کێ بە رفرە ھ دناف خە لکی دا , بە لێ سە بارە ت کوردێن ئاکنجییێت پارێزگە ھا دھوکێ لکوردستانا عیراقێ ھیچ دانە یە ك لبە ردە ست نینە. ز بە ر قێ چە ندێ ئە ڤ ڤە کولینە ھاتە ئـە نجامـدان بو دیارکرنا گرێدانا پە یدابونا ئێشێت پدیێ و کێم بوونا زنکی . ئارمانج ز قێ فە کولینێدیارکرنا کارتێکرنا داناماددێ زنکی لسە ر پـدیێ دناف نە خوشێن شە کرێ ز جورێ ۲.

رێکێن ڤە کولینێ: ۳۰۰ نە خوشێن شە کرێ ئە وێن ئێشێن پدیێ ھە ین ھاتنە زێگرتن . نە خوش ھاتنە دابـە ش کـر ن بـو سـێ گروپـا. گروپـێ ئێکی : ئە وێن ماددێ زنکی وە ردگرن . گروپـێ دووێ: ئە وێن جارە سە ریا پدیێ وە ردگرن. گروپـێ سیێ: ئە وێن مـاددێ زنکـی و جارە سە ریا پدیێ وە ردگرن . د سە رە دانا ئێکێ دا یا نە خوشا خوین دێ ز ھە میـا ھێتـە وە رگـرتن. نـە خـوش د گروپـێ ئێکـێ و دوویـێ دا دێ ۵۰ ملغم زنکی روزێ سێ جارا وە رگریت بو ماوێ شە ش ھە یڤا.

ئە نجام: ل دە ستپێکێ. چ جباوازییێن دیار دناڤ بە را ھە رسیً گروپان دا نە بو. پشتی بورینا شە ش ھە یڤا. تیکراییً ھە زمارا یا گرێدانا ریشالی و کووراتیا ڤالا ھییَن پدیيً ب شیَوە کیً بە رجاڤ کیمتر بو د گروپـیً سیً دا بە راورد دگە ل گروپـیً دوو . رێزا گھورینـێ دناڤ بە را گرێدانا ریشالی و کووراتیا ڤالا ھییَن پدیيً ب شیَوە کیً بە رجاڤ بلند تر بو د گروپـیً سیً دا بە راورد دگە ل گروپـیً دوو .

دە رئە نجام: دانا مادێ زنکی بو ھاولاتییێن خو بە خش ئە وین رێزا زنکی کیم د لە شێ وان دا وە کی نە خوشێن جوری دوو ئێشێن شە کرێ دە لیڤا پە یدابونا ئێشێن پدیێ دێ کێمتربیت.

الخلاصة

تأثير اعطاء الزنك على حالة اللثة

خلفية واهداف البحث: عامل الريس وفصائل الدم المنتشرة تم دراستها بين الشعوب المختلفة ومع ذلك لا توجد معلومات متوفرة للناس الكورد الدين يعيشون في دهوك؛ العراق. ولهذا السبب تمت الدراسة لتحديد العلاقة بين حدوث التهاب اللثة ونقصان الزنك. وكان الهدف من البحث لتحديد تاثير اعطاء الزنك على حالة اللثة في المرضى السكري النوع الثاني.

طرق البحث: ٣٠٠ مريض سكري مصابين التهاب اللثة المزمن معدل اعمارهم ٤٥-٦٥ سنة تم اختيارهم. المرضى تم تقسيمهم الى ثلاث مجموعات: المجموعة الاولى تم اعطائهم الزنك والمجموعة الثانية تم لهم تنظيف اللثة والمجموعة االثالثة تم اعطائهم الزنك مع تنظيف اللثة ومن الزيارة الاولى تم سحب عينات الدم لجميع المرضى ليتم فحص الزنك والكلكوز في المصل. حالة اللثة للمرضى تم قياسها بمقياس المجموعة الاولى والثانية للمرضى وافقوا لتناول ٥٠ مليغرام زنك ثلاث مرات في اليوم لمدة ستة اشهر .حالة اللثة تم قياسها مرة ثانية بعد المقابلة وبنفس الطريقة.

النتائج: في البداية لا يوجد فروقات معنوية في اي مقياس بين المجاميع الثلاثة .في نهاية فترة الستة اشهر,معدل قيم فقدان الترابط النسيجي السريري وعمق الجيوب اللثوية كان قليل معنويا في المجموعة الثالثةعندما تم مقارنتها بالجموعة الثانية. النسبة المئوية للتغيير في فقدان الترابط النسيجي السريري وعمق الجيوب اللثوية كان كثير معنويا في المجموعة الثالثة عندما تم مقارنتها بالمجموعة الثانية

الاستنتاج: اعطاء الزنك للناس المتطوعين وعندهم نقص بالزنك مثل مرضى السكري النوع الثاني يقلل فرصة حدوث التهاب اللثة الحاد.

PREVALENCE OF IRON DEFICIENCY IN B-THALASSEMIA TRAIT IN ERBIL GOVERNORATE

KAWA MOHAMEDAMIN HASAN, MBChB, MIM, PhD clinical haematology*

Submitted 3 Dec 2014; accepted 31 Dec 2014

ABSTRACT

Background and objectives Anemia is a common clinical disorder that could be seen by clinician in Iraqi Kurdistan hospitals and private clinics, iron deficiency anemia perform the vast majority of such cases, and the prevalence of β-thalassemia trait in our community is about 7.5-8%. We examined a consecutive cohort of patients with β-thalassemia trait to detect the frequency of iron deficiency among them.

Method A descriptive cross sectional study performed in Erbil-Rizgary teaching hospital, the study was conducted among 162 individuals with β-thalassemia trait over a period extending from October 2013 to October 2014. The individuals had their diagnosis confirmed by a combination of blood counts and High Performance Liquid Chromatography. They were then investigated for Iron status by determining Transferrin saturation and Serum ferritin.

Results Among the 162 individuals with β-thalassemia minor enrolled, the prevalence of iron deficiency was 34.6%. There were no significant difference in the frequency of iron deficiency between adults and children (p = 0.99) or males and females (p= 0.477). The mean haemoglobin (Hb) and mean corpuscular volume (MCV) were significantly lower in those with concomitant iron deficiency (ID) than those without it (p= 0.009, p= 0.021 respectively) while mean red cell distribution width (RDW) was higher among those with ID than those without ID (p = 0.01). However, no significant differences were noted in the Hb A2 % in those with concomitant ID (p= 0.52).

Conclusions Iron deficiency is frequent among our β-thalassemia trait people, serum ferritin was low in only 16% of cases while the prevalence of ID counting on both serum ferritin and transferrin saturation (Tsat%) was 34.6%; so serum ferritin shuold not be the only ultimate tool for iron assessment among such people.

Duhok Med J 2014;8(2): 38-46.

Keywords: Iron deficiency, β thalassemia trait, Erbil

Thalassemia is the most common genetic disorder worldwide.[1,2] It affects men and women equally and occurs in approximately 4.4 of every 10,000 live births.[3] They are inherited in autosomal recessive manner that cause hemolytic anemia because of the decreased or absent synthesis of a globin chain.[4] In its heterozygous state β-thalassemia trait (minor), is asymptomatic and results in microcytosis and mild anaemia.[5] Prevalence of β-thalassemia trait in Mediterranean region, Africa and Southeast Asia is about 5-30% and in Erbil is 7.7%.[6,7]

Thalassemia syndromes and iron deficiency anemia (IDA) are the two most common etiologies of microcytic hypochromic anemia in children and adults. It has long been considered that iron deficiency does not exist in thalassemia syndromes, including

* *Lecturer, Department of Internal Medicine, College of Medicine, Hawler Medical University, Erbil, Kurdistan, Iraq. mah_kawa@yahoo.com*

thalassemia major as well as trait.[8] It has been suggested that the trait confers an advantage in maintaining iron balance in which case the prevalence of iron deficiency should be lower in those with this trait.[9] However; studies have shown the occurrence of iron deficiency in patients with beta thalassemia trait.[9-11]

The aim of the study: to detect the frequency of iron deficiency among β - thalassemia trait people, and to see the impact of iron deficiency on red cell count, RDW and RBC indices like MCV and MCH in such individual.

METHODS

The study was conducted in Erbil-Rizgary teaching hospital over a period extending from October 2013 to October 2014; a total of 162 patients were enrolled in this study. These patients were seen either for assessing anemia or they were detected by chance with low mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH) from complete blood count that was arranged for other reasons. Patients of both sex and all age groups with MCV below 80 fimtoliter (fL) and MCH less than 27 picogram (pg), and with HbA2 more than 3.5% and thus labeled as β-thalassemia minor were deemed eligible for the study, while those with MCV more than 100 fl, subjects taking iron preparation, and other haemoglobinopathies were excluded from the study. The data was collected by a direct interview of patients through a special questionnaire designed for the current study containing; demographic description of each enrolled individual, chief complaint, physical findings and laboratory data then the purpose of the study was carefully explained to each participant. The study was approved by the scientific and ethical committees of the College of Medicine- Hawler Medical University. The purpose of the study was demonstrated to each participant individually or for the parent of the enrolled children during personal interviews, and an informed verbal consent was obtained from all enrolled individuals.

A blood sample was taken for complete blood picture by automated haematology analyzer (Celttac alpha 6410 Japan). The following blood biomarkers reflecting iron metabolism were assessed directly: serum concentrations of iron (µg /dl), total iron-binding capacity (TIBC, µg/dl). Transferrin saturation (Tsat) was calculated as a ratio serum iron (µg/dl) and TIBC (µg/dl), multiplied by 100 and expressed in percent and serum ferritin (µg/L). The later was measured using immunoassay (Roche Diagnostics GmbH, Mannheim, Germany). Serum iron and TIBC were assessed using a substrate method with Feren S (Thermo Fisher Scientific, Waltham, MA, USA). Iron deficiency was defined prospectively as serum ferritin <15 µg/L and or Tsat <15%. High performance liquid chromatography (HPLC) (D10, Biorad USA); arranged for haemoglobin analysis and estimation of HbA2.

Statistical Analysis

Statistical package for social sciences (SPSS) software (version 19) was used for data entry and analyzing, aided by Microsoft excel 2010 for plotting graphs and tables. Descriptive data were presented

for continuous variables as mean ± SD, while qualitative data description done by calculating number and percentage. t-test was used to compare between two means and Chi-square(x2) tests was used to compare between proportions , p value ≤ 0.05 considered statistically significant.

RESULTS

Out of 162 patients with β-thalassemia trait enrolled in this study, 101 (62.3%) were females, and 61 (37.7%) were males with female: male ratio of (1.6:1). The Mean (±SD) of age was 29.6±16 years ranging from 1.4-70 years, 26 (16%) of them were ≤ 12 years (pediatric age group), 25 (15%) of the patients belong to age group (10-19) years, followed by 43 (27%) of the patients in the age group (20-29) years, and 34 (21%) patients in the age group (30-39) years as shown in (Figure 1).

The basic haemogram parameters concerning Hb%, haematocrit (%), red cell count, MCV, MCH, RDW and HbA2 are illustrated in (Table 1). The result of iron status including serum iron, TIBC, serum ferritin and Tsat also demonstrated in (Table 1).

The prevalence of iron deficiency (ID) was 34.6% (56 patients) among the 162 enrolled individuals, with no significant difference between children and adults (p = 0.996). Moreover, there was no significant difference in prevalence of ID in relevance to gender among the enrolled individuals (p= 0.477) (Table 2). Comparisons between the subjects with β-thalassemia trait and ID and those without ID are shown in (Table 3), and revealed that there were significant difference in mean Hb, MCV and RDW between those with ID and those without ID; the mean Hb and mean MCV were both lower while mean RDW was higher in those in the ID subgroup (p= 0.009, p= 0.021 and p= 0.01 respectively), but there were no significant difference between both subgroups regarding MCH, RBC count and HbA2.

Prevalence of anemia among the studied individuals was 88.3% but there was no significant difference between those with ID (87.5%) and those without it (88.7%) (p = 0.824) as shown in (Table 4).

Serum ferritin and transferrin saturation (Tsat %) both were assessed in all 162 studied individuals, (Table 5) shows that Transferrin saturation was more likely to detect iron deficiency than S. ferritin, and there was a significant correlation (p < 0.001).

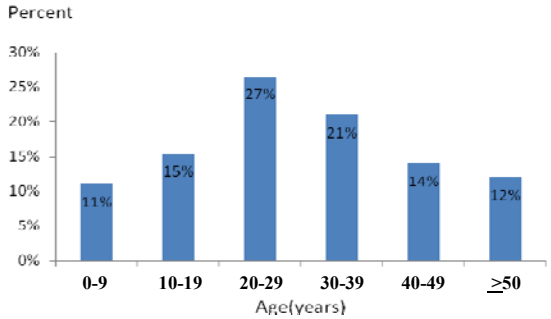


Figure 1 Distribution of enrolled patients by age

Table 1. Overall Mean and SD of the studied parameters

	Mean	SD	Mini.	Maxi.
Hb g/dl	10.74	1.38	6.6	14.3
Hct %	33.76	4.48	22	45
MCV fL	61.9	4.99	47.4	76
MCH pg	19.63	1.99	14.3	26.9
RDW %	16.43	2.52	11	25
RBC ×1012	5.51	0.61	3.3	7.45
HbA2 %	4.89	0.77	3.51	6.9
S. ferritin µg/L	78.34	78.92	0.05	424
S. iron µg/dl	67.07	35.19	8	153
TIBC µg/dl	316.37	78.54	151	576
Tsat %	22.39	12.75	2	59

Table 2. The prevalence of ID according to age and sex

	N	Prevalence ID%		P value
		No.	%	
Age				
≤ 12 years	26	9	34.6	0.996
> 12 years	136	47	34.6	
Sex				
Male	61	19	31.1	0.477
Female	101	37	36.6	

Table 3. A comparison between β-thalassemia trait with ID and those without ID

	ID	N	Mean	SD	SE	P value
Hb_g/dl	Yes	56	10.436	1.499	.173	.009
	No	106	11.005	1.224	.131	
MCV fL	Yes	56	60.997	5.511	.636	.021
	No	106	62.801	4.356	.467	
MCH pg	Yes	56	19.447	2.401	.277	.287
	No	106	19.793	1.562	.167	
HbA2 %	Yes	56	4.941	.810	.093	.520
	No	106	4.862	.745	.080	
RBC ×1012	Yes	56	5.433	.661	.076	.125
	No	106	5.582	.573	.061	
RDW %	Yes	56	16.9747	2.68051	.30952	.011
	No	106	15.9690	2.30219	.24682	

Table 4. The prevalence of anemia among enrolled people

Prevalence of ID	Hb%						P value
	Low		Normal		Total		
	No.	%	No.	%	No.	%	
No	94	88.7	12	11.3	106	65.4	0.824
Yes	49	87.5	7	12.5	56	34.6	
Total	143	88.3	19	11.7	162	100	

Table 5. The correlation between S. ferritin and Tsat%

Ferritin	Tsat%						
	Low (ID)		Normal (No ID)		Total		
	No.	%	No.	%	No.	%	P value
low	23	88.5	3	11.5	26	100	< 0.001
Normal	30	22.1	106	77.9	136	100	
Total	53	32.7	109	67.3	162	100	

DISCUSSION

Iron status in β-thalassemia trait had always been an area of interest to haematologist. The common held notion is that iron deficiency is unlikely coexist in thalassemia trait. Moreover, conflicting data came up from different studies regarding the iron metabolism in β-thalassemia trait. In 1980 Economidou et al. showed that iron deficiency was a common finding in female thalassemia trait of reproductive age not receiving iron supplement.[12] However in 1987 Mehta and Pandya showed that the β-thalassemia trait group had an advantage in maintaining iron balance.[13] In 1995 a study done among British Asian children showed that coincident iron deficiency and thalassemia trait can coexist and it should not be presumed that the trait protects iron status or that the two are in any way mutually exclusive, at least in the early years.[14] In 2000 a study in Iran concluded that, iron level should be examined in subjects with the trait especially in men, to avoid harmful effects of iron overload in early stages of the disorder.15Thus the exact role of thalassemia trait in iron metabolism still remains an area to be explored.

In the current study the prevalence of iron deficiency was 34.6% among 162 individuals with β- thalassemia trait, with no significant difference regarding both the age and the sex of enrolled individuals. The high prevalence of ID may be explained by the fact that ID still is the most frequent nutritional disorder in our community, and it may also be related to a false belief among the public and even among physician that individuals with thalassemia are always iron overload and thus advised to avoid iron-rich meals and iron supplements. Our result is much higher than results of Qureshi in Pakistan[10] of 13.5%, Dolai et al, and Madan et al of 19.3 % and 27.2% in India.[11, 16]

The mean Hb and MCV were lower in those with ID as compared to those without it; our finding is in consistence with Dolai et al in India11, while mean RDW was higher among traits with ID, RDW was introduced as an important parameter for differentiating IDA from β-thalassemia trait.[17]

We observed that mean HbA2 was not significantly different in those with ID versus those without it. Mean HbA2 was even marginally higher in the subgroup with ID. Our finding is in agreement with Madan et all[16] and Passarello et al[18], this indicate that the presence of iron deficiency did not preclude the detection of thalassemia trait in this population, reduction of HbA2 has been reported to be linked to the severity of anemia[9] so that possibly the concomitant ID is not sufficiently severe or not sufficiently prolonged to significantly reduce the level of HbA2, but our result is in contrary to Harthoorn et al[19] conclude that patients with β-thalassemia trait and concomitant ID can show normal HbA2 and Steinberg et al[20] reported reduced HbA2 in β-thalassemia trait coincident with ID.

Concerning the prevalence of anemia; the majority (88.3%) of the studied individuals were anemic but there was no significant difference between those with

ID and those without ID (p = 0.824), which means that ID contribution to the anemia in the studied cohort was not significant, on the other hand about 12% of the enrolled cases were not anemic so normal Hb level should not preclude such individual from iron state evaluation.

Diagnosis of IDA may be less straight forwards in patients with acute or chronic inflammatory conditions, since most of the biochemical markers of iron metabolism are affected by acute phase reaction.[21] We have estimate both serum ferritin and Tsat in all the studied cases and the correlation was significant (p < 0.001), serum ferritin was low in 26 (16%) cases only while the prevalence of ID counting on both serum ferritin and Tsat was (34.6%); so we can not consider serum ferritin alone as the only reliable ultimate tool for iron state evaluation in such individuals.

Iron deficiency is frequent among β-thalassemia trait in our population, and one clue to its concomitant presence is high RDW. Thus the coexistence of both should not be dismissed and the best approach to securing a diagnosis is a combination of serum ferritin and transferrin saturation.

REFERENCES

1. Najmabadi H, Teimourian S, Khatibi T, Neishabury M, Pourfarzad F, Jalil-Nejad S, et al. Amplification Refractory Mutation System (ARMS) and reverse hybridization in the detection of beta – thalassemia mutations. Arch Iran Med. 2001; 4: 165-70.
2. Usman M, Moinuddin M, Ghani R, Usman S. Screening of five common beta thalassemia mutations in the Pakistani population: a basis for prenatal diagnosis Sultan Qaboos Univ Med J. 2009; 9: 305-10.
3. Quek L, Thein S. Molecular therapies in β-thalassaemia Br J Haematol. 2007;136: 353-65.
4. Di Fraja D, Sarno L, Migliucci A, Acampora E, Napolitano R, Maruotti GM et al. Prenatal diagnosis of beta-thalassemia: nuchal translucency in affected fetuses. Minerva Ginecol. 2011; 63 (6): 491-4.
5. Muncie HI, Campbell JS. Alpha and Beta Thalassemia. Am Fam Physician. 2009; 15: 80 (4): 339-44.
6. Rund D, Rachmilewitz E. Beta – thalassemia. NEJM. 2005; 353: 1135-46.
7. Abdulkadir A, Huda A. Prevalence of β-thalassemia carriers among a cohort of university students in Hawler province of Iraqi Kurdistan. Iraqi J Pharm Sci. 2009; 18(2):15-19
8. White HM, Richards R, Jelenski G, Byrne M, Ali M. Iron state in alpha and B thalassaemia trait. J Clin Pathol. 1986;39:256-9.
9. Alperin BJ, Dow AP, Petteway BM. Hemoglobin A2 levels in health and various hematologic disorders. Am J Clin Pathol. 1977;67:219-26.
10. Qureshi TZ, Anwar M, Ahmed S, Ahmed Khan D, Saleem M. Serum ferritn levels in carriers of beta thalassemia trait. Acta Hematol. 1995; 94(1):7-9.
11. Dolai TK, Nataraj KS, Sinha N, Mishra S, Bhattacharya M, Ghosh MK. Prevalence of iron deficiency in thalassemia minor: a study from

tertiary hospital. Indian J Hematol Blood Transfus. 2012; 28:7-9.

12. Economidou J, Augustaki O, Georgiopoulou V, Vrettou H, Parcha S, Loucopoulos D. Assessment of iron stores in subjects heterozygous for beta-thalassemia based on serum ferritin levels. Acta Haematol. 1980; 64(4):205–8.
13. Mehta BC, Pandya BG. Iron status of beta thalassemia carriers. Am J Hematol. 1987: 24(2):137–41.
14. Hinchliffe R, Lilleyman J. Frequency of coincident iron deficiency and beta-thalassemia trait in British Asian children). J Clin Pathol. 1995; 48(6):594–5
15. Hoorfar H, Sadrarhami S, Keshteli A, Ardestani S, Ataei M, Moafi A. Evaluation of iron status by serum ferritin level in Iranian carriers of beta thalassemia minor. Int J Vitam Nutr Res. 2008; 78(4–5):204–7.
16. Madan N, Sikka M, Sharma S, Rusia U. Phenotypic expression of hemoglobin A2 in beta-thalassemia trait with iron deficiency. Ann Hematol. 1998; 77 (3): 93-6.
17. Romero J, Carbia CD, Ceballo MF, Diaz NB. Red cell distribution width (RDW): its use in the characterization of microcytic and hypochromic anemias. Medicana (Buenos Aires) 1999; 51 (1):17-22.
18. Passarello C, Gimbona A, Cannata M, Vinciguerra M, Renda D, Mggio A. Iron deficiency dose not compromise the diagnosis of high HbA2 B thalassemia trait. Haematologica. 2012; 97:472-3.
19. Hathoorn-Lasthuizen EJ, Lindemans J, Langenhuijsen M. Influence of iron deficiency anemia on HbA2 level: possible consequences for β-thalassemia screening. Scan J Clin Lab Invest. 1999; 59: 65-70.
20. Steinberg MH, Adams JG. Hemoglobin A2: Origin, evolution and aftermath. Blood. 1991; (78) 9: 65-77.
21. Brugnara C. Iron deficiency and erythropoiesis: new diagnostic approaches. Clin Chem. 2003; 49:1573–8.

پوختە

ڕێژەی هەبوونی کەمی مادەی ئاسن لە نێو هەڵگرانی نەخۆشی پالاسیمیا جۆری بێتا لە شاری هەولێر

پێشەکی و ئامانج: کەم خوێنی بەربڵاوترین نەخۆشیە کە پزیشك روبەروی دەبێتەوە لە نەخۆشخانەکان و کلینیکە تایبەتیەکان لە کوردستانی عێراق. کەم خوێنی بەهۆی کەمی مادەی ئاسن ڕێژەیەکی زۆری ئەم نەخۆشانە پێك دێنێت. ڕێژەی ئەوکەسانەی کە هەڵگری نەخۆشی پالاسیمیا جۆری بێتا لە کۆمەڵگەی ئێمە نزیکەی 7.5-8%. ئێمە هەستاین بە پشکنین و لێکۆلینەوەی چەند گروپێکی یەك لە دوای یەکی ئەو کەسانەی کە هەڵگری نەخۆشی پالاسیمیا جۆری بێتا ن بۆ دۆزینەوەی ڕێژەی کەمی ماددەی ئاسن لە نێوانیاندا.

نەخۆشەکان و شێواز: توێژینەوەیەکی وەسف کراوی پانە برگەیی ئەنجامدرا لە نەخۆشخانەی رزگاری فێرکاری لە شاری هەولێر. توێژینەوەکە ئەنجامدرا لە نێوان ١٦٢ کەس کە هەڵگری نەخۆشی پالاسیمیا جۆری بێتا لە ماوەی تشرینی یەکەمی ٢٠١٣ تا تشرینی یەکەمی ٢٠١٤ ئەم کەسانە نەخۆشی پالاسیمیا تییایاندا دەستنیشانکرا بە پشکنینی خوێنی کشتی لەگەل پشکنینی HPLC پاشان پشکنینیان بۆ کرا بۆ هەڵسەنگاندنی باری مادەی ئاسن لە خوێن بە هەریەك لە ڕێژەی فێریتینی ناو خوێن و ڕێژەی تێربونی ترانسفێرین.

ئەنجام: لە نێوان ١٦٢ کەس کە هەڵگری نەخۆشی پالاسیمیا جۆری بێتا کەوا بە شدار بوون لە م لیکولینەوەیە ڕێژەی هەبوونی کەمی مادەی ئاسن لە نێو ئەو کەسانە ٣٤,٦٪ بو. هیچ جیاوازیەکی بەرچاو نەبوو لە نێوان مندال و گەورە (P=0.99) وە هەروەها لە نێوان هەردوو ڕەگەزی نێر و مێ (P=0.477). ڕێژەی هیمۆگلۆبین و ڕێژەی قەبارەی خرۆکە سورەکان کەمتر بوون لەو کەسانە کە هەڵگری نەخۆشی پالاسیمیا جۆری بێتا و کەمی مادەی ئاسنیان هەیە بە بەراورد لەگەل ئەو کەسانە کە کەمی مادەی ئاسنیان نیە. بەڵام تێکرای (RDW) کە پێوانەی جیاوازی قەبارەی خرۆکە سورەکانە زیاتر بوو لە نێو ئەو کەسانەی کەمی مادەی ئاسنیان هەیە بە بەراورد لەگەل ئەو کەسانە کە کەمی مادەی ئاسنیان نیە. بەهەرحال جیاوازیەکی بەرچاو نەبو لە ڕێژەی HbA2 % لەو کەسانەی کە هەڵگری نەخۆشی پالاسیمیا جۆری بێتا و کەمی مادەی ئاسنیان هەیە (P= ٠,٥٢).

دەرئەنجام: کەمی مادەی ئاسن بەربڵاوە لە نێو ئەو کەسانەی کە هەڵگری نەخۆشی پالاسیمیا جۆری بێتا ن لە کۆمەڵگەکەمان. لە کۆی ١٦٢ کەس کە هەڵگری بێتا پالاسیمیان کەوا بە شدار بوون لەم لیکولینەوەیە تەنها 16%یان ڕێژەی فێریتینی ناو خوێنیان کەم بو بەلام ڕێژەی هەبوونی کەمی مادەی ئاسن لە نێو ئەو کەسانە ٣٤,٦٪ بو بەپشت بەستن بەهەریەك لە ڕێژەی فێریتینی ناو خوێن و ڕێژەی تێربونی ترانسفێرین. بویە پێوانی ڕێژەی فێریتین لە خوێن بەتەنها نابێت بە پشکنینی سەرەکی دابنرێت بۆ هەلسەنگاندنی مادەی ئاسن لە خوێنی ئەو کەسانەی کە هەڵگری بێتا پالاسیمیان.

الخلاصة

انتشار نقص الحديد بين حاملي مرض الثلاسيما من نوع بيتا في محافظة أربيل

الخلفية والأهداف: فقر الدم هو اضطراب سريري شائع التي يمكن أن يواجه الطبيب في المستشفيات والعيادات الخاصة في كوردستان العراق ، وفقر الدم نتيجة نقص الحديد يشكل الغالبية العظمى من هذه الحالات، نسبة انتشارحامل مرض الثلاسيما (الثلاسيميا الصغرى) من نوع بيتا في مجتمعنا حوالي ٧.٥-٨٪. قمنا بدراسة مجموعات متتالية من حاملي مرض الثلاسيما من نوع بيتا للكشف عن نسبة نقص الحديد بينهم.

المرضى والطرق: دراسة وصفية مقطعية أجريت في مستشفى رزكاري التعليمي في اربيل. وقد أجريت الدراسة بين ١٦٢ شخصا من حاملي مرض الثلاسيما نوع بيتا على مدى فترة امتدت من أكتوبر ٢٠١٣ إلى أكتوبر ٢٠١٤. لقد تم تشخيص مرض الثلاسيما عند هؤلاء الاشخاص عن طريق تحليل الدم العام و تحليل السائل الكروماتوكرافي عالي الاداء (HPLC) بعد ذلك تم التحري عن نسبة الحديد بواسطة كل من نسبة الفيرتين في مصل الدم ونسبة تشبع الترانسفيرين.

النتائج: بين ١٦٢ شخصا من حاملي مرض الثلاسيما نوع بيتا الذين شملتهم الدراسة بلغت نسبة انتشار نقص الحديد ٣٤.٦٪، لم يكن هناك اختلاف بشكل ملحوظ بين الكبار والأطفال (P= ٠.٩٩) و بين كلا الجنسين (P=٠.٤٧٧). معدل نسبة خضاب الدم ومعدل حجم كريات الدم الحمراء (MCV) كان أقل وبشكل ملحوظ بين حاملي مرض الثلاسيما نوع بيتا المتزامن مع نقص الحديد (ID) من تلك دون نقص الحديد (P= 0.009، P= 0.021 على التوالي)، في حين معدل توزيع خلايا الدم الحمراء (RDW) كان أعلى بين ذوي نقص الحديد (ID) من دون تلك ID (P=٠.٠١). على اية حال لم يلاحظ اي اختلاف ملحوظ في خضاب (HbA2 %) عند حاملي مرض الثلاسيما نوع بيتا المتزامن مع نقص الحديد (P= ٠.٥٢).

الاستنتاج: نقص الحديد شائع و منتشر لدى الاشخاص الحاملين لمرض الثلاسيما نوع بيتا، نسبة الفيرتين كان اقل من الحد الطبيعي عند 16% فقط من مجموع ١٦٢ شخصا اجريت عليهم الدراسة بينما بلغت نسبة انتشار نقص الحديد ٣٤.٦٪ معتمدا على كل من نسبة الفيرتين في مصل الدم ونسبة تشبع الترانسفيرين، لذلك فان قياس نسبة الفيرتين في مصل الدم لا يمكن ان تكون الفحص الاساسي الوحيد لتقييم نسبة الحديد بين هؤلاء الشخاص.

EXTRACORPOREAL SHOCK WAVE THERAPY VERSUS LOCAL INJECTION OF STEROID IN TREATMENT OF PLANTAR FASCIITIS: AN INTERVENTIONAL STUDY

MOHAMMAD T. RASOOL, FRCP-G, FRCP, DRMR (London)*
ZOLYKHA M. MERZA, MBCHB**

Submitted 17 Sep 2014; accepted 31 Dec 2014

ABSTRACT

Background and objectives Plantar fasciitis is a damage and / or inflammation of the fascia of the plantar surface of the foot usually at its calcaneal attachment causing painful heel. The first line treatment is conservative. For refractory cases two other methods may be tried before surgery namely local injection of steroid and Extracorporeal Shock Wave Therapy.
Aim is to compare the results of local injection of steroid and extracorporeal shock Wave therapy.

Methods This study was conducted at Duhok Center for Rheumatic Disorders during the period from April 2013 till February 2014. It included those patients with chronic plantar fasciitis whose symptoms extended for more than 3 months. The study sample which comprised 119 cases (with 132 painful heels) was subdivided into two groups: Group 1 (51 patients with 55 painful heels) was treated by local injection of steroid and Group 2 (68 patients with 77 painful heels)was treated by Extracorporeal Shock Wave Therapy (6 sessions with 2 session per week).

Results The mean body mass index was 33.6 kg/m2. According to the 10 points visual analog scale for pain, the mean pain severity level dropped from 7.9 to 2.3 after 3 months in Group1, while in group 2 the pain level dropped from 8 to 2.9. The result of treatment of each group was statistically significant, but the difference between both modalities of treatment did not achieve statistical significance.

Conclusions Both local injection of steroid and Extracorporeal Shock Wave Therapy are effective ways for treatment of chronic plantar fasciitis with the latter being non-invasive and safer.

Duhok Med J 2014;8(2): 47-56.

Keywords: plantar fasciitis, local injection, extracorporeal shock wave therapy

Plantar fasciitis is defined as a damage and/ or an inflammation of the fascia of the plantar surface of the foot usually at its calcaneal attachment causing painful heel.[1,2]

The plantar fascia is a broad and strong connective tissue structure that runs along the full length of the plantar aspect of the foot from its origin at the inferior surface of calcaneal bone to its complex insertion at the level of the heads of the metatarsals. The plantar fascia is made up of predominantly longitudinally oriented collagen fibers. It is the principle static and dynamic stabilizer of the longitudinal arch of the foot. It also acts as a shock absorber and helps to protect the underlying soft tissues.[3-11]

* *Assistant Prof. of Rheumatology, Department of Surgery, Faculty of Medical Sciences, University of Duhok, Kurdistan Region, Iraq*
** *Senior House Officer (permanent resident) of rheumatology at Duhok center for rheumatic diseases and medical rehabilitation*
Correspondence author: Assistant Prof. M.T Rasoul e-mail: mzakholi@yahoo.com Mobile: 07504552497

With aging process, there is gradual reduction in collagen and water content in the elastic fibrous tissues. So plantar fascia becomes less pliable and more stiff with age. Plantar fasciitis occurs when the plantar aponeurosis is over stretched or over used. This mechanical cause of structural strain can result in micro-tears in the plantar fascia. Repetition of such events together with aging degenerative changes may cause impairment of normal healing processes and result in chronic inflammatory reaction in the plantar fascia.[2,4,6,12-14]

Ten per cent of the population experience plantar heel pain at some point during their life time.[6] The main symptom is pain in the plantar area of the heel, which is particularly more severe with first few steps taken in the morning or after a period of rest. Palpation typically reveals localized tenderness at the antero-inferior medial aspect of calcaneal tuberosity at the origin of the plantar fascia. The duration of symptoms varies from a few weeks to several months or even years.[5,13-19]

Diagnosis is usually clinical and rarely needs to be investigated further. Radiographs reveal a calcaneal spur in about 50% of patients, but the exact significance of this finding is uncertain. Thickening of the plantar fascia insertion more than 5mm either on ultrasound or MRI is suggestive of plantar fasciopathy.[5, 6, 20-22]

The first line treatment is conservative by relative rest, stretching exercises, heat or ice application, shoe inserts and NSAIDs. If the patient does not improve by this method and the condition becomes recalcitrant, then other methods may be tried before surgery. Two of these methods are local injection of the heel by steroid or using Extracorporeal Shock Wave Therapy (ESWT) which delivers focused shock waves to the body.[5,6,11,13,23,24] The aim of this study is to compare the results of treatment of patients with chronic plantar fasciitis by two methods: ESWT and local injection of steroids.

PATIENTS AND METHODS

This study was conducted in Duhok Center for Rheumatic Diseases and Medical Rehabilitation and Azadi Teaching Hospital during the period from April 2013 till February 2014. The type of study was quantitative, analytic, interventional, therapeutic clinical trial study. It included those patients with chronic plantar fasciitis whose symptoms extended more than 3 months and failed to improve by conservative measures such as relative rest, NSAIDs, stretching exercises and shoe inserts as heel pads.

The study sample comprised 119 cases with 132 painful heels. The sample was subdivided into two groups:

Group 1 included 51 cases with 55 painful heels. Those were treated by local injection of 40mg of methyl prednisolone. (Figure 1)

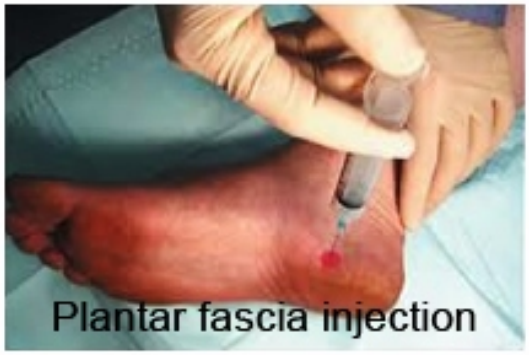


Figure 1. Local injection of plantar fascia

Group 2 included 68 cases with 77 painful heels. Those were sent to Azadi Teaching Hospital/ Department of Physiotherapy for treatment by ESWT. This method of treatment was conducted by using Sonocur Plus machine (a product of Siemens company). Each patient underwent a total of 6 sessions at a rate of 2 sessions per week. At each session the patient was in semi-sitting position with neutrally positioned leg, 2000 pulses of low energy shock waves type were applied to the maximum painful area of the heel over 15 minutes (Figure 2).

Figure 2. The extracorporeal shock waves therapy machine used in Azadi Teaching Hospital for treatment of plantar fasciitis.

For each patient, a special data form was prepared to accommodate the required data which included: name, age, sex, occupation, duration of symptoms, past medical history ,past surgical history ,past drug history ,body weight, height and severity of pain depending on the patient's personal judgment according to a Visual Analog Scale (VAS). Figure 3. In addition, his (her) written consent was taken together with personal mobile phone number or of one of his(her) close relatives, and lastly severity of pain after treatment.

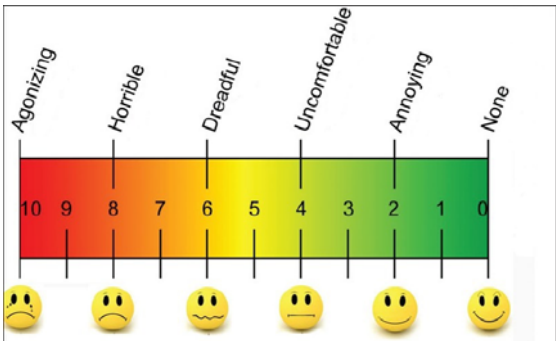


Figure 3. Visual analog scale for pain

After treatment, patients of both groups were followed up for a period of 3 months and their symptoms reviewed at the end of the 1st and 3rd month, some of them by direct interview at the outpatient clinic and the others by phone calls.

Statistical analysis was done by using SPSS software program, version 14.

The mean and standard deviation were used to summarize and describe data. The paired student's t-test was used to compare the mean pain scores of each group before and after 3 months of treatment.

The unpaired student's t-test was used to compare the mean pain scores between the two groups after 3 months of treatment. The level of statistical significance was set at a p value ≤ 0.05.

RESULTS

The total number of patients included in this study was 119 cases comprising 96 female (80.7%) and 23 male (19.3%) with 132 painful heels. (Table 1)

Table 1. Baseline characteristics of the study sample

Characteristics		Number (%)
Total cases		**119 (100%)**
Gender	**Females**	**96 (80.7%)**
	Males	**23 (19.3%)**
Job	**Indoor workers**	**89 (74.8%)**
	Outdoor workers	**30 (25.2%)**
Calcaneal spur	**Positive**	**115 (87.1 %)**
	Negative	**17 (12.9 %)**

Their age ranged from 29 to 63 years with a mean ± SD of 44.7 year. The height of patients ranged from 142 to 185 cm with a mean ± SD of 158.5 cm, while their weight ranged from 60 to 155 kg with a mean ± SD of 84.5 kg and their body mass index ranged from 19.2 to 63.7 kg/m2 with a mean ± SD of 33.6 kg/m2. (Table 2)

Table 2. Study sample by age, height, weight and BMI

Variables	Range	Mean value
Age	29-63 year	44.7 year
Height	142-185cm	158.5cm
Weight	60-155kg	84.5kg
Body Mass Index	19.2-63.7kg/m^2	33.6kg/m^2

Results of Group 1:

In accordance with the 10 degree (VAS) scale, patients in this group assessed the severity level of the pain before treatment as a mean value of 7.9. After one month the mean value became 4.6 and after three months dropped further to 2.3. The differences proved statistically significant with a p value <0.01. (Table 3)

Table 3. Summary statistics comparing pre and post treatment results of both groups

Group	Before treat.	After 1 month	After 3 months	Student's t-test	P-value
Group 1	7.9	4.6	2.3	14.9 (Paired sample)	< 0.01
Group 2	8	4.6	2.9	15.4 (Paired sample)	< 0.01
Comparison between results of both groups				-1.2 (independent)	0.218

Results of Group 2:

As judged by patients in this group according to the same pain scale, the severity level of the pain before treatment amounted to a mean value of 8. After one month the mean value became 4.6 and after three months dropped further to 2.9. The differences proved statistically significant with a p value <0.01. (Table 3)

Comparison between the results of both groups:

By comparing the results of response to both modalities of treatment in both groups, the independent sample Student's t-test was -1.2 and the P-value was 0.218. (Figure 4)

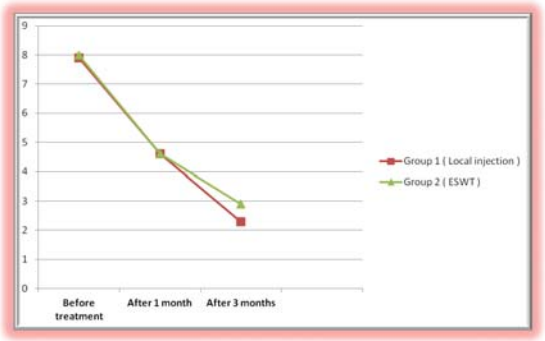


Figure 4: Pre and Post treatment Pain Scores of Both Groups by Time

Complications of treatment:

In both methods of treatment no significant complications occurred in the patients included in this study apart from one case with local injection who developed local infection and was treated by antibiotics (amoxicillin+clavulanic acid) for 5 days.

DISCUSSION

In this study most of the patients 80.7% were females (96 out of 119), and their average age was 44.7 years. Most of them 74.8% (89 case out of 119) were indoor workers (mainly housewives) with an average body mass index of 33.6 kg/m2

which is considered to be obesity class I.25-27

In group 1 there were 18.2% (10 out of 55) of patients who did not show any improvement in their heel pain, and in group 2 there were 15.6% (12 out of 77) who also did not show any response to the treatment. All these patients were obese and their body weights were around or more than 100 kg and their body mass indices were more than 40kg/m2 (i.e. obesity class 3). Saber et al, also found that 7% of their patients who did not respond to either modality of treatment were obese.[28]

Obesity not only increases the risk of plantar fasciitis but also increases the level of disability, which is proportional to the body mass index.[6] In other studies also there were high relation-ship between obesity and plantar fasciitis. Frey et al, found that plantar fasciitis, tendinitis, and osteoarthritis of ankle and foot joints usually are secondary to overuse and increased stress on the soft tissues and joints, which may be directly related to increased weight on these structures in over weight and obese patients.[29] Irving et al, also found that obesity is associated with chronic painful heel syndrome and may be a risk factor for the development of the condition.[30]

In those patients who had been treated by local injection into their heel, the average of their pain severity level dropped from 7.9 to 2.3 after 3 months with a difference of 5.6 degree from 10 according to VAS. This result was statistically significant and it is comparable with the results of other studies. Saber et al, and Crawford et al, in their studies also had a statistically significant improvement of pain of their patients' heels according to VAS by local injection of methylprednisolone.[28,31]

The other group of patients who had been treated by ESWT also had a statistically significant improvement in their heel pain level from an average of 8 to 2.9 degree from 10 according to VAS after 3 months. Saber et al, also notice similar results in their patients who had been treated by ESWT.[28] Gollwitzer et al, in their study compared ESWT for chronic painful heal with placebo in 40 participant by 3 sessions of ESWT and they found 73.2% reduction in severity of pain by VAS at 12 weeks.[32] Also Chuckpaiwong et al, notice 70.7% success rate in treatment of their patients by ESWT.[33]

In group 1 of our patients, the average of pain level dropped from 7.9 to 2.3 (i.e. the difference was 5.6), while in the group 2 the pain level dropped from 8 to 2.9 (i.e. the difference was 5.1). By comparing the results of response to both modalities of treatment, the difference between both groups was statistically not significant. This means that both methods were effective with no much difference between both of them. Although the results of local injection showed slight superiority but because it is an invasive way of treatment with more risk of complications (it occurred for one of our cases who had been treated by local injection and then developed local infection) and in practice we noticed that most of our patients were worry about the local injection, so we recommend for use of ESWT for treatment of chronic plantar fasciitis as it is a non-

invasive way of treatment and relatively safe.

From the results we could notice in both groups of patients that there was a gradual improvement of pain level after treatment (at 1st month to 3rd month); in group 1 the average of pain dropped from 7.9 before treatment to 4.6 at 1st month to 2.3 at 3rd month and in group 2 from 8 before treatment to 4.6 at 1st month then to 2.9 at 3rd month. So we recommend reassurance of the patients about the gradual improvement of their heel pain with time.

In conclusions plantar fasciitis is more common in overweight and obese patients and obesity is a risk factor for failure of different methods of treatment for plantar fasciitis including: conservative, local injection by steroid and ESWT. Local injection by steroid and ESWT are both an effective ways for treatment of chronic plantar fasciitis but the last one is more preferable for treatment because it is non-invasive way of treatment and relatively safer. Reassurance of the patients about the gradual improvement of their heel pain with time is recommended.

REFERENCES

1. Newman WA. Dorland's illustrated medical dictionary. 32nd edition. Philadelphia: Elsevier-Saunders, 2012.
2. Medlineplus medical encyclopedia, available from: [http://www.nlm.nih.gov/medlineplus/ency/article/007021.htm]
3. Darke RL, Vogl AW, Mitchell AWM. Gray's anatomy for students. 2nd edition. Philadelphia: Churchill Livingstones, 2010.
4. Snow SW, Bohne WH, DiCarlo E, Chang VK. Anatomy of the Achilles tendon and plantar fascia in relation to the calcaneus in various age groups. Foot Ankle Int. 1995; 16(7): 418-21.
5. Murphy GA. Disorders of tendons and fascia. In: Canale ST, Beaty JH. Campbell's Operative Orthopaedics. 12th edition. Philadelphia : Elsevier-Mosby; 2013. p. 3952-9.
6. Puttaswamaiah R, Chandran P. Degenerative plantar fasciitis: A review of current concepts. The foot (2007); 17:3-9. Available online at [www.sciencedirect.com]
7. Thordarson DB, Kumar PJ, Hedman TP, Ebramzadeh E. Effect of partial versus complete plantar fasciotomy on the windlass mechanism. Foot Ankle Int. 1997; 18(1): 16-20.
8. Kitaoka HB, Luo ZP, Growney ES, Berglund LJ, An KN. Material properties of the plantar aponeurosis. Foot Ankle Int. 1994; 15(10):557-60.
9. Arangio GA, Chen C, Kim W. Effect of cutting the plantar fascia on mechanical properties of the foot. Clin Orthop Relat Res. 1997;(339): 227-31.
10. Gefen A. The in vivo elastic properties of the plantar fascia during the contact phase of walking. Foot Ankle Int. 2003; 24(3): 238-44.
11. Stuber K, Kristmanson K. Conservative therapy for plantar fasciitis: a narrative review of randomized trials. J Can Chiropr Assoc. 2006; 50(2): 118-133.
12. Riddle DL, Pulisic M, Pidcoe P, Johnson RE. Risk factors for plantar fasciitis: a matchedcase-control study.

J Bone Joint Surg Am. 2003; 85A(5): 872-7.

13. Bowyer G. The ankle and foot. In: Solomon L, Warwick D, Nayagam S. Apley's system of orthopaedics and fractures. 9th ed. London: Hodder Arnold; 2010. p. 576-578.
14. Kwong PK, Kay D, Voner RT, White MW. Plantar fasciitis. Mechanics and pathomechanics of treatment. Clin Sports Med. 1988;7(1): 119-26.
15. Biundo JJ. Musculoskeletal signs and symptoms: D. Regional rheumatic pain syndromes. In: Klippel JH, Stone JH, Crofford L J, White PH, editors. Primer on the rheumatic diseases. 13th edition. New York: Springer; 2008.
16. Kumai T, Benjamin M. Heel spur formation and the subcalcaneal enthesis of the plantar fascia. J Rheumatol. 2002;29(9): 1957-64.
17. Banks AS, Downey MS, Martin DE, Miller SJ. McGlamy's comprehensive textbook of foot and ankle surgery. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2001. p 467.
18. Riddle DL, Schappert SM. Volume of ambulatory care visits and patterns of care for patients diagnosed with plantar fasciitis: a national study of medical doctors. Foot Ankle Int. 2004; 25(5): 303-10.
19. Young CC, Rutherford DS, Neidfeldt MW. Treatment of plantar fasciitis. Am Fam Physician. 2001; 63(3): 467-74.
20. Tanz SS. Heel pain. Clin Orthop Relat Res. 1963; 28: 169-78.
21. Lapidus Pw, Guidotti Fp. Painful Heel: Report Of 323 Patients With 364 Painful Heels. Clin Orthop Relat Res. 1965; 39:178-86.
22. McNally EG, Shitty S. Plantar fascia: imaging diagnosis and guided treatment. Semin Musculoskelet Radiol. 2010;14(3): 334-43.
23. Haake M, Buch M, Schoellner C, Goebel F, Vogel M, Mueller I, et al. Extracorporeal shock wave therapy for plantar fasciitis: randomised controlled multicentre trial. BMJ. 2003 12; 327 (7406): 75.
24. Calle EE, Thun MJ, Petrelli JM, Rodriguez C, Heath CW Jr. Body-mass index and mortality in a prospective cohort of U.S. adults. N Engl J Med. 1999; 7;341(15): 1097-105.
25. de Onis M, Habicht JP. Anthropometric reference data for international use: recommendations from a World Health Organization Expert Committee. Am J Clin Nutr. 1996; 64(4): 650-8.
26. Saber N, Diab H, Nassar W, Razaak H. Ultrasound guided local steroid injection versus extracorporeal shockwave therapy in the treatment of plantar fasciitis. Alex JM. 2012 march; 48 (1): 35–42.
27. Frey C, Zamora J. The effects of obesity on orthopaedic foot and ankle pathology. Foot Ankle Int. 2007 Sep; 28 (9): 996-9.
28. Irving DB, Cook JL, Young MA, Menz HB. Obesity and pronated foot type may increase the risk of chronic plantar heel pain: a matched case-control study. BMC Musculoskelet Disord. 2007; 8: 41.

29. Crawford F, Atkins D, Young P, Edwards J. Steroid injection for heel pain: evidence of short-term effectiveness. A randomized controlled trial. Rheumatology (Oxford). 1999; 38(10): 974-7.
30. Gollwitzer H, Diehl P, von Korff A, Rahlfs VW, Gerdesmeyer L. Extracorporeal shock wave therapy for chronic painful heel syndrome: a prospective, double blind, randomized trial assessing the efficacy of a new electromagnetic shock wave device. J Foot Ankle Surg. 2007; 46(5): 348-57.
31. Chuckpaiwong B, Berkson EM, Theodore GH. Extracorporeal shock wave for chronic proximal plantar fasciitis: 225 patients with results and outcome predictors. J Foot Ankle Surg. 2009; 48(2): 148-55.

پوختە

لیکدانا چارەسەری یا ژدەرڤەی لەشی بەرامبەر دانانا دەرزیکا کورتیزونی

بو چارسەریا هەودانا پەردا پانیا پێی: ڤەکولینەکا کلینیکی

پێشەکی هەودانا پەردا پانیا پێی تێکچونا سەروبەر و هەودانا پەردا پانیا بنێ پێ یە ل جهێ گرێدانا ڤێ پەردێ د گەل هەستیێ بنێ پێی کو دبیتە ئەگەرێ ئێشانا پانیا پێی ل دەف مروڤی. دەھ ژ سەدێ ژ مروڤا گازندێ ژ ئێشانا بنێ پێی دکەن د دەمەکی دژیانا خودا. دەمێ ڤێ گازندێ ڤەدکێشیت ژچەند حەفتیەکا تا چەند هەیڤەکا یان چەند سالا. پێنگاڤا دەسپێکێ بو چارەسەریا ڤێ ئێشێ بریکا بهنڤەدانەکا سنوردای، هندەك کارێن وەرزشی، ب کارئینانا گەرمێ یان سەرمایێ، بکارئینانا هندەك پارچێت متاتی د ناف پێلاڤێدا، و بکارئینانا دەرمانێت دژی هەودانا پێت نە پێت ستیرودی. و ئەگەر نەخوشی مفا ژ ڤان ریکا نەدیتن، هندەك ریکێت دی پێت هەین بو چارەسەریێ وەك بکار ئینانا لیکدانا چارەسەری یا ژدەرڤەی لەشی و دانانا دەرزیکا کورتیزونی. مقارنا ئەنجامێت هەردو ریکێت چارەسەریا هەودانا پەردا بنێ پیێ: لیکدانا چارەسەری یا ژدەرڤەی لەشی و دانانا دەرزیکا کورتیزونی.

ریکێن ڤەکولینێ ئەڤ ڤەکولینە هاتە ئەنجام دان ل بنگەهێ ئێشێن گەهان و نەخوشخانا ئازادی یا فیزکرنێ/ بەشێ چارەسەریا سروشتی ل دهوکێ هەر ژ نیسانا ٢٠١٣ تا شواتا ٢٠١٤. ئەڤێ ڤەکولینێ ئەو نەخوش ب خوڤە ڤەگرتن ئەویت توشی هەودانا پەردا بنێ پێی بوین بو پتر ژ ماوێ سێ هەیڤا و بێ مفا ژ ریکێن دەسپێکی بیت چارەسەریێ. ئەو ژی ١١٩ نەخوش بون و وان ١٣٢ پانییت ب ئێش هەبون، و هاتنە دابەشکرن بو دوو گروپا: گروپێ ئێکێ هاتنا چارەسەرکرن ب ریکا دانانا دەرزیکا کور تیزونی بو پانیا پێی ئەوژی ٥١ نەخوش بون و٥٥ پانییت ب ئێش هەبون. گروپێ دوێ هاتنە چارەسەرکرن ب ریکا لیکدانا چارەسەری یا ژدەرڤەی لەشی ئەوژی ٦٨ نەخوش بون و وان ٧٧ پانییت ب ئێش هەبون. ئەڤ نەخوشە هاتنە دیتن پشتی ١ هەیڤ و ٣ هەیڤ ژ چارەسەریێ.

ئەنجام بەهرا پتر ژ نەخوشان مێ بون (٨٠,٧٪) و ناڤەراستا ژیێ وا ٤٤,٧ سال بون، و ناڤەراستا درێژیا بەژنا وان ١٥٨,٥ سم، و ناڤەراستا سەنگێ وان ٨٤,٥ کغم، و ناڤەراستا تێراتیا لەشێ وان ٣٣,٦ کغم/م٢ ئەوا تێتە هژمارتن قەلەوی جورێ ١. ئەو نەخوشێت چ مفا نە دیتین ژ هەر ریکەکا چارەسەریێ سەنگێ وان نێزیکی یان پتر بو ژ ١٠٠ کغم ان و تێراتیا لەشێ وان پتر بو ژ ٤٠ کغم/م٢ (ئەڤەژی قەلەوی یە جورێ ٣).

د گروپێ ئێکێ دا پلا ئێشێ کێم بو ژ ٧,٩ بو ٢,٣ پشتی ٣ هەیڤا ژ چارەسەریێ ل دیف پیڤەرێ ئێشێ ب چاڤ ئەوێ پێك تێت ژ ١٠ پلا ، و دگروپێ دوێ دا پلا ئێشی کێم بو ژ ٨ بو ٢,٩ پلە. و بکارئینانا پیڤەری قوتابی یێ جوت بو پشکنینا ئەنجامێت هەر گروپەکی جودا ئەنجامێت وان ژ لایێ هژماریڤە یێ بەرچاڤ بو، بەڵێ ل دەمێ مقارنا ئەنجامێت هەردو گروپا دگەل ئێك ب ریکا پیڤەرێ قوتابی یێ سەربەخو ئەنجام ژ لایێ هژماریڤە نە یێ بەرچاڤ بو.

دەرئەنجام هەودانا پەردا بنێ پێی یا بەربەلاڤە د ناڤ نەخوشێت قەلەو. قەلەوی ئەگەرە بو نە مفا دان ژ هەمی جورێت چارەسەریێ. بکار ئینانا لێکدانا چارەسەری ژ دەرڤەی لەشی و دانانا دەرزیکا کورتیزونی بو بنێ پێی هەردوك ریکێت باشن بو چارەسەریا هەودانا پەردا بنێ پێی. چارەسەری ب ریکا لێکدانا چارەسەری ژدەرڤەی لەشی باشترە چونکو زیانێت وێ کێمترن.

الخلاصة

العلاج الخارجي بالموجة عالية التردد مقابل الزرق الموضعي للكورتيزون في علاج التهاب غشاء بطانة القدم: دراسة تداخلية

الخلفية وأهداف البحث التهاب غشاء بطانة القدم هو تضرر مع التهاب تفاعلي للغشاء المبطن لاسفل القدم عادة في منطقة اتصال الغشاء بعظم كعب القدم مسببة حالة الكعب المؤلم. ان الخط الاول من العلاج تحفظي عن طريق راحة محدودة، تمارين المط، استخدام موضعي للحرارة او البرودة، مساند مطاطية داخل الحذاء واستخدام الادوية المضادة للالتهاب غير الستيرودية. و اذا لم يستجب المريض لهذه الطريقة واصبحت الحالة مزمنة، فهناك طرق اخرى للعلاج مثل العلاج الخارجي بالموجة عالية التردد او الزرق الموضعي لمادة الكورتزون. هو مقارنة نتائج العلاج الخارجي بالموجة عالية التردد مقابل الزرق الموضعي لمادة الكورتزون.

طرق البحث أجريت الدراسة في مركز أمراض المفاصل ومستشفى آزادي التعليمي/ قسم العلاج الطبيعي في مدينة دهوك للفترة من نيسان ٢٠١٣ لغاية شباط ٢٠١٤. شملت الدراسة المرضى المصابين بالتهاب غشاء بطانة القدم المزمنة والذين لم يستجيبو للعلاج التحفظي لمدة ثلاثة اشهر او اكثر. كان عدد المرضى ١١٩ لديهم ١٣٢ حالة كعب قدم مؤلمة وتم تقسيمهم الى مجموعتين: المجموعة الاولى عولجت بطريقة زرق ابرة الكورتزون في بطانة القدم وكانوا ٥١ مريضا و لديهم ٥٥ حالة كعب مؤلمة. المجموعة الثانية عولجت بالعلاج الخارجي بالموجة عالية التردد و كانوا ٦٨ مريضا و لديهم ٧٧ حاة كعب مؤلمة. تم متابعة المرضى بعد شهر و ثلاثة اشهر من تلقي العلاج.

النتائج معظم المرضى كانوا اناثا (٨٠.٧%) و معدل اعمارهم ٤٤.٧ سنة، و معدل اطوالهم ١٥٨.٥ سم، ومعدل اوزان اجسامهم ٨٤.٥ كغم ، ومعدل مؤشر كتلة الجسم ٣٣.٦ كغم/م٢ و الذي يعتبر سمنة صنف ١. المرضى الذين لم يظهروا اي تحسن في حالتهم كان اوزان اجسامهم حوالي او اكثر من ١٠٠ كغم و مؤشر كتلة اجسامهم اكثر من ٤٠ كغم/ م٢ (وهذا يعتبر سمنة صنف ٣). في المجموعة الاولى انخفض شدة الالم من ٧.٩ الى ٢.٣ بعد ثلاثة اشهر من العلاج حسب مقياس الالم النظري و المؤلف من عشر درجات، بينما في المجموعة الثانية انخفض شدة الالم من ٨ ال ٢.٩. وباستخدام اختبار (paired t test) لفحص نتائج كل مجموعة على حدة كانت النتائج بمستوى احصائي معنوي عالي، في حين عند مقارنة نتائج طريقتي العلاج باستخدام اختبار (unpaired t test) لم تبلغ النتيجة المستوى الاحصائي المعنوي.

الاستنتاجات التهاب غشاء بطانة القدم اكثر شيوعا عند المرضى السمان. السمنة احد عوامل فشل علاج حالة التهاب غشاء بطانة القدم. ان استخدام العلاج الخارجي بالموجة عالية التردد و الزرق الموضعي لابرة الكورتزون طريقتان فعالتان لعلاج التهاب غشاء بطانة القدم. العلاج الخارجي بالموجة عالية التردد مرغوبة اكثر لانها اكثر امانا.

P53 IMMUNOHISTOCHEMISTRY IN CHRONIC PERIODONTITIS; RELATION TO SMOKING AND HISTOPATHOLOGIC PARAMETERS

CHINAR M. SULAIMAN,BDS, MSc*
AMEERA K. KHALEEL, BDS, MSc**

Submitted 1 Nov 2014; accepted 31 Dec 2014

ABSTRACT

Background and objectives Smoking is one of the main and important risk factors that increase risk of oral health problems. There is a dose-response relationship between number of cigarettes smoked and the development of periodontal diseases, in addition, to an elevation of p53 in oral mucosa of smokers. The aim of the study was to examine p53 immune expression in the gingival tissue samples in patients with different severity of chronic periodontitis in relation to different histopathological parameters and smoking status.

Methods Gingival tissue biopsies were taken from (30) smokers and (30) nonsmoker subjects with different severity of chronic periodontitis. Staining profiles were classified according to the number of positive cells as well as to the location of the positive cells in the different epithelial layers of the specimens.

Results No significant difference was found between the median p53 labeling indices and any of the smoking status, severity of chronic periodontitis, epithelial thickness and number of blood vessels in the connective tissue. However, a significant association was found between p53 immunostaining and number of inflammatory cells.

Conclusions Chronic periodontitis may accelerate smoking effects on p53 gene mutation.

Duhok Med J 2014;8(2): 57-77.

Key words: P53, Immunohistochemistry; Periodontitis, Smoking

Chronic periodontitis is an inflammatory disease caused by different types of microorganisms. Mechanisms responsible for gingival tissue damage are poorly understood; both immune-mediated reactions and direct bacterial cytopathic effects may be involved.[1] Based on a direct effect of bacteria in cell cultures, it has been suggested that apoptosis might play an important role in periodontitis. Apoptosis is important phenomenon in regulation of the inflammatory response against chronic bacterial accumulation with increasing cellularity and affecting the extent of the inflammatory infiltration.[2] A recent study demonstrated that p53 plays a fundamental regulatory role in apoptosis and is responsible for regulation of cell cycle. This protein is also implicated in the regulation of tissue dynamics and is specifically thought to induce apoptosis in terminally differentiated cells, including inflammatory cells.[3]

Recent studies which took into account oral hygiene status showed that smokers had a greater risk of periodontal disease regardless of oral hygiene.[4] Studies

*Assistant lecturer, Department of Oral Surgery and Diagnosis, School of Dentistry, Faculty of Medical Science, University of Duhok, Duhok, Kurdistan Region – Iraq
**Assistant professor, College of Dentistry, Hawler Medical University, Kurdistan Region – Iraq

Correspondence author: Chinar M. Sulaiman. Email: chinar82@gmail.com

in vitro have shown a direct inhibition of neutrophil and monocytes-macrophage defensive functions by high concentrations of nicotine that may be achieved in patients using tobacco. Smoking appears to affect both B and T lymphocyte function; inducing functional unresponsiveness in T cells.[5] p53 mutation has been associated with several factors, such as prolonged exposure to various external carcinogens, such as benzopyrene in cigarette smoke. Husgafvel-Pursianien et al[6] found that p53 was overexpressed in human tumors linked to carcinogens found in tobacco products. Gamonal et al[7] studied the apoptotic events in the gingival tissue of adult patients with chronic periodontitis; they demonstrated overexpression of p53 only in the inflammatory infiltrate. Bulut et al[3] selected eight patients with generalized aggressive periodontitis and ten healthy (control) individuals, they observed no significant difference between the two groups with respect to grades of p53 expression.

This study was an attempt to study p53 immunoexpression in the gingival tissue samples obtained from moderate and heavy smoker patients having chronic periodontitis with different severity in relation to the thickness of the epithelium, number of inflammatory cells and blood vessels in the connective tissue.

METHODS

Thirty smokers persons (study group) of (35-55) years old, and (30) nonsmokers subjects (control group) matched in the age with the study group, with chronic periodontitis, selected from the Duhok Health Centers, in the period from November 2010 to March 2011. In each smoking status category, an equal number of cases with mild, moderate and severe chronic periodontitis based on pocket attachment loss (PAL) were included. The data which included the laboratory serial number, patient name, age, gender, smoking status and date of taking the biopsy were registered in a special form. None of the subjects had any known systemic disorders or had used antibiotics and anti-inflammatory medications in the last 3 months and no history of comprehensive periodontal treatment nor were they under orthodontic treatment. Patients and control subjects with active infectious diseases as well as females, who were lactating, women taking contraceptive pills, or pregnant as well as participants with history of alcohol drinking were also excluded from the study. Approval of the Research Ethic Committee at Duhok Directorate General of Health for examining the patients was taken. The smokers group was subdivided into two categories according to previous studies[8]:

Moderate (5-15 cigarettes per day for >1-10 years)

Heavy (≥ 15 cigarettes per day for >10 years)

The severity of chronic periodontitis at the site level was classified based on the degree of PAL [1] and the gingival biopsies were taken from clinically diagnosed patients from the buccal or labial region using sterile surgical blade and involving the gingival epithelium with underlying connective tissue.

Sections made were stained with hematoxylin and eosin, and additional sections were processed and put on positively charged slides for immunohistochemical study. Running with each batch test immunostain, we applied positive tissue control (strongly positive breast ductal carcinoma tissue section) and negative tissue controls (using a non-immune serum by applying the antibody diluents alone).

Five biopsy specimens of healthy gingiva obtained during surgical removal of impacted upper canine were used as controls for normal p53 expression.

For immunohistochemical staining, thin tissue sections (4μ m) were cut from paraffin blocks and mounted on sialinized slides and placed in oven overnight at 55°C. Sections were deparaffinized in xylene for 5 minutes, then hydrated in 100% ethanol, 90% ethanol and 70% ethanol, each for 5 minutes respectively then rinsed by distilled water for 5 minutes. Slides were put in antigen retrieval and placed in pressure cooker for 50 minutes at 75°C. Then the container with the slides was removed from the steamer and allowed to cool slowly for 10-20 minutes at room temperature. Slides were rinsed in PBS solution. The excess buffer was tapped off gently and sections are wiped around by gauze pad and a circle around the section was made by pap pen. Enough hydrogen peroxidase block was applied to cover all the tissue and incubated for 10 minutes in order to block endogenous peroxidase activity. Slides were rinsed in PBS for 5 minutes, incubated with protein block for 5 minutes, washed in PBS for 5 minutes, incubated with primary antibody for 30 minutes at room temperature, washed in PBS for 5 minutes, incubated with post primary block for 30 minutes, washed in PBS for 5 minutes, incubated with NovoLinkTM Polymer (UK) for 30 minutes, then rinsed in 2 jars of Tris-Buffer Solution (TBS) for 5 minutes each respectively with gentle rocking.

Diaminobenzidine (DAB) working solution was prepared by adding 50μl of DAB Chromogen to1ml of NovoLinkTM DAB substrate buffer and sections were incubated with this solution for 5 minutes which resulted in a brown colored precipitate at the antigen sites. Slides were rinsed with tap water, hematoxylin was used as nuclear counter stain for 30 seconds, then slides were washed in running water gently, sections then were dehydrated in graded ethanol (70%, 90%, 100%) for 2 minutes each respectively, transferred to xylene, then slides were mounted, dried and examined under light microscope.

All hematoxylin and eosin stained slides were examined in relation to:

A. The major epithelial thickness (MET), which is distance between the external epithelial surface and the epithelial crista tip, and the epithelial base thickness (EBT) which is distance between the external epithelial surface and basal membrane located between the two cristae. The measurements were taken using an image analyzed system that comprised a light microscope (Nikon, Japan) equipped with a digital camera (Nikon,

Japan). Pictures captured at 10X magnification and then transferred to a personal computer with image processing software(AutoCAD 2010) for morphometric analysis. MET and EBT were evaluated in five different areas in each of the three different fields, totaling 15 measures per slide. The final data for each parameter represent the mean for the quantification in the analyzed fields.[9,10]

B. The number of inflammatory cells (with 40X magnification) and blood vessels (with 20X magnification) in the connective tissue, in three microscopic fields per slide. Positive expression of p53 gives a clear-cut nuclear staining of brown color. Staining profiles were classified according to the relative number of positive cells as well as to the location of the positive cells in the different epithelial layers of the specimens. Three categories for p53 immunostaining were defined[11]:
    1) Negative: No expression of p53 detected in any epithelial nucleus.
    2) Nuclear staining confined to the basal cell layer.
    3) Clear suprabasal nuclear staining (in addition to basal cell layer).

For quantitative analysis of p53 positive cells, at first the cells were counted under a light microscope, then the counting was repeated by two independent pathologists and the average of the readings was used. Only the number of cells showing nuclear expression of p53 was quantified by counting at least 1000 epithelial cells in five representative fields at 400X objective in each case. Calculation of the labeling index (LI) is based on the ratio of the number of immune positive cells per 1000 counted cells per case studied, and then divided by 10 to express the index in percentage.[12,13] The intensity of staining was not considered.

RESULTS

Total number of patients was sixty, 40 males (66.67%) (10 nonsmokers and 30 smokers) and 20 females (33.33%) (20 nonsmokers and zero smoker). The age ranged between (35-55) years with a mean age of (47.73) years for nonsmokers, (46.20) years for moderate smoker, and (43.73) years for the heavy smokers.

Mild chronic periodontitis histopathologic parameters and smoking status:

The results showed marked increase in median MET and EBT with increase severity of the smoking status in cases (Table 2). Kruskal-Wallis test indicates significant differences was found in the median MET, EBT and the median number of blood vessels among the different groups of smoking ($p<0.05$) while no significant difference was found in the median number of inflammatory cells ($p>0.05$).

Results of post-hoc Mann-Whitney U test indicated significantly higher median MET, EBT and blood vessels in moderately smokers compared with non smokers ($p=0.008$, 0.014 and 0.006 respectively). In addition, significantly

Table 1. Distribution of examined patients by smoking status and severity of chronic periodontitis

Pocket attachment loss	Non smoker No. (%)	Smoker		Total
		Moderate No. (%)	Heavy No. (%)	
Mild (PAL=1-2 mm)	10 (16.67)	5 (8.33)	5 (8.33)	20
Moderate (PAL=3-4 mm)	10 (16.67)	5 (8.33)	5 (8.33)	20
Severe (PAL=≥5 mm)	10 (16.66)	5 (8.34)	5 (8.34)	20
Total	30 (50)	15 (25)	15 (25)	60

PAL: Probing attachment loss

Table 2. Histopathological parameters in patients with mild chronic periodontitis (PAL= 1-2 mm) in relation to the smoking status

Parameter	Non smoker	Smoker		p-value
		Moderate	Heavy	
Median MET (µm)	488	513	520	0.003
Median EBT (µm)	338	410	412	0.008
No. of inflammatory cells	25.5	47	27.6	0.252
No. of blood vessel	0.8	2	1.6	0.022

PAL: Probing attachment loss
MET: Major epithelial thickness
EBT: Epithelial base thickness

higher median MET and EBT were demonstrated among heavy smokers compared with the nonsmokers (p=0.005 and p=0.014 respectively). In contrast, no significant difference was found in median MET and median EBT between moderate smokers and heavy smokers (p=0.344 and p=0.243 respectively).

In contrast, no significant difference was found in median number of blood vessels between heavy smokers and non smokers (p=0.193), and between moderate smokers and heavy smokers (p=0.243).

Figure 1-3 shows the microscopical pictures of the gingiva with mild chronic periodontitis in nonsmokers, moderate and heavy smoker patients respectively.

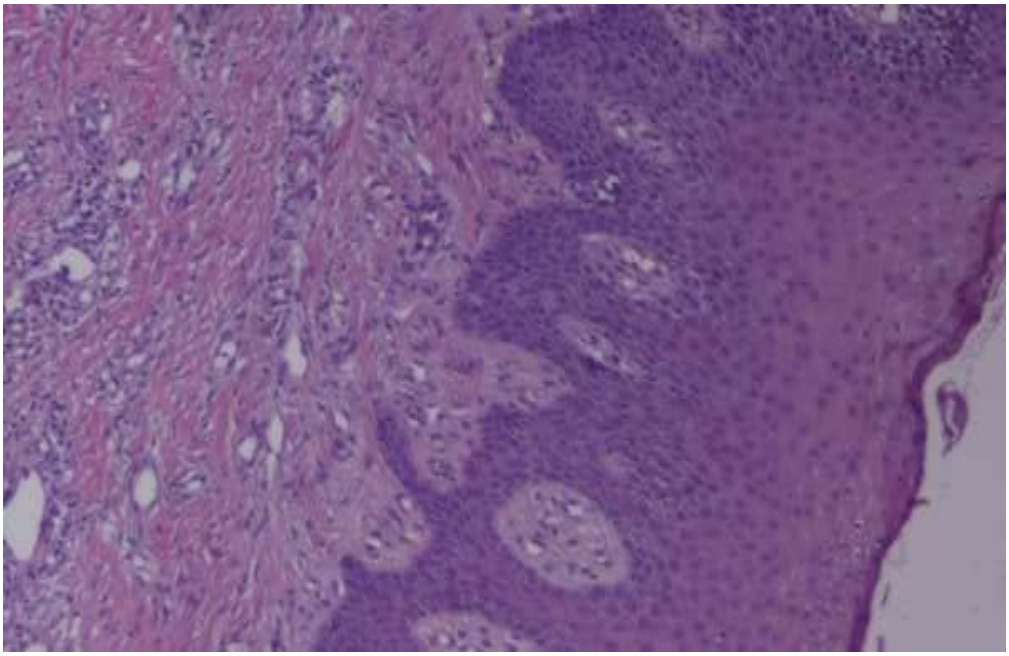


Figure 1. Microscopical picture of the gingiva with mild chronic periodontitis in nonsmoker patient, showing the gingival epithelium and connective tissue (H &E, X 10)

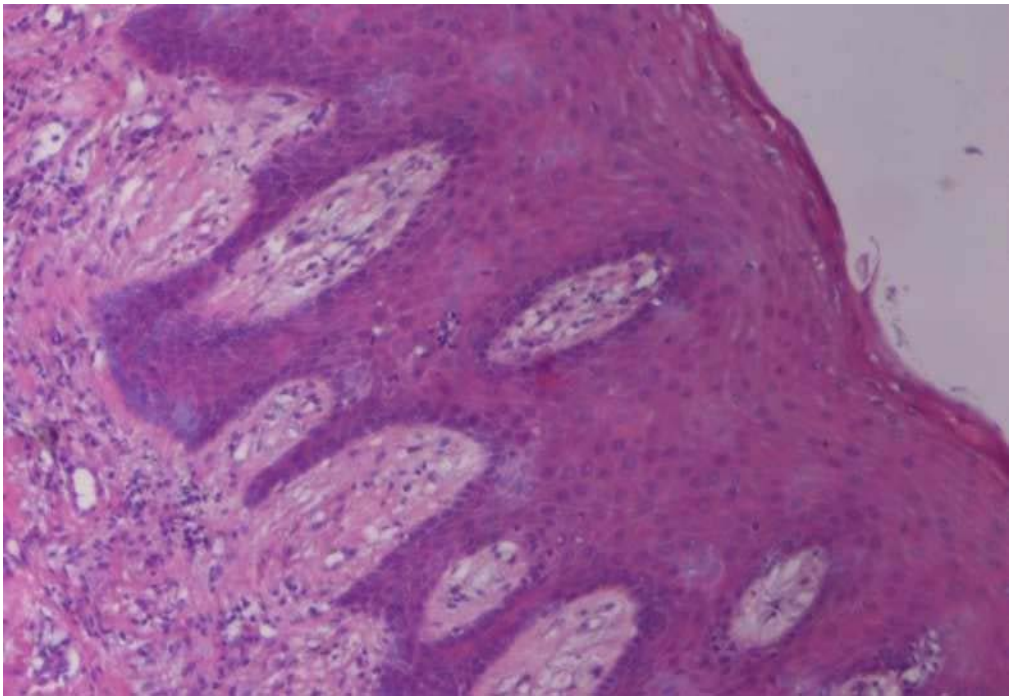


Figure 2. Microscopical picture of the gingiva with mild chronic periodontitis in moderate smoker patient, showing increase in the MET and EBT (H&E, X 10)

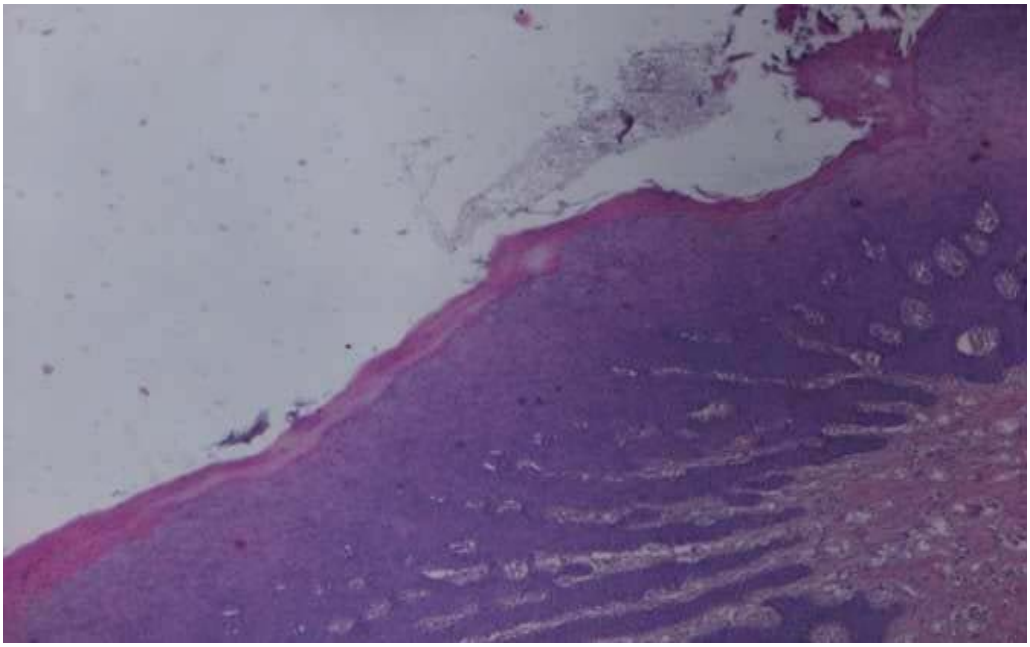


Figure 3. Microscopical picture of the gingiva with mild chronic periodontitis in heavy smoker patient, showing increase thickness of keratin and elongated rete pegs (H &E, X 10) periodontitis (PAL=3-4mm), in relation to the smoking status

Moderate chronic periodontitis histopathologic parameters and smoking status:

There was a marked increase in median MET and EBT with increase severity of the smoking status (Table 3). Kruskal-Wallis test indicated significant differences in the median MET, EBT and median number of blood vessels between the three smoking categories in the ($p<0.05$) and no significant difference in the median number of inflammatory cells ($p>0.05$).

Results of post-hoc Mann-Whitney U

Table 3. Histopathological parameters in patients with moderate chronic periodontitis (PAL= 3-4 mm) in relation to the smoking status

Parameter	Non smoker	Smoker		p-value
		Moderate	Heavy	
Median MET (µm)	484	509	536	<0.001
Median EBT (µm)	335	340	419	0.006
No. of inflammatory cells	43.9	53.6	49.5	0.075
No. of blood vessel	2.6	5	2.61	0.023

PAL: Probing attachment loss
MET: Major epithelial thickness
EBT: Epithelial base thickness

test indicated a significantly higher median MET among moderate smokers and among heavy smokers compared with nonsmokers (p=0.002). In addition, a significantly higher median MET was found among heavy smokers compared with moderately smokers (p=0.009).

In the same line, a significantly higher median EBT among moderate smokers and among heavy smokers compared with nonsmokers (p=0.035 and 0.013 respectively) and significantly higher median EBT among heavy smokers compared with moderately smokers (p=0.008).

Regarding the blood vessels, significantly higher median number of the blood vessels was observed among moderate smokers compared with nonsmokers and heavy smokers (p=0.012 and 0.026 respectively). In contrast, there was no significant difference in the number of blood vessels present between heavy smokers and nonsmokers (p=0.622). Figure 4-6 shows the microscopical pictures of the gingiva with moderate chronic periodontitis in nonsmokers, moderate and heavy smokers.

Severe chronic periodontitis histopathology and smoking status:

A marked increase in median MET and EBT with increase severity of the smoking status was demonstrated (Table 4). Kruskal- Wallis and post-hoc Mann-Whitney U tests indicated significantly higher median MET among moderate and heavy smokers compared with nonsmokers with severe chronic periodontitis (p= 0.002), and among heavy smokers compared with moderate smokers (p=0.009). No significant difference was found in the median number of inflammatory cells and in the median number of blood vessels between the three smoking categories (p> 0.05).

In the same line, a significantly higher median EBT among moderate smokers and among heavy smokers compared with nonsmokers (p=0.005 and 0.002 respectively).

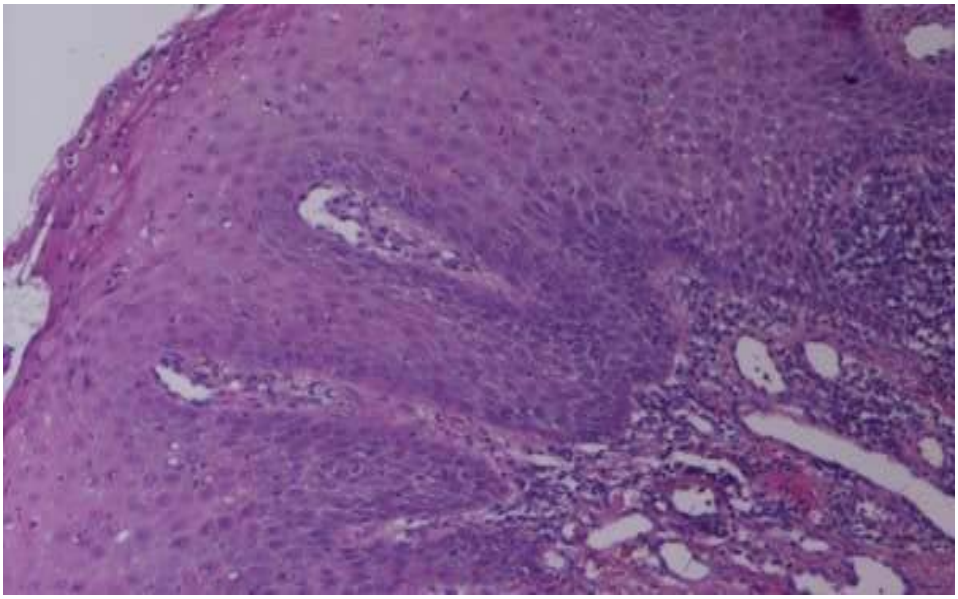


Figure 4. Microscopical picture of the gingiva with moderate chronic periodontitis in non smoker patient, showing an increase in the number of inflammatory cells and blood vessels in the connective tissue compared with that of mild chronic periodontitis (H&E, X10)

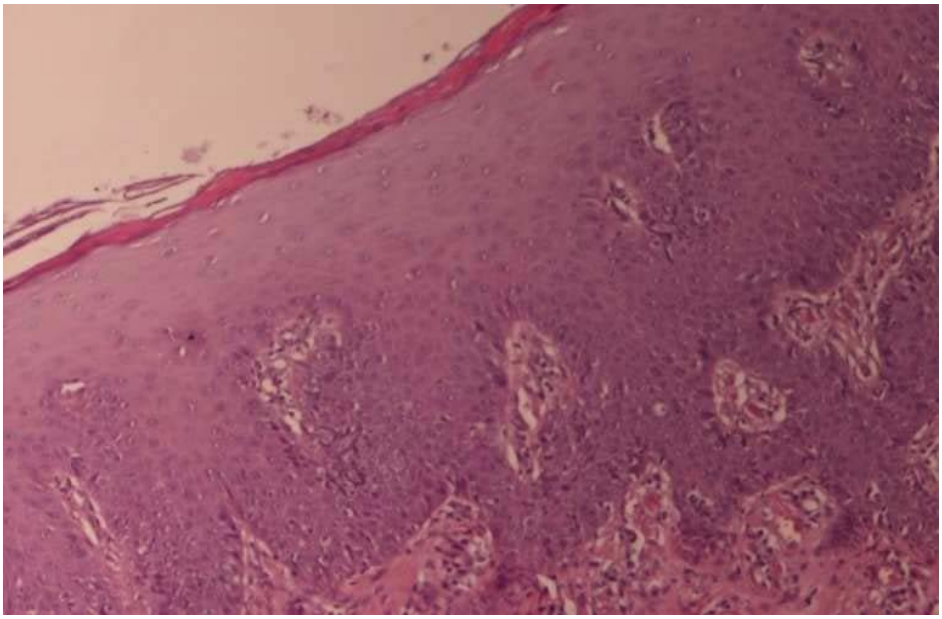


Figure 5. Microscopical picture of the gingiva with moderate chronic periodontitis in moderate smoker patient, showing an increase in the thickness of the epithelium with short irregular rete pegs (H &E, X 10)

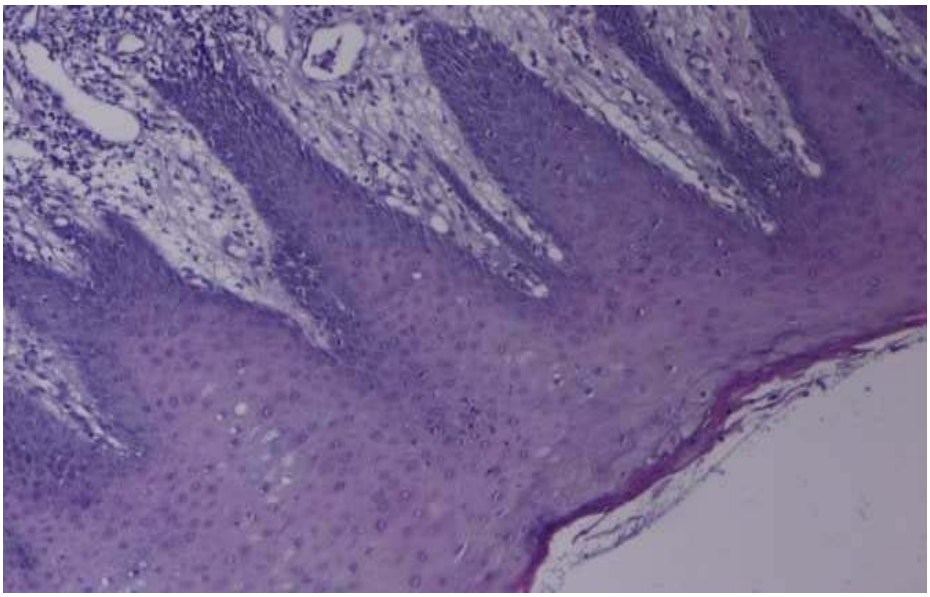


Figure 6. Microscopical picture of the gingiva with moderate chronic periodontitis in heavy smoker patient, showing an increase in thickness of the epithelium with long rete pegs (H&E, X10)

In contrast, no significant difference was found in the median EBT between moderate and heavy smokers (p=0.115). Figure 7, Figure 8, and Figure 9 show the microscopical pictures of the gingiva with severe chronic periodontitis in non-smokers, moderate and heavy smokers.

p53 immunohistochemical results:

Immunohistochemically, p53 stained the basal cell layer only in normal gingival epithelium. The total number of positive p53 cases was 55 (91.67%). Twenty eight cases were smokers of whom 11 (36.67%) and 17 (56.66%) showed basal and

Table 4. Histopathological parameters in patients with severe chronic periodontitis (PAL ≥ 5mm) in relation to the smoking status

Parameter	Non smoker	Smoker		p-value
		Moderate	Heavy	
Median MET (µm)	412.5	495	596	<0.001
Median EBT (µm)	329	340	430	0.001
No. of inflammatory cells	68.7	68	77.6	0.224
No. of blood vessel	3.1	3.6	3.3	0.642

PAL: Probing attachment loss
MET: Major epithelial thickness
EBT: Epithelial base thickness

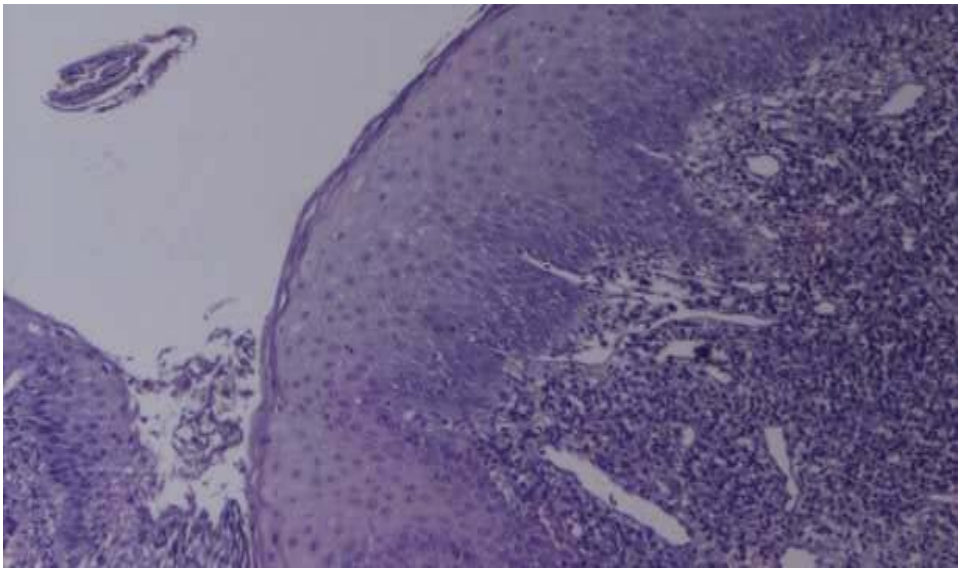


Figure 7. Microscopical picture of the gingiva with severe chronic periodontitis in non smoker patient, showing an decrease in the thickness of the gingival epithelium, and increase in the number of inflammatory cells and blood vessels in the connective tissue compared with that of mild chronic periodontitis (H&E, X10)

suprabasal expression of p53, respectively. The p53 expression in two cases had extended beyond the suprabasal layer close to the surface of the epithelium. In nonsmokers with positive p53 expression (27 cases), 21 (77.78%) showed basal expression compared to only six (22.2%) individuals with suprabasal expression.

The remaining two cases, p53 positive cells reached nearly the surface epithelium (Table 5). The number of of positive p53 cases in mild chronic periodontitis was 18 (90%). The number of basal p53 positive cases in nonsmoker patients was (8) and it was higher than that of smokers (3) but the number of suprabasal p53 positive cases in the smokers (6) was higher than that of nonsmokers (1).

In moderate chronic periodontitis, number of basal p53 positive cases in nonsmoker patients was (6) which was higher than that of smokers (3), whereas the number of suprabasal p53 positive cases in the smokers (7) was higher than that of nonsmokers (3).

In severe chronic periodontitis, number of p53 positive cases was 18 (90%). The number of basal p53 positive cases in nonsmoker patients was (7) which was higher than that of smokers (5) while the numbers of suprabasal p53 positive cases in the smokers was four (two for heavy smokers and two for moderate smokers); it was higher than nonsmokers (2).

Figure 10-12 shows p53 immune expression in the gingiva of nonsmoker, moderate smoker, and heavy smokers with different severity of chronic periodontitis. Both heavy smokers and moderate smokers showed more p53 median labeling index than nonsmokers, but statistically not significant. The highest percentage of labeling index was seen among heavy smokers with severe chronic periodontitis (Table 6). No significant associations were demonstrated between the median percentage of p53 labeling index and any of the median MET, EBT, and the number of blood vessels in the connective tissue ($p>0.05$). In contrast a significant direct association was present between the median number of inflammatory cells and p53 labeling index ($p<0.05$) (Table 7).

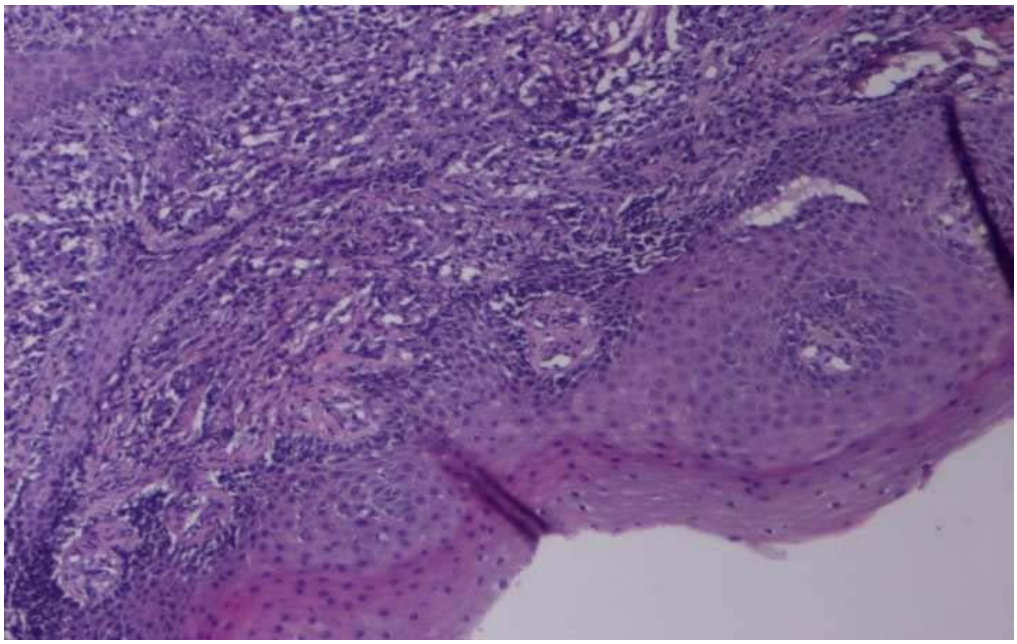


Figure 8. Microscopical picture of the gingiva with severe chronic periodontitis in moderate smoker patient, showing increase in the thickness of the stratum corneum (H&E, X10)

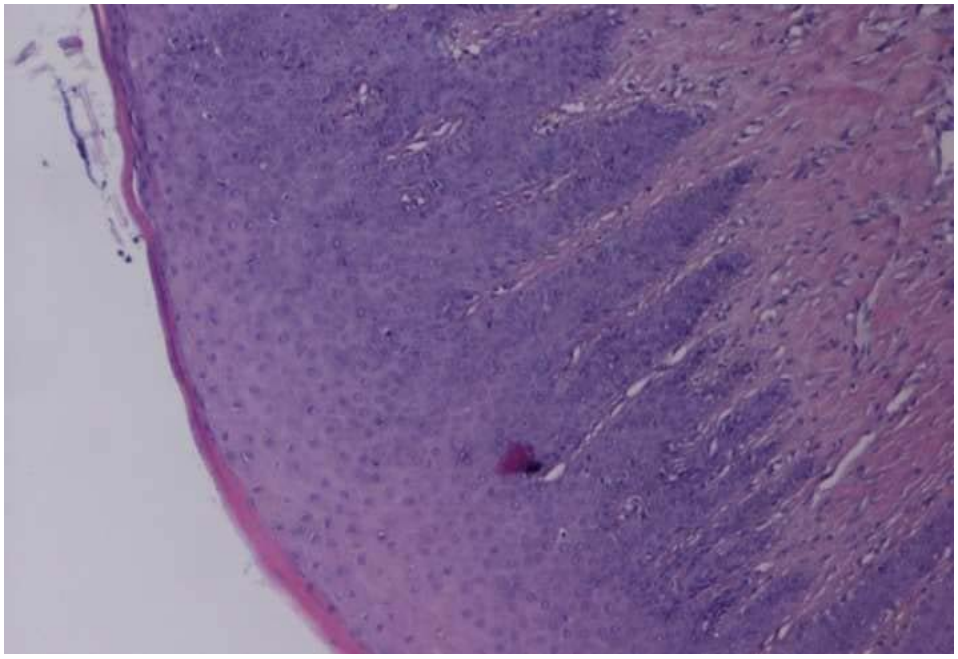
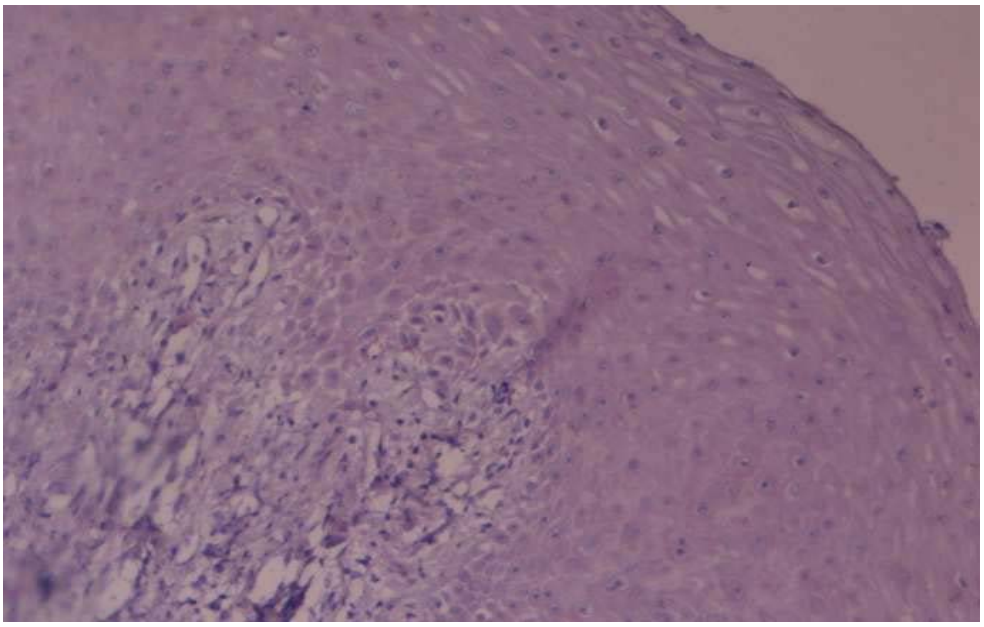


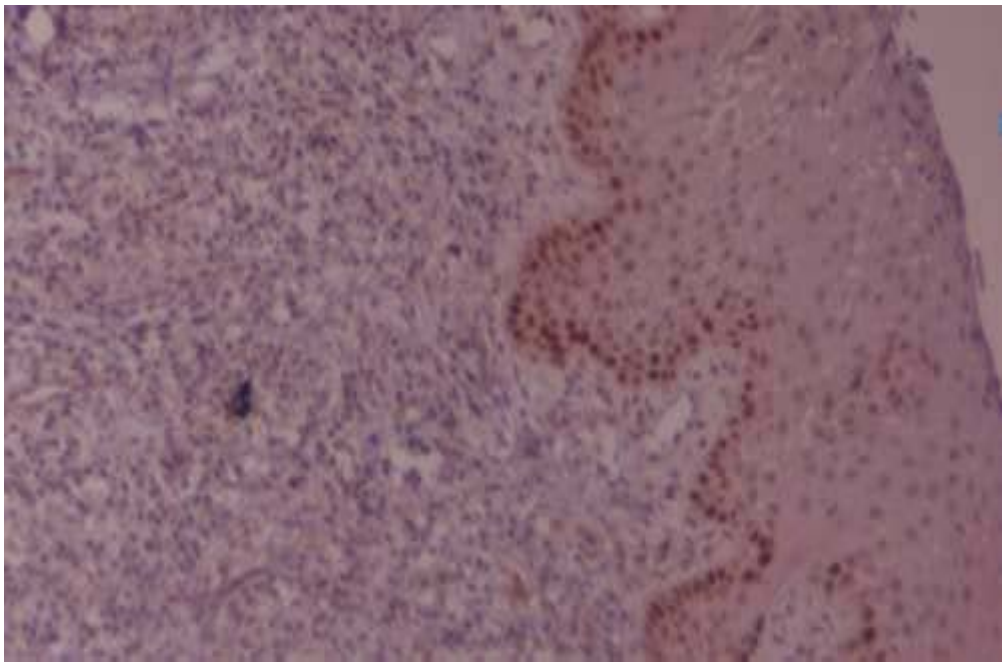
Figure 9. Microscopical picture of the gingiva with severe chronic periodontitis in heavy smoker patient, showing increase in the thickness of both stratum corneum and stratum spinosum layer and elongated rete pegs (H&E, X10)

Table 5. P53 Expression in oral epithelium of patients with mild, moderate, and severe chronic periodontitis, in relation to the smoking status expressed in number of individual

p53 immune expression			Smoking status				
			Non smoker (n=10)	Smoker			Total
				Moderate (n=5)	Heavy (n=5)	Total	
Mild chronic periodontitis	Negative		1	1	0	1	2
	Positive	Basal	8	2	1	3	11
		Suprabasal	1	2	4	6	7
		Total	9	4	5	9	18
Moderate chronic periodontitis	Negative		1	0	0	0	1
	Positive	Basal	6	2	1	3	9
		Suprabasal	3	3	4	7	10
		Total	9	5	5	10	19
Severe chronic periodontitis	Negative		1	0	1	1	2
	Positive	Basal	7	3	2	5	12
		Suprabasal	2	2	2	4	6
		Total	9	5	5	9	18

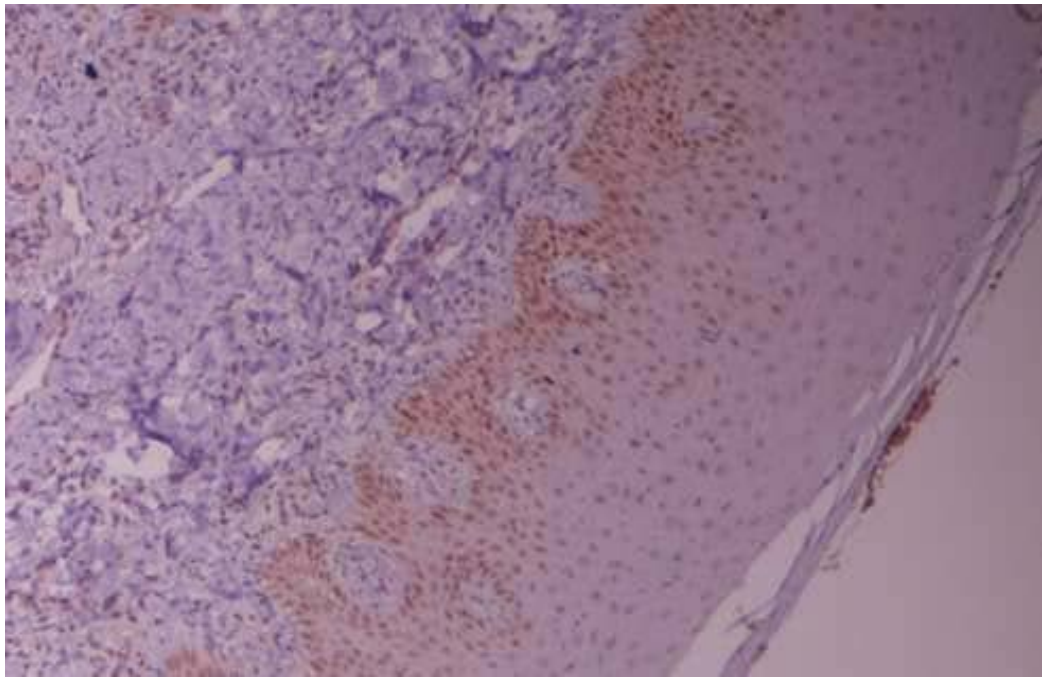


A

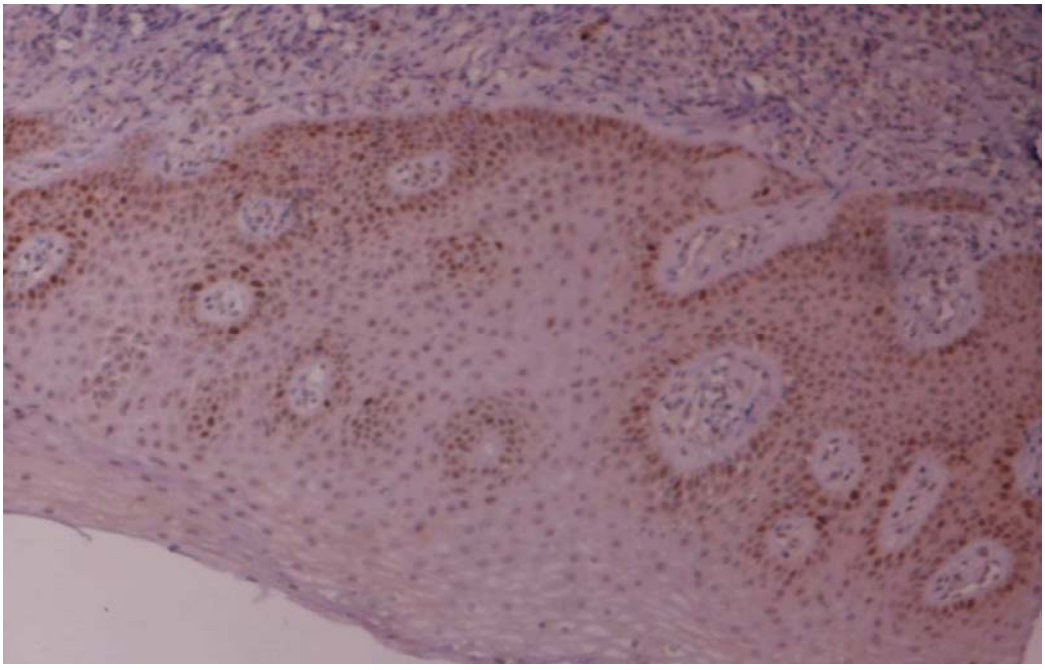


B

Figure 10. Microscopical picture of the gingiva in a nonsmoker patients with mild chronic periodontitis showing (A) Negative p53 expression. (B) Basilar p53 expression (IHC, X10)

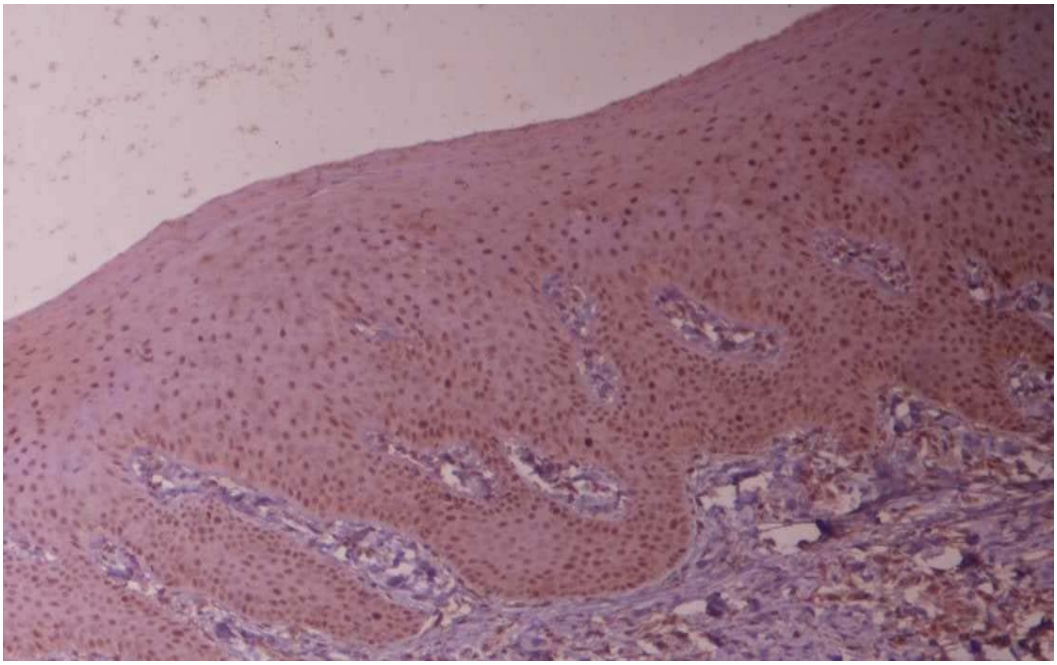


A

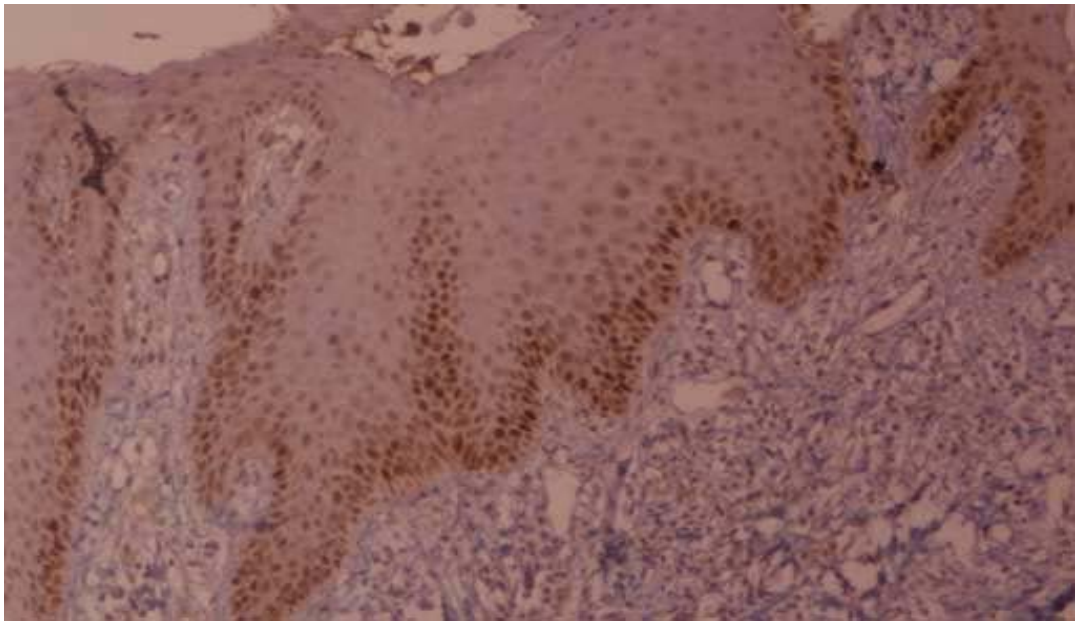


B

Figure 11. Microscopical picture of the gingiva in a moderate smoker patients with (A). Moderate chronic periodontitis showing suprabasilar p53 expression. (B) Severe chronic periodontitis showing suprabasilar p53 expression (IHC, X 10)



A



B

Figure 12. Microscopical picture of the gingiva in a heavy smoker patients with (A) Moderate chronic periodontitis showing supra basilar p53 expression reaching nearly to the surface of the epithelium; (B) Severechronic periodontitis showing supra basilar p53 expression (IHC, X 10)

Table 6. Median p53 labeling index in patient with mild, moderate, and severe chronic periodontitis in relation to the smoking status

Smoking status		P53 Immunoexpression	
		Median (LI)% for positive	P- value
Mild PAL	Non smoker	13.00	0.891
	Moderate smoker	13.70	
	Heavy smoker	14.94	
Moderate PAL	Non smoker	16.24	0.522
	Moderate smoker	16.66	
	Heavy smoker	17.95	
Severe PAL	Non smoker	16.56	0.412
	Moderate smoker	17.78	
	Heavy smoker	18.9	

PAL: Probing attachment loss
LI: Labeling index

Table 7. Correlation between median LI for p53 positive cases and the thickness of epithelium, the number of inflammatory cells and blood vessels in the connective tissue

Attribute	Correlation coefficient	p-value
MET	- 0.07	0.961
EBT	0.031	0.815
Number of inflammatory cells in the connective tissue	0.299	0.021
Number of blood vessels in the connective tissue	0.026	0.84

LI: Labeling index
MET: Major epithelial thickness
EBT: Epithelial base thickness

DISCUSSION

Periodontitis is a chronic inflammatory disease caused by a variety of risk factors, of which smoking is demonstrated to detrimentally affect the periodontal health. The regulation of the inflammation and host immune response is coordinated by apoptosis mechanism. p53, a tumor-suppressor protein, induce this apoptosis process. The protein is normally present in

healthy tissues; however its expression is undetectable. When it became activated, the protein get stabilized and detected by immunohistochemical technique.[14] Our study examined the expression of p53 in the gingival tissue samples taken from moderate-heavy smokers who have chronic periodontitis in relation with some pathological parameters such as MET, EBT and numbers of inflammatory cells and presence of blood vessels.

In the present study, both MET and EBT were elevated significantly in smokers compared to nonsmokers regardless of the perdiodontal health conditions. This results confirms findings of Villar and de Lima[9] and Gültekin et al[15] which can be explained by the proliferating effects of smoking toxins on the epithelial tissues of gingiva. Another study by Bajagic et al[10] found a statistically non-significant difference in the MET between smokers and nonsmokers but this evidence is compromised by the very small size of the sample taken from each group to justify the statistical significance testing.

The relationship between the intensity of the inflammatory cells in the gingival connective tissues and smoking across the different categories of periodontitis has been reported with variable findings. In our study, the difference did not show statistical significance similar to what is demonstrated in Rahman et al[16] study. Al-Tayeb[17] found an inverse significant correlation with smoking while Loos et al[5] indicated that the total inflammatory cell count was significantly higher in smokers than in nonsmokers.

The number of blood vessels in the gingival connective tissue of smokers was higher than that of nonsmokers; the smokers reveal more blood vasculature than nonsmokers with significant differences in mild and moderate chronic periodontitis and non-significant difference in severe chronic periodontitis. This result coincides with the results of Al-Sherbini et al,[18] but in contrary with that of Rezavandi et al and Al-Tayeb.[16,19] The vasoconstriction or vasodilatation effect of smoking is probably related to the degree of inhalation of the tobacco and the nicotine absorption rate. Independent of the smoking status, inflammation by itself causes vascular changes in the gingiva and this could justify the non-significant changes in the blood vessel numbers among the three groups of smokers (nonsmokers, moderate smokers, and heavy smokers) who have severe periodontitis.[20]

Majority of study samples reveals basal layer p53 expression even in nonsmokers. This is probably due to physiological response to physical, chemical and microbiological agents that may exhibit in the oral cavity leading to p53 accumulation.[11,21] Yu et al[22] found that exposure to cigarette smoke can increase apoptosis in stratum spinosum cells of human gingival epithelium and that could justify our results which showed more labeling index (LI) in smokers than non smokers but of not significance, that could be related to that, the use of tobacco did not increase the number of p53 positive cells, and the abuse of tobacco alone is probably not enough to cause significant

p53 over expression.[23]The present study showed more suprabasilar p53 positivity in heavy smokers than moderate and non smokers. This difference in suprabasilar p53 expression was not the case in patients with severe chronic periodontitis (this could be due to the sample size).

A significant association was present ($p<0.05$) between p53 expression and number of inflammatory cells in the connective tissue, and as the number of inflammatory cells increase the p53 labeling index(LI) was increased. This also suggested that apoptosis-associated DNA damage and expression of the p53 are prevalent phenomena in inflamed human gingival tissue.[24]

In conclusion, chronic inflammation of the gingiva may accelerate the smoking effect on p53 expression and together may have synergistic effect. Further studies on a larger sample and on a prospective basis would help to delineate this synergism and any progression to malignancy.

REFERENCES

1. Lindhe J, Lang NP, Karring T. Clinical periodontology and implant dentistry. 5th ed. London: Blackwell; 2008.
2. Fridman JS, Lowe SW. Control of apoptosis by p53. Oncogene. 2003; 22(56):9030-40.
3. Bulut S, Uslu H, Özdemir BH, Bulut ÖE. Expression of caspase-3, p53 and Bcl-2 in generalized aggressive periodontitis. Head Face Med [Internet]. 2006 [cited 2010 Sep 21];2:17 [7 pages]. Available from: http://www.head-face-med.com/content/2/1/17
4. Kinane DF, Chesstnutt IG. Smoking and periodontal disease. Crit Rev Oral Biol Med. 2000; 11(3):356-65.
5. Loos BG, Roos MT, Schellekens PT, van der Velden U, Miedema F. Lymphocyte numbers and function in relation to periodontitis and smoking.. J Periodontol. 2004;75(4):557-64.
6. Husgafvel-Pursiainen K, Boffetta P, Kannio A, Nyberg F, Pershagen G, Mukeria A, et al. p53 mutations and exposure to environmental tobacco smoke in a multicenter study on lungcancer. Cancer Res. 2000; 60(11):2906–11.
7. Gamonal J, Bascones A, Acevedo A, Blanco E, Silva A. Apoptosis in chronic adult periodontitis analyzed by in situ DNA breaks, electron microscopy, and immunohistochemistry. J Periodontol. 2001 ;72(4):517-25.
8. Ralhan R, Sandhya A, Meera M, Bohdan W, Nootan SK. Induction of MDM2- P2 Transcripts correlates with stabilized wild-type p53 in betel- and tobacco- related human oral cancer. Am J Pathol. 2000;157(2):587-96.
9. Villar CC, de Lima AF. Smoking influences on the thickness of marginal gingival epithelium. Pesqui Odontol Bras. 2003;17(1):41-5.
10. Bajagic V, Pejcic A, Zivkovic V, Petrovic A. Histochemical study of gingival epithelium in smokers and nonsmokers. Acta Facultatis Medicae Naissensis. 2006; 23:151-4.
11. Cruz IB, Snijders PJ, Meijer CJ, Braakhuis BJ, Snow GB, Walboomers JM, et al. p53 expression above the basal cell layer in oral mucosa an early

event of malignant transformation and has predictive value for developing oral squamous cell carcinoma. J Pathol. 1998;184(4):360-8.

12. Bansal S, Sircar K, Joshi SK, Singh S, Rastogi V. A comparative study of p53 expression in hyperplastic, dysplastic epithelium and oral squamous cell carcinoma. Brazilian Journal of Oral Sciences. 2010;9(2):85-8.
13. Abrahao AC, Bonelli BV, Nunes FD, Dias EP, Cabral MG. Immunohistochemical expression of p53, p16, and hTERT in oral squamous cell carcinoma and potentially malignant disorders. Braz Oral Res. 2011;25(1):34-41.
14. Shivanaikar SS, Faizuddin M, Bhat K. Effect of smoking on neutrophil apoptosis in chronic periodontitis: an immunohistochemical study. Indian J Dent Res. 2013;24(1):147. doi: 10.4103/0970-9290.114935.
15. Gültekin SE, Sengüven B, Karaduman B. The effect of smoking on epithelial proliferation in healthy and periodontally diseased marginal gingival epithelium. J Periodontol. 2008;79(8):1444-50.
16. Rahman BU, Raman MM, Arslan A. The effects of cigarette smoking on human gingival tissues (a histopathological study). J Pak Med Assoc. 1994; 44(9):210-2.
17. AL-Tayeb D. The effect of smoking on the periodontal condition of young adult Saudi population. Egyptian Dental J. 2008;54(3):1-11.
18. Al-Sherbini M, Murshid Z , Darwish Z. Clinical and immunohistochemical study on the effect of cigarette smoking on the periodontium of Saudi. Egyptian Dental J. 2004; 50(2):757-71.
19. Rezavandi K, Palmer RA, Odell EW, Scott DA, Wilson RF. Expression of ICAM-1 and E-selectin in gingival tissues of smokers and non-smokers with periodontitis. J Oral Pathol Med. 2002;31(1):59-64.
20. Kumar V, Faizuddin M. Effect of smoking on gingival microvasculature: a histological study. J Indian Soc Periodontol. 2011; 15(4): 344–8.
21. Humayun S, Prasad VR. Expression of p53 protein and ki-67 antigen in oral premalignant lesions and oral squamous cell carcinomas: an immunohistochemical study. Natl J Maxillofac Surg. 2011; 2(1): 38–46. doi: 10.4103/0975-5950.85852
22. Yu XJ, Li S, Xue LD, Xiao CJ. Influence of smoking on apoptosis in human gingival epithelium. Shanghai Kou Qiang Yi Xue. 2006;15(4):351-5. [Article in Chinese]
23. Van Oijen MG, van De Craats JG, Slootweg PJ. p53 overexpression in oral mucosa in relation to smoking. J Pathol. 1999;187:469-74.
24. Jarnbring F, Somogyi E, Dalton J, Gustafsson A, Klinge B. Quantitative assessment of apoptotic and proliferative gingival keratinocytes in oral and sulcular epithelium in patients with gingivitis and periodontitis. J Clin Periodontol. 2002;29(12):1065-71.

پوختە

بەرگری شانەزانی کیمیایی p53 لە هەوکردنی درێژخایەنی پووکی دەوروبەری ددان وپەیوەندی بەخوێی جگەرەکێشان و راگە ێین شانەزانی نەخوشی

پێشەکی و ئارمانج: هەوکردنی شانەکانی دەوروبەری ددان بریتی یە لە توشبونێك کە هۆکارەکەی جۆری جیاوازەلە زیندەوەرە ووردبینەکان وجگەرەکێشان یەکێکە لەو هۆکارانەی کە مەترسی هەوکردنەکە زیاتردەکات. مەبەستی لێکۆڵینەوەیە بریتییە لە دۆزینەوەی ئەستووری توێکارە شانەی پوك،وە هەروەها ژمارەی خانە هەوکردووەکان و موولوولەکانی خوێن لە شانەی بەستەری پووك (بەستەرەشانەی پووك). هەروەها هەڵسەنگاندنی ڕوخساری زۆر دەڕبڕینی پڕۆتینیp٥٣ لە نموونەکانی وەرگیراوی شانەی پووك بۆ کەسانی زۆر جگەرەکێش و کەم جگەرە کێش و جگەرە نەکێش.

ریکێن ڤەکولینێ: سی کەسی جگەرە کێش و سی کەسی جگەرە نەکێش کە پلەی جیاوازیان هەبوو لە هەوکردنی شانەکانی دەوروبەری ددان درێژ خایەن ، هەڵبژێردران لە بنکە تەندروستیەکانی دهۆك لە ماوەی نێوان کانوونی یەکەمی ٢٠١٠ تاوەکو ئازاری ٢٠١١ و نموونەی شا نەی پووکیش کۆکرایەوە لە نەخۆشەکان بە مەبەستی ڕەنگ کردنی بە مادەی هیماتو کسیلین و ئایۆسین و بە مەبەستی ڕەنگ کردنیان بە ڕەنگکردنی بەرگری شانەیی کیمیاوی بۆ لێکۆڵینەوەی دەربرینی p٥٣ بە کارهینانی Leica NovoLink MT Polymer (UK).

ئەنجام: ئەوەیان دەرخست کە زیادبوونێکی بەرچاو هەیە لە ئەستورایی چینی ڕوکە شی گەورە و ئەستورایی چینی ڕوکە شی بنکە لەگەڵ زیادبوونی تینی جگەرەکێشان (ڕێژا p کێمتر ژ ٠,٠٥)، وەجیاوازیەکی نا مەعنەوی مامناوەندی ژمارەی خانە هەوکردووەکان (ڕێژا p پتر ژ ٠,٠٥) تێبینی کرا لە نێوان کەسانی جگەرە نەکێش و کەم جگەرە کێش و زۆر جگەرە کێش. هە ڕوەها کەمترین ژمارەی موولەکانی خوێن بە دی کرا لە کەسانی زۆرجگەرە کێش. تاقیکردنەوەکان ئەوەیان دەرخست لە کەسانی زۆر جگەرە کێش کە زیادبوونێکی نا مەعنەوی (ڕێژا p پتر ژ ٠,٠٥) لە سەر کومەڵەکان لە مامناوەندی تیکرای پیوەری p٥٣ وپەیوەندی نامەعنەوی تێبینی کرا لەبەینی مامناوەندی تیکرای پیوەریp٥٣ لەگەڵ ئەستورایی چینی ڕوکە شی گەورە و ئەستورایی چینی ڕوکە شی بنکە و ژمارەی موولوولەکانی خوێن لەشانەی بەستەری پووك (ڕێژا p پتر ژ ٠,٠٥). بە پێ چەوانەوەوە پە یوەندی مەعنەوی تێبینی کرا لە لەگەل ژمارەی خانە هەوکردووەکان (ڕێژا p کێمتر ژ ٠,٠٥).

دەرئەنجام: دەرئەنجامەکانی ئەم لێکۆڵینەوەیە دەری خست کە p٥٣ ڕۆڵی هە یە لە نە خوشی هەوکردنی شانەکانی دەوروبەری ددان.

الخلاصة

الإظهار الكيميائي النسيجي المناعي ل p53 في التهاب ما حول الأسنان وعلاقته بالتدخين و مؤشرات نسيجية مرضية

خلفية واهداف البحث: إلتهاب أنسجة ما حول الأسنان هو أصابة سببها مختلف أنواع الأحياء المجهريه والتدخين هو واحد من أهم عوامل الخطورة. الهدف من الدراسة هو إيجاد سمك الطبقة الطلائية للثة، عدد الخلايا الإلتهابية والأوعية الدموية والتعبيرالمناعي للبروتين p53 فى نماذج نسيج اللثة للمرضى المدخنين وغير المدخنين الذين عندهم إلتهاب أنسجة ما حول الأسنان المزمن.

طرق البحث: ثلاثون شخص مدخن و ثلاثون شخص غير مدخن عندهم مختلف درجات إلتهاب أنسجة ما حول الأسنان المزمن أختيروا من المركز الصحي فى دهوك فى الفترة من تشرين الاول ٢٠١٠ الى كانون الثانى ٢٠١١. نماذج اللثة جمعت ومررت للتصبيغ بمادة هيماتوكسيلين والإيوسين وللتصبيغ الكيميائي النسيجي المناعي لبروتين p٥٣ باستعمال (Leica NovoLink MT Polymer UK).

النتائج: أظهرت النتائج زيادة واضحة فى سمك الطبقة الطلائية الكبير و سمك الطبقة الطلائية فى القاعدة مع زيادة شدة حالة التدخين (قيمة p اقل من ٠,٠٥)، وفرق غير معنوى وجد فى متوسط عدد الخلايا الإلتهابية (قيمة p اكثر من ٠,٠٥) بين غير المدخنين والمعتدلين وكثيرين التدخين، بالاضافة الى ذلك، كثيري التدخين أظهروا أقل عدد من الأوعية الدموية فى اللثة مقارنة بمعتدلي التدخين. كثيري التدخين أظهروا زيادة غير معنوية (قيمة p اكثر من ٠,٠٥) في متوسط معدل مقياسp53 بين المجاميع. علاقات غير معنوية أيضا وجدت بين متوسط معدل مقياس p53 مع سمك الطبقة الطلائية الكبيرو سمك الطبقة الطلائية فى القاعدة وعدد الأوعية الدموية فى النسيج الرابط للثة (قيمة p اكثر من ٠,٠٥). وعلى العكس علاقة معنوية وجدت مع عدد الخلايا الإلتهابية (قيمة p اقل من ٠,٠٥).

الاستنتاجات: أشارت نتائج الدراسة الحالية أن بروتين p53 له دور مهم في إلتهاب أنسجه ما حول الاسنان المزمن.

EVALUATION OF IN VITRO PRODUCTION OF CYTOKINES BY MONOCYTES/MACROPHAGES IN PATIENTS WITH HEART FAILURE

SERGIY FEDOROV, MD, PhD*
LIUBOMYR GLUSHKO, MD, PhD, DSci*
IVANO-FRANKIVSK*

Submitted 18 Sep 2014; accepted 31 Dec 2014

ABSTRACT

Abstract Recent studies showed an important role of inflammation in heart failure (HF). Monocytes/macrophages are main cells in immune response. The aim was to investigate spontaneous cytokines production by monocytes/ macrophages in patient with ischemic heart failure.

Methods Ninety six patients with HF of ischemic genesis were observed. The spontaneous production of interleukin 1β (IL-1β), interleukin 6 (IL-6), and interleukin 10 (IL-10) by monocytes/macrophages in vitro was detected by ELISA method.

Results The in vitro spontaneous production of pro inflammatory cytokines IL-1β and IL-6 by monocytes/ macrophages in patients with HF was significant higher and anti-inflammatory IL-10 was lower than in control group. The progression of HF caused to increase of spontaneous production by monocytes/ macrophages of IL-1β and IL-6 but decrease of IL-10.

Conclusion The monocytes/macrophages in patients with ischemic HF are in condition of chronic activation which manifests of overproduction of pro inflammatory cytokines and poor secretion of anti-inflammatory IL-10.

Duhok Med J 2014;8(2): 78-84.

Keywords: Heart failure, Monocytes/macrophages, Cytokines

Heart failure (HF) is a complex clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection of blood.[1] It is a major health issue in society today, because it is associated with health, death and consumption of healthcare resources. HF affects approximately 1-2% of adults in developed countries, and prevalence increases markedly with age: 10% in cohort 75 years and older.[2]

A US study has predicted that the prevalence of HF will increase by 3 millions (25%) in the next 20 years; a similar study based on data from Scotland predicts a 21% increase in the number of admissions for HF by year 2020.[3,4]

It is estimated that 1-2% of all healthcare expenditure is devoted to HF in developed countries. Myocardial dysfunction, which take place in HF, leads to activation of several neurohormonal compensatory mechanisms aimed at improving the mechanical environment of heart. In addition to causing further myocardial injury, the neurohormonal responses have detrimental effects on the blood vessels and organs of human body, and create a pathophysiological "vicious circle", accounting for many of the clinical features of the HF syndrome, including electrical instability of myocardium.[5]

* *National Medical University, Ukraine.*
Correspondence author: SERGIY FEDOROV

Different models indicate a role of innate immunity independent of HF etiology. Innate immunity is activated in the myocardium early by recognition of rather unspecific stimuli, summarized as danger-associated molecular patterns. This form of sterile inflammation is prototypically initiated by engagement of innate pattern recognition receptors, like toll-like receptors.[6]

It is likely that inflammation is also initiated in human myocardium by innate recognition of pathogen-associated molecular pattern even well before the heart failure becomes symptomatic/ diagnosed. However, clinical data to corroborate findings made in animal studies are widely limited to the demonstration of increased circulating levels of soluble mediators, mainly cytokines, in a variety of patient cohorts with heart failure.[7]

Monocytes play an important role in immune defence, inflammation, and tissue remodelling and they do so by phagocytosis, antigen processing and presentation, and by cytokine production. Activated, monocytes/macrophages produce many cytokines, chemokines, and growth factors, including IL-1α and -β, IL-6, tumor necrosis factor-α, macrophage inflammatory proteins 1 α/β etc.[8]

More recent studies reported a strong association between peripheral monocytosis, left ventricle (LV) dysfunction, and LV aneurysm formation after myocardial infarction (MI).[9]

Consequently, inhibition of monocytes activation is a tempting therapeutic target in the prevention of ischaemia-related HF. The present experimental data about spontaneous production of cytokines by macrophages in HF patients are contradictory.[10,11]

The purpose of study was to investigate spontaneous cytokines production by monocytes/ macrophages in patient with ischemic heart failure.

METHODS

The study was performed during period of 2013 year in Ivano-Frankivsk Central City Hospital (Ukraine) in accordance with the Helsinki Declaration and Good Clinical Practice Guideline. All patients gave written informed consent and the local ethics committee approved the study protocol. 96 patients with HF of ischemic genesis were observed. The diagnosis was verified by clinical, laboratory and instrumental methods according to European Society of Cardiology recommendations (2013, 2014). Patients were divided into 3 subgroups (according New-York Heart Association (NYHA) functional class (FC) classification of HF): FC II (NYHA)–27 patients, FC III (NYHA)–39 patients and FC IV (NYHA)–30 patients. Control group consist of 19 practically healthy persons. Suspension of monocytes from blood obtained by Recalde H. method.[12]

The isolated cells were labeled with a monoclonal antibody (Daco, Glostrup, Denmark) against the monocyte specific positive antigen CD14. The procedure yielded a population of 89-96% CD14-positive cells in the isolated fraction. Cell viability was confirmed by trypan blue test and was 89-93%. Monocytes were suspended in 199 medium supplemented

with 30% blood autoserum, 100U/ml penicillin, 100 μg/ml streptomycin and 10 μg/ml fungizone (Gibco, Grand Island, NY, USA). The cells were counted and the monocyte concentration was adjusted to 1×10^6 cells/ml. A constant number of monocytes (1×10^6 monocytes per well) was placed in a plastic 24-well microtiter plate (Becton-Dickinson, Franklin Lakes,NJ, USA) and left intact for 2 h to allow them to adhere. The medium was then changed, and the cultures were incubated for additional 24 h. Incubations were performed in triplicate at 37°C in a humidified atmosphere containing 5% CO2 in air. Interleukin 1β (IL-1β), interleukin 6 (IL-6), and interleukin 10 (IL-10) levels in culture supernatant were determined using commercial ELISA kits (ProCon, Russia; Amersham Pharmacia Biotech, UK) according to the manufacturer's instructions. Statistical analyses were performed using the Statistica 12.0 (StatSoft, Tulsa, OK, USA). Statistical significance was assumed at $p<0.05$.

RESULTS

The average age of observed patients with HF was (68.24±9, 87) years. In this cohort 22 (22.9 %) were females. 68 (70.8 %) persons had history of myocardial infarction (MI). As concomitant diseases more frequent were: arterial hypertension, permanent atrial fibrillation, type 2 diabetes mellitus and chronic kidney diseases.

The in vitro spontaneous production of pro inflammatory cytokines IL-1β and IL-6 by monocytes/macrophages in patients with HF was significant higher than in control group: (119.50±4.12) pg/10^6 cells vs (51.39±3.71) pg/10^6 cells ($p<0.001$) and (6.62±0.41) pg/106 cells vs (2.79±0.28) pg/10^6 cells ($p<0.001$) respectively. Instead the spontaneous production of anti-inflammatory IL-10 was lower in HF: (3.79±0.41) pg/10^6 cells vs (5.86±0.76) pg/106 cells ($p<0.01$).

The severity of HF was associated with increased production by monocytes/ macrophages of IL-1β and IL-6 and with decreased production of IL-10 (table 1).

Table 1. The in vitro spontaneous production of cytokines by monocytes/macrophages in HF patients (M±SE)

Parameter	HF patients, n=96			Control group, n=19
	FC II, n=27	FC III, n=39	FC IV, n=30	
IL-1β, pg/10^6 cells	96.27±3,14 $p_1<0.01$	115.12±4.75 $p_1<0.001$ $p_2<0.05$	147.11±4.34 $p_1<0.001$ $p_2<0.001$ $p_3<0.001$	51.39±3.71
IL-6, pg/10^6 cells	5.11±0.45 $p_1<0.001$	6.41±0.37 $p_1<0.001$ $p_2<0.05$	8.34±0.44 $p_1<0.001$ $p_2<0.01$ $p_3<0.01$	2.79±0.28
IL-10, pg/10^6 cells	5.21±0.45 $p_1>0.05$	3.21±0.47 $p_1<0.05$ $p_2<0.05$	2.96±0.33 $p_1<0.01$ $p_2<0.01$ $p_3<0.05$	5.86±0.76

Remarks: HF – heart failure; FC – functional class of heart failure (NYHA); p_1 – difference with control; p_2 – difference with FC II group; p_3 – difference with FC III group.

DISCUSSION

It's known, in vitro macrophages can be generated from bone marrow precursors by various means. Macrophages generated in the presence of interferon-gamma (IFNg) or lipopolysaccharide (LPS) have been termed M1, or classically-activated, inflammatory, macrophages. Macrophages generated in the presence of IL-4 or IL-10, however, have been called M2, or alternatively activated macrophages, and carry a pro-resolution profile.[13]

In our case we can allow about M1 (proinflammatory) pathway of monocytes activation which could leads to HF destabilization.

Some recent studies showed the similar results. In particular, CD14 expression and monocyte cytokine production (IL-1β, IL-6, TNF-α), both unstimulated and after LPS stimulation, are increased in moderate-severe CHF when compared with mild CHF.[14] Another study showed that IL-10, as strong anti-inflammatory cytokine, profoundly inhibits TNF-α release from monocytes/ macrophages isolated from patients with chronic HF.[15] These data suggest that circulating monocytes, possibly via overproduction of pro inflammatory cytokines, may play a significant role in the immunologic dysbalance observed in advanced CHF.

The study concluded that monocytes/ macrophages in patients with ischemic HF are in condition of chronic activation which manifests of overproduction of pro inflammatory cytokines and poor secretion of anti-inflammatory IL-10.

CONflICT OF INTEREST

none declared.

REFERENCES:

1. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Drazner MH, et al. ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation /American Heart Association Task Force on practice guidelines Circulation. 2013; 128(16):e240-327.
2. Park D, McManus D, Darling C, Goldberg JH, Gore JM, Lessard D, et al. Recent trends in the characteristic and prognosis of patients hospitalized with acute heart failure. Clin Epidemiol. 2011; 3: 295-303.
3. Heiderich P.A., Trogdon J.G., Khavjou O.A. Butler J, Dracup K, Ezekowitz MD, et al. Forecasting the future of cardiovascular diseases in United States: a policy statement from the American Heart Association. Circulation. 2011; 123: 933-44.
4. Stewart S, MacInture K, Capewell S. McMurray JJHeart failure and the aging population: an increasing burden in the 21-th century? Heart. 2003; 89: 49-53.
5. Hofmann U, Frantz S. How can we cure in "heart in flame"? A translational view on inflammation in heart failure. Basic Research in Cardiology. 2013; 108: 1-23.
6. Kleinbongard P, Heusch G, Schulz R. TNFalpha in atherosclerosis, myocardial ischemia/reperfusion and heart failure. Pharmacol Ther. 2010;127:295–314.

7. Swirski FK., Weissleder R, Pittet M. Heterogeneous in vivo behavior of monocyte subsets in atherosclerosis. Arterioscler. Thromb Vasc Biol. 2009; 29: 1424-32.
8. Maekawa Y, Anzai T, Yoshikawa T, Asakura Y, Takahashi T, Ishikawa S. et al. Prognostic significance of peripheral monocytosis after reperfused acute myocardial infarction: a possible role for left ventricular remodeling. JACC. 2002; 39: 241-6.
9. Jovinge S, Ares M, Kallin B, Nilsson J. Human monocytes/macrophages release TNF-α in response to Ox-LDL. Arterioscler Thromb Vasc Biol. 1996; 16: 1573-9.
10. Leor J, Rozen L, Zuloff-Shani A, Feinberg MS, Amsalem Y, Barbash IM, et al. Ex Vivo activated human macrophages improve healing, remodeling, and function of the infarcted heart. Circulation. 2006; 114: 94-100.
11. Recalde HR. A simple method of obtaining monocytes in suspension. J Immunol Meth. 1984; 69: 71-7.
12. Mosser DM, Edwards JP Exploring the full spectrum of macrophage activation. Nat Rev Immunol. 2008; 8: 958–969.
13. Conraads V, Bosmans J, Schuerwegh A, Goovaerts I, De Clerck LS, Stevens WJ, et al. Intracellular monocyte cytokine production and CD14 expression are up-regulated in severe vs mild chronic heart failure. J Heart Lung Transplant. 2005; 24 (7): 854-59.
14. Bolger A, Sharma , von Haehling S, Doehner W, Oliver B, Rauchhaus M et al. Effect of interleukin-10 on the production of tumor necrosis factor-alpha by peripheral blood mononuclear cells from patients with chronic heart failure. Am J Cardiol 2002; 90: 384-9.

پوختە

چێکرنا خوپ خویی یا سیتوکینات حوکرتێ یا دژی حوکرتیا ژ خانێن ئێکانە/ البالعة ل دەف نەخوشێن دلاوازبوونا دلی

پێشەکی و ئارمانج: ڤەکولینێن دوماهیێ روڵەکێ گرنگێ حوکرتێ دلاوازبوونا دلی دا بومە دیارکر . سوود وەرگرتن ژ ڤێ ڤەکولینێ، لێگرین ژ چێکرنا خوپ خویی یا سیتوکینات ژ خانێن (البالعة) ل دەف نەخوشێن لاوازبوونا دلی ژ ئەنجامێ کێم ئاڤیە .

ڕێکێن ڤەکولینێ: پشکنین بۆ ٩٦ نەخۆشێن لاوازبوونا دلی هاتەکرن کو ئەگەرێ وێ کێم ئاڤی بوو، وبەر هەمهینانا خۆ ب خۆیی یا ئەنترلوکینی تێدا هاتە دیارکرن (IL-10)، (IL-6)، (IL-Ib)، خانێن ئێکانە بوون ل تاقیگەهێ ، ب ڕێکا پشکنینا ئەنزیمێ هەڤبەندێ بەرگریا لەشی (ELISA) .

ئەنجام: ئەنجامێن ناقیگەهێ دیارکر کو بەرهەمهینا خوب خویی یا سایتوکینات هەوکرێ (IL-Ib) ، (IL-6)ژخانێن ئێکانە/(بالعة) لدەف نەخۆشێن لاوازبوونا دلی بلنتربوو، ودژە تەنێن هەوکرنێ (K-Ib) دکێمتربوو ژئەویێن دناڤ کۆما پیڤەری دا، وزێدەبوونا لاوازبوونا دلی بەرهەمهینانا خانێن ئێکانە/(بالعة) (IL-b) و(IL-6) زێدە ترلێکر، بەڵێ (IL- 10) کێمتر لێکر .

دەرئەنجام: لدەف نەخۆشێن لاوازبوونا دلی ژ ئەنجامێ کێم ئاڤیێ، خانێن ئێکانە / البالعة ددۆ خەکێ چالاکێ دوم درێژ دانە ئەوێن کو زیدەبوونا بەرهەمهینانا سایتوکوناتێ هەوکرنێ (IL- 10) بۆ مە دیارکرییە .

الخلاصة

الأنتاج التلقائي للسيتوكينات الالتهابية والمضادة للألتهاب من الخلايا الوحيدة / البالعة عند مرضى قصور القلب

خلفية وأهداف البحث: لقد أظهرت الدراسات ألاخيرة دورا هاما للألتهاب في قصور القلب. وان الخلايا الوحيدة / البالعة هي الخلايا الرئيسية في الاستجابة المناعية. هو البحث عن الانتاج التلقائي للسيتوكينات من الخلايا البالعة عند مرضى قصور القلب الناتج عن نقص التروية.

طرق البحث: تم معاينة ٩٦ مريضا يعاني من قصور في القلب سببه نقص التروية وتم الكشف عن الانتاج التلقائي للأنترلوكين (IL-1b),(IL-6), (IL-10), من الخلايا الوحيدة في المختبر بواسطة فحص الانزيم المرتبط المناعي (ELISA).

النتائج: لقد أظهرت النتائج في المختبر أن الانتاج التلقائي للسيتوكينات الالتهابية (IL-1b) و(IL-6) من الخلايا الوحيدة /البالعة عند مرضى قصور القلب كان أعلى، ومضادات الالتهاب (IL-10) كان أقل مما كانت عليه في المجموعة القياسية. وأن تفاقم قصور القلب أدى لزيادة أنتاج الخلايا الوحيدة / البالعة (IL-1b)و(IL-6) ولكن ادى لنقصان (IL-10).

الاستنتاج: أنه عند مرضى قصور القلب الناتج عن نقص التروية ,الخلايا الوحيدة /البالعة هي في حالة تنشيط مزمن الذي كشف عن زيادة أنتاج السايتوكينات الالتهابية ونقص أفراز مضادات الالتهاب (IL-10).

MUSCLE-SPARING TREATMENT OF MUSCLOSKELETAL HYDATID CYSTIC DISEASE

HAYDER H. IBRAHIM, MBChB, FRCSEd*

Submitted 14 Nov 2014; accepted 31 Dec 2014

ABSTRACT

Background and objectives Muscloskeletal hydatid cystic disease are rare surgical problems in comparing to other organs in the body. To show the benefit of muscle-sparing operation in treating such pathology and to be considered in differential diagnosis of soft tissue muscloskeletal mass particularly in endemic areas.

Methods Case series study of 10 patients operated upon in the period between 1995-2010 for muscloskeletal hydatid cyst in Mosul and Duhok hospitals . All patients were evaluated by history, physical examination, complete blood picture, ultrasounds of the muscle mass and liver, and chest x-ray. Patients were operated upon under general anaesthesia. Muscle-sparing operation was performed in the form of drainage of the content of the mass after evacuation of its content without excision of the ectocyst .

Results The operation for muscloskeletal hydatid cysts (muscle-sparing) was without complications, without mortality but one patient developed recurrence after one year from operation.

Conclusions Muscle sparing surgical operation is effective method of treatment without morbidity and mortality. Muscloskeletal hydatidosis should be considered in differential diagnosis of soft tissue tumor paticularly in endemic area.

Duhok Med J 2014;8(2): 85-92.

Keywords: Muscloskeletal hydatid cyst, Muscle-sparing surgery, Morbidity, Mortality Recurrence

Hydatid disease or echniococcosis is classified as parasitic infestation caused by tapeworm echnicoccus granulosus, multilocularis, vogeli and oligarthrus. Echinococcus granulosus is the most common type and is most prevalent in sheep-and cattle-breading areas. Human are infected following the accidental ingestion of eggs from environmental sources.[1]

Surgeons meet with hydatid cysts of the liver and lungs with a reasonable frequency. However when the cyst appears in the unusual sites such as muscles of the extremities, the clinical suspicion is unlikely.[2] Muscloskeletal hydatidosis is rare, accounting only for 0.5–4% of all cases[3]. Nevertheless, some cases of primary muscular hydatidosis at various sites have been reported as, sartorius, supraspinatous, bicep barachii, thoracic wall, and gluteus muscles.[4-9]

We report our experience in the management of patients with muscloskeletal hydatid cysts both isolated (without liver involvement) and with liver involvement types with less trauma to the site of lesion . Also to point out that, this zoonotic infestation should be included in the differential diagnosis of muscular masses especially in endemic areas such as Iraq.

** Ass. Prof. in General Surgery, School of Medicine / Faculty of Medical Sciences. Duhok University, Kurdistan, Iraq Email: hayder1950@yahoo.com*

METHODS

Ten patients, seven females and three males, with mean age of 34.9 years (range 18–61 years) with muscloskeletal hydatidosis were operated upon from February 1995–December 2010. All of them presented with mass, some with pain and others without pain. The location of the mass was medial aspect of the thigh in 3 patients, posterior thigh (hamstring) in 1 patient, rectus abdominis muscle in 3 patients, chest wall in 1 patient and scapular area in 2 patients (Table1) and figures 1. Size of the cyst was ranging from 3–10cm by Ultrasound examination . None of the patients had significant co morbidities.

Figure 1 Multivesicular hydatid cysts with multiple daugher cysts in the supraspinatous muscles.

Clinical presentation and presence of patients in endemic area raised the suspicion of hydatid disease, to be included in the differential diagnosis. Routine blood test were within normal limit, 3 patients had high ESR. Ultrasound Imaging for the mass and abdomen were performed in all patients as well as chest X-ray. Serology test was not performed.

Elective surgery in the form of muscle –sparing, drainage of the content of the cyst was performed for all patients , followed by a course of Albendazole treatment for 3 months.

RESULTS

The clinical presentations are outlined in Table 1.

In all patients the cyst were confined into the skeletal muscles, not affecting neurovascular structures or bones and the diagnosis was confirmed by operative findings such as outer fibrous layer and inner germinal layer contained fluid, laminated membrane and /daughter cysts (univesicular and multivesicular type) as shown in Table 2. Primary cyst was observed in 6 patients , while in 4 patients the liver were involved by hadatid cyst. One patients had history of hepatic hydatid cyst operation . None of them had pulmonary hydatid cyst .

During follow-up period ranging from 1-3 years there were no local or systemic complications but one patient who had hydatid of supraspinatous muscle developed recurrence (cyst was multivesicular type and contains multiple small daughter cysts) Figure 1 which was confirmed by ultrasonography after one year from operation. All other patients regained full range of movement and returned to their normal activities.

Table 1. Muscloskеtal cyst presentation, age, gender, cyst dimension and location

Patient	Clinical presentation	Gender, Age	Dimension of the cyst	Location
Case 1	Painful mass	F, 18- year	10 × 10 cm	Hamstring muscle
Case 2	Painless mass	F , 20-year	3 × 4 cm	Medial aspect of thigh
Case 3	Painless mass	F , 25-year	5 × 3 cm	Medial aspet of thigh
Case 4	Painful mass	F, 30- year	4.5 × 6 cm	Medial aspect of thigh
Case 5	Paiful mass with distension	M , 35- year	10 × 10 cm	Right and left Rectus abdominis muscle
Case 6	Painless mass	M , 45-year	3 × 5 cm	Left rectus abdominis muscle
Case 7	Painful mass	M , 32- year	4 × 5.5 cm	Left rectus abdominis muscle
Case 8	Painless mass	F , 23-year	3.5 × 5 cm	Left side chest wall
Case 9	Painful mass	F , 60- year	7 × 6.5 cm	Right supraspinatous muscle
Case 10	Painful mass	F, 61-year	5 ×6 cm	Right supraspinatous muscle

M = Male F= Female

Table 2. Muscloskeletal hydatid cyst, type of the cyst, liver involved and recurrence

Patient	Univesicular	Multivesicular	Liver	Recurrence
Case 1		Multivesicular	Not involved	No recurrence
Case 2	Univesicular		involved	No recuurence
Case 3	Univesicular		Not involved	No recurrence
Case 4	Univescular		Involved	No recurrence
Case 5	Univesicular		Involved	No recurrence
Case 6	Univesicular		Not involved	No recurrence
Case 7		Multivesicular	Not involved	No recurrence
Case 8	Univesicular		Involved	No recurrence
Case 9		Multivesicular	Not involved	Recurrence
Case10		Mutivesicular	Not involved	No recurrence

DISCUSSION

The hydatid disease parasites are members of the flatworm cestodes . The parasite may affect any organ; however, muscle is supposed to be unfavorable site for infestation. Several factors would explain the exceptional nature of muscle localization of hydatid cysts:, unfavorable muscle environment for the growth of hydatid larvae due to high lactic acid content and muscles contractility which hinders intramuscular growth of the cysts, in addition to the efficiency of the hepatic and pulmonary barriers[7,10]. The predominant localization in the proximal muscle could be explained by the volume of the muscle mass and its rich blood supply as seen in our patients where the cyst detected in thigh , shoulder and rectus muscles.

Intramuscular hydatid cysts grow gradually and may mimic a soft tissue tumor;[11] thus , the diagnosis of muscular hydatid cyst needs a high index of suspicion. Ultrasonography still remains the main non-invasive test to discover the

mass and is the diagnostic tool of initial work-up.[12,13] Computerized tomography and Magnetic resonance imaging were not available in some cases and can be used in complicated cases such as rupture or infection of the cyst.[14]

A variety of serological tests are used in diagnosis of hydatid disease but are unreliable. There is high false negative and false positive results so does not exclude the diagnosis.[15] However, the best way to establish the diagnosis is histopathological examination of surgical specimen.

Usually intramuscular hydatid cysts are associated with hepatic hydatid cyst, resulting either from the spread of cysts or viable larval tissues after spontaneous or trauma-induced cyst rupture or after operation for hydatidosis in distant regions[16].

In current study, six patients had isolated cysts and four patients had muscular cysts with liver cyst.

Multivesicular cyst were observed in four patients and the cyst was located in large muscles and exposed to more movement which might be explained as a result of trauma induced by muscular action leading to internal rupture of the cyst and causing multivesicular type of the cyst.

Surgical procedures vary from radical (i.e pericystectomy) to conservative method (evacuation of the cyst content, with the pericyst left in place).[17]

In the literature, some studies report the disadvantages of radical treatment.[17,18] According to these studies reason to adopt conservative operation include less bleeding, without excision of muscle (pericyst) then less post-operative mortality and morbidity. Further, conservative procedures were recommended by some authors because they require no organ resection, short hospital stay, and minimal blood loss.[18,19] In all cases under study the conservative operation (muscle-sparing) were performed which consist of drainage of the cyst cavity, removal of laminated membrane, daughter cysts and fluid without muscle excision and with hospital stay ranging from 1–3 days .

In cases affecting skeletal muscles - without other organ involvement - where surgical excision is possible, the rationale of adjuvant chemotherapy is to reduce the risk of dissemination during surgery and to prevent recurrence.[20] Bone involvement makes recurrence more likely after surgical excision, compared to muscle echinococcosis alone[20] but in this study there were no patients with bone involvement.

Post-operatively all patients received Albendazole treatment 10mg/kg/day for 3 months to reduce or avoid recurrence and no side effects of drug therapy noticed . No morbidity or mortality were noticed in any of the patients operated upon in this study. Follow up was from 1–3 years. Recurrence was noticed only in one patient with supraspinatous hydatid, it was multivesicular type and contains multiple small daughter cysts, the recurrence was due to multiple and small size cyst as shown in Figure 1.

In conclusion muscle-sparing surgery as treatment modality seems to be effective, well tolerated, and without

morbidity or mortality so such option should be taken into account in patients with muscloskeletal hydatid cyst. Hydatid cyst as soft tissue mass in the skeletal muscle should be in the differential diagnosis in the endemic area.

REFERRENCES

1. Babu KS, Goel D, Prayaga A, Rao IS, KumarA. Intra abdominal hydatid cyst: a case report. Acta Cytol 2008: 52(4);464-6
2. Merkle E, Schulte M, Vogel T. Musculoskeletal involvement in cystic echnicoccosis. report of eight cases and review of literature. AJR AmJ Roentgenol 1997; 168: 1531
3. Garcia-Alvarez F., Torcal J., Salinas JC., Garcia-Alvarez I., Navarro-Zorraquino M., Tejero E., Lozano R. Musculoskeletal hydatid disease: A report of 13 cases. Acta Orhop Scand 2002; 73 (2): 227–231
4. Ates M, Karakaplan M. Hydatid cyst in the biceps and gluteus muscles: case report. Surg Infect (Larchmt). 2007;8: 475–8
5. Haque F, Harris SH, Khan R, Abbas SZ. Primary hydatidosis of gluteus maximus. J Postgrad Med 2006; 52:300–1.
6. Tatari H, Baran O, Sanlidag T, Göre O, Ak D, Manisali Met al et al. Primary intramuscular hydatidosis of supraspinatus muscle. Arch Orthop Trauma Surg 2001;121:93–4.
7. Duncan GJ & Tooke SMT: Echinococcus infestation of the biceps brachii Clin Otrhop 1990, 261: 247 - 250.
8. Rask MR & Lattig GJ: Primary intramuscular hydatidosis of the sartorius. J Bone Joint Surg Am 1970, 52: 582 - 584
9. Orhan Z, Kara H, Tuzuner T, Sencan I, Alper M. Primary Subcutaneous cyst hydatic disease in proximal thigh an unusual localisation: a case report. BMC Musculoskelet Disord 2003; 4: 25.
10. Garcia-Alvarez F, Torcal J, Salinas JC, Navarro A,Garcia-Alvarez I, Navaro-Zorraguino Met al .Muscloskeletal hydatid disease: A report of 13 cases . Acta Orthp Scand 2002; 73: 227-31.
11. Sahni JK, Jain M, Bajaj Y, Kumar A, Jain A. Submandibular hydatid cyst caused by Echinococcus Oligarthus. J Laryngol Otol 2000;114: 473 - 476.
12. Turgut AT, Akhan O, Bhatt S, Dogra VS. Sonographic spectrum of hydatid disease. Ultrasound Q 2008;24:17- 29.
13. WHO Informal Working Group. International classification of ultrasound images in cystic echinococcosis for application in clinica field and epidemiological settings. Acta Trop 2003; 85: 253-61
14. Pedrosa I, Saíz A, Arrazola J, Ferreirós J, Pedrosa CS. Hydatid disease: Radiologic and pathologic features and complications. Radiographics 2000; 20: 795-817.
15. White CJr, Weller PF, Echinococcosis. In: Braunwald E, Fauci AS, Kasper DL, Lngo DL, Jameson JL. editors. Harrison,s principles of internal medicine 15th edition McGraw Hill; 2001. 1250pp..

16. Guidelines for treatment of cystic and alveolar echniococcosis in humans . WHO International Working Group on Echinococcosis Bull World Health Organ 1996; 74: 231-42.
17. Sayek I, Tirnaksiz MB, Dogan R. Cystic hydatid disease: Current trends in diagnosis and treatment. Surg Today 2004; 34: 987-96.
18. Saidi F, Treatment of Echinococcal cyst. In: Nyhus LM, Baker RJ, Fischer JE, editors. Master of surgery. 3rd edition . Boston Little Brown 1997 p 350-4.
19. Bülent C. Yüksel, Serkan Akbulut, and Suleyman Hengirmen A minimally invasive treatment option in primary muscular hydatid cyst: report of 2 cases. Can J Surg.2008; 51(2): 153-154.
20. Arazi M, Ericoglou M, Odev K, Memik R, Ozdemir M. Primary echinococcus infestation of the bone and muscles. Clin Orthop Rel Res. 2005; 432: 234–241.

چارەسەرکرنا برینا بێی برینا ماسولکێ بۆ چارەسەرکرنا جورکێن ئافێ بێن ماسولکێن لەشی بێن دەرڤە

پوختە

پێشەکی و ئارمانج: جورکێن ئافێ ئەوێن تو شی ماسولکێن ڕەخاوسینگی و زگی دبن ئێکە ژجوورین پزیشکی یێن زۆر کێم، بۆ دیتنا مفایێ ل نەشتەرگەریا بێی ل نەشتەرگەریا بێی برینا ماسولکێ بۆ چارەسەرکرنا جورکێن ئافێ بێن ماسولکا، بەلێ دبیت بەرچاڤ بهێە وەرگرتن دەست نیشانکرنا ئستیربوونا ماسولکێ و ب تایبەتی ئەو وولاتێ کو تێدا جورکێن ئافا ماسولکا گەلەك هەبیت.

ڕێکێن ڤەکولینێ: هاتە دەست نیشان کرن (دەهـ) نەساخێن جورکێ ئافا ماسولکا هەین ل دەست پێکا هەیڤا شواتێ سالا ١٩٩٥ هەتا دیماهی یا هەیڤا کانونا ئێکێ سالا ٢٠١١ ل میسل و دهوکێ و نەشتەرگەری یا وان هاتەکرن. پێش وەخت هاتبوو دەست نیشانکرن ب ئامیرێ سونارێ یێ بارستە بو ماسولکێ و سونارێ زك بو جەرگی و گرتنا فیلمێ تیشکێ بو سینگی.

ئەنجام: نەشتەرگەری یا جورکێن ئافێ بو ماسولکا یا بێ ئالوزی و رویدانێن مرنێ بوو و رازیبوون لسەر هەبوو و ئێك نەساخ بتنێ هاتە سەرەدانێ پشتی نەشتەرگەریێ.

دەرئەنجام: نەشتەرگەری یا پاراستی (بێ برینا ماسولکا) بو چارەسەرکرنا ئەڤان جورا ڕێکەکا ئەکتیڤە و ئالوزی یا ناکەت ئانکو مرن نینە، دیسان جور کێن ئافێ یێن ماسولکا، دبیت بهێنە دانان دەست نیشانکرنا هەرە سەرەتایی بو ئستیربوونا ماسولکێ بتایبەتی ل وولاتێن ئەڤ جورکە تێدا هەین گەلەك.

الخلاصة

العلاج الجراحي بدون استئصال العضلة في علاج الاكياس المائية لعضلات الجسم الخارجية

الخلفية والأهداف: الأكياس المائية التي تصيب عضلات الأطراف وجدار الصدر والبطن هي حالات طبية نادرة. لرؤية فائدة العمليات الجراحية بدون استئصال العضلة لمعالجة الأكياس المائية في العضلات وكذلك يجب أن تؤخذ بنظر الاعتبار في حالة تشخيص أورام العضلات خاصة في البلدان الموجود فيها الاكياس المائية بكثرة.

طريقة البحث: تم تشخيص عشرة حالات مرضية لديهم اكياس مائية في العضلات للفترة من بداية شباط سنة ١٩٩٥ ولغاية نهاية كانون الاول سنة ٢٠١١ في الموصل ودهوك واجريت لهم عمليات جراحية بعد اجراء التشخيص بواسطة جهاز السونار للكتلة في العضلة وسونار البطن للكبد واخذ فلم شعاعي للصدر.

النتائج: العمليات الجراحية للاكياس المائية في العضلات كانت بدون مضاعفات وعدم حدوث حالة وفيات، وكانت حالة مرضية واحدة لكيس مائي راجع بعد العملية.

الأستنتاج: العمليات الجراحية التحفظية (بدون استئصال العضلة) لمعالجة هذة الحالات هي طريقة فعالة وبدون مضاعفات أو وفيات. كما أن الأكياس المائية في العضلات يجب أن تعتبر من ضمن التشخيص الأولي لأورام العضلات خاصة في البلدان التي توجد فيها الأكياس بكثرة.

پەربەندا ٨ ژمارە ٢
كانونا ئێكێ ٢٠١٤

زانكويا دهوك
كوليژا پزيشكى

گوڤارا پزيشكى يا دهوكێ

گوڤارا فەرمى يا كوليژا پزيشكى يا دهوكێ

ISSN: 2071 - 7326