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FREQUENCY OF THYROID CANCER AMONG PATIENTS WITH GOITRE

HAYDER H. IBRAHIM, MBChB , FRCSEd*

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ABSTRACT

Background Thyroid diseases are common surgical problems and the incidence of malignancy is increasing particularly in patients with non-toxic goitre.
Aim To show the frequency of thyroid cancer in patients with goitre.
Materials and Methods Case Series Study of 216 patients operated upon in the period between 1992 - 2009 for non- toxic and toxic goitre in Mosul and Duhok hospitals, 172 patients with non-toxic goitre and 44 with toxic goiter. Hyperthyroidism was diagnosed by elevated tri-iodothyroinine and thyroxin ratio and low thyroid stimulating hormone (TSH). All patients were evaluated with ultrasound, fine needle aspiration cytology for nodular cases and some of them by scintigraphy. Histopathology reports of patients treated surgically with a preoperative diagnosis of non-toxic and toxic goitre were reviewed to identify the thyroid cancer frequency. Patients having a history of neck irradiation or radioactive iodine therapy were excluded from the study.
Results The incidence of malignancy was 11.6% for non-toxic goitre group and no case of malignancy was detected in toxic group.
Conclusions The incidence of malignancy in non-toxic group is increasing in contrast to toxic goitre in which no case was detected.

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Key words: Toxic goiter, Non-toxic goiter, Solitary nodule, Thyroid cancer

Presentation of the patient with lump or multiple lumps in the thyroid is an important clinical problem. The commonest pathological changes is non-toxic goitre, other changes are toxic goitre, thyroid cancer, inflammation and rarely dyshormonogenesis. The fact that few patients with multinodular goitre not having surgery develop clinically evident thyroid cancer suggests that these are not clinically aggressive malignancies. Recent change in any goitre should always alert the clinician to the possibility of malignant change.

The incidence of malignancy is lower in patient with toxic goitre (TG) than in those with non-toxic goitre (NG), and many authors claimed that hyperthyroidism protect against thyroid cancer.[1] Other authors reported in different studies that the incidence of malignancy with TG was not as low as previously thought. [2,3,4,5]

In the present study, the frequency and types of thyroid cancer in patients with goitre are identified.

MATERIAS AND METHODS

Two hundred and sixteen patients operated upon between 1992 - 2009 for non- toxic and toxic goitre. None of the patient had history of radioactive iodine therapy or neck irradiation.

In the NG group (20 males, 152 females), indications for surgery were pressure effects, cosmetic, or a dominant nodule increasing in size or showing cytological features raising the possibility of malignancy, or retrosternal extension. All patients were evaluated with ultrasound and some with scintigraphy. Fine needle aspiration cytology was performed in nodular cases. Subtotal, near total thyroidectomy or lobectomy with isthmusectomy was the

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procedure performed. All patients with papillary and follicular carcinoma received postoperative suppressive Eltroxin therapy.

In TG group (12 males, 32 females), recurrent hyperthyroidism after medical treatment, enlarging nodule, persistent drug side-effects, cytological suspicion of malignancy, and symptoms of tracheal or oesopgageal compression were the criteria of surgery, and only performed after euthyroidism was achieved by Neomercazole or Propyl thiouracil. Hyperthyroidism was diagnosed by elevated triiodothyronine/thyroxine ratio and low thyroid stimulating hormone associated with clinical signs and symptoms. All patients were evaluated with ultrasound and some with scintigraphy. The operation achieved was total or near total thyroidectomy.

RESULTS

Non-toxic goitre (including solitary nodule) was found in 172 patients, 152 females and 20 males (F/M 7.6: 1). Age range was 20 - 60 years, with a mean ± SD of (39.66 ± 10.12). Nodule size ranged from 10mm to 100mm, with a mean ± SD of (57.07±25.00). Toxic-goitre group (including thyroid nodule) was seen in 44 patients, 32 females and 12 males (F/M 2.6:1). Age ranged from 20- 60 years, with a mean ± SD of (37.26±9.76). Nodule size ranged from 10-90 mm, with a mean ±SD of (45.59±21.75). Total solitary nodules were 90 patients (both toxic and non-toxic), Females 76 and males 14 cases. 12 patients with solitary nodules had toxic goiter (Table 1).

Histopathology reports in all series were as follows: 128 cases non-toxic colloid, 38 toxic goitre, 22 with Hashimoto's thyroiditis (18 with non-toxic goitre, 4 with toxic goitre), 8 follicular adenoma (6 females, 2 males) and 20 (18 females and 2 males) with carcinoma (Table 2).

In non-toxic goitre the frequency of malignancy was 11.6%. It was 11.84% (18/152) in female, and 10% (2/20) in male patients. The frequency of malignancy in non-toxic solitary nodule was 15.7% which is higher than that in non-toxic multinodular goiter (5.4%).

Types of malignancy was as follow: 14 papillary carcinoma (including two cases with Hashimoto's thyroiditis) and 4 follicular carcinoma. There was one case of non-Hodgkin's lymphoma and another case of anaplastic carcinoma (Table 3). In papillary carcinoma 12 were females; their age ranged from 25- 60 year and 2 males aged 40 and 45 year showed multifocality. In follicular carcinoma 4 patients were females aged 40 - 65 year and all were of Hurthle's cell variant. Histological examination revealed no cancer in any patients with toxic goitre.

Table 1. Age, sex, size and number of solitary nodule in all cases

Variables	NG No. 172	TG No. 44
Age		
Years	**20-60**	**20-60**
Mean (SD)	**39.66 (±10.12)**	**37.26 (±9.76)**
Sex		
M	**20**	**12**
F	**152**	**32**
Size of nodule		
mm	**10 – 100 mm**	**10 – 90 mm**
Mean (SD)	**57.07(±25.00)**	**45.59(±21.75)**
No. of solitary nodule		
M 14	**M 14**	**M 0**
F 76	**F 73**	**F 3**

M: male; F: female; SD: standard deviation; NG: non-toxic goiter; TG: toxic goitre

Table 2. Histopathology reports in all patients

Types	Non-toxic group	Toxic group
Colloid	128	38
Hashimoto's thyroiditis	18	4
Malignancy	20	0
Adenoma	6	2

Table 3. Frequency of malignancy in all series

Types	Non-toxic group N = 172	Toxic group N= 172
Papillary	14 (8.1%) (2M,12F)	0
Follicular	4F (2.3%)	0
Lymphoma	1F (0.5%)	0
Anaplastic	1F (0.5%)	0
Total	20 (11.3%) (2M, 14F)	0

M: male; F: females

DISCUSSIONS

The frequency of cancer in our series was 11.6% in NG while in TG it was zero. It was reported that the risk of thyroid cancer in hyperthyroidism was as low as 1-2 %, [1] and the frequency of carcinoma in TG is less than 1%[3] Some investigators found that the incidence of cancer is as high as 21 %[6] . In a recent study, the incidence of malignancy in TG was found to be 7 % and most of them were papillary microcarcinoma.[4] On the other hand, the incidence of cancer in NG was reported between 6.2 - 9.7 % in several studies.[7,8] It has been suggested that upward incidence trends in thyroid cancer have also been associated with increased diagnostic activity because of more sensitive tests.[9]

All benign thyroid nodules showed predominance in women. From epidemiological studies it appears that the gender factor may influence the risk of benign thyroid disease and thyroid cancer in women.[10,11] On the other hand, some studies pointed out that the incidence of thyroid cancer showed male/female parity in patient from endemic areas compared with patients from non-endemic areas.[12,13] Male/Female ratio was 2/18 (11.11%) in NG group and no malignancy in toxic group in our study.

The types of malignancy were as follows: 14 papillary (8.1%), 4 follicular (2.3%), 1 lymphoma (0.5%), and 1 anaplastic carcinoma (0.5%). Papillary carcinoma was the commonest malignancy; 2 of them of micropapillary type as defined by World Health Organanization as papillary carcinoma measuring $\leq$ 10mm in the greatest dimension.

However, many autopsy series[14-16] showed that papillary microcarcinoma was a very frequent incidental finding, corroborating the idea that small papillary cancer was 'quite the normality' and that most of these tumors did not progress to clinical cancer. There were also some reports of clinical evidence of massive lymph node metastases in some micropapillary carcinoma which further indicated the potential aggressiveness of small cancers.[16-19] Moreover, treatment should be advocated because

microcarcinoma has an excellent prognosis.[20-22]

The increasing incidence of cancer in thyroid could be attributed to better nodule detection, difference in extent of thyroid resection and the number of histological sections examined per specimen.

CONCLUSION

The incidence of thyroid cancer in non-toxic goitre is increasing particularly in solitary nodule which may be due to better diagnostic activity while the incidence of cancer in toxic goitre is not the same as reported in some literature.

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پوختە

بەربەلاڤبوونا شێرپەنجا پەریزادێ لجەم نەخوشێن تووشی پەریزادێ بووین

پاشکا لێکولینێ: نەخوشیێت پەریزادێ ژوان نەخوشیێت بە ربە لاڤن وریژا تووشبوونا شێر یەنجا پەریزادێ بەرەڤ زێدەبوونێ یە بتایبەت بەریزادا نەژەهراوی.

ئارمانج: ئەڤ لێکولینە ریژا شێر پەنجێب پەریزادێ لنك نە خوشێت تووشی مەزن بوونا پەریزادێ یا ژەهراوی و نە ژەهراوی دیاردکەت.

ریکێن ڤەگولینێ: لێکولینەکا نەخوشێت لدویڤ ئێك ودوو مە (216) دوو سەد وشازدە نەخوش هەبوون کو تووشی مەزن بوونا پەریزادێ بووین (44)نەخوش بێت پەریزادا ژهراوی و (172) نەخوش بێت نەژهروای بوون). نشتەرگەریا ژێکرنا پەریزادێ بو هاتەکرن لناڤ بەرا (2009-1992) ێ ل پارێزگەهێن میسل ودهوك. ئەو نەخوشێت پێشوەخت چارەسەری وەرگرت (یودا پرشنگدرا و تیشکا قوول ناکەڤتە دناڤ ڤێ لێکولینێ دا). هەلسەنگاندنا نەخوشا هاتەکرن بریکێت پێلێت لسەر دەنگی دا بو هەمیا و پشتکیننا خانەی بدەرزیکێ و کەرەستێ پرشنگدا بو هندەك نەخوشا. نەخوشێت پەریزادا ژهراوی هاتنە دەست نیشانکرن بریکا پشکنینا هورمونێت تایبەت. پشکنینا شانەی هاتەکرن بو هەمی نەوخوشا پشتی نەشتەرکەریێ و بڤێ ریکێ جور و چەشنێت شێر پەنچێن هاتنە دەست نیشانکرن.

ئەنجام: ریژا تووشبوونا شێر پەنچا پەریزادێ گەهشتە 11.6% ژ نەخوشێت پەریزادا نە ژهراوی و دیار بووکو نەخوشێت پەریزادا ژەهراوی هەی شێرنجەناگریت.

دەرئەنجام: تووشبوونا نەخوشێت شێر پەنجا پەریزادێ یادزێدبوونێ دا لنك نەخوشێت مەزینا پەریزادێ هەمی یا نەژەهراوی و نەبوونا شێر پەنجێ لنك نەخوسیێت پەریزادا ژهراوی.

الخلاصة

نسبة الإصابة بسرطان الغدة الدرقية لدى المرضى المصابين بالدراق

خلفية البحث: أمراض الغدة الدرقية هي من الأمراض الجراحية الشائعة ونسبة الإصابة بسرطان الغدة الدرقية في زيادة وخاصة لدى المرضى ذو الغدة الدرقية غير السامة.

الهدف: هذا البحث يبين نسبة حالات سرطان الغدة الدرقية لدى المرضى المصابين بتضخم الغدة الدرقية السامة والغير السامة.

طريقة البحث: تم دراسة سلسلة حالات .مائتان وستة عشر مريض لديهم تضخم الغدة الدرقية (السامة 44 حالة والغير السامة172 حالة) أجريت لهم عمليات استئصال الغدة للفترة من 1992–2009 في محافظتي الموصل ودهوك. المرضى الذين لديهم علاج سابق باليود المشع أو بالأشعة العميقة غير مشمولين بهذه الدراسة. تم تقييم الحالات المرضية بواسطة فحص الأمواج فوق الصوتية لجميع الحالات والفحص الخلوي بالإبرة والمادة المشعة لبعض الحالات . حالات الغدة السامة تم تشخيصها بواسطة فحص الهرمونات الخاصة بالغدة. تم إجراء الفحص النسيجي لكافة المرضى بعد العملية ومن خلالها تم معرفة حالات ونوع سرطان الغدة .

النتائج: إن نسبة الإصابة بسرطان الغدة الدرقية هو 11.6% من حالات الغدة الغير السامة مع عدم وجود حالات سرطانية بين مرضى الغدة السامة.

الاستنتاجات : حالات الإصابة بسرطان الغدة الدرقية في زيادة لدى المرضى المصابين بتضخم الغدة الدرقية الغير السامة ولأيوجد لدى مرضى الدرقية السامة.

FACTORS AFFECTING THE EFFICACY OF PHOTOTHERAPY AS TREATMENT FOR NEONATAL HYPERBILIRUBINMIA IN DUHOK

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ABSTRACT

Background Phototherapy is an effective and safe management for neonatal hyperbilirubinemia that decreases the need for exchange transfusion. Its efficacy depends mainly on the light irradiance and wavelength as well as the distance between the phototherapy lamp and the patient.

Aim To determine the efficacy of phototherapy in lowering total serum bilirubin level in neonates managed in neonate care unit in Azadi General Hospital in Duhok and to find out any significant effect on this efficacy by each of maturity, age, weight, cause of hyperbilirubinemia and initial total serum bilirubin level.

Patients and Methods The study included 102 neonates with hyperbilirubinemia managed by phototherapy. Total serum bilirubin was measured for all patients at the beginning of phototherapy and 4 hours after that. The patients were divided into different groups according to their maturity, weight, age, initial total serum bilirubin and the cause of hyperbilirubinemia (hemolytic or non hemolytic). The mean rate of total serum bilirubin lowering in 4 hours was found for all the patients and also for each group separately. The results were statistically analyzed using t-test and Pearson correlation.

Results The mean rate of total serum bilirubin lowering was found to be 0.97 mg/dl/4 hours and percentage of lowering was 6.4% of the initial total serum bilirubin in 4 hours. This result is close to the results found in other studies in different parts of the world. The mean rate of total serum bilirubin lowering was found to be higher in preterms than in full terms (0.82 mg/dl/ 4 hours versus 0.64 mg/dl/4 hours) but no significant difference was found(P=0.71). The mean rate of total serum bilirubin lowering was higher in hemolytic than the non hemolytic cases of hyperbilirubinemia (0.95mg/dl/4hours versus 0.74mg/dl/4hours) but no significant difference was found (P=0.97). The mean rate of total serum bilirubin lowering was found to be increasing with increasing age but no significant correlation was found (P=0.61), r =0.05. Also there was no significant correlation of mean total serum bilirubin lowering and body weight (P=0.66), r =0.044 and with initial total serum bilirubin level (P=0.74), r =0.033.

Conclusion The efficacy of phototherapy in our neonate care unit is close to its efficacy elsewhere and this efficacy is not affected significantly by age, maturity, weight, initial total serum bilirubin and the cause of hyperbilirubinemia.

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Key words: Neonate, Hyperbilirubinemia, Phototherapy

Hyperbilirubinemia is a common problem of neonatal period and it is usually benign but may result in lifelong neurologic sequelae in infants who are not treated.[1] Thus, treating hyperbilirubinemia at the appropriate time is of high importance in neonates.[2]

Increased bilirubin production, hepatic uptake reduction, impaired bilirubin conjugation and increased enterohepatic circulation are the pathologic etiologies of hyperbilirubinemia in the newborns.[3]

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Phototherapy serves as the primary treatment in neonates with uncojugated hyperbilirubinemia.[4,5] Phototherapy is a useful method for treating neonatal hyperbilirubinemia because it is easily available and devoid of all complications of double-volume exchange transfusion.[6]

The efficacy of phototherapy depends on the dose and the wavelength of light used and surface area exposed.[7] The efficacy can also be increased by moving lights closer to baby.[8] Light at a wavelength absorbed by bilirubin (blue or white spectrum) is used. The uncojugated bilirubin in the skin is converted by such light to a stereoisomer compound that is water soluble able to be excreted in bile without conjugation.[9] The infant's eyes should be shielded from light to prevent damage to retinal cells.[10]

Although phototherapy has been shown to decrease the likelihood of exchange transfusion, the long term benefits of its use in infants with less severe jaundice are unknown.[11]

Unless the photobilirubin that enters the small bowel is converted rapidly to other water-soluble products or is excreted rapidly, some enterohepatic circulation of bilirubin via reconversion to bilirubin IX-a may occur. Therefore; even with rapid conversion of bilirubin to its products, a rapid decline in serum bilirubin level may not always be seen. A marked advantage of phototherapy is conversion of 10-20% of circulating bilirubin to water-soluble isomers which should be less likely to cross the blood brain barrier.[12]

No studies were found in medline that reveal the effect of body weight, gestational age, initial TSB level, age or the cause of hyperbilirubinemia on the rate of lowering of TSB level with phototherapy. This study will try to find any such correlation in addition to determining the efficacy of phototherapy as treatment of neonatal hyperbilirubinemia.

To determine the efficacy of phototherapy in lowering total serum bilirubin(TSB) level in jaundiced neonates in the neonate care unit in Azadi Hospital in Duhok and to find out any significant correlation between the rate of lowering of TSB and each of maturity, age, weight, initial TSB level and the cause of hyperbilirubinemia.

PATIENTS AND METHODS

This study was conducted in the period from August 2007 to February 2008 in the neonate care unit in Azadi General Hospital in Duhok in Iraqi Kurdistan Region.

The study included 102 neonates who had hyperbilirubinemia for which they were treated by phototherapy according to criteria of the American Academy of Pediatrics. All the neonates were put in incubators and subjected to blue light, wavelength of 450 nanometers and the distance between the phototherapy lamp and the patients was 65 cm.

All the patients were investigated for reticulocyte count,serial hematocrit measurements, Coomb's test and blood group and Rh and accordingly they were divided into hemolytic (when there is gradually decreasing hematocrit over time and raised reticulocyte count) and non hemolytic causes of hyperbilirubinemia. Most of the hemolytic cases were those caused by Rh isoimmunization followed by ABO incompatibility. The patients were adequately hydrated with intravenous fluids and oral feeding was given to those who tolerated it.

The neonates were weighed and categorized according to their weights in kilograms. Total serum bilirubin was measured at the beginning of phototherapy and the patients were divided into groups accordingly. Also the patients were classified according to their ages and maturity. Total serum bilirubin was measured for all the patients 4 hours after starting phototherapy and rate of lowering was found for each neonate. The mean rate of lowering was found for all the patients

and also for each group of patients separately.

All these results were statistically analyzed using t-test and Pearson correlation to find out any significant correlation between the rate of lowering of total serum bilirubin and each of these variables.

RESULTS

One hundred and two neonates were studied. The mean rate of lowering of TSB after 4 hours from the onset of phototherapy was 0.97 mg/dl in 4 hours. The range of lowering was from 0.11 to 3.92 mg/dl in 4 hours. The percentage of lowering ranged from 0.56% to 26% of initial TSB in 4 hr with the mean being 6.4% in 4 hr.

According to maturity, the patients were divided into two groups; full term and preterm (gestational age <37 weeks). The full term babies were 54 (52.94%) and the prematures were 48 (47.06%). The mean rate of lowering of TSB in the full terms was 0.64 mg/dl/4 hr while in the preterms it was 0.82 mg/dl/4 hr. On statistical analysis, it was found that (P=0.7) which means there is no significant difference in the rate of lowering TSB between preterms and full terms.

The patients were also classified according to the cause of hyperbilirubinemia to hemolytic 14 (13.72%) which were mainly caused by Rh isoimmunization and ABO incompatability and non hemolytic 88 (86.28%). The mean rate of total serum bilirubin lowering in the hemolytic cases was 0.95 mg/dl/ 4 hr while in the non hemolytic it was 0.74 mg/dl/4 hr. The P value is 0.97 which means there is no significant difference between the both groups.

As shown in table 1, there are 8 groups of patients according to age with different mean rates of total serum bilirubin lowering in 4 hours. Although it is shown that the mean rate of total serum bilirubin lowering increases with increasing age, there is no significant correlation (P=0.61), r = 0.05.

Table 2 divides patients into 4 groups according to total serum bilirubin level at the beginning of phototherapy. There were different mean rates of total serum bilirubin lowering which were increasing with increased initial total serum bilirubin level but no significant statistical correlation was found (P=0.74), r = 0.033.

In table 3, the patients were divided into 6 groups according to weights. The mean rate of TSB lowering increased with increasing age but no significant correlation between these two variables was found (P=0.66), r =0.044.

Table 1. The ages of patients and mean rate of TSB lowering

Age (days)	Number	Mean rate of TSB lowering(mg/dl/4hr)
1	**4**	**0.28**
2	**17**	**0.95**
3	**23**	**0.65**
4	**20**	**0.92**
5	**13**	**1.55**
6	**9**	**1.16**
7	**8**	**1.52**
>7	**5**	**0.68**

P= 0.61 not significant
r =0.05 not significant

Table 2. The initial TSB level and mean rate of TSB lowering

Initial TSB (mg/dl)	Number	Mean rate of TSB lowering(mg/dl/4hr)
Equal to and less than 10	17	0.5
More than 10 to equal to and less than 15	42	0.55
More than 15 to equal to and less than 20	30	1.38
More than 20	13	1.6

P=0.74 not significant
r=0.033 not significant

Table 3. Weights of neonates and mean TSB lowering

Weight (Kg)	Number	Mean rate of TSB(mg/dl/4hr)
Equal to &less than 1Kg	10	0.38
More than 1Kg to equal to &less than 1.5 Kg	20	0.68
More than 1.5 Kg to equal and less than 2 Kg	32	0.8
More than 2 Kg to equal to &less than 2.5 Kg	22	0.74
More than 2.5 kg to equal to &less than 3 kg	11	1.1
More than 3 Kg	7	0.96

P=0.66 not significant
r=0.044 not significant

DISCUSSION

In this study all the neonates were subjected to fixed phototherapy dose & wavelength and the distance between the lamp of phototherapy and the body of the infant. Adequate hydration was maintained for all patients by intravenous fluids since dehydration that results from heat produced by phototherapy will elevate total serum bilirubin level.[13] Those neonates who could feed orally were given milk every 2-3 hours to enhance bowel motion and interrupt the enterohepatic circulation which can increase total serum bilirubin level.[14]

We found in our study that the mean rate of decline of toyal serum bilirubin is (0.97mg/dl/4hr) with a wide range from 0.11mg/dl/4hr to 3.92mg/dl/4hr. The percentage of lowering total serum bilirubin level ranged from 0.56% to 26% with a mean of 6.4% . Hansen found that the decline of total serum bilirubin with phototherapy was as high as 10 mg/dl in a few hours with a rate reduction of 30-40% in the first 24 hours.[15] Here we can find that the percentage is equal to 5-6% of TSB in 4 hours which is similar to the result of this study.

Graranti et al found that the rate of total serum bilirubin lowering with phototherapy was 0.163 mg/dl/hr.[16] which means 0.652 mg/dl/4hr and this result is lower than the result of this study. Itani et al showed a much higher result when they found that the rate of total serum bilirubin lowering was 5mg/dl/hr[17] which means 20 mg/dl/4hr. Porter found the rate of total serum bilirubin lowering with phototherapy to be 1-2 mg/dl/4hr[18] which is close to our result. Seidman et al found the rate of this lowering was 0.2 mg/dl/hr[19] which is 0.8 mg/dl/4hr which is not remote from the result of this study.

Since it is supposed that efficacy of phototherapy is more in the larger babies because of larger area of exposure,[20] we divided the neonates into 6 groups according to their weights. There is an

increase in rate of TSB lowering with increasing weight but statistical analysis found no significant correlation. The best explanation for this is that the effect of weight is blunted by the equality of the dose and wavelength of the light used and the distance between the body of the neonate and the phototherapy lamp.

The patients were divided into 4 groups according to the initial total serum bilirubin level and on analysis no significant correlation was found although the total serum bilirubin lowering increased with increasing initial total serum bilirubin. Tan et al found that the maximal efficacy of phototherapy was in the severely jaundiced neonates.[21] Rubultelli et al also showed that the rate of total serum bilirubin lowering with phototherapy was higher at high baseline total serum bilirubin.[22]

The premature neonates usually have a higher rate of bilirubin production because of immaturity of hepatic conjugation and enhanced enterohepatic circulation.[14]

Therefore; we compared mean rates of total serum bilirubin lowering between the pre term and full term neonates and although the mean was higher in the preterms no significant difference was found between these two groups.

The efficacy of phototherapy is higher when there is hemolysis[21] and in this study the mean rate of total serum bilirubin lowering was higher in the hemolytic cases but no statistically significant differences were found between hemolytic and non-hemolytic cases.

Also we found no significant correlation between the ages of neonates and the mean rate of total serum bilirubins lowering.

The best explanation for the results above is that the effect of these factors is blunted by the equal dose & wavelength of phototherapy and the same distance between the body of the neonates and the phototherapy lamp.

CONCLUSION

The efficacy of phototherapy as treatment for neonatal hyperbilirubinemia in our unit is similar to efficacy of phototherapy elsewhere and this efficacy is not significantly affected by the age, the weight and maturity of the patient nor by the cause of hyperbilirubinemia and the initial TSB level.

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پوختە

کاریگەریا چارەسەریا ب روناهی یێ بو چارەسەرکرنا بلند بونا ئاستێ بلیروبینا خوینێ لدەڤ زاروکێن نەوزاد ل دهوکێ

پێشەکی: چارەسەریا ب روناهی یێ ریکەکا بهێزو کێم مە ترسیە بو چارەسەرکرنا بلند بونا ئاستێ بلیرونینێ لناڤ خوینا زاروکێن نەوزاد وگەلك پێدڤیاتیا گهورینا خوینێ کێم دکەت. هاوکارێت سەرەکی بو کاریگەریا ڤی جورێ چارەسەریێ هیزا رونا‌هی یە. و دریژیا شەپولا وێ ودیراتیا چرایا روناهی یێ ژ لەشێ زاروکێ.

ئارامانج: دیارکرنا کاریگەریا چارەسەریا ب روناهی یێ دچارەسەرکرنا بلند بونا بلیروبینا خوینێ لهوبا چارەسەریا زاروکین نەوزاد(فرنیکی) ل نەخوشخانا ئازادی یاگشتی ل دهوکێ وهەر وسادیارکرنا ئاستێ کارتێکرنا ژیێ زاروکی گەهشتناوی . سەنگاوی .ئاستی بلیروبینێ ل دەست پێکا چارەسەریا ب روناهی یێ و ئەگەری بلند بونا بلیروبینێ(شکەستنا تەپکێن سورین خوینی یان نە) لسەر کاریگەریا ڤی چارەسەریی.

ئەنجام: رەیژەیا گشتی یاکیمبونا ئاستێ بلیروبینێ 0.97ملغ /دل/ 4دەم ژمیرا دا بو(0.64٪ لماوی 4 /دەم ژمیرا دا) ئەڤ ئەنجامە یێ نێزیکە بو ئەنجامێت گەلەك شروڤە کرنا یێن هاتینە کرن لسەر نسەری جیهانێ . ریژا نزم بونا ئاستی بلیروبینێ لدەڤ زاوکێن نەگەهشتی پتر بوژ ئەوین گەهشتی (0.82بەرامبەر0.64 ملغ /دل/ 4دەم ژمیرا دا) بەلێ شروڤەکرنا ئاماری دیارکر کو ئەڤ جیاوازیە نەیا گرنگە p=0.7 ودیار بو کو ریژا کیمبونا ئاستێ بلیروبینا خوینێ لنەڤ زاروکێن شکستنا تەپکێن خوینی لدەڤ هەیی بلند تره ژ وان ئەوین نەهەی بەلێ شروڤەکرنا ئاماری دیارکر کو ئەڤ جیاوازیە نەیا گرنگە(0.95بەرامبەر 0.74ملغ /دل /4دەم ژمیرا). کیمبونا ئاستی بلیروبینێ پترلێت دهێت لگەل مەزبنونا ژیێ زاروکی بەلێ چ بیکڤە گریدانا گرنگ نەهاتە دیتن پشتی شروڤەکرنا ئاماری هاتیە کرن r =+0.05, p=0.61 هەروەسا چ پیکڤە گریدانا گرنگ نەهاتنە دیتن لناڤبەرا کیمبونا ئاستی بلیروبینێ وهەرئیك ژ سەنگا زاروکی (r=0.044, p= 0.66) وئاستێ بلیروبینێ لدەسپێکێ(r=0.033 ,p=0.74).

الخلاصة

فعالية العلاج الضوئي في معالجة ارتفاع بليروبين الدم عند الأطفال حديثي الولادة في دهوك

المقدمة: العلاج الضوئي وسيلة علاجية فعالة وامينة لمعالجة ارتفاع بليروبين الدم عند حديثي الولادة و يقلل الحاجة الى اجراء عملية تبديل الدم. تعتمد فعالية هذا النوع من العلاج على شدة الضوء وطوله الموجي والمسافة بين المصابيح وجسم الرضيع.

هدف الدراسة: تحديد فعالية العلاج الضوئي المستخدم لمعالجة ارتفاع بليروبين الدم عند حديثي الولادة في مستشفى آزادي العام في دهوك و كذلك تحديد ما اذا كانت هذه الفعالية تتأثربالعمر'النضج'الوزن'مستوى بليروبين الدم اوسبب ارتفاع البليروبين.

جمع الحالات و طريقة البحث: شملت هذه الدراسة 102 طفل رضيع يعانون من ارتفاع بليروبين الدم ويتلقون العلاج الضوئي. تم قياس مستوى البليروبين لكل مريض عند بدء العلاج الضوئي و بعد مرور 4 ساعات من ذلك وثم حساب معدل انخفاض مستوى البليروبين.تم تصنيف المرضى المشمولين الى مجاميع من حيث النضج'العمر' الوزن' مستوى البليروبين عند بدء العلاج الضوئي و سبب ارتفاع مستوى البليروبين (تحللي او غير تحللي) و تم حساب معدل انخفاض البليروبين لكل من هذه المجاميع على حده. تمت مقارنة وتحليل هذه النتائج إحصائيا.

النتائج: المعدل العام لانخفاض مستوى البليروبين هوسبع و تسعون من المئه مليغراملكل دسيليترلكل اربع ساعات.هذه النتيجة مقاربة لنتائج دراسات اخرى اجريت في مختلف انحاء العالم. معدل هذا الانخفاض عند الخدج وجد اعلى مما عند الناضجين ولكن التحليل الاحصائي اثبت ان هذا الفرق غير ذي اهمية. كذلك و جد ان معدل الانخفاض في حالات الدموي اعلى مما في غيرها ولكن هذا الفرق غير ذي اهمية عند تحليل هذه النتائج إحصائياز وجد ايضا ان معدل انخفاض البليروبين يزداد مع زيادة العمر وكذلك مع ازديادالوزن ولكن التحليل الاحصائي اثبت عدم وجود ترابط احصائي ذي اهمية مع هذين المتغيرين.

ألاستنتاج: فعالية العلاج الضوئي في وحدتنا مقاربة لفعاليته في مناطق مختلفة من العالم ولا يوجد تأثير مهم على هذه الفعالية من قبل العمر'النضج'الوزن'مستوى البليروبين او سبب ارتفاع البليروبين.

INTRAUTERINE INSEMINATION TREATMENT IN SUB FERTILITY: ANALYSIS OF FACTORS AFFECTING OUTCOME

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ABSTRACT

Background Intra uterine insemination is an assisted reproductive technique using husband or donor sperm, at the time of ovulation in natural or stimulated cycle put in the uterine cavity or in the cervical canal.
Objective To identify factors that can predict successful outcome in intrauterine insemination.
Methods a prospective study, 193 cycles of intrauterine insemination were analyzed to identify prognostic factors regarding treatment outcome. The variables selected for analysis were: female age, infertility duration and etiology, types of infertility, sperm parameters after preparation (count and progressive motility), number of preovulatory follicles, thickness of endometrium and type of ovarian stimulation. The data were analyzed with chi – square test.
Results The overall pregnancy rate was 7.8%; the miscarriage rate was 60%, and no ectopic pregnancy or multiple pregnancies were encountered. Five significant variables were identified for successful outcome: endometrial thickness (P=0.001), number of treatment cycles (P=0.002), number of preovulatory follicles (P=0.038), progressive motility of sperm after preparation (P=0.05), and female age (P=0.05).
Conclusion intrauterine insemination should be considered prior to more invasive and expensive other assisted reproductive techniques as in vitro fertilization and gamete intra-Fallopian transfer. Careful couple's selection is a crucial factor in enhancing conception with this method.

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Key words: IUI, Infertility, ART

Intrauterine insemination (IUI) is one of assisted conception techniques in which a sample of washed, prepared motile sperm is deposited in the uterus at the time of ovulation in a natural or stimulated cycle.[1] IUI is a form of therapeutic insemination (TI) using the husband's (AIH) or donor (AID) sperms. IUI has a significant cost saving and less invasive compared with other forms of assisted reproductive techniques such as in vitro fertilization (IVF) or gamete intra-Fallopian transfer (GIFT).[2]

Controlled ovarian stimulation (COS), with IUI has been another important factor to the increased use of IUI treatment. It was first described by Sher et al.[3]

The indications of IUI are: nonsevere male factor infertility, unexplained infertility, cervical mucus hostility, ovulatory disturbance, and for some couples with immunologic abnormalities.[3,4] The male factors which benefit from using IUI with Controlled ovarian hyperstimulation COH[5] are: decreased sperm motility ≥30 %[6] and decreased sperm quality, disorders of sperm function, defects of the penis, and other form of ejaculatory dysfunction as spinal cord injury patients.[7]

Female factors that may benefit from IUI are: Scant or unreceptive mucus, persistent cervicitis, and cervical

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stenosis.[7,8] IUI with superovulation is favored as the treatment of choice for unexplained subfertility.[9]

There was a trend toward an increased success rate with increased total motile sperm count> 5 million.[10,11] According to the World Health Organization (WHO) Manual criteria: motility is graded from a to d, as follows: Grade (a) sperm are those that swim forward fast in a straight line, Grade (b) sperm swim forward, but either in a curved or crooked line, or slowly. Grade (c) sperm move their tails, but do not move forward and Grade (d) sperm do not move at all. WHO previously accepted 30% as normal, Kruger et al (1986) have described 'strict criteria' where less than 14% normal morphology would indicate the need for assisted conception.[6,12,13] The live birth rate per insemination declines with advancing age. IUI is useful for cervical mucus hostility, cervical infection, or the presence of antisperm antibodies.[14]

The main contraindications to IUI are: the presence of persistently less than 5 million motile sperms.[15] and pelvic inflammatory disease as the incidence of ectopic pregnancy is about 1 in 6.Other complications include bleeding, uterine cramping, infectious and allergic reactions.[1,16,17]

There are currently many different hormonal treatment protocols for COH combined with IUI. The use of clomiphene and Gonadotrophins is to induce COH.[7,18,19]

Success rate are in the region of 5 - 30 %,[20-24] and depend upon many factors including: cause of infertility as IUI is of more value for infertility caused by male and cervical factors. The quantity and quality of sperms produced are important.[25] Also it's stated that sperm DNA quality may predict IUI outcome and that the stability of the sperm DNA status is a parameter for positive outcome, while the extent of its fragmentation is an indicator of poor IUI outcome.[3] Women with healthy Fallopian tubes and who ovulate regularly have a higher chance of achieving pregnancy than those whose tubes are not healthy or do not ovulate regularly.[24] The younger the woman the higher the chance of conception.[25] The chance of conception declines with the longer period of infertility.[26,27] It is generally accepted that re-evaluation and discussion about other forms of treatment such as IVF and GIFT should be carried out with the couples after 6 consecutive failed cycles.[11,27-29]

PATIENTS AND METHODS

In this prospective study, evaluation of 223 IUI cycles was done for 170 couples. All cycles were carried out between March 2004 and December 2004 at the infertility clinic of Al - Batool Maternity Teaching Hospital in Mosul city.

The studied couples had at least one year of infertility, or less than this period if there were already identifiable risk factors such as female age above 35years or known male factor for infertility .The enrolled had a basic infertility evaluation as semen analysis for the male partner, hormonal assay (FSH, LH, serum prolactin, serum testosterone, thyroid function test, and mid luteal serum progesterone), transvaginal ultrasound to assess ovulation and structural normality of the female genital organ. Tubal patency was investigated by laparoscopy or hysterosalpingography and all women with tubal abnormalities were excluded from the study. If pregnancy was not achieved after two to three ovarian stimulation/IUI cycles, tubal patency was re evaluated and 5 cycles were excluded.

Another 25 cycles were excluded from the study because they didn't return to the clinic after performing IUI, which made the total number of the cycles 193.

The mean female age was 31.3 (range 18 – 47) years and the mean duration of infertility was 6.96 (range 1 – 25) years.

Women in the study had transvaginal ultrasound performed on the second day of the menstrual cycle as a baseline, and then

underwent ovarian stimulation. The first group used clomiphene citrate alone, 100 - 200 mg on day 2 - 6 of the cycle. The second group where those who didn't respond to clomiphene citrate alone, human menopausal gonadotrophins (HMG)/gonalf Serono were added, started on day 5, 1 – 2 ampoules/day until the follicle reached the acceptable size. The third group were women who didn't respond to the above two regimes, and HMG alone used with standard set up method. Sometimes IUI was performed on natural cycles when the women attended the clinic at the time of mid cycle, and discovered to have one or more mature follicles.

Ovarian and endometrial response were monitored by transvaginal ultrasound on cycle day's 9 – 13 (every 2 – 3 days after HMG injection), and 10000 I.U of hCG (pregnyl) was administered when at least one follicle was more than 16mm in mean diameter and endometrial thickness of 8 – 10 mm. Standard IUI was performed at approximately 36 hours after administration of hCG.

Semen was collected by masturbation into a sterile jar or condom after 2 - 4 days of sexual abstinence. After liquefaction and initial sperm analysis, the standard swim up technique was used for preparation, employing Medi - cult medium supplemented with human serum albumin and no antibiotic was added. The sperm sample was centrifuged at 500g for 15 minutes. The supernatant was discarded and the pellet diluted in 2.5 ml of medium and recentrifuged. After removing the supernatant the final pellet was gently covered with medium and incubated for one hour at 370C in an incubator.

IUI was performed using an intrauterine catheter with 1 ml syringe. The catheter was gently passed through the cervical canal and the sperm suspension expelled into the uterine cavity. Insemination volumes ranged from 0.5 - 1 ml. The woman remained supine for 10 - 15 minutes after IUI. If menstruation was delayed, a serum hCG test was performed 10 days after a missed period. All pregnancies were confirmed by ultrasonography.

A chi-square test was used to identify significant variables that contribute to the success of ovarian stimulation / IUI treatment, and to predict the probability of pregnancy for each treatment cycle. The variables selected for the initial analysis were female age, duration of infertility, type and diagnosis of infertility, sperm concentration and progressive motility (grade a+b) after preparation, number of preovulatory follicles (> 16 mm in diameter), thickness of endometrium, number of the treatment cycles and drug used for ovarian stimulation.

Female age was treated as dichotomous variable: <40 or ≥ 40 years and duration of infertility as <6 or ≥6 years. The categories of sperm concentration were <5×106, 5 – 10×106 or > 10×106 and progressive motility (grade a+b) of <40% or ≥ 40%. The number of follicles and treatment cycles were categorized as follows: 1, 2, 3 or 4 (more than 4 follicles were recorded as 4) and 1,2,3,4 or 5 cycles (more than 5 cycles was recorded as 5) respectively. The thickness of the endometrium was also treated as categorical variables, <6, 6 - 10, or >10 mm. The chosen level of significance was $p < 0.05$.

RESULTS

A total of 193 cycles were analyzed. The overall pregnancy rate per cycle was 7.8% (15/193). Of the 15 pregnancies, 6 (40%) were viable, 9 (60%) resulted in miscarriages, all the pregnancies were in different couples so we can say results were per couples. There was no ectopic pregnancy or multiple pregnancies. Pregnancy outcome is presented in table 1.

Table 2 summarized the pregnancy rate according to the female characteristics. Couples with combined factors were excluded from the study. The

pregnancy rate in women <40 years was significantly higher than in older women (9.6% versus 0 %), although the difference was statistically not significant (p=0.05). The pregnancy rate in women with duration of infertility of 6 years or less was higher than those with duration of more than 6 years (9.2% versus 6.0%) but was statistically insignificant (p=0.407). Regarding infertility etiology, highest pregnancy rate was achieved in those with ovarian dysfunction (9.1%), followed by unexplained infertility (7.9%), and male factor (6.9%). No pregnancy was obtained in those with endometriosis. However the difference was statistically insignificant (p=0.935).Higher pregnancy rate was demonstrated among those with secondary infertility when compared to primary infertility (11.3% versus 6.4%) the difference was statistically not significant (p=0.257).three cases of primary infertility had term pregnancies with living child, and 6 had miscarriages. Three cases with secondary infertility went into spontaneous labor at term and 3 had miscarriages.

Intrauterine insemination pregnancy rate according to sperm parameters is shown in table 3. The highest pregnancy rate was achieved among couple with sperm count more than 10 million (8.7%), followed by those with sperm count between 5 – 10 million (6.7%), while no pregnancy was observed in those with sperm count of less than 5 million. However the difference was statistically not significant (p=0.688).There was statistically significant difference (p=0.047) in pregnancy rate among couple in whom progressive motility of sperm after preparation was ≥40% as compared to those with <40% (10.2% versus 1.8%).

The pregnancy rate according to numbers of follicles were (19 %), (14.3%), (7.7%) and (2.5%) with four or more, 3, 2, and1 preovulatory follicles respectively, the difference was statistically significant (p=0.038) as sown in table 4.

Table 1. Pregnancy outcome of the intrauterine insemination cycles

Pregnancy outcome	*No. of patients*	*No. from total*	*%from total*
Pregnancy cycle	**15**	**15/193**	**7.8**
Live births /cycle	**6**	**6/193**	**3.1**
Miscarriages/cycle	**9**	**9/193**	**4.7**

Table 2. Intrauterine insemination and pregnancy rate according to female characteristics

Female character	Pregnancy/cycles	Percent rate	% total	P-value
Age (years)				
<40	**15/156**	**9.16%**	**7.8**	**0.050**
≥40	**0/37**	**0%**	**0**	
Infertility duration (years)				
≤6	**10/109**	**9.17%**	**5**	**0.407**
>6	**5/84**	**5.95%**	**2.6**	
Infertility etiology				
Unexplained	**3/38**	**7.89%**	**1.6**	**0.935**
Male factor	**6/87**	**6.89%**	**3**	
Endometriosis	**0/2**	**0%**	**0**	
Ovarian dysfunction	**6/66**	**9.09%**	**3**	
Types of infertility				
Primary	**9/140**	**6.4%**	**4.7**	**0.257**
Secondary	**6/53**	**11.3%**	**3**	

Table 5 demonstrates IUI pregnancy rate according to endometrial thickness. The highest pregnancy rate was observed among those with endometrial thickness of >10 mm time of insemination (50%), followed by those with thickness between 6-10 mm (4.5%), while no pregnancy was observed among those with endometrial thickness <6mm. The finding was statistically significant (p=0.001).

The relation of numbers of treatment cycles with pregnancy rate are demonstrated in table 6.The rate were (33.3%), (28.6%), (9.5%) and (3.9%) with treatment cycle 4, 3,2 and 1, there was no pregnancy when the number were≥ 5 cycles, a statistically significant variable (p=0.002) was found.

Highest pregnancy rate was observed in those receiving both clomiphene citrate and human menopausal gonadotrophins for ovarian stimulation (20%), HMG alone (8.6%) and CC alone (5.2%) each as shown in table 7. No pregnancy was observed in those who underwent IUI on spontaneous cycle. The difference between these variables were statistically not significant (p=0.101).

Table 3. Intrauterine insemination pregnancy rate according to sperm parameters (after preparation

Sperm parameters	Pregnancy/cycles	Percent rate	% total	P-value
Sperm count(×106/ml)				
<5	**0/6**	**0%**	**0**	**0.688**
5-10	**4/60**	**6.7%**	**2**	
>10	**11/127**	**8.7%**	**5.7**	
Progressive motility:				
<40%	**1/56**	**1.8%**	**0.5**	**0.047**
≥40%	**14/137**	**10.2%**	**7**	

Table 4. Intrauterine insemination pregnancy rate according to number of preovulatory follicles

Number of follicles (≥16mm)	Pregnancy/cycles	Percent rate	% total	P-value
1	**2/79**	**2.5%**	**1**	
2	**5/65**	**7.7%**	**2.6**	
3	**4/28**	**14.3%**	**2**	
≥4	**4/21**	**19.0%**	**2**	**0.038**

Table 5. Intrauterine insemination pregnancy rate according to endometrial thickness

Thickness of endometrium (mm)	Pregnancy/cycles	Percent rate	% total	P-value
<6	**0/2**	**0%**	**0**	
6-10	**8/177**	**4.5%**	**4**	
>10	**7/14**	**50%**	**3.6**	**0.001**

Table 6. Intrauterine insemination pregnancy rate according to the number of treatment cycle

Number of treatment cycle	Pregnancy/cycles	Percent rate	% total	P-value
1	**5/127**	**3.9%**	**2.6**	
2	**4/42**	**9.5%**	**2**	
3	**4/14**	**28.6%**	**2**	
4	**2/6**	**33.3**	**1**	**0.02**
≥5	**0/4**	**0%**	**0**	

Table 7. Intrauterine insemination pregnancy rate according to drugs used for ovarian stimulation

Drug used for ovarian stimulation	Pregnancy/cycles	Percent rate	% total	P-value
CC (group1)	4/77	5.2%	2	
HMG (group2)	7/81	8.6%	3.6	
Both (group3)	4/20	20%	2	0.101
Spontaneous	0/15	0%	0	

DISCUSSION

The aim of the current study is to uncover prognostic factors for successful outcome in IUI treatment in our practice. Five significant variables were identified. They were endometrial thickness, number of treatment cycles, number of preovulatory follicles, progressive motility of sperm after preparation and the female age.

The overall pregnancy rate per cycle was 7.8%. The success rate of IUI varies considerably between infertility clinics, and the same clinic between different couples. Success rate are in the region of 5-30 %.[24] The relatively low success rates in this study explained by the limited facilities of the center due to the condition of the country, the media used for sperm preparation, and irregular availability of drugs used for ovulation induction, especially HMG.

The spontaneous abortion rate in this study was 60 %(9/15), while the live birth rate was 40 %(6/15). There were no cases of multiple pregnancies. This may be due to the relatively small numbers of those who achieved pregnancy which did not provide a reflection of the entire possible outcome and the fear of ovarian hyperstimulation syndrome that made the gynecologists abandon the cycles with more than four follicles.

The pregnancy rate in younger women (<40 years) was significantly higher than in older women (≥40 years) , this result was similar to many previous studies. Both Stone et al[26] and Rojanasakul et al.[27] in their studies found that the success rate appeared to be higher in the younger age groups. The age related decline in female fecundity has been suggested to be a result of reduced uterine receptivity, and/or decreased oocytes quality.[3]

The pregnancy rate was higher for those with shorter duration of infertility (< 6) years, but the difference was statistically not significant. The impact of the duration of infertility on the success of IUI varied between studies. Nuojua - Huttunen et al[3] found that the duration of infertility is a prognostic factor for live birth among untreated subfertile couples. Also Iberico et al[29] found that homologous IUI achieved the best results with infertility duration <3 years. Thus IUI cannot be recommended to patients with a long standing duration of infertility.

The lowest pregnancy rate was observed with endometriosis (0%) inspite of very small number of patient. Nuojua Hutunen et al.[3] found a significantly lower pregnancy rate in endometriotic patients. The causal relationship between reduced fertility and endometriosis without tubal involvement is not clear. Extensive investigations suggest a multifactorial etiology for endometriosis associated infertility, which includes, for example, an altered follicular environment, impaired oocytes quality and reduced implantation rate. Immunological alterations observed in women with endometriosis are also thought to interfere with fertility via a direct cytotoxic effect on the gametes and the embryo.[3]

For other causes of infertility, the results varied between studies, Rojanasakul et al[27] found that the success rate appeared to be higher in unexplained infertility.

In this study, the difference between

infertility etiologies in relation to the success of IUI was statistically not significant. Higher pregnancy rate was observed in those with secondary infertility than primary infertility. A result was in agreement with the result reported by Rojanasakul et al.[27]

Higher pregnancy rate was observed in those with higher sperm count but what is more important than the sperm count, was the sperm motility. This was also demonstrated in other studies. Pasqualotto et al[30] found that the percentage of post wash sperm motility, and not the post wash total motile sperm count, can predict successful IUI outcome.

In this study, progressive motility of sperm after preparation was a good predictor of successful IUI outcome, which was in agreement with many studies in this subject. Tomilson et al[31] found that progressive motility of sperm was one of the predictive variables of IUI success. Tsai et al[23] found that the post prepared sperm motility was the only parameter predicting the successful rate of IUI. This was also found by Shulman et al[25] who reported that the degree of sperm motility after appropriate preparation for IUI is the only parameter to be correlated with treatment outcome.

The number of follicles was a prognostic variable for successful IUI outcome. In this regard, a significantly higher pregnancy rate seen in cycles with four or more preovulatory follicles, this being remarkably higher than in cycles with only one follicle. This result was in agreement with the result of other studies. Khalil et al[15] reported that the number of mature follicles at the time of insemination was positively and significantly related to a successful outcome of IUI, however, with an unacceptable high rate of multiple pregnancies with more than 4 mature follicles. Also Iberico et al[29] in their study reported that the number of preovulatory follicles was a significant predictor of pregnancy.Multifollicular development may result in an increased number of fertilizable oocytes and a better quality endometrium and luteal phase, thereby improving fertilization and implantation rates.[3] The poor outcomes in cycles with only one preovulatory follicle indicate the necessity of using ovarian stimulation in combination with IUI.[3]

The current study also showed that highest pregnancy rate was observed among those with endometrial thickness > 10mm which was statistically significant variable that can predict successful IUI outcome, this result is in line with the result of other studies including those of Tomlinson et al[31] who found that the endometrial thickness was a predictive of IUI success. Also Wang et al demonstrated that the pregnancy rates were statistically correlated with endometrial thickness at the day of hCG injection. Zollner et al[32] used three dimensional ultrasound to measure endometrial volume and found that an endometrial volume <2ml at the day of insemination is associated with a poor likelihood of pregnancy. They suggested that the endometrial volume predict endometrial receptivity. However, other studies did not show endometrial thickness as a significant factor for successful IUI outcome.[33]

A significant higher pregnancy rate was observed in the fourth treatment cycle in the current study. This is in contrast to the finding of Khalil et al[15] who demonstrated that the first treatment cycle compared to the following up to six treatment cycle was associated with highest pregnancy. Duran et al[3] in his study also found highest pregnancy rate in the first treatment cycle and thereafter it remained constant up to the fourth cycle. The result may be explained by small number of patients who had four cycles. However it has been demonstrated that fecundity has been shown to be relatively constant for the first three to seven cycles and that most of pregnancies occur within the first four treatment cycles, favoring a maximum of four IUI cycles before IVF.[3,34]

Highest pregnancy rate was observed among those who received both CC-HMG which is inconsistent with previous studies.[15]

CONCLUSION

IUI is an option for many couples prior to considering more complicated and expensive assisted reproductive techniques such as IVF, and that factors including endometrial thickness, number of treatment cycle, number of preovulatory follicle, progressive motility of sperm after preparation and female age, can predict IUI success, thus careful patient selection criteria combined with ovarian stimulation is the model for IUI success.

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پوختە

Intrauterine insemination وەك ریکەك بو چارەسەریا نەزوکیێ

پێشەکی: Intrauterine insemination ئێکە ژ ڕێکێن دهێنە ب کارئینان ژ بو چارەسەریا نەزوکیێ ب ڕێکا کارئینانا تۆمێ نێرینە ژ زەلامی یان ژ کەسەکێ خوبەخش و دانا ئافا زەلامی دناف منداڵدانێ دا یان گەردەنا منداڵدانێ دا ل دەمێ (ovulation).

ئارمانج: دیارکرنا فاکتەرێ گرێدای ب سەرکەفتنا ئەنجامێن چارەسەریا نەزوکیێ ب ڕێکا (Intrauterine insemination).

ریکا ئەکولینێ: ئەکولینەکا (prospective) هاتە کرن. 193 خول ژ Intrauterine insemination هاتنە شلوڤەکرن. ئەو فاکتەرێن کریدای ب ئەنجامێن باش بێن چارەسەریێ هاتنە دەست نیشان کرن و ئەوژی ئەڤەبوون: ژیێ ئافرەتێ، میّژوو و ئەگەرێ نەزوکیێ، ژمارا کیسولێن پێش (ovulation)، ستویراتیا پەردا دناڤ منداڵدانێ دا، و جورێ وریاکرناهێلکەدانێ. شلوڤەکرنا ئەنجاما یا ئامارا هاتە کرن ب ڕێکا (Chi-square).

ئەنجام: ڕێژا زگبریێ دناڤ ئافرەتا دا 7.8٪ بوو. ڕێژا بەرچوونا بچویکی 60٪ بوو و چێ ژ وان زکپربوون ل دەرڤەی منداڵدنێ دا یان دوگیان بن ب جمکا. سەرکەفتنا چارەسەریێ یا کریدای بوو ب ستویراتیا پەردا دناڤ منداڵدانێ دا ($p = 0.001$)، ژمارا خولێن چارەسەریێ ($p = 0.002$)، ژمارا کیسولێن پێش (ovulation) ($p = 0.38$)، لڤینا تۆمێ نێرینە ($p = 0.05$) و ژیێ ئافرەتێ ($p = 0.05$).

دەرئەنجام: Intrauterine insemination دڤێت بهێتە بەرجاف وەرگرتن بو چارەسەریا نەزوکیێ پێش ڕێکێن دی بێن گرانتر و ب زەحمەت تر وەك in vitro fertilization یان gamete intra-Fallopian transfer. دەسنیشانکرنا دروست یا هەڤڕینا بو چارەسەریێ فاکتەرەکێ گرنکە ژ بو زێدەبوونا ڕێژا زگبریێ.

الخلاصة

التلقيح الاصطناعي كعلاج لنقص الخصوبة:تحليل العوامل التي تؤثر على النتائج

الخلفية: التلقيح الاصطناعي هي احدى طرق تقنيات الخصوبة باستعمال السائل المنوي من الزوج او من متبرع, بعد اجراء بعض المعاملات عليه وحقن السائل داخل الرحم او عنق الرحم في فترة الاباضة.

الهدف: ايجاد العوامل المساعدة لانجاح النتائج في حالات التلقيح الاصطناعي داخل الرحم.

الطرق: دراسة مستقبلية ل193 دورة تلقيح داخلي ,حيث تم تحليلها لايجاد الطرق الافضل لتحسين النتائج. العوامل التي اخذت بنظر العتبار كانت: عمر الزوجة, مدة وسبب العقم, نوع العقم, ومواصفات السائل المنوي بعد التحضير, عدد البويضات الناضجة, ثخن بطانة الرحم ونوع الادوية المنشطة المستعملة. تم تحليل النتائج باستخدام (Chi-square test).

النتائج: كان معدل حدوث الحمل 7.77%, نسبة الاجهاض عند الحوامل كان 60% , لم تحدث حالة حمل خارج الرحم ولا حالة حمل متعدد. لوحظ وجود خمسة موثرات مفيدة على النتائج وكانت: ثخن بطانة الرحم (P=0.001) ,عدد الدورات التي تم التلقيح فيها (P=0.002), عدد البويضات الناضجة قبل التلقيح (P=0.038), نشاط الحيامن بعد عملية التنشيط (P=0.05) واخيرا عمر الزوجة (P=0.05).

الاستنتاج: الاستعانة بالتلقيح الاصطناعي في حالات العقم قبل اللجوء الى العمليات الاخرى لتقنيات الخصوبة مثل عملية اطفال الانابيب. ونسبة النجاح تعتمد على الاختيار الامثل للزوجين.

COMPLIANCE OF HYPERTENSIVE PATIENTS TO MANAGEMENT IN DUHOK GOVERNORATE USING MORISKY-GREEN TEST

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ABSTRACT

Background Hypertension forms a major public health problem in Kurdistan region, Iraq Good compliance to antihypertensive drugs is a key factor in controlling blood pressure.
Aim To study compliance of patients toward management of hypertension in Duhok city, Iraq.
Patients and Methods A cross-sectional study was conducted during four months period in 2007. The inclusion criteria were patients eighteen years of age and above who were known to be hypertensive for not less than one year. Information was obtained by direct interview. A Morisky-Green test was adopted to assess compliance to medication.
Results A total of 707 patients were recruited for the study. The study revealed a 54.6% compliance rate. Statistically significant associations were found between compliance rate by Moriskey-Green test and old age, female gender, low level of education, average socioeconomic status, long history of disease, knowledge of using medication, perception of hypertension as a health risk, presence of associated illnesses and practicing of life style changes.
Conclusions and Recommendations More attention should be paid by health authorities and patients to the hypertension problem. Patients should be aware about the importance of compliance to medications. Emphasis on Health education of hypertensive patients that attend primary health care centers about importance of compliance to medication and complication of hypertension through planned health education program.

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Key words: Hypertension, Compliance, Morisky-Green test

Hypertension is the most prevalent cardiovascular disorder all over the world. In the United States, for example, more than half of the entire population over 60 has hypertension. Similarly, community surveys in industrialized countries show a prevalence of 15%-38% in people aged 30 years and more.[1] A steady increase in the prevalence of hypertension has also been reported in developing countries; mainly due to westernization of life style.[2]

In the Eastern Mediterranean Region hypertension affects more than 20% of people. In Egypt For example, hypertension affects about 26.3% of total population.[3,4] Also Hypertension and its complications are increasing in Arabian Gulf countries.[5]

In Iraq a survey about risk factors of non communicable disease conducted in 2006 showed a prevalence of 40.4%.[6]

The main impact of hypertension is in its effect as being a leading cause of morbidity and mortality from coronary heart disease (CHD), stroke and renal failure.[7] Secondary prevention by antihypertensive drugs (AHD) has shown

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to decrease the risk by about 25% for CHD and stroke.[8] Achieving and monitoring the control of hypertension is a problem which is shared by the patients and their physicians. An important issue in the failure to control hypertension is low compliance with treatment, which remains a universal problem. Compliance involves not only taking the prescribed medications but also adherence to follow-up appointments and maintaining the recommended lifestyle modifications.[9,10]

Several studies have shown a low compliance rate. In Saudi Arabia and Egypt, for example, compliance rates of only 34.2% and 15.9% have been reported respectively.[3,10]

The aim of this study is to examine compliance of hypertensive patients to management and explore factors determining such compliance.

METHODS

A cross sectional design study was conducted in Duhok city from the 1st of January 2007 to the 30th of April 2007. Duhok is the centre of Duhok governorate which is one of the three governorates making Iraqi Kurdistan Region. The total population of Duhok governorate is about one million, while the population of Duhok city alone is 225246 inhabitants.[11]

Patients were collected from three main health facilities: the out patients department of Azadi general teaching hospital; which is the only referral tertiary care hospital in the governorate and from 2 primary health care centers (PHCCs), selected randomly out of the total 19 such centers in Duhok city. The PHCCs are delivering primary care services to people of Duhok city and use referral system for further management.

Cases were patients over eighteen years of age of both sexes known to be hypertensive for not less than one year who attended the study setting during the study period. All pregnant women were excluded. One researcher visited alternatively one of the settings during the period of study. The doctor in charge was requested to send hypertensive cases according to case definition for further evaluation. The aim of the study was explained to each patient.

Data were obtained from hypertensive patients by a detailed questionnaire form which was filled for each patient by the researcher. The form included general and specific information; the general included data regarding age, gender and some variables to estimate the socioeconomic status as low, intermediate or high (Table 1).[12]

The specific information were about compliance to treatment of hypertension and some associated determinants of compliance. For patients who were not on regular medication a more detailed evaluation was conducted about causes of not taking medication.

Morisky-Green test was also used for evaluating patient's compliance to medications; the Morisky-Green test consists of the following questions:

(1) Have you ever forgotten to take your medicine?

(2) Are you sometimes neglectful in regard to your medicine hours?

(3) Do you skip your medicine hours when you are feeling well?

(4) When you feel badly due to the medicine, do you skip it? According to the protocol of the Morisky-Green test, patients are considered adherent to the treatment when they obtain the maximum score of 4 points, and patients are considered nonadherent when they obtain 3 points or less.[13,14]

Data analysis was done using SPSS 15. Chi-square (X^2) test was used in the analysis of contingency tables. $P \leq 0.05$ was considered significant.

RESULTS

A total of 707 hypertensive patients were interviewed all agreed to participate in the study. A total of 33.1% of the study

population were interviewed in Azadi general teaching hospital, while the remainders were interviewed in PHCC. The distribution of study population by age and gender is shown in table 2. The total number of males was 302 in comparison with 405 females making a male to female ratio of (0.74:1).

Table 3 shows the socio-demographic characteristics of the study population. A total of 70.3% of study sample were illiterate or having only primary education, with only 8.9% have had university or higher education. Table 3 also reveals that more than 60% of the patients lived in intermediate socio-economic conditions.

Table 4 shows aspects of medication among the study population. A total of 94.5% of patients were on medication and 97.8% of them were using them at the time of study. Table 4 also reveals that 84.1% of the patients had their medications prescribed by physician, while 15.9% were prescribed by paramedical staff. Also it shows that only 21.0% of the study sample knew the name of the medicine used by them, while the majority of the patients were unaware of the name of medicine. Finally, table 4 illustrates that 54.6% of the patients were taking their medications regularly and are compliant with their treatment according to Morisky- Green test.

Table 1. Estimation of socio-economic status

Main Question	Category	Score
Type of housing	Owned complete	8
	Owned shared	6
	Rent	2
	Tent/Mud huts	0
Possession of car	Yes	2
	No	0
Crowding index	≥ 5	0
	3-4	1
	1-2	2
Educational level	Illiterate	0
	Primary	1
	Intermediate and secondary	2
	University and higher education	3
Occupation	Jobless(unemployed, retired)	0
	Unskilled(self employed, manual worker)	1
	Skilled (civil servant)	2
No. of electrical machines	Up to 2	1
	3-4	2
	6 and more	3

Table 2. Age and gender distribution of the study population

Age (years)	Male No. (%)	Female No. (%)	Total No. (%)
Less than 30	7 (2.3)	12 (3.0)	19 (2.7)
30-39	18 (6.0)	31 (7.7)	49 (6.9)
40-49	49 (16.2)	85 (21.0)	134 (19.0)
50-59	94 (31.1)	119 (29.4)	213 (30.1)
60-69	96 (31.8)	78 (19.3)	174 (24.6)
≥70	38 (12.6)	80 (19.8)	118 (16.7)
Total	302 (100.0)	405(100.0)	707 (100.0)

Table 3. Socio-demographic characteristics of the study population	
Socio-demographic characteristic	**No. (%)**
Occupation	
Jobless (unemployed, retired)	**454 (64.2)**
Unskilled (self employed, manual worker)	**144 (20.4)**
Skilled (civil servant)	**109 (15.4)**
Educational level	
Illiterate and primary	**497 (70.3)**
Intermediate and secondary	**147 (20.8)**
University and higher education	**63 (8.9)**
Socio-economic status	
Low	**59 (8.3)**
Intermediate	**470 (66.5)**
High	**178 (25.2)**

Table 4. Aspect of medication among hypertensive patients	
Aspect of medication	**No. (%)**
Medication prescription (N= 707)	
Medication prescribed to patient	**668 (94.5)**
Medication not prescribed	**39 (4.5)**
Current use of medication (N= 668)	
Currently using	**653 (97.8)**
Currently not using	**15 (2.2)**
By whom medication was prescribed (N= 668)	
Physician	**562 (84.1)**
Paramedical staff	**106 (15.9)**
Clarification of how to use medication (N= 668)	
Clarified	**644 (96.4)**
Not clarified	**24 (3.6)**
knowledge of drugs name (N= 668)	
Yes	**140 (21.0)**
No	**528 (79.0)**
Regularity of medicine intake (N= 668)	
Regular	**365 (54.6)**
Irregular	**303 (45.4)**
Morisky –Green test (N= 668)	
Compliant	**365 (54.6)**
Noncompliant	**303 (45.4)**

A total of 34.9% of the study sample had ever forgotten to take medicine. Also, 37.0% of participants were sometimes neglectful in regard to the schedule of medicine. Also 37.1% of the patients skipped medicine because of feeling well and 25.7% of patients experienced bad feelings about their medication.

Table 5 demonstrates a significant association ($p<0.001$) between compliance to AHD(antihypertensive drugs) according to Morisky-Green test and age of patients, as the compliance was highest among patients aged 70 years and more (78%) followed by those less than 30 years old (64%). Females were significantly ($p<0.001$) more compliant to AHD than males. Table 5 also reveals a significant association ($p<0.001$) between compliance and the level of education among patients,

where those with low level of education (illiterate and primary education) were more compliant than those with high level of education (intermediate and higher). Compliance has also found to be significantly associated with the socioeconomic status of patients ($p<0.001$), where 61.7 % of patients who were of intermediate socioeconomic status were compliant in comparison with 41.1% and 41% of patients from low and high socioeconomic status respectively.

Finally, table 6 illustrates a significant association ($p<0.001$) between compliance to AHD according to Morisky-Green test and the following variables: presence of the disease for more than 10 years, clarification of how to use medication, perception of hypertension as a health risk or as a chronic disease, presence of associated illnesses and practicing three methods of life style changes.

DISCUSSION

Hypertension is a serious public health problem due to its high prevalence and good control of the disease has always considered to be essential for reducing its morbidity and mortality.[14]

Non-adherence is a serious problem and should be understood as one of the major obstacles to the success of the treatment of hypertension. Identifying factors determining low compliance of hypertensive patients to treatment is, therefore, of vital importance in applying therapeutic strategy and in obtaining satisfactory results. [15,16]

In Iraq very little information is available about knowledge, attitude, practice and compliance of patients to AHD. Similarly, no data has been encountered in Kurdistan region.

A cross-sectional design was adopted

Table 5. compliance rate by Morisky Green test according to socio-demographic characteristics

	Morisky-Green test		Total No. (%)	X^2 (d.f.)	p- value
	Compliant No. (%) N= 365	Not compliant No. (%) N= 303	N= 668		
Age in years					
Less than 30	**11(64.7)**	**6(32.3)**	**17(100)**		
30-39	**18(48.6)**	**19(51.4)**	**37(100)**		
40-49	**59(47.6)**	**65(52.4)**	**124(100)**		
50-59	**92(44.9)**	**113(55.1)**	**205(100)**	**37.585 (5)**	**< 0.001**
60-69	**93(55.7)**	**74(44.3)**	**167(100)**		
Equal or more than 70	**92(78)**	**26(22)**	**118(100)**		
Gender					
Female	**234(62.7)**	**139(37.3)**	**373(100)**	**22.325 (1)**	**< 0.001**
Male	**131(44.4)**	**164(55.6)**	**295(100)**		
Level of education					
Illiterate and primary	**290(62.4)**	**175(37.6)**	**465(100)**		
Intermediate and secondary	**48(33.3)**	**96(66.7)**	**144(100)**	**39.450 (2)**	**< 0.001**
Higher education	**27(45.8)**	**32(54.2)**	**59(100)**		
Socioeconomic status					
Low	**23(41.1)**	**33(58.9)**	**56(100)**		
Intermediate	**271(61.7)**	**168(38.3)**	**439(100)**	**25.976 (2)**	**< 0.001**
High	**71(41)**	**102(59)**	**173(100)**		

Table 6. compliance rate by Morisky-Green test according to hypertension related factors

	Morisky-Green test		Total No. (%) N= 668	X^2 (d.f.)	p-value
	Compliant No. (%) N= 365	Not compliant No. (%) N= 303			
Duration of hypertension (in years)					
1-<2	**21(51.2)**	**20(48.8)**	**41(100)**		
2-<5	**89(44.1)**	**113(55.9)**	**202(100)**		
5-<10	**85(46.2)**	**99(53.8)**	**184(100)**	**39.192 (3)**	**< 0.001**
≥10	**170(70.5)**	**71(29.5)**	**241(100)**		
Clarification of how to use medication					
Clarified	**360(56.0)**	**284(44.0)**	**644(100)**	**11.480**	**< 0.001**
Not clarified	**5(20.8)**	**19(79.2)**	**24(100)**	**(1)**	
Perception of hypertension as a health risk					
Yes	**343(58.7)**	**241(41.3)**	**584(100)**		
No	**2(18.2)**	**9(81.8)**	**11(100)**	**31.706**	**<0.001**
Don't know	**20(27.4)**	**53(72.6)**	**73(100)**	**(2)**	
Perception of hypertension as a chronic disease					
Yes	**298(62.9)**	**176(37.1)**	**474(100)**		
No	**12(41.4)**	**17(58.6)**	**29(100)**	**45.231**	**< 0.001**
Don't know	**55(33.3)**	**110(66.7)**	**165(100)**	**(2)**	
Presence of associated illnesses					
Yes	**170(65.4)**	**90(34.6)**	**260(100)**	**19.826**	**< 0.001**
No	**195(47.8)**	**213(52.2)**	**408(100)**	**(1)**	
Practice of life style changes*					
Not Practice	**43(47.8)**	**47(52.2)**	**90(100)**		
Practice one method	**38(44.2)**	**48(55.8)**	**86(100)**	**12.453**	**< 0.001**
Practice two methods	**140(53.0)**	**124(47.0)**	**264(100)**	**(3)**	
Practice three methods	**144(63.2)**	**84(36.8)**	**228(100)**		

** includes salt restriction, saturated fat restriction and weight reduction*

and the sample was expected to be representative of the Duhok population. All registered hypertensive patients are supplied by AHD almost free of charge during their visits to hospitals and PHCCs. A history of one year or more on AHD was determined in order to give a more stable compliance. The 18 year of ages was selected as a cutoff point as hypertension among those of age less than 18 years is mainly due to secondary causes.[17] Pregnancy was excluded as some cases of hypertension during pregnancy are transient and no continuous treatment is required. Direct interviews adopted in the study are expected to increase the accuracy of data in comparison to self completed questionnaires.

The study showed that more than 50% of patients were between ages 50-69 years. This is similar to the result observed in several other studies where the median age of patients was about 50-60 years.[18-20] The male to female ratio was 0.74:1. This is similar to a study conducted in Iran in 2004, as well as in other countries.[19] This might be due to the fact that females are having more visits to clinics and more complaint than males. The study illustrated that 64% of the study populations was retired and /or unemployed. This is expected since unemployed are more frequently using public clinics for receiving drugs. Moreover hypertension is an age related disease and its prevalence will be higher at old ages.[6,21]

The study showed that about 70% of the study population was either illiterate or with primary education. This might reflect the general expected illiteracy rate in the community due to the cohort effect as most patients were old. This is in disagreement with similar data from USA,[20] which is expected due to very low illiteracy rate in western communities. Moreover some of our high educated patients might seek private rather than public clinics.

The study revealed that about 95% of patients have been been given medications to control their hypertension; and about 97% of them were currently using those medications. This is expected as those patients were traced while they were attending health centers for receiving their medication and /or for follow up. Similar results have been observed in Malaysia and the USA.[20-25]

About 84% of the study populations have been on AHD prescribed for them by physician and about 16% by paramedical staff. This is a good practice as the majority of our patients had been examined by physician.

The study showed that only 20% of patients knew the name of their AHD. This might be due to the high rate of illiteracy among our sample. It is a usual custom in our localities that patients usually describe their drugs by the color or size of the tablets. This has turned to be difficult in the last years due to importation of drugs from different sources and companies. This has made it difficult for doctors to follow up their patients' AHD, unless they provide them with the pack of the drug.

Several studies have shown a significant association between treatment regularity and the control of blood pressure.[19,26,27] Reasons behind irregularity of medicine intake may be related to the type of the disease (Hypertension) as being asymptomatic and chronic. Chronic diseases usually associated with a high incidence of defaulter. Moreover, old age patients frequently forget to take their treatment regularly. Another explanation is that complications attributed to hypertension are remote and hence the patient does not realize the importance of sticking to his /her treatment regimen.[28,29]

Similarly our study revealed that about half of the patients were not taking their medication regularly. This rate is slightly lower than the 75% reported in Baghdad in 2000, and this might be due to differences in the sample or collection site.[30]

Morisky-Green test was used for estimation of compliance of patients with AHD and this might be the first time that such a test is used in Iraq, and probably in neighboring countries[13,14]. The study found that 54%of our patients were complaint to medication according to the test. Similar result have been reported in Argentina and Brazil.[31,14]

Compliance to AHD have been estimated in other countries using methods other than Morisky-Green test; mainly counting the remaining pills for the month and /or using the therapeutic outcome method where diastolic blood pressure of <90mm Hg was considered indicative of compliance with treatment.[10,26,32,33]. Compliance rates using those methods were 66% and 47% in two studies in Saudi Arabia,[10,26] 41% in Sudan,[32] 54% in Nigeria[33] and 37% in Hong Kong.[29]

The study showed that patients older than 70 years were more compliant than younger patients. This probably reflects the traditional emphasis on family care for the elderly in the community when the disease is more frequently associated with more severe symptoms and complications.[21,34] Similar result have been observed in other studies.[10,19,35]

The study also revealed that female patients were more compliant than males. Similarly in the USA females tended to adhere better to AHD and to reach blood pressure control than males did.[36] Conflicting results have been reported in other studies.[10,26] This might reflect the general tradition in our society that

females are more compliant with medical advice than males. Also males are responsible for looking after families and are usually the one who work for the family. The latter might lead to forgetting to take medication in a busy daily work.

Compliance rate was higher among patients with a low level of education. Similar results have been observed in developing countries[10]; but the reverse was found in developed countries.[37] This might indicate that poor people with low education might be more easily motivated to treatment by doctors, media and colleagues in developing countries.

In Iraq AHD are usually available almost free of charge to patients. Accordingly the noncompliance observed in this study was associated with reluctance to take drugs rather than non-availability. The latter was frequently found to be an important cause in other countries.[38,39]

The study showed that compliance score was higher in those patients who had hypertension for more than 10 years. The rate of compliance was low in the newly diagnosed patients. This might partially be due to the fact that young patients are more afraid of taking a life long medication than patients in older age group. It might also be, as mentioned earlier, that the course of the disease is usually more severe in old age group.[21,34] This is against the result reported in Brazil[15] but similar to that observed in Iran.[19]

The study revealed that patients to whom the use of AHD was properly clarified and who were more aware of the health risk of the disease were more compliant to AHD than other patients. This indicates that information about hypertension and its treatment and complications is an important means to increase patients' motivation to take AHD regularly. Similar results have been observed in a study carried out in Czecho-Slovakian population.[37]The presence of an associated illnesses was found to increase compliant rate. This might be due to the more severe symptoms expected in such patients or to intense concern about life and health expected among this group. Similar result has been observed in Iran.[19]

The study also showed that patients who practiced three methods for life style changes (salt and saturated fat restriction and weight reduction) were more compliant to AHD than other patients. This is expected as patients who are keener about conducting life style changes will be more likely to be keen about observing their medication.

RECOMMENDATIONS

The study found that about half of our patients were not complaint to AHD. This necessitate a quick and well organized program designed according to local customs and believes in order to solve this important problem and its sequel.

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پوختە

پێگیریا نەساخێن بلندبونا فشارا خوینێ ب چارەسەریێ ل پارێزگەها دهوکێ

بنەکوك: بلندبوونا فشارا خوینێ ئاریشەکا ساخلەمی یا سەرەکی یە ل هەرێما کوردستانێ. دەستڤەئینانا پێگیریەکا باش ب چارەسەریێ گرنگیا خو یا هەی ژ بو کونترولکرنا نەساخیێ.

ئارمانج: ئارمانجا سەرەکی ژ ڤی کاری خواندنا پێگیریا نەخوشاب چارەسەریێ ل باژێرێ دهوکێ.

نەساخ و رێبازا کاری: رێکا ڤەکولینا برگەیی بو ب دەستڤەئینانا ئارمانجێن ڤی کاری هاتە بکارئینان د ماوێ چوار هەیڤان ژ سالا2007 کو ژیێ وان 18 سال و پتر بوون و نە کێمتر ژ سالەکی بووری بیت ل سەر دەستنیشانکرنا نەساخیێ. پرسیارنامەکا تایبەت هاتە ب کارئینان. تاقیکرنا Moriskey-Green هاتە ب کارئینان بو هەلسەنگاندنا پێگیریا وان ب دەرمانێن نزمکرنا فشارا خوینێ.

ئەنجام: دڤێ ڤەکولینێ دا 707 نەساخ هاتنە وەرگرتن. ڤەکولینێ دیارکر کو رێژا پێگیریێ ب دەرمانان 54.6٪ یە. هەڤبەندیەکا بەرچاڤ یا هەی دناڤبەرا رێژا پێگیریێ و فاکتەرێن وەکی پیراتیێ, رەگەزێ مێ, ئاستێ نزم یێ خواندەڤانیێ, بارودوخێ ژیار وئابوری یێ ناڤنجی, هەبوونا نەساخیێ بو دەمەکێ درێژ, زانینا چەوانیا ب کارئینانا دەرمانان, دیتنا نەساخیێ وەك مەترسیەکا ساخلەمی و دومدرێژ, هەبوونا نەساخیێن دی بێن دومدرێژ, و گوهورینێن شێوازێ ژیانێ.

دەرئەنجام و راسپاردە: پویتەپێدانەکا باشتر پێدڤی یە دەستهەلاتێن ساخلەمی و نەساخ ب دەنە ئاریشا بلندبوونا فشارا خوینێ. نەساخ پێدڤی یە د ئاگەهـ بن ل سەر گرنگیا پیڤانا فشارێ گەلەك جاران, گوهورینا شێوازێ ژیانێ, هەڤبوونا ئالوزیان, زێدەباری دوپاتکرن ل سەر گرنگیا پێگیریێ ب دەرمانان.

الخلاصة

التزام العلاج لدى مرضى ارتفاع ضغط الدم في محافظة دهوك

خلفية البحث: يعد ارتفاع ضغط الدم مشكلة صحية رئيسية في اقليم كوردستان. الالتزام بالعلاج ذات اهمية قصوى للسيطرة على المرض.

الهدف: يهدف البحث الى دراسة الالتزام بالعلاج لدى مرضى ارتفاع ضغط الدم في مدينة دهوك.

المرضى وسياق العمل: تم اعتماد نمط الدراسة المقطعية خلال فترة اربعة اشهر من سنة 2007. شملت الدراسة المرضى المصابين بارتفاع ضغط الدم لاكثر من سنة و الذين اعمارهم كانت 18 سنة فما فوق. تم جمع المعلومات بواسطة استبيان خاص, كذلك تم استخدام اختبار Moriskey–Green لمعرفة مدى التزام المرضى بالادوية المخفضة لضغط الدم.

النتائج: شملت الدراسة 707 مريض. اظهرت الدراسة بان نسبة التزام المرضى بالادوية المخفضة لضغط الدم كانت 54.6%. وجدت الدراسة بان هناك ارتباط معنوي بين نسبة الالتزام بالادوية المخفضة لضغط الدم والعوامل التالية: الشيخوخة, الجنس الانثوي, انخفاض المستوى التعليمي, المستوى المعيشي والاقتصادي المتوسط, الاصابة بالمرض لفترة طويلة, معرفة كيفية استعمال الادوية, وجود امراض مزمنة اخرى و مزاولة تغيير اسلوب الحياة.

الاستنتاجات والتوصيات: يجب ان تولي السلطات الصحية والمرضى مشكلة ارتفاع ضغط الدم اهمية اكبر. على المرضى ادراك اهمية قياس ضغط الدم بصورة منتظمة وتغيير نمط الحياة بما يهدف الى معالجة المرض والمضاعفات الناتجة عنه, اضافة الى التاكيد على اهمية اخذ العلاج بصورة منتظمة.

FAMILY PLANNING UNMET NEED PROFILE IN MOSUL CITY, NORTH OF IRAQ: A CROSS-SECTIONAL STUDY

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ABSTRACT

Background Contraceptive use has increased markedly in the recent years in most developing countries, as has the desire for smaller families, however, millions of women, more than 150 million women, want to delay or avoid pregnancy but are not using contraception, these women are considered to have unmet need for family planning.
Aim and Objectives The aim of the present study is to assess the level of unmet need in Mosul City in the north of Iraq, and determining reasons.
Methods and Participants A cross sectional survey was done covering1786 currently married fecund women attending the immunization unit of the chosen primary health care centers. A standard questionnaire formula was used and filled by direct interview with the participants.
Results The most important reasons of unmet need were health concerns/side effects which were responsible for 49.3% of causes of unmet need, followed by low perceived risk of pregnancy (20.1%), family and religious opposition (14.4%), lack of knowledge and accessibility concerns (10.6%) and other causes (5.3%).
Conclusion It is important to study the unmet need in a longitudinal perspective. This is the only research design that permits evaluating transitions in family planning status over time.

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Key words: Family planning, Unmet needs, Mosul city, Cross-sectional

Understanding of unmet need for family planning (FP), has passed through a series of stages, each one is an outgrowth of the once before.[1]

The causes of unmet need are complex, surveys and other in depth researches from 1990 revealed a range of obstacles and constrains that can be undermine a woman's ability to act on her childbearing preference.[2] Generally speaking, the reasons of unmet need can be grouped into two categories. Weak motivation for fertility control and high perceived cost of contraception. Couples have weak motivation for fertility regulation if their perceived benefits from preventing the birth of a next child are slight or their perceived chances of conceiving are slight.[3] Weak motivation for fertility control accounts for 20 - 40% of the reasons of unmet need among women surveyed between 1990 and 1994, and a special reason for unmet need in Sub-Saharan Africa.[3]

Weak motivation for fertility control includes; ambivalence about future child birth; this condition occurs mainly in women with unmet need for spacing births, so the ambivalence is only about the timing of the next birth.[4] Also it includes perceived low risk of conception which includes infrequent sexual activity, low perceived fecundity, breast feeding or lack of knowledge about the

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relationship between sexual intercourse and conception.[5] The last reason is the most important among adolescents who involved in illegal sexual relationships which occur mainly in the western countries. Low perceived fecundity occur among older women, on the other hand some women do not use contraception because they think that they are too young to become pregnant.[3]

The perceived cost of fertility regulation may play an important role in reproductive decision-making.[3] High perceived cost of contraception includes 3 types of costs. Physiological cost; that is the fear from the side effect of contraception and other health concerns.[6] While social cost is the societal and familial disapproval for FP which includes; respondent oppose, husband oppose, family oppose and religious causes.[7]

Monetary cost so called "non access barriers", which includes; the price of contraceptive method, its availability, transport, distance, time to reach the nearest center for FP and knowledge of contraceptive method.[8]

One still important cause of non using contraception is simply that, the woman wants more children. Women with unmet need for limiting births has different causes than those for spacing births.[3]

While ambivalence is the most important cause among spacers, lack of exposure to sexual activity and lack of knowledge are the important causes for limiters, limiting women appear to be more strongly motivated than spacers.[3]

There is another point which may lay a role in the causation of unmet need that is, low motivation to encourage contraceptive use among health care providers for various reasons including: lack of training, financial gain from providing abortion and a historical reliance on abortion to regulate fertility.[9]

The aim of the present study is to assess level of unmet needs and to pin point reasons behind this problem in Mosul City in the north of Iraq.

MATERIALS AND METHODS

Official permission was taken from Nineveh Health Office, to facilitate data collection from the involved primary health care centers (PHCCs).

The present study was conducted in Mosul City, the center of Nineveh Governorate. It is the third biggest city in Iraq with total population of 1317594. It is divided by the Tigris River into right and left banks. Each bank is served by the corresponding health sector (i.e. right and left health sectors). The right health sector includes 13 PHCCs and the left has 16 PHCCS.

To achieve the aim of the present study, a cross-sectional study design was adopted. Multistage non random sampling design was carried out, in which Mosul City was divided into two parts: right and left health sectors, from each health sector, three PHCCs were chosen i.e. six PHCCs from both parts in a try to cover most of city areas; north, middle and south.

The unit of the present study was currently married fecund woman at childbearing age (15-49 years) attending the immunization unit in the PHCCs at the time of the survey for immunization of any of her children and live in Mosul City.

Information was obtained from the women after an informed consent was taken. A detailed questionnaire form was prepared depending on WHO modules and literatures relevant to FP unmet needs of women at childbearing. Reliability (repeatability) and validity were assessed. The calculated reliability index was 84% and validity was 85.5%.

In this study, the precise estimation of the sample size was done depending on the catchment's area of each PHCC by following the equation of sample size determination in a simple surveys.[10]

The sum results from the six chosen

PHCCs gave the desired sample size which was 1572 women.

Because there might be some incomplete forms present among the questionnaire results and none response; the total sample size collected was 1800 women, which makes about 3.2% from the total number of women at child bearing age living within the catchment area of the chosen PHCCs. The period of data collection was from 1st of September to 31st of December 2007.

The information regarding each woman was transferred into code sheets and data entry was done using computer Pentium IV. SPSS package version (11.5) was used for the statistical analysis. To achieve the aim of this study, the following indicators were used:

1. Total number of women with current unmet need for FP; which is the total number of fecund women who do not want to have any more children or want to postpone their next birth for at least two more years and they do not use any type of contraception (standard formulation).[11] This indicator also includes pregnant or amenorrheic women whose current or most recent pregnancy was unwanted or mistimed.[12]
2. The expanded formulation of unmet need includes the standard formulation plus unmet need for modern contraception.[13]

Chi-square test was used to detect the presence of association between educational background of women and reasons behind unmet need. P-value of =< 0.05 is considered significant.

RESULTS

Calculation of the current unmet need for FP according to the standard formulation is exhibited in figure 1. The total number of women with unmet need for FP is 360 (20.2%) out of the total women surveyed (n=1786). On the other hand, figure 2 portrays the current unmet need for FP according to the expanded formulation which is 34.9%.

Table 1 shows reasons of unmet need as stated by all women with unmet need in the present study. Fear from side effects is the most important reason of unmet need (27.6%) followed by health concerns (21.7%) and low perceived risk of pregnancy (20.4 %), the rest of causes are mainly those concerned with family opposition (9.1%), religious causes (5.3%), ambivalence (4.5%) and lack of knowledge about methods and types of contraceptives (4.3%).

Table 2 depicts reasons of unmet needs among 181 women with unplanned pregnancy. Just less than half (47.7%) witnessed contraceptives none use; in one third (32%) traditional methods were blamed. The rest (20.4%) have used modern contraceptives incorrectly.

Table 3 illustrates that among the 31 amenorrheic women who have had unwanted childbirth, 64.5% claimed not using contraception and the rest follow incorrect way of use (35.5%). None of them reported using traditional methods.

Table 4 indicates presence of highly significant association between causes of unmet need and education level of women with various degree of significance. Low perceived risk of pregnancy is the most frequent stated reason among illiterate women (34.3%). On the other hand health concerns and side effects are the reasons number one among educated women with various fractions varied from 60.1% among women with secondary education to 41.2% among those with higher degrees.

DISCUSSION

The present study showed that health concerns and side effects were on the top of the list of common reasons for unmet need for FP, which reaches 49.3%. Sedgh et al.[14] in their research

conducted in 53 countries in Asia, Africa and Latin America found that, 60% of women mainly in North Africa, West Asia and nearly half of women in Latin America did not use contraception due to low perceived risk of pregnancy. The same group found that health causes only form 32% in those regions. The finding of the present study may be due to the fact that Iraqi women may become easily affected from the side effects of the modern contraceptives regardless of types, which may be due to the circumstances that they have been living with during the last decades such as low standards of living as a result of successive wars in addition to the sanction which affect all aspects of life particularly women at childbearing age, children as well as elderly.

The second common reason found in the present study was low perceived risk of pregnancy (20%). The third reason was family opposition (9.1%), which occurs when the most influential person in the family like mother in law or the husband oppose the use of contraception.[12]

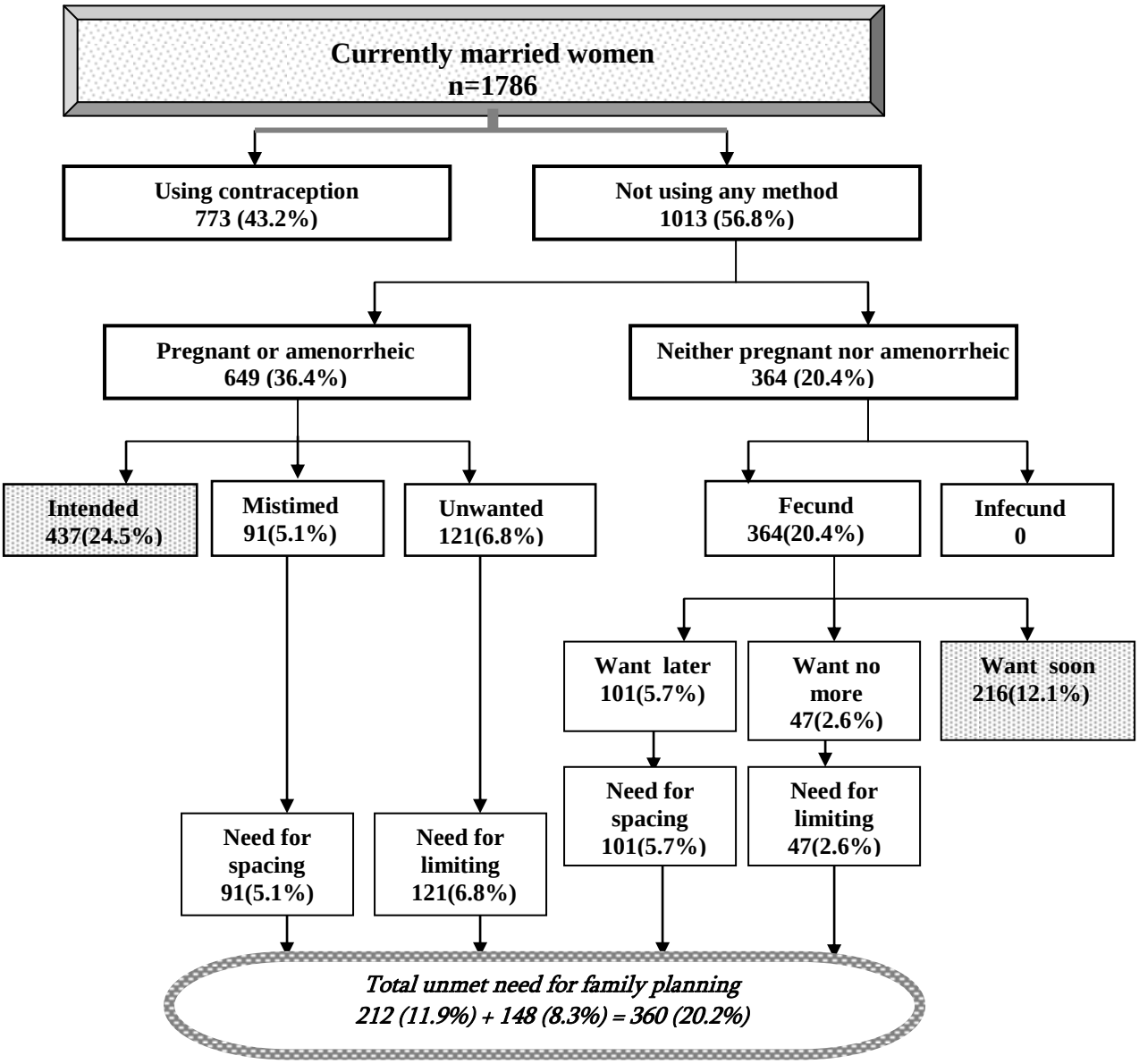

Figure 1. Calculation of current unmet need for FP according to the standard formulation, (September–December 2007)

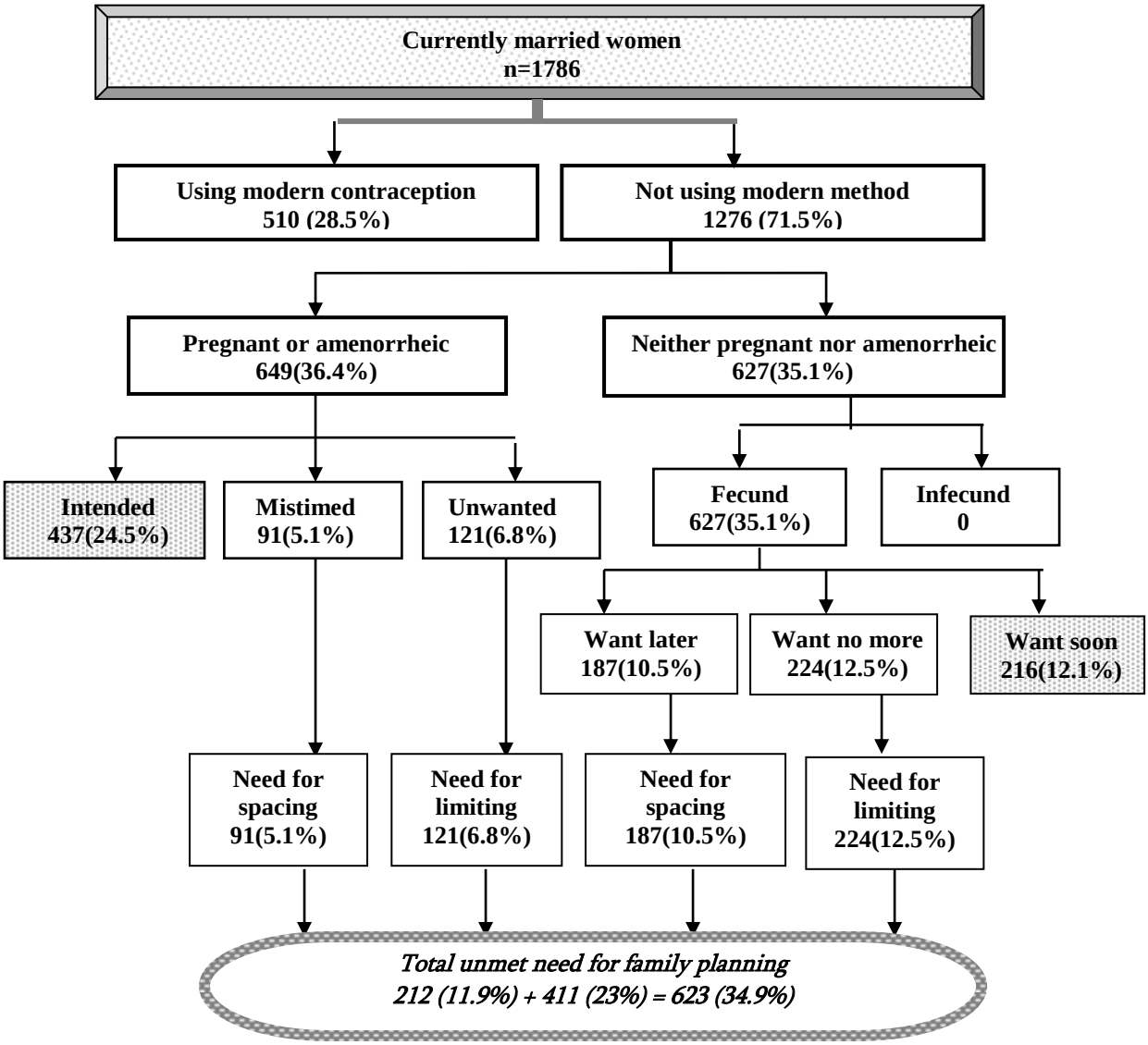

Figure 2. Calculation of current unmet need according to the expanded formulation (September–December 2007)

Table 1. Reasons of unmet need as stated by study subjects, (September–December 2007)

Reasons of unmet need	No. of contraceptive non-users	%
Side effects	172	27.6
Health concerns	135	21.7
Low perceived risk of pregnancy	127	20.1
Family opposition	57	9.1
Religious causes	33	5.3
Ambivalence	28	4.5
Don't know how to use contraception	19	3.0
Hard to get contraception	13	2.1
Bad services at FP center	10	1.6
Don't know types of contraception	8	1.3
Hard to go to FP center	8	1.3
High price of contraception	8	1.3
Other reasons	5	0.8
Total	623	100.0

Table 2. Special reasons of unmet need stated by women with unplanned pregnancy (September–December 2007)

Reasons of unmet need	No. of women with unplanned pregnancy	%
Not using contraception	86	47.5
Using traditional contraception	58	32.0
Using contraception incorrectly	37	20.4
Total	181	100.0

Table 3. Special reasons of unmet need stated by amenorrheic women with unwanted childbirth (September–December 2007)

Reasons of unmet need	No. of amenorrheic women with unwanted childbirth	%
Not using contraception	20	64.5
Using contraception incorrectly	11	35.5
Using traditional contraception	0	0.0
Total	31	100

Table 4. Association between level of education of women and the reasons of unmet need (September–December 2007)

Reasons of unmet need	Level of education										Total		p value*
	Don't read and write		Primary		Secondary		University graduate		Post graduate				
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	
Health concerns / side effects	31	31.3	111	50.6	80	60.1	78	50.3	7	41.2	307	49.3	0.001
Low perceived risk of pregnancy	34	34.3	34	15.5	20	15.0	38	24.5	1	5.9	127	20.4	0.000
Family opposition and religious causes	15	15.2	38	17.4	18	13.5	14	9.0	5	29.4	90	14.4	0.079
Lack of knowledge and ambivalence	17	17.2	17	7.8	7	5.3	17	10.9	2	11.8	60	9.6	0.031
Accessibility reasons	2	2.0	19	8.7	8	6.0	8	5.2	2	11.8	39	6.3	0.170
Total	99	100.0	219	100.0	133	100.0	155	100.0	17	100.0	623	100.0	0.000

** Using χ^2 test , d .f = 4*

Big proportion of women with unmet need are forced by the husband and his family to follow their commands and bring as many children as they want. So unmet need from this women's rights, is considered as an indicator of violation of such rights and one of the several basic rationales for women's empowerment.[15] In Sedgh et al.[14] research family opposition was stronger in Sub-Saharan African countries where 23% of women gave this reason for contraceptive non-use, as the women who face opposition to FP are conceptually less likely to be served by the provision of contraception supplies.

Cost and accessibility have been identified as barriers to the use of FP services for poor rural women.[16] The

present study indicated that accessibility causes form 6.3%. One of these causes is the cost of the contraception which makes only 1.3%. A very much higher figure was found in Burkina Faso, where 12% of women cited expensive contraception as a reason for contraceptive non use.[14]

Adair[16] in his study in Sub-Saharan Africa during 2007 found that, contraceptive prevalence rate is more than five times higher among women in the highest wealth quintile compared with those in the lowest. Finger[17] in his study in Sub-Saharan Africa too suggested that, educated and wealthier women are more likely to be able to pay for their contraception and may get it from a private sector, while poor uneducated women may rely on the public sector for their method supply where narrow range of contraceptive choice is a usual situation.

In the present study cost reason is not frequently suggested as an obstacle for contraceptive non use mainly because the most important types of modern contraceptives namely intrauterine devices, oral contraceptives, injections and male condom are provided almost free of charge in the FP centers in the city.[18] Religious causes form 5.3% of the unmet need causes indicated by the present study. Almost a similar figure was reported by Chaudhury[2] in his study in South Asia where he stated that religious causes was claimed by 3.2% of respondent women.

A number of studies has indicated that ambivalence towards pregnancy (by which women do not know whether they want children or not), is a barrier to early and continuous prenatal care as well as professional delivery care.[19] In the present study, ambivalence about pregnancy makes about 4.5%. A similar result was indicated by Sedgh et al[14] which was about 5%.

A large proportion of women in Mosul get married at a very young age, i.e. 13-15 years, within one year or two become pregnant leading to the problem of adolescent pregnancy. Adolescent marriage occurs in some eastern countries including Iraq particularly in rural areas and even urban regions have adopted adolescent marriage for girls.

Most of adolescent mothers are ambivalent, they do not know whether they want to get pregnant or not. They are young and got a long fertile life to spend, at the same time they want to complete their families or most of it within the first five years of their marriage. So they are hesitated whether to take contraception or not. Furthermore, ambivalent users may also be more likely to use methods inconsistently.[20]A similar picture of adolescent pregnancy is found in developed countries too, like USA; with high prevalence of illegal sexual relationship.[21]

Other causes make 0.8% which include few minor causes like rural to urban migration. David et al[6] in their study suggested that migrants possess limited knowledge of modern contraceptive methods, therefore, may experience unmet need for contraception or may have a limited choice of modern contraceptive methods during their first year in an urban district.

On testing the presence of association between level of unmet need and maternal education, low perceived risk of pregnancy happened to be the reason with highest significant association (p=0.000) by which the fraction of women with unmet need is higher among illiterate compared to high education grades. Women with no education frequently miss judge the possibility of pregnancy, and its relative risk when it is unplanned.

The same was true for lack of knowledge and ambivalent causes. Health concerns and side effects showed an inverse picture where the higher fraction of unmet need women is seen among educated women. Educated women are frequently conservative, think about the side effects of the modern contraceptives more seriously than those with no education.

On the other hand, family opposition and religious causes were not significantly associated with the level of maternal education as those reasons arise from old and deep beliefs of the family itself and got nothing to do with the level of women's education.

The present study describes the unmet need for FP among married women in child bearing age in Mosul City in the north of Iraq. It is useful to describe it's reasons and association with educational background of the women. An important point that gives strength to the present study is the relatively large and city wide representative sample with an excellent response rate (97%). However, causal association and extent of over and under reporting of the level and reasons of unmet need cannot be determined, although the study questionnaire is valid and reliable.

It is important to study unmet need in a longitudinal perspective; which is the only research design that permits evaluating transition in FP status over time.

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پوختە

پروفایلێ ڕێکخستنا خێزانی لجەم ئافرەتێن باژێرێ موسلێ ل باکورێ ئیراقێ ئەوێن پیویستی پێ هەی بەس ب کار نائینن: ڤەکولینەکا برگەیی

پێشەکی: ل ڤان سالێن چوویی بکارئینانا دژی ئافزبوونێ ل گەلەك دەولەتێن پاشکەفتی زێدە بوویە دگەل حەزا وان بو پێکئینانا خێزانێن ب کێمتر پچویك. نێزیکی 150 ملیون ئافرەتا ل جیهانێ نەڤێن ب زگپریێ کەڤن یان ژ ی گیروکەن. ئەڤ جورە ئافرەتە دهێنە نیاسین کو پیویستی ڕێکخستنا خێزانی بەس ب کار نە ئینانە.

ئارمانج: دیارکرنا ڕێژا ئەوان کەسێن کو پیویستی ب ڕێکخستنا خێزانی بەس ب کار نە ئینانە ل باژێرێ موسلی ل باکووری عێراقێ و دیارکرنا ئەگەرا.

ڕێکێن ڤەکولینێ: ڤەکولینەکا برگەیی هاتە کرن و 1786 ئافرەتێن د ماوێ ئافزبوونێ دا هاتنە وەرگرتن ل یەکا ڤاکسیندانێ دا ل بنگەهێن ساخلەمیێن بێن هاتینە دەستنیشانکرن. فورمەکا پرسیارا یا ستاندەرکرێ هاتە ب کارئینان ب ریکا چاڤپێکەتنا دگەل کەسێن پشکدار.

ئەنجام: ئەگەرێن سەرەکی بو نەکائینانا ڕێکخستنا خێزانی ئەگەرێن گریداین ب ساخلەمیێ و خرابییێت دەرمانا (49.3٪) و لدویف دا نەزانینا ئافرەتا لدور مەترسیا ئافزبوونێ دا (20.1٪)، ئەگەرێن ئاینێ و خێزانێ (14.4٪)، نەزانین لدور هەبونا ڕێگرێن ئافزبوونێ و چەوانیا ب دەست ڤەئینانا وان (10.6٪)، و ئەگەرێن دی (5٪).

دەرئەنجام: یا گرنگە کو دراسەتەکا یا پاشەرۆژی بهیتە کرن. ئەڤە باشترین ریکە ژ بو هەلسەنگاندنا گهورینێن بێن د چێدبن ل کائینانا ڕێکخستنا خێزانی.

الخلاصة

الاحتياجات الغير الملباة للنساء المتزوجات في مدينة الموصل, شمال العراق

خلفية الموضوع: هناك زيادة مطردة في استعمال موانع الحمل في السنوات الأخيرة في معظم البلدان النامية, وعلى الرغم من هذا فقد لا يتم استخدام أي طريقة لتحقيق هذه الرغبة. هذه المجموعة من النساء تعاني من احتياجات غير الملباة إلى تنظيم الأسرة.

هدف الدراسة: إن هدف هذه الدراسة هو تقييم الاحتياجات الغير ملباة للنساء المتزوجات في سن الإنجاب والأسباب المؤدية إليها في مدينة الموصل في شمال العراق

النتائج: أظهرت الدراسة إن من أهم الأسباب المسئولة عن الاحتياجات الغير ملباة هي الجوانب الصحية وحيث شكلت (49%) من الأسباب , تليها قلة إدراك خطورة الحمل غير المنظم(20%), الأسباب الدينية والعائلية لاستخدام موانع الحمل (14%), ثم عدم المعرفة بموانع الحمل وكيفية الحصول عليها (10,6%). أما الأسباب الأخرى فقد شكلت نسبة لاباس بها (5%) .

الاستنتاج: إن من الأهمية بمكان هو إن يتم تصميم وتطبيق دراسة مستقبلية لهذا الموضوع وذلك للتعرف على التغييرات التي تحصل في واهم أسبابها.

GENETIC RELATIONSHIP ASSESSMENT AMONG *STAPHYLOCOCCUS AUREUS* ISOLATES IN KURDISTAN REGION-IRAQ USING AMPLIFIED FRAGMENT LENGTH POLYMORPHISM (AFLP) MARKERS

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ABSTRACT

Background AFLP-PCR is a highly sensitive and reproducible tool used in molecular biology to detect DNA polymorphisms and had become widely used for the identification of genetic variation and phylogentic studies of many organisms including strains of Pathogenic bacteria. *Staphylococcus aureus* is one of the most important pathogens causing nosocomial and community acquired infection. Typing of *St. aureus* strains is necessary for proper epidemiological investigation of both sources and modes of the spread of different strains and subsequently, to design appropriate prevention and control measures.
Aim The use of AFLP markers to evaluate the phylogenetic diversity and genetic distance among isolates collected from different sites of infection in different geographical places in Kurdistan Region-Iraq.
Methods Eight isolates were collected from three major hospitals in Kurdistan region in Iraq including (Dr. Khalid General Hospital in Koya city, Teaching Hospital in Erbil city and Azadi General Hospital in Duhok city) these isolates were isolated from Urine, skin and burn infections. These isolates were subjected to AFLP-PCR markers using different combination of selective primers *PstI/True91*.
Results The values of genetic distance among eight isolates ranged from (1.289 to 0.320). It was clear that the lowest genetic distance (0.5025) was found between isolates number 7 and 8 which were isolated from urine and burn infections in Erbil respectively, whereas the highest genetic distance (1.5090) was found between isolates number 5 and 7 representing burn sample from Duhok and urine sample from Erbil respectively. Phylogenetic diversity analysis among different *S. aureus* isolates. Indicated that all eight isolates were classified completely into four major genetic groups named as *Sa*-1, *Sa*-2, *Sa*-3 and *Sa*-4. The first group included sub-division number 1, 5 and 3. The second group included sub-division number 2 and 6. The third group included sub-divisions number 7 and 8. The fourth group included sub-division number 4.
Conclusions AFLP banding pattern revealed a high degree of DNA polymorphisms among the selected isolates which could clearly be noticed. The high polymorphism was reflected in a high genetic variation among the geographically isolated strains of *St aureus*.

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Key words: *Staphylococcus aureus*, AFLP, Genetic relationship

Staphylococcus aureus is one of the most successful and adaptable human pathogens causing nosocomial and community settings.[1] Typing of *St. aureus* strains is necessary for proper epidemiological investigation of both sources and modes of the spread of different strains and subsequently, to design appropriate prevention and control measures.[2] The goal of genotyping studies is that epidemiologically related isolates collected from hospitals are able to be linked to one another. The incorporation of molecular methods for typing of

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nosocomial pathogens has assisted in efforts to obtain a more fundamental assessment of strain and inter-relationship.[3]

Establishing clonality of pathogens can aid in the identification of the source (environmental or personnel) of organisms and distinguish infectious from non-infectious strains.[4] One of the molecular typing methods is the Amplified Fragment Length Polymorphism. AFLP Originally was applied to the characterization of plant genomes, which proved to be a powerful procedure for genetic mapping, genotyping, identification and in taxonomic studies.[5] AFLP has been applied to bacterial typing.[6- 10] Studies of [6, 8,10] demonstrated that AFLP is reproducible and has good ability to differentiate clonally derived strains.[6-10] AFLP is a genome fingerprinting technique based on the selective amplification of a subset of DNA fragments generated by restriction enzyme digestion.[5] The combination of different restriction enzymes and the choice of selective nucleotides in the primers for PCR make AFLP a useful and new system for molecular typing of microorganisms.[11] The aim of this study was to use AFLP markers to evaluate the phylogenetic diversity and genetic distances among isolates were collected from different site of infection in different geographical places.

MATERIAL AND METHODS

Bacterial isolates and DNA isolation

Eight of isolates were collected from three hospitals in Kurdistan region include Dr. Khalid General Hospital in Koya city, Teaching Hospital in Erbil city and Azadi General Hospital in Duhok city kindly supplied by Scientific Reseach Center-Duhok University. They were identified and characterized using enrichment and selective media in addition to biochemical tests such as catalase, coagulase, and DNase tests. These isolates were selected according to different sources including; Urine, skin and burn infection as well as different geographical location including Koya, Duhok and Erbil cities. Genomic DNA was extracted from these isolates according to Roder and Broda method[12] with minor modification.

AFLP Preparation

The AFLP markers performed as described by[5] with minor modification and as follow; 500ng of DNA from each sample was double digested with 5U each of the two restriction enzyme, *Tru91* (recognition site 5'T↓TAA3') and *PstI* (recognition site 5'CTGCA↓G3'), in 30µl final volume of reaction mix containing, 1x one phor all buffer (Pharmacia Bioteh, Uppsala, Sweden). The reaction was incubated for three hours at 37C. The generated DNA fragments were then ligated with *Pst I* and *Tru91* adapters with concentration (5 and 50 pmol) respectively, 1U of T4-DNA ligase, 1Mm rATP and 1X of one phore-Buffer were then added and the reaction was incubated for 3hr. at 37C. After the ligation, the reaction mixture was diluted to 1:5 using sterile distilled water. Preselective PCR amplification was performed in a reaction volume of 20 µl containing 50ng of each of the oligonucleotid primers (P00, M82) corresponding to the *Tru91* and *Pst I* adapters, 2µl of template- DNA, 1U *Taq* DNA polymerase, 1XPCRbuffer and 5mM dNTPs. The PCR amplification was performed in (M.W.G.Biotech., UK) thermal cycler using following program: 30 cycles of 30s at 94 Cº, 1min at 60Cº, 1min at 72 Cº. The preamplification product was then diluted to 1:5 and 2µl was used as template for selective amplification. Five different reactions were prepared using *Tru91* and *Pst1* selective primers combinations (listed in table 1). The Amplification was performed

Table 1. Represents the selective primers and their sequences used in this study

No.	Selective primer ('5-----3')	
1	P109	GACTGCGTACATGCAGAATG
2	P237	GACTGCGTACATGCAGGATA
3	M289	GATGAGTCCTGAGTAATAAA
4	M181	GATGAGTCCTGAGTAACCCC
5	M184	GATGAGTCCTGAGTAACCGA

in program for 36 cycles with the following cycle profile: a 30s DNA denaturating step at 94 Cº, 30s annealing step, and a 1 min extension step at 72Cº. The annealing temperature was varied in the first cycle it was 65Cº; in each subsequent cycle for the next 12 cycle it was reduced by 0.7 Cº (touchdown PCR), and for the remaining 23 cycles, it was 56 Cº. The selective amplification products were loaded onto 6% denaturating polyacrylamid gels, and DNA fragments were visualized using silver staining kit (Promega, Madison, Wis) as described by the supplier, silver – stained gels were scaned to capture digital images of the gels after air drying.[13]

Data analysis

Positions of scorable AFLP bands were transformed into binary character matrix (" 1" for the presence and "0" for the absence of a band at a particular position); only polymorphic bands were used in the analysis. Jaccard's similarity index [14] between any pairs of strains was determined. The Jaccard similarity matrix was used for cluster analysis (UPGMA) to study the genetic relationships among the strains. Jaccard's similarity index estimation and UPGMA were done using the software package NTSYS-PC version 2.0.[15]

RESULTS

In this study eight isolates of *St aureus* have been selected from different site of infections and collected from different hospitals in Kurdistan regions Iraq, supplied by scientific Reseach Center in Duhok University to study phylogenetic diversity and genetic distance to these isolates using AFLP markers. Five reactions have been performed on these isolates using different combinations of selective primers. Figure 1 shows the amplifications results of these primers and reveals the polymorphisms among these isolates. Phylogenetic tree was created by the unweighted pair-group method arithmetic (UPGMA) average cluster analysis.[16] This program is based on the Nei formula[17] for detecting genetic variability; therefore the results of all primers were introduced in a matrix to be calculated by the computer program. Table 2 summarizes the values of genetic distance of eight *S. aureus* isolates from Urine, skin and burn infections.

The genetic distance values range from (1.289 to 0.320). It was clear that the lowest genetic distance (0.5025) was found between isolates number 7 and 8 which were isolated from urine and burn infection in Erbil respectively, This indicates the close genetic relationships of these isolates although they are from different source infection sites, whereas the highest genetic distance (1.5090) was found between isolates number 5 and 7 representing burn sample from Duhok and urine sample from Erbil respectively. Genetic fingerprinting and phylogenetic diversity among different *S. aureus* isolates were determined by converting AFLP data into a Jaccard similarity matrix

and analyses by UPGMA to produce a phylogenetic tree. Results in table 2 were further used to design a dendrogram. Diagram 1 showed the cluster analysis and phylogenetic tree depending on genetic distances in order to reveal the genetic relationship between the eight isolates subjected to AFLP-PCR analysis. Analyzing this dendrogram show the results of the five selective primer combinations are presented in figure 1. The overall result indicated that all 8 isolates were classified completely into four major genetic groups named as *Sa*-1, *Sa*-2, *Sa*-3 and *Sa*-4. The first group included sub-division number 1, 5 and 3. The second group included sub-division number 2 and 6. The third group includes sub-divisions number 7 and 8. The fourth groups include sub-division number 4.

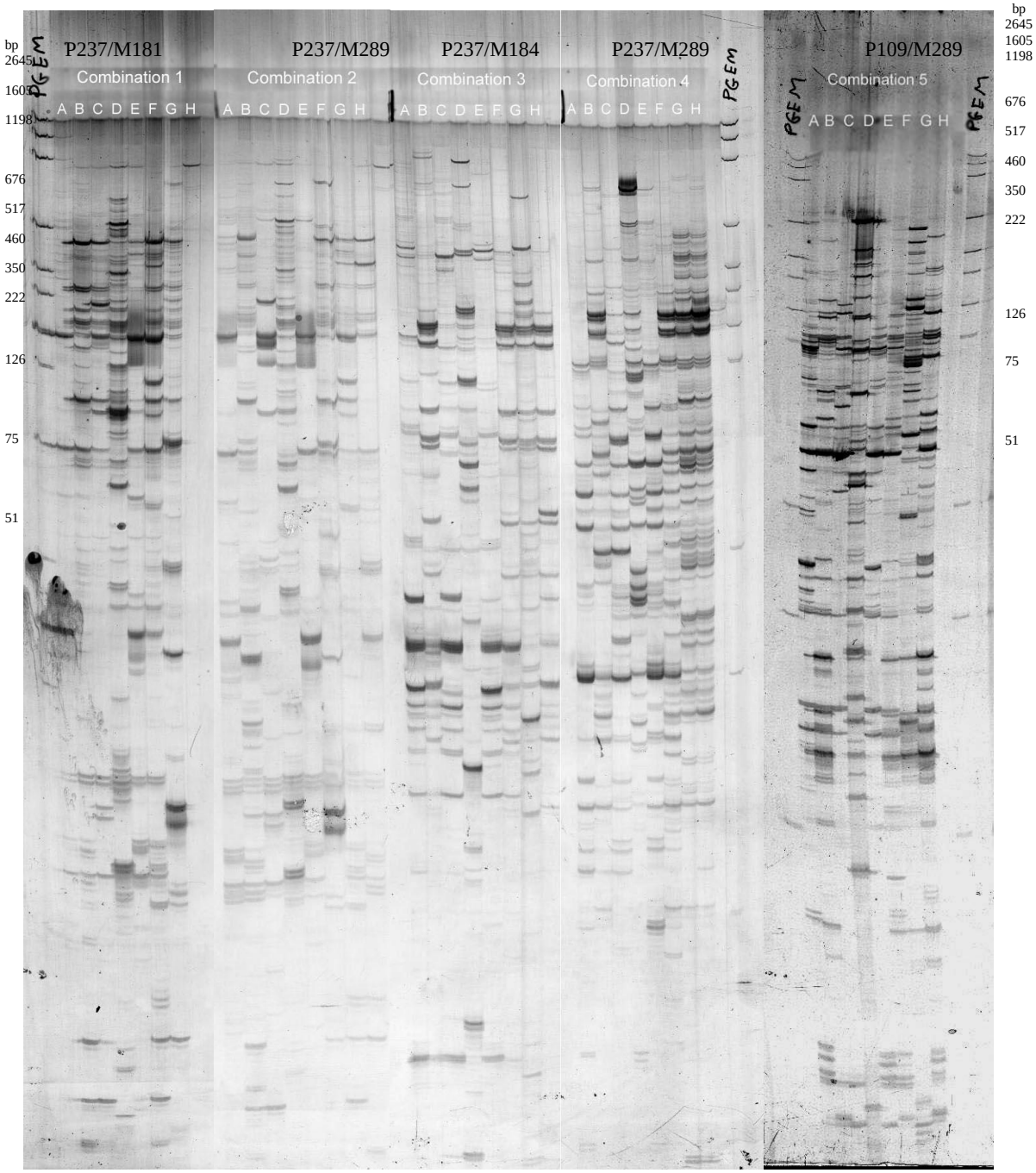

Figure 1 Represent the amplification pattern of AFLP markers in eight isolates of *St. aureus* collected from different sources (A: Urine-Koya; B: Skin-Koya, C: Burn-Koya; D:Urine-Duhok; E: Burn-Duhok; F: Skin-Duhok; G: Urine-Erbil; H: Burn-Erbil) by five selective primers combinations

Table 2. the genetic distance values for *S. aureus* isolates used in AFLP analysis

1 0
2 1.0030 0
3 0.7264 1.0096 0
4 1.2131 0.9829 1.2196 0
5 0.5212 1.0929 0.6254 1.4305 0
6 0.9852 0.5525 0.8899 1.1998 0.9369 0
7 1.2059 0.8014 1.1071 1.2590 1.5090 0.7996 0
8 1.2643 0.6366 0.9831 1.1423 1.3029 0.5578 0.5025

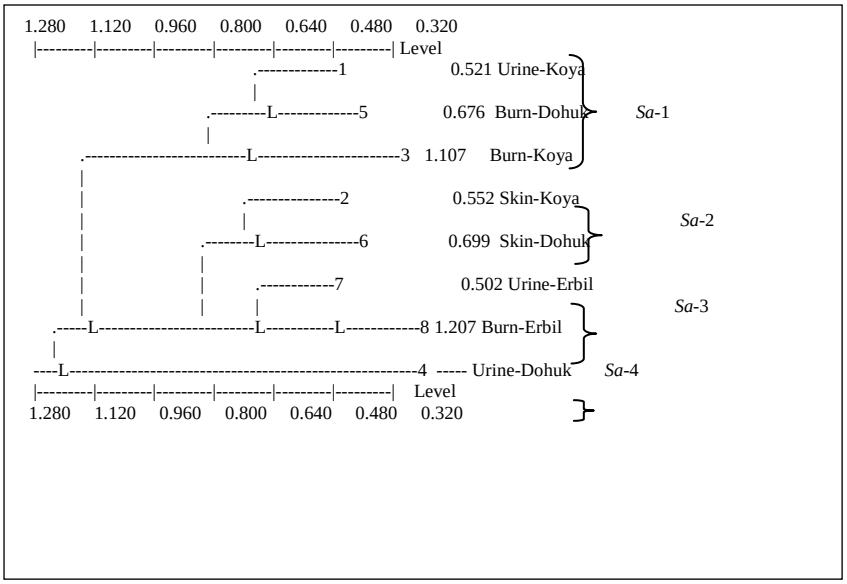

Diagram 1. Phylogenetic diversity of *St. aureus* by using AFLP markers

DISCUSSION

The results of this study find much evidence that genotypic clusters were not associated with site of infection or geographical place. For instance the isolates in subdivision *Sa-2* were originated from the same source of infection (skin) but from different city, whereas isolates in subdivision *Sa-3* were originated from different source include (urine and burn) collected from same city. AFLP banding pattern revealed a high degree of polymorphisms among the selected isolates. The high polymorphism reflected a high genetic variation among the geographically isolates strain. DNA polymorphism was indeed clearly noticed within isolates collected from the same infection. The results may also suggest possible and frequent occurrence of mutations in *St. aureus* in different sources and location and this may provide empirical for the idea that the genetic clusters in bacteria maintained in the absence of adaptation to different niches, these results to be agreed on the results conducted in Switzerland to study the genetic Diversity of *Staphylococcus aureus* Strains Colonizing Humans.[18] Determination of genetic distance is very important in different fields, for example in bacteriology, in order to understand evolutionary relationships, determine the specific source of infection and route of transmission of specific isolate clones. Diverse genotype may have different levels of invasiveness and virulence and may originate from various sources within the hospital environment, therefore the infection control measures should consider this finding.[19] Such highly polymorphic

AFLP has been reported,[18, 20] in *St aureus* as well as in other microorganisms.[21-26] Suggesting the usefulness of AFLP markers used in molecular typing of microorganisms.

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پوختە

هە لسنگاندنا پە یوەندیا زك ماکی دنا ف برا تیرێت (*Staphylococcus aureus*) ل هەریما کوردستانا عیراق

–بکارئینانا نیشاندە رێن جێوازین دریژبونا پارچێن DNAهندە جارAFLP

بشتە وانی: نیشاندە رین جیوازێین دریژبونا پارچێن DNA.هندەجار AFLPدهێتە هە ژمارتن کو گە لە ك هە ستە دارە و شیان بو وە رگرتنا ئە نجامێنوەك یێن پشتگیر لسەر زنجیرا کارلیکادوو هند بوونی PCRدهێتە بکارئینان وەك ئا میرەك ل زیندە واری گە ردی بو دیار بونا جێوازیا ت dnaبشێوەیەکێ بەر فرە هاتە بکار ئینان بو دەست نیشان کرنا جێوازیێن زك ما کی و خاندنا پە یوە ندیێن زك ما کی بو گەلەك زیندە وەرا وژ وان زیندەوەرا بەکیریا نەخوشیا چێ دکەت ,وژ وان Staphylococcus aureus دهیتە هە ژمارتن ژ گرنکترین نە خوشیێن ل نە خشخانا ودنا ف کو مە لیدا بە لاف دکەت. دابە شکرنا تیرێن گرنگ بو فە کولینا پەژی یا ساخلەم ژ ژ یدەرا وریگێن بەلاڤە بوون وبڤێ چەندێ پیڤە رەك بو پاراستنێ و کونترەلکرنێ هاتە دانان

ئارمانج: بکارئینانا نیشاندەرێن AFLPبو هەلسە نگاندنا جێوازیا ودەست نیشانکرنا درێژبونا زك ماکی دناڤ بەرا تیرێن خریا ئیشداریین و ئە ڤێت هاتینە کومکرن ژ هندەك تووشبوونێت جورە و جور و جهێن جوگرافی یێن جێواز ل کوردستانا عیراقێ

متا و رێکێن ڤە کولینێ: هەشت تیرە هاتنە کومکرن وژ سێ نە خوشخانێت گشتی لکوردستانا عیراق و ئەوژی نە خشخانا خالد ل کوێیە و نە خوشخانا فێر کرنێ یا گشتی ل هە ولێرێ و لنە خوشخانا ئازادی یا گشتی ل دهوکێ ئە ف تیرە هاتنە وە رگر تن ژ تووشبووییێن جورە و جور ژ وان میز ,پیستو تو شبوو نێت سووتنێ و ئە ڤ تیرە هاتە مە لکە چیکرن بوو نیشاندەرا AFLP-PCR.بکار ئینانا تێکەل کرنا دەست پێکەرییێن جێواز یێن ژێ گرتی *PstI_Tru91*

ئە نجام : بهایێن دیراتیا زك ما کی دناڤبە را تیرادا ژ(0.320_1.289) و کێمترین دیراتیا ز کماکی هندە بو (0.525) دنا ڤبە را تیرا ژمارە 7,8 وئەوژی هاتینە وەر گرتن ژ میز و سووتنێ ل نەخوشخانا هە ولێر لدیف ئێك. بلند ترین دیراتیا زك ماکی هندە بو (1.5090)دناڤ بەرا تیرا 5,7 ئە ڤا هاتیە وەر گرتن ژ تووشبوونێن سووتنێ ل نە خووشخانا دهو کێ و میز ل هەو لێرێ. بو شلو ڤە کرنا پیوە ندیێن زك ماکی دیارکر کو ئە ڤ هەشت تیرە دابەش بوون بو چوار گروپێ سەرەکی و هاتنە نیاسین بڤی شێوەی Sa1,Sa2, Sa3,Sa4. گروپێ ئێکێ Sa1پێك هات ژ سێ گرو پێن ناوەندی 3,5,1 و گروپێ دووێSa2 هایە دابە شکرن بو دوو گرو پێ ناوەندی 2,6 گرپێ سیێ Sa3 پێك هات ژ دوو گرو پێ ناوەندی7.8 و گرو پێ چارێ Sa4پێك ژ گروپەکێ ناوە ندی پێك هات ئە وژی ژمارە 4

دە ر ئە نجام: شێوین کورزا یێن AFLP دیارگر پلەیە کا بلند ژ جێوازیا لسەر ئاستێ DNAدناڤ بەرا تیریێن هژمارتن تهێنە تیصبینە ر کرن ب شیچوە یە کی ئاشکرا وئەڤ جێوازییێن دیار دکەت جێوازیا زك ماکی دنا ڤبەرا تیریێن هاتینە وە رگرتن ژ ژێدەرییێن جێواز.

الخلاصة

تقييم العلاقة الوراثية بين عزلات *Staphylococcus aureus* في منطقة كردستان- العراق باستخدام مؤشرات تباين اطوال قطع الدنا المتضاعفة (AFLP)

الخلفية: تعتبر مؤشرات تباين اطوال قطع الدنا المتضاعفة (AFLP) والمعتمدة على سلسلة التفاعل التضاعفي (PCR) في غاية الحساسية و القدرة للحصول على نتائج ثابتة تستخدم كاداة في البايولوجي الجزيئي لاكتشاف الاختلافات في الدنا واصبحت واسعة الاستخدام في تشخيص الاختلافات الوراثية ودراسات العلاقات الوراثية للعديد من الكائنات من ضمنها البكتريا المرضية ومنها المكورات العنقودية *Staphylococcus aureus* حيث *تعتبر* واحدة من اهم الممرضات المسببة عدوى المستشفيات والمجتمع المكتسبة. ان تنميط العزلات ضروري في التحري الوبائي السليم لكلا من المصادر وطرق الانتشار وبالتالي وضع قياسات للوقاية والسيطرة.

الاهداف: استخدام مؤشرات AFLP لتقييم التباينات وتحديد البعد الوراثي بين عزلات المكورات العنقودية والتي جمعت من اصابات مختلفة ومناطق جغرافية مختلفة في كردستان العراق.

مواد وطرق البحث: جمعت ثمانية عزلات ومن ثلاث مستشفيات عامة في كردستان العراق وتشمل (مسشفى خالد العام في كويا, المستشفى التعليمي العام في اربيل ومستشفى ازادي العام في دهوك). أخذت هذه العزلات من اصابات مختلفة منها الادرار, الجلد واصابات الحروق وقد خضعت هذه العزلات الى مؤشرات AFLP-PCRباستخدام مزيج من بادئات مختلفة مختارةPstI/True91 .

النتائج: كانت قيمة البعد الوراثي بين العزلات تتراوح مابين 1.289- 0.320 وكان اقل بعد وراثي 0.525 بين عزلة رقم 7 و 8 المأخوذة من الادرار والحروق في في مسشفى اربيل على التوالي. اما اعلى بعد وراثي كان 1.5090 بين عزلة رقم 5و7 المأخوذة من اصابة الحروق من مستشفى دهوك والادرار من اربيل. في تحليل العلاقة الوراثية اظهرت ان العزلات الثمانية قسمت الى اربع مجاميع اساسية سميت كالاتي *Sa2* ,*Sa3*, *Sa*1و *Sa4*.المجموعة الاولى *Sa1* شملت ثلاث مجاميع ثانوية 1,5و3 اما المجموعة الثانية *Sa2*قسمت الى مجموعتين ثانويتين 2و6 اما المجموعة الثالثة *Sa3* فشملت مجموعتين ثانويتين 7و 8 والمجموعة الرابعة *Sa4* فقد شملت مجموعة ثانوية واحدة هي رقم 4.

الاستنتاجات: طراز الحزم للAFLP يظهر درجة عالية من التباينات على مستوى الدنا بين العزلات المختارة والتي من الممكن ملاحظتها بشكل واضح . ان هذه الاختلافات تعكس التباين الوراثي بين العزلات الماخوذة من مصادر مختلفة.

THE ASSOCIATION BETWEEN IRON DEFICIENCY ANEMIA AND FIRST FEBRILE SEIZURE: A CASE-CONTROL STUDY

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ABSTRACT

Background Febrile seizures (FS) are the most common type of seizures in children. The relationship between iron deficiency anemia (IDA) and first FS has been examined in several studies with conflicting results.
Purpose The purpose of this study was to determine the association between IDA and first FS.
Patients and Methods In this prospective case-control study we assessed 112 children with a diagnosis of first FS, aged between 5 months and 4 years who were admitted to the emergency unit of Hevi Children's Hospital in Duhok/Kurdistan region/Iraq, or who visited private office of the authors, during January 2006 to July 2009. The control group consisted of 120 febrile children without convulsion; controls were matched to the cases by gender and age. Patients and controls were reviewed to determine iron status using the hemoglobin concentration (Hb), mean corpuscular volume, S. iron, and total iron binding capacity.
Results A total of 35 (31.2%) of cases had IDA, compared to 14 (11.6%) of controls, which is statistically significant, P = 0.003.
Conclusion IDA was more frequent among children with FS than those with febrile illness alone. The results suggest that IDA may be a risk factor for FS and screening for IDA should be considered in children presenting with the first FS.

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Key words: Febrile convulsion, Iron deficiency, Anemia

Febrile convulsions (FCs), also referred to as febrile seizures (FSs), are the single most common type of seizure in children, affecting 2% to 4% of youngsters before their fifth birthday. It is defined as a seizure in a healthy infant or young child, between 3 months and 5 years of age that is associated with febrile, usually viral, illness (rectal temperature >38° C), but not with intracranial infection or dehydration or a history of nonfebrile seizures.[1] Most FSs occur between 6 months and 36 months of age, peaking at 18 months.[2] The occurrence of a child's first (initial) FSs has been associated with: first or second-degree relative with history of febrile and afebrile seizures,[3] day care attendance,[4,5] developmental delay,[3] Influenza A viral infection,[6,7] human herpesvirus-6 infection,[8,9] and iron deficiency anemia.[10]

There is a controversy regarding the role of iron status in FSs.

The aim of this case-control study was to evaluate the relation of IDA with first FS.

PATIENTS AND METHODS

Children with first FC who were admitted to the emergency unit of Hevi Children's Hospital in Duhok/Kurdistan region/Iraq, or who visited private office of the authors, between January 2006 and July 2009 were included. Children with prior afebrile seizure history were not included. The diagnosis of FC was made clinically by a pediatrician based on the history given by the mothers and observation of

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the fit and exclusion of CNS infection by normal CSF examination (lumber puncture was done only for children < 18 mo of age).

At the same time children of the same age group with acute febrile illness without convulsion were used as control group.

Age, sex, developmental milestones, family history of febrile seizures or epilepsy, mean of the temperature peak at admission, and the underlying illness were recorded for all cases and controls. The best up to date method for diagnosing IDA is the serum level of transferrin receptors, however, this technology is not within our reach, therefore patients and control group were evaluated to determine iron status using the Hb, mean corpuscular volume (MCV), S. iron, and total iron binding capacity (TIBC). Iron deficiency anemia was defined as the presence of hemoglobin concentration < 10.5 gm/dl, MCV < 70 fl, serum iron concentration of < 22 µg/dl, and TIBC > 400 µg/dl.[11]

The ethics committee at college of Medicine / University of Duhok approved the study. Chi square was used for statistical evaluation.

RESULTS

The study group consisted of 67 (59.8%) boys and 45 (40.2%) girls; a total of 112 children. The control group consisted of 70 (58.3%) boys and 50 (41.7%) girls; a total of 120 children.

The age groups and the number of patients and controls with IDA are shown in table 1. There was a significantly higher rate of IDA among children with febrile convulsions than in controls (31.2% vs. 11.6%), p = 0.003.

The hematological indices of patients and controls with IDA are shown in table 2. The development, family history of FC or epilepsy, the cause of fever and the mean of temperature peak on admission in patients and controls are shown in table 3.The differences were not statistically significant

DISCUSSION

The association between IDA and impaired neurocognitive function is well established, and this association holds even when potential confounders such as psychosocial and environmental factors are taken into account,[12] whereas, the association between IDA and febrile seizures has been described in the last decade with contradictory results. Infants and toddlers, who are undergoing critical neurocognitive development, may be at particular risk for such effects.[12]

In this study, IDA was more prevalent among the cases with febrile convulsion, as compared to the controls (31.2% vs. 11.6%); these findings are in accord with those of previous studies. Daoud et al[13] observed a significantly lower plasma ferritin in the first febrile convulsion group than in the reference group (49 of 75 vs.

Table 1. Age groups and number of anemic patients and controls

Age groups (mo)	Patients No. (%)	Patients with IDA	Controls No. (%)	Controls with IDA
< 6	2 (1.8)	0	2 (1.7)	0
7-12	14 (12.5)	3	17 (14.2)	1
13-18	39 (34.8)	14	43 (35.8)	6
19-24	32 (28.6)	10	34 (28.3)	4
25-32	9 (8)	2	11 (9.2)	1
33-36	6 (5.3)	2	8 (6.7)	0
37-48	10 (8.9)	4	5 (4.2)	2
Total	112 (100)	35 (31.2%)*	120 (100)	14 (11.6%)*

**p = 0.003*

Table 2. The hematological indices of anemic patients and controls (ranges)

	Patients with IDA (n=35)	Controls with IDA (n=14)
Hb (g/dl)	8.2-9.6	8.8-9.4
MCV (fl)	55-63	61-66
S. iron (µg/dl)	8-14	11-17
TIBC (µg/dl)	438-575	430-544

Table 3. The development, family history of FC or epilepsy, cause of fever, and tempt. peak on admission in patients and controls

	Patients No. (%)	Controls No. (%)	P value
Delayed motor development	7(6.3)	13 (10.8)	0.25*
•Delayed expressive speech	5(4.5)	3(2.5)	0.42*
•Family history of FC	13(11.6)	7(5.8)	0.15*
•Family history of epilepsy	8 (7.1)	7(5.8)	0.7*
•Cause of fever			
-URTI	62 (55.3)	89 (79.5)	0.16*
-LRTI	11 (9.8)	7 (5.8)	0.33*
-GE	14 (12.5)	10 (8.3)	0.34*
-Other viral infections	25 (22.3)	14 (11.7)	0.06*
•Mean tempt. on admission	38.8 ±5 ºC	38.8 ±8 ºC	

** Not significant*

24 of 75), and Dawn et al[14] and Pisacane[15] reported a significantly higher rate of IDA among children with febrile convulsions than in controls (15% vs. 9% and 30% vs. 12%, respectively), whereas, in contrast, Kobrinsky[16] reported that iron deficiency raises the threshold for seizures. Unfortunately, there are no national data on the prevalence of IDA among children in Iraq or in Duhok. Two large scale studies, the Third National Health and Nutrition Examination Survey (NHANES III) and the third report on nutrition monitoring in the United States, reported the prevalence of IDA in 1-2 year olds to be 3 % and in one to three year olds to be 15 %.[17] A more recent study, conducted in an urban setting with an equal mix of lower and middle socioeconomic groups, noted that 10 % of one to three year olds had IDA.[18]

The mechanism by which iron deficiency impairs neurologic function is unknown. Iron deficiency could impair neurotransmitter mechanisms, and it has been shown to decrease expression of dopamine receptors in the rat brain.[19] It may also interfere with myelination and alters myelin proteins and lipids in oligodendrocytes.[20] In addition, several enzymes in neural tissue require iron for normal function,[21] and monoamine and aldehyde oxidase are reduced in IDA,[22] which is common during the second and the third year of life and has been associated with behavioral and development disturbances.[23] Fever can worsen the negative effects of iron deficiency on the brain and a seizure can occur as a consequence.[15]

Although the family history of FSs and family history of epilepsy were higher

among cases than controls, the differences were not statistically significant. FCs are sometimes associated with inheritance of the so-called FC trait, a tendency to convulse with fever because of a low seizure threshold. Most studies suggest a dominant mode of inheritance with reduced penetrance and variable expression and increased frequency of FCs when a first degree relative has FCs.[24] In a child with FC trait, the risk of an FC is 10% for the sibling and almost 50% for the sibling if a parent has FCs as well.[24] Cases and controls also did not differ in other risk factors for FS (e.g. delayed development), as shown in table 3.

Lead toxicity, which interferes with the use of iron, is associated with low serum iron concentrations, lowers the seizure threshold, and could easily account for the apparent association between iron deficiency and seizures in these children.[15] However, lead poisoning is very unlikely in our patients and no data are available from the clinical records that might indicate whether lead poisoning was present in our patients, and children with febrile seizures are usually children who are well before and after fit, and afebrile convulsions are uncommon among them.

In conclusion, IDA may be a risk factor for the first febrile convulsion and a full blood count and screening for IDA will therefore be warranted in the work up of children with the first febrile convulsion.

However, further larger studies are required and other measures of iron sufficiency including plasma ferritin should be measured to confirm the findings in this study.

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پوختە

پەیوەندی دناڤ بەرا کەم خوینی یا کێم بوونا ئاسنی و ئێکەمین لەرزینا تایێ

بنەکوك: لەرزینا تایێ ژ مشەترین جورێن لەرزینا یە(فیی) ل نك زاروکا, گەلەك ڤەکولین بو شروڤەکرنا پەویەندیێ د ناڤ بەرا بەرا کەم خوینی یا کێم بوونا ئاسنی و ئێکەمین لەرزینا تایێ هاتینە کرن ب ئەنجامێن هەڤ دژ.

ئامانج: ئامنج ژ ڤێ ئەوە بو دیارکرنا پە وەندی دناڤ بەرا کەم خوینی یا کێم بوونا ئاسنی و ئێکەمین لەرزینا تایێ.

شێواز: رێژا خوینێ , تێکرایا قەبارێ خروّکیچن سور , و رێژا ئاسنی دناڤ خوینێدا هاتە پیڤان بو 112 نەخوشێن تووش بوی ب ئێکەمین لەرزینا تایێ ئەوێن ژییّن وان دناڤ بەرا 5 مەها تا 4 سالان دماوێ ژ کانینا دووێ 2006 تا تیرمەهێ 2009 ,ل هەمان کات دە ئەو پیڤەر هاتنە کرن بو 120 زاروکێن تووشی تایێ بووین بێ لەرزین وەك گروپێ کونترول.

ئەنجام: کەم خوینی یا کێم بوونا ئاسنی هاتە دوست نیشانکرن ل نك 35 نەخوشا بەراوەدکرن دگەل 14 زارروکا ژ گروپێ کونترول.

دەرئەنجام و شیرەت: کەم خوینی یا کێم بوونا ئاسنی پتر یا بەربەلاڤە ل نك زاروکێن تووش بوی ب ئێکەمین لەرزینا تایێ.

الخلاصة

العلاقة بين فقر الدم الناتج عن نقص الحديد والاختلاجات الحرارية

الخلفية: الاختلاجات الحرارية هي من اكثر انواع الصرع شيوعا لدى الاطفال. اجريت عدد من البحوث لتفسير العلاقة بين فقر الدم الناتج عن نقص الحديد والاختلاجات الحرارية الاولى مع نتائج متناقضة.

الاهداف: الغرض من هذا البحث هو لمعرفة العلاقة بين فقر الدم والاختلاجات الحرارية الاولى.

الطرق: تم قياس نسبة الهيموكلوبين وحجم الكريات الحمرو نسبة الحديد في الدم ل(112) مريض مصاب باختلاج حراري اول,ممن تراوحت اعمارهم بين خمسة اشهر واربع سنوات للفترة من كانون الثاني 2006 ولغاية تموز2009 . وفي نفس الوقت تمت دراسة 120 طفلا مصابا بحمى بدون اختلاجات كمجموعة سيطرة.

النتائج: ظهر فقر الدم الناتج عن نقص الحديد في 35 مريضا مقارنة ب 14 طفلا من مجموعة السيطرة.

الاستنتاج والارشادات: فقر الدم الناتج عن نقص الحديد اكثر شيوعا بين الاطفال المصابين بالاختلاجات الحرارية , لذلك يجب التحري عن ذلك.

ZINC STATUS AMONG SMOKERS AND NON-SMOKERS: RELATION TO OXIDATIVE STRESS

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ABSTRACT

Objective To assess zinc status in cigarette smokers and to ascertain the relationship between the levels of serum zinc and oxidative stress.
Methods A cross-sectional study was carried out at Azadi Teaching Hospital, Duhok, Iraq, from December 2007 to June 2008.The study included 254 apparently healthy males(127 smokers and 127 non-smokers, aged 20-61 years), .Exclusion criteria were: a)minerals supplements, b)medication, c) recent or chronic infections. All the participants were invited for medical health examination. Data were collected from subjects according to self-administered questionnaire. Several biochemical parameters were estimated such as, serum zinc, serum antioxidant markers (ceruloplasmin and total glutathione), serum pro-oxidant by-products (malondialdehyde and peroxynitrite), and dietary zinc intake.
Results The percent of marginal zinc deficiency in smokers was significantly higher than that of non-smokers (50.1% Vs 42.6%, $p<0.05$). Smokers had significantly higher malondialdehyde (1.6±0.5 nmol/L) and peroxynitrite (1.7±0.34 mmol/L) serum levels than that of non-smokers (1.2±0.1 nmol/L and 1.4±0.32 mmol/L respectively,($p<0.05$) for both parameters. Serum zinc, ceruloplasmin, and total glutathione levels, were not significantly differed between the two groups, whereas the percent of abnormally high levels of oxidative stress markers were significantly higher in smokers than in non-smokers($p<0.01$). In respect to dietary zinc intake for smokers and non-smokers, no significant difference was found in daily dietary zinc intake for both groups ($p=0.45$).
Conclusion This study demonstrated that cigarette smoking is associated with marginal hypozincemia which may render smokers more susceptible to oxidative stress.

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Key words: Zinc, Smoking, Oxidative stress

Accumulating evidence suggests a link between cigarette smoking and oxidative stress.[1] Smokers are at greater risk than non-smokers of having intracellular oxidizing agents, particularly free radicals.[2] Tobacco smoke contains numerous compounds, many of which are oxidants and pro-oxidants capable of producing free radicals and enhancing the oxidative stress in vivo.[3] The high production of these oxidants and pro-oxidants associated with smoking may exceed the capacity of the oxidative defense system resulting in oxidative damage to certain proteins, lipids and DNA.[4] Data on the other hand, suggest that zinc is a necessary factor in a variety of "antioxidant", enzymes, particularly superoxide dismutase, catalase, and peroxidase. Alteration of zinc metabolism such as adequate zinc which is unavailable for these enzymes may contribute

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to the oxidative damage observed in smoking.[5] It has been reported that cigarette smoking decreases appetite and may decrease the amount of nutrients consumed by the smokers.[6] Cigarette smokers may be less likely to consume micronutrient supplements and more likely to consume alcohol and other substances that interact with nutrient metabolism. Tobacco leaves contain a significant amount of cadmium which is absorbed into the body when a person smokes or chews tobacco. This cadmium can replace the bivalent metals like zinc(Zn), copper(Cu), and manganese (Mn) from superoxide dismutase (SOD) which is a powerful antioxidant.[7] A recent study indicates that even though dietary intake of minerals in smokers was adequate, the habitual diet was not able to maintain the serum zinc concentration in the normal ranges, and thus making smokers more susceptible to oxidative stress.[8] Therefore the present study was designed to assess zinc status in a sample of cigarette smokers in comparison with that of non-smokers and to ascertain the relationship between the levels of serum zinc, oxidant and antioxidant variables.

METHODS

This study was carried out on 254 apparently healthy males aged 20-61 years. They were recruited by consecutive sampling procedure from different areas of Duhok city. One hundred twenty seven were smokers and 127 were non-smokers. Both smokers and non-smokers underwent medical health examination at Azadi Teaching Hospital, Duhok, Iraq. None of the participants was being on mineral supplements, medication, or having recent infection or chronic disease. Verbal consent was obtained from the subjects after the nature of the study had been fully explained to them. The study protocol was approved by postgraduate committee of the University of Duhok/Medical Branch.

A pre-tested questionnaire was designed to obtain information on age, smoking habit, and habitual food consumption patterns of each participants.

Selection of smokers was done according to the number of cigarettes smoked per day. For a better assessment of the impact of smoking status on parameters under testing, this study included only heavy smokers who used to smoke at least 20 sticks per day and excluded mild or casual smokers to leave a buffer zone of comparison between smokers and non-smokers. All smokers included were males, because female smokers in our society are rare. Dietary intakes of selected nutrients and zinc were calculated from the computerized food-frequency questionnaire using Food Composition Tables recommended by Hands Es.[9].

A 24-hours recall procedure was used to assess the dietary intakes of these participants. The quantity of food was estimated in portions of common household measures. A known weight or volume of household measures and some weighted food items were used as model. Marginal hypozincemia was identified by serum zinc between 50-70 ug/dl.

Participants were instructed to attend the laboratory of the Department of Clinical Biochemistry at Azadi teaching Hospital at morning after overnight fasting for 12-14, avoiding smoking and heavy physical activity for a minimum of 2 hours before examinations. Blood samples were collected between 9:00-11:00 am. Ten ml of blood was withdrawn by venipuncture using vacutainer from the antecubital vein and collected in blood vacutainer system CAT-plain tubes. After 25-30 minutes, the serum was separated and divided into number of plain tubes for the estimation of serum zinc and oxidative stress biomarkers. The pro-oxidant by-products (malondialdehyde and peroxynitrite), and antioxidant markers (serum ceruloplasmin and glutathione) were

Ceruloplasmin was measured by modified method of Menden et al 1977.[10] This assays measure only native, copper-containing caeruloplasmin. Serum total glutathione concentration was determined by modified method of Ellman.[11] Estimation of MDA was done according to the method Beuge and Aust.[12] Serum peroxynitrite level was measured by the modified method of Vanuffelen et al[13] Serum zinc concentration for the target group of this study was measured by atomic absorption spectrophotometer (AAS) method. Flame Atomic Absorption (Varian 220, Australia) was used as standardized procedure. The coefficient of variation (CV) for zinc in pooled serum samples was 3.5 % (n=30). Values for the internal control sera (Randox,Ltd.England) were 73.0 (SD 4.7) ug/dl compared with certified value of 69.0 (SD 6.7) ug/dl. The atomic absorption spectrophotometer was adjusted according to the instruction of the manufacture.

Differences between groups and correlations between different variables were evaluated by paired student t-test and Spearman's Correlation Coefficient. They were calculating using the statistical package for social science SPSS. P value of <0.05 was considered statistically significant. The cut off values >(mean+2SD) for non-smokers were applied to determine the percent(%) of risk in any of the parameter in smokers.

RESULTS

Among 254 eligible male participants, 115 (45.4%) had marginal zinc deficiency (serum zinc 50-70 ug/dl), a level indicated by others.[16] The univariate analysis showed that marginal zinc deficiency was more frequent in smokers (50.1% Vs 42.6%) compared to non-smokers. Of 127 smokers, 10(7.9%) had high serum ceruloplasmin levels (>0.430 g/L) and 40(31.5%) had high serum total glutathione levels (>1.7 umol/L), whereas in non-smokers (n=127)the values were relatively lower, i.e. 5 (4.2%) and 27(21.3%) respectively, though, no significant difference was observed between the two groups (serum zinc of smokers 72.7±22.4 Vs non-smokers 75.9±17.7 ug/dl; caeruloplasmin 0.340±0.087 Vs 0.339± 0.045 g/L, and total glutathione 1.27±0.25 Vs 1.20±0.22 umol/L). Regarding pro-oxidant by-products,30(23.6%) of smokers had elevated serum MDA (>1.4 nmol/l) and 35(27.5%) had elevated serum peroxynitrite(>2.09 mmol/l) compared to 8(6.3%) and 11(8.7%) of non-smokers respectively (p<0.01). The mean serum values of MDA in smokers was 1.6±0.5 Vs 1.2±0.1 nmol/l in non-smokers (P=0.025), and for peroxynitrite was 1.7±0.34 Vs 1.4±0.32 mmol/l (P=0.021), the differences were statically significant. We examined the association between hypozincemia and the oxidative stress biomarkers. In this analysis, the results of spearman's correlation coefficient(r) revealed that hypozincemia had weak, positive association with these related variables, (ceruloplasmin; r =0.176 , p=0.1; total glutathione; r=0.193, p= 0.08; MDA; r=0.195, p=0.08 and peroxynitrite; r= 0.209, p= 0.06).

The average percentage contribution of different food sources of dietary zinc intake of participants reveled that cereal products were the major source of dietary zinc, 46.3% of all participants depend on cereal products as a source of dietary intake. Among cereal products, wheat bread contributed to 16.5% of the daily dietary zinc intake of male smokers and non-smokers. No difference in daily dietary zinc intake for male smokers and non-smokers was observed (smokers % zinc intake Vs non-smokers: cereal products 43.0 % Vs 47.0%; vegetables and vegetables products 14.0% Vs 19.0%: Legumes, seeds and related products 15.0% Vs 13.6%; Meat 15.0% Vs 7.8%; milk and diary products 5.0% Vs 4.6%; eggs 5.0% Vs 4.0%; fruits and fruit products 2.3% Vs 2.8%; and miscellaneous items 0.7 Vs 1.2%.

DISCUSSION

There have been reports of marginal zinc deficiency in Iraqi population.[14-15] In our sample, marginal zinc deficiencies do exist, even among non-smokers. Although there have been several studies investigating the effects of cigarette smoking on zinc status , there are few published data on zinc status in our population. This study revealed low concentration of zinc in our sample compared with other population. For example, in adults a study performed on Saudi Arab males in 2006 , serum zinc concentrations were markedly higher than the levels reported in this locality (i.e. 84.5± 11.8 vs. 74.2 +19.0)[5] as well as in western populations.[16] A low serum zinc concentration in Iraqi population was also observed in an earlier study of adults where mean serum zinc concentration for adult males was 78.0+11.7 ug/dl[17] Such a difference is especially note worthy because several factors are known to impact negatively on biochemical zinc status.[18] Of these, dietary factors have the most marked negative effect on serum zinc concentration .The present study shows that around half of total subjects had marginal hypozincemia and a relatively higher frequency in smokers compared to non-smokers. The higher frequency of marginal zinc deficiency among smokers may have resulted from deficient absorption of zinc caused by a tobacco chelating effect. In view of the confounding effect of dietary zinc intake on biochemical zinc status, no significant difference in this parameter for male smokers and non-smokers was observed. Thus, our results suggest that smoking-induced hypozincemia is an additive factor to low dietary bioavailability among subjects living in Duhok city.

Several studies documented that cigarette smoking may increase oxidative stress and impair oxidant defense system, particularly antioxidant enzymes, and some trace elements such as selenium, zinc and copper, which protect the body against reactive oxygen species.[19] Our data shows that a high frequency of smokers had low serum zinc levels and high oxidative stress biomarkers, Thus our results suggest that cigarette smoking is associated with marginal hypozincemia , which renders smokers more susceptible to oxidative stress. However, it is unlikely that the changes in serum zinc were caused solely by dietary imbalance. Oxidative stress, a common disorder associated with smoking habit, can disturb zinc metabolism, this withstanding 51.1% of the smokers were at high risk of oxidative stress (increased levels of MDA and/or peroxynitrite). This may reflect the high prevalence of marginal zinc deficiency in smoker males. There may be a complex interaction between zinc, antioxidant (ceruloplasmin and glutathione) and pro-oxidant (MDA and peroxynitrite) markers that increases oxidative stress risk in smokers. However, it is not exactly clear that plasma zinc plays the major role as antioxidant against oxidative damage induced by cigarette smoking.

The study has few limitations. Firstly, the data from males living in Duhok city may not represent all subjects living in other parts of the Duhok governorate. Secondly, the serum zinc analyses were not indicative of zinc status for all subjects. Finally the number size of the participant was relatively low.

Even though, this study demonstrated a significance association between cigarette smoking and zinc status which may render smokers more susceptible to oxidative stress. The effects of zinc have received great deal of interest, through effects on oxidant defense system; zinc may decrease the risk of oxidative stress. Larger prospective studies are needed to confirm our observations, and experimental data may further elucidate the biological mechanisms of the associations.

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پوختە

باریٚ کەرستیٚ زنك لدەف کەسێن جگارکێش و جگارنەکێش: هەڤبەندی دگەل ئەرکیٚ ئوکسیدکرنیٚ

ئارمانج: هەلسەنگاندنا باریٚ کەرستیٚ زنك لدەف نمونەکا جگارکێشان ب بەراوردی دگەل جگارنەکێشان ژبو دەستنیشانکرنا کارتێکرنا زنکی وە کەرستەکیٚ پارێزکەر دژی زیانا ئوکسیدکرنیٚ.

شێواز: ڤیٚ ڤەکوینیٚ (254) کەس بخوڤە گرتن کو هەمی نێر بوون و د ساخلەم بوون و ل جهێن جورەوجور ل باژێریٚ دهوکیٚ دژین. 127 ژوان جگارکێش بوون و 127 ێن دی جگارنەکێش بوون. هەمی هاتنە داخوازکرن بو بەشداریبوون د تاقیکرنەکا نوژداری ل نەخوشخانا ئازادی یا فێرکرنیٚ لدهوکیٚ/عێراق. پێزانین هاتنە وەرگرتن ژ بەشداران برێکا پرسەنامەیێن کەسایەتی و ژمارەکا تاقیکرنێن کیمیاوی لسەر خوینا وان هاتنە کرن سەبارەت کەرستیٚ زنك و نیشانێن دژە ئوکسیدکەران و ئەنجامێن ئوکسیدەران, هەروەسا چەندییا زنکی د خوراکیٚ روژانە یێ بەشداربوویان.

ئەنجام: رێژا ژسەدیٚ یا ئاستیٚ کێمییا زنکی لدەف جگارکێشان بلندتر بوو ب بەراوردی دگەل جگارنەکێشان(Vs , P< 0.05 50.1 % 42.6%). سەبارەت ئاستیٚ دژەئوکسیدکەران چ جیاوازی نەهاتە دیتن دناڤبەرا هەردوو گروپان دا, بەلیٚ رێژەکا بلند ژ جگارکێشان ئاستەکیٚ بلند ژ نیشانێن ئەرکیٚ ئوکسیدکرنیٚ هەبوون ب بەراوردی دگەل جگارنەکێشان (P< 0.01). ئەنجامان دیارکر کو چ جیاوازیا گرنگ نەبوو د چەندییا زنکی د خوراکیٚ روژانە یێ هەردوو گروپان دا.

دەرەنجام: ڤەکولینیٚ گرێدانەك دیت دناڤبەرا جگارەکێشانیٚ و کێماتییا کەرستیٚ زنك و ئەڤەیە کو جگارکێشان پتر بەرهەڤدکەت بو توشبوونیٚ ب زیانێن ئەنجامێن ئەرکیٚ ئوکسیدکرنیٚ.

الخلاصة

حالة الخارصين في الأشخاص المدخنين وغير المدخنين : العلاقة مع جهد الأكسدة

الهدف: تقيم حالة الخارصين في عينة من المدخنين بالمقارنة مع غير المدخنين وكذلك لاكتشاف تأثير الخارصين كعنصر وقائي ضد الضرر التاكسدي .

طريقة العمل: شملت الدراسة على (254) شخصا من الذكور الأصحاء الذين يعيشون في مناطق مختلفة من مدينة دهوك ومنهم (127) شخص مدخن و (127) غير مدخن. وقد تم دعوة هؤلاء المشاركين إلى الفحص الطبي في مستشفى ازادي التعليمي

في محافظة دهوك / العراق . تم تجميع البيانات في الأشخاص المشاركين طبقا للاستبيانات الذاتية. عدد من الاختبارات الكيماوية تم إجرائها في مصل الدم شملت على الخارصين, دلالات مضادات الأكسدة , نواتج المؤكسدات

كما تم احتساب كمية الخارصين الغذائية اليومية للمشاركين .

النتائج: أظهرت النتائج ان النسبة المئوية لمستوى نقص الخارصين في الأشخاص المدخنين كان اعلى بالمقارنة مع غير المدخنين ($P< 0.05$, 42.6% Vs 50.1 %). أما بخصوص مستوى دلالات مضادات الأكسدة لا تباين معنوي وجد بين تلك المجموعتين, بينما نسبة عالية من المدخنين كان عندهم مستوى عالي من دلالات جهد الأكسدة بالمقارنة مع غير المدخنين ($P< 0.01$).

تشير النتائج إلى عدم وجود تباين معنوي في كمية الخارصين الغذائية اليومية لكلتا المجموعتين .

الاستنتاج: بينت الدراسة وجود ترابط بين تدخين السكائر ونقصان الخارصين وهذا ما قد يعد المدخنين أكثر عرضة للضرر الناتج عن جهد الأكسدة .

PRIMARY PLEURAL LIPOSARCOMA. CASE REPORT

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SUMMARY

Primary Liposarcoma of the pleural cavity is one of the rarest cases. Only few cases were reported all over the world. A 32 year old pregnant lady presented with severe cough and dyspnea, low grade fever, high ESR, and diffuse bilateral ronchi. Chest X-ray revealed an irregular radio opaque shadow in the right middle zone of the chest, diagnosed as ruptured pulmonary hydatid cyst. Thoracotomy done revealed a very big lobulated mass occupying about two thirds of the pleural cavity and attached to the pleura and middle lobe, Excision of the mass with right middle lobectomy was done. Histopathology revealed dedifferentiated myxoid liposarcoma. Pregnancy was terminated two weeks after surgery, and then chemotherapy regime started.

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Key words: Primary, Pleural, Liposarcoma

The main primary malignancy of the pleura seen with any regularity is malignant mesothelioma.[1] The existence of pure mesenchymal tumours arising from the lung parenchyma has now been well recognized. Theoretically, any given type of tumour affecting the soft tissue may arise, but uncommonly, in the lung as well.[2-4] Although liposarcoma forms one of the more common subtypes of soft tissue sarcoma and makes up to 15% of chest wall sarcomas, rarely it arises in the chest.[2] Most liposarcomas are low grade tumors; they have a propensity to recur locally, given their infiltrative nature.[2] Out of 1067 cases of liposarcoma reported by the Armed Forces Institute of Pathology, 29 were located in the chest, with a majority being in the mediastinum, and only 9 cases have ever been described as arising in the pleural space. These tumors tend to be very large at presentation, the smallest pleural liposarcoma reported is 1 kg weight.[3] Both adults and children can be affected & both sexes are equally involved, There is no predilection for a particular pulmonary lobe or lung. Because the lung is a common site for secondary deposits from soft tissue sarcomas, care must be taken to exclude the possibility metastatic sarcoma prior to rendering a diagnosis of primary sarcoma of the lung.[4] The first case of primary pleural liposarcoma was reported by Ackerman and Wheeler in 1942, until 2006 only 14 cases were reported in the English literatures.[5] Iwao Takanami and Tetsuo Imamura in 2003 reported the first case in Japan.[6] Angel Uchikov, Elena Poriazova, Zaprian Zaprianov and Desislava Markova published a case of pulmonary myxoid liposarcoma in 2005 in Bulgaria.[7] A small series of 4 cases of primary pleural liposarcoma from the files of the Armed Forces Institute of Pathology (Washington, DC) which are published

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and compared with previous 9 cases in literatures before.[8] Paul Goldsmith when reported 2 cases he mentioned that review of medline revealed a total of six reported cases of primary pleural myxoid liposarcoma.[9] We presented this case as the first case reported in Iraq[§].

CASE PRESENTATION

A 32 year old lady has a history of 3 missed periods; she was a house wife from Shengal, North West of Iraq. The lady was complaining of repeated attacks of vomiting for the last 2 months, diagnosed as morning sickness and treated conservatively. For the last 2 weeks, the woman developed severe dyspnea, with loss of appetite and repeated vomiting. On examination, the lady was febrile, dyspnoeic, and looked ill. There was a restriction in movement of the right side of the chest with diffuse ronchi, stony dullness on percussion, and decreased air entry in the same side mainly the middle and lower zones. Investigations revealed that apart from high ESR (131 mm/hr), the complete blood picture, renal and liver functions tests were within normal limits. Chest X-ray revealed a complete opacity in the right middle and lower zones, with pleural effusion (Figure 1 and 2). Ultrasound examination of the chest showed masses of mixed echogenecity (cystic to solid) with pleural effusion. Ultrasound of the uterus, revealed a single viable foetus, 13.3 weeks gestational age. CT-scan was not requested because the patient was pregnant. The condition was diagnosed as complicated hydatid cyst as the patient was from an endemic area.

Surgery Right posterolateral thoracotomy was done and a big lobulated mass was found occupying almost the whole pleural cavity, attached to the right middle lobe (Figure 3). Excision of the mass with right middle lobectomy was done (Figure 4 and 5). Postoperatively, the patient recovered smoothly and the chest X-ray showed fully expanded lung (Figure 6).

Histopathology Grossly, the specimen consisted of a nodular, white to gray mass measuring 200x190x150 mm and weighing 1400 gm, bossolated at one surface (Figure 7 A and B). On sectioning, the specimen was nodular, mucoid, white-gray. Areas of hemorrhage and necrosis were present. The lung lobe was dark brown, shrunken, measuring 90x60x30 mm and weighing 300 gm.

Microscopically, the mass was formed of variable admixture of malignant spindle cells and interspersed lipoblast-like vacuolated cells. Mitosis was frequent with evidence of aberrant mitoses. There were foci of malignant fibrohistocytoma-like differentiation (MFH). The stroma was myxoid and there were areas of necrosis and hemorrhage (Figure 8-11). The tumor was attached at one site to the pleural surface (Figure 12). The lung parenchyma was free from malignancy. Immunohistochemically, the malignant cells showed positivity for vimentin and S100 protein (Figures 13 and 14) while negative for keratin, EMA, actin, Desmin, HMB45, and CD34. The appearances were consistent with dedifferentiated myxoid liposarcoma of the pleura.

After surgery, Pregnancy was terminated uneventfully and the patient started chemotherapy after that. Then CT-scan was requested for thorax and abdomen for assessment the site of surgery and to exclude any distant metastasis; it revealed mild right side pleural effusion (Figure15).

Chemotherapy The case in question was adherent to the pleura and appeared to be incompletely excised so combined chemotherapy was applied after 3 weeks. This regimen included, after good

§ *Because of the lack of proper registration and poor recording in our hospitals and centers in Iraq we reviewed the available literatures and personal contact with the thoracic surgeons we didn't found any previous recorded case so we regard this case as the first case reported in Iraq.*

hydration, Doxorubicin 50 mg/m² over 3-5 minutes on day 1 every 21 days, Mesna 600mg/ m² in 200 ml 0.9% NS over 15 minute, Ifosfamide 5000 mg/m²+ mesna 2500mg/ m² in 3000 ml 0.9% NS/GW over 12 hours on day 2 every 21 days. Doxorubicin and ifosfamide. Doxorubicin 85 mg given directly intravenously over 3-5 minute on day 1 followed by ifosfamide 8500 mg in combination with mesna 4250 mg in 3000 0.9% NS and 5% GW over 12 hours on day 2 every three weeks. The treatment was given for 4 cycles only due to non compliance of the family with treatment.

Three months later, recurrence was noticed ipsilaterally and contra laterally in the other lung (Figure 16) and treatment was continued conservatively but unfortunately the patient died 9 months after surgery.

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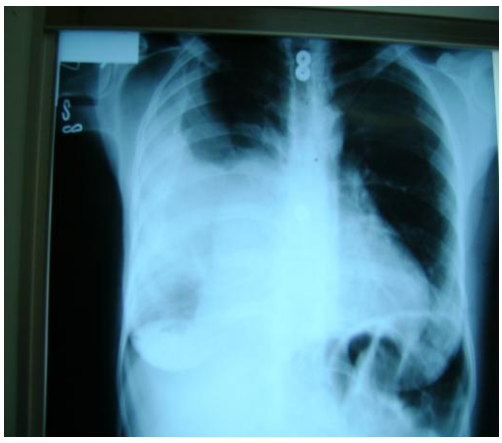


Figure1. Plane X-Ray

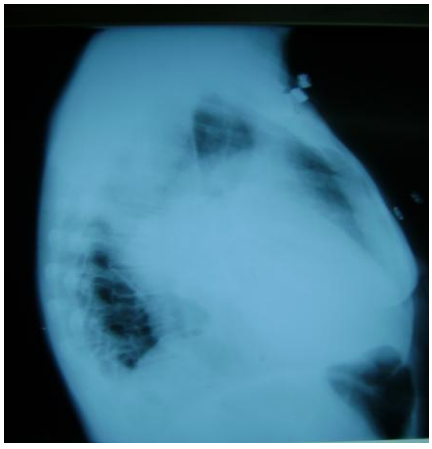


Figure2. Right lateral X-ray

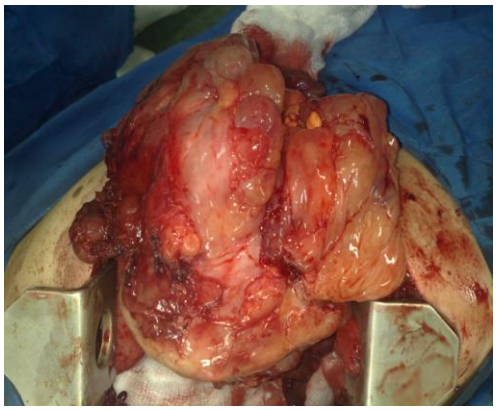


Figure3. Separation of the mass from nearby tissues

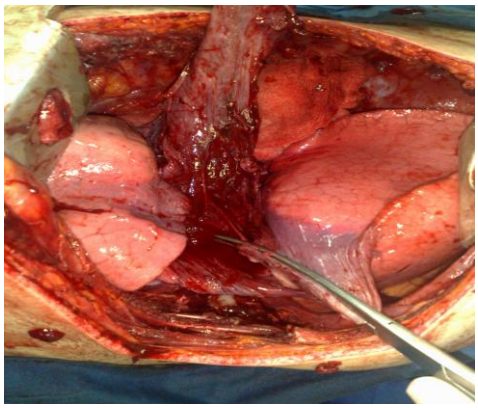


Figure4. Right middle lobectomy

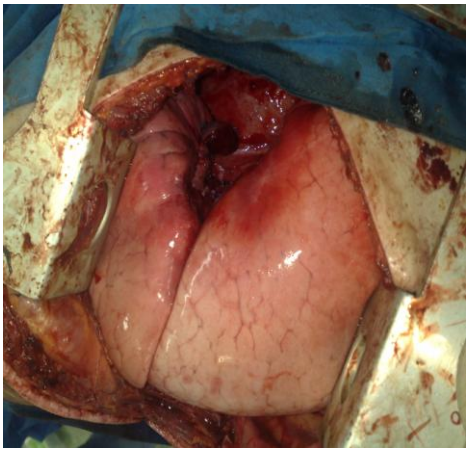


Figure 5. The mass excised with the right middle lobe

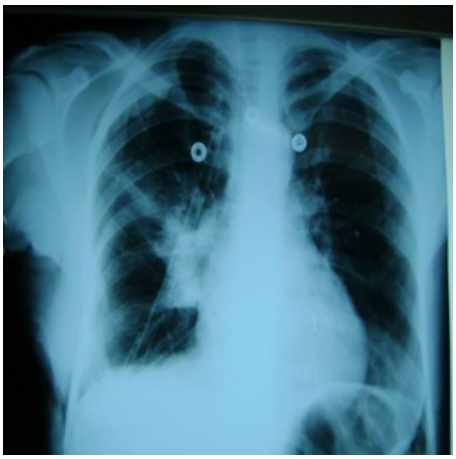
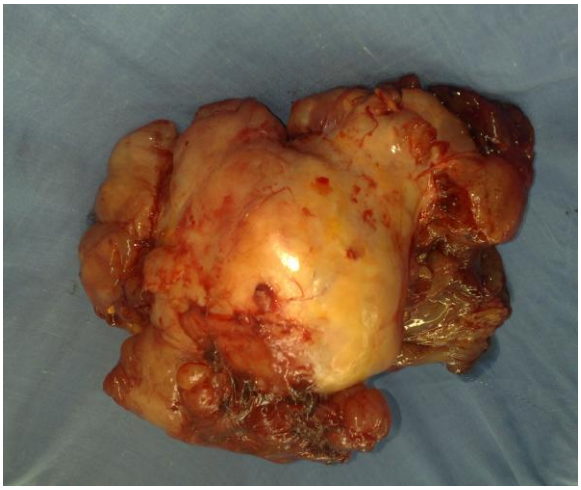
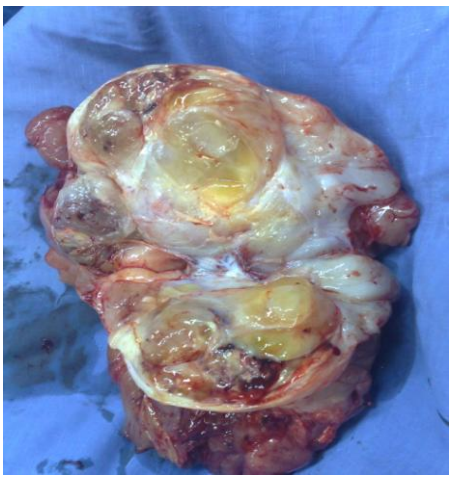


Figure 6. Post operative plane X-ray



A



B

Figure 7 (A and B). The gross appearance of the excised mass

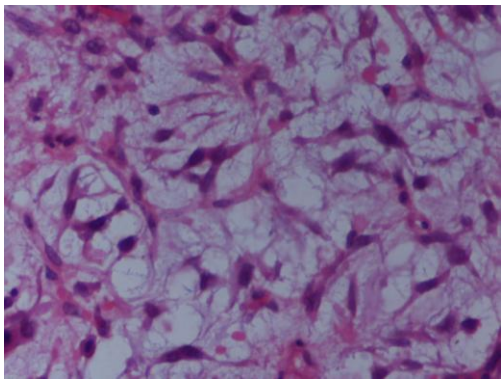


Figure 8. Lipoblasts within a myxoid stroma (X200)

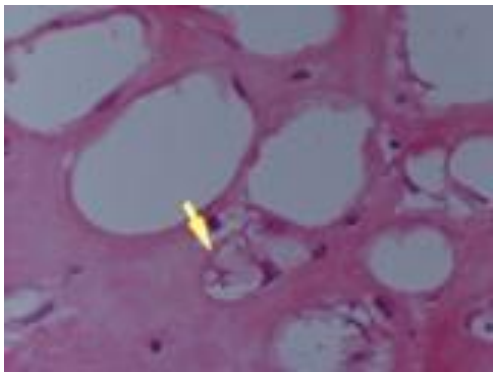


Figure 9. Multi-vacuolated lipoblast (arrowed) (X400)

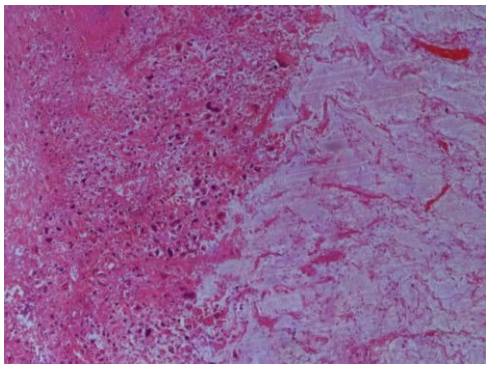


Figure 10. Extensive necrosis with a myxoid area (X100)

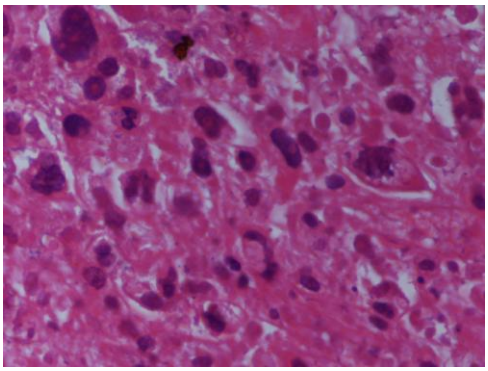


Figure 11. MFH-like area (X400)

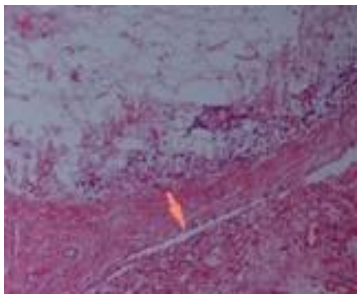


Figure12

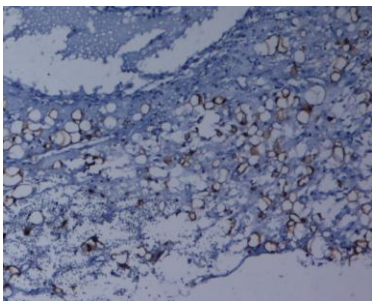


Figure13

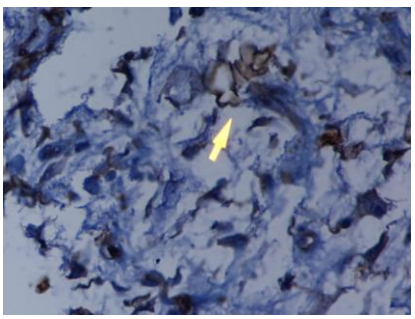
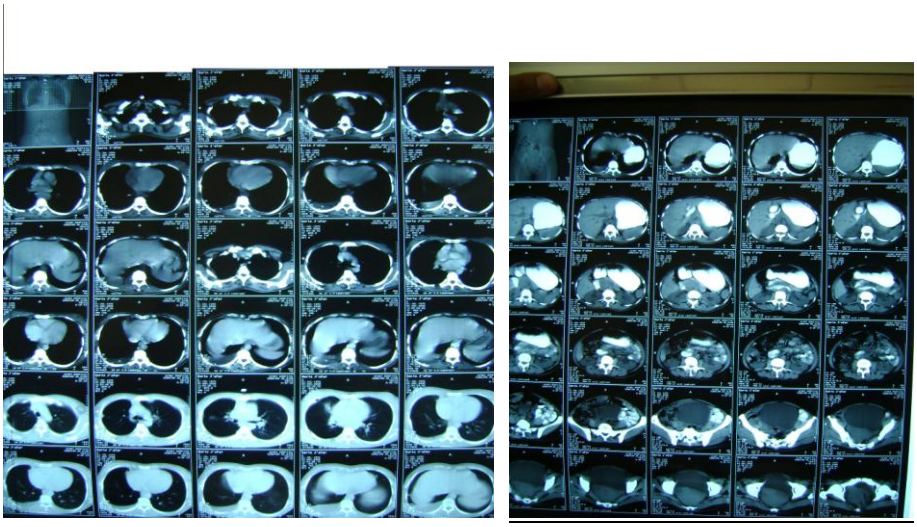


Figure14

Figure 12. Evidence of attachment of the tumor to the pleural surface; myxoid changes are clear (X100)
Figure 13. S100 positivity high lightening the lipoblasts
Figure 14. Positive malignant cells for Vimentin (X400)



A B

Figure 15. Postoperative CT-scan of the chest (A), and abdomen (B)

Figure 16. Recurrent mass in right upper zone

كورتى

لايپوسارکوما پێشینی یا چالاً پەردا سەر مێلاکێت سوور. راپورتا حالەتەکێ

لايپوسارکوما پێشينى يا چالاً پەردا سەر مێلاکێت سوور، ئێکە ژ دەگمەنترين نە خوشيا، بتنێ چەند نەخوشەك پێت هاتينە رابورت كرن لهەمى جيهانێ. مە ئەڤ نەخوشە پێشكێشكر وەك نەخوشێ ئێكێ ل عيراقێ.ژنەكا دووگيان يا 32 سالى ئامادەبوو لگەل كوخكەكا دژوار وبێن تەنگيێ،تايەكا سفك و (ESR) يا بلند بوو ولگەل سيخسيخەكا دژواريا هەردووك لايا. تيرێژا سنگى ديايكر كو سيبەرەكا نەرێك وپێك يا هەى لرەخێ راستێ ل زونا ناڤنجى يا سنگى،هاتە دەست نيشانكرن وەك كيسەكێ هايداتدى يێ پەقى. سنگێ وێ هاتە ڤەكرن ولمچەكا مەزن يا گرێ گرێ هاتە ديتن كو نێزيكى دوو سێكا ژ چالا پەردا سەر مێلاكێت سوور ڤەگرتبوو ويا بپەردێ وپارچا مێلاكا سوورڤە يا نيسيای بوو.لمچا وەرەمێ هاتە ژێڤەكرن ولگەل ژێڤەكرنا سێكا مێلاكا سوور يا ناڤنجى يا رەخێ راستێ. پشكنينا هيستوپاتولوجى ديايكر كو ئەڤە لايپوسارکوما ميكسويدە يا ديايكرى،دووگيانيا نەخوشێ هاتە بدوماهيك ئينان پشتى دووحەفتيا ژ نشتەرگەريێ ،وپاشى رژێما كيمياوى دەست بێ كر.

الملخص

ورم الخلايا الشحمية الأولي الخبيث لغشاء الجنب. اشهار حالة

ورم الخلايا الشحمية الأولي الخبيث لغشاء الجنب واحد من أندر الحالات , بعض الحالات فقط سجلت عالميا , نقدم هذه الحالة كأول حالة في العراق , سيدة حامل بعمر 32 سنة تقدمت بأعراض ضيق التنفس وسعال شديد مع ارتفاع طفيف في درجة الحرارة, وارتفاع نسبة ترسب كريات الدم الحمراء, أزيز منتشر في جانبي الصدر, أشعة الصدر أظهرت وجود عتمة شعاعيه غير منتظمة في النطاق الوسطي الأيمن , شخصت الحالة ككيس مائي رئوي منفجر. أجريت لها عملية فتح الصدر التي كشفت عن وجود كتلة كبيرة مفصصة تشغل حوالي ثلثي تجويف الجنب وملتصقة بغشاء الجنب والفص الوسطي, تم استئصال الكتلة مع الفص المذكور . الفحص النسيجي اظهر نوع الورم كورم خبيث غير متميز للنسيج ألدهني لغشاء الجنب , انهي الحمل بعد أسبوعين من الجراحة وبوشر بنظام للعلاج الكيماوي.