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1 Sanford Guide to Microbial Therapy 2008 (38th edition)
2 Chodosh, S. et al. (1998) Clin Infect Dis 27, 722–729
3 Chodosh, S. et al. (1998) Clin Infect Dis 27, 730–738

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SALINE SONOHYSTEROGRAPHY VALIDITY IN ABNORMAL UTERINE BLEEDING DURING THE REPRODUCTIVE AGE

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ALAA YOUSIF, MRCOG**

Submitted 10 February 2016; accepted 18 March 2016

ABSTRACT

Background: To study the Sonohysterography accuracy and to compare results with the hysteroscopy and histological study. One of the tools for investigation in patients with Abnormal Uterine Bleeding (AUB), is Vaginal Ultra sound (VU/S), as an initial investigation. Saline Sono-Hysterography (SSHG), is more reliable for focal and generalized endometrial lesions. The technique was introduced in 1987 where by Installation of Isotonic Saline Solution into the cavity of the uterus was found to improve the endometrial cavity's Transvaginal Sonographic imaging outcome. This study was conducted for the comparison of the accuracy of (VU/S), and (SSHG) as a first step in the diagnostic approach of endometrial abnormities of women presenting with (AUB), and to compare the results with hysteroscopy and histopathological findings.

Patients and Methods: Ethical approval was properly taken. Patients were collected from Private and Azadi Teaching Hospital Consultation Clinics. A prospective study was started from June 1st. 2013 to March 1st. 2014 and conducted in 200 women in their reproductive years of age presented to Private and Azadi Teaching Hospital Consultation Clinics complaining from (AUB). All of them underwent (VU/S), and (SSHG) Transvaginal ultrasound, and Sonohysterography. Focal or generalized endometrial abnormalities were noticed, and classified into seven types (normal endometrium, thickened endometrium, endometrial hyperplasia, endometrial polyp, submucous myoma, uterine synechiae, and suspesious of malignancy). Those women with positive findings then underwent hysteroscopy and diagnostic curettage, the histopathologic findings was compared with the results of (SSHG). Finally, the correlation between sonographic results with definitive diagnoses that were obtained by hysteroscopy& endometrial biopsy was used to calculate the test predictive values.

Results: The sensitivity and specificity of (SSHG) was 92.9% and 89.7% respectively, in contrast to the sensitivity and specificity of (VU/S) which was71.4% and 67.7% respectively. The (SSHG) and Hysteroscopy were 91% in agreement to each other while (VU/S) and Hysteroscopy were in agreement to each other in 69% of cases only, ($p = 0.002$). The diagnostic efficiency of (SSHG)in three main endometrial abnormalities (endometrial hyperplasia, polyps and sub mucous fibroids) were superior to that (VU/S). with the best results being seen in patients with sub mucous myoma where the level of both sensitivity and specificity reached 100% for (SSHG), this was in contrast to those of (VU/S) which reached 61.55 and 97.7% respectively.

Conclusions: The results of our study have concluded that (SSHG) is a much better assessment tool than traditional (VU/S) in dealing with intrauterine lesions. Decision making in selecting cases for hysteroscopy and directed biopsy would be much better supported by having an accurate differentiation between focal and generalized endometrial abnormalities beforehand. Hence the use of (SSHG) as a first step in the diagnostic approach of (AUB) is strongly recommended by this study.

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Keywords: Abnormal Uterine Bleeding, Vaginal Ultra sound, Saline Sono – Hysterography.

Abnormal uterine bleeding (AUB) is a well-recognized gynecologic problem in women attending outpatient clinics[1]. The reasons for this complaint may range from simple causes like Dysfunctional Uterine Bleeding (DUT) to Carcinoma of the endometrium. Such a variety of possible presentations needs an

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in depth workout to identify the exact cause weather organic, hormonal or systemic, bearing in mind that 10% to 15% of endometrial cancer cases occur women at premenopausal and postmenopausal age group[2-4]. The use of blind endometrial sampling to evaluate the endometrial cavity is an inaccurate way for diagnosing pathological condition. The diagnostic hysteroscopy with directed biopsy will insure the recognition of the abnormalities, however, it is invasive.[5]

Vaginal Ultra sound (VU/S) has a major role as a first step modality in the assessment of AUB, however its efficiency is limited it's as a screening tool for the proper assessment of endometrial lesions[1,6,7].

The (VU/S) finding of a thickened l endometrium is mostly non-specific and may be caused by a diversity of lesions like endometrial: polyps; hyperplasia; carcinoma; cystic atrophy or sub mucosal fibroids. Besides its limited ability in differentiating between myometrial and endometrial lesions, focal lesions are also under diagnosed by this modality because of the restrictions in the evaluation of double-layer thickness.3,8,9 The proper evaluation of single layer endometrial lining is best achieved by applying the (SSHG), which is a technique in which the endometrial cavity is filled with sterile isotonic saline solution during vaginal ultrasound examination helping the sonographer to reliably distinguish focal from diffuse lesions of the endometrial cavity. A lot of studies have recently indicated that (SSHG) can improve the specificity of (VU/S) in differentiating focal from diffuse endometrial thickening.[10-16] .This study was conducted for the comparison of the ability of (VU/S), and (SSHG) as a first step in the diagnostic approach of endometrial abnormities of women presenting with (AUB), and correlating the results with hysteroscopy and histopathological findings.

PATIENTS & METHODS

This study was done at Azadi Teaching Hospital, the main tertiary care facility in Duhok - Kurdistan. Approval was granted by the research ethics committee of Duhok University College of Medicine, and an informed consent was taken from all the patients. The study was started from June 1st. 2013 to March 1st. 2014, Two hundred women were seen in the consultation clinic with AUB. Initially (VU/S) was done for all of them, those with no sonographic abnormalities did not needed any further imaging evaluation and were excluded from the study (No. = 100).

The remaining patients were followed by SHG, hysteroscopy and biopsy (No. 100). The age ranged from 25 to 50 years with mean age of 37.5 years. Hysteroscopy and Biopsy was arranged for the inclusion group within 10-14 days from the initial examination day. The interval between (VU/S) and (SSHG) to hysteroscopy was between, 2–14 days.

SALINE HYSTEROSONOGRAPHY (SSHG) TECHNIQUE

Initially a detailed history, concentrating on the presenting symptoms and duration should be obtained. Patient with Pregnancy, acute PID, ovarian pathology, large intramural fibroid, a very tight cervix, a recently abnormal pap smear, or those who refused further intervention were excluded. A baseline (VU/S) is

performed to assess the uterus, endometrium and adnexal structures. Under aseptic technique, a sterile Casco's speculum is inserted in the vagina to identify the cervix which should be cleaned with butadiene antiseptic solution. Then a size 5-French hysterosonography sterile catheter (Lyco HSG Catheter; Model 06-105F) is placed into the uterine cavity. The speculum is then removed, leaving the catheter in place.

transvaginal 5-7MHz multi frequency ultrasound transducer is then inserted into the vagina, and the catheter balloon is properly inflated and gently drawn toward the internal Os to avoid the saline from leaking during the examination. Approximately 10cc of sterile isotonic saline solution is then pushed through the catheter to symmetrically distend the uterine cavity. Sagittal and coronal images of the uterus are then obtained. The measurement of the endometrial thickness on SHG is obtained by adding the thickness of the opposite endometrial linings. Noting that the total added thickness should not exceed 5mm. normally and the endometrium should appear symmetrical and uniformly distended with no masses distorting or be present within the uterine cavity. On conventional TVUS, a uniform endometrial thickness of the two coapted layers of <5 mm is considered normal in the postmenopausal woman.[1,3-5] Adhesions or uterine synechiae on SHG are seen as thick bridging bands of tissue which distort the uterine cavity, and, may make it difficult to properly distend the uterine cavity. Endometrial polyps on (VU/S) are seen as a thick endometrium. While On (SSHG), an intracavitary polyp is outlined by the anechoic saline and can be clearly demarcated.[6] Leiomyomas on Conventional (VU/S) can be used to identify the relationship with the endometrial interface, and any distortion of the myometrial/ endometrial interface. (SSHG) can be helpful for further localization of the leiomyomas, whether it is sub mucosal or intramural. Endometrial carcinoma On (SSHG) can appear as an irregularly thickened endometrium of variable echogenicity.[1] An endometrial thickness >5 mm in a postmenopausal woman should be further evaluated for the possibility of endometrial carcinoma[3,4,7].

Endometrial (SSHG) findings of patients on tamoxifen therapy include polypoid lesions, endometrial hyperplasia, and sub-endometrial micro cystic lesions.[8,9] These changes are located in the proximal myometrium on a background of a thin and atrophic endometrium and they are thought to represent reactivation of foci of adenomyosis due to tamoxifen estrogenic effects.[10]

RESULTS

A 200 cases of (AUB) exposed to Transvaginal ultrasound (VU/S), normal uterine cavity found in 33%cases with (VU/S), 38% of cases with (SSHG) and 44% of cases in hysteroscopy and histopathologic study. The other finding was endometrial polyp which showed in 32% of cases with (VU/S), 31% with (SSHG), histopathology Submucous myoma in 18,19, and 19% with (VU/S), (SSHG) and histopathology respectively. Chronic endometritis found in 0,0, and 1% with (VU/S), (HSSG) and histopathology respectively. Adhesion found in 0,2, and 2% with (VU/S), (SSHG) and histopathology respectively. Hyperplasia was found in17, 10, and 11% respectively in (VU/S), SHG and histopathology. As is shown in table (1)

Table 1: The pathology in 100 Patients with AUB according to the diagnostic test Modalities. (P value statistically significant).

Type Diagnosis	TVU no of The Patient	%	SHG diagnosis no of patient	%	Hysteroscopy Histopathology Diagnosis number of patient	%	P VALUE
Homogenous endometrial thickening	33	33	38	38	44	44	
Endometrial polyp	32	32	31	31	23	23	
Submucous myoma	18	18	19	19	19	19	0.000
Chronic endometritis	0	0	0	0	1	1	0.00506
Adhesion	0	0	2	2	2	2	0.00771
hyperplasia	17	17	10	10	11	11	0.00771
Total	100	100%	100	100%	100	100%	

The sensitivity and specificity in this study of (SSHG) and (VU/S) is seen in table 2 The sensitivity in (VU/S) and (SSHG) were 73.3% and 88.8% respectively, and the specificity were 43.2% and 74.4% respective

Table 2: Diagnostic performance of (SSHG) & (VU/S)

Test	sensitivity	specificity	Ppv	Npv	Likelihood ratio	
TVU	73.7%	43.2%	62.1%	55,9%	positive	negative
SHG	88.5%	74.4%	84.4%	80.6%	1.289	0.620
					3.452	0.154

Table 3: Comparisons between sensitivity, specificity, PPV, NPV, PLR AND NLR in different ways of diagnostic aids

Diagnosis	Endometrial Hyperplasia		Endometrial Polyp		Sub Fibroid	mucous
Test Performance	TVS	SHG	TVS	SHG	TVS	SHG
Sensitivity	58.8	58.8	85	100	73.7	100
Specificity	90.4	97.6	82.5	89.6	96.3	100
PPV	55.6	83.3	54.8	74.2	82.4	100
NPV	91.5	92	95.7	100	94.0	100
PLR	6.103	24.412	4.857	9.63	19.895	0.00
NLR	0.456	0.422	0.182	0	0.273	0.00

DISCUSSION

Abnormal Uterine Bleeding has been extensively evaluated by (VU/S) .A number of studies have demonstrated that (VU/S) is a sensitive tool in evaluating AUB. Being an operator depended on modality, the diagnostic accuracy of (VU/S) has a wide range of variability , the sensitivity being 87% (range 24–96%) and the specificity 82% (range 29–93%).[14,20,21] Our study has showed a 71.4% sensitivity, and a 67.7% specificity, with 54.4% PPV and 81.5% NPV for (VU/S) in investigating AUB.

Despite the wide spread use of onventional (VU/S) for the initial assesment of AUB, a growing number of studies in the literature is showing that (VU/S) has an inherent limitation in picking up small isoechoic endometrial nodular lesions.[20,21,22,23]. In the same way, (VU/S) cannot easily distinguish sub mucosal from intramural fibroid lesions in many cases, which is an essential prerequisite step for further interventions.[24,25] Our study results revealed that out of 13 cases of submucous fibroids, 5 were misinterpreted as intramural by (VU/S) but correctly localized by SHG. This study has also showed that eight cases diagnosed as normal by TVS exhibited different endometrial abnormalities on SHG, and 10 cases showing endometrial abnormalities on TVS were found to be normal on SHG. These results are in agreement with those of Laifer-Narin et al.[22] who claimed that 14% of 114 patients showing normal TVS findings revealed abnormalities on SHG. The use of (SSHG) as an initial test in approaching patients with AUB has a great value, taking in consideration its efficiency in showing small lesions and in differentiating focal from diffuse endometrial pathologic abnormalities, making it a perfect tool in the diagnostic workup of such cases. The sensitivity and specificity of SHG have been reported range from 85-91% and 83-100%, respectively[3,14,16,26], these results were very near to those that have been obtained in our study which revealed 92.9% Sensitivity, 89.7% Specificity, 86.7% PPV, and 94.5% NPV for SHG to diagnose intra-cavity endometrial lesions. This study has also shown an overall diagnostic accuracy of 91%. Which was in good agreement with accuracy rates ranging from 84% to 96% that have been reported by other authors.[11,26,27] A near total concordance (96%) between SSGH and hysteroscopy in the diagnosis of focal lesions has been reported by Epstein et al.[11]. Both tests had a sensitivity of approximately 80% with regard to diagnosing endometrial polyps, whereas VU/S had missed 50% of them. Kamel et al[28] have achieved 93.3% sensitivity, 94.6% positive predictive value and 93.3% diagnostic accuracy in the detection of endometrial polyps by SHG in 106 patients with AUB. Soares et al. and Nanda et al[29-30] have both reported 100% sensitivity, 100% positive predictive value and 100% diagnostic accuracy for polypoid lesions by SHG. According to Leone et al.[5] A total of 48 cases (100%) submucosal fibroids were correctly diagnosed using (SSHG). Our study results are in perfect agreement with the previously mentioned publications, with an overall accuracy level of 100% in differentiating submucosal from intramural fibroids by SSHG The major drawback of SSHG is in

the possibility of missing the presence of endometrial carcinoma, the most serious cause of AUB. In the present study, only one case of carcinoma was detected and it was misdiagnosed as endometrial hyperplasia by both TVS and SSHG modalities. Retrospectively it was found to be a very small lesion associated with adenomatous hyperplasia detected on endometrial biopsy. Epstein et al.[11] has reported that hysteroscopy is superior to both SSHG and TVS for discriminating between benign and malignant lesions (sensitivity, 84%, 44%, and 60%; false-5 positive rate, 15%, 6% and 10%, respectively). However, neither Hysteroscopy nor saline contrast Sonohysterography can reliably discriminate between all the benign and malignant focal lesions and biopsy is usually indicated to further evaluate such lesions. No complications related to SSHG were found in this study. However in the literature some exceptional complications have been mentioned like vasovagal syncope, bleeding, infection, perforation and possibility of spreading of carcinoma. Dubinsky et al[31] found two cases of endometritis after SHG in their study (n=89 patients). The risk of infection following SHG is estimated to be 1 %.10 Hysterosonography is a simple painless day care procedure, well accepted by the patients can be done in an outpatient clinic and does need an operating theater or anesthesia. No ionizing radiation or contrast media are required. It confers a great value in differentiating of intracavitary, endometrial, and sub mucosal uterine abnormalities.

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پوختە

دروستیا سونوهیستێروگرافیا خوێیی ل خوین بەربونا نە نورمالا مالزاروك ل دەمێ تەمەنێ زاروکبونێ

پێشەکی: ب مەرەما خواندنا دروستیا سونوهیستێروگرافی و هەلسەنگاندنا ئەنجامان دگەل هیستێروسکوپی و خواندنا شانەناسی. ئێك ژ ئامیرەیێن لێکولینێ بۆ نەخوشێن ب خوین بەربونا نە نورمالا مالزاروك (AUS)، سونارا ناڤ ئەندامێ مێینە (VU/S) وەکو لێکولینا دەستپێکی یە، سونوهیستێروگرافیا خوێیی (SSHG)، پتر بۆ برینێن ناڤەندی و گشتی یێن ناڤ ئێندومێتریال باوەرپێکرییە، ئەڤ تەکنیکە ل سالا ١٩٨٧ هاتە راگەهاندن و داکوکی دکر کۆ دانانا ئاڤا نیزوتونیکا خوێیی لناڤ ڤالاهیا مالزاروك دکاریت ئەنجامێن وێنەگرتن ب سونارا ناڤ ئەندامێ مێینە باشتر بکەت. ئەڤ ڤەکولینە هاتە ئەنجامدان ب مەرەما هەلسەنگاندنا دروستیا VU/S وSSHG وەکو یەکەم پێنگاڤ ل شێوەیا ناسینی یا دەرئاسایی یێن ئێندومێتریال ل ژنێن بـAUB، و هەروەسا هەلسەنگاندنا ئەنجامان دگەل ئەنجامێن هیستوپاتولوجیکی و هیستێروسکوپی.

ڕێکێن ڤەکولینێ: روخسەتا ئەخلاقی هاتە وەرگرتن نەخوش ژ نەخوشخانەیا ئازادی یا فێرکرنێ و کلینیکێن تایبەت هاتن کومکرن، ڤەکولینەکا پێشەروژی ژ ئێکێ هەیڤا پێنج سالا ٢٠١٣ حەتا ئێکی هەیڤا سێ یا سالا ٢٠١٤ هاتە دەستپێکرن و لناڤ ٢٠٠ ژنێن ل تەمەنێ زاروکبوونێ و سەرەدانکەرێن نەخوشخانەیا ئازادی یا فێرکرنێ و کلینیکێن تایبەت هات دان. سونارا ناڤ ئەندامێ مێینە (VU/S)، سونوهیستێروگرافیا خوێیی (SSHG)، سونارا ناڤ ئەندامێ مێینە و سونوهیستێروگرافی بۆ هەمو ژنان هاتەکرن، دەرئاسایێن ناڤەندی یان گشتی یێن ئێندومێتریال هاتە دیارکرن، ب حەفت جورا هاتن دابەشکرن (ئێندومێتریوما نورمال، ئێندومێتریوما ستور، زێدەبونا خانیکێن ئێندومێتریال، زێدەگوشتا ئێندومێتریال، تیومرا ماسولکەیا ژێر موخاتی، چربونا مالزاروك، و گومارا رزینێ)، لدوڤ دا ژنێن ب ئەنجامێن نەرێنی لژێر هیستێروسکوپی و نەشتەرگەریا ناسینی هاتن دانان و ئەنجامێن شانەناسی دگەل ئەنجامێن SSHG هاتە هەلسەنگاندن. لدوماهیێ پەیوەندیا ئەنجامێن سونوگرافی ب ناسینا پشت راستکری کو ب هیستێروسکوپی و نمونەیا ئێندومێتریال بدەست هاتی، هاتن بکارئینان دا کو ئەنجامێن پێش دیتنێ هەژمار بکەین.

ئەنجام: دروستی و تایبەتمەندیا SSHG ٩٢.٩٪ و ٨٩.٧٪ بو ب رێژ، ل هەمبەر دروستی و تایبەتمەندیا VU/S ٧١.٤٪ و ٦٧.٧٪ بو ب رێژ. SSHG و هستێروسکوپی ب رێژەیا ٩١٪ لهەڤهاتن دگەل ئێك هەبو، لێ VU/S و هیستێروسکوپی ل ٦٩٪ ژ نمونەیان لهەڤهاتن هەبو، (p=0.002) بکێرهاتنا ناسینی SSHG ل سێ دەرئاسایێن سەرتر ژ VU/S بون. ب باشترین ئەنجامێن هاتن دیتن ل نەخوشێن ب تیومرا موسولکەیا ژێر موخاتی کو هەردوو دروستی و تایبەتمەندی ب رێژەیا ١٠٠٪ بو SSHG گەهشت نیشان دا کو دگەل ئەنجامێن VU/S ب رێژەیێن ٦١.٥٥٪ و ٩٧.٧٪ ب رێز ل هەڤهاتن نەبو.

دەرئەنجام: ئەنجامێن ڤەکولینا مە نیشان دان کو SSHG ژ VU/S یا کەڤنەشوپ ژبو سەرەدەریکرن ب برینێن ناڤ مالزاروکی شێوەیەکا باشترە، بریار وەرگرتن بو هەلبژارتنا نمونەیێن هیستێروسکوپی و نمونەیێن راستەوخو باشترە ب جوداکرنەکا دروست دناڤبەرا دەرئاسایێن ناڤەندی و گشتی یێن ئێندومێتریال بهێتە پشتەڤانیکرن، لەورا بکارئینانا SSHG وەکو پێنگاڤا یەکەم ل شێوەیا ناسینی بو AUB بشێوەیەکێ بهێز ژ ئالیێ ڤەکولینێ دهێتە پێنشیارکرن.

الخلاصة

دقة سونوهستيروغرافي الملحية (سالين) في النزف الرحمي الشاذ أثناء العمر المنتج

الخلفية والأهداف: لدراسة دقة سونوهستيروغرافي ولمقارنة النتائج مع هيستيروسكوبي مع دراسة النسيج. إحدى الأدوات للتحقيق في المرضى بالنرف الرحمي الشاذ AUB، الكشف المهبلي بالأمواج فوق الصوتية VU/S، كتحقيق أولي. سونوهستيروغرافي الملحية SSHG، موثوق به أكثر لالضرار او االذى في بطانة الرحم البؤرية والمعممة. التقنية قدمت في ١٩٨٧ حيث بتركيب محلول ايزوتونيك الملحي إلى تجويف الرحم وجدت لتحسين نتيجة تصوير سونار خالل التجويف المهبلي في بطانة الرحم. هذه الدراسة أجريت لمقارنة دقة VU/S، وSSHG كخطوة اولية للنظرة التشخيصية لحالات الشذوذ أولاً في بطانة الرحم عند النساء المتقدمات مع AUB، ولمقارنة النتائج مع هيستيروسكوبي ونتائج هستوباثولوجي.

طرق البحث: الموافقة الأخلاقية أخذت بشكل صحيح. المرضى جمعوا من مستشفى آزادي التعليمي وعيادات خاصة. دراسة متوقعة بدأت من الأول من يونيو–حزيران ٢٠١٣ إلى الأول من مارس ٢٠١٤ وأجريت على ٢٠٠ امرأة بعمر السنوات المنتجة من مستشفى آزادي التعليمي وعيادات خاصة. كلهم مروا بهم VU/S, SSHG، وسونوستيروغرافي. حاالت الشذوذ في بطانة الرحم البؤرية أو المعممة لوحظت، وصنفت إلى سبعة أنواع (بطانة الرحم طبيعية، تثخن بطانة الرحم، تضخم كمي في بطانة الرحم، زائدة لحمية في بطانة الرحم، لزوجة في الرحم، ارتياب من الخبث). أولئك النساء ذوات النتائج الإيجابية تم اجراء الهستروسكوبي والكيورتاج التشخيصي، والنتائج الهستوباثولوجية قورنت بنتائج SSHG. أخيرا، الارتباط بين نتائج سونار جازم يشخص الذي حصل عليه من قبل هستروسكوبي وفحص عينة في بطانة الرحم كان يستعمل لحساب قيم الاختبار التنبؤية.

النتائج: الحساسية والتحديد SSHG كان ٩.٩٢% و٧.٨٩% على التوالي، بالمقارنة مع الحساسية والتحديد VU/S الذي كان ٤.٧١% و٧.٦٧% على التوالي. SSHG وهستروسكوبي كانت ٩١% موافق بينما VU/S وهستروسكوبي كانت موافقة إلى بعضهم البعض في ٦٩% من الحالت فقط ($p=0.002$) الكفائة التشخيصية SSHG في ثالث حاالت شذوذ في بطانة الرحم رئيسية (تضخم كمي في بطانة الرحم، زوائد لحمية وأورام تحت االغشية المخاطية) كانت أرفع من تلك VU/S. بأفضل النتائج أن ترى في المرضى المصابين بالأورام تحت االغشية المخاطية الفرعي حيث مستوى كلتا الحساسية والتحديد وصال ١٠٠% ل SSHG، هذا كان بالمقارنة مع أولئك VU/S الذي وصل ٥٥.٦١% و٧.٩٧% على التوالي.

الاستنتاجات: إن نتائج دراستنا إستنتجت بأن SSHG هي احد الأدوات لتقييم أفضل بكثير من تلك التقليدية VU/S في التعامل من الأضرار او الأذى داخل الرحم. لذا إتخاذ القرارات في إختيار الحالات لهستروسكوبي وفحص عينة موجه سيكونان أفضل بكثير ومدعوم من قبل إملاك تفاضل دقيق بين حالات الشذوذ في بطانة الرحم البؤرية والمعممة مقدما. لذلك إستعمال SSHG يمثل الخطوة الأولى للوصول الى التشخيص عن طريق AUB ويوصى بقوة باجراء هذه الدراسة.

ZINC STATUS IN WOMEN WITH UNEXPLAINED INFERTILITY IN DUHOK CITY, KURDISTAN REGION, IRAQ

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ABSTRACT

Background: Alterations in the status of nutrients and minerals including zinc should be considered in the etiology of unexplained infertility. The aim of this study was to determine serum zinc status in women with unexplained infertility and compare it with that of fertile controls.

Methods: A case-control study was conducted at Infertility center in Duhok city/Kurdistan region/ Iraq, during the period from beginning of February to end of July 2014, fifty patients with unexplained infertility and 100 age matched apparently healthy fertile control were enrolled. For each one blood sample was obtained for the measurement of serum Zinc.

Results: The mean age of infertility patients was 30.9(±5.95) years. The mean serum Zinc was significantly lower in infertile patients than in the controls group (59.13±15.21 µg/dl) and (76.32 ±14.75 µg/dl) respectively. There were no statically significant associations between mean serum Zinc types and duration of infertility.

Conclusion: Zinc may have an important etiological role in the pathogenicity of unexplained infertility and therapeutic intervention might be considered.

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Keywords: Serum Zinc, Infertility, Kurdistan region.

Infertility is a common health problem. Nutrition and nutritional imbalances of trace elements, including zinc, have been attributed in its etiology. Zinc deficiency is usually due to inadequate zinc intake or absorption, increased losses from the body, or increased requirements for zinc.[1-5]

Zinc is an essential element for many functions including protein synthesis, regulation of gene function and immune responses. Zinc is also important for reproduction, genetic expression of steroid hormone receptors, homeostasis of reproductive hormones estrogen and progesterone, with anti apoptotic and antioxidant properties. Also, it has a therapeutic role in preventing and treatment of menstrual irregularities and impotence.[5-8]

Zinc deficiency was reported to be associated with infertility, an ovulation, miscarriage, failure of implantation, intrauterine Growth retardation, delayed sexual maturation, impotence, hypogonadism in males and an increase in the incidence of congenital malformations.[9-11]

The aim of this study is to determine serum Zinc status in women with unexplained infertility and to compare that with a fertile control group in Duhok city, Iraq.

PARTICIPANTS AND METHODS

The present study was performed at infertility center at Azadi teaching hospital which is the main tertiary care hospital in Duhok province, Kurdistan region, Iraq.

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The data were collected from beginning of February to end of July 2014 .A case–control study design was adopted .The cases composed of 50 infertile women of unknown causes (Primary & secondary infertilities) diagnosed by specialist gynecologist specialist depending on scientific definition of unexplained infertility where all investigations were normal. The Control group composed from 100 normal and healthy fertile non pregnant women who were accompany their sick babies to Heevi pediatric teaching hospital. All who were receiving multivitamins or zinc supplementation or who were suffering from acute or chronic illnesses were excluded from the study.

The study protocol was approved by Ethical Committee of Kurdistan Board of Medical Specialization. Official permission from Duhok General Directorate of health was obtained. An informed verbal consent was obtained from all women prior to participation in the study. The purpose of the study was carefully explained to each participant, with assurance of the privacy and confidentiality of collected data.

Age at marriage, type and duration of infertility were recorded for all cases. A blood sample was collected from patients and controls for the measurement of serum Zinc. Blood specimens were collected in metal-free plain tubes. Specimens were then centrifuged and the serum was separated and kept in tubes and stored at –20 centigrade until analysis. The zinc concentrations in serum were measured by means of spectrophotometer (CE 2021), LTA reagents were used (LTA s. r. l via Milano 15/F). The serum and reagents were mixed and read at wavelength 578 nm. The serum Zinc levels were classified to Severe zinc deficiency (< 50µg /dl), Marginal Zinc deficiency (50-70 µg /dl), Normal serum Zinc (> 70–130 µg /dl) and Hyperzincemia (> 130 µg / dl).[12]

Statistical analysis was done using SPSS version[19]. All categorical variables were presented as percentage and continuous variable as means & standard deviation with 95% CI. Differences between two groups for continuous variables were determined by Odds Ratio & independent student t test, while difference between more than two groups determined by one way ANOVA test. Chi square test was used for categorical variables. Statistical significance was set at a P value ≤0.05.

RESULTS

The mean age of infertility patients was 30.9(±5.95) years and the mean age at marriage was 25.8(± 5.41) years. Table 1 shows that the mean serum Zinc level was significantly lower in patients with Infertility in comparison with control; (59.13±15.21µg/dl) and (76.32±14.75µg/dl) respectively.

Table 1: Mean Serum zinc levels in Infertile and control groups.

Groups	No.	rum zinc level(µg/dl) Mean(±SD.)	P-value
Infertility	**50**	**59.13(±15.21)**	**0.001**
Control	**100**	**76.32 (±14.75)**	

Table 2 reveals that the prevalence of sever hypozincemia was 42% in infertility patients in comparison to 1% in among controls. Moreover it also shows that the

majority of control group had normal serum Zinc (66%) in comparison to only (22%) among infertile

Table 2: Distribution of Serum zinc levels in Infertile and control groups.

S. Zinc	Infertility patients	Control group	Total
Sever Hypozincemia (<50 µg/dl)	21(42%)	1(1%)	22(14.7%)
Marginal zinc deficiency (50 t0 70 µg/dl)	18(36%)	31(31%)	49(32.7%)
Normal S.Zinc (70-130 µg/dl)	11(22%)	66(66%)	77(51.3%)
High S.Zinc (> 130 µg/dl)	0(0%)	2(2%)	2(1.3%)
Total	50(100%)	100(100%)	150(100%)
X2 = 52.03	df= 3		P-Value= 0.001
Odds ratio= 7.5	95 % CI= 3.41-16.6		P-Value= 0.001

Table 3 reveals that 58% of participants had primary infertility, and the mean serum Zinc was slightly lower in this group when compared to those with secondary infertility; (56.53±15.47) & (62.71 ±14.44 µg/dl) respectively, but the results were statistically not significant. Moreover the study shows that the prevalence of hypozincemia was higher, but also not significant, in those with primary infertility than those with secondary infertility, (82.7%) and (71.4%) respectively.

Table 3: Mean Serum zinc levels according to the types of infertility

Groups	No.	Serum zinc level(µg/dl) Mean(±SD.)	P-value
Primary Infertility	29	56.53(±15.47)	0.1
Secondary Infertility	21	62.71 (±14.44)	
Total	50	59.13(±15.21)	

Table 4: Distribution of Serum zinc levels according to the types of infertility

S.Zinc	Primary Infertility	Secondary Infertility	Total
Low S.Zinc (<70 µg/dl)	24(82.7%)	15(71.4%)	39(78%)
Normal S.Zinc (70-115 µg/dl)	5(17.3%)	6(28.6%)	11(22%)
Total	29(100%)	21(100%)	50(100%)
X2 = 0.91	df= 1		P-Value= 0.3
Odds ratio= 1.9	95 % CI= 0.49-7.41		P-Value= 0.3

Finally table 5 shows that the mean serum Zinc was reducing with increasing the duration of infertility, where the lowest mean serum Zinc were reported in those with duration of infertility more than six years (52.80±6.49 µg/dl) compared to (58.96 and 64.50 µg/dl) respectively among those with 3-<6 years and 1-<3

years of infertility; but the differences were statistically not significant.

Table 5: Mean Serum zinc levels according to the duration of infertility

Duration of Infertility	No.	Serum zinc level (µg/dl) Mean(±SD.)	P-value
1-<3 year	14	64.50(±18.32)	0.3
3-<6 years	23	58.96 (±14.08)	
6+years	8	54.18(±15.31)	
>9 years	5	52.80(±6.49)	
Total	50	59.13(±15.21)	

DISCUSSION

The mean age of marriage among infertile cases was 25.8(±5.41) years. The average age of marriage in the Kurdistan Iraq.13 Fertility declines with age, and female fertility is at its peak between the ages of 18 and 24 years. 14

The study showed that the mean serum Zinc was significantly lower in women with unexplained infertility in comparison to control group. Similar results were observed by a study done in Iraq on smaller number of cases and controls by Al-saraf et al in 2005. 15Conversely, another old study conducted in 1983 by Soltan and Jenkins in United Kingdom found that Plasma zinc concentration was not appreciably different in infertile and fertile women .16 In Egypt, mosad and Shalaan (2006) found thatserum Zinc was significantly lower among women suffering from repeated abortions.17 The study also found that the mean serum Zinc was lower in women with primary governorates currently featuring the highest in Iraq ; with an average of 26 years as opposed to 22 years in the rest of infertility when compared to those with secondary infertility. Moreover serum Zinc was found to be reduced with increasing the duration of Infertility with the lowest mean serum zinc reported among those with long duration of infertility. Nevertheless both associations were found not to be significant and this might be due to the small number of cases in the study.

Zinc affects a women's fertility in a multitude of ways such as; hormone regulation, ovulation, follicular fluid levels, sexual development, menstrual cycle and antioxidant properties. 5,6,18

In conclusion Zinc might be important in unexplained infertility among women and supplementation for this group might be considered.

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پوختە

دەستنیشانکرنا پلەیا توتیایێ ل دەڤ ژنێن نەزوکیا بێ ئەگەر هەین:
ڤەکولینەکا نەخوشی – کونترلی یە

پێشەکی: یا گرنگە هزر د گهورینا پلەیا کەرەستێن خوراکی و کانزایدا بهێتەکرن وەك ئەگەرەك بو نەزوکیا بێ ئەگەر، و ژوان کەرەستێن زێدە گرنگ توتیایە کو بدیتنا مە دبیتن فاکتەرەکێ گرنگ بیتن بو ڤێ نەزوکیا بێ ئەگەر. ئارمانج ژ ئەڤێ ڤەکولینێ ئەوبوو دیارکرنا پلەیا توتیایێ ل سەر بنەمایێ پەیتا توتیایێ دناڤ خوینێ (سیروم)ی دا، ل دەڤ ژنێن نەزوکیا بێ ئەگەر هەی و بەراوردکرنا وێ لگەل پلەیا توتیایێ دکونترولێن ساخلەمیدا.

ڕێکێن ڤەکولینێ: ئەڤ ڤەکولینا نەخوشی–کونترولی یە، ل بنگەهێ نەخوشییێن نەزوکی ل باژێرێ دهوکێ/ هەرێما کوردستانا عیراقێ ژ هەیڤا شواتێ تا هەیڤا تیرمەها ٢٠١٤ هاتیە ئەنجامدان، پێنجی نەخوشێن نەزوکیا بێ ئەگەر ب خوڤەگرت و ١٠٠ کەسێن ئاشکرا کو دساخلەمن و ژلایێ تەمەنی ژیڤە دگونجای بوون وەکو گروپێ کونترولی، هەر ژنەکێ چ نەخوشبیتن یان کونترول چەندین پرسیار ژێ هاتنەکرن، کێش و درێژاهیا وان هاتە پیڤان و سامپلەکێ خوینێ ژێ هاتە کێشان ژبو دەستنیشانکرنا ئاستێ توتیایێ دناڤ خوینێدا.

ئەنجام: دناڤ نەخوشاندا تەمەنێ ناڤنجی ٣٠.٩ سال بو، تێکراییا توتیایێ دناڤ خوینێدا ل دەڤ نەخوشێن نەزوك ٧٦.٣٢ µg/dl، ب شێوەکێ گرنگ نزمتر بو ژ یێ کونترولا ٥٩.١٣ µg/dl چ پەیوەندییێن ژمێریاری یێن بەرچاڤ نەهاتنە تێبینیکرن دناڤبەرا تێکراییا توتیایێ دناڤ خوینێدا ل دەڤ نەخوشێن نەزوك و جورێن نەزوکیێ، ماوێ نەزوکیێ و پیڤەرێ زێدەکێشیێ.

دەرئەنجام: دڤێ ڤەکولینێدا دیاربوو کو کێمبوونا توتیایێ دناڤ خوینێدا ل دەڤ نەخوشێن نەزوکیا بێ ئەگەر دبیتن رولەك هەبیت دهەبوونا ڤێ کێشێ، و دانا کەرەستێ توتیایێ بو نەزوکێن کێم توتی دناڤ لەشیدا دبیتن دەرگەهە بیت بو چارەسەرکرنا ڤێ کێشا بێ سەروشین.

الخلاصة

مستويات الخارصين في مصل الدم لدى النساء المصابات بالعقم غير المفسر: دراسة العينة والشاهد

الخلفية والأهداف: ينبغي النظر في التغيرات في المواد المغذية والمعادن بما في ذلك الخارصين كمسببات العقم غير المفسر. كان الهدف من هذه الدراسة هو تحديد حالة الخارصين على أساس تركيز الخارصين في مصل الدم للنساء المصابات بالعقم غير المفسر ومقارنتها مع االصحاء.

طرق البحث: أجريت دراسة الحاالت والضوابط في مركز العقم في مدينة دهوك /اقليم كردستان /العراق، خالل الفترة من بداية شباط الى نهاية تموز 2014. خمسون مريضة من اللواتي يعانين من العقم غير المفسر و100 من االصحاء كمجموعة ضابطة شملن بالدراسة. لكل واحدة منهن ملئ استبيان عن طريق المقابلة المباشرة، وتم الحصول على عينة من الدم لقياس الخارصين في مصل الدم.

النتائج: كان متوسط عمر مريضات العقم هو 30،9 سنة. وكان متوسط مستوى الخارصين في مصل الدم أقل لدى المريضات اللواتي يعانين من العقم مما كان عليه في المجموعة الضابطة 59،13 ± 15،21 ميكروغرام/ ديسيلتر و76،32 ± 14،75 ميكروغرام/ ديسيلتر على التوالي ولا يوجد عالقة معتدة احصائيا بين مستوى الخارصين في مصل الدم وأنواع العقم، ومدة العقم

الاستنتاجات: من هذه النتائج تم التوصل إلى أن مستوى الخارصين في مصل الدم قد يكون له دور مهم في العقم غير المفسر، والتدخل العالجي في هذا الصدد قد يكون مفيداً في عالج هذه الحالة.

HEALTH EDUCATION ROLE IN IMPROVING AWARENESS ABOUT PREECLAMPSIA /ECLAMPSIA AMONG TRADITIONAL BIRTH ATTENDANTS IN DUHOK GOVERNORATE

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ABSTRACT

Background: Preeclampsia/Eclampsia was the second most common cause of maternal death in Duhok Governorate during the period 2007-2014.The aim was to measure the value of a health education program in improving knowledge and practice toward Preeclampsia/ Eclampsia among traditional birth attendants in Duhok.

Methods: A quasi experimental study was conducted during the summer of 2014 on 91 traditional birth attendants registered in Duhok governorate. Their knowledge and practice about Preeclampsia/ Eclampsia were evaluated using a standardized questionnaire before and 8 weeks after an education program. The program comprised lectures, videos and an education booklet which contains basic knowledge supported by pictures and distributed to all participants.

Results: The study showed that most of traditional birth attendants had correct basic knowledge, and practice toward Preeclampsia /Eclampsia; with a statistically significant post education improvement in most of knowledge and practice toward both conditions.

Conclusion: Health Education has a significant role in improving knowledge and practice of traditional birth attendants toward Preeclampsia / Eclampsia

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Keywords: Preeclampsia/ Eclampsia, Health education, Traditional birth attendants.

Ten million women develop Preeclampsia (PE) around the globe each year, with 76.000 deaths. Women in the developing countries are seven times more likely to develop PE; with mortality rates 14 times higher than in developed countries.[1-3]

In Duhok, PE and eclampsia were the second cause of maternal death during the period of 2007-2014.[4] Health education about risk factors and early detection of PE cases, play a major role in the prevention of the disease and its complication.[5-6] Traditional Birth Attendants (TBAs) are still playing important role in caring for pregnant women, particularly in developing countries.[7-9] Their practice based primarily on knowledge and experience acquired informally through the practices and traditions of the communities where they originated.[10] Globally a number of reasons were reported for the women to seek TBAs care. Those include: cost, proximity, lack of trust in nurses and doctors, history with the TBA, availability, accessibility, reliability, privacy, and desire for sincere attention.[11-13] Another important consideration is that women do not see a risk in using the TBA's facilities.[11] The WHO supported programs aiming to educate TBAs and to provide them with proper skills and

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knowledge.[1,15] In Duhok especially in rural districts, where women lack proper antenatal knowledge and practice, TBAs are still essential health providers. The study aimed to measure the effect of an educational program in improving their knowledge and practice towards PE and eclampsia.

METHODS

The study was conducted in Duhok governorate which is one of three governorates in Kurdistan Region of Iraq during the summer of 2014.

An education booklet was prepared using basic information regarding health education for PE and eclampsia, which have then been reviewed, modulated and approved by specialists in the field. The contents were designed in small colored booklet. The instructions emphasized the importance of good nutrition, activities, checking weight, perception of fetal movement, observation of abdominal enlargement, the use of folic acid, the risk of smoking and drugs on maternal health and on the fetus and the alarming signs and symptoms of PE and eclampsia, supported with many photos as an aid to make it easy to be understood and was written in Kurdish and Arabic languages.

A questionnaire was designed which included personal information, the age, number of years in experience, and if she had seen any case of PE/eclampsia, her behavior, the referring, transportation difficulties, the maternal and fetal outcome of that case; also if she has an interest to participate in education programs.

A total of 107 TBAs were registered at Duhok health department. All were approached and 91 responded to the invitation. Interviews were arranged to be conducted in the nearby health center for groups of 15-20 participants. All appointments were arranged with the local health staff.

The aim was first explained then the questionnaire was filled for each TBA individually. Thereafter a lecture about the risk of PE/eclampsia to the life of the mother and her babies was given and then all supplied with a copy of the education booklet and they were asked to understand the contents by themselves or by assistants in their family. Lastly, they were asked to come back after eight weeks where the second evaluation was done using the same questionnaire and answers were recorded and stored in the designed database file.

Statistical analyses were done by using computer software SPSS version 22.0.

Comparison of pre and post education findings was made by using McNemar's (paired chi square) tests .The differences were considered significant at p -value $\leq$ 0.05.

RESULTS

All the 91 TBAs came to the second meeting and showed interest in the subject and in the education booklet. Table (1) shows that about three quarters of TBAs were between 51-70 years of age. More than one third was from Akre district. More than half of them have had long practice experience of about 10-20 years and have attended between 1-4 lectures or conferences on maternal health education, also nearly three quarters of TBAs have seen women with PE and more than quarter of them have seen cases of eclampsia.

Table 1: Characteristics of TBAs.

Characteristic		No.	%
Age	30 – 40	3	3.3
	41 – 50	13	14.3
	51 – 60	29	31.8
	61 – 70	41	45.1
	71 – 80	5	5.5
Sector	Duhok	18	19.8
	Sumel	21	23.1
	Akre	33	36.3
	Amedy	19	20.8
Registration& practice	4 – 10	13	14.3
	11 – 20	53	58.2
	21 – 30	25	27.5
Attended conferences	Nil	13	14.3
	1 - 4	53	58.2
	5 and more	25	27.5
Have seen PE	Yes	65	71.4
	No	26	28.6
Have seen Eclampsia	Yes	25	27.5
	No	66	72.5
Total		91	100.0

Table (2) illustrates that more than three quarters of TBAs, have correct knowledge about PE, where nearly all of them believed that they can save the life of the women by health education, also more than three quarters of them have basic correct practice of managing PE in labor, and only four TBAs have wrong basic practice of managing eclampsia in labor. The table shows statistically significant post education improvement in most of knowledge and practice toward PE. Finally most of TBAs have basic correct practice by referring women to the nearest health center

Table 2: TBAs knowledge and practice before and after intervention

Knowledge or practice area		Before No. (%)	After No. (%)	p*
Knowledge about PE and eclampsia	Correct	73 (80.2)	87 (95.6)	
	Incorrect	11 (12.1)	3 (3.3)	0.001
	Do not know	7 (7.7)	1 (1.1)	
Answer to the question: "Can you save the life of the woman by health education"	Yes	88 (96.7)	90 (98.9)	0.480
	No	3(3.3)	1(1.1)	
Knowledge about health education and ANC practice	Correct	78 (85.7)	86 (94.5)	0.006
	Incorrect	13 (14.3)	1 (1.1)	
	Do not know	0 (0.0)	4 (4.4)	
Practice regarding PE in labor at home	Refer her	71 (78)	80 (87.9)	0.008
	Deliver her	20 (22)	11 (12.1)	
Practice regarding eclampsia in labor at home	Refer her	87 (95.6)	91 (100)	0.134
	Deliver her	4 (4.4)	0 (0.0)	
Total		91 (100)	91 (100)	

* Based on McNemar's test.

DISCUSSION

Health education is an important tool to achieve good protection to several health problems, including pregnancy complications, and to increase the quality of services delivered to the public.[1,10]

The TBAs are still essential health providers in many developing countries, and improving their knowledge and practices will have a significant effect in reducing maternal mortality and morbidity.[12-14]

The TBAs in Duhok are distributed mainly in the suburban areas in Akre and Amedy. Those are the biggest districts with mountainous areas which are likely to be isolated by the deposits of snow during winter. Such families may be obliged to ask the help of TBAs in pregnancy and

labor Moreover they are dominated by strict social and cultural behaviors especially those related to obstetrical care. Accordingly a well trained TBA is essential and vital for pregnant women.[10, 15,18]

The education booklet was accepted by the TBAs as its contents were selected on practical bases with colored pictures to make it more understandable by the target persons or their relatives, as there was a great variation in their educational levels.

Health education is more successful if the health planners focus on the target group and supply them with the necessary knowledge, practice and equipment to prepare them to be more skilled and accepted by the community.[19]

Most TBA training evaluations lack a baseline background of trainees. Background surveys, may provide important information about the areas within which TBAs operate. These are essential information which can help to design a training program that is focusing on the learners, the specific knowledge and practice that need to be applied.[15]

The study revealed that the majority of TBAs have correct basic knowledge and practice about PE. This is against the result reported in a similar study in Nigeria 5 , which might be due to the fact that the majority had attended many conferences about maternal health care.[20] Other possibility is that some knowledge might be gained by the practice of accompanying pregnant women to the health center during medical consultation or in labor. The study also showed that the majority of TBAs were illiterate, as the case in most of the developing countries. Also most of them showed an interest in health education and antenatal care, and this will have a more significant outcome on the training program.[10]

Nevertheless still few TBAs had incorrect knowledge .This might have a significant impact on the related village as dangerous practice may have a fatal outcome on the pregnant and her baby. A successful policy is to integrate TBAs in the public-health system, as a member of a team of health providers for all levels of care. The integration of TBAs with formal health systems increases skilled birth attendants.[10, 21]

The study revealed a significant improvement in the knowledge and practice of TBAs after implementing of the education program. Other studies also showed that training of TBAs has improved their knowledge and skills for proper antenatal care and improved pregnancy outcome.[10, 18, 19]

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پوختە

رولێ رەوشەنبیرکرنا ساخلەمی دپێشڤەبرن و باشکرنا هوشمەندیێ لدور بریکلامبسیا/ ئیکلامبسیا دناڤبەرا داپیرکێن کلاسیکی ل پارێزگەها دهوکێ

پێشەکی: ڤەلەرزینێ و پێشەکیێن وێ دووەمین گرنگترین هۆکارێن مرنا دایکان ل پارێزگەها دهوکێ یە دناڤبەرا ٢٠٠٧-٢٠١٤. بو پشکنینا زانین و پێرابوونا داپیرکێن کلاسیکی دبابەتێ ڤەلەرزینێ و پێشەکیێن وێ بەری و پشتی بەرنامێ رەوشەنبیرکرنێ.

ریکێن ڤەکولینێ: ڤەکولینەکا کومەلگەییە دناڤێکدا چوونەکا رەوشەنبیریە ل پارێزگەها دهوکێ ژ ئێکی خزیرانا ٢٠١٤ تا هەشتی شواتا ٢٠١٥. و نامیلکەکا رەوشەنبیرکرنێ هاتە ئامادەکرن دگەل دوو لیستەیێن راپرسینێ بەری و پشتی رەوشەنبیرکرنا داپیرکێن کلاسیکی، پەیوەندی ب ٩١ نوت و ئێك داپیرکان هاتەکرن ژبو کومبوونێ ب ریێا داخازکرن بو کومبوونێ بەری و پشتی رەوشەنبیرکرنێ ب ماوەیەکێ ناڤبەرا شەش تا هەشت حەفتیان، هەڤدیتن هاتنەکرن ل پشکا ساخلەمیا خوپاراستنێ ل بنگەهێ دهوك و ل هەر هەست بنگەهێن ساخلەمیێ بێن دەستنیشانکری ل بنگەهێ دهوك و هەر چار کەرتان ئاکرێ، ئامێدیێ، سێمێلێ و زاخو.

ئەنجام: باشبوونەکا ئاماریێ یا بەرچاڤ هاتە دیتن دزانین و پێرابوونا گروپێ داپیرکان پشتی رەوشەنبیرکرنێ لدور بابەتێ ڤەلەرزینێ و پێشەکیێن وێ.

دەرئەنجام: ڤەکولینێ باشبوونەکا بەرچاڤ دیارکر، پشتی رەوشەنبیرکرنا ساخلەمیێ دزانین و پێرابوونا گروپێ ڤەکولینێ لدور ڤەلەرزینێ و پێشەکیێن وێ و ب جیاوازیەکا ئاماریێ ٠.٠٠١.

الخلاصة

دور التعليم الصحي في تحسين الوعي حول بريكلامبسيا / إكلامبسيا بين المتلقين التقليديين للولادة في محافظة دهوك

الخلفية والأهداف: يمتاز الاضطراب التحويلي بوجود اعراض متعلقة بالجهاز العصبي غيرمفسرة مع وجود اسباب نفسية ورائها, الهدف من البحث كان لبيان نسبة انتشار الاضطراب التحويلي، وعوامل الاختطار، اضافة الى الاعراض الرئيسية المنتشرة بين المرضى والضغوطات النفسية التي ورائها.

طرق البحث: من خلال دراسة مقطعية تم اختيار (٦٣٧) مريض من الذين كانوا يراجعون استشارية الامراض النفسية بين يوم واخر في مستشفى ازادي التعليمي في مدينة دهوك للفترة من تموز ٢٠٠٨ الى تموز ٢٠٠٩. تم الاعتماد على الدليل التشخيصي والاحصائي الرابع للاضطرابات النفسية المعروف بـ(DSM-IV) لتشخيص حالات الاضطراب التحويلي، وقد تم معالجة البيانات احصائيا باستخدام برنامج (SPSS).

النتائج: أظهرت النتائج ان نسبة انتشار الاضطراب التحويلي قد بلغ ١٨.٢% (١١٦ حالة)، وكان منتشراً أكثر بين الاناث (٨٠.٢٥%)، والفئة العمرية الشابة بين ١٨ الى ٢٥ سنة (٦٤.٧%)، والمستوى التعليمي الابتدائي (٣٦.٢%) وربات البيوت (٤٢.٢%)، مع وجود علاقة احصائية ايجابية معنويا بين الاضطراب والتغيرات المذكورة. وعلى الرغم بانه كان منتشراً أكثر بين المتزوجين (٥٢.٧%) وضمن المناطق الحضرية (٥٦%) ولكن العلاقة كانت غير مهمة إحصائياً. كان العرض الاكثر انتشاراً هو عدم الاستجابة (٤٩.١%) (نوبات سقوط مع فقدان الوعي لفترات طويلة)، تلاه نوبات الصرع الكاذب (٢١.٦%) (نوبات سقوط قصيرة مع حركات غير منتظمة)، ونوبات الاغماء (١٠.٣%)، ثم الحركات الغير طبيعية (٨.٦%). كان الصراع المنزلي هو الضغط النفسي الاكثر انتشار (٢٧.٦%) وكانت جميع الحالات اناثاً، تلاه العلاقة الغرامية (١٧.٢%) ثم المرض (١٣.٨%) والذي كان الضغط النفسي الاكثر انتشاراً بين الذكور.

الاستنتاجات: نسبة انتشار الاضطراب التحويلي كان مرتفعاً، وشملت عوامل الاختطار كل من الاناث، والفئات العمرية الشابة، والمستوى العلمي المنخفض، إضافة الى ربات البيوت.

THE PREVALENCE OF GARDNERELLA VAGINALIS IN BACTERIAL VAGINOSIS AMONG SYMPTOMATIC WOMEN IN DUHOK CITY

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ABSTRACT

Background: *Gardnerella vaginalis* is considered the most common bacteria that associated to Bacterial Vaginosis syndrome (BV), which is leading to vaginal disorder, and it is the most common cause of unpleasant vaginal odor and discharge in women during reproductive age.

Objectives: The main aims of this study were To identify the prevalence of Gardnerella vaginalis in the Bacterial Vaginosis cases in symptomatic women with BV in Duhok city by using VITEK2 system, and determine the susceptibility of some isolates of this bacteria against (14) different antibiotics by using the disc diffusion method.

Methods: A total of 500 vaginal samples taken from women of reproductive age range between (18 – 50) years suffering from symptoms of bacterial vaginosis such as vaginal discharge, burning, and itching complaints, and others. Sampling period was from November 2014 until March 2015, and the samples were taken from two major hospitals in Duhok province, Maternity hospital and VIN Private hospital.

Results: From Out of 500 high vaginal swabs, 63(12.2 %) cases of bacterial vaginosis were detected depending on Nugent criteria and (56) isolates of G. vaginalis distinguished from them, with a prevalence (11.2%) in all samples tested, and (88.8%) in bacterial vaginosis cases. According to the age range, the highest prevalence rate of G. vaginalis was seen in age 20-30 years (46.4%). Due to the antibiotics susceptibility test, the results revealed that G. vaginalis isolates showed a good sensitivity toward Clindamycin (89.5%), while the study showed that only one isolate (5%) of Gardnerella vaginalis was sensitive to Metronidazole

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Keywords: Conversion disorder, frequency, risk factors, stressors

Gardnerella vaginalis is considered the most common bacteria that associated to Bacterial Vaginosis syndrome (BV), which is leading to vaginal disorder, and it is the most common cause of unpleasant vaginal odor and discharge in women during reproductive age[1]. This bacterium at the beginning known as Haemophilus vaginalis, is affiliated to the family Bifidobacteriaceae and primary was identified as the main cause of bacterial vaginosis.[2]

Bacterial vaginosis, also known as vaginal bacteriosis or Gardnerella vaginitis, is a disease of the vagina caused by excessive bacteria. Common symptoms include increased vaginal discharge that often smells like fish, the discharge is usually white or gray in color, burning with urination may occur; occasionally there may be no symptoms. Having Bacterial vaginosis increases the risk of infection by a number of sexually transmitted infections including HIV/AIDS. It also increases the risk of early delivery among pregnant women.[3-4]

With the increasing incidence of bacterial vaginosis around the globe, there is a need to fully understand about this type of

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syndrome and its pathogenicity to enable us to control the complications associated to these type of infections, it was found that 300 million women worldwide are thought to be acquired bacterial vaginosis each year5. The essential participants in pathological polymicrobial associations, which could be used as markers for bacterial vaginosis, are Gardnerella vaginalis (that grow under appropriate microaerophilic conditions).[7] Other microorganisms involved in bacterial vaginosis microbiota are very diverse and include anaerobes, such as Peptostreptococcus spp., Mobiluncus spp., Prevotella spp., Bacteroides spp., and Fusobacterium spp.[9]

This study will focus on Gardnerella vaginalis bacteria and its association with vaginal disorder and genital infections because this bacterium is the predominant organism in vaginal fluid from women with bacterial vaginosis1. This will help to highlight the role of this bacterium in certain cases, and how to improve and update laboratory isolation and detection of this bacterium which commonly associated to bacterial vaginosis.

It is not clear yet if the Gardnerella vaginalis is a sexually transmitted disease, bacterial vaginosis can be an independent and increased risk factor for acquisition of any sexually transmitted infections10. It has also been shown to be a cause for serious health problems as preterm birth, postpartum fever, development of endometritis, post-hysterectomy or postabortal sepsis, and pelvic inflammatory disease[8].

The reason of interest in this microorganism (Gardnerella vaginalis) was based on fact of being the mostly isolated microorganism and more virulent than other associated anaerobes in cases of bacterial vaginosis, which is regarded as one of the most common vaginal disorders in women of reproductive age, this makes bacterial vaginosis including Gardnerella vaginalis paramount importance.[11]

Currently there is only few limited studies to bacterial vaginosis occurrence in the Kurdistan population, and as such our study is relevant for the characterization of that infection in Duhok, Therefore, the main objective of the current study was to Identification and determination the prevalence of G.vaginalis in the bacterial vaginosis in symptomatic women of Duhok city including pregnant, aborted, and women used IUD.

MATERIALS AND METHODS

Samples Collection

From November 2014 until March 2015 a total of 500 cases (each sample include 2 swabs) taken from all tested patients of reproductive age range between 18-49 years suffering from symptoms of suspected bacterial vaginosis such as vaginal discharge, burning, and itching complaints, and others, sampling also include pregnant, aborted, and women used IUD.

The samples were taken from two major hospitals, Maternity hospital, and VIN Private Hospital in Duhok city, Kurdistan region.

Two vaginal swabs were obtained from each woman, one of them for culture and Gram stain, while the other swab was for PH measurement, Whiff test, and wet preparation.

Bacterial Vaginosis Diagnostic tests a- Amstel's clinical criteria

Diagnosis of bacterial vaginosis depending on the clinical criteria was done according to Amsel (12), as follow:

1- The presence of vaginal discharge
2- Measurement of vaginal pH
3- Detection of clue cells in the vaginal fluid,
4- Whiff test (KOH test)

b-The Nugent criteria

In the Nugent method, the swab which stained by Gram stain, was read, and the number of morphotypes was evaluated based on a standardized scoring method for the following morphotypes under oil immersion (1000×magnification):[13]

• large Gram-positive rods (Lactobacillus morphotypes),
• small Gram-variable rods (G. Vaginalis morphotypes),
• Curved Gram-variable (Mobiluncus species morphotypes) Rods (Tables 1&2).

Table 1: show the Laboratory examination of vaginal smears and the determination of the Nugent Score.

Number of organism morphotypes per high power field

lactobacillus morphotypes	SCORE	G.vaginalis morphotypes,	SCORE	Curved gram-negative bacilli	SCORE	Sum=*N SCORE
30 or >	0	0	0	0	0	0
5-30	1	<1	1	<1	1	3
1-4	2	1-4	2	1-4	1	5
<1	3	5-30	3	5-30	2	8
0	4	30 or >	4	30 or >	2	10

*** N Score = the sum of the scores for each bacterial morphotype listed above. (Number of Organisms seen /100X objective). (13, 16)**

Table 2: explain the Interpretation of Nugent Score

Interpretation of Nugent Score

If (N) Score is:		
0-3	Normal	Not BV case
4-6	Intermediate score	May be BV
>7	High score	BV case

Note: our study takes only the high score cases (7-10) which regard as BV because the study focuses on symptomatic patients only.

Isolation of G. vaginalis:

For Isolation of G. vaginalis bacteria, the samples were cultivated on Colombia Blood Agar (CBA) base with Selective Supplement (CONDA-Spain), in microaerophilic condition (5–10% CO2) at 37◦C for 48–72 hours. The suspected colonies on Columbia human blood agar were sub-cultured on a new plate of this medium, then the obtained pure colonies were subjected to gram stain, catalase, oxidase, VITEK 2 system.

Diagnosis of G. vaginalis by VITEK2 System

a. Description

The VITEK2 system (biomerieux) is highly automated and uses very compact plastic cards (credit card size) that performs rapid identification based on colorimetry, this system repetitive turbidimetric monitoring of bacterial growth during an abbreviated incubation period.

b. Preparation of suspension

A sterile swab was used to transfer a sufficient number of colonies of a pure culture and suspended in 3.0 ml of normal sterile saline (0.45% to 50%) with a PH (4.5–7.0) in a clear plastic polystyrene test tube. The turbidity was adjusted according to the tables provided by manufacturer recommendation on McFarland turbidity range for Gram positive (0.5-0.63), and measured using a turbidity meter called the DensiChek TM.

A test tube containing the bacteria suspension was placed into a special rack (cassette) and the identification card (type VITEK® 2GP ID card for Identification of Gram-positive bacteria) was placed in neighboring slot while inserting the transfer tube into the corresponding suspension tube and the filled cassette was placed manually after reading the barcode of the cards.

Antibiotics

Fourteen of different antibiotic disks have been used in this study, supplied by (Bioanalyse/ Turkey).

Antibiotic Susceptibility Test

The susceptibility of G. vaginalis isolates towards different antibiotics, were examined by using the disc diffusion method (Kirby-Bauer method) on Colombia agar according to the National Committee for Clinical Laboratory Standards and Manual of Antimicrobial Susceptibility Testing guidelines (14,15).

RESULTS

The prevalence of Gardnerella vaginalis in vaginal swabs and bacterial vaginosis cases

Out of 500 cases examined in this study, (56) isolates of G.vaginalis distinguished with a prevalence (11.2%) in all samples tested, while (63) cases of bacterial vaginosis which had a Nugent score (7-10) detected by using Nugent laboratory criteria with a prevalence (12.6%) in all samples tested in this study.

Morphology of Gardnerella vaginalis cells

Under the oil immersion (1000 X), the microscopic examination of G.vaginalis which was taken from the growth of this bacteria on Colombia Blood Agar media and stained with Gram stain, showed that they were polymorphic cells to double cocco-bacilli or single, Gram positive to Gram variable bacterial cell as explained in Figure (1).

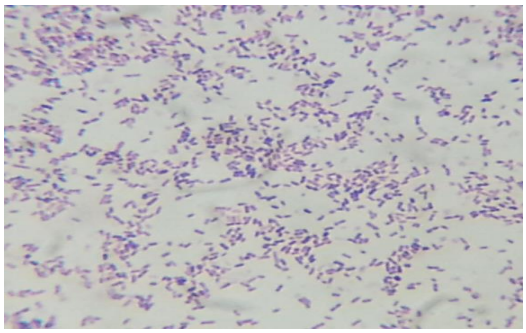

Figure 1 The cells of Gardnerella vaginalis stained with Gram staining, taken from Columbia Blood Agar, which appeared as Gram virable cocco-bacilli Bacteria (1000 X).

Culture of Gardnerella vaginalis

Fifty six (11.2%) isolates of *G.vaginalis* obtained from 500 cases examined in this study by using supplemented selective media (Colombia blood agar).The characteristics of Gardnerella vaginalis colonies that grew on Columbia blood agar under 10 % CO2, at 37°C for 48 hr. were appeared as small, circular, gray to white, with diffused edges, surrounding by β-hemolysis, as in Figure (2).

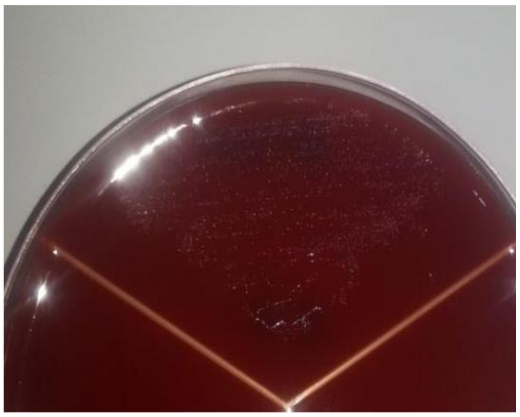

Figure 2 Colonies of Gardnerella vaginalis that grew on Columbia blood agar

The infection rate of *Gardnerella vaginalis* according to age range

Age range distribution in table (3) showed that the highest prevalence rate of G.vaginalis was seen in age ranged between (20-30) years (46.4%) and followed by age ranged between (30-40) years (39.4%) years.

Table 3 The Occurrence rate of Gardnerella vaginalis according to age group.

age group (years)	Number	Number of Gardnerella vaginalis isolates (n=56) %
<20	4	0 (0)
20-30	215	26 (46.4)
31-40	191	22 (39.3)
41-49	90	8 (14.3)
Total	500	56 (100)

***Gardnerella vaginalis* in relation with Pregnant, abortion cases, and use of intrauterine device (IUD).**

The table (4) showed that (5) from (10) pregnant women had G. vaginalis While (9) of G.vaginalis isolates from (36) recent abortion cases detected, and (4) isolates of G. vaginalis detected in (8) women used IUD.

Table 4: Occurrence rate of Gardnerella vaginalis in Pregnant, abortion cases, and Women use IUD.

Condition	Number	Number of G.vaginalis isolates	The rate %
Pregnant women	10	5	50%
Abortion	36	9	25%
Use of IUD	8	4	50%

The Occurrence rate of *G. vaginalis* according to diagnosis and important clinical signs

From the 56 samples of G. vaginalis which obtained in the study, discharge was found in 49 (87.5%) cases, while clue cells found in 51 (91%) cases, and 48(85.7%) of samples which had PH more than (4.5) were found to be positive for G. vaginalis. Amine test was moderately related to the presence of G.vaginalis 37(66%), as explained in the Table (5)

Table 5: The occurrence rate of G.vaginalis according to diagnosis and important signs.

Clinical signs	Number of G. vaginalis share with sign (n=56) %
Vaginal discharge	49 (87.5)
Pus cell>10	21 (37.5)
Clue cell	51 (91)
pH>5	48 (85.7)
Fishy odor	37 (66)
BV case (n=63)	56 (88.8)

Susceptibility of *Gardnerella vaginalis* to antibiotics:

The susceptibilities of G.vaginalis against different locally available antibiotics were studied by disk diffusion method (Kirby Bauer test), and the results were presented in tables (6&7).

The results explained that *G. vaginalis* isolates were showed a good sensitivity toward the following antibiotics: Clindamycin (89.5%), Rifampicin (84.2%) and Ciprofloxacin (84.2%), while the study showed that only one isolate of G. vaginalis was sensitive to Metronidazole (5%) and the remaining isolates were resistant (95 %) to this antibiotic.

Table 6: The susceptibilities of (19) isolates of G. vaginalis towards (14) locally available antibiotics measured by using Kirby-Bauer method

Ab Gv	RA	CIP	AX	DA	KF	PRL	TOB	GN	SXT	E	CFM	TE	AK	MET	S	R
1	S	S	S	S	S	S	R	R	R	R	R	R	R	R	6	8
2	S	S	R	S	S	R	R	R	R	S	R	R	R	R	5	9
3	R	S	R	S	R	R	S	S	S	R	R	S	R	R	6	8
4	S	S	S	S	R	S	R	R	R	R	R	R	R	R	5	9
5	S	S	R	S	R	R	R	R	R	S	R	S	R	S	5	9
6	S	S	S	S	S	R	S	S	S	R	R	R	R	R	8	6
7	S	S	S	S	S	R	R	R	R	R	R	S	R	R	6	8
8	S	S	S	S	S	R	R	R	R	R	R	R	R	R	5	9
9	R	S	S	S	S	S	S	R	R	S	S	S	S	R	12	2
10	S	S	S	R	S	S	R	R	R	R	R	R	S	R	6	8
11	S	S	S	S	R	S	S	S	R	R	S	R	S	R	8	6
12	S	S	S	S	R	S	S	S	R	R	S	R	R	R	8	6
13	S	R	R	S	S	R	S	S	R	R	S	R	R	R	6	8
14	S	s	R	R	R	S	R	R	R	S	S	R	S	R	5	9
15	S	R	S	S	R	R	S	S	R	R	S	S	R	R	7	7
16	R	S	S	S	R	S	R	R	R	R	S	R	R	R	5	9
17	S	R	S	S	S	S	R	R	R	R	S	R	R	R	6	8
18	S	S	S	S	R	S	R	R	S	R	S	R	R	R	7	7
19	S	S	R	S	S	S	R	R	R	R	S	R	R	R	6	8
Tot.	16 S 3R	16 S 3 R	14 S 6 R	17 S 2 R	13 S 6 R	11 S 8 R	8 S 11 R	8 S 11 R	3 S 11 R	4S 15 R	10 S 9 R	5S 14 R	4S 15 R	1S 18 R		

S = sensitive, and R = resist, RA= Rifampicin , CIP=Ciprofloxacin , AX= Amoxicillin , DA=Clindamycin , KF= Cephalothin, PRL=Pipracillin, TOB=Tobramycin, GN=Gentamycin, SXT= Co-trimaxazol, E=Erythromycin, CFM=Cefaxime, TE= Tetracycline, AK=Amikacin, MET= Metronidazole

Table 7: The susceptibility of (19) G. vaginalis isolates towards (14) different locally available antibiotic.

	Nineteen isolates of G. vaginalis	
ANTIBIOTIC	Sensitive No.(%)	Resistant No.(%)
Clindamycin	17 (89.5)	2 (15.8)
Rifampicin	16 (84.2)	3 (10.5)
Ciprofloxacin	16 (84.2)	3 (10.5)
Amoxicillin	14 (73.6)	5 (26.4)
Cephalothin	13 (68.4)	6 (31.6)
Pipracillin	11(57.9)	8 (42.1)
Cefaxime	10 (52.7)	9 (47.3)
Tobramycin	8 (42.1)	11 (57.9)
Gentamycin	8 (42.1)	11 (57.9)
Erythromycin	4 (21.0)	15 (79)
Co-trimaxazol	3 (15.8)	16 (84.2)
Tetracycline	5 (26.4)	14 (73.6)
Amikacin	4 (21)	15 (79)
Metronidazole	1 (5)	18 (95)

DISCUSSION

Due to the prevalence of G.vaginalis , the prevalence of our study is (11.2%) , other studies in Baghdad and Basra- Iraq Suzan et al 17 and Jihan et al 18 found that the prevalence of G. vaginalis were (5.2%), (7.7%) respectively.

The percentage of G. vaginalis isolated in this study was close to that seen obtained in a study done by Esim et al 19 in Turkey which showed the prevalence of this bacteria was (10.2%). Recent study in Iran revealed the prevalence of G. vaginalis was (8.7%). 20, while other a study in Pakistan 21 showed that the prevalence of this bacteria was (30 %).

In Portugal-Europe a study found the prevalence of these bacteria was (28%)22, in Nigeria a study detected (17.0%) of Nigerian women had G.vaginalis, while in USA one study, 23 found that the prevalence of this bacteria was (35%).

The previous studies showed that the prevalence of G.vaginalis varies from one country to others. The diversity in prevalence of this bacteria reported by various workers, may be related to that different authors have studied different types of population which differ in ethnicity, environment, age of women, and have considered different criteria for selecting the cases of bacterial vaginosis. These factors along with poor viability and fastidiousness of this organism to grow on different culture media, and also since different methods for isolation and identification were used, all these factors may explain this variation in isolation and prevalence rate of this bacteria.

At last can be concluded that the prevalence of G. vaginalis obtained in this study was almost low among the studied population from other countries like USA (35%), Portugal (28%) Pakistan (30%) and others. Due to The prevalence of bacterial vaginosis (12.2%), it's also varies considerably between ethnic groups within the countries. Many factors responsible for decreasing or increasing the prevalence of bacterial vaginosis in the population, poor socio-economic status, improper sanitation, poor hygiene, malnutrition, all

these factors rise the bacterial vaginosis cases.[24] You can't say these things because you did not discuss them.

In our population the good hygiene, good sexual behavior and medium socio-economic status relatively may be responsible for the low bacterial vaginosis infection. The sexual behavior among different population is regarded as very important factor to increase or decrease the bacterial vaginosis infection in population[25].

Gardnerella vaginalis was found in samples from 88.8% of women with bacterial vaginosis. The high rate of this bacteria in bacterial vaginosis cases obtained in the study illustrated the significant relationship between bacterial vaginosis and G.vaginalis bacteria, which also confirmed by other studies that found about (88-98%) of women with bacterial vaginosis were colonized with G.vaginalis,[26-28] and these studies also indicated that this bacteria plays an important role in the etiology of bacterial vaginosis.

The presence of this microorganism in high concentrations with decreasing in Lactobacillus spp. can be a microbiological indicator of the occurrence of bacterial vaginosis[27.] Nevertheless, it should be noted that *G. vaginalis* can be part of the normal vaginal micro-flora and may be present in healthy women, but it has been recently reported that the biotypes of *G. vaginalis* isolated from healthy women differ from those isolated from women with bacterial vaginosis, the isolates from bacterial vaginosis cases were significantly more cytotoxic than the isolates from non-bacterial vaginosis which taken from healthy women.[29]

The current study used the laboratory criteria (Nugent) as a diagnostic procedure with the individually clinical signs for the detection of bacterial vaginosis cases in order to increase the identification of real cases of bacterial vaginosis infections.

The Nugent criteria based on Gram staining procedure, the advantage of using Gram-stain for the smears of vaginal fluid is the observing of the different morphotypes of the bacteria presented in the sample enabling quantifying the amount of the three individual organisms (Lactobacillus morphotypes, *G. vaginalis* morphotypes, and Mobiluncus species morphotypes which are present in bacterial vaginosis cases, also this criteria can visualize the clue cells Figure (1) (epithelial cells colonized by bacteria) which is regarded an important sign of bacterial vaginosis and an indicator of G. vaginalis presence. 30 Recall that there are two main criteria for diagnosis of bacterial vaginosis which include Nugent and Amsel criteria, but the current study used the laboratory criteria (Nugent) as a diagnostic procedure for detection bacterial vaginosis and then *G. vaginalis*, because the use of Amsel's criteria was based on some clinical symptoms that could not be standardized 31, for example, conduct of the whiff test is subjective for each individual examiner and lacks sensitivity, assessment of vaginal pH also lacks specificity, errors and false results in pH measurement may happen because an increase in vaginal pH may be due to many other lower genital tract conditions, which might be happened by presence of cervical mucus rather than vaginal discharge which has a higher pH or due to the presence of cervical infection which increases the pH

by increasing the flow of cervical secretions into the vaginal canal 32, and identification of clue cells may vary according to the skill and interpretation of the examiner and the quality of sample collection33, for the reasons above, the method which depend on microbial diagnosis, such as the Nugent score, is good election method for diagnosis of bacterial vaginosis.

Although the diagnosis of bacterial vaginosis by Amsel criteria is simple, it is relatively insensitive, in a study done by Schwebke et al[27], which considered Nugent criteria the gold standard for diagnosing bacterial vaginosis, they reported that the sensitivity of Amsel criteria compared to Nugent was less sensetive, and poorly predictive the bacterial vaginosis, and because that, the current study used Nugent criteria and didn't include Amsel criteria in the assessment, also this study found that the combination between the Nugent criteria and the detection of clinical symptoms of bacterial vaginosis individually and separately, like abnormal vaginal discharge, fishy odor, PH, itching, and other abnormal factors which may be indictors for bacterial vaginosis infection were gave a significant result in detection of bacterial vaginosis cases[16].

At last some studies suggested that Amsel criteria is ideally suited to clinical settings where microscopy is not available because the test is easy performed, rapid, inexpensive diagnostic test [34].

Due to the reaction with Gram stain procedure, Although the cell wall of *G.vaginalis* is gram-positive, the peptidoglycan layer can be thinner than many gram-positive organisms, which may resulting in negative gram staining and this makes this bacteria to be Gram variable and sometime appear as Gram negative bacteria[29].

Due to the culture, the growth of Gardnerella vaginalis was not observed on any of the primary cultures before 48 hours of incubation or it appears as very small colonies before this period, and usually the growth of this bacteria on the media was light.

Gardnerella vaginalis bacteria is a fastidious organism and requires complex medium for growth[22]. Columbia Blood Agar (with human blood) that used in this study for isolation of G.vaginalis is a suitable media that typically used in the culture of fastidious and pathogenic microorganisms.

Regarding to the age, The finding in table (3) is in agreement with results obtained from several studies which indicated that highest rate of G.vaginalis demonstrated in women at sexually active ages or reproductive ages[35-36].

Table (3) noted that the rate of G.vaginalis in age < 20 was Zero (0), that's may be the High Vaginal Swab test done only for married women who are rare in this age. Due to the presence of Gardnerella vaginalis in Pregnant, abortion cases, and Women use IUD that explained in table (4), the number of samples in this table, which includes pregnancy, abortion cases, and women use IUD, were relatively very low therefore numbers and prevalence of *G. vaginalis* in conditions that showed in the table (4), may not be revealed the real and true rate of G.vaginalis in these cases , therefore it needs further number and larger studies to explain the real and true

prevalence of *G.vaginalis* in these condition.

But in general some studies explained the relationship between *G.vaginalis* and these conditions, a study mentioned that bacterial vaginosis is associated with pregnancy and non-pregnancy in relation to infections of upper genital tract, and *G.vaginalis* is relatively being in non-pregnant women18. Other study revealed that *G.vaginalis* was not significantly associated with the frequency of postabortal, and not present at the time of abortion.[37], while others showed that *G.vaginalis*–associated bacterial vaginosis is a risk factor for poor obstetric and gynecologic outcomes and has been related to many gynecologic conditions and complications of pregnancy endometritis, amniotic fluid infection, preterm delivery, preterm labor, premature rupture of the membranes, and, possibly, spontaneous abortion38,39. Other clinical studies have demonstrated a relationship between *G.vaginalis* and preterm delivery[40,41].

McDonald (42) reported a 2-fold increase in preterm labor and delivery among women harboring *G. vaginalis*.

Due to the use of intrauterine device (IUD), *G.vaginalis* infection may be associated with IUD, this finding is supported by other studies43,44, which indicated that IUD is a risk factor for bacterial vaginosis infections, and showed that (13.8%) of women who used (IUD) were infected with *G.vaginalis*.

From the table (5), the relationship between the clinical signs and the presence of *G.vaginalis* in the sample is very clear, by use of clinical signs in the diagnosis of bacterial vaginosis, the study found that there was a good correlation between the presence of vaginal discharge with clue cells and the occurrence of *G.vaginalis* in the samples.

This study also revealed that there was a good relationship between the discharge, clue cells and then pH>4.5 with presence of *G.vaginalis*, while, others found18, that there was a good correlation between the amine test and pH>4.5 with the occurrence of *G.vaginalis* and then the presence of clue cells. Amine test was moderately related to the presence of *G.vaginalis* and this may be related to the accuracy of results obtained by the examiner, therefore the result may be differ from one person to another.

Due to the susceptibility test the results that obtained in this study (tables 6&7) were agreed and close to other studies in Iraq[17,47] which found that *G.vaginalis* isolates were (100%) resistant to Metronidazole, in contrast to many studies that referred to the good sensitivity of *G.vaginalis* against Metronidazole[23,45]. The difference between the previous studies and local isolates susceptibility to the Metronidazole may be attributed to the exaggerated use of Metronidazole in Iraq, it has been used to treat many parasitic and anaerobic bacterial infections for about[47] years[17,46], possibly for its low price and the absence or low of side effects, and this long time using of this drug may induce the bacteria to produce new resistant strains by mutation[29,47], and the most well-characterized mechanism of resistance to metronidazole due to mutation is inactivation or deletion of genes with nitroreductase activity enzymes which are considered attractive targets for nitroimidazole-based intervention

therapies and play important role in converting metronidazole from a prodrug to a mutagenic that damages bacterial DNA, resulting in cell death. Therefore, factors that lead to the loss of or a decrease in the activities of the nitroreductase activity enzymes may contribute to metronidazole resistance[48,49] Also it was found that the biofilm formation capability provides *G.vaginalis* resistance to orally administered metronidazole[29,50]. The rest of antibiotics were showed different rate of sensitivity against *G.vaginalis* isolates for example the sensitivity of Cephalothin was found to be (68.4%), Cefaxime (52.7%), Tobramycin (42.1%), and Pipracillin (42.1 %), while the antibiotics Erythromycin (21.0%), Co-trimaxazol (15.8%) and Tetracycline (26.4%) (Table 7) revealed low sensitivity of *G.vaginalis*. The pattern of *G.vaginalis* sensitivity to antibiotics in table (6) showed: isolates No. 2, 4, 8, 14, 16, were resistant to nine antibiotics, while, the isolates No. 1, 3, 7, 10, 13, 17, 19, were resistant to eight antibiotics; and isolates No. 15 and 18, resistant to seven antibiotics; and the isolates No. 6, 11 and 12, were resistant to six antibiotics; and finally the isolate No.9, was only resistant to two antibiotics.

These results were agreement with that reported by Suzan et al,[17] and Al-saady et al,[46]. However, and in general no one of the isolates were revealed a high resistance towered the antibiotics, the study found that each isolate was sensitive at least against five types of antibiotics, and this may be due to the lack of resistant plasmid in this bacteria, which is responsible for the transfer of antibiotic resistance genes between bacterial cells[22].

Although the sensitivity of Amoxicillin against *G.vaginalis* was found to be (73.6%) (Table 7), but the use of this antibiotic for the treatment the bacterial vaginosis are limited and may be associated with failure to eradicate G. vaginalis, this is probably due to inactivation of Amoxicillin by the B-lactamases produced by vaginal anaerobes. However, this agent may have a role in treating Gardnerella-associated infections at extravaginal sites[51]. Also the use of erythromycin may be limited in patients with bacterial vaginosis because of the acidic environment of the vagina which decreases the activity of this antibiotic[52]. Current study found that Clindamycin antibiotic, was the most effective antibiotic against *G.vaginalis*; it has been used both orally and as a local utilizing, and this in agreement with other studies which found the same result and mention that, currently Clindamycin antibiotic is the preferred approach (oral or intravaginal administration) for treatment of bacteria vaginosis[51,53].

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پوختە

هۆکارێن مەترسیێ بێن تێکچوونا ڤەکوهێزەر (هستیریا) ل پارێزگەها دهوکێ / کوردستانا عیراقێ

پێشەکی: بەکتیا *Gardnerella vaginalis* ژ هەمی بەکتریا پتر تێتە دیتن دناڤ نەخوشیا بەکتیریال ڤە جینوسیس و گرنگترین بەکتیریایە بو هەبونا ڤێ نەخوشیێ. دەستنیشانکرنا بەکتریا *Gardnerella vaginalis* دناڤ نەخوشیا بەکتیریال ڤەجینوسیس دا، هەروەسا تاقیکرنا هەستەوەریێ ب ریکا بکارئینانا ١٤ دژێن زیندوی بێن جورە وجور.

ریکێن ڤەکولینێ: ٥٠٠ نمونە هاتنە وەرگرتن ل ئافرەتان ل ٢ دوو نەخوشخانەیێن مەزن ل پارێزگەها دهوکێ و هاتینە کومکرن دماوێ هەیڤا چریا ئێکێ ٢٠١٤ تا ئاداریێ ٢٠١٥، و تاقیکرنا هەستەوەریێ ب ریکا بکارئینانا ١٤ دژێن زیندوی بێن جورە و جور هاتەکرن.

ئەنجام: (٥٦) پێنجی و شەش نمونە هاتنە دەستنیشانکرن بەکتیریا *Gardnerella vaginalis* ب ریژا ١٠.٧٪ و (٦٣) نمونە ژ نەخوشیا بەکتیریال ڤەجینوسیس Bacterial vaginosis هاتنە دەستنیشانکرن ب ریژا ١٢.٧٪ ریژا بەکتیریا *Gardnerella vaginalis* دناڤ وان (٦٣) نمونادا بێن نەخوشیا بەکتیریال ڤەجینوسیس دا دیاربو کو ٨٨.٩٪ و ئەڤ ریژا بلند یا ڤێ بەکتیریایێ دناڤ ڤێ نەخوشییدا نیشانە بو رولێ گرنگ یێ بەکتیریا *Gardnerella vaginalis* دناڤ نەخوشیا بەکتیریال ڤەجینوسیس Bacterial vaginosis.

هەروەسا هاتە دیتن کو ریژا بەکتریا *Gardnerella vaginalis* یا بلندبوو دناڤ وان ئافرەتاندا ئەوێن تەمەنێ وان ژ (٢٠–٤٠) سالی بوون. هەروەسا دڤێ خواندنێ دا (١٩) تەنیتێن *Gardnerella vaginalis* هاتنە تاقیکرن ب تاقیکرنا هەستەوەریێ ب ریکا بکارئینانا ١٤ دژێن زیندوی بێن جوراوجور، و ئەڤان تەنیتیا ریژەیەکا مەزن یا بەرگریێ کر بو دژێ زیندوی میترونیدازول (٩٥٪) و هاتە دیتن کو چێترین انتیبایوتیکە دژی بەکتریا *Gardnerella vaginalis* کلیندا مایسین بو (٨٩٪) و هەر وەسا زیندوێ ریفامبسین و سیبروفلوکساسین ب ریژەکا باش هەبو دژی ڤێ بەکتریایێ.

الخلاصة

عوامل الاختطار للاضطراب التحويلي في محافظة دهوك/ كوردستان العراق

الخلفية والأهداف: تعتبر بكتريا الغاردنال المهبلية *Gardnerella vaginalis* من أكثر الأحياء المجهرية ذات الصلة بحاالت التهاب المهبل البكتيري Bacterial Vaginosis (BV) والتي تسبب مشاكل وعدم راحة في منطقة المهبل عند النساء. هدفت الدراسة الى التعرف على مدى انتشار الغاردنريلة المهبلية في حالات التهاب المهبل البكتيري لدى النساء الحاملة لأعراض المرض في مدينة دهوك، وكذلك إجراء فحص الحساسية للمضادات الحيوية لعزلات الغاردنريلة المهبلية، كما هدف البحث أيضاً إلى استخدام تقنيات متقدمة مثل تقنية VITEK2 للكشف عن هذه البكتيريا

طرق البحث: أجريت الدراسة خلال الفترة من شهر تشرين الثاني 2014 وحتى شهر آذار 2015؛ حيث تم جمع حوالي (٥٠٠) عينة مهبلية (كل عينة تشمل 2 مسحات) والتي اخذت من نساء بين الفئة العمرية من 50–18 سنة واللواتي يعانين من أعراض التهاب المهبل البكتيري؛ والتي تتمثل بالافرازات المهبلية، والحرقة، والحكة، وغيرها من هذه االعراض المصاحبة لهذه الحالة؛ وقد تم أخذ هذه العينات من اثنين من المستشفيات الرئيسية في محافظة دهوك وهي كل من مستشفى الولادة، ومستشفى فين الأهلي. استخدمت الدراسة طريقة نوجنت التشخيصية (Nugent criteria) واالستدلال ببعض العلامات السريرية للكشف عن حالات التهاب المهبل البكتيري كما تم إجراء فحص الحساسية للمضادات الحيوية لـ(14) عزلة من بكتريا الغاردنريلة المهبلية باستخدام طريقة الانتشار القرصي.

النتائج: من بين 500 مسحة مهبلية تم جمعها في هذه الدراسة، تم الكشف عن 63 حالة 12.2% من حالات التهاب المهبل البكتيري والتي تم تشيخصها حسب معايير طريقة نوجنت (Nugent criteria) والمعتمدة في تشخيص هذه الحالة. كما تم عزل 56 عزلة من بكتريا الغاردنيال المهبلية وبنسبة 10.7% في جميع العينات التي تم اختبارها، و88.8٪ في حالات التهاب المهبل البكتيري. إن ارتفاع معدل هذه البكتيريا في حالات التهاب المهبل البكتيري والتي تم تشيخصها في هذه الدراسة، دلالة على العالقة الوثيقة بين التهاب المهبل البكتيري، وبكتيريا الغاردنريال المهبلية.

وبالاعتماد على الفئات العمرية وجدت الدراسة بأن أعلى معدل انتشار للغاردنال المهبلية كانت في الفئة العمرية ٢٠–٣٠ عاماً 46.4%، وتليها الفئة العمرية ٣٠–٤٠ عاماً 39.4%، مما يشير إلى أن معدل هذه البكتريا يزيد عند النساء في سن الانجاب والنشاط الجنسي.

أما دراسة فحص الحساسية لـ14 نوع من المضادات الحيوية ولـ19 عزلة من بكتريا الغاردنال المهبلية؛ باستخدام طريقة االقراص؛ فقد أوضحت النتائج أن عزلات بكتيريا الغاردنال المهبلية قد أظهرت حساسية جيدة تجاه المضادات الحيوية التالية: الكليندامايسين 89.5%، ريفامبيسين 84.2 وسيبروفلوكساسين 84.2%، في حين أظهرت الدراسة أن عزلة واحدة فقط من الغاردنال المهبلية كان حساسة إلى المضاد الحيوي ميترونيدازول 5% وبقية العزالت 95% أبدت مقاومة لهذا المضاد الحيوي والذي يمكن أن يعزى إلى المبالغة والافراط في استخدام هذا المضاد الحيوي في منطقتنا لعلاج الالتهابات المهبلية، بينما خلصت الدراسة الى ان المضاد الحيوي كليندامايسين، كان الأكثر فعالية ضد بكتيريا الغاردنريلة المهبلية.

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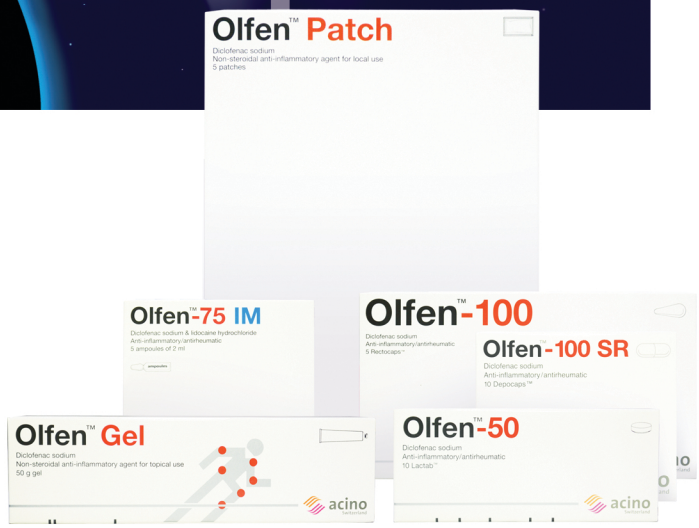

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PREMARITAL PERCEPTION ON OBESITY AND GESTATIONAL WEIGHT GAIN

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ABSTRACT

Background: Increasing prevalence of overweight and obesity among women in the childbearing age and during pregnancy is a growing global public health problem. The study aimed to assess pre-marital women's perception as to their own weight and future gestational weight gain.

Methods: Four hundred women selected by systematic random sampling from the Premarital Clinic at the Central Laboratory of Duhok city, have been directly interviewed, during the period from June 1, to July 31, 2014. They answered questions related to perceptions on their current own weight and future healthy gestational weight gain.

Results: The overall prevalence of overweight/obesity was 44.3%. Seventy-three percent of the overweight/obese women underestimated their body mass index, in comparison to 26.6% of the normal weight women. Only 10.8% of all the women possessed proper knowledge on the best gestational weight gain for themselves. Relations of socio-demographic factors with perception of own weight and gestational weight gain guidelines, were statistically not significant. However, obese women had prevalence of high perception on gestational weight guidelines of 16.3%, compared to 0% and 1.4% for the underweight and normal-weight respondents, respectively (P= 0.001).

Conclusion: Premarital women's level of perception as to their own weight and proper gestational weight gain was low.

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Keywords: Premarital, Perception, Overweight, Obesity, Gestational Weight Gain.

Increases in average body mass index (BMI) are being observed among women in developed countries as well as urban areas of developing countries; many women are becoming pregnant at the time they are overweight or obese and many are gaining excessive weight during pregnancy.[1] In 2006, a survey in Duhok showed that 82% of mothers in the reproductive age were either overweight or obese.[2] This situation puts mothers and their babies' health at risk. Unnecessary Gestational Weight Gain (GWG) is related to increased risks among mothers including pregnancy-induced hypertension and preeclampsia, gestational diabetes mellitus and cesarean section delivery; it also increases risk of structural anomaly affecting infants such as macrosomia, stillbirth, traumatic delivery and future obesity.[3]

To improve maternal and child health, women have to understand that they should be within a normal BMI range when they start pregnancy, and should gain weight within the known healthy range. To optimize the recommended GWG, it is important to know the level of knowledge women have regarding this subject. These perceptions are needed

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when planning services for the control of overweight and obesity, and where future education strategies are required. Therefore, the objectives of this study were to assess the perception of premarital women as to their current own weight and of GWG, and to examine the association of such awareness with their socio-demographic factors and current BMI.

SUBJECTS AND METHODS

A cross-sectional study was conducted on 400 women who have been interviewed while presenting to perform premarital investigations at the Premarital Clinic of the Central Laboratory in Duhok city, from June 1, to July 31, 2014. The sample size was calculated as equals $(pqZ^2)/e^2$, where p (prevalence of awareness) = 0.5, q = 1 – p, Z (95% confidence level) = 1.96, e (accepted standard error) = 0.05. Systematic random sampling was used: every third presenting woman was selected. The second author, a female physician, directly interviewed verbally consenting women, to fill a pretested questionnaire. First, each woman was asked about her age, place of residence, highest level education attained and occupation. Then the respondent was asked to identify herself as currently being underweight, normal weight or overweight/obese (i.e., to identify her BMI category). Each participant was then asked to indicate what they think the ideal weight before pregnancy, on a photograph linking BMI to nine silhouettes of contour drawings of women with increasing measures, from thinner to wider drawings, and mean BMI from 17.5 to 37.5.4 The respondent was then asked about the meaning of healthy weight gain during pregnancy: if there should be no weight gain, or a steady gain within certain limits, or it is not impotant how much weight a pregnant woman gain. Lastly, each woman was asked, "What would be on average the healthier pregnancy weight gain for herself in kgs?"

Each woman was weighed, bare-footed and lightly clothed, to the nearest 100 grams, using seca electronic scale. The height was measured to the nearest 0.5 cm, using a wall-mounted stadiometer. The BMI was calculated as the weight in kilograms divided by height in meters squared.

At the end, the interviewer provided each woman with information on her BMI and guidelines for healthy gestational weight gain.

Collected data were analyzed using SPSS version 22. First, the socio-demographical data, BMI and level of awareness/ perception were described using frequency tables. Second, the relationship between women perception as to their own weight, and their actual BMI classification, was tested using Chi-square test. Third, the respondents' level of perception as to their own weight was dichotomized into correct and incorrect, while the level of awareness of GWG guidelines was classified as low if there was one correct answer, medium if there were two correct answers or high if the three questions were answered correctly. Then, relationships between perception levels and socio-demographic factors and BMI were analyzed using the Chi-square test. A P-value < 0.05 was used to indicate statistical significance.

RESULTS

Mean age for the participant women was 22.86 years with a standard deviation of 4.84, and a range from 15-41 years.

Women aged 20-24 years were the commonest group (41.8%); only 8.5% were 30 or more. There were relatively more respondents from rural areas (55%) than from urban areas (45%). Illiterate women made around 10% and those with primary school education nearly 40%. Only 18.2% of the women have been employed outside home. Regarding BMI, 44.3% of the women were overweight or obese, whereas only 4% were underweight (Table 1).

Table 1: Socio-demographic characteristics and BMI of the studied population

Characteristic		No. (%)
Age (years)	15-19	103 (25.8)
	20-24	167 (41.8)
	25-29	96 (24.0)
	≥ 30	34 (8.5)
Residence	Urban	180 (45.0)
	Rural	220 (55.0)
Education	Illiterate	41 (10.3)
	Primary	157 (39.3)
	Secondary	100 (25.0)
	Higher	102 (25.5)
Occupatio n	Housewife	327 (81.8)
	Working	73 (18.2)
BMI	Underweight	16 (4.0)
	Normal weight	207 (51.8)
	Overweight	134 (33.5)
	Obese	43 (10.8)
Total		400 (100)

Table 2 shows that from 207 normal weight women, 142 (68.6%) correctly identified themselves to be of normal weight. From 177 overweight/obese women, only 48 (27.1%) correctly identified their weight category; 121 (68.4%) considered themselves as of normal weight and eight women (4.5%) as underweight.

Table 2: The distribution of women perception as to their own weight, according to the estimated BMI

Estimated BMI	What you consider your weight?					Total no.
	Underweight no. (%)		Normal weight no. (%)	Overweight no. (%)		
Underweight	10	(62.5)	6 (37.5)	0	(0.0)	16
Normal weight	55	(26.6)	142 (68.6)	10 (4.8)		207
Overweight or obese	8	(4.5)	121 (68.4)	48	(27.1)	177
Total	73	(18.3)	269 (67.3)	58	(14.5)	400

$P < 0.001$

Table 3 shows no significant associations between the level of women's perception and the sociodemographic variables of age, residence, education and occupation.

Table 3: Women's perception of their own weight by selected socio-demographic factors

Factor	Correct no. (%)	Incorrect no. (%)	Total no.	P
Age (years)				
15-19	51 (49.5)	52 (50.5)	103	0.660
20-24	88 (52.7)	79 (47.3)	167	
25-29	47 (49.0)	49 (51.0)	96	
≥ 30	14 (41.2)	20 (58.8)	34	
Residence				
Urban	89 (49.4)	91 (50.6)	180	0.841

Factor	Correct no. (%)	Incorrect no. (%)	Total no.	P
Rural	111 (50.5)	109 (49.5)	220	
Education				
Illiterate	17 (41.5)	24 (58.5)	41	0.522
Primary	77 (49.0)	80 (51.0)	157	
Secondary	55 (55)	45 (45.0)	100	
Higher	51 (50.0)	51 (50.0)	102	
Occupation				0.224
Housewife	168 (51.4)	159 (48.6)	327	
Employed	32 (43.8)	41 (56.2)	73	
Total	200 (50)	200 (50)	400	

Table 4 illustrate the perception of women according to GWG guidelines. About half of the women pointed to the women of normal weight on the picture presented to them. Nearly 70% said that pregnant women should gain weight steadily during pregnancy. However, only 10.8% of the women gave correct answer concerning a suitable GWG for themselves in future pregnancy.

Table 4: Distribution of perception as to the GWG guidelines

GWG guideline	Perception	No.	(%)
Ideal weight before	Underweight	114	28.5
pregnancy on picture	Normal weight	204	51.0
	Overweight	79	19.8
	Obese	3	0.8
Healthy weight gain	No gain	60	15.0
during pregnancy	Steady gain	278	69.5
	Does not matter	62	15.5
The ideal weight gain for	Correct	43	10.8
herself during pregnancy	Incorrect	201	50.3
	Do not know	156	39.0
Total		400	100

Finally, Table 5 shows no significant associations between women's perception of GWG recommendations and their demographic factors. However, when it comes to BMI, the obese women were better than the under/normal weight respondents (prevalence of high knowledge of 16.3%, compared to 0% and 1.4%, respectively; P= 0.001). Overweight women had the highest prevalence of low knowledge in GWG guidelines (59.7%) compared to other weight groups, though normal weight women also displayed a high frequency of low knowledge (58.9%).

Table 5: Women's perception of GWG guidelines by socio-demographic factors and BMI

Factor	Low perception no. (%)		Medium perception no. (%)		High perception no. (%)		Total no.	P
Age (years)								0.29
15-19	67	(65.0)	33	(32.0)	3	(2.9)	103	9
20-24	92	(55.1)	66	(40.1)	8	(4.8)	167	

Factor	Low perception no. (%)		Medium perception no. (%)		High perception no. (%)		Total no.	P
25-29	49	(51.0)	74	(41.7)	7	(7.3)	96	
≥ 30	20	(58.8)	140	(41.2)	0	(0.0)	34	
Residence								
Urban	105	(58.3)	64	(35.6)	11	(6.1)	180	0.256
Rural	123	(55.9)	90	(40.9)	7	(3.2)	220	
Education								
Illiterate	31	(75.6)	10	(24.4)	0	(0.0)	41	0.120
Primary	88	(56.1)	64	(40.8)	5	(3.2)	157	
Secondary	57	(57.0)	37	(37.0)	6	(6.0)	100	
Higher	52	(51.0)	43	(42.2)	7	(6.9)	102	
Occupation								
Housewife	187	(57.2)	128	(39.1)	12	(3.7)	327	0.229
Employed	41	(56.2)	26	(35.6)	6	(8.2)	73	
BMI								
Underweight	8	(50.0)	8	(50.0)	0	(0.0)	16	0.001
Normal weight	122	(58.9)	82	(39.6)	3	(1.4)	207	
Overweight	80	(59.7)	46	(34.3)	8	(6.0)	134	
Obese	18	(41.9)	18	(41.9)	7	(16.3)	43	
Total	228	(57.0)	154	(38.5)	18	(4.5)	400	

In the present study, 44.3% premarital women were overweight or obese, from whom only 27.1% women classified their weight correctly. Thus, overweight/obese women seem to be prone to underestimate their weight status (BMI). Rates of correct perception were 50% in Canada8, 16% in Brisbane[9] and 30% in Canberra[10], Australia. The perception of pre-pregnancy weight and BMI seems to be generally poor, particularly among overweight and obese women. The inaccurate classification of women's own weight indicates that women may not percept how overweight or obese they are to take care of their GWG in future pregnancies. Post et al. concluded that awareness of health risk associated with increased weight is

poor in people who underestimate their own weight, decreasing their desire to seek education on proper GWG and to join in healthy behaviors such as physical activity.[11]

Nearly half (51.8%) of the women in our study had normal weight, from whom only 68.6% considered themselves normal compared to 93.8% in Canada.8 Herring et al. reported that 87% of women with normal pre-pregnancy BMI accurately perceived their weight.[12]

More than one third (37.5%) of underweight women in the present study overestimated their weight. The 2009 California Women's Health Survey showed that among under-weight women, 2.6% thought they were overweight and 60.5% thought their weight was about right.[13]

No statistical association was found with any socio-demographic factor, which indicates that the pattern of perception found in this study is common across all socioeconomic levels with no specific tendency.

There was a clear lack of knowledge regarding GWG guidelines in our study population. About half of the women were unaware of the best weight before pregnancy shown on a photograph; they pointed to thin more than to overweight/obese silhouettes. The highest prevalence of "low knowledge" was among the overweight women. Current commercial mass media might have affected the perception of the community of what is accurately normal weight with a shift toward thinness. Supervised mass media should be directed to these women to rectify their perception.

Regarding the pattern of a healthy GWG, we found that nearly 70% of our participants chose the "steady gain" way; the "high knowledge group" was the obese women. This can help these women in making informed healthy choices regarding nutrition and physical activity during pregnancy, provided they receive guidance and motivation from their maternity care providers about "steady gain" of weight.

The most challenging question for the respondents was to give an appropriate GWG for themselves in a future pregnancy; only 10.8% could correctly identified that. In New Zealand, Hooker found that 69.4% of pregnant women were unable to correctly identify appropriate weight gain for pregnancy; overweight and obese women were more likely to overestimate GWG, compared to healthy weight women.[14] In Egypt, Kavle et al. concluded that pregnant women have little to no knowledge about the best weight gain during pregnancy.[15]

In conclusion, premarital women's level of perception as to their own weight and proper gestational weight gain was low among the current study population, and needs to be promoted by health care providers and the mass media. Pregnant women's perception on these topics also needs to be investigated.

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پوختە

تێگەهشتنا پێش هەڤژینیێ لدور قەلەوی و بدەست ئینانا کێشەیا دووگیانی

پێشەکی: زێدەبونا ڕێژەیا زێدەکێشیێ و قەلەوی لناڤ ژنان ل تەمەنێ بەرداری و ل دەمێ دووگیانی ئاریشەیەکا جیهانیا تەندروستیا گشتیە، هیڤیا ڤەکولینێ هەلسەنگاندنا تێگەهشتنا ژنان پێش هەڤژینیێ لدور کێشەیا ئەوان و بدەستئینانا کێشەیا دووگیانی بۆ.

ڕێکێن ڤەکولینێ: چوارسەد ژن ب شێوەیەیێ نمونە وەرگرتنا چانسی و سیستەماتیك ژ کلینیکا پێش هەڤژینیێ ل تاقیگەها باژێرێ دهوکێ هاتن هەلبژارتن، دناڤبەرا ٥/١ حەتا ٢٠١٤/٧/٣١، هەڤپەیڤین دگەل هاتەکرن، ژنان بەرسڤا پرسیاران لدور تێگەهشتنا خو لدور کێشەیا نها و بدەستئینانا کێشە ل دەمێ دووگیانی دان.

ئەنجام: ڕێژەیا گشتی یا زێدەکێشیێ/ قەلەوی ٤٤.٣٪ بو، حەفتی و سێ ژ سەدێ ژ ژنێن خودان کێشەیا زێدە و قەلەو BMI یا خو بچویك دیتن، ل هەمبەر ٢٦.٦٪ ژنێن ب کێشەیا نورمال ب تنێ ١٠.٨٪ ژ ژنان خودان تێگەهشتنا دروست و باشترین زێدەکێشەیی یا دووگیانی بون، پەیوەندی بێن فاکتەرێن جڤاکی و دەموگرافی یێن کێشە و بدەست خستنا کێشە لدەمێ دووگیانی ژ ئالیێ ئاماریێ بەرچاڤ نەبوون، لێ ژنێن قەلەو و خودان ڕێژەیەکا بلند لدور پیڤەرێن کێشەیا دووگیانی بون ١٦.٣٪، ل هەمبەر ٠٪ و ١.٤٪ لناڤ بەرسڤدەرێن خودان کێم کێشە و کێشەیا نورمال، ب ڕێز ($p=0.001$).

دەرئەنجام: تێگەهشتنا ژنان ل دەمێ پێش هەڤژینیێ ل کێشەیا خو و کێشەیا گونجاوا دووگیانی ل ئاستەکێ خوارێ بو.

الخلاصة

إدراك النساء قبل الزواج للسمنة وازدياد الوزن أثناء الحمل

الخلفية والأهداف: ان الارتفاع الحاصل في معدل انتشار زيادة الوزن والسمنة بين النساء في سن الانجاب وأثناء الحمل يعد مشكلة عالمية متنامية في مجال الصحة العامة. والهدف من هذه الدراسة هو تقييم إدراك النساء قبل الزواج لأوزانهن، والزيادة في الوزن أثناء الحمل في المستقبل.

طرق البحث: تمت مقابلة ٤٠٠ امرأة اخترن بطريقة العينة العشوائية المنتظمة من وحدة رعاية النساء قبل الزواج في المختبر المركزي في مدينة دهوك، خلال الفترة من ١ حزيران الى ٣١ تموز، ٢٠١٤. تم طرح أسئلة عليهن مباشرة لمعرفة ادراكهن فيما يخص تصنيف اوزانهن ومعدل زيادة الوزن المناسب لهن اثناء الحمل.

النتائج: كانت نسبة النساء اللواتي لديهن زيادة في الوزن او سمنة هي ٤٤%. من تلكم النساء ٧٢.9% قللن من قيمة مؤشر كتلة الجسم لديهن، يقابلهن فقط ٢٦.6% من ذوات الوزن الطبيعي. فقط ١٠.8% من النساء كانت لديهن معلومات صحيحة عن معدل زيادة الوزن المناسب لهن اثناء الحمل. لم تظهر العالقات بين االدراك للوزن ولزيادته أثناء الحمل، والعوامل االجتماعية–الديموغرافية، دالالت إحصائية معنوية. مع ذلك، أظهرت النساء البدينات معدل إدراك عالي لزيادة الوزن أثناء الحمل بنسبة ١٦.٣% مقارنة مع ٠% و ٤.١% للنساء ذوات الوزن المنخفض والطبيعي، على التوالي .P= 0.001

الاستنتاجات: كان إدراك النساء منخفض في مجالي تقييم اوزانهن وتقدير معدل الزيادة المناسب لهن في الوزن اثناء الحمل.

FUNCTIONAL AND COSMETIC LABIA MINORA REDUCTION

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ABSTRACT

Background: Aesthetic surgery of female genitalia is an uncommon procedure, and of the techniques available, labia minora reduction can achieve excellent results. Recently, more conservative labia minora reduction techniques have been developed, because the simple isolated strategy of straight amputation does not ensure a favorable outcome. This study was designed to review a series of labia minora reductions using inferior wedge resection and superior pedicle flap reconstruction. The purpose of this article is to present recent modify labial pedicle flap for management aesthetic and functional of problems associated with protrusion of the labia minora.

Method: Twenty-one patients underwent inferior wedge resection and superior pedicle flap reconstruction. The mean follow-up was 14 months. Aesthetic results and postoperative outcomes were collected retrospectively and evaluated.

Results: for idiopathic labia minora enlargement. Postoperative result, there was no wound infections. Minor wound dehiscence found in one patient and one painful hematoma not necessitate surgical drainage in anther, one patient sustained retention of urine that necessitate bladder catheterization. All women were fulfilled with cosmetic results, no recurrence of chief complained were reported. The mean follows up none have consequently required or requested revision surgery.

Conclusions: modified labial based flap was establish to be straight forward and useful technique of labia minora reduction using single procedure in small series cases this technique give favorable cosmetic and purposeful outcomes for the patient.

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Keywords: Labia minora, Cosmetic.

Vaginal labia minora occasionally become bigger, protrude in various extent of projection on medial side of the labial majora, Enlargement of the labia minora can be congenital or acquired[1-3] Factors like: mechanical irritation by chronic local infections, dermatitis secondary to urinary incontinence, vaginal lymph edema, myelodysplastic disease, exogenous androgen hormones. Labia minora may expand and protrude above labia majora may functionally or psychologically be harassing. This condition may lead to loss of self stem and embarrassment in those women as they feel abnormal and disFigured. Functional causes for labia minora reduction comprise hygienic issues because of extra labial tissue leading to regional irritation, hindrance with sexual intercourse, and trouble when dressing, sitting and walking[1-7].

Several techniques are present for hypertrophic labia minora reduction, which are: continues W-fashioned excision[1], epithelial removing of labia

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minora with reduction[5], an easy and in a straight line deletion of the extra portion plus over sewing the border[1-6,8]. Method end up with direct excision procedure, the labial border is substituted via a flimsy and ridged suture line that is usually accompanied with regional annoyance and even discomfort during walking[7]. Furthermore, linear scars have a propensity to contract leading to partial occlusion of vaginal introits.

This technique was adjusted by carrying out an advanced labial based flap Reconstruction, to prevent such undesirable outcome. The outcome of this technique is more natural, softer, hid scar and more rounded labial edge.

PATIENTS AND METHODS

From February of 2012 to Jun of 2015, 21 women with mean age of 40 years (between, 21-52 years) went through labia minora surgical reduction between twenty to fifty years of ages all patients were sexually active, only two patients out of four were not active in total 50.

All women seek surgical management for practical reasons, and the majority of them be displeased of the shape of labia see (Table1):

Table 1: Chief patients complain

Complaining of patient	Number
Hygiene problem	3
Walking discomfort	4
Clothing discomfort	8
Exercise discomfort	8
Intercourse discomfort	8
Aesthetic	9
Total	50

Any patients exposed to androgenic management or having disease related to androgenic hormone have being excluded in the study. Labial relation between length, width and excision in mm have being recorded preoperatively (table.2). The operation done as day case procedure were patients came on the day of procedure to the Suliamany and Duhok plastic and reconstructive centers. 1ntravenous cefotaxim (one gram) and Metronidazole (500 mg) were given before the surgical procedure. The procedure done through the saddle block, and in the position of lithotomy. Caudal anesthesia and in the lithotomy, (Figure. 1). With a small forceps, the middle portion of the labia minora is stretched inferiorly until the posterior part of the vaginal introitus (pinching test)[9]. The surgical markings are designed. A wedge-shaped area located between the two points is then designed and represents the area of tissue to be resected. The angle and extent of the wedge resection vary, depending on the excess tissue and the cutaneous-mucosal laxity. The optimal point cached by forceps in the intermediate part of the labia minora is recognized and the posterior part of the vagina is chosen also. It must be in mind not to over incise into the frenulum at the proximal of the clitoris, and should take caution that incision not reach the dorsal hood . By no way the incision allow to reach fourchette, because this maneuver lead to future scar contraction and may Lead to difficulty in sexual intercourse.

Table 2: Relation between length, width and excision in mm

No.	Side	length mm	width Mm	excision mm
1	L	37	15	4
	R	35	15	4
2	L	30	20	4
	R	35	27	6
3	L	32	17	6
	R	32	19	7
4	L	35	12	4
	R	40	12	4
5	L	30	10	3
	R	40	12	4
6	L	62	20	6
	R	60	20	6
7	L	70	30	10
	R	65	35	5
8	L	65	35	15
	R	35	25	5
9	L	40	25	5
	R	80	15	3
10	L	55	18	6
	R	45	25	5
11	L	30	10	3
	R	40	12	4
12	L	62	20	6
	R	60	20	6
13	L	70	30	10
	R	65	35	5
14	L	45	25	5
	R	30	10	3
15	L	40	12	4
	R	62	20	6
	L	60	20	6
16	R	70	30	10
	L	65	35	5
	R	66	34	4
17	L	30	10	3
	R	40	12	4
18	L	62	20	6
	R	60	20	6
19	L	70	30	10
	R	65	35	5
20	L	65	35	15
	R	35	25	5
21	L	40	25	5
	R	35	23	4

By this method, the Urethral orifice will not be damaged by possible over excision. Whenever possible we try to make our advance flap inferiorly based as it has more profound blood supply than the upper one.

The tissue of labial are distillated with 1% lidocaine and adrenaline (1:200,000) to produce vasoconstriction and decrease bleeding. This technique can add in performing an easy dissection between lateral and medial flaps. After resection of the surplus tissue and extensive hemostasis, with cauterization. The thin tissues of the labium minus are re-approximated in an interdigitated manner using vertical mattress to favorite suture for reliable skin edge approximation and eversion (Figure.3b) generally, the length is kept to at least of 10 mm letting the labia minora to some extend to the level of the major labia. The labial flap is advanced superiorly to attach through 6/0 vicryl suture in a transverse mattress, and through several suture to the muscle then approximate the outer and inner layer and without tension via 5/0 vicryl sutures. Bupivacaine Hydrochloride Injected near the sutures lines to provide long anesthesia. There was no need to use the folly catheter. Most patients in our series were discharged on the day of surgery, Follow-up ranged from two months to two years and continues for some patients.

Figure 1 (pinching test), using forceps pulling upward the labia minora in slightly stretch manner and then pulled upward until the anterior part of valvular intoitus Intra-operative

RESULTS

Out of the 21 patients, 18 of them had an uneventful postoperative recovery, first patient developed a minor blood collection in the ventral part of right labia minora, drainage without surgical interference, second patient developed minor wound dehiscence as a result of suture opening, the wound healed by secondary intension within three weeks, resulted in unrestricted function and satisfactory appearance. And third patient sustained retention of urine that necessitate baldder catheterization through next postoperative day.

All patients had minimal postoperative discomfort and, 2 weeks after surgery, reported no pain. Swelling subsided within 4 weeks. By that time, all patients were pleased with the appearance of their genitalia and the resolution of their original problems (Figure 4a & b). All patients reported that their sexual intercourse was free of pain with no distress (Figures 2 a&b to figure 5 a&b).

Figure. 2b

Figure.2a

Figure.3a

Figure 3b

Figure.4b

Figure 4a

Figure.5a

Figure .5b

DISCUSSION

There are vast discrepancy in size of the labia minora in women with complain[13]. It could be result from congenital anomalies[14] but may also be result from androgens during intrauterine live,[15] continues manual thrust out or weight bearing,[16] and rebound eczema secondary to incontinence of urine habitually, both labia minora are widely spread from the clitoral hood to the posterior fourchette, but the enlargement also may involve a single labia minora and contra lateral one many be normal[17]. Although some authors have quantified this as greater than 40 to 50mm from the base 9 and agreed that a normal labium tissue calculated less than 50mm during slight pulling , most Women have a clue of what assemble normal function and appearance of the labia 20. Labia minora reduction may ameliorate physical as well as psychosocial uncomfortability and sexuality in some patients.[19]

Labioplasty complications with straight-line trimming excisions are often technique dependent. This procedure has some inherent problems, such as loss of normal pigmentation and contour of the labial edges, difficulty achieving symmetry, and a tendency to over resects or under-resects the labia. The tendency for separations along the labial length is high, especially if the labium is thick. In addition, it is difficult using the trimming technique in many women to achieve a natural transition at the junction of the clitoral frenulum, the clitoral hood, and the labia minor[20,21]. Excessive advancement of labial tissue at the time of the operation will end up in ever excision and absolute loss of the medial part of the labium.[20,22] additionally, the more the protuberance of labia minora over labia major the more label for wedge exactions[23]. In addition, the extra lightly colored anterior labial edge joint harshly with the darker pigmented posterior labial edge when the V-shaped is approximated. we modified labial pedicle flap[6,9,10] as we deepened on pinch test prior wedge excision and more superiorly based labial flap as we found more preserving normal contour, texture, good vascularity that prevent wound necrosis[12] and may be sensation[24], beside that it has the ability to end up with non continues nonlinear scar. The study concluded that the procedure maximize function through preserving normal optimal size of labial mucosal secretions and minimize disfiguring through preserve the distance that extend near labia majora, and restore cosmetic via preserving tissue which look like the natural spherical

contour of the border. The anteroposterior color is steady and shown natural for these reason this constructive understanding in[19] cases, we recommend this procedure for reduction labia minora.

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پوختە

نشتەرگەری بچویکرنا شێوێ دوولێڤێن بچیك ژلایێ کاری و جوانکاریێ ڤە

پێشەکی: گەورەبونا دوولێڤێن بچیك بێت (مهبل) دبیت ببیتە ئەگەرێ ئاریشێت کارکرنێ و جوانکاریێ و دەروونی، ئەگەر ژڤێ گوتنێ ئەوە پیشاندانا دوماهیك راستڤەکرن بکارئینانا (السدلە) ل لێڤا بچیك بو چارەسەریا ئاریشێن دهێنە پێش ژ بەرزبوونا دوولێڤێن بچیك.

ئەنجام: ژ حالەتێن گەورەبونا دوولێڤێن بچیك ژنەدیاربوونا ئەگەرا و ژ ئەگەرێ نشتەرگەریا چ هەودان و کولبون ل نشتەرگەریێ دیارنەبون، بەس ڤەبوونەکا بچیك ل نشتەرگەریێ هاتە دیتن ل نەخوشەکێ و هەروەسا هەبوونا کومبوونا خوینێ یا بێ ئێش ل نەخوشەکا دی، هەروەسا توشبوونا نەخوشەکا دی بو گیروبوونا میزێ کو پێتڤی بو ب چێکرنا (قسگرە) میزلدانکێ لەورا هەمو ئافرەت درازیبون و دلخوشبون ژ ئەنجامێن جوانکاریێ و کارکرنێ و نواندا دیڤچوونا ڤێ خواندنێ (١٤) چاردە حەفتی بوون.

دەرئەنجام: نشتەرگەریا بچویکرنا دوولێڤێن بچیك بکارئینانا راستڤەکرنا (السدلە) لێڤا بچیك دهێتە هژمارتن تەکنیکەکا گەلەك ب مفا و ئەنجامێن زور باش بو هەنە ژلایێ کارکرنێ و جوانکاری دئێك دەمدا.

الخلاصة

جراحة تصغير أو تصحيح شكل الشفرين الصغيرين من الوجهة الوظيفية والجمالية

الخلفية والأهداف: تضخم الشفرين الصغيرين (المهبل) يمكن أن يسبب مشاكل وظائفية التجميلية والنفسية، الغرض من هذه المقالة هو عرض آخر تعديل في استعمال السدلة الشفة الصغرى لمعالجة المشاكل الناتجة عن بروز الشفرين الصغيرين.

النتائج: لتضخم الشفرين الصغيرين مجهولة السبب، نتيجة العملية لم يكن هناك أي التهاب في الجرح، فتح طفيف في الجرح وجدت في مريضة واحدة، وجود جمع دموي غير مؤلم في مريضة أخرى، كما أصيبت مريضة واحدة باحتباس البول التي تطلبت قسطرة المثانة، وكانت جميع النساء راضيات من نتائج الجراحة التجميلية والوظيفية، وكان متوسط المتابعة أربعة عشر أسبوعاً.

الأستنتاجات: إن عملية تصغير الشفرين الصغيرين باستعمال السدلة الشفة الصغرى التعديلي تقنية مفيدة جداً وتعطي نتائج باهرة من الناحية الوظيفية والتجميلية في آن واحد.

ASSESSMENT OF SERUM HOMOCYSTEINE LEVEL IN PATIENTS WITH MISSED MISCARRIAGE

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ABSTRACT

Background: Accumulative reports documented that homocysteine (hcy) was implicated in many diseases. In recurrent missed miscarriage, the reports are limited and scarce. The objective was to evaluate the effect of hyperhomocysteinemia in the etiology of recurrent missed miscarriage.

Methods: This study involved sixty seven patients with confirmed diagnosis of missed miscarriage. The second group served as control group and included ninety four ladies subdivided into three subgroups: a) Thirty five normal pregnant ladies with matched gestational age' .b) Twenty nine apparently healthy non-pregnant ladies with matched age. c) Thirty apparently healthy full term pregnant ladies with matched age. The following main parameters were measured: Total serum homocysteine levels, Serum Human Chorionic Gonadotropin concentration(HCG), Serum progesterone concentration, complete blood count. Placental Histopathological Specimens Examination: Placental tissues were obtained from women after delivery and women with recurrent missed miscarriage and were examined histologically by using hematoxyline and eosin stain and also using CD34 immunohistochemistry.

Results: Serum homocysteine in cases of single missed abortion was significantly higher compared to recurrent missed miscarriage cases, non-pregnant cases and pregnant with matched gestational age groups (13.1 VS 9.8, 8.5, 8.7µmol/L, P< 0.009). Serum Human Gonadotropin was significantly higher in pregnant controls compared to that of missed miscarriage groups(10000 VS 2198.5 mlu/ml, P<0.001). Serum progesterone level was significantly higher in pregnant controls than recurrent missed miscarriage group (30.06 VS 3.64 ng/ml, P< 0.001). In missed miscarriage group, serum Hcy significantly negatively correlated with gravity and parity. Histopathological Results: There were histopathological changes of placental tissues of missed abortion cases in comparison to placenta of normal healthy fullterm pregnant cases including hyalinization of villi with focal or total losing of cytotrophoblast, hydropic degeneration, vasculitis of blood vessel and hemorrhage within decidua.

Conclusion: Data of the present study demonstrated that elevated homocysteine level has an important role in the pathogenesis of missed miscarriage.

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Keywords: Recurrent missed miscarriage, Homocysteine.

Pregnancy loss is a common problem that affects many women and their partners. Losing a pregnancy is extremely difficult for the expectant parents, and even early losses cause frustration and grief. Among women who know they are pregnant, the miscarriage rate is roughly 15-20%[1] and it is the most common complication of early pregnancy in humans.

According to the Royal College of Obstetricians and Gynecologists (RCOG) Green-top Guideline No. 17, a miscarriage can be defined as the spontaneous loss of a pregnancy before the fetus has reached viability at 24 weeks[2]. This includes all pregnancy losses from the time of conception until 23 completed weeks of gestation.

The American Society for Reproductive Medicine defines recurrent missed miscarriage as two or more failed

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pregnancies (documented by ultrasound or histopathological examination) and suggests some assessment after each loss with a thorough evaluation after three or more losses.[3]

Recurrent pregnancy loss (RPL) can be considered a primary or secondary process: primary RPL refers to repeated miscarriages in which a pregnancy has never been carried to viability, while in secondary RPL, a live birth has occurred at some time[4,5]. The prognosis for successful pregnancy is better with secondary RPL[5].

Homocysteine is one of the non-protein amino acids synthesized in blood. It is a sulfur containing amino acid with a free thiol (sulphhydryl-SH) group and is formed from methionine through s-adenosyle methionine[6]. High level of homocysteine in the serum, above 15µmol/L, is called hyperhomocysteinemia. This has been claimed to be a significant risk factor for the development of a number of diseases including cardiovascular disease and thrombosis[7]. Hyperhomocysteinemia makes a person more prone to endothelial cell injury, which leads to inflammation in the blood vessels, which in turn may lead to atherogenesis, and subsequent ischemic injury[8]. Recently, high levels of homocysteine have been associated with certain pregnancy complications that include: congenital malformations, recurrent miscarriages, chromosomal anomalies, preeclampsia and placental disorders[9]. Hyperhomocysteinemia has also been associated with early pregnancy loss[10] and with neural tube defects[11].

Subjects, Materials and Methods:

The design of the present study is a case–control study. This study was conducted at the Department of Physiology, School of Medicine, Faculty of Medical Sciences, University of Duhok and Duhok Maternity Hospital during the period of 1st May 2014 to 30 July 2014.

Two groups of ladies were included in this study, as follows:

1- The first group included sixty seven patients admitted to Gynecology and Obstetrics Department in Duhok Maternity Hospital with confirmed diagnosis of missed miscarriage for termination of pregnancy.

This group was subdivided into two subgroups:

Forty six patients with history of recurrent missed miscarriage.

Twenty one patients with history of single missed miscarriage.

The enrollment of both subgroups was according to the criteria of WHO for recurrent miscarriage[12].

2- The second group served as control group and included ninety four ladies subdivided into three subgroups:

Thirty five normal pregnant ladies with matched gestational age.

Twenty nine apparently healthy non-pregnant ladies with matched age.

Thirty apparently healthy full term pregnant ladies with matched age.

Data acquired at study entry included age, address, education, occupation, residence, economic status of family, weight, height, body mass index, gravidity, parity, abortion ,duration of pregnancy past medical history, obstetrical history (including history of recurrent missed miscarriage and history of metabolic diseases) and gynecological history (polyp, leiomyoma).

8ml of venous blood were obtained from a suitable forearm vein, 2ml sent for complete blood count using hematology auto analyzer, the remaining 6mls were put in plain plastic tubes, then centrifuged at 3000 rpm for 10 minutes at 4°C. The obtained serum was divided into 3 parts, stored in epiendrof capped tubes and stored frozen at -28°C. until the time of analysis for Homocysteine, HCG and Progesterone concentrations using ELISA Technique.

Placental tissue preparation was done for patients included in the first group (single missed and recurrent missed miscarriage), as soon as evacuation of uterus done: the placental tissue was collected in a small size glass beaker, rinsed thoroughly with cold normal saline until all the blood and debris were removed, then a small piece of the placental tissue was taken and stored in 4 ml of formalin solution 10%.

Also placental tissue preparation was performed for normal pregnant fullterm ladies at labor as a control group. Placental tissues were blunt dissected to remove visible connective tissue again a small piece of the placental tissue is taken and stored in 4ml of formalin solution 10%. We investigated chorionic villous vascularization by both histopathology and an image analysis system combined with CD34 immunohistochemistry in 10 women miscarriage group, compared with 10 women of healthy full term. Subsequently, we studied the vascular profile parameters (number of vascular elements per measured chorionic area and per ten filed).

The data were transferred into SPSS version 22 statistical package .Unpaired t-test, Mann-Whitney and LSD were used for comparison between two groups, one-way analysis of variance (ANOVA) and Kruskal-Wallis tests used for comparison between three groups or more. Receiver operating characteristic (ROC) analysis and ROC curves were used to examine the validity of studied parameters in the differentiation between missed abortion and normal pregnancy. Spearman's rank correlation and scatter diagrams were used to test the association among the studied parameters. The significance level was set at $P< 0.05$[13].

RESULTS

Comparison of blood parameters showed, Total WBC count was significantly different between the studied groups (ANOVA p=0.001) (table 1). There was an obvious significant high WBC count in the single missed miscarriage compared with that of recurrent missed miscarriage cases, pregnant and non- pregnant controls (10.6Vs 8.7, 8.3 and 7.3, $P < 0.001$), on the other hand the WBC count was higher in the miscarriage groups (single and recurrent) than that of non-pregnant group (10.6Vs, 7.3. 8.7Vs 7.3, $P< 0.001$, $P<0.033$) respectively.

Platelet count was significantly different between the studied groups which was lower in pregnant control group than non-pregnant control and single missed miscarriage (192.1 Vs.240.2and 224.2, p=0.003, p=0.023 respectively). In addition, platelet count was significantly lower in recurrent miscarriage group compared to non –pregnant (205.7Vs, 240.2, P=0.023).

Table1: Measurement of blood parameters in the studied group

Parameter	Single missed miscarriage 21(16%)	Recurrent missed miscarriage 46(35.1%)	Non-pregnant controls 29(22.1%)	Pregnant controls 35(26.7%)	P (ANOVA)
WBC (cells/mm3) x103					0.001
Mean ± SE	10.6± 0.98	8.7± 0.42	7.3± 0.46	8.3± 0.31	
P (LSD) for difference in mean between:					
Single missed miscarriage X Recurrent missed miscarriage = 0.017					
Single missed miscarriage X Non-pregnant controls < 0.001					
Single missed miscarriage X Pregnant controls = 0.005					
Recurrent missed miscarriage X Non-pregnant controls < 0.033					
Hb (g/dl)					0.181
Mean ± SE	11.7± 0.46	11.5± 0.23	12.2± 0.29	12.1± 0.21	
Platelets /mm3) x103					0.018
Mean ± SE	224.2± 8.33	205.7± 9.43	240.2± 14.30	192.1±10.52	
P (LSD) for difference in mean between:					
Recurrent missed miscarriage X Non-pregnant controls = 0.023					
Non-pregnant controls X Pregnant controls = 0.003					
Single missed miscarriage X Pregnant controls = 0.023					

The value of HCG was significantly higher in normal pregnant control compared with all other studied groups. (10000Vs5201, 2198.5 and 0.1, p=0.026, p=<0.001 and P=<0.001 respectively),(Table 2).Lowest median HCG values were observed among non-pregnant and recurrent missed miscarriage groups.

The median values of serum progesterone level was significantly higher in normal pregnant control group with matched gestational age than other study groups (30.06Vs 6.08, 5.99 and 3.64). In addition, serum progesterone level in recurrent missed miscarriage was lower than all other groups (3.64 Vs6.08).

Highest median value of homocysteine was observed in single missed miscarriage group (13.1 µmol/L) in addition, serum homocysteine level was significantly higher in recurrent missed miscarriage compared with non-pregnant control (9.8Vs 8.5, p<0.016)(figure.1).

Although the median value of serum homocysteine was higher in recurrent missed miscarriage compared with pregnant control (9.8Vs8.7), but the difference was statistically not significant (P =0.059).

Table 2: Measurement of Serum hCG & Progesterone and Homocysteine in the studied group

	Single missed miscarriage 21(16%)	Recurrent missed miscarriage 46(35.1%)	Non-pregnant controls 29(22.1%))	Pregnant controls 35(26.7%)	P (Kruskal-Wallis)
Serum human chorionic Gonadotropin (mlu/ml)					< 0.001
Median	5201	2198.5	0.1	10000	
Interquartile range	2220 – 10000	938.4 – 7071	0.1 - 491.9	10000 -10000	
P (Mann-Whitney) for difference in mean between:					
Single missed miscarriage X Non-pregnant controls = 0.020					
Single missed miscarriage X Pregnant controls = 0.026					
Recurrent missed miscarriage X Non-pregnant controls < 0.001					
Recurrent missed miscarriage X Pregnant controls < 0.001					
Non-pregnant controls X Pregnant controls < 0.001					
Serum Progesterone(ng/ml					< 0.001
Median	5.99	3.64	6.08	30.06	
Interquartile range	3.97 - 15.63	1.60 - 10.53	0.48 - 15.15	19.20 - 42.50	
P (Mann-Whitney) for difference in mean between:					
Single missed miscarriage X Pregnant controls = 0.035					
Recurrent missed miscarriage X Pregnant controls < 0.001					
Non-pregnant controls X Pregnant controls < 0.001					
Single missed miscarriage X Recurrent missed miscarriage = 0.203					
Homocysteine µmol/L)(					0.001
Median	13.1	9.8	8.5	8.7	
Interquartile range	11.0 - 13.5	8.2 - 10.7	6.9 - 9.6	6.9 - 10.2	
P (Mann-Whitney) for difference in mean between:					
Single missed miscarriage X Recurrent missed miscarriage = 0.009					
Single missed miscarriage X Non-pregnant controls = 0.001					
Single missed miscarriage X Pregnant controls < 0.001					
Recurrent missed miscarriage X Non-pregnant controls = 0.016					
Recurrent missed miscarriage X Pregnant controls = 0.059					

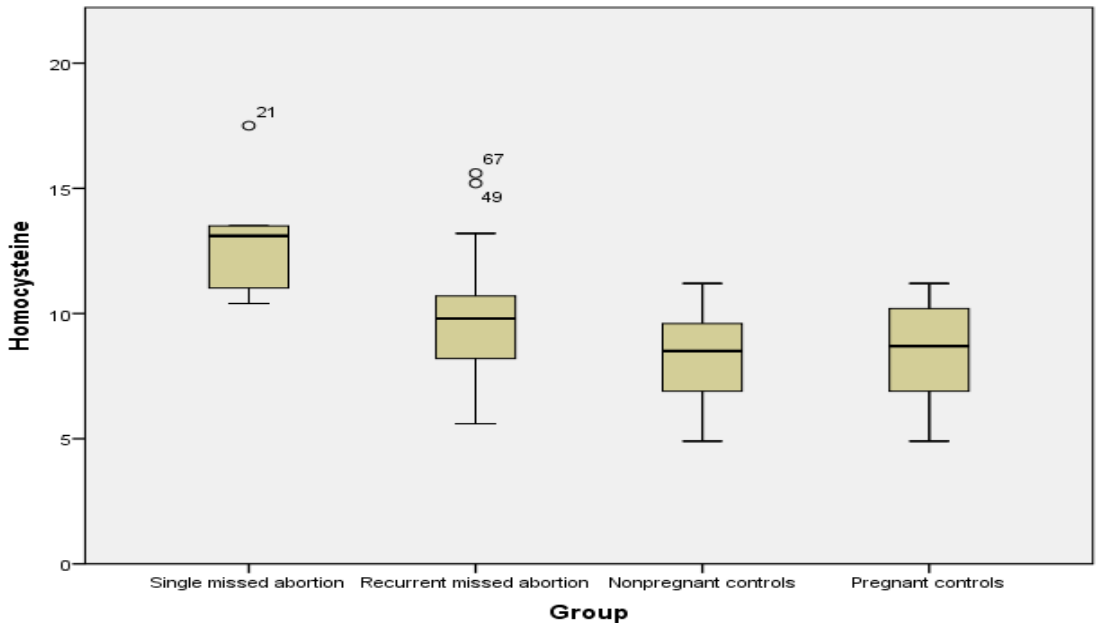

Figure 1 Box plot of serum homocysteine concentration of the four study groups

In missed miscarriage group, serum homocysteine level is significantly negatively correlated with gravidity (r = -0.518, p = 0.001)(Figure.2) , parity (r= -0.519,p=0.001) and hemoglobin level.

There were also significant negative correlations of gravidity with WBC count (r= - 0.250, p = 0.041, figure 3 and platelet count (r= -0.257, p= 0.036, figure 4).

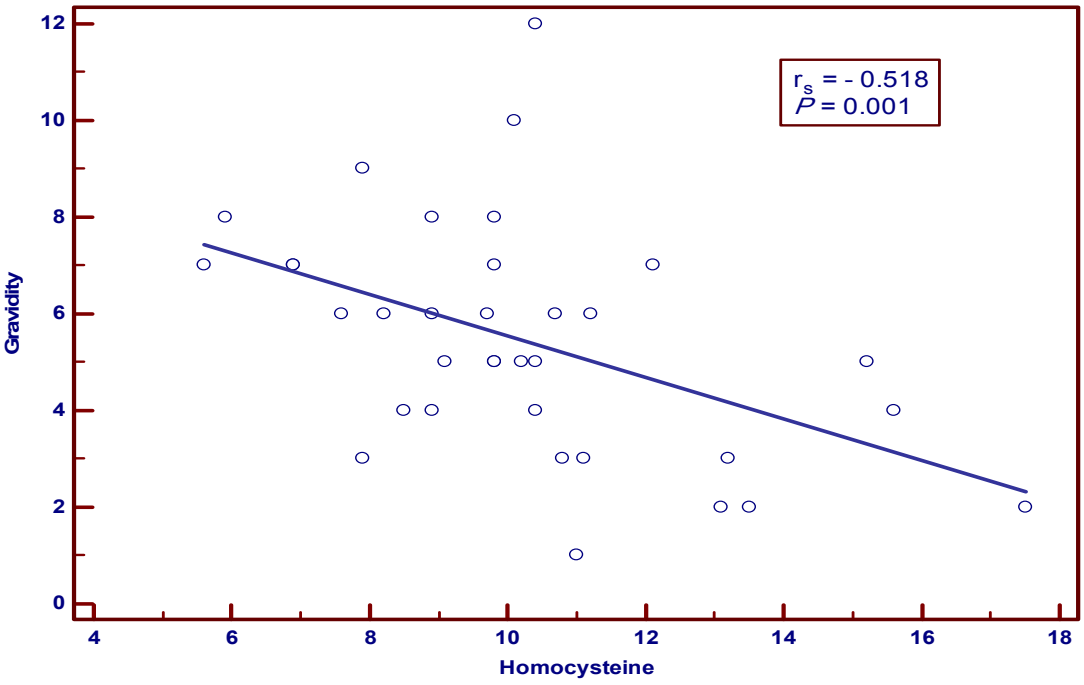

Figure 2 Correlation of gravidity with serum homocysteine concentration in missed miscarriage.

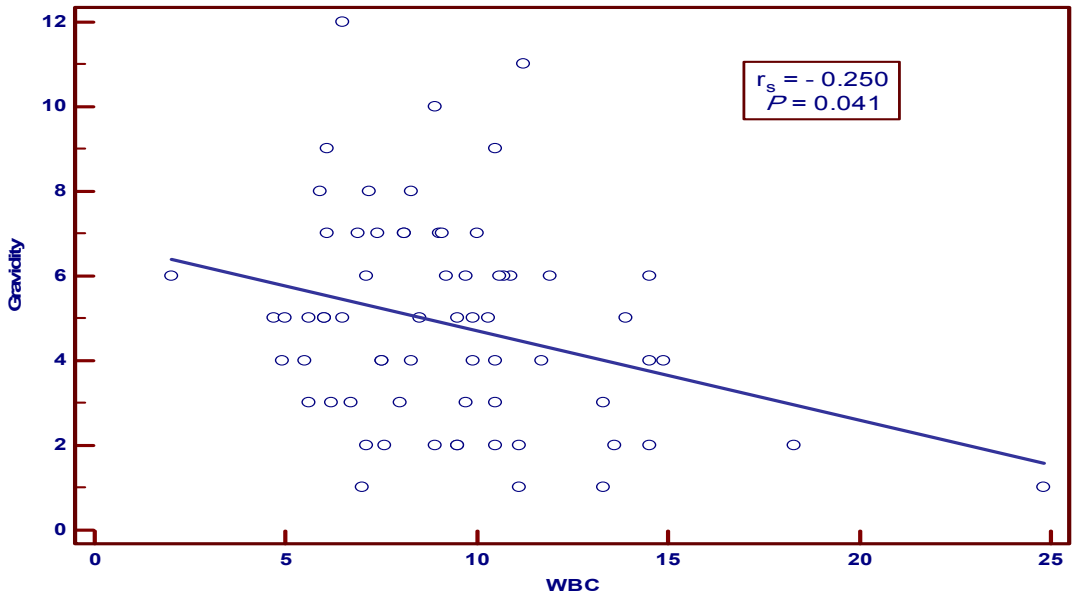

Figure 3 Correlation of gravidity with total WBC in missed miscarriage.

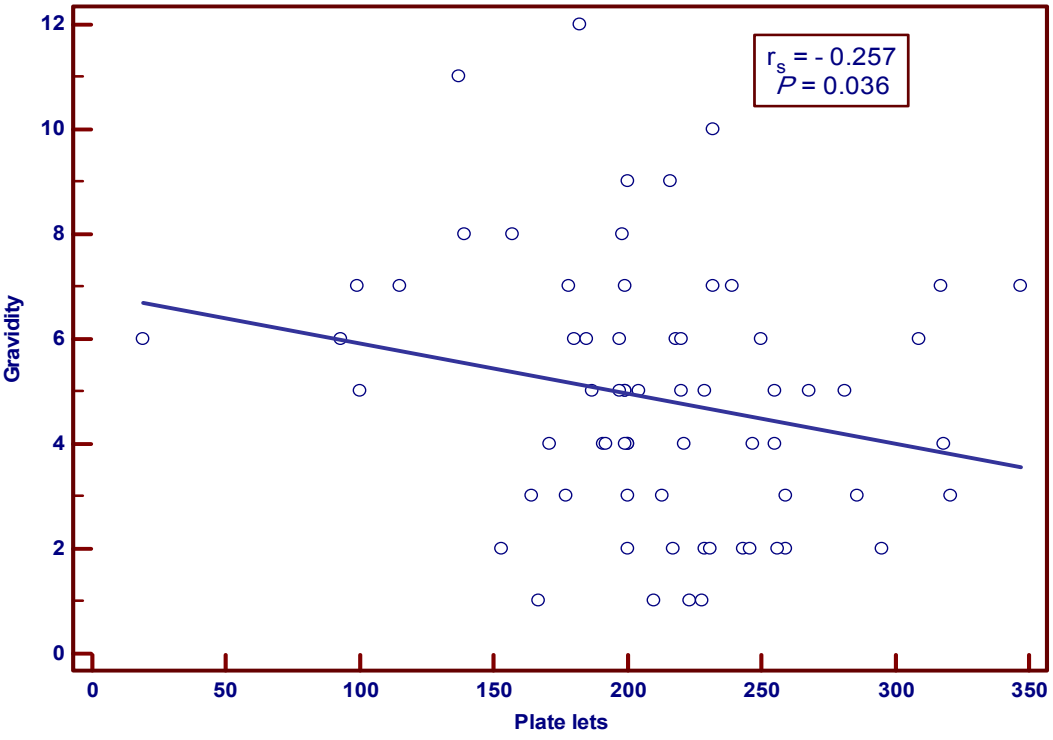

Figure 4 Correlation of gravidity with platelets counts in missed miscarriage

Receiver Operating Characteristic (ROC) curve analysis showed that serum progesterone was of highest validity with an area under curve (AUC) of 0.888, P =< 0.001), when used to differentiate between missed miscarriage cases from normal pregnancy followed by serum HCG (AUC= 0.870, p = <0.001, Figure 5). Serum Homocysteine was also of good validity (AUC =0.691, p=0.006) when

used to differentiate between missed miscarriage cases from normal pregnancy (Figure 6).

Using of cut-off point equal or less than 9932 mlu/ml, the sensitivity of the HCG hormone for differentiating missed miscarriage from normal pregnancy was 85.7% and the specificity was 83.3%.Also using cut-off point equal or less than10.53 ng/ml, the sensitivity of the progesterone for differentiating missed miscarriage from normal pregnancy was 74.3 % and specificity was 100%.

Distribution of study subject to the cutoff value of more than 9.1 µmol/L for homocysteine for differentiating of missed miscarriage from normal pregnancy the sensitivity was62.9% and specificity was 68%.

Table 3: ROC (receiver operating characteristic) analysis of hormones and homocysteine for differentiating missed miscarriage from normal pregnancy.

Parameter	AUC	SE	95% CI	Cut-off point	Sensit-ivity (%)	Speci-ficity (%)	P-value
HCG(mlu/ml)	0.870	0.047	0.757 - 0.944	≤ 9932	85.7	83.3	< 0.001
Progesterone(ng/ml)	0.888	0.045	0.778 - 0.955	≤ 10.53	74.3	100.0	< 0.001
Homocysteine(µmol/)	0.691	0.069	0.559 - 0.804	> 9.1	62.9	68.0	0.006

AUC= Area under the curve.

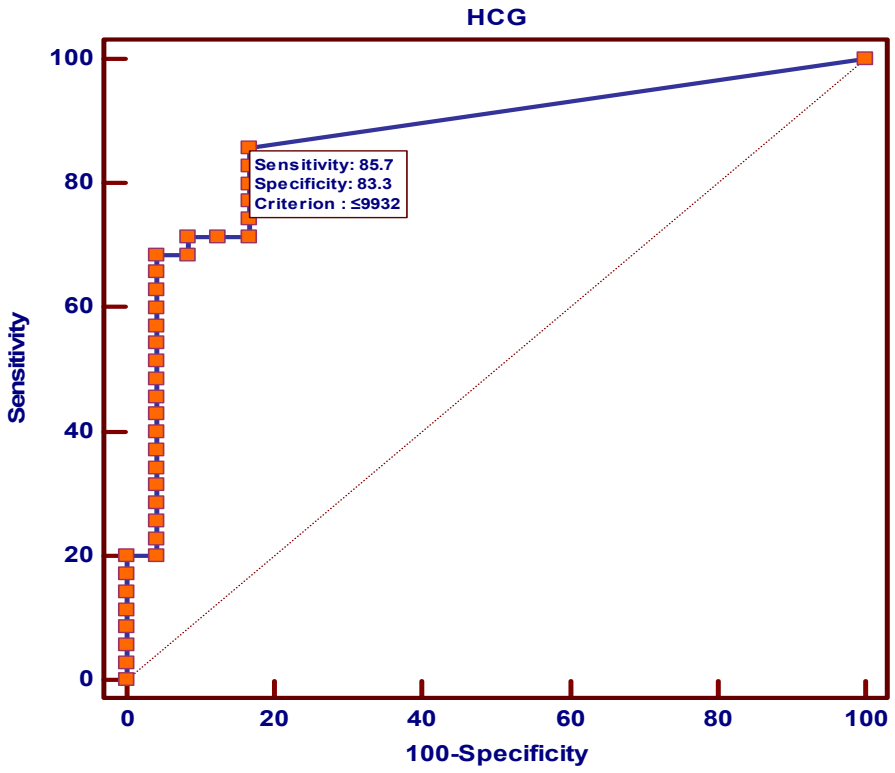

Figure 5 ROC curve showing the tradeoff sensitivity (rate of true positive and specificity rate of false positive) for Human Chorionic Gonadotropin(HCG) mlu/ml for differentiating missed miscarriage from normal pregnancy.

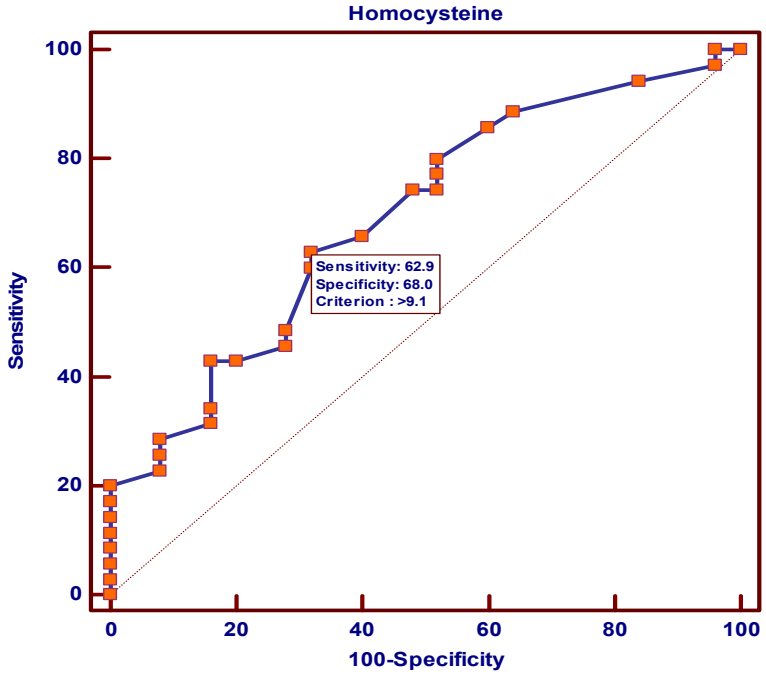

Figure 6 ROC curve of homocysteine for differentiating missed miscarriage from normal pregnancy.

The total number of vascular elements measured per mm chorionic tissue was lower in placenta of women with recurrent missed abortion than that of normal placental tissue (229.8 Vs 3.41, p = < 0.001)(table 4).

Table 4: Comparison of mean number of blood vessels of placental tissue, between cases of missed miscarriage and cases of normal pregnancy

	Normal pregnancies (n= 10)	Missed miscarriage (n= 10)
Mean number of blood vessels of placental tissues per 10 fields	229.80	3.41
SE	10.24	0.95
P*	< 0.001	

* Based on unpaired t-test.

Figure (7) shows the normal microscopic appearance of placental tissue with normal chorionic villi and normal vascularization.

Figure (8, 9) show histopathological changes in placental tissue of a recurrent missed miscarriage patient. There is decrease in number of syncytiotrophoblast cells, some of villi are replaced subtotaly by hyalinization and others show loss of covering trophoblastic with necrotic debris.

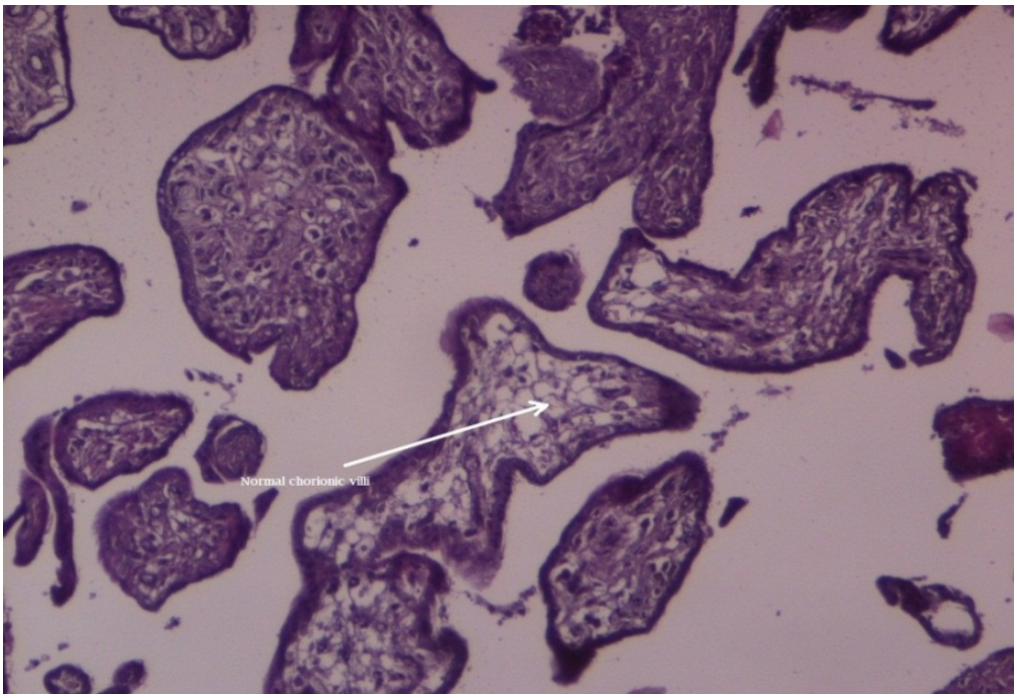

Figure 7 Microscopic appearance of normal placental tissue showing chorionic villi (10x10) the decidua, composed of well vascularized polygonal and faint eosinophilic cytoplasm.(H& E Stain) .

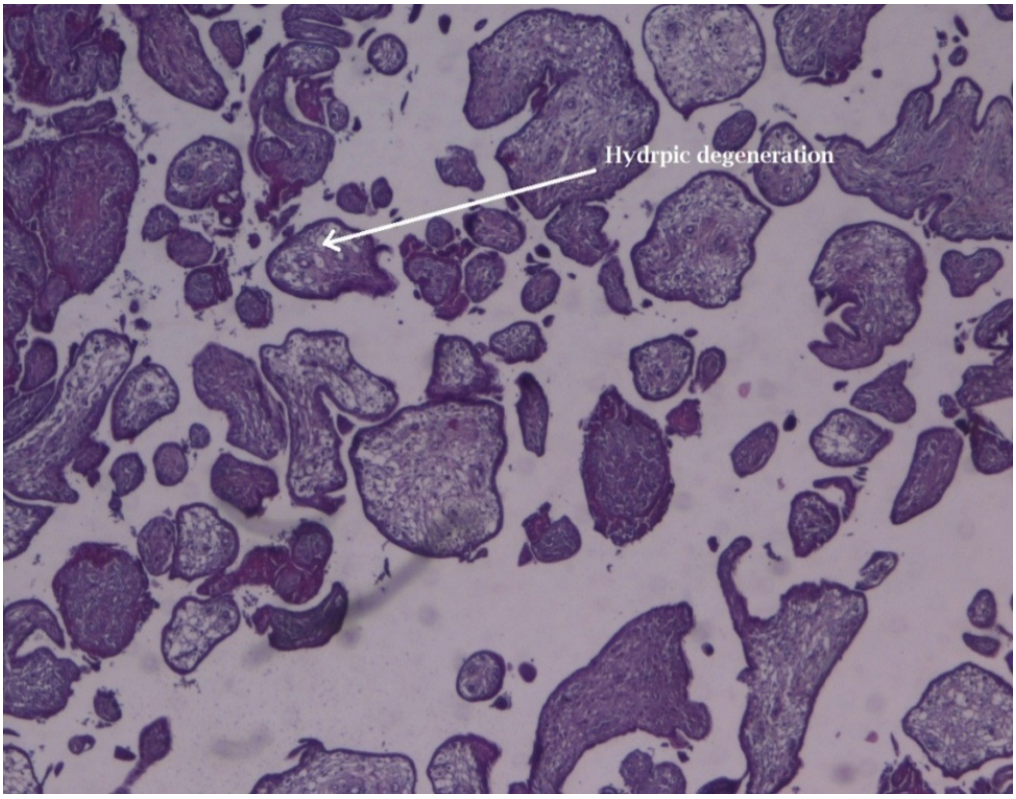

Figure 8 Large villi with hydro pic degeneration in placental tissue of recurrent missed abortion patient (10x10) (H&E stain)

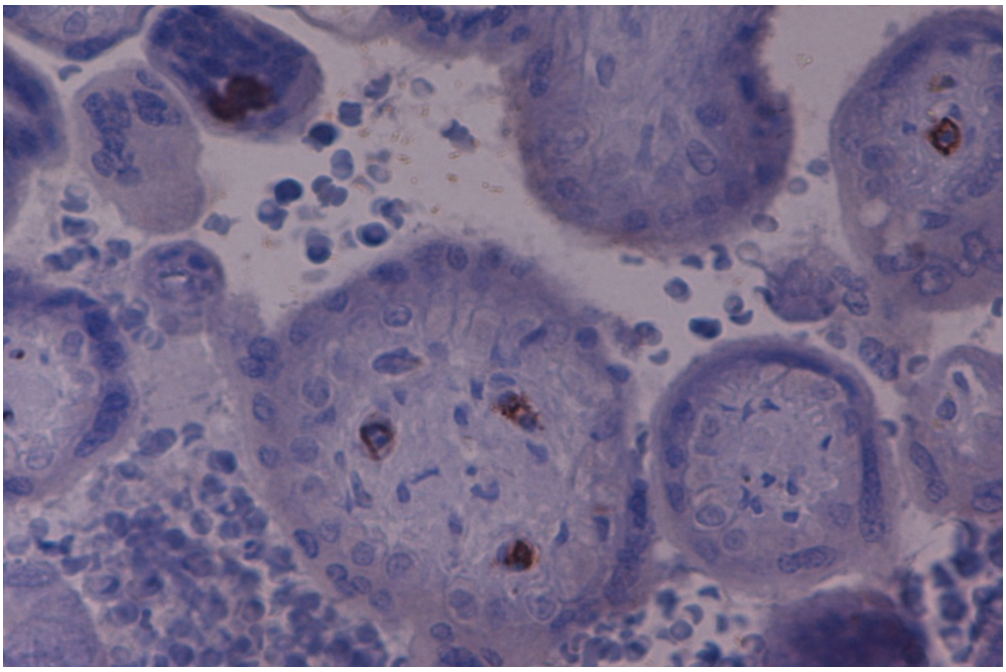

Figure 9 large villi with hydropic degeneration in placental tissue of recurrent missed abortion patient 40x10 (CD34) stain

DISCUSSION

Several reports, described an association between homocysteine and early missed miscarriage, but the present study is carried out for the first time in this locality. The pooled estimates for elevated hcy concentrations support the postulation that hyperhomocysteinemia is a risk factor for missed miscarriage.

Normal levels of serum homocysteine are considered to be between 5 and15 µmol/L[14]. The present study found that the median value of serum homocysteine in the single missed miscarriage patients was (13.1) µmol/L, and in the recurrent missed miscarriage was (9.8) µmol/L,which were significantly higher than that of non–pregnant and pregnant controls(8.5and 8.7) µmol/L respectively. The same findings were observed by Coumans et al[15]. In addition, Gris et al[16] reported an association between increased levels of hcy and a first early pregnancy loss.

A study found that 25% of women with recurrent missed miscarriage have hyperhomocysteinemia or at least a pathological methionine loading test[17].

Moreover, elevated homocysteine levels > 18 µmol/L were considered by the authors to be a risk factor for recurrent pregnancy loss[18]. Another study showed that women with recurrent miscarriage had a direct relationship between high levels of homocysteine and defective chorionic vascularization[19].

Results of the present study showed that there was no significant difference in homocysteine level in non-pregnant control (8.5) µmol/L compared with pregnant control (8.7) µmol/L. The same findings were observed by others[20]. In contrast, it was shown that homocysteine concentrations were 29–60% lower in pregnant women than in non-pregnant women[21].Various hypothesizes have been proposed explaining the decrease in

homocysteine concentration during pregnancy, Rolf et al.[22] and Cikot et al.[23], reported only a slight reduction in homocysteine concentration during early pregnancy, the homocysteine concentration decreases during normal pregnancy either due to the physiological changes of pregnancy, and increase in the level of estrogen, or increased the demand for methionine by both mother and the fetus.

The current study showed a significant negative correlation between serum homocysteine and gravidity, in addition to its correlation with parity. The same findings were observed by other researchers[24]. In contrast to these results, homocysteine levels were found to be positively associated with increased number of deliveries[25].

The capacity of homocysteine to differentiate between cases of missed miscarriage and healthy controls was assessed with a receiver operating characteristic (ROC) curve analysis .The ROC area for serum homocysteine was (0.691, p=0.006) in differentiating cases with missed miscarriage and normal pregnant control. Elevated homocysteine can be considered risk factors for miscarriage with cut-off point >9.1µmol/L, sensitivity 62.9%, specificity 68%.

In the present study we used vascular image technique to investigate single vascular profiles in miscarriage tissues. A smaller median percentage vascular area was found in women with elevated homocysteine concentration. In agreement with this, significantly smaller median areas per chorionic vascular element were observed as well as, a negative correlation between the median vascular perimeter and total homocysteine concentration .This suggests that elevated maternal total homocysteine concentration may be a cause of defective chorionic villus vascularization.

A defective chorionic villous vascularization, demonstrating inadequate vasculogenesis and abnormal development of the vasculosyncytial membrane, are seen in pregnancies complicated by embryonic death and is even more pronounced in un embryonic pregnancies[26].

A study on chorionic villous vascularization found deficient vascularization in cases of embryonic death[27] this is agreed with our study when we found a significant difference of number of blood vessels between placenta of normal pregnancy and placenta of missed miscarriage cases (229Vs 3.41, p= < 0.001).

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پوختە

هەلسەنگاندنا ئاستێ هوموسیستینا سیرەم ل نەخوشێن ب بەرچونا زوو و بەرزە

پێشەکی: راپورتێن ل دوهەڤ نیشان دانە کۆ هوموستین (hcy) ل گەلەك نەخوشیان هاتیە دیتن، ل بەرچونێن زوو و بەرزە یا دوبارە، راپورت سنوردار و کێمن، ئارمانجا ڤەکولینێ هەلسەنگاندنا کارتێکرنا زێدەبونا پرۆتینا هوموسیتین لناڤ خوینێ ل ئەگەرناسینا بەرچونا زوو و بەرزەیا دوبارەیە.

ریکێن ڤەکولینێ: ڤەکولین ژ ٦٧ نەخوشێن پشت راست کری ب بەرچونا زوو و بەرزە پێك هاتن، گروپێ دویەم وەکو کونترول هاتن بکارئینانا و ژ٩٤ ژنان پێك دهات کۆ بۆ سێ ژێر گروپ هاتن دابەشکرن أ- ٣٥ ژن ب دوگیانیا نورمال ب تەمەنێن دوگیانی یێن هەڤسەنگ. ب- ٢٩ ژنێن نە دووگیان و دیار ساخلەم ب تەمەنێن هەڤسەنگ. ج- ٣٠ ژنێن دووگیان تەمام و دیار ساخلەم ب تەمەنێن هەڤسەنگ. پیڤەرێن سەرەکی یێن خوارێ هاتن پیڤان: ئاستێن هوموسیستینا تەماما سیرەم، تیری یا هورمونا گونادو ترۆپینا کوریونیك یا سیرەما مرۆڤ (HCG)، تیری یا هورمونا پرۆجیستێرونا سیرەم، هەژمارا تەماما خوینێ، ئەزمونا نمونەیێن هیستوپاتولوجیکی یێن نافکێ (هەڤالوکی): تەڤینەکێن نافکێ ژ ژنان پشتی پەیدابوونا زاروك و ژانێن بەرچوونا زوو بەرزەیا دوبارە هاتن بدەستئینان و ب رەنگێن ئێنوزین و هێماتوکسیلین و هەروەسا ب هاریکاریا CD34 immunohistochemistry هاتن پشکنین کرن.

ئەنجام: هوموسیستینا سیرەم ل نمونەیێن تەك بەرچوونا درەنگ و بەرزە ل هەمبەر نمونەیێن بەرچوونا زوو و بەرزەیا دوبارە، نمونەیێن نەدوگیان ب تەمەنێن دوگیانی یێن هەڤسەنگ بشێوەیەکێ بەرچاڤ پتر بو (١٣.١ ل هەمبەر ٩.٨، ٨.٥، ٧.٨) مایکرومول/ لیتر، P<0.009). هورمونا گونادوتروپینا سیرەما مرۆڤان ب شێوەیەکێ بەرچاڤ ل ژنێن دوگیان ل گروپێ کونترول ل هەمبەر گروپێ بەرچوونا زوو و بەرزە پتر بو (١٠٠٠٠ ل هەمبەر ٢١٩٨.٥ mlu/ml P<0.001).

ئاستێ پروجێستێرونا سیرەم ب شێوەیەکێ بەرچاڤ ل ژنێن دوگیانێن کونترول ل هەمبەر گروپێ پەرچوونا زوو و بەرزەیا دوبارە پتر بو (٣٠.٠٦ ل هەمبەر ٣.٦٤ نانوگرم/ میلی لیتر، P<0.001). ل گروپێ بەرچونا زوو و بەرزە هوموسیستینا سیرەم ب شێوەکێ بەرچاڤ و نەرێنی پەیوەندی دگەل زاروکبوون و زاروك هەبونێ هەبو.

ئەنجامێن هیستوپاتولوجکی کو هەرینێن هیستەپاتولوجیکی یێن تەڤینەکێن نافکێ ل نمونەیێن بەرچونا درەنگ و بەرزە هەبو ل هەمبەر نمونەیێن ب دوگیانیا تەمام و دیار ساخلەم، گوهەرێن پێك دهاتن ژ شیشەیی بونا موخاتی ب ژدەست دانا ناڤەندی یا تەمام یا cytotrophoblast، تێکچوونا ئافێ، کولبونا رهێن خوینێ و خوین بەربونا دناڤ موخاتا ئێندومێتریوم.

دەرئەنجام: زانیاری یێن ڤەکولینا بەردەست سەلماند کو ئاستێ هوموسٓیتینا بلند رولەکێ گرنگ ل پەیدابوونا بەرچونا زوو و بەرزە هەیە.

الخلاصة

تقييم مستوى الـ(هوموسيستين) في مصل في المرضى بالفشل المفتقد

الخلفية والأهداف: وثقت عديد من التقارير المتراتبة بأن هوموسيستين متداخل في العديد من الأمراض، في الفشل المتفقد المتكرر، التقارير محدودة ونادرة، الهدف كان أن لتقييم تأثير فرط هوموسيستينميا في المسببات للفشل المتفقد المتكرر.

طرق البحث: تضمنت هذه الدراسة سبعة وستون مريضاً بالتشخيص المؤكد من الفشل المتفقد، عملت المجموعة الثانية كالمجموعة القياسية وتضمنت أربع وتسعون سيدة قسمت إلى ثلاث مجاميع فرعية: أ- ٣٥ سيدة حبلى طبيعيات بالعمر الحملي المتناظر. ب- ٢٩ سيدة غير حبلى صحيات على ما يبدو بالعمر المتناظر. ج- ٣٠ سيدة كتعبير صحي على ما يبدو الحمل كامل بالعمر المتناظر، البارامترات الرئيسية التالية قيست: المستويات للمصل الكلي هوموسيستين، تركيز مصل كوريونيك جونادوتروبين (HCG)، تركيز بروجسترون في المصل، احصاء دم كامل، وفحص نماذج النسيج المشيمي: الأنسجة المشيمية حصلت عليها من النساء بعد الولادة والنساء بالفشل المفتقد المتكرر وفحص بالطريق النسيجي باستعمال هيماتوكسيلين وصبغة أينوزين ويستعملان CD34 immunohistochemistry أيضاً.

النتائج: المصل هيماتوكسيلين في حالات الإجهاض المفتقد هو الوحيد مقارنة كان أعلى جداً إلى الفشل المفتقد المتكرر ومؤشر إلى حد كبير، حالات غير حبلى وحبلى بمجموعة الأعمار الحملية المتناظرة (١٣.١ مقابل ٩.٨، ٨.٥، ٨.٧ مايكروميل/ لتر، P<0.009). مصل جونادوتروبين البشري كان أعلى جداً في السيطرة الحبلى مقارنة إلى تلك الأخرى من مجموعات الفشل المفتقدة (١٠٠٠٠ مقابل ٢١٩٨.٥ mlu/ml, P<0.001). مستوى بروجسترون المصلي كان أعلى جداً في السيطرة الحبلى من مجموعة الفشل المفتقدة المتكررة (٣٠.٠٦ مقابل ٣.٦٤ نانوجرام/ ميليلتر P<0.001) في مجموعة الفشل المفتقدة، ربط مصل Hcy بشكل ملحوظ سلبياً بالجاذبية والتكافوء، نتائج الهستوباثولوجي كان هناك تغييرات هستوباثولوجية للأنسجة المشيمية للإجهاض المفتقد مؤشرة إلى حد كبير بالمقارنة مع مشيمية لحالات كامل الطبيعية الحبلى الصحية التي تزجيج الزغابات المعوية بالخسران البؤري أو الكلى للأورمة الخلوية، انحطاط ماء، التهاب الأوعية الدموية للوعاء الدموي والنزف ضمن السقوط.

الاستنتاجات: بيانات الدراسة الحالية بينت بأن مستوى هوموسيستين مرتفع له دور مهم في النشوء المرضي من فشل مفتقد.

OUTCOME OF ANTENATALY DIAGNOSED HYDRONEPHROSIS AMONG NEWBORNS IN DOHUK CITY

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ABSTRACT

Background: Fetal hydronephrosis is a common finding on antenatal ultrasound examination occurring in 0.5 to 1 percent of pregnancies,

Methods: In this study 67 newborn were evaluated soon after delivery by ultrasound examination and for those with moderate and severe hydronephrosis IVU & VCUG were done, the severity of the hydronephrosis and time of diagnosis were correlated with the cause whether it is physiological or pathological.

Results: One third of cases showed no pathological causes and the hydronephrosis resolved during follow up, while two third of cases had pathological causes and the most common two causes were VUR 34% and UPJ obstruction 30% and other causes include lower ureteric obstruction in 10%, posterior urethral valve in 6%, MCDK in 6% and lower ureteric ureterocele in 1.4% , and most cases diagnosed in first trimester seems to have severe hydronephrosis while most of the cases diagnosed in second trimester revealed mild cases with no pathological causes and cases diagnosed in third trimester usually showed to have pathological causes behind hydronephrosis.

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Keywords: Hydronephrosis, Newborn, Duhok.

Fetal hydronephrosis (dilatation of the renal pelvis with or without dilation of the renal calyces) is a common finding on antenatal ultrasound examination occurring in 0.5 to 1 percent of pregnancies[1]. It can be detected as early as 9th to 12th week of gestation[2] they are usually easy to identify because of their relatively hyperechogenic aspect in the first trimester. Although renal pelvic dilatation could be transient and these physiological in most of the cases, it's important to detect anatomical causes as these conditions can prevent normal renal development and/or cause renal injury. Therefore the goal of postnatal management is to detect those cases of antenatal hydronephrosis that will impact the health of the infant and require postnatal evaluation and possible intervention to minimize adverse outcomes. The majority of cases of antenatal hydronephrosis are not clinically significant, and therefore excessive concern may lead to unnecessary investigating the newborn baby and anxiety for parent and healthcare providers.

OBJECTIVES

We evaluate those newborns with antenatal hydronephrosis who had been referred from obstetrician with antenatal ultrasound revealing hydronephrosis , and the goal was to determine whether its

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transient and physiological or there is an anatomical cause behind it and if intervention is required or not, the second goal was to correlate between the severity and time of antenatal hydronephrosis with the etiology diagnosed postnataly.

MATERIAL & METHODS

During the period between December 2014 and January 2016, 67 newborn infants were referred to the pediatric surgery center in Dohuk with history of antenatal hydronephrosis. In this study all newborns were evaluated two weeks after delivery with ultrasound examination to assess the grade of hydronephrosis and APPD and those with mild hydronephrosis (APPD <7 mm) were followed by U/S examination every three months till resolution of hydronephrosis occurred, while those newborn with moderate hydronephrosis (APPD 10-15mm) and sever hydronephrosis (APPD>15mm) were further evaluated with intravenous urography (IVU) and voiding cystourthrography (VCUG) at age of six weeks. Renal function test were done for those with moderate to sever hydronephrosis and monthly general urine examination (GUE) were done for all cases to assess for urinary tract infection.

List off abbreviations

VUR, vesicoureteral reflux
PUJ, pelvo-uretric junction obstruction
LUO, lower uretric obstruction
PUV, posterior urethral valve
MCDK, multicystic dysplastic kidney
APPD. anterio-posterior pelvic diameter
VCUG, voiding cystourethro graph
IVU, intravenous urography
U/S, ultrasound

RESULTS

The total number of cases were 67 among these cases twenty one (31%) have only mild hydronephrosis and they resolve with follow up by ultrasound examination every three months for six months and no anatomical causes were found, while 46 cases (68%) have moderate to severe hydronephrosis and they were further evaluated with IVU & VCUG among these 46 cases fourteen cases (30%) showed to be PUJ Obstruction (left sided in ten cases and right sided in four cases), VUR were the finding in sixteen patients 34.7% (bilateral in 9 cases, right in 5 cases and left in 2 case), lower ureteric obstruction in seven cases 15% (left in 4 cases and right in 3 cases), posterior urethral valve in four cases 8.6% with significant renal impairment, left sided uretrocele in one cases 2% and congenital renal disease in four cases MCDK 8.5% (despite MCDK is not a true hydronephrosis but they were encountered antenatal as hydronephrosis by US that is why they were included in this study). And among these 67 newborn infants 11 cases (16.4%) where diagnosed in the first trimester (9 cases 82% have anatomical cause), 24 cases (35.8%) were diagnosed in second trimester (9 cases 37.5% have anatomical cause) and 32 cases (47.7%) were diagnosed in third trimester (28 cases 87.5% have anatomical cause). Cases with anatomical causes diagnosed in first trimester include 4 cases with PUV, 4 cases with VUR and one case with PUJ obstruction, the anatomical causes diagnosed in 2end trimester include 5 cases with PUJ obstruction, 3 cases with VUR and one case with LUO and the anatomical causes diagnosed in the third trimester include 9 cases with VUR, 8 cases with PUJ obstruction, 6 cases with LUO, 4 cases with MCDK and one case with left side uretrocele.Table.1, Figures1,2,3.

Table 1: Incidence of anatomical causes of hydronephrosis in each trimester

	pathology	1st trimester	2end trimester	3rd trimester	Total % (67)
1	Physiological ,resolved	2 cases 18%	15cases 62.5%	4 cases 12.5%	31.3%
2	VUR	4 cases 25%	3 cases 18%	9 cases 56%	23.8%
3	PUJ	1 case 7%	5 cases 35%	8 cases 57%	20.8%
4	LUO	No case	1 case 14%	6 cases 85.7%	10.4%
5	PUV	4 cases 100%	No case	No case	5.9%
6	MCDK	No case	No case	4 cases 100%	5.9%
7	uretrocele	No case	No case	1 case 100%	1.4%

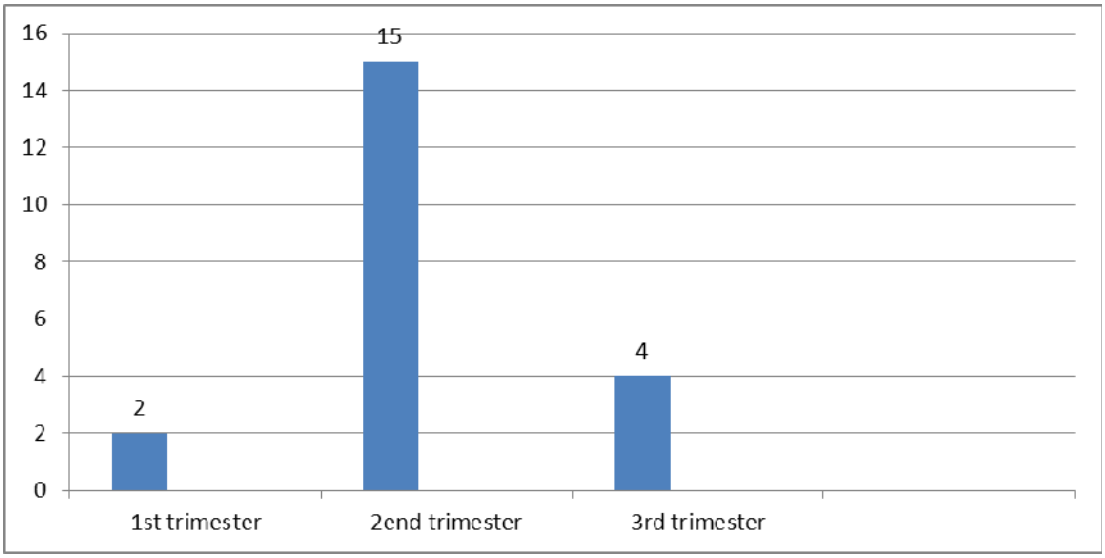

Figure 1 Antenatal diagnosed physiological hydronephrosis

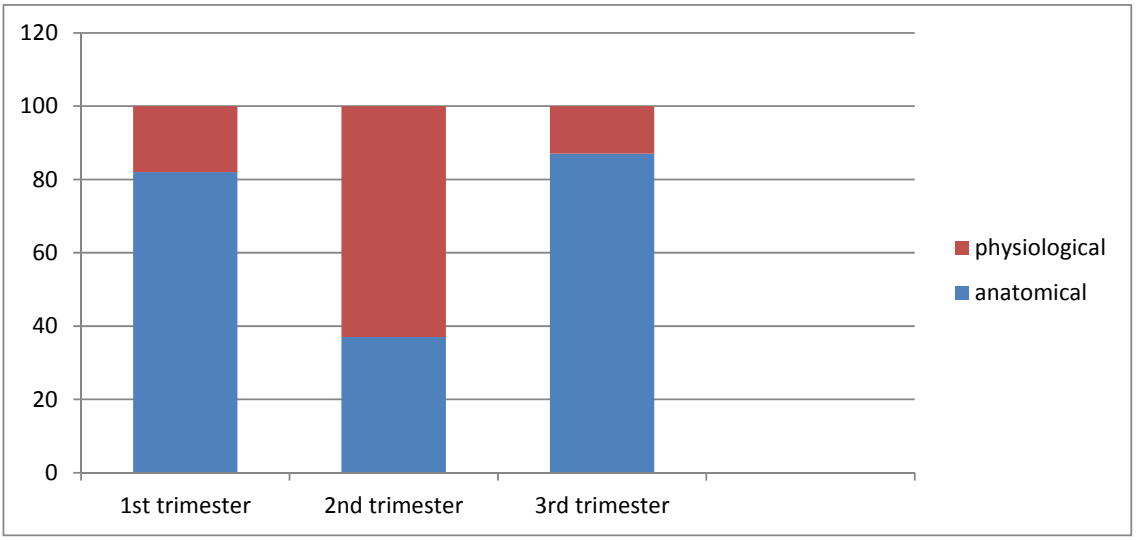

Figure.2 Ratio between anatomic and physiological causes in each trimester

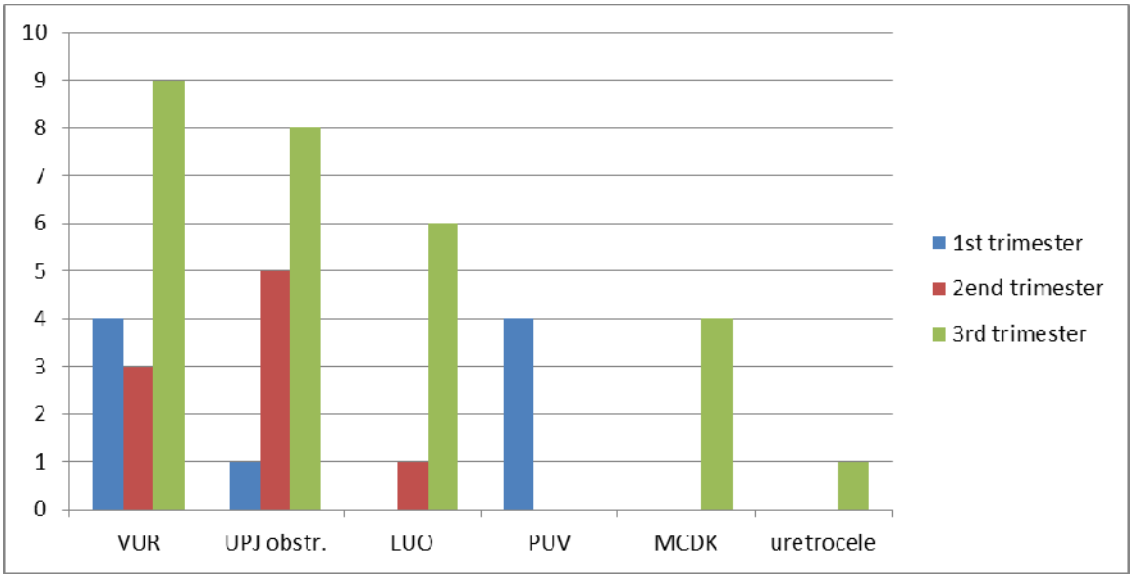

Figure 3 incidence of different anatomical pathologies in each trimester

DISCUSSION

In this study 21 cases 31.3% of antenatally diagnosed hydronephrosis appear to be physiological and spontaneous resolution occurred comparing with other study 40%3 and most of our cases show improvement and reduction in degree of dilatation by age of three month and nearly return to normal by age of six month among those infants 14 were male (66%) while 7 were female (34%) male to female ratio 2:1 same result founded by Blyth et al1, and majority of physiological hydronephrosis cases 62.5% were diagnosed in 2nd trimester but during follow up period antenatally there was no much difference or worsening during third trimester[3].

While 46 cases 68% had anatomical causes, majority of these cases were diagnosed in 1st trimester 9 cases out of 11 cases (82%) and in 3rd trimester 28 cases out of 32 cases (87%) while 9 cases out of 24 cases (37%) diagnosed in 2nd trimester showed anatomical causes.

VUR was the commonest cause 16 cases 23.8% (9 female, 7 male) and in other studies it account for 30%[4,5,6]. It was bilateral in 7 cases (43.7%), left sided in 5 cases 31% and right sided in 4 cases (25%). And it's mainly the cause of hydronephrosis in 3rd trimester 56% and male: female ratio was 1:1.3. UPJ obstruction is one of the most common anatomical cause of antenatal hydronephrosis[7,8]. In this study it was the 2end most common cause of antenatal hydronephrosis 14 cases (20.8%), male to female ratio 1.8:1, Boys are affected with UPJ obstruction more commonly than are girls[9,10]. The majority were diagnosed in the 3rd trimester (57%). Most cases of LUO were found to be diagnosed in third trimester (85.7%), right to left ratio 1.4:1 and in all cases grade V hydronephrosis were evident. All cases of PUV were diagnosed in the 1st trimester, in 3 cases (75%) it was associated with oligohydramnies and its usually diagnosed between 10-12 week of gestation[11]. Four cases of MCDK 5.9% in some studies it account for 7% of antenatal hydronephrosis[12,13,14], all cases were

diagnosed in third trimester. Only one female case of left ureterocele was diagnosed in 3rd trimester, female are more commonly affected, female: male ratio 4:1[15,16].

Finally, we can conclude that: most of the antenatal diagnosed hydronephrosis is physiological and resolve spontaneously and most of cases diagnosed in 1st & 3rd trimester have anatomical causes. Also ,cases that diagnosed in first trimester have poor prognosis while cases diagnosed in second trimester have favorable prognosis .On another hand, cases diagnosed in 3rd trimester have the highest rate of postnatally confirmed pathology .VUR and UPJ are the most common two causes of antenatal hydronephrosis.

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پوختە

ئەنجامێن کومبونا میزێ پێش ژدایکبون دناڤ نوژدایك بویان ل باژێرێ دهوك

پێشەکی: کومبونا میزێ ل جهم کورپەلەیان ئاریشەیەکا بەربەلاڤە کو ل دەمێ ئەنجادانا سوناریّ ل ۰.۵ حەتا ۱٪ ژدووگیانان پەیدا دبیت.

ڕێکێن ڤەکولینێ: ل ڤەکولینا بەردەست ٦٧ نوژدار بو ب دەمەکێ زوی و پشتی ژدایك بونێ ب سوناریّ هاتن فەحسکرن، ئەوێن ب ب کومبونا میزێ ب رەوشا سڤك و گران ب IVU وVCUG هاتن پشکنینکرن، پەیوەندیا گرانیا کومبونا میزێ و دەمێ ناسینێ هاتە هەلسەنگاندن دگەل ئەگەرێ فیزیولوجیکی و پاتولوجیکی.

ئەنجام: سێکا نمونەیان ئەگەرەکێ پاتولوجیکی نەبون و کومبونا میزێ ل دەمێ دوڤچونێ دا هات دروستبون، لێ دوو ژ سێکێن نمونەیان ئەگەرێ پاتولوجیکی هەبون و دوو ئەگەرێن بەربەلاڤ VUR ب ۳۰٪ و گرتنا UPJ ب ۳۰٪، ئەگەرێن دیتر ژ گرتنا ئالیێ خوارێ میزبەر ل ۱۰٪ بوریا پاشین ل ٦٪ MCDK ل ٦٪ و ڤەگەریانا ئالیێ خوارێ میزبەر ل ۱.٤٪.

دەرئەنجام: پرانیا نمونەیێن هاتینە ناسین ل شەش هەیڤێن یەکەم خودان کومبونا میزێ یا ئاست گران بون، لێ پرانیا نمونەیێن هاتینە نیاسین ل نەھ هەیڤێن دووگیانیێ هیچ جورە ئەگەرەکێ پاتولوجیکی ل پشت کومبونا میزێ پەیدا نەبوو.

الخلاصة

نتائج استسقاء الكلية عند حديثي الولادة المشخصة في فترة الحمل في مدينة دهوك

الخلفية والأهداف: استسقاء الكلية من المشاكل الشائعة التي تشخص عند الجنين في فترة الحمل وتحصل بنسبة ١%.

طرق البحث: هذه الدراسة شملت ٦٧ حالة، تم إجراء فحص السونار للأطفال بعد الولادة، في الحالات التي كانت تعاني من استسقاء شديد أو متوسط الحدة تم إجراء فحص الأشعة الملونة للتمييز بين الحالات المرضية والحالات الفسلجية المسببة لاستسقاء الكلية الولادي.

النتائج: تبين من خلال هذا البحث أن ثلث حالات استسقاء الكلية المشخصة قبل الولادة هي فسلجية، وتتحسن تلقائياً خلال متابعة المريض، وفي ثلثي الحالات تبين وجود سبب عضوي أو مرضي مسبب لاستسقاء الكلية، وهذه الأسباب المرضية شملت بالدرجة الأولى ارتداد البول من المثانة إلى الكلية بنسبة ٣٤% وانسداد حوض الكلية بنسبة ٣٠%، وهناك أسباب أخرى مسببة للاستسقاء وهي انسداد أسفل الحالب في ١٠%، صمام الإحليل الخلفي في ٦%، تكيس الكلية الولادي في ٦% وتوسع أسفل الحالب في ١.٤% من الحالات.

الاستنتاجات: معظم حالات استسقاء الكلية التي تم تشخيصها في الثلث الأول من الحمل كانت شديدة مع وجود سبب عضوي، بينما تبين أن معظم الحالات التي شخصت في الثلث الثاني من الحمل كانت فسلجية مع عدم وجود مسبب عضوي، والحالات التي شخصت في الفترة الأخيرة من الحمل كانت معظمها مرضية مع وجود سبب عضوي.

MATERNAL SERUM AND TISSUE LEPTIN IN FIRST TRIMESTER SPONTANEOUS MISCARRIAGES

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ABSTRACT

Background: Spontaneous miscarriage is a term used for a pregnancy that ends on its own, within the first (20) weeks of gestation, mostly occur during the 1st thirteen weeks of pregnancy. This study investigates the role of maternal serum and tissue leptin expression as a possible endocrine cause for early spontaneous miscarriages.

Methods: The study included three groups of women; (34) cases presented with 1st trimester spontaneous miscarriage, (34) cases with normal ongoing 1st trimester pregnancy, and (34) cases of normal non pregnant women with comparable age range regarded as a control group. Serum leptin concentration determined for study groups and trophoblastic immunohistochemical expression of leptin was studied in miscarriage group.

Results: Serum leptin concentration in miscarriage group was significantly lower than both pregnant and the non-pregnant (control) women. Also pregnant women show significantly higher leptin concentration as compared to non- pregnant control group and the correlation between maternal serum concentration and trophoblastic immunohistochemical expression of leptin was statistically significant.

Conclusion: Low level of maternal leptin hormone concentration in miscarried women and its significant correlation with trophoblastic immunohistochemical expression of leptin indicate the important role of leptin hormone in spontaneous miscarriage and maintaining normal pregnancy.

Duhok Med J 2016; 10 (1): 85-92.

Keywords: Leptin, Miscarriage, Immunohistochemical.

Spontaneous miscarriage refers to a pregnancy that ends spontaneously before the fetus has reached a viable gestational age[1]. It implies delivery of all or any part of the products of conception, with or without a fetus weighing less than500g[2].

There are many causes of miscarriage including chromosomal abnormality[3], infections[4], feto-maternal hemorrhage5 and endocrine abnormalities[6].

Leptin is a circulating 16 KD polypeptide consisting of 167 amino acids, encoded by obese gene (Ob) and is located on chromosome 7 in humans, primarily regulates energy homeostasis[7].

Its role in pregnancy was suggested by the findings that plasma levels during gestation are greater than in non-gravid individuals and that is synthesized within the fetoplacental unit[8].

Although leptin is mainly produced and secreted to the blood stream by white adipocytes, it is also produced by a variety of tissues and the placenta, uterus and ovaries have also been shown to be able to produce small amounts of leptin[9].

Leptin receptor transcripts were identified in the villous and extravillous trophoblast[10] and decreased leptin levels seem to be

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associated with miscarriage[11].

Although, the exact role of leptin in pregnancy is not known, it is thought to be important in the control of the functional integrity of the feto-placental unit and is implicated in the pathogenesis of recurrent miscarriage and pre-eclampsia[12]. It has also been shown that leptin is involved in early embryogenesis[13].

Leptin may orchestrate and coordinate the reproductive status of an organism by acting as a cross-talk molecule between nutrition and reproduction[14]. The human placenta shows substantial expression of leptin mRNA and protein[15].

The aims of the study were to investigate the relation of serum leptin hormone level with miscarriage and to study its relationship with the expression of this hormone in trophoblastic cells of women with spontaneous 1st trimester miscarriage.

MATERILAS AND METHODS

A prospective cohort study conducted during the period of December 2013 to May 2014.This work was approved by the ethical committee of Koya University and it included one hundred and two (102) women .All patients were personally interviewed and verbal consent obtained individually to participate in the study.

The study population divided into three groups:

Group A, included 34 cases of first trimester spontaneous miscarriages. Selection criteria include:

1- Spontaneous miscarriage (absence of elective medical or surgical measures to terminate the pregnancy)[16].
2- Gestational age is sonographically less than 13 weeks[16].
3- History of previous one or more miscarriages.
4- No previous history of medical problems.

Group B, included 34 cases of normal ongoing first trimester pregnancy.

Group C, included 34 cases of married, non-pregnant females of comparable age group as a control group.

Five milliliter of peripheral venous blood collected from the patients in sterile plane tube and left to clot for (15-30) minutes at room temperature, then centrifuged for 5 minutes at 3000 round per minutes (rpm). Sera were separated, divided into Eppendorf tubes and stored in deep freeze at –20ºC till assay day. Serum leptin concentrations in study groups were determined by solid phase competitive ELISA. (LDN Labor Diagnostica ,Leptin Elisa, Cat No.ME E-0300).and miscarried placental tissue was immediately washed by normal saline and fixed in 10% formalin, processed for routine Hematoxylin and Eosin stained tissue sections and for immunohistochemical staining of leptin expressed in placental trophoblastic cells by using commercially available kit (LeptinAntibody-NBP2-21618-Unit Size: 0.1 mg-Novus Biologicals co. Canada).

Immunohistochemical staining of trophoblastic cells showed a granular brown cytoplasmic staining. The best preserved and best stained area of trophoblastic cells sections were assessed that can see both stained and unstained cells in the same section.

A quantitative, proportion score was visually assessed as any cytoplasmic reaction for leptin was recorded as positive

as a percentage of total 100 trophoblastic cells (regardless the intensity of staining).

Analysis of data was performed by using Graphpad Prism 6 (GraphPad software, USA version 6.05), and Statistical Package for Social Science (SPSS) Version 19. Results are expressed as (Mean ± S.E), Percentage, the significance of the mean differences was assessed by one way ANOVA (Newman-Keuls multiple comparisons test), unpaired Student's t-test and spearman correlation coefficient (r) depending on SPSS program. p value <0.05 was considered to be statistically significant.

RESULTS

Mean serum leptin concentration in miscarriage group (24.58 ± 2.108) ng/ml was significantly (P<0.001) lower than both pregnant (66.81± 2.47) and the non-pregnant control (55.73 ± 2.86) ng/ml. Table (1).

Table 1: Serum leptin concentrations in studied groups

Parameters	Groups			
	Miscarriage	Pregnant	Non- Pregnant	P- value (ANOVA)
Serum leptin (ng/ml)	24.58 ± 2.108	66.81 ± 2.47	55.73 ± 2.86	<0.001

Results expressed as Mean ± S.E

Also pregnant women show significantly higher leptin concentration as compared to non-pregnant control group (P<0.001).Figure (1)

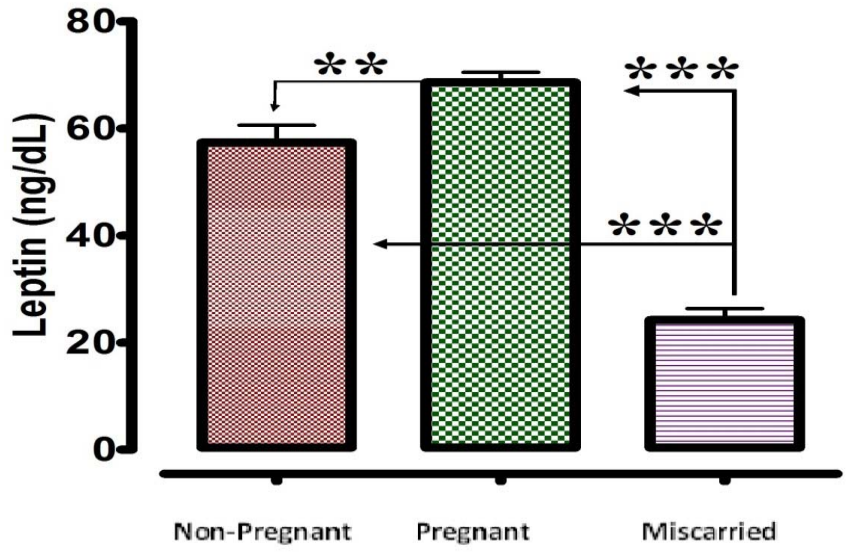

Figure 1 Serum leptin concentrations in studied population groups

(*** Significant P<0.001, ** Significant P<0.01)

Histological results

Leptin showed a brown granular cytoplasmic expression in the trophoblastic cells of first trimester spontaneous miscarriage. Figure 2.

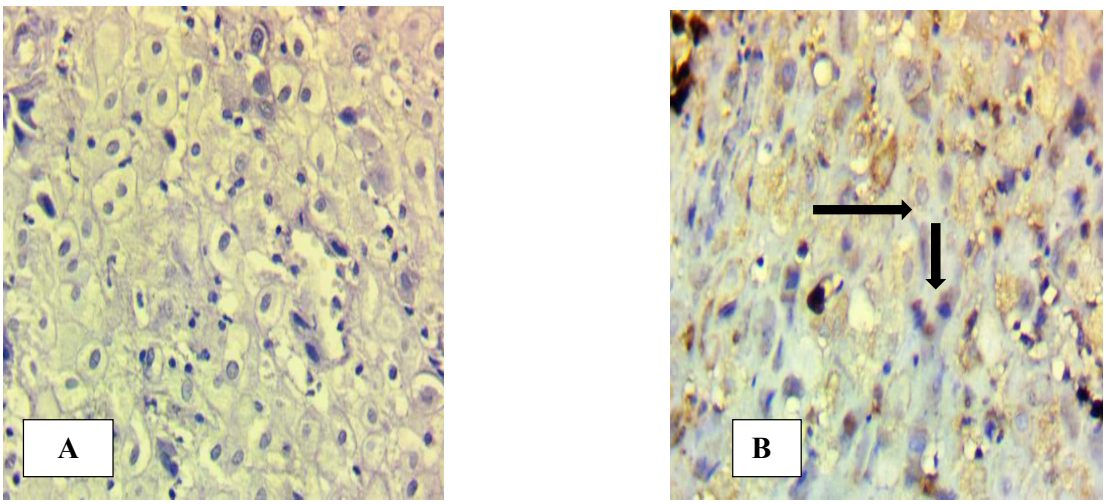

Figure 2 A; Photomicrograph showing the trophoblastic cells of 1st trimester spontaneous miscarriage (H&E, 400X) B; Photomicrograph showing the immunohistochemical expression of leptin in trophoblastic cells (arrows) of 1st trimester spontaneous miscarriage, note the brown cytoplasmic granular staining (400X).

The tissue leptin immunohistochemical score was (52.91 ± 4.55 %).The correlation between serum concentration and tissue expression of leptin was statistically significant. Table 2.

Table 2: Correlation between serum concentration and tissue leptin immunohistochemical score (IHC) in miscarriage group

Serum leptin (24.58 ± 2.108) ng/ml			
Parameters	**Mean ± S.E**	**Spearman correlation (r)**	**P-value**
Tissue leptin IHC score (%)	**52.91 ± 4.55**	**0.363***	**0.035**
* Correlation is significant at the level 0.05			

DISCUSSION

Early pregnancy loss is perhaps the most common medical problem in women of reproductive age. , and many causes have been postulated to explain these losses, but few other than genetic are well established[17].

Reasons for early pregnancy loss may be an abnormal embryo, infection, hormone imbalance problems with implantation of the embryo into the uterus wall, problems with the placenta and how it is formed, an inability of the cervix to stay closed[18].

Table (1) showed that serum levels of leptin were high in normal pregnant group as compared to miscarriage and non-pregnant control groups this is an indication that leptin may play a role in the maintenance of pregnancy as shown by Al-Atawi et al[19] who found that serum concentration of leptin increased significantly in the pregnant females during the first trimester as leptin produced by the placenta[20]. it raises an attractive hypothesis that leptin may act as a regulator of gestational weight gain and postpartum weight retention[21].

The low levels of serum leptin in miscarriage group in the current study are in agreement with Lage et al[22]. which indicated that abnormally low serum leptin levels were observed in women suffering spontaneous miscarriages in the first

trimester of pregnancy and Laird et al[23], reported that the significantly lower concentrations of leptin in women who subsequently miscarried suggest that leptin may play a role in preventing miscarriage.

While table (2) showed highly significant correlation between serum leptin concentration with its expression in trophoblastic cells of 1st trimester spontaneous miscarriage, these results agree with Tessier[24], who demonstrated that placental leptin expression patterns coincide with maternal serum leptin levels. The expression of leptin and leptin receptor in human placenta[25], and the observation that leptin may also augment the conceptus ability to sustain embryonic development, as it potentiates a down-regulation of apoptosis in the early blastocyst[26].

The Current study concluded that low level of maternal serum leptin and it significant correlation with trophoblastic immunohistochemical expression of leptin suggests an important role of leptin hormone in spontaneous miscarriage and maintaining a healthy early pregnancy.

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پوختە

بەرچوونا خوبخو و رولێ هورمەنێ لیپتین د رویدانا ویدا ل دەف دووگیانا

پێشەکی: ل بەرچوونا لەخووە زاراوەیەکە بەکاردێت کاتێك دووگیانی لە خووە لە ٢٠ هەفتەی سەرەتادا کۆتایی پێ دێت زۆربەی لە ماوەی ١٣ هەفتەی سەرەتادا دووگیانی دەبێت، ئەم توێژینەوە رولی هورمونی لیپتین لە ناو زەردەوی دایك و رەنگکردنی بەرگری شانەیی کیمیاوی بۆ دەربرینی لیپتین لە لایەن خانە بنچینەکانەوە.

رێکێن ئەکولینێ: کومەلەی ژن گرتوە: ٣٤ حالەتی لەبارچوونی لە خووە و ٣٤ حالەتی دووگیانی بەردەوام لە سێی مانگی یەکەم و ٣٤ حالەتی ئاسایی لە ژنان کە دووگیان نەبوون و هاوشێوە لە تەمەن وەك گروپی کونترول.

ئاستی هورمونی لیپتین لە ناو زەرداو و رەنگکردنی بەرگری شانەیی کیمیاوی بۆ دەربرینی لیپتین لە لایەن خانە بنچینەکانەوە.

ئەنجام: ئاستی هورمونی لیپتین لە ناو زەرداوی کومەلەی دووگیانی ئاسایی زۆر نزمتر بوو بەراورد لە گەل کومەلەکانی دووگیانی ئاسایی و کونترول، و ئاستی هورمونی لیپتین لە کومەلەکانی دووگیانی ئاسایی زۆر بەزترە کە ئاماژەیە بۆ کومەلەی کونترول هەروەها هورمونی لیپتین لەخووە زور پەیوەندی دار لە گەل وەرگیراوی بەرگری شانەیی کیمیاوی لیپتین لە لایەن خانە بنچینەییەکانەوە.

دەرئەنجام: نزمبوونی ئاستی هورمونی لیپتین لە ناو زەرداوی کومەلەی لە بارچوون لەخووە زور پەیوەندی لە گەل وەرگیراوی بەرگری شانەیی کیمیاوی لیپتین لە لایەن خانە بنچینەیەکانەوە کە ئاماژەیە بو ئەوەی هورمونی لیپتین رۆلێکی گرنگی هەیە لە پارێزگاری کردن لە دووگیانی سروشتی.

الخلاصة

الإجهاض التلقائي ودور هورمون اللبتين في حدوثه

الخلفية والأهداف: الإجهاض التلقائي هو مصطلح يستخدم للحمل الذي ينتهي تلقائيا خلال الأسابيع العشرين الأولى للحمل وتحدث معظمها خلال االسابيع الثالث عشر الأولى، تتحرى هذه الدراسة دور هورمون اللبتين في مصل االم والتعبير النسيجي للهرمون في الخاليا الغاذية كسبب غدي لألجهاض التلقائي.

طرائق العمل:

شملت الدراسة ثالث مجاميع من النساء: 34 امرأة عانت من االجهاض التلقائي و34 امرأة حامل في الثلث ألول من الحمل و34 امراة غير حامل وباعمار مقاربة كمجموعة سيطرة.

تم تقدير مستوى هورمون اللبتين في المصل والتعبير النسيجي الكيمياوي المناعي للهرمون في الخاليا الغاذية للسقط.

النتائج:

مستوى هورمون اللبتين في مجموعة االجهاض كانت معنويا اقل من كال مجموعتي السيطرة والنساء الحوامل في الثلث الأول من الحمل. كما ان النساء الحوامل أظهرن مستويات معنوية اعلى للهورمون بالمقارنة مع مجموعة السيطرة كما ان العالقة بين مستوى الهورمون في المصل مع التعبير النسيجي الكيمياوي المناعي للهرمون في الخاليا الغاذية كانت عالقة معنوية.

الاستنتاجات:

انخفاض تركيز هورمون اللبتين في مصل الأمهات اللاتي أجهضن تلقائياً والعالقة المعنوية مع التعبير النسيجي الكيمياوي المناعي للهرمون في الخلايا الغاذية تؤشر الى دور مهم لهورمون اللبتين في الإجهاض التلقائي و دوره في المحافظة على الحمل الطبيعي.

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PREOPERATIVE ASSESSMENT TO ANTICIPATE DIFFICULT INTUBATION IN CESAREAN SECTION

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ABSTRACT

Background: Incidence of difficult intubation increases during pregnancy due to physiological and pathological changes. Risks associated with general anesthesia for Cesarean Section are generally related to airway problems such as difficult intubation and aspiration pneumonia. High risk of morbidity and mortality associated with difficult intubation or failure of intubation in Cesarean Section necessitates the anesthesia team to use the best way for evaluation of the airway and anticipation of difficult intubation. The aim of this study is to detect the best method for airway evaluation that anticipates difficult intubation in Cesarean Section.

Methods: This study was conducted at Duhok Maternity Hospital during the period from May 2013 till October 2013. It included 100 pregnant patients admitted for Cesarean Section under general anesthesia, they evaluated for difficult intubation by Mallampati scoring system, (Thyromental, Sternomental, Hyomental) distances, Upper Lip Bite Test and Body Mass Index before induction of general anesthesia and the results were compared with the Cormack and Lehane grading system (the gold standard) after induction of anesthesia.

Results: The sensitivity and specificity of the methods for anticipating difficult intubation were; Mallampati Scoring System (sensitivity 75%, specificity 97.82%), Upper Lip Bite Test (sensitivity 71.42%, specificity 90.69%), Body Mass Index (sensitivity 88.88%, specificity 45.05%), Sternomental Distance (sensitivity 60%, specificity 97.89%), Tyhromental Distance (sensitivity 50%, specificity 97.95%), Hyomental Distance (sensitivity 33.3%, specificity 97.93%).

Conclusions: Mallampati scoring system is the best method for anticipating difficult intubation in Cesarean Section.

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Keywords: Difficult intubation, Cesarean Section, Mallampati scoring system, Cormack & Lehane.

The incidence of difficult intubation increases during pregnancy due to physiological and anatomical changes.[1]

Risks associated with general anesthesia are generally related to airway problems such as inability to intubate, inability to ventilate or aspiration pneumonia. Regardless the time of last oral intake, all obstetric patients are considered to have a full stomach and to be at risk for pulmonary aspiration.[1,2]

So, when there is a high risk of morbidity and mortality associated with difficult intubation or failure of intubation especially in emergency Cesarean Section, this necessitates the anesthesia team to search for and use the shortest and the best way to evaluate the airway and to anticipate difficult intubation.

Pregnancy leads to engorgement of the

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capillaries and edema of the upper airways, the mucosa will become friable, which may increase the risk of bleeding during manipulation or in response to trauma. These changes in the upper airways and increasing of breast mass of pregnant patients increases the incidence of difficult laryngoscopy and intubation.[2-6]

During pregnancy the oxygen consumption will increase and the functional residual capacity (FRC) will decrease which put pregnant patients in a high risk of hypoxia and desaturation during apneic periods.[1,5,6]

The gravid uterus normally will displace the stomach upward and this will leads to shifting of the gastroesophageal junction; the tone of the lower esophageal sphincter will decreases and this will increase the risk of reflux. The expanding uterus will increases the pressure inside the stomach, in combination these will lead to increase the risk of regurgitation and aspiration in pregnant ladies.[4,6-8]

Time of gastric emptying will prolong and gastric motility will decrease, so the pregnant patients are always regarded to have a full stomach.[3]

The lower esophageal sphincter is regarded as the primary protective mechanism against gastroesophageal reflux. Its length is about 2-5cm, with inspiration and expiration it will move upward and downward respectively. Normally the resting pressure of the LES is higher than gastric pressure. "barrier pressure" is the difference between these pressures. Reflux will occur when the LES pressure decreases or the gastric pressure increases.[7-10]

Other mechanism for protection against reflux is the angle at which the esophagus encounters the stomach; high intragastric pressures are needed to produce reflux when the angle is oblique. While, when the small angle is present e.g. (morbidly obese patients and pregnancy) lower gastric pressures may leads to reflux.[4,11,12]

Other structure that protect patients against regurgitation is the upper esophageal sphincter, practically most of the anesthetic agents that used for general anesthesia including the muscle relaxants lead to relaxation of this sphincter.7,13

The intrinsic airway reflexes e.g. cough reflex, expiration reflex and laryngospasm also have a role for protection against regurgitation. All of these reflexes eliminated by the effect of general anesthetic agents.[5,12,13]

Aspiration of the gastric contents during general anesthesia is rare (1:4000 to 1:9000). But when it occurs, it may leads to a fatal problem. (Mendelson's syndrome); chemical pneumonitis may result from gastric aspiration, which may happen if the pH of the gastric aspirate is <2.5 and the volume of the aspirate is >0.4 ml/kg.[11,12]

Furthermore, large gastric particles aspiration may obstruct the airways anyplace along the broncho–tracheal pathway creating difficulty in ventilation.[4,15]

Finally, aspiration of the gastric contents may happen during the perioperative period at any time. It may happen pre-induction, during induction of anesthesia, during manual ventilation, during laryngoscopy and intubation, during and after extubation.[7,14,15]

PATIENTS AND METHODS

This study was conducted in Duhok Maternity Hospital during the period from May 2013 till October 2013. The type of study was cross sectional study. A total of 100 pregnant patients admitted for Cesarean Section under general anesthesia were enrolled in this study. Each patient was evaluated for Mallampati scoring system, (Thyromental, Sternomental, Hyomental) distances, Upper Lip Bite Test and Body Mass Index before starting general anesthesia.

Preoxygenation with 100% FiO2 for 3-5 minutes through a standard face mask followed by induction of general anesthesia by sodium thiopental in dose of 3-6 mg/Kg (sleeping dose) followed by succinylcholine (scolin) 1.5mg/Kg in a rapid sequence induction & intubation technique.

The laryngeal view (Cormack & Lehane test), which is the gold standard test, was graded for the level of difficult intubation while intubating the trachea.

the data was collected and evaluated for the sensitivity and specificity of each test in comparison with Cormack and Lehane grading system (the gold standard) to identify the most sensitive and the most specific test which will be regarded as the best way for anticipating difficult intubation in pregnant patients undergone Cesarean Section under general anesthesia.

RESULTS

The total number of patients included in this study was 100 cases; all of them were evaluated for Mallampati scoring system, (Thyromental, Sternomental, Hyomental) distances, Upper Lip Bite Test and Body Mass Index before induction of general anesthesia.

Evaluation of Mallampati classification revealed the incidences among (100) cases of cesarean section, it was highest in Mallampati class I (59 patient; 59%) of the sample followed by Mallampati class II (33 patients; 33%), whereas the lowest incidences were Mallampati class III & IV (8 patients; 8% & no patient; 0%) respectively, which are suspected to be difficult to intubate. (Figure 1)

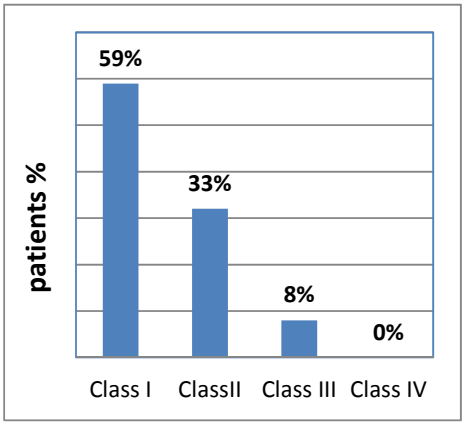

Figure 1: Incidences of Mallampati classification (pharyngeal view) in 100 patients

Evaluation of Upper Lip Bite Test (ULBT) shows 82 patients were able to do the test successfully, whereas 18 patients were failed. (Figure 2)

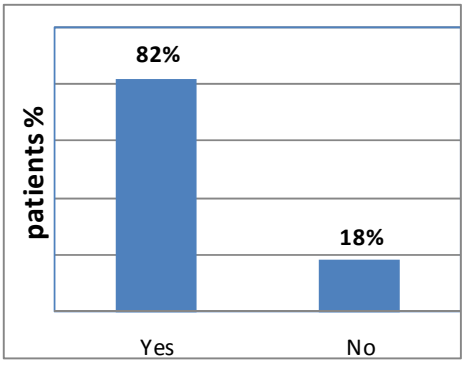

Figure 2: incidences of ULBT in 100 patients.

Evaluations of Thyromental (TMD), Hyomental (HMD) and Steromental (SMD) distances shows; 3 patients were have TMD less than 6.5cm, 3 patients had HMD less than 4cm, whereas 5 patients had SMD less than 12 cm. all of these are suspected to be difficult to intubate. (Figure 3)

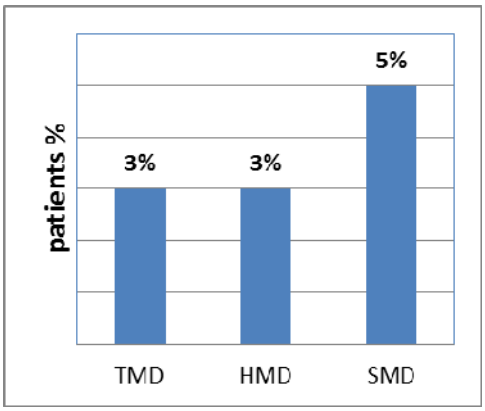

Figure 3: Incidence of TMD, HMD, and SMD distances <6.5 cm, <4cm & <12cm respectively.

Evaluation of Body Mass Index (BMI) in 100 patients shows that Healthy weight women were (12%), Overweight women (30%), Obesity class I (33%), Obesity class II (15%) & Morbid Obesity were (10%). (Figure 4)

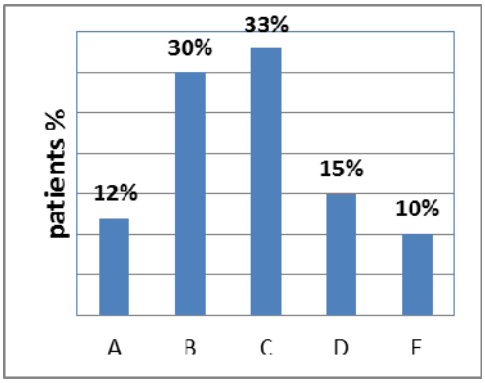

Figure 4: Incidences of BMI in 100 patients A: Healthy weight, B: Overweight, C: Obesity class I, D: Obesity class II, E: Morbid obesity.

Comparison between results of Mallampati scoring system with Cormack & Lehane grading system revealed that; the sensitivity and specificity were 75% and 97.82% respectively. (Table 1)

Comparison between results of Upper Lip Bite Test with Cormack & Lehane grading system revealed that; the sensitivity and specificity were 71.42% and 90.69% respectively. (Table 2)

Comparison between results of measured distances with Cormack & Lehane grading system revealed that; the sensitivity and specificity were 50% and 97.95% respectively for Thyromental Distance (TMD). The sensitivity and specificity were 33.3% and 97.93% respectively for Hyomental Distance (HMD). Whereas The sensitivity and specificity were 60% and 97.89% respectively for Sternomental Distance (SMD). (Table 3)

Comparison between results of Body Mass Index (BMI) with Cormack & Lehane grading system revealed that; the sensitivity and specificity were 88.88% and 45.05% respectively. (Table 4)

sensitivities and specificities of the methods for anticipating difficult intubation that are considered in (100) cases of Cesarean Section in this study according to their validity were illustrated. (Table 5)

Table 1: Validity of Mallampati scoring system in comparison with Cormack & Lehane test.

Mallampati Classification		Cormack & Lehane G I	G II	G III	G IV	Sensitivity	Specificity
Class I	59	47	12	-	-	75 %	97.82 %
Class II	33	21	10	2	-		
Class III	8	-	2	6	-		
Class IV	0	-	-	-	-		

Table 2: Validity of the ULBT in comparison with the Cormack & Lehane test.

ULBT		Cormack & Lehane G I	G II	G III	G IV	Sensitivity	Specificity
Yes	82	62	16	4	-	71.42 %	90.69 %
No	18	3	5	8	2		

Table 3: Validity of the measured distances in comparsion with Cormack & Lehane test.

Distance		Cormack & Lehane G I	G II	G III	G IV	Sensitivity	Specificity
TMD>6.5cm	97	80	16	1	-	50 %	97.95 %
TMD≤6.5cm	3	-	2	1	-		
HMD>4cm	97	74	21	2	-	33.3 %	97.93 %
HMD≤4cm	3	-	2	1	-		
SMD>12cm	95	83	10	2	-	60 %	97.89 %
SMD≤12cm	5	-	2	3	-		

Table 4: Validity of the BMI in comparison with the Cormack & Lehane test.

BMI		Cormack & Lehane G I	G II	G III	G IV	Sensitivity	specificity
Healthy weight	12	11	1	-	-	88.88 %	45.05 %
Overweight	30	25	4	1	-		
Obesity class I	33	23	8	2	-		
Obesity class II	15	4	8	3	-		
Morbid obesity	10	4	3	2	1		

Table 5: Validities of all the methods included in this study.

Method	Sensitivity	Specificity
Mallampati scoring system	75 %	97.82 %
ULBT	71.42 %	90.69 %
SMD	60 %	97.89 %
TMD	50 %	97.95 %
HMD	33.3 %	97.93 %
BMI	88.88 %	45.05 %

DISCUSSION:

In this clinical study, multi screening methods considered for anticipating difficult intubation in Cesarean Section (Mallampati scoring system, ULBT, TMD, HMD, SMD & BMI) and compared with the gold standard method Cormack and Lehane (laryngeal view).Most of international studies regarding difficult intubation or airway management are based on a comparison of just one or two methods with the gold standard, or multi screening tests but in nonspecific sample.

In 2006, T.Randell studies (prediction of difficult intubation), included a comparison between the Mallampati and the TMD, and proved that the Mallampati is more sensitive than the TMD in predicting difficult intubation in a general surgical unit[16]. In 2011, Subramanian H., N.V. Nagalakshmi did preoperative assessment to predict difficult airway using multiple screening tests, included the Mallampati classification, TMD, Head and Neck movement and Inter incisor gap in a random sample, proved that the Mallampati had a higher sensitivity than the Head and Neck movement[17].

In 2013, E. Allahyary, S. R. Ghaemei, S.Azemati, compared five methods for predicting difficult intubation in obstetric patients, used the ULBT, Mallampati, TMD, Inter incisor gap and the Horizontal length of the mandible for predicting difficult intubation in obstetric patients, recommended that the best combination of tests for anticipating difficult intubation is ULBT with the Mallampati scoring system(18),but that study didn't included the SMD test which was described by Savva in 1994 or the BMI which are important predictors for difficult intubation in pregnant patients.

Therefore, in our study we used the most important methods that concern on anticipating difficult intubation collectively and apply it on 100 pregnant patients admitted for Cesarean Section under general anesthesia which is suspected to improve the practicing with this type of patients and to a great extent, it will decrease the incidence of morbidity and mortality for both mother and fetus.

Out of the 100 patients of Cesarean Section, only 8 patients were Mallampati class III & IV (difficult intubation), but when these were compared with Cormack & Lehane (the gold standard), only 6 cases were Cormack III & IV (difficult intubation). Calculating these data shows that the sensitivity of Mallampati scoring system was (75%), whereas the specificity was (97.82 %).

For ULBT, 18 patients were not able to bite their upper lips precisely, whereas only 10 of them were Cormack III & IV. So, the sensitivity of this test was (71.42%), i.e. the possibility of difficult intubation increases when the patient fails to do this test in (71.42 %), while the specificity of ULBT was (90.69 %). The BMI used in this study as a method for anticipating difficult intubation. 58 patients were obese (obesity class I, II & III), whereas direct laryngoscopy (Cormack and Lehane grading) for those revealed that 8 of them have (Grade III, IV) and considered to be difficult for intubation. So, the BMI in this study was sensitive in (88.88%), whereas the specificity was just (45.05%).

Comparing the results of the measured distances with the gold standard test revealed that only 3 patients had TMD less than 6.5 cm which result in 50% sensitivity and 97.95% specificity, 3 patients had HMD less than 4 cm which result in 33.3% sensitivity and 97.93% specificity, 5 patients had SMD less than 12 cm which result in 60% sensitivity and 97.89% specificity. These results shows that SMD test is the most sensitive among the measured distances.While, HMD test was least sensitive among the measured distances.We found that the results of this study meet the international results regarding assessment of difficult intubation in obstetric unit.

In conclusion; Mallampati scoring system is the best way and the most valid method to anticipate difficult intubation in Cesarean Section under general anesthesia.

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پوختە

هەلسەنگاندنا کلینیکی یا بەری نشتەرگەریا سیزیریەن بو پێشبینکرنا زەحمەتا لولەککرنێ

پێشەکی: هەبوونا زەحمەتا لولەککرنێ بلندبیت ل دەمێ دووگیانیێ ژبەر گهورینا فەسلەجی و نەساخیێن ئافرەتا دووگیان، مەترسیێت پەیدابن ژ ئەنجامێ بێهوشکرنا گشتی ب رەنگەکێ گشتی گرێداینە ب ئاریشێن جوبارێن هەناسێ وەك بوارێ لولەککرنێ و باخوشکرنێ یان هەلکێشانا سیهان بو تشتێن دناڤ گەدەیدا، ئەڤجا دەومێ بوارکێ بلند هەبیت بو دوژانکا یان مرنێن گرێدای ب زەحمەتا لولەککرنێ وەك بوارێ لولەککرنێ و باخوشکرنێ ب تایبەت دسیزێریەنێن بلەزدا پێتڤی ب نوژداریێ بێهوشکرنێ و تیمێن وێ باشترین ریّك بکاربینن بو هەلسەنگاندنا جوبارا هەناسێ ژبو پێشبینکرنا زەحمەتا لولەککرنێ بەری نشتەرگەریێ.

ریّکێن ڤەکولینێ: ئەڤ ڤەکولینە هاتە پێکئینان ل نەخوشخانا دایکینیێ یا فێرکرنێ ل دهوکێ ناڤبەرا هەیڤا گولانا ٢٠١٣ تا چریا ئێکێ ٢٠١٣، سەد (١٠٠) بارێن ژدایك بونێن سێزیریەن ل هولا نشتەرگەریێ بریّکا بێهوشکرنا گشتی و پشتی هینگێ هەر بوارەك هاتە هەلسەنگاندن لدویڤ: پولینکرن Mallampati، دوراتی (Thyromental, Sternomental, Hyomental) تاقیکرنا لەقدانا لێڤا بلند (Upper Lip Bite Test)، و رابەرێ بارستا لەشی (Body Mass Index)، ئەوژی بەری پولینکرنە بنواشە کە (Golf Standard) بو ئاستێ زەحمەتا لولەککرنێ لدەمێ لولەککرنا بوریا هەوایی پشتی دانانا بێهوشکرنا گشتی.

ئەنجام: هەستیاری و تایبەتمەندی یا ریّکێن دهێنە بکارئینان دڤێ ڤەکولینێ دا دا ژبو پێشبینیکرنا زەحمەتا لولەککرنێ د (١٠٠) باران دا ژ نشتەرگەریێن سێزیریەن ب ڤی رەنگی بوون: پولینکرن Mallampati (هەستیاری ٧٥٪، تایبەتمەندی ٩٧.٨٢٪)، تاقیکرن Upper Lip Bite Test (هەستیاری ٧١.٤٢٪، تایبەتمەندی ٩٠.٦٩٪)، رابەرێ بارستا لەشی Body Mass Index (هەستیاری ٨٨.٨٨٪، تایبەتمەندی ٤٥.٠٥٪، دوراتی Sternomental (هەستیاری ٦٠٪، تایبەتمەندی ٩٧.٨٩٪، دوراتی Thyromental (هەستیاری ٥٠٪، تایبەتمەندی ٩٧.٩٥٪)، دوراتی Hyomental (هەستیاری ٣٣.٣٪، تایبەتمەندی ٩٧.٩٣٪).

دەرئەنجام: پولینکرن Mallampati باشترین ریّکە بو پێشبینیکرنا زەحمەتا لولەککرنێ د سیزێرن دا.

الخلاصة

التقييم السريري ما قبل العملية القيصرية لتوقع صعوبة التنبيب

الخلفية والأهداف: احتمالية صعوبة التنبيب تزداد خالل فترة الحمل بسبب التغيرات الفسلجية والمرضية للمرأة الحامل. المخاطر الناتجة عن التخدير العام مرتبطة عموما بمشاكل المجرى التنفسي كاستحالة التنبيب او استحالة التهوية او االسنتشاق الرئوي لمحتويات المعدة. عندما تكون هناك احتمالية عالية للمضاعفات او الوفاة المتعلقة بصعوبة التنبيب او استحالة التنبيب وخاصة في العمليات القيصرية الطارئة سيحتم على فريق التخدير استخدام افضل طريقة لتقييم المجرى التنفسي لتوقع صعوبة التنبيب قبل العملية. الهدف من هذه الدراسة هو الوصول الى أفضل طريقة لتقييم المجرى التنفسي لتوقع صعوبة التنبيب في العمليات القيصرية.

طرق البحث: أجريت هذه الدراسة في مستشفى االمومة التعليمي في دهوك خالل الفترة من آيار 2013 الى تشرين ألول 2013. تتضمن 100 حالة حمل أدخلت الجراء العملية القيصرية تحت التخدير العام, تم تقييم المرضى لصعوبة التنبيب بأستخدام نظام Mallampati مسافات (Thyromental, Sternomental, Hyomental) اختبار عض الشفة العليا (Upper Lip Bite Test) ودليل كتلة الجسم (Body Mass Index) قبل البدء باعطاء التخدير العام وتمت مقارنة النتائج مع نظام التصنيف (Cormack and Lehane) والذي يعتبر (المعيار الذهبي) بعد البدء بالتخدير.

النتائج: الحساسية والخصوصية للطرق المعتمدة في هذه الدراسة لتوقع صعوبة التنبيب في ال 100 حالة من العمليات القيصرية كانت: تصنيف (Mallampati) الحساسية 75%، الخصوصية 97,82% اختبار (Upper Lip Bite) الحساسية 71,42%، الخصوصية 90,69%، دليل كتلة الجسم (Body Mass Index) الحساسية 88,88% الخصوصية 45,05%، مسافة Sternomental (الحساسية 60% الخصوصية 97,89%)، مسافة Thyromental (الحساسية 50% الخصوصية 97,95%)، مسافة Hyomental (الحساسية 33,3% الخصوصية 97,93%).

الاستنتاج: نظام تصنيف Mallampati هو الطريقة ألفضل لتوقع صعوبة التنبيب في العمليات القيصرية.

EFFECTIVENESS AND SAFETY OF CURRENT ANTICONVULSANT THERAPY DURING PREGNANCY: CASE SERIES FROM DUHOK

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ABSTRACT

Background: Epilepsy is a very common chronic neurological disease that affects both male and female populations; there has been an association between epilepsy and course and outcome of pregnancy. The study aimed to study the effects of few currently used anticonvulsant drugs on pregnancy, labour, and the newborn in a small group of female patients.

Methods: This retrospective, clinical case-series included women suffering from focal/complex partial/generalized epilepsy, with/without aura, before and after their marriage, who eventually became pregnant and presented to the Neurology/ Neurosurgery Consultation Clinics and Private Clinics at Duhok during the period January 2005–December 2015. The enrolled 28 women with epilepsy came from Duhok Governorate, and their ages ranged between 15–40 years. A suitable format sheet has been designed in which relevant patient's notes were recorded. All of patients had standard routine haematological and biochemical profile, including alpha fetoprotein measurement, skull X-rays, abdominal ultrasound, contrast computed tomography and magnetic resonance imaging scanning examination; all had electroencephalographic records. Patients were given anti-convulsant medication at presentation, 5mg daily folic acid supplements 2 months before and during pregnancy, plus other symptomatic drugs when appropriate; most of them were also given multivitamins and minerals preparation as additional nutritional support. The anticonvulsant drugs included Carbamazepine, Levetiracetam, Lamotrigine, and Valproic Acid, within standard dosage necessary to achieve an adequate control (seizure-free life). Duringthe follow-up period,routine blood tests were done every 6 months to monitor the effects of those drugs on the bone marrow and the liver.

Results: All have achieved good epilepsy control before, during, and after pregnancy, and during the follow-up period. Clinical examinations, blood tests, skull X-ray, computed tomography, magnetic resonance imaging were within normal; however, alpha-fetoproteins value was only abnormal in the patient who gave birth to the newborn with facio-oral defect. The course of pregnancy, labour, and post-partum period was smooth in all of the patients. All gave birth to healthy single viable newborns, having normal gestational age, birthweight or APGAR score, except one of the patients who was taking Valproic acid, her newborn had cleft lip and palate. The latter patient was switched over to carbamazepine and gave rise to a healthy newborn baby in subsequent pregnancy.

Conclusions: WWE treated by CBZ, LVC, LTG and VPA showed good seizure control during pregnancy and labour whether vaginal or cesarean section.Unlike CBZ, LVC and LTG, only VPA use was associated with one case of facio-oral congenital abnormality.

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Keywords: Pregnancy, women with epilepsy, safety of anticonvulsants

Epilepsy is the most common chronic neurological condition, affecting 0.6 to 1% of the population[1-2]. Given that approximately a third of patients receiving antiepileptic drugs (AEDs) are of reproductive age and almost half of pregnancies are unplanned[3], the fetus may be exposed to these in the first trimester of

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pregnancy, including during the critical stage of embryogenesis[4].

In general, there are few known gender related differences in pharmacokinetics or efficacy of antiepileptic drugs (AEDs). Conversely, gender has a significant influence on the susceptibility to certain adverse effects, not the least those involving alterations in sex hormone metabolism. Particularly relevant are the teratogenic effects of AEDs, with important differences among AEDs in their potential to cause adverse effects on the fetus when used during pregnancy. Pregnancy can also markedly affect the pharmacokinetics of several AEDs, and dose adjustments are often needed during pregnancy to maintain seizure control[5].

Women with pregnancy (WWE) have several gender based problems pertaining to social and biological domains. The stigma of epilepsy and its consequences appear to be more for women than men. They have more difficulty in getting married and sustaining a married life. The cyclical variations in the reproductive hormones can adversely impact the seizure pattern in WWE. Epileptiform discharges in the brain can influence the hypothalamic functions and lead to sexual dysfunction. The AEDs may alter their metabolic and hormone profile and contribute to this disorder. Most WWE tend to have uneventful pregnancies and healthy babies. Nevertheless, the risk of fetal malformations appears to be increased when AEDs are used during pregnancy. This risk is higher for those who are on polytherapy, or using valproate. Recent studies have also demonstrated that antenatal exposure to AEDs could lead to neurocognitive and developmental impairment, low IQ or language problems in exposed infants. Clinicians need to consider these special issues while initiating AED therapy in adolescent girls. All WWE need to have a detailed pre conception evaluation wherein the need to continue AEDs, the ideal AEDs and dosage are reassessed. The AEDs therapy would have to be individualized according to the clinical situations, obstetric background and family concerns. Folic acid should be prescribed to all women who could potentially become pregnant. Detailed screening for fetal malformations by estimation of serum alpha fetoprotein and fetal ultrasonography need to be carried out between 14-18 weeks of pregnancy. The dosage of AEDs may have to be escalated in the second half of pregnancy in selected patients. The family should be provided detailed counseling and information on how to cope with the pregnancy, childbirth, lactation, and contraception[6].

The aim of this study is to show the effects of few currently used anticonvulsant drugs on pregnancy, labor, and newborn in a small group of women who presented to the Neurosciences Clinics in Duhok City between January 2005 and December 2015.

MATERIALS AND METHODS

A suitable format sheet has been designed in which relevant patient's notes were recorded. All of 28 patients had routine hematological and biochemical profile, including alpha fetoprotein measurement (α-FP), abdominal ultrasound (US),skull X-ray (SXR), computed tomography (CT) and magnetic resonance imaging (MRI)/ contrast studies, and electro-encephalographic (EEG) records. They all

hadstandard history taking and neurological examination. Patients were given anti-convulsant medication at presentation, folic acid supplements before and after pregnancy, plus other symptomatic pharmacological treatment when appropriate. The current anticonvulsant drugs which were prescribed to the patients and that achieved adequate seizure control before marriage, during, and after pregnancy included Carbamazepine (CZB), Levetiracetam (LVC), Lamotrigine (LMG), and Valproic Acid (VPA), within standard dosage range. Labor and post-partum complication(s), if any, were recorded. Newborn infants were assessed regarding their gestational age, birth weight or APGAR score.

RESULTS

There were 28 women; their ages ranged between 15–40 years; they came from Duhok City and many other districts around it. Those presented at the age of 15, got married and were pregnant at the age 20 (Table 1). Five WWE had complex partial seizure and the rest (23) suffered idiopathic generalized epilepsy. Routine blood and imaging tests were within normal, except the patient whose child had cleft lip and palate; she had higher α-FP than normal. The EEG records show epileptiform, sharp, and spike and wave discharges that confirm the clinical diagnosis of epilepsy. Those patients using CZB, LVC, and LTG delivered healthy babies. However, within the VPA group, the woman who was only controlled with VPA gave birth to a newborn with cleft lip and palate; she suffered idiopathic generalized epilepsy. There were neither maternal obstetric nor pediatric post-natal complications.

Table 1: Included patients by clinical findings

Patients number	Age (range) in years when pregnant	Anticonvulsant medication(s) and dosage given	Course of pregnancies and labour*	Outcome of pregnancy
20	20-40	Carbamazepine 400 mg CR/SR▪ twice daily	Uneventful vaginal delivery 17; cesarean section 3	All healthy newborns
2	25	Levetiracetam 500 mg in the morning 1000 mg in the evening	Uneventful vaginal delivery	All healthy newborns
2	25	Lamotrigine 100 mg in the morning 150 mg in the evening	Uneventful vaginal delivery	All healthy newborns
4	35	Valproic Acid 500 mg twice daily	Uneventful vaginal delivery	One newborn had cleft lip and palate

Table 2.Included patients by type of convulsive disorder.

Type of epilepsy	Number of patients
Complex partial seizure	5
Idiopathic generalised epilepsy	23
Total	28

DISCUSSION

Medical treatment of epilepsy is quite different for women than for men[7]. It is known that estrogen facilitates while progesterone inhibits the generation of epileptic seizures. Due to the direct neuronal effects of estrogen, progesterone, and their metabolites, as well as the cyclical nature of sex hormone release, women are particularly susceptible to the effects of these hormones on seizure frequency and severity. AEDs may result in reproductive endocrine disorders, decreased effects of oral contraceptives, or congenital malformations. On the other hand, if AED treatment is insufficient, seizures may influence reproductive endocrine disorders or cause fetal death. Physicians should minimize these risks through preconception counseling and appropriate treatment of women with epilepsy who are of reproductive age[8].

The prevalence of active epilepsy is that of 3.33 per 1000 among pregnant women, with about one percent having a past history of seizure from eclampsia8. Seizures in pregnancy are particularly challenging, as their management requires careful consideration of not only the etiology of the seizure, but also the physiologic changes of pregnancy as well as potential adverse effects on the developing embryo or fetus. In spite of achieving satisfactory epilepsy control and less teratogenic effects with new AEDs during pregnancy[9], however, researchers have documented the increased risk of anomalies among newborns of WWE taking AEDs during pregnancy as well as the increased occurrence of seizure events during later months of pregnancy, during labor and puerperal course. Furthermore, they have more complications, e.g., hypertension, miscarriages, and need for Cesarean section[10]. As far as the ages of patients, medications that were prescribed, and outcome of pregnancy, labor and newborn health, as well as type of convulsive disorder, these are shown in Table1and 2. Obviously, in the setting of managing epilepsy, for both sexes, of all age groups, every effort should be tried to achieve a satisfactory control in order to promote a seizure-free life. In the medical literature, there is plenty amount of evidence that pregnant epileptic women, having optimal seizure control, should continue taking their anticonvulsive medication(s) in order to avoid unwanted events that may affect the course of pregnancy, labor, post-partum course, and physical and future mental health of their newborns. Researchers have found that achieving proper epilepsy control would not be possible in WWE not taking AEDs; physicians would need to put WWE back on anticonvulsant medication. They also found that, by excluding VPA and Topiramate, the risk of anomalies in the newborns would be the similar in WWE whether taking AEDs or not[11]. Two of our patients have achieved good seizure control and drug safety on pregnancy by using LVC. They both had smooth labor and given healthy newborns. This is in accordance with other studies, who also have prescribed sustained-release preparations[12,13]. Our patients were using standard tablet preparation not the extended-release form as the latter is unavailable in our markets. It is well established in the clinical practice that anomalies among newborns of WWE occur many folds more than those born to

non-epileptic women; this is either attributed to teratogenic risk of AEDs or genetic susceptibility, especially those using CZB, LTG, and VPA; especially associated with the latter drug anomalies of neural tube, oral, facial and heart organs[14-16]. Others have found an association between autism and VPA17. However, one of our four patients who were taking VPA had given birth to a newborn with cleft lip and palate. Many clinicians have setup and suggested guidelines for prescribing VPA to WWE; among the regulations avoiding VPA to women of childbearing age and finding alternative AEDs for the seizure control18. Not only in those taking VPA but also other AEDs, e.g., Topiramate, childbearing WWE should take folate to reduce the risk of congenital anomalies that has been proved in many epidemiological studies[18-21]. In this study, however, TPM has not been used; all of our patients were given Folic acid orally before and during pregnancy. Furthermore, researchers pointed out that significant number of WWE may suffer psychiatric disturbances, e.g. anxiety, depression during pregnancy and puerperium[22]. In our study, five of the pregnant patients had anxiety and were well controlled with 0.5 mg of Alprazolam twice daily. The present study shows that our patients have not encountered any untoward obstetric event, although others have mentioned that WWE consuming AEDs have higher risks of toxemia of pregnancy, Cesarean section, post-partum hemorrhage, and premature birth. Concerning mortality, none of our patients died throughout the study period; however, other authorities stress upon an optimal epilepsy control during pregnancy, labor and afterwards in order to avoid risk of death that might be increased many folds than the cases with women without seizure[23-25]. Concerning breast lactation, it is advisable that WWE should receive encouragement for breastfeeding their newborns in spite of contradictory findings about maternal milk AEDs effects; however, the infants should be monitored well[26-27].

In the present study we have not taken into consideration the neurodevelopmental, and the cognitive profile, of those children born to WWE receiving AEDs; however, studies have shown the harmful effect of AEDs, e.g., VPA, Phenobarbital on cognitive functions. The latter occur more often with the use of polypharmacy than the use of monotherapy; furthermore, polypharmacy is found to be associated with more intrauterine deaths than monotherapy[28-29]. In this context, it is recommended that neuroscientist should seek safer anti-convulsive medications as more and more advances have been made in the pharmaceutical manufacturing. The present study has shown that most of childbearing WWE have given births to healthy newborns. This goes with other studies[30].

Eating habits of pregnant WWE have received attention by researchers; they recommend avoiding binge (comorbid) eating disorder as the latter habit is found to statistically associated with more toxemia, psychiatric, and post-partum disorders[31]. Although this aspect has not been investigated in our community, it is hoped that this may prompt local researchers to consider it in their future studies. Finally, We can conclude that, WWE treated by CBZ, LVC, LTG and

VPA showed good seizure control during pregnancy and labour whether vaginal or cesarean section. Unlike CBZ, LVC and LTG, only VPA use was associated with one case of facio-oral congenital abnormality. A more rigorous design including a bigger sample and a longer follow up period is required to further verify the effectiveness and the long term safety profile of AEDs on the mother and her baby. Avoidance of prescribing VPA to women during their childbearing age is highly recommended until further studies clarify its safety profile.

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پوختە

کارتێکرنا و سلامەتیا دەرمانێن دژی تەپێ ل ماوێ دووگیانی ئافرەتا قەکولینەك بۆ هندەك نەخوشا ل باژێرێ دهوکێ

پێشەکی: کارڤەدانێن تەپێ ژ نەخوشیێن دەمارا بێن بەربەلاڤە ل سەر رەگەزێ نێر و مێ هەنە و پەیوەندیا تەپێ ل سەر دووگیانیێ هەیە، و ئەڤ شلوڤەکرنە ل سەر کارتێکرنێن هندەك دەرمانێن چارەسەریا کارڤەدانێن تەپێ ل سەر دووگیانیێ و زاروکبونێ و زاروکێ دبیت ژبو کومەکا ژنان هاتەکرن.

ڕێکێن ڤەکولینێ: شلوڤەکرن هاتە ڤەگرتن بو چەند جورێن نەخوشان ئەوێن هاتینە نڤاندن کو پێکهاتبوون ژ نەخوشێن ڤەکرنا تەپێ یا تیشك سەرکری و یا گشتی ل گەل چێبوونا قەلەویێ یان بێ قەلەویێ بو ژنان بەری و پشتی شویکرنێ و دووگیانیێ کو هاتبونە چارەسەرکرن ژلایێ تایبەتمەندێن دل و هناڤا و تایبەتمەندێن نشتەرگەریا کوما دەمارا ل نەخوشخانە و کلینیکێن پارێزگەها دهوکێ دناڤبەرا کانونا ئێکێ و کانونا دووێ ل سالا ٢٠١٥ێ زاینی، دشلوڤەکرنا مەدا (٢٨) ژن بەشداربوون تەمەنێ وان ژ ١٥–٤٠ سالا بون، فورمەکا تایبەت هاتە ڕێکخستن بو تومارکرنا پێزانینێن پەیوەندی ب شلوڤەکرنا مەڤە هەی، تاقیکرنێن خوینێ بو هاتنەکرن هەر ژ هیموگلوبینی و کێمستریا ژیانێ و ئەلفافیتو و تیشکا مێشکی و سونار و میفراسا مەگناتیکی ب رەنگ و رەنینا مەگناتیسی ب رەنگ و فیکراکێشانا ئەلکتریکی بو مێشکی، دەرمانێن دژی کارڤەدانێن تەپێ هاتنە دان بو نەخوشی و ٥ملگم ژ ترشوکا فولیك بو ماوەی دوو هەیڤان بەری و پشتی دووگیانیێ دگەل هندەك دەرمانێن دی، هەروەسان هندەك ڤیتامین و ئامرازێ ئاسنی هاتنە دان بو نەخوشان ژبو گەرەنتیا خارنا قورچێن پێتڤی ژبو کونترولکرنا تەپێ ب شێوەکێ دروست. ل دەمێ چارەسەری و چاڤدێریا نەخوشان بەردەوام پشکنینێن خوینێ دهاتنەکرن ژبو چاڤدێریا مەژیێ هەستیکی و مێلاکێ.

ئەنجام: کونترولا کارڤەدانێن مێشکی ب شێوەکێ گشتی هاتەکرن و پشکنینێن نەخوشان سروشتی بوون ب تنێ ئالفافیتو ل دەف نەخوشەکێ ئەوا دزاروکێ وێ دا کێماسیێن زکماکی دسەروچاڤ و دفنێ دا دیاربووین و ئەو ەنخوشا ترشوکا فالبروك دساخلەم بوون و کێشەیا وان یا سروشتی بو، و هەروەسا سلم أبکور، ژبلی زاروکێ بووی دکێماسیا زکماکی دلێڤێن کێوریشکێ و بنیا دەڤی واللهاە، مە دەرمانێن ڤێ نەخوشێ گوهارتن و پشتی وی دەمی زاروکەکێ سروشتی بوون.

دەرئەنجام: ل دویڤ ڤێ شلوڤەکرنێ دا بو ڤان نەخوشان ژمارەکا کێم یا نەخوشان مفا ژ ڤان دەرمانان وەرگرت کاربامازین و لیفتابرسیتام و لاموتریجین، ژبلی وی نەخوشا کێماسیا زکماکی دزاروکێ وێ دا دەرکەتی، ئاموژگاریا مە ئەوە شلوڤەکرنەکا تێر و تەسەل و پتر نەخوشان بخوڤەبگریت و هندەك نەخوشێن دووگیان بەشداربن بێن توشی کارڤەدانێن تەپێ دبن دا بزانین باشیا دەرمانان دخون و ئاموژگاریێ دەین دویربن ژ ترشوکا الفابرویك.

الخلاصة

تأثير (فعّالية) وسالمة مضادّات الاختلاجات الصرعية خلال الحمل، دراسة حالات متتالية من دهوك

الخلفية والأهداف: إختلاجات الصرع أمراض عصبية شائعة تؤثر على الجنسين الذكور والاناث وهناك ارتبط بين الصرع ونتائج الحمل. هذه دراسة تأثير بعض الدوية المستعملة لمعالجة الاختالجات الصرعية على الحمل والوالدة، والطفل المولود في مجموعة من الاناث.

طرق البحث: دراسة استرجاعية سريرية لحالات متتالية شملت الاختلاجات الصرعية البؤرية العامّة مع أو بدون حدوث النسمة على إناث قبل وبعد الزواج والحمل عولجن من قبل إختصاصيي الباطنية الجراحة العصبية في مستشفيات وعيادات في مدينة دهوك بين كانون الثاني وكانون الأوّل من عام 2015 ميلادي. شملت الدراسة 28 إمرأة تتراوح أعمارهن بين 15–40 سنة. تم تهيئة استمارة لهذا الغرض لتسجيل المعلومات ذات العالقة بالبحث. خضع اليضات لفحوص الدم القياسية و منها الهيموغلوبين والكيمياء الحياتية زلال الألفافيتو وأشعة الجمجمة والسونار ومفراس الدماغ بالصبغة والرَنين المغناطيسي بالصبغة والتخطيط الكهربائي للدماغ. أعطي المرض االدوية المضادَة لإلختالجات الصرعية مع 5 ملغم حمض الفوليك لشهرين قبل بداية الحمل و أدوية أخرى مناسبة، كما وأُعطيت معظم المريضات الفيتامينات والمعادن لضمان التغذية الالزمة. الأدوية المضادّضة للصرع شملت عقار الكاربامازين والأيفتايرسيتام والالموتريجين وحمض الفالبرويك ضمن الجرع الالزمة للسيطرة على نوبات الصرع سيطرة تامَة. خلال فترة المتابعة والمعالجة كانت تجرى فحوصات الدم لمتابعة صحة نخاع العظام والكبد.

النتائج: تمَت السيطرة التامَة على الاختالجات الصرعية وكانت الفحوصات السريرية طبيعية باستثناء زلال الألفافيتو عند المريضة التي ظهر في مولودها شَوَه خَلقي في الوجه والفم والتي كانت تتناول حمض الفالبرويك. كذلك كانت طبيعية حالة الحمل والوالدة وما بعد الوالدة. كان المولودين في صحة وأوزان الجسم طبيعية وكذلك سلَم أبكور، باستثناء الطفل الذي ولد مع الشَوَه الخَلقي في شفة الأرنب وفتحة سقف الفم واللهاة. تم تبديل العقار لهذه المريضة وولدت طفالً طبيعياً بعد ذلك.

الاستنتاجات: هذه (العينة) المجموعة الصغيرة من المريضات شوهد سالمة أدوية الكاربامازين والليفتايرسيتام والالموتريجين باستثناء المريضة التي ظهر في مولودها شَوَه خَلقي في الوجه والفم والتي كانت تتناول حمض الفالبرويك. نوصي بإجرء دراسة ولفترة طويلة وبأكثر شموليةً وعدداً من المريضات الحوامل المصابات باإلختالجات الصرعية لبيان سالمة استعمال االدوية وينصح بتجنُب حمض الفالبرويك.

DOES OXIDATIVE STRESS INCREASE FOLLOWING IRON THERAPY DURING THE 2ND AND 3RD TRIMESTERS OF PREGNANCY

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ABSTRACT

Background: Pregnancy contributes to the processes of oxidation and free radical formation, the causes may be due to mitochondria rich placenta and a number of transitional metals, especially iron, which is particularly abundant in the mammalian placenta, are important in the production of free radicals.

Objective: to evaluate the oxidative stress status at the 3rd trimester of pregnancy in two groups of pregnant women according to the iron supplement therapy.

Methods: Enzyme linked immune sorbent assay (ELISA) technique was used for assessing the serum oxidative stress biomarker ; malondialdehyde (MDA), total antioxidants capacity , ferritin and complete blood picture were studied in 81 pregnant women at the 3rd trimester of pregnancy who were routinely visited the Duhok maternity hospital for checking up their pregnancy , forty one of them who were took Iron therapy continuously during the 2nd and 3rd trimester of pregnancy and forty women who didn't took iron at all during their pregnancy. The inclusion criteria were young pregnant women below the age 35 years with their hemoglobin > 11 g% and absence of any chronic medical problem.

Results: serum MDA, ferritin, Hb and pack cell volume were significantly higher in pregnant women who took iron than those who didn't took any iron supplement.

Conclusion: higher oxidative stress and lipid peroxidation was found in women at the late stage of the 3rd trimester of pregnancy in iron treated group was shown by increased serum MDA levels due to increase serum ferritin. The higher serum MDA and ferritin during the 3rd trimester of pregnancy in ladies who took iron continuously will probably provide the need of guidance for planning the iron supplement dosage regime.

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Keywords: Iron, Pregnancy, Oxidative stress, Ferritin, Total antioxidants

Pregnancy is a physiological condition in which women are prone to oxidative stress due to imbalance oxidative stress status, that occur between pro-oxidant and antioxidant factors[7]. In the first trimester, establishment of blood flow into the intervillous space is associated with a burst of higher oxidative reactions and lipid peroxidation. There is a strong evidence that oxidative stress plays a major role in the pathogenesis of many human diseases[1,2,5]. During a normal pregnancy, oxidative stress activate antioxidant mechanisms that are capable of reacting by way of enzyme activity and non-enzyme free radical deactivators. However, pregnancy is also a state in which this adaptation and balance may be easily disrupted. There is strong evidence that a chronic inflammatory reaction combined with the presence of a local oxidizing environment may play a vital role in the etiology and development of complications during pregnancy[3]. The

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dangerous effect of oxidative stress which may multiply in the 3rd trimester of pregnancy when the demand of oxygen and oxidation mechanism are highly increased by the fast growing of the fetal organs. The more oxidation processes, the more free radicals, hydrogen peroxide and the lipid peroxides production will increase the chances for DNA damage and appearance of pregnancy disorders, such as miscarriages, pre-eclampsia, preterm birth, gestational diabetes, intrauterine growth restriction and may be the death of mothers[6]. Ferritin is protein has a 24 subunit protein composed of two subunits, H and L. Ferritin has the capacity to sequester up to 4500 atoms of iron in a ferrihydrite mineral core and functions to store iron not required for immediate metabolic needs[8]. Experimentally a 6-fold induction of ferritin synthesis was observed in liver slices from rats treated with phorone, a glutathione-depleting drug that increases intracellular levels of oxidative stress[9].

SUBJECTS AND METHODS

This study is a part of MSc study. It was conducted at the Department of Physiology/ College of Medicine/ University of Duhok and Duhok Maternity Hospital from the 1 November to 20 December 2015. Eighty-one pregnant women who visited Duhok Maternity Hospital were participated in this study.

They divided into two groups according to continuous taking (n= 41) or not taking iron supplemental therapy at all (n= 40) during the 2nd and 3rd trimesters of pregnancy. The inclusion criteria are, pregnant women with uncomplicated pregnancy at age below 35 years with their hemoglobin > 11 g% at the late stage of the 3rd trimester > 32 weeks of pregnancy and absence of any chronic illness. Informed consent was obtained from each subject before study entry and the study was approved by the local medical research ethics committee of the College of Medicine/ University of Duhok.

Serum totalantioxidants capacity (TAC), serum oxidative stress biomarker; malondialdehyde (MDA) and ferritin were measured using specific ELISA kits supplied Bioassay Technology laboratory`s Mission Complete blood analysis was done in Duhok Maternity Hospital using Medonic M Series Blood Analyzer ; M20M-GP product Code-1400004, Manufacture 2015.

RESULTS

The mean ± standard deviation of demographical characters of the women in the two studied groups was shown in table 1. No significant differences were found between the two groups in the ages, height and weight. Body mass index (BMI) before delivery and after delivery were also found to be insignificantly changed. Most of our subjects are illiterates (46%), read and write or finished primary school is 7.1%. Intermediate and secondary school finished is 27.1% while women with high education is 19.8%. Most of the studied women are Multipara (48.2%), then Primipara (40.7%) and Grand para (11%). Absence of smokers in the both studied groups, while higher number (53%) of negative smokers (living or working with smokers) are present. Table 2 showed the mean ± standard deviation of the hematological measurements in the present study. Packed cell volume (PCV), hemoglobin and serum ferritin were significantly higher in the women taking

iron therapy during the 2nd and 3rd semesters of pregnancy when compared to the women group don't take iron. Mean cell hemoglobin, Mean cell hemoglobin concentration, mean cell volume, total white blood cell count and platelets count were non-significantly differed between the two groups.

Table 3 showed the mean ± standard deviation of the serum MDA and total antioxidants capacity in the two studied groups. The serum MDA was significantly higher in the women group 1 taking iron therapy (Figure 1), while the unexpected results of the present study, that the total antioxidants capacity was non-significantly increased in the iron taking group (Figure 2). The results of spearman`s correlation (table 4) revealed that serum MDA in the group 1 women taking Iron a significant correlations present with RBC count (<0.05) MCH (0.03) MCHC (<0.001) and TAC (0.001). In comparing with the same results of serum MDA in the group 2 in women do not take iron revealed that a significant correlations only with TAC (<0.0004), RBC (<0.047) and platelets count (<0.02)

Table 1: Demographical characters of the studied women groups

Parameters	Group 1 women take Fe treatment (N=41)		Group 2 women don't take Iron treatment (N=40)		Mann-Whitney test	
	Mean + SD		Mean + SD		U-value	P-value
Age (years)	27.30 + 4.42		26.58 + 6.34		721.00	0.45
Height (cm)	160.35 +4.65		161.43 + 4.74		698.00	0.33
Weight (kg)	84.23 +15.40		79.60 +18.18		665.50	0.20
BMI (Kg/m2) before delivery	32.76 ± 6.35		30.35 ± 6.29		639.50	0.08
BMI (Kg/m2) After delivery	N= 14		N= 10			
	27.31 + 6.06		30.04 + 7.45		62.00	0.41
Education Illiterate	Number	%	Number	%	Total number	%
	14	17.6	23	28.4	37	46
Read& write and completed primary	5	6.1	1	1	6	7.1
Intermediate and 2nd school	15	18.5	7	8.6	22	27.1
Higher education	7	8.	9	11.1	16	19.8
Parity	Number	%	Number	%	Total number	%
Primipara =1	15	18.5	18	22.2	33	40.7
Multipara 2-5	22	27.2	17	21.0	39	48.2
Grand para >5	4	4.9	5	6.2	9	11.1
Smoking habits	Number	%	Number	%	Total number	%
Smoker	0	0	0	0	0	0
Negative smoker	20	24.7	23	28.4	43	53.1
Absence of smoking risk	21	25.91	17	20.99	38	46.9

Table 2: Comparison of the hematological variables measured between the Two studied groups

Parameters	Group 1 women take iron treatment (N=41)	Group 2 women don't take iron treatment (N=40)	Mann-Whitney test	
	Mean +SD	Mean +SD	U-value	P-value
PCV (%)	33.85+ 2.38	32.68+ 1.91	553.00	0.02**
RBC (1012/l)	4.15+0.39	4.10+0.34	746.50	0.61
Hb (g/dl)	12.37+ 0.77	12.00+ 0.69	576.00	0.03**
S. ferritin (ng/ml)	21.0٣+ 11.4٦	15.37+ 11.66	460.00	0.001***
MCH (pg)	29.99+1.67	29.43+2.14	704.00	0.36
MCHC (g/dl)	36.63+0.74	36.51+0.78	743.50	0.59
MCV (fl)	81.83+3.75	80.55+5.04	699.50	0.33
WBC (109/l)	10.96+2.90	10.91+2.92	771.00	0.78
PL (109/l)	211.88+61.11	212.38+57.47	781.00	0.85

Table 3: Comparison of the oxidative stress biomarkers (MDA) and antioxidants values measured in the two groups of women

Parameters	Women take Iron treatment (N=41)	Women don't take Iron treatment (N=40)	Mann-Whitney test	
	Mean + SD	Mean + SD	U-value	P-value
MDA (nmol/ml)	22.91 ± 17.14	16.96 ± 11.57	586.00	0.04***
TAO (U/ml)	30.00 ± 14.82	29.16 ± 16.75	773.00	0.80

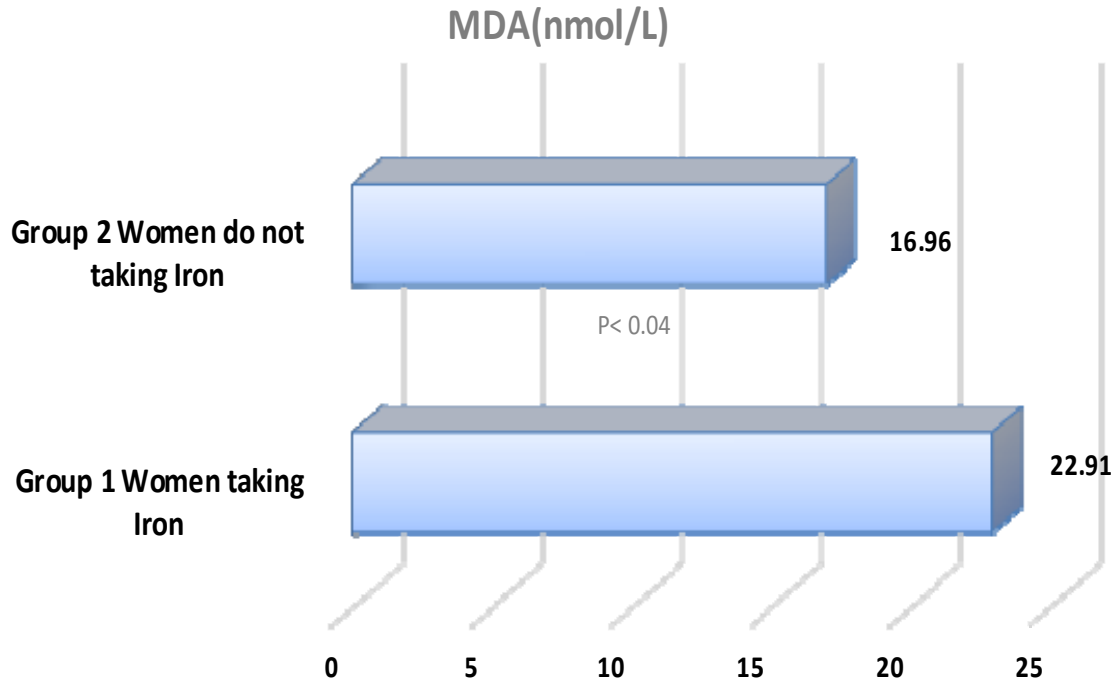

Figure 1 Serum MDA of the group 1 women taking Iron and group 2 women do not taking iron during the 2nd and 3rd semesters of the pregnancy

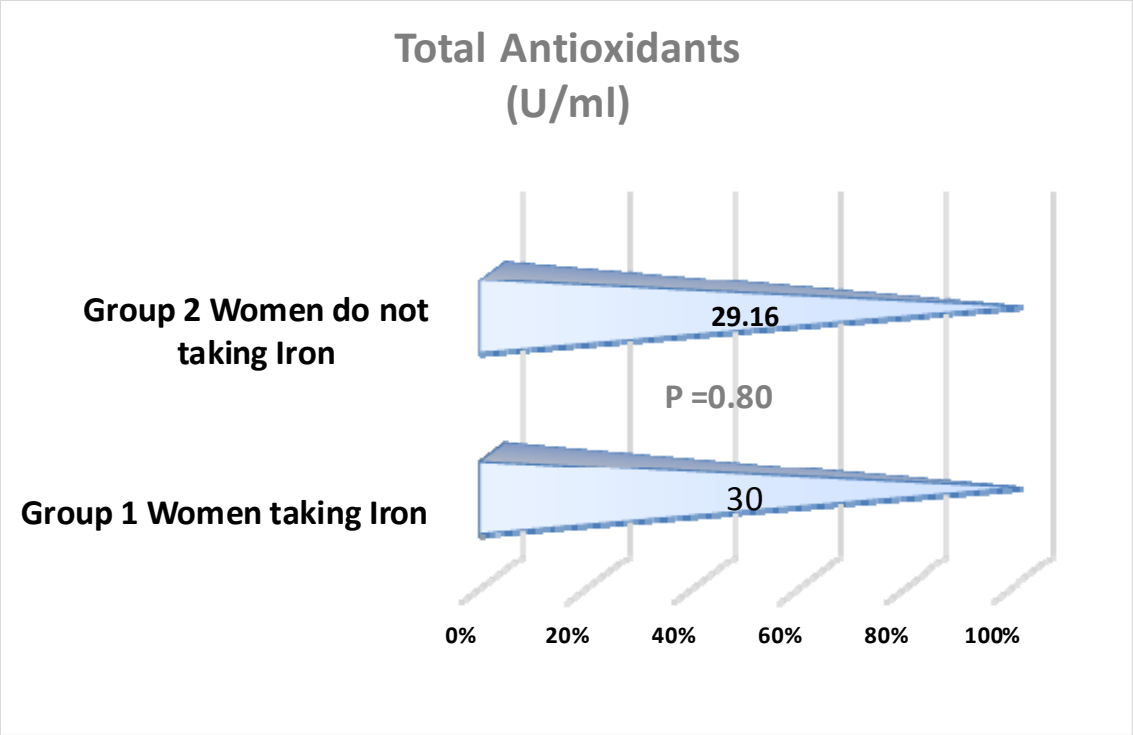

Figure 2: Serum Total antioxidants of the group 1 women taking Iron and group 2 women do not taking iron during the 2nd and 3rd semesters of the pregnancy.

DISCUSSION

The results of the present study provide further evidence that a combination of serum oxidative stress biomarker (MDA), total antioxidants capacity, ferritin and hemoglobin measurement give an idea about the state of oxidative stress and iron storage capacities present in pregnant women at the 3rd trimester of pregnancy.

There is convincing evidence that imbalanced oxidative stress status can induced a chronic inflammatory reaction combined with the presence of a local oxidizing environment, which may play a vital role or can act as risk factor in the etiology and development of complications during pregnancy (10) by decreasing the body antioxidant defense mechanism and increasing inflammatory biomarkers which growing into imbalance oxidative stress status (increased oxidative stress and decreased total antioxidants), decrease whole body immunity and development of different pathophysiological disorders. A number of studies have discussed the influence of the mother's oxidative stress on the later stages of pregnancy and resulting complications[11]. For these reasons the medical and nutritional interventions to overcome oxidative stress in pregnancy is important. The higher serum MDA and ferritin, also the high correlations of serum MDA with RBC, MCH, MCHC in group 1 women taking iron may give us the presence of high relation of oxidative stress produced by the iron therapy. Iron therapy will probably provide the need of guidance, dosage regime and a limited duration of the iron supplement therapy especially in the non-anemic women. The advisement of strengthening of antioxidants defense mechanisms is a supportive idea for normal safe and healthy pregnancy especially in illiterate and low education pregnant women.

Table 4 Spearman's Rank Correlation for the Studied Groups

Women Taking Iron Supplement (+ve Fe)																
			Hb	**WBC**	**PL**	**RBC**	**PCV**	**MCV**	**MCH**	**MCHC**	**weight**	**length**	**BMI**	**TAO**	**Ferritin**	**MDA**
Women do not king Iron (-ve Fe)	**Hb**	**U =**		0.08	-0.28	0.79	0.95	-0.20	-0.27	-0.26	0.09	-0.02	0.06	0.13	0.05	0.15
		P=		0.60	0.08	**<0.0001**	**<0.0001**	0.20	0.09	0.10	0.56	0.90	0.70	0.43	0.75	0.37
	WBC	**U =**	0.05		0.24	0.19	0.09	-0.17	-0.12	-0.03	0.28	0.06	-0.32	0.20	-0.01	0.03
		P=	0.74		0.13	0.25	0.59	0.30	0.45	0.86	0.08	0.72	**0.05**	021	0.97	0.86
	PL	**U =**	0.24	0.28		0.07	0.22	-0.22	-0.17	-0.09	0.36	0.02	0.32	-0.14	0.02	0.04
		P=	0.13	0.08		0.68	0.18	0.18	0.29	0.60	**0.02**	0.91	0.04	0.40	0.90	0.80
	RBC	**U =**	0.52	0.11	0.26		0.87	-0.71	-0.78	-0.54	0.01	0.09	0.001	0.18	0.06	0.31
		P=	**0.0006**	0.52	0.10		**<0.0001**	**<0.001**	**<0.0001**	**0.0003**	0.93	0.58	0.99	0.26	0.70	**0.05**
	PCV	**U =**	0.84	0.06	0.30	0.68		-0.30	-0.43	-0.51	-0.06	0.05	-0.05	0.19	-0.05	0.22
		P=	**<0.0001**	0.72	0.06	**<0.0001**		0.06	**0.005**	**0.0008**	0.70	0.76	0.74	0.24	0.74	0.17
	MCV	**U =**	0.16	-	-0.04	-0.69	-0.12		0.94	0.32	-0.14	-0.08	-0.10	0.18	-0.12	-0.34
		P=	0.34	0.12	0.79	**<0.0001**	0.45		**<0.0001**	0.046	0.40	0.63	0.52	0.26	0.45	**0.03**
				0.47												

MCH	**U =**	0.17	-	-0.01	-0.71	-0.18	0.93		0.58	-0.11	-0.06	-0.08	-	-0.07	-0.39
	P=	0.30	0.05	0.93	**<0.000**	0.28	**<0.00**		**0.000**	0.51	0.70	0.62	0.23	0.68	**0.01**
			0.77		**1**		**01**		**1**				0.15		
MCH	**U =**	0.03	-	0.04	-0.41	-0.29	0.31	0.58		-0.17	-0.02	-0.14	-	0.10	-0.24
C	**P=**	0.83	0.11	0.80	**0.009**	0.07	**0.05**	**0.0001**		0.29	0.91	0.40	0.28	0.53	0.14
			0.52										0.08		
	U =	0.08	0.07	0.03	0.22	0.11	-0.21	-0.30	-0.33		-0.08	0.94	0.06	0.21	-0.06
Weight	**P=**	0.91	0.68	0.86	0.18	0.51	0.19	0.06			0.62	**<0.00**	0.71	0.23	0.72
									0.035			**01**			
	U =	0.04	0.13	0.17	-0.08	0.08	0.18	0.09	-0.16	0.34		-0.38	-	0.02	0.33
Length	**P=**	0.82	0.44	0.30	0.62	0.61	0.26	0.58	0.31	**0.03**			0.09	0.89	**0.03**
												0.015	0.60		
BMI	**U =**	0.000	0.08	0.005	0.31	0.13	-0.30	-0.38	0.34	0.96	0.15		0.03	-0.34	-0.18
	P=	7	0.63	0.97	**0.05**	0.42	0.06	**0.01**	**0.030**	**<0.000**	0.37		0.85	**0.03**	0.27
		0.99								**1**					
TAO	**U =**	0.06	0.45	0.06	0.21	0.07	0.16	0.13	-0.5	0.12	0.22	0.07		0.01	0.40
	P=	0.70	**0.00**	0.74	0.20	0.67	0.32	0.44	0.36	0.45	0.18	0.67		0.96	**0.01**
			4												
Ferriti	**U =**	0.10	0.25	0.03	0.01	0.16	0.14	0.20	0.002	0.06	0.01	0.04	0.13		-0.24
n	**P=**	0.27	0.11	0.87	0.93	0.32	0.38	0.21	0.99	0.69	0. 95	0.79	P=0.		0.14
													42		
MDA	**U =**	-0.23	0.16	-0.36	-0.32	-0.21	0.11	0.10	-0.06	0.16	0.14	0.12	0.60	0.10	
	P=	0.16	0.30	**0.02**	**0.047**	0.19	0.49	0.55	0.74	0.34	0.30	0.47	**0.00**	0.56	
													01		

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پوختە

ئەرێ تێکچوونا ئەکسەدێ زێدەدبیت پشتی وەرگرتنا ئاسنی دماوێ سێیەکا دووێ و سێیێ ژ دووگیانیێ؟

پێشەکی: دووگیانی کارتێکرنێ دکەت دکریارا ئەکسدێ دا و پێکئینانا رهێن ئازا ژ ئەگەرێ هەڤال بچیکی زەنگین ب مایتوکوندریا و کانزایێ ڤەگوهاستی و ب تایبەت ئاسن ئەوێ مشە و بشێوەکێ روهن دهەڤال بچویکی دا و یێ گرنگ بو بەرهەمئینانا رەهێن ئازا بو هەلسەنگاندنا ئاستێ ئەکسدێ بو دوو گروپێن ژنێن دووگیان ل سێیەکا سێیێ ژ دووگیانیا وان لسەر بناغێ وەرگرتنا وان بو دەرمانێ ئاسنی.

رێکێن ئەکولینێ: تەکنیکا (ئیلایزەر) بکارئینایە بو هەلسەنگاندنا نیشانێن سروشتی (بایولوجی) بو ئەکسدێ و MDA و هەمی شانێن هەڤدژی ئەکسدێ و ڤرتینێ دسیرومێ خوینێ دا ووێنێن تەمام یێ خوینێ (CBC) هاتە لێکولینکرن بو ٨١ ژنێن دووگیان ل سێیەکا سێیێ ژ دووگیانیا وان ئەوێن کو سەرەدانا نەخوشخانا دهوك یا زاروکبوونێ کری ب شێوەیەکێ روتینی بو پشکنینا دووگیانی یا خو ٤١ چل وئێك ژ وان ئەوێن کو چارەسەری یا ئاسنی ب شێوەیەکێ بەردەوام دماوێ سێیەکا دووێ و سێیێ ژ دووگیانیێ و ٤٠ چلێن دی چارەسەری یا ئاسنی نەوەرگرتبوون دماوەیێ دووگیانیێ دا ب هیچ رەنگەکی و ئەڤ ژنێن مە ڤەکولین لسەر کرین هەمی دژیەکی دابوون کو پتر نەبوون ژ ٣٥ سالیێ کو پلا هیموگلوبینێ (١١گرام/ دسلیتر) یە دگەل نەبوونا هیچ ئاریشەکا دوم درێژ.

ئەنجام: (MDA) و ڤێریتینێ و هیموگلوبینێ دسیرومێ خوینێ دا و قەبارەیێ خانێن تێکرای (PCV) ب شێوەیەکێ گەلەك بلند لدەف ژنێن دووگیان ئەوێن کو چارەسەری یا ئاسنی وەرگرتین، دگەل وان یێن چارەسەری یا ئاسنی نە وەرگرتین.

دەرئەنجام: زێدەبوونا تێکچوونا ئەکسدێ و رونێ بیروکسیدی دیاربوون دسییەکا سێیێ لدەف ژنێن دووگیان و ئەوێن ئاسن بکارئینان دماوێ دوگیانیا خودا و ئەوێن دیارکرن ب زێدەبوونا ئاستێ MDA دسیرومی دا ژ ئەگەرێ زێدەبوونا ڤرتینێ سیرومی، ئاستێ بلندبوونا MDA و ڤرتینێ دسێیەکا سێیێ دا ژ دووگیانیێ لدەف وان ژنا ئەوێن بەردەوام ئاسنی وەردگرن یا پێدڤیە رێبەرەك هەبیت بو پلاندانانا وەرگرتنا ئاسنی.

الخلاصة

هل يزيد االجهاد التاكسدي بعد اخذ عالج الحديد خالل الثلثين الثاني والثالث للحمل؟

الخلفية والأهداف: يساهم الحمل في عملية الأكسدة وتكوين الجذور الحرة والذي قد يكون بسبب المشيمة الغنية بالماتوكوندريا والمعادن الانتقالية وخصوصاً الحديد، الذي يتوفر بشكل واضح في مشيمة الثديات والمهم في إنتاج الجذور الحرة.

الهدف: لتقييم حالة االجهاد التاكسدي في الثلث الثالث من الحمل لمجموعتين من النساء الحوامل بناءً على العلاج التكميلي للحديد.

طرق البحث: تقنية الايلايزا استعملت لتقيم العلامات البيولوجية للإجهاد التاكسدي؛ مالونديالديهايد (MDA) والقدرة الاجمالية لمضادات االكسدة والفيريتين في مصل الدم, وتم ايضا دراسة الصورة الكاملة للدم لواحد وثمانين امرأة حامل في الثلث الثالث من الحمل اللواتي زرن مستشفى دهوك للولادة بشكل روتيني لفحص حملهن (واحد وأربعون منهن أخذن العلاج الحديدي بشكل مستمر خلال الثلثين الثاني والثالث من الحمل وأربعون امراة حامل لم يأخذن الحديد خلال فترة الحمل على الاطلاق). وكانت معايير إدراج النساء الحوامل الصغيرات دون سن 35 عاما وكان درجة الهيموكلوبين > 11غم/ دسي لتر مع عدم وجود أي مشكلة طبية مزمنة.

النتائج: مالونديالديهايد (MDA) والفيرتين والهيموكلوبين في مصل الدم وحجم رزمة الخلية (PCV) أعلى بكثير لدى النساء الحوامل اللاتي أخذن الحديد من أولئك الذين لم يأخذن أي مكملات للحديد.

الاستنتاجات: ارتفاع االجهاد التأكسدي والدهن البيروكسيدي في الثلث الثالث من الحمل للنساء الحوامل اللاتي استعملن ادوية الحديد خلال الحمل كما هي ظاهرة في ازدياد مستويات الـ(MDA) في المصل بسبب ارتفاع الفيريتين في المصل. المستوى العالي للـ(MDA) والفيريتين خلال الثلث الثالث من الحمل في النساء اللاتي اخذن علاج الحديد باستمرار ربما توفر حاجة إلى توجيه لتخطيط جرعة الحديد المستعملة.

RELATIONSHIP BETWEEN AGE AND SERUM ANTI-MULLERIAN HORMONE IN FERTILE AND SUBFERTILE FEMALES

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ABSTRACT

Background: Infertility is a common problem in our society, female fertility declines with age due to decrease in the number of growing ovarian follicles. Anti-Mullerian hormone, is a glycoprotein produced in the ovaries by the granulosa cells of ovarian follicles, maily in preantral and small antral stages. The aim of this study is to measure the level of serum Anti-mullerian hormone in both fertile and subfertile females of the same age group (20-40)years and to find whether Anti-Mullerian hormone level changes with age and to compare its level between the two groups and their age subgroups ,this could be useful to evaluate ovarian reserve and female fertility.

Methods: A case control study was conducted on 130 females ,70 (53.84%) subfertile females (patients) with a mean± SD 28.75±6.76 years and 60(46.15%) fertile female (controls) with a mean ± SD 31.26±5.98 years ,in Mosul city / fertility and IVF center in Al- Batool Teaching Hospital during the period from 1st of November 2013 to 30th of April 2014 . Serum Anti-Mullerian hormone concentration was measured in both patients and controls.

Results: In this study, there was a significant negative correlation between serum concentration of Anti-Mullerian hormone and age. The Anti- Mullerian hormone level was inversely correlate with the age of whole sample (r=-0.53), age of subfertile females (r=-0.50) and age of fertile females (r=-0.73).The serum Anti-Mullerian hormone level of subfertile females was significantly lower than its level in fertile females (p=0.006), a significant higher Anti-Mullerian hormone in fertile younger and older females in comparison to subfertile females (p=0.001 and p=0.006 respectively); a significant decrease in Anti-Mullerian hormone after the age of 30 years in both fertile and subfertile females (p=0.0001).

Conclusions: The present study, concluded that there was a significant negative correlation between serum Anti-Mullerian hormone and age ,a decline in Anti-Mullerian hormone level with increasing age in both fertile and subfertile females and its level can be considered a useful test to predict ovarian reserve in females, and should be done routinely.

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Keywords: Age, Anti-mullerian hormone, Fertile and subfertile females

Anti-Mullerian hormone (AMH), also called Mullarian Inhibiting Substance (MIS), is a 140 kilodalton dimeric glycoprotein composed of 535 amino acid, it is a member of the transforming growth factor- ß (TGF-ß) super family.[1,2] AMH is produced in the ovaries by granulosa cells of the ovarian follicles, the highest hormone production is in the preantral and small antral stages which are less than 4mm in diameter, these follicles contain more developed micro vasculature and larger numbers of granulosa cells so they are considered the primary source of AMH, the hormone production deceases and then stops as follicles grow and reach size over 8 mm. Although its functions is primarily as an

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autocrine and paracrine regulator of follicle development, AMH appears in measurable amount in the serum. There is a strong correlation between the size of the residual follicular pool and the number of small antral follicles. Serum AMH level decreases gradually as the female gets older ,then becomes undetectable near the menapause .The AMH levels are gonado tropin –independent, and show very little variation within and between the menstrual cycles, because this hormone derives from pre antral and small antral follicles.[2,3] AMH also has a role in fetal lung maturation and in males it is produced in immature sertoli cells during fetal sex differentiation and it causes the regression of the mullerian ducts which are the precursors to the uterus, fallopian tubes, and upper vagina, during normal male reproductive tract development, then continues to be produced by the testes throughout male life .In females, AMH is only produced by the ovaries, nearly un detectable in the fetal and postnatal ovaries. At puberty, its production by the granulosa cells of the ovary significantly increases while levels in the follicular fluid and serum are maintained similar to those in the testes. AMH plays a role in the regulation of folliculogenesis,[4,5,6,7] AMH belongs to the TGF-ß multigene family along with activin, inhibin, bone morphogenetic protein (BMP) and the growth and differentiation factor (GDF).[7] In the ovaries it inhibits the primordial follicle recruitment and the responsiveness of growing follicles to follicle stimulating hormone (FSH). Since hormone production is only in pre antral and small antral follicles, measuring its level in the blood reflects the size of the ovarian follicle pool in women.[8,9,10] In the ovaries , it may influence the changing of primordial follicles from the resting stage to growing follicles.[11] In addition it may has a role in the recruitment of ovarian follicles which are sensitive to FSH in the early antral stage.[12] The secretion of this hormone depends on the degree of gonads development, at birth, the level is barely detectable, then after puberty it increases to high levels and continues to be secreated by granulosa cells in the reproductive period,[13,14] in normal female, the baseline serum range of AMH is 2–5 ng/ml. Some reports describe very littile variation in serum AMH levels with the menstrual cycle in premenopausal women. After menopause, serum AMH levels decrease gradually to reach undetectable levels, while in males, it stays detectable throughout life. 15,16 This hormone is used to represent both the quantity and the quality of the ovarian follicles ,so it is considered as an important test for measuring ovarian reserve.[17] Studies on this hormone indicate that ,with increasing female age, AMH level declines gradually[18] and in vitro fertilization (IVF) patients with normal FSH levels ,the intial AMH level is associated with the ovarian response.[19] It is also thought to be involved in the inhibition of steroid hormone production in women of reproductive age.[20] The receptor is a heterometric complex (consisting of a type l and type ll trans membrane serine/ therionine kinase receptor complex). Current studies suggest that MIS/AMH type l receptor (MIS/AMHR l) is an activin receptor-Like kinase (ALK) ligand such as BMP and GDF type l receptors of the IGF-ß family. The growth inhibitory function of

MIS/AMH begins with ligand binding with the MIS/AMH type ll receptor (MIS/AMH Rll).[21]

Recent Studies have demonstrated that AMH was associated with the cycle irregularity and the onset of the menopausal transitions within four years. In addition, higher AMH serum levels are associated with in vitro fertilization (IVF) outcomes, such as the number of the retrived mature oocyte, also the number and quality of embryos. Since AMH is considered as the earliest marker to decrease with age, and has the least intercycle and intracycle variability, it has been used as a marker for ovarian reserve.[22] In addition other studies considered AMH a diagnostic marker and therapeutic agent in ovarian cancer as in granulosa cell tumors (GCT), also it has been shown to correlate well with the course of the disease.[23] The performance of AMH as a screaning test of ovarian reserve has been examined in the general IVF population and in population of women at low or high risk of diminished ovarian reserve. Over all, lower AMH levels have been associated with poor response to ovarian stimulation and low oocyte yield, embryo quality, and pregnancy rate, but studies correlating mean AMH levels with IVF outcomes have not yielded threshold values that can be applied comfidently in clinical care[3].

Behringer et al[24] showed that in transgenic female mice, over expression of AMH causes abnormal ovarian development in addition to Mullarian duct regression. AMH recently is considered as a reliable and accurate predictor of ovarian reserve and IVF cycle outcome in some centers of the world.[25,26,27,28,29] Evaluation of MIS/AMH might be useful in the diagnoses and management of ovarian reproductive diseases.30

Materials and Methods

MATERIALS

This study is a case control study; it was carried out in fertility and IVF center in Al- Batool Teaching Hospital from 1st of November 2013 to 30th of April 2014

Prior to data collection and test performance, essential official permissions were obtained from Nineveh Health Office, AL-Batool Teaching Hospitals in Mosul city. This study included 130 females, classified into two groups:

Group 1 (patients). Seventy sub fertile females, aged 20-40 years used as case. This group was sub classified into two subgroups: group 1 aged 20-29 years and group 2 aged 30-40 years.

Group II (Controls). Sixty fertile females aged 20-40 years used as control (from relatives, friends, and sub staffs). This group was also classified into two subgroups: group 1 aged 20-29 years and group 2 aged 30-40 years.

All subjects enrolled in this study were interviewed and the general information was taken to fill the questionnaire, a written informed consent was obtained from all participants.

Inclusion criteria

The inclusion criteria for fertile women were age between 20-40years having regular menstrual cycles varying from 21-35 days, proven natural fertility with at least one pregnancy carried to term.

The inclusion criteria for subfertile women were age between 20-40 years having regular menstrual cycles varying from 21-35 days with infertility.

Specimens Five milliliters (ml) of venous blood was obtained from each participant of both groups and collected in a plain tube then incubated at 37ºC for 15 minutes in water bath, centrifuged for 10 minutes at 1000 rotation per minutes (rpm), then aspirated supernatant serum was freezed at-20oC till time of assay. Hormonal analyses was performed in the laboratory of Al–Batool teaching hospital, The following instruments were used throughout this study:

AMH normal range in females according to fertility status shown in table 1.

Table 1: AHM normal range in females according to fertility status

Optimal fertility	**4.0 - 6.8 ng/ml**
Satisfactory fertility	**2.2 – 4.0 ng/ml**
Low fertility	**0.3 – 2.2 ng/ml**
Very Low / undetectable	**0.0 - 0.3 ng/ml**
High Level	**> 6.8 ng/ml**

Exclusion criteria: for fertile and sub fertile groups

The exclusion criteria for both groups include:

- Hypertension, Diabetes and heart disease.
- Venereal disease.
- Hyperthyroidism, hypothyroidism, Hyperprolactinemia, Acromegaly and cushing disease.
- Polycystic ovarian syndrome (PCOS).
- History of ovarian surgery, Women with ovaries of abnormal morphology on ultrasound examination.
- Smoking.
- Women on hormonal therapy (contraception or induction therapy) for the last three months.
- Women on Chemotherapy , steroids and antihypertensive drugs.
- General laboratory centrifuge, Hettich, Germany.
- Automatic micropipettes, to deliver 10 to 1000µl, Rudolf brand, Germany, and pipette tips.
- Plain tubes and gel containing tubes are used.
- ELISA Bio-Tek, ELX 800 (Instru. Inc., USA).

Reagent Human AMH ELISA Kit. Copyright © 2014-2015 Elabscience Biotechnology Co., Ltd.

Statistical analysis: Standard statistical methods were used to determine the mean, standard deviation (SD) and range. The unpaired Z–test, unpaired student t-test and Chi-square tests were used. All values quoted as the mean ± SD. The accepted level of statistical significance was considered at $p<0.05$. (31)

RESULTS

One hundred thirty woman participate in this study. The studied sample include 70 (53.84%) subfertile females and 60 (46.15%) fertile females.

1. The comparison of chronological age between fertile and subfertile studied sample:

The fertile females were in average 2.5 years older than subfertile females ($p=0.02$), as shown in table 2.

Table 2: comparison of chronological age in between fertile and subfertile females

Parameters	subfertile females N=70 Mean ± SD	Fertile females N=60 Mean ± SD	P-value
Chronological age (years)	**28.75 ±6.76**	**31.26 ± 5.98**	**0.02**

2. The comparison of AMH level between fertile and subfertile females:

The difference between the two groups was statistically significant.

The serum AMH level of subfertile females was significantly lower than its level in fertile females (p=0.006), as shown in table 3.

Table 3: comparison of AMH level between fertile and subfertile females.

Parameters	Infertile females N=70 Mean ± SD	Fertile females N=60 Mean ± SD	P-value
AMH (ng/ml)	2.39 ± 1.24	3.07 ± 1.54	0.006

3. The AMH level of subfertile and fertile females according to different subclasses of age: The results revealed the following: a significant higher AMH in fertile younger and older females in comparison to subfertile females (p=0.001 and p=0.006 respectively); a significant decrease in AMH after the age of 30 years in both fertile and subfertile females (p=0.0001), as shown in table 4.

Table 4: comparison of AMH between subfertile and fertile females according to subclasses of chronological age

Parameters	subfertile Mean ± SD	Fertile Mean ± SD	P-value in raw	
Chronological age	<30 years	2.84 ±1.26	4.17 ± 1.15	0.001
	30+ years	1.66 ± 0.77	2.28 ± 1.28	0.006
P-value in column	0.0001	0.0001		

4. The correlation of age with AMH in the whole sample and in each subgroup of the study: The AMH level was inversely correlate with the age of whole sample (r=-0.53), age of subfertile females (r=-0.50), age of fertile females (r=-0.73), as shown in table 5, and in figures 1 and 2 respectively.

Table 5: Correlation of age with AMH in the whole sample and the subgroups of the study (subfertile and fertile females)

Variables	Whole sample		subfertile group		Fertile group	
	R	P-value	R	P-value	R	P-value
Age(year)	-0.53	0.0001	-0.50	0.0001	-0.73	0.0001

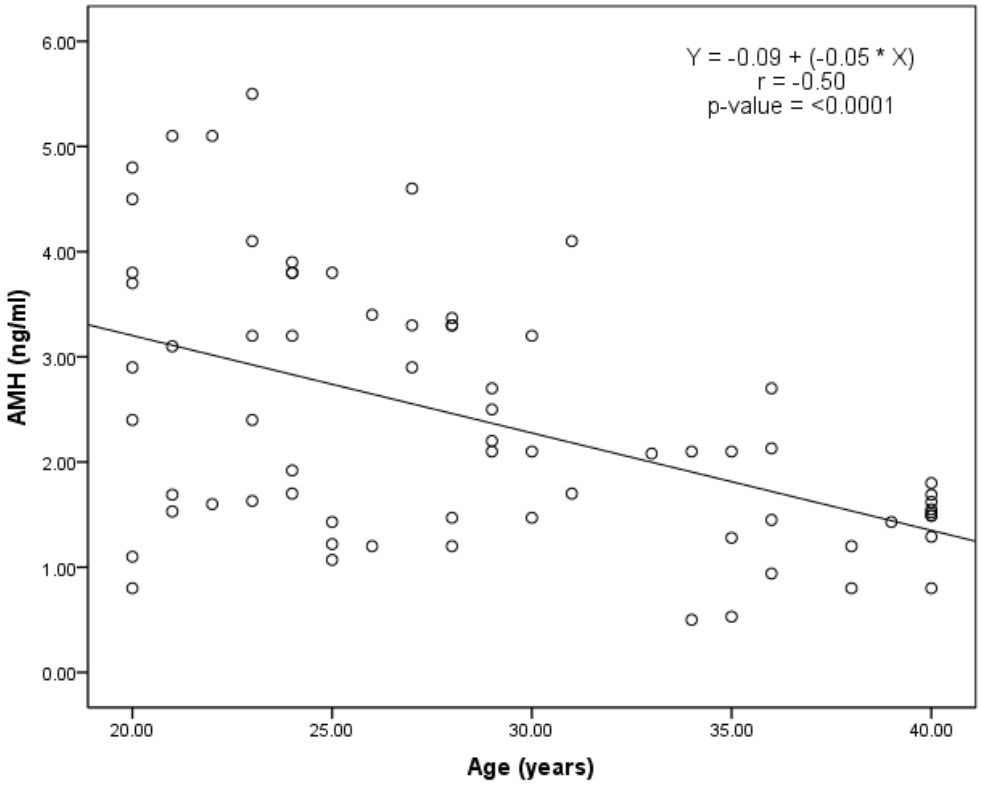

Figure1 Correlation between age and AMH in subfertile group.

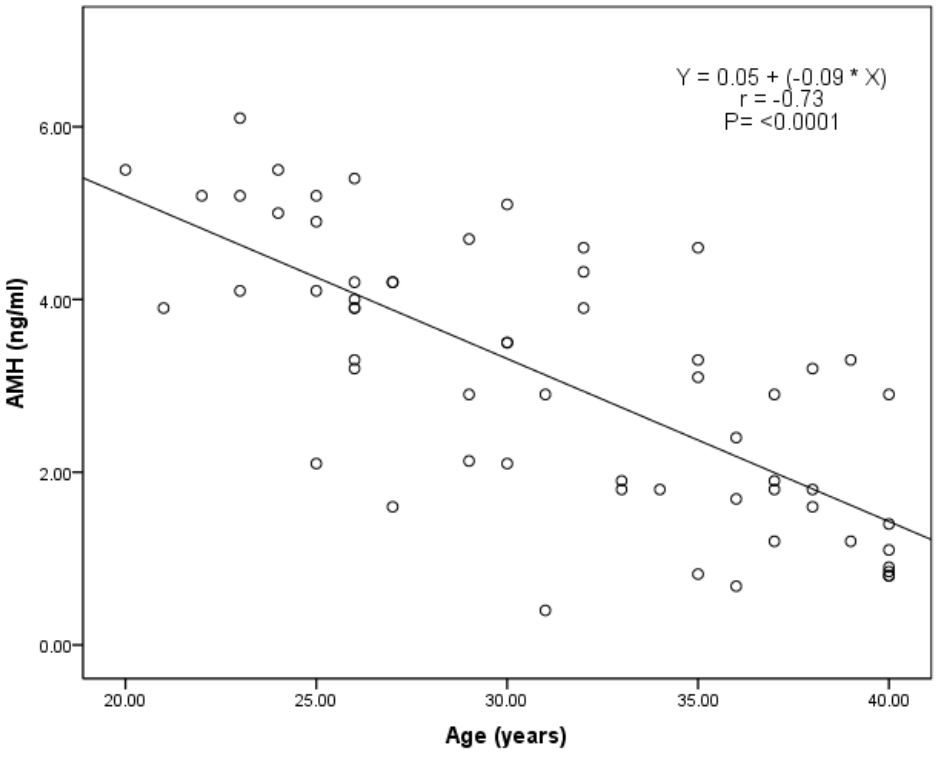

Figure 2 Correlation between age and AMH in fertile group.

DISCUSSION

Mullarian Inhibiting Substance (MIS), is glycoprotein, produced by the granulosa cells in ovarian follicles of pre antral and small antral stages ,they are likely the primary source because they contain larger number of granulosa cells and more developed micro vasculature .The number of small antral follicles correlate with the size of the residual follicular pool and AMH serum levels are thought to reflect the size of the remaining egg supply or ovarian reserve, its levels decline progressively ,becoming undetectable near the menopause.[3,8,9,10]

Recent observations indicate that with increasing female age, AMH levels declines so it has been recognized as a biological marker of ovarian function and /or reserve, during natural aging in healthy women and those with infertility.[18,22,23]

The present study assessed serum AMH level in 70 subfertile females and 60 fertile females with normal regular menstrual cycles varying from 21-35 days, aged (20-40) years, each group was sub classified into two subgroups: group 1 aged (20-29) years and group 2 aged (30-40) years.

In the present study There was a significant higher AMH in fertile younger and older control females in comparison to subfertile females ($p=0.001$ and $p=0.006$ respectively) and a significant decrease in AMH after the age of 30 years in both fertile and subfertile females ($p=0.0001$). There was a decline in serum AMH level with age, AMH level was inversely correlate with the age of whole sample ($r=-0.53$;$p<0.0001$), age of subfertile females ($r=-0.50$; $p<0.0001$), age of fertile females ($r=-0.73$; $p<0.0001$), this is in agreement with other recent observations.[32,33,34]

La Marca et al.,[32] found that with increasing age there is a decline in female reproductive function due to the reduction of the ovarian follicle pool. The present study, concluded that there was a significant negative correlation between serum Anti-Mullerian hormone and age, a decline in Anti-Mullerian hormone level with increasing age in both fertile and subfertile females due to the ovarian aging process and the reduction in the number of small pre antral and early antral follicles. Anti-Mullerian hormone can be considered a useful test to predict ovarian reserve in females.

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پوختە

پەیوەندیا دناڤبەرا تەمەن و هورمونا مولێریەنا سیرەم ل رەگەزێن مێ بێن بەردار و بەردارێن ڤەشارتی

پێشەکی: نەزوکی ئاریشەیەکا بەربەلاڤە ل جڤاکا مەدایە، بەردار بونا ژنان ب زێدەبونا تەمەن ب ئەگەرا مەزن بونا فولیکولێن هێلکەدانێ یە، هورمونا دژە مولێریەن، گلایکوپروتینەکە کو ل هێلکەدانان ب رێیا خانیکێن دندکینێن فولیکۆلێن هلێکەدانی، سەرەکی ل قوناغێن ئانترالێن بچوك و پێش ئانترال دروست دبیت.

هیڤیا ئەڤێ ڤەکولینێ پیڤانا ئاستێ هورمونا دژە مولێریەن ل رەگەزێن مێ بێن بەردار و بەردارێن ڤەشارتی ل تەمەنێن بەرامبەرێن ٢٠–٤٠ سالی یە، هەروەسا پەیداکرنا گوهەرینێن ئاستێ هورمونا دژە مولێریەن ل تەمەنێن جودا و هەلسەنگاندنا ئاستێ وێ دگەل دوو گروب و ژێر گروپێن تەمەنی. ئەڤە رەنگە ب مەرەما هەلسەنگاندنا بەردارێا ژنان و پاراستنا هێلکەدان مفادار بیت.

رێکێن ڤەکولینێ: ڤەکولینەکا نمونە کونترول لناڤ ١٣٠ رەگەزێن مێ، ٧٠ (٥٣.٨٤٪) ژنێن ب بەردارێا ڤەشارتی (نەخوش) ب سنورێ ژیێ ٢٨.٧٥ + ٦.٧٦ سال و ٦٠ (٤٦.١٥٪) ژنێن بەردار (کونترول) ب سنورێ ژیێ ٣١.٢٦ + ٥.٩٨ سال، ل باژێرێ موسل ل سەنتەرێ نەزوکی و IVF ل نەخوشخانەیا ئەلبەتول یا فێرکرنێ ل بەروارێن ئێکێ نوڤەمبەرا ٢٠١٣ حەتا ٣٠ ئەپریلا ٢٠١٤ هاتە ئەنجامدان. تیری یا هورمونان دژە مولێریەن یا سیرەم ل هەردوو گروپێن نەخوش و کونترول هاتن پیڤان.

ئەنجام: ل ڤەکولینا بەردەست، پەیوەندیەکا نەرێنی یا بەرچاڤ دناڤبەرا تیری یا ناڤ سیرەمیا هورمونا دژە مولێریەن و تەمەن هەبو، ئاستێ هورمونا دژە مولێریەن بشێوەیەکێ بەروڤاژی پەیوەندی دگەل تەمەن هەمو نمونەیان هەبو (r=-0.53)، تەمەنێ ژنێن ب بەردارێا ڤەشارتی (r=-0.5)، و تەمەنێ ژنێن بەردار (r=-0.73).

ئاستێ هورمونا دژە مولێریەنا سیرەم یا ژنێن بەردارێن ڤەشارتی بشێوەیەکێ بەرچاڤ کێمتر ل ژنێن بەردار بو (p=0.006)، ئاستێ هورمونا دژە مولێریەن ل ژنێن بەردار ب تەمەن مەزنتر و گەنجتر بشێوەیەکێ بەرچاڤ پتر بو ل هەمبەر ژنێن بەردارێا ڤەشارتی (p=0.001 و p=0.006) ب رێز، کێمبوونەکا بەرچاڤ ل هورمونا دژە مولێریەن پشتی تەمەنێ ٣٠ سالی ل هەردوو ژنێن بەردار و بەردارێن ڤەشارتی هەبو (p=0.0001).

دەرئەنجام: ڤەکولینا بەردەست نیشان دا کو پەیوەندیەکا نەرێنی یا بەرچاڤ دناڤبەرا هورمونا دژە مولێریەن و تەمەن هەیە، کێمبون ل ئاستێ هورمونا دژە مولێریەن ب زێدەبوونا تەمەن ل هەردوو ژنێن بەردار و بەردارێن ڤەشارتی و ئاستێ وێ دکاریت وەکو فەحسەکا مفادار ب مەرەما پێشبینیا پاراستنا هێلکەدان ل ژنان بشێوەیەکێ روتینی بهێتە بکارئینان.

الخلاصة

العالقة بين العمر وتركيز هرمون انتيموليريان في مصل الدم عند االناث الخصبات والعقيمات

الخلفية والأهداف: يعد العقم مشكلة شائعة في بلدنا وان الخصوبه عند االناث تنحدر بشكل تدريجي مع تزايد العمر بسبب تناقص في عدد الجريبات الغارية في المبايض.

ان هورمون انتيموليريان هو بروتين سكري يتم انتاجه في المبايض بواسطة الخلايا الحبيبيه الموجودة في جريبات المبيض بالاخص في المراحل الغارية الصغيرة وقبل الغارية.

ان الهدف في هذه الدراسة هو قياس نسبه هورمون انتيموليريان في أألناث الخصبات والعقيمات وبنفس الفئة العمرية 20-40 سنة وايجاد فيما اذا كانت نسبة هذا الهرمون تتغير بتقدم العمر ومقارنة نسبته بين المجموعتين وبين مجموعات العمر الفرعية وهذا يمكن ان يكون مفيدا في تقييم مخزون المبايض وخصوبة المراة.

طرق البحث: ان هذه الدراسة هي مقارنه الحالة ثم تطبيقها على 130 انثى ,70 انثى عقيمة (مقياس حالة) بمعدل 53,84% وبوسط حسابي 6.76±28.75 سنة و 60 انثى خصبة بمعدل 46.15% وبوسط حسابي 5.98±31.26 سنة في مدينة الموصل/ مركز الخصوبة واطفال االنابيب في مستشفى البتول التعليمي خالل الفتره الزمنية من اليوم أألول من نوفمبر 2013 الى اليوم الثالثون من ابريل 2014، تم قياس تركيز هرمون انتيموليريان في كال المجموعتين.

النتائج: في هذه الدراسة كانت هنالك عالقه معنوية عكسية بين تركيز هرمون انتيموليريان في مصل الدم والعمر. لقد كان مستوى الهرمون في مصل الدم متناسبا تناسبا عكسيا مع العمر في العينة الكاملة r=-0.53 ومع عمر الإناث العقيمات- r= 0.50 ومع عمر الإناث الخصبات r=-0.73 لقد كان مستوى هورمون انتيموليريان في مصل الدم عند الإناث العقيمات أقل بشكل معنوي عن مستواه في مصل الدم عند الإناث الخصبات p=0.006 وكانت هناك زيادة معنوية في مستوى الهرمون في الإناث الخصبات االصغر سنا والأكبر سنا بالمقارنة بالنساء العقيماتp=0.006&p=0.001 كذلك نقصان معنوي في مستوى الهرمون بعد عمر 30 سنة في كلتا المجموعتين p=0.0001 .

الاستنتاجات: الدراسة الحالية تستنتج بأن هناك عالقة عكسية معنوية بين تركيز هرمون انتيموليريان في مصل الدم والعمر، وتراجع في مستوى الهرمون مع تقدم العمر في النساء الخصبات والعقيمات وان مستوى هذا الهرمون يعتبر فحص مهم للتنبؤ باحتياطي المبايض عند أألناث وينبغي ان يتم فحصه بشكل روتيني.

IMPACT OF OXIDATIVE STRESS IN RECURRENT MISSED ABORTION

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ABSTRACT

Background: Recurrent pregnancy loss is a frustrating and heart-wrenching experience for both the patient and the physician. There is strong evidence that oxidative stress has a role in the pathogenesis of many human diseases and early aging processes.
The aim of the study was to determine the impact of oxidative stress on recurrent pregnancies loss via the evaluation of the oxidative stress status in blood and placenta of women with recurrent missed miscarriage.
Methods: This study was conducted at the Department of Physiology, College of Medicine, University of Duhok and Azady Teaching Hospital. Two groups of women were included: the 1st group was (88) patients women admitted to Gynecology and Obstetrics Department in Azady Teaching Hospital with confirmed diagnosis of missed miscarriage; for termination of pregnancy, it was subdivided into (73) patients with a history of recurrent missed miscarriage, and (15) patients with a previous one missed miscarriage. The 2nd group, (84) women, served as a control group, and subdivided into 3 subgroups: a. thirty pregnant women with matched gestational age, b. thirty apparently healthy non- pregnant women with matched women's age, c. twenty four apparently healthy full-term pregnant ladies with matched women's age .
Serum total antioxidants capacity (TAC), serum and placental tissue oxidative stress biomarkers;, 8-iso prostaglandin F2α (8-Isoprostane), and inhibin A were measured using specific ELISA kits,
Results: showed the significant increase in serum and placental tissue of 8-Isoprostane suggests that the oxidative stress is a feature of the patho-physiological changes and the damage of placental syncytiotrophoblast which had seen in recurrent missed miscarriage. Serum total antioxidants capacity and Serum inhibin A, were significantly lower in missed recurrent miscarriage group compared with the control group.
Conclusion: Oxidative stress was found to be present in the group women with recurrent pregnancy loss which indicates its role as a cause of missed miscarriage, especially in those women with low concentrations of total serum antioxidants capacity and inhibin A.

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Keywords: Oxidative stress, Antioxidants, Recurrent Pregnancy loss. 8-Isoprostane, inhibin A.

Missed Miscarriage refers to a pregnancy in which there is a fetal demise without outside intervention, but the myometrium activity is absent to expel the products of conception before 20 weeks of pregnancy[1].

The World Health Organization (WHO) defines a miscarriage as the loss of a fetus or embryo weighing ≤ 500g, which would normally be at 20-22 complete weeks of gestation[2]. Women who miscarry two or more consecutive pregnancies deserve an evaluation to look for the cause, which sometimes can be treated. They can also be reassured that approximately 70% of women in this situation ultimately succeed

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in having a baby, even though the cause of recurrent miscarriage can be determined in only about half of the cases[3]. Repeated or recurrent pregnancy loss (RPL) classically refers to the occurrence of 3 or more consecutive losses of clinically recognized gestation prior to the 20th week of pregnancy4. (Togas and Al-Fozan, 2011). (Togas and Al-Fozan, 2011).

The prevalence of miscarriage is influenced by the age of the mother and by a number of pregnancy-related factors, including a history of a previous full-term normal pregnancy, the number of previous spontaneous miscarriages, a previous stillbirths, and a previous infant had born with malformations or known genetic defects, which may influence the rate of spontaneous miscarriage. An emerging confluence idea suggests that oxidative stress is one of the main underlying mechanisms in the pathogenesis of a continuum of disease processes such as spontaneous miscarriage, hydatidiform mole and preeclampsia[5].

The correlations of in vivo and in vitro data suggests that overwhelming oxidative stress of the placental tissues represents a common pathophysiological mechanism for the various etiologies of RPL[6]. The healthy individual body antioxidants scavenge ROS before causing damage to the biological molecules, slowing and prevent oxidative damage from spreading by interrupting the free radical chain reaction. Unfortunately, a limited information and research work is present in Duhok population about the possible role of oxidative challenge on recurrent pregnancy loss. The study aim was to evaluate the impact of oxidative stress and antioxidants defense via the measurement of the oxidative stress biomarker (8-Isoprostane) and total antioxidants capacities in the blood and placenta of women with recurrent missed abortion.

MATERIALS AND METHODS

This study was conducted at the Department of Clinical Physiology, College of Medicine, University of Duhok and Azady Teaching Hospital. Two groups of women were included in this study, as follows:

The first group was 88 patients admitted to Gynecology and Obstetrics Department in Azady Teaching Hospital, with confirmed diagnosis of missed miscarriage for termination of pregnancy.This group was subdivided into 2 subgroup: a. 73 Patients with a history of repeated missed miscarriage. b. 15 Patients with a history of previous one missed miscarriage.

All patients were at child bearing age (15-45 years) and were referred from different areas of Duhok City. The duration of their pregnancy was between (7-14) weeks of pregnancy. The exclusion criteria were cases of missed abortion with known causes, like infectious diseases like TORCH, metabolic diseases like diabetes mellitus, anatomical causes like uterine septum (the anomaly most commonly associated with pregnancy loss), hemiuterus (unicornuate uterus), bicornuate uterus, incompetent cervix, leiomyomas, and uterine polyps. The second group, served as control group and included 84 women subdivided into 3 subgroups

a. Thirty normal pregnant women with matched gestational age.
b. Thirty apparently healthy non-pregnant women with matched women's age.

c. Twenty four apparently healthy full term pregnant women with matched age.

The 2nd group, (84) women, served as a control group, and subdivided into 3 subgroups: a. thirty pregnant women with matched gestational age, b. thirty apparently healthy non- pregnant women. c. twenty four apparently healthy full-term pregnant women, both last groups with matched women's age .

Informed consent was obtained, the diagnosis of missed miscarriage already had confirmed, prior to evacuation of uterus and any intervention, 10ml. venous blood were obtained from a suitable forearm vein, 2ml was placed in EDTA containing tubes which used for complete blood count using auto-hematology analyzer, the remained 8ml were put in plain plastic tubes and stored in cooling ice bag, then centrifuged at 3000 rpm for 30 minutes at 4 Co. The obtained serum was divided into 3 parts, stored in epiendrof capped tubes and stored frozen at -28 Co until the time of analysis. The control group, all volunteers were kept in a calm place at suitable room temperature (20-25 C°), blood samples were taken from the pregnant control as that of the studied group after exclusion of cases with a history of previous abortion, and after their approval, a questionnaire was completed and blood samples were collected, the blood sampling, centrifugation and storage of serum samples were carried out using the same procedure applied for other groups. About the Known cases of missed miscarriage, evacuation of uterus was done by the obstetrician. The preparation of the placental tissue was done for patients in the group of (one missed and recurrent missed abortion), as soon as evacuation was done; then the placental tissue was collected in a small size glass beaker, rinsed thoroughly with cool normal saline (4 C o) until all the blood and debris were removed, then 1gm of the placental tissue is taken and stored in 4ml of physiological saline solution. Also placental tissue preparation was performed for normal pregnant full-term women at labor as a control group. A placental lobule (cotyledon) was removed from the central region of the placenta, the basal plate and chorionic surface were removed from the cotyledon, and villous tissue was obtained from the middle cross section. Placental tissues were blunt dissected in order to remove visible connective tissue. Placental tissue taken from patients with missed miscarriage and those with full-term normal pregnancy were homogenized carefully in 4ml physiologic buffer solution using ground glass electrical homogenizer. Then centrifugation of the homogenized tissue was done at 3000 rpm for 30 minutes, at 4 Co, the supernatant was taken and stored frozen at -28 Co until the time of analysis[7].

RESULTS

Table 1 shows that the mean age of repeated missed miscarriage group was significantly higher than that of pregnant control with matched gestational age and also higher than full-term control group (30 Vs 26.7 years, P= 0.009 and mean 30 Vs 26.9 years ,P = 0.02) respectively. The mean body mass index (BMI) was higher in repeated missed miscarriage group than that of pregnant control with matched gestational age (26.5 Vs 24.5 Kg / m2, P = 0.045). These results revealed that the women with higher BMI more were more

prone to the pregnancy loss. Heart rate was significantly higher in missed groups (single and repeated) compared to non-pregnant and full-term groups. However, no significant differences in mean blood pressure were observed among the studied groups.

Table 1: Comparison of Some Characteristics of the Studied Groups

Groups Parameters	Single missed abortion N=15 Mean ±SD	Repeated missed abortion N=73 Mean ±SD	Non-pregnant controls N=30 Mean ±SD	Pregnant Matched gestational age controls N=30 Mean ±SD	Full term control N=24 Mean ±SD	ANOVA Test P value
Age (years)	29.3 ±7.1	30 ± 6.1	29.4 ±5.3	26.7 ± 4.4	26.9 ± 5.7	0.041*
BMI (Kg/m2)	24 ± 2.9	26.5 ± 4.7	26.7 ± 3.5	24.5 ± 3.6	28.2 ± 5.7	0.009*
Heart rate (beats/min.)	85.4 ± 1.21	84±0.86	79.4±0.68	83.6±1.24	80.6±0.87	0.001*
Systolicblood pressure (mmHg)	110.3±2.21	111.8±1.76	111.7±1.73	114.7±2.02	115.6 ±2.36	0.52[NS]
Diastolic blood pressure (mmHg)	72 ± 2	72.9 ±1.39	74.3±1.57	71±1.39	74.6 ± 1.7	0.62[NS]
Mean blood pressure (mmHg)	84.8 ±1.97	85.8 ±1.46	86.8 ±1.29	85.6 ±1.54	88.3 ±1.88	0.82[NS]

NS=non-significant, * = significant

Table 2 .shows an obvious significant high WBC count in full-term group compared with that of single missed ,repeated missed abortion cases, non- pregnant and pregnant matched gestational age controls (13.9 Vs 10.5,9.7,8.3and 9.2, P= 0.002,P=0.001) respectively, on the other hand the WBC count was higher in the missed groups (single and repeated) than that of non-pregnant groups (10.5 Vs 8.3,9.7 Vs 8.3, P =0.03,P = 0.04) respectively. Mean blood hemoglobin level was significantly lower in repeated missed group compared with non-pregnant group (11.7 Vs 13, P< 0.001) and also lower than pregnant with matched gestational age (11.7 Vs 12.5, P= 0,017). Mean blood hematocrit percentages were significantly lower in missed groups (both single & repeated) than non-pregnant group (35.5 and 34 Vs 39.3, P=0.005, P=0.001). Moreover, the hematocrit percentage was significantly lower in repeated missed group compared to pregnant with matched gestational age (34 Vs 36.8, P=0.004) Mean corpuscular volume (MCV) was significantly lower in a single missed group compared with non-pregnant and pregnant with matched gestational age (81.5fL Vs 86.8 and 88.2, P=0.047 and P=0.01 respectively). In repeated missed group, MCV was lower than that in non-pregnant and pregnant with matched age group. (83.1fL Vs 86.8 & 88.2, P=0.04 & P= 0.05) respectively). Highly significant differences in platelets count were observed among the studied groups. Platelet count was lower in a single missed group compared with non-pregnant and full-term groups. (190.4 Vs 285.3 and 239.7, P= 0.001, P=0.03 respectively). In addition, platelet count was significantly lower in repeated missed group compared to non- pregnant, pregnant with matched gestational age and full-term groups (197 Vs 285.3, 228.7 and 239.7, P=0.001, P= 0.047 and P= 0.01 respectively).

Table 2: Blood Parameters Measured in the Studied Groups

Parameters / Groups	Single missed abortion N=15 Mean ±SE	Repeated missed abortion N=73 Mean ±SE	Non-pregnant controls N=30 Mean ±SE	Pregnant Matched gestational age controls N=30 Mean ±SE	Full term control N=24 Mean ±SE	ANOVA Test P value
WBC COUNT (cells/mm3) × 103	10.5 ± 0.71	9.7 ± 0.44	8.3 ± 0.35	9.2 ± 0.47	13.9 ± 0.86	<0.001*
Blood Hematocrit %	35.5 ± 0.77	34 ± 0.61	39.3 ± 0.75	36.8 ± 0.52	36 ± 0.7	<0.001
Mean corpuscular volume(fL)	81.5 ± 2.42	83.1 ± 0.95	86.8 ±1.38	88.2 ± 1.33	84.5 ± 1.94	< 0.016
Platelet count (mm3) ×103	190.4 ± 17.4	197 ± 9.12	285.3 ±12.88	228.7 ±10.06	239.7 ± 14.9	<0.001

*= Significant

Table 3 shows the results obtained from the measurement of total antioxidants capacity (TAC) among the studied groups. Serum TAC in missed abortion cases was significantly lower compared with control groups (non-pregnant and pregnant with matched gestational age). For a single missed group it was 784, and for recurrent missed abortion was 590.1 Vs 1211.4 and 1260.3 µmol/L respectively. However, no statistically significant difference in serum TAC levels was observed between pregnant controls and pregnant with matched gestational age (Table 3, Figure.1). Serum concentration of Isoprostane in cases with repeated missed abortion was significantly higher compared to single missed abortion cases, non-pregnant control cases and pregnant with matched gestational age groups (6755.5 VS 734.9, 1325.9 and 1653.6 pg/ml, P< 0.001, P= 0.047 and P= 0.040, respectively), (Table 3, Figure 2). A highly significant increase of placental Isoprostane concentration in patients with repeated missed abortion compared to placental tissue of full-term pregnant (17991 Vs 6676.7pg/ml, P< 0.001), the same for repeated missed abortion if compared to patients with single missed abortion and placental tissue of full-term pregnant (17991 Vs 6184.8 and 6676.7pg/ml, P=0.039 and P< 0.001, respectively). Pregnancy loss biomarker, serum Inhibin A was found to be significantly lower in recurrent missed abortion compared to the single missed, and pregnant with matched gestational age groups.

A significantly higher median values of serum progesterone level was found in pregnant with matched gestational age groups with other groups.

Table 3. Measurement of Serum and Placental Variables in the Studied Groups

Parameters / Groups	Single missed abortion N=15 Median	Repeated missed abortion N=73 Median	Non-pregnant controls N=30 Median	Preg. Matched gestational age controls N=30 Median	P value (Kruskal-Wallis)
Serum TAC (µmol/L)	784	590.1	1211.4	1260.3	<0.001*
Serum Isoprostane (Pg/ml)	734.9	6755.5	1325.9	1653.6	<0.001
Serum Inhibin-A (pg/ml)	68.8	21.3	23	103.5	0.006
Serum Human chorionic gonadotropin (mIU/ml)	>1500	>1500	1	>1500	<0.001
Serum progesterone (ng/ml)	3.8	5.85	1.12	30.78	
Placental Oxidative Stress Biomarker		Single missed abortion	Repeated missed abortion	Full term pregnant controls	
Placental Isoprostane (pg/ml)	Median	6184.8	17991	6676.7	<0.001

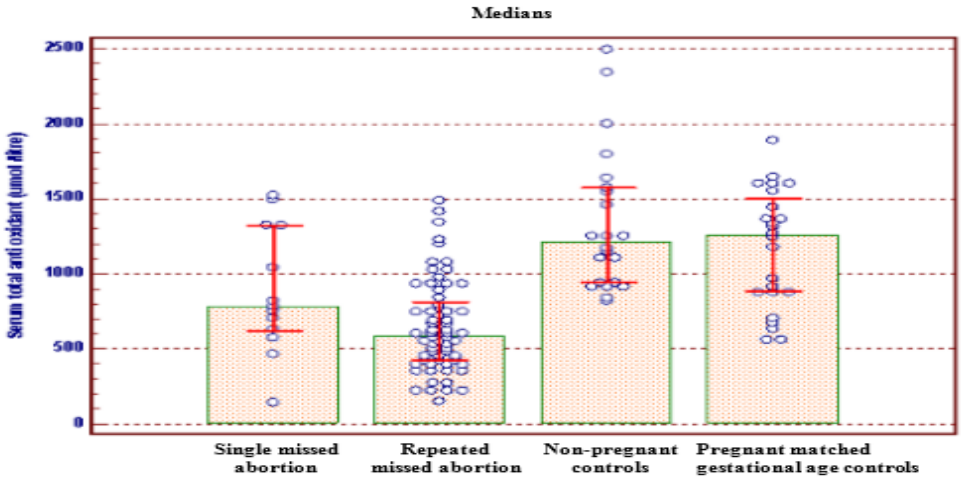

Figure 1 Comparison of Median Serum TAC among the studied Groups

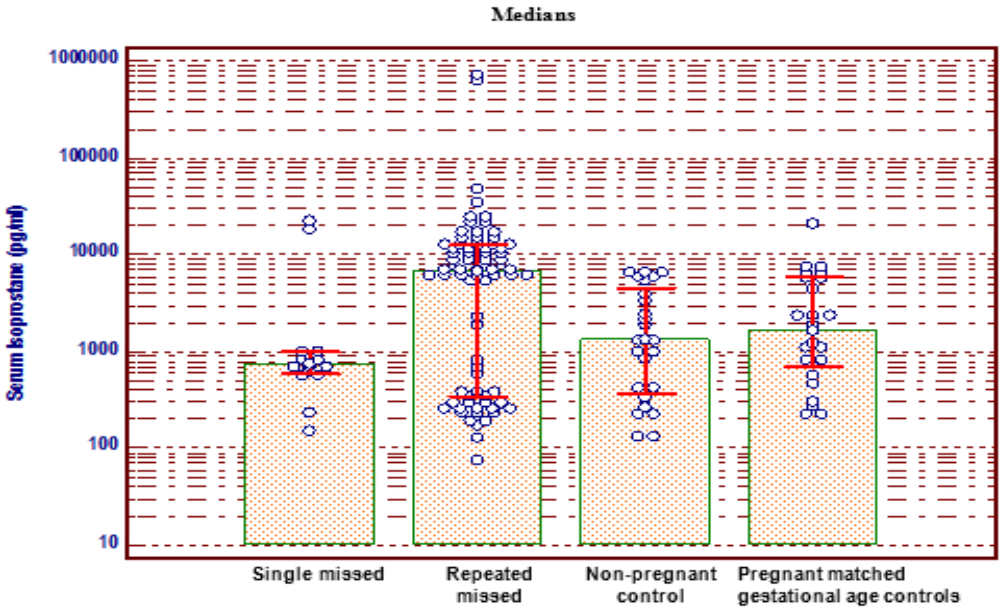

Figure 2 Comparison of Median Serum Isoprostane in the Studied Groups

DISCUSSION

The findings of this study provide further evidence that currently the most effective method for predicting missed abortion is by a combination of co-variables such as oxidative stress, antioxidants, and pregnancy loss biomarkers. The median value of serum Isoprostane in non-pregnant controls was 1325.9 pg/ml versus its level in pregnant with matched gestational age of 1653.6 pg/ml). The level was found to be higher in pregnant with matched age and this is due to the fact that women at labor are subjected to high oxidative stress[8].

Serum concentration of Isoprostane in cases with recurrent missed abortion was significantly higher compared to non-pregnant control (P=0.046), which was compatible with previous studies correlated oxidative stress with missed abortion. Moreover, there was significant difference in serum concentration of Isoprostane between repeated missed abortion with matched gestational pregnant. (P=0.04). The results of the present study demonstrate the elevated values of serum and placental tissue of Isoprostane which provides important evidence in the involvement of oxidative stress in pathophysiology of repeated missed abortion. The circulation is one of the prime requirements for a successful pregnancy. Initially, the tips of the spiral arteries are occluded by plugs of trophoblast cells arising from the trophoblast shell. The dislocation of these plugs due to invasion of trophoblast allows circulation of maternal erythrocytes in the intervillous space, with a subsequent rise in O2 tension between weeks 10 and 12, thus establishing the uteroplacental circulation. The rise in oxygen tension is associated with a burst of placental oxidative stress as a result of the reperfusion of the ischemic tissue 9The same result was obtained by other researchers (Gupta et al., 2007), incidence of repeated abortion increases with age; from 15% at 25 years of age to 35% in women older than 38 year 9, the age primarily, affects the oocyte, women in the advanced reproductive age who have a reduced ovarian reserve are prone to be at higher risk of repeated miscarriages, such miscarriages are due to decreased egg quality 10 . The highest risk of miscarriage was when a woman was 35-44 years old[11]. The increased oxidative stress also seems to be responsible for diminishing oocyte quality, thereby leading to oocyte aging[12]. The conclusions of this study is a marked increase in serum Isoprostane suggests that oxidative stress is a feature of the pathophysiological changes seen in recurrent missed abortion. The significant increase in placental tissue Isoprostane indicates that placental oxidative stress with resultant damage to the syncytiotrophoblast may provide a final common mechanism of recurrent missed abortion. Serum total antioxidants capacity in missed abortion cases were significantly lower compared with control groups. Decreased serum inhibin A is a specific marker of early pregnancy loss before the onset of the clinical symptoms of recurrent miscarriage.

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پوختە

کارتێکرنا ئوکسیدتیڤ ستریّس ل بەرچوونا درەنگا بەرزە

پێشەکی: ژدەست دانا دوگیانیا دوبارە سەربورەکا ماندوکەر و دل ئێشێن بۆ نەخوش و نوژداری یە، بەلگەیەکێ بهێز هەیە کو ئوکسیدتیڤ ستریّس رولەك ل پەیدابونا گەلەك نەخوشان و پێڤاژویا پیربونا دەم زوو لناڤ مرۆڤان هەیە. هیڤیا ڤەکولینێ دیارکرنا کارتێکرنا ئوکسیدتیڤ ستریّس لسەر ژدەست دانا دوگیانی یێن دوبارە ژ ریّیا هەلسەنگاندنا رەوشا ئوکسیدتیڤ ستریّس لناڤ خوین و هەڤالوکا (placenta) ژنێن ب بەرچونا زوو و بەرزەیا دوبارەیە.

ریّکێن ڤەکولینێ: ئەڤ ڤوکولینە ل پشکا فسیولوجی، کولیژا پزیشکی زانکویا دهوك و نەخوشخانەیا ئازادی یا فێرکرنێ هاتە ئەنجامدان، دوو گروپ ژ ژنان ل ڤەکولینێ دا هاتن دانان: گروپێ یەکەم ژ ٨٨ نەخوشێن ژن وەرگرتی ل پشکا ژنان و زاروکبونێ ل نەخوشخانەیا ئازادی یا فێرکرنێ ب ئەرێ بو نەناسینا بەرچوونا زوو و بەرزە، بۆ ب داوی ئینانا دوگیانی، هاتن دابەشکرن ب ٧٣ نەخوشێن ب دیروکا بەرچونا زوو و بەرزەیا دوبارە، و ١٥ نەخوش ب هەبونا ئێك بەرچونا زوو و بەرزە. گروپێن دویەم ژ ٨٤ ژنان پێکدهات و وەکو کونترول هاتن بکارئینان، و ب سێ ژێر گروپ هاتن دابەشکرن: أ– ٣٠ ژنێن دووگیان ب تەمەن دووگیانی یێن هەڤسەنگ، ب– ٣٠ ژنێن دیار ساخلەم و نەدووگیان ب تەمەنێن هەڤسەنگ. ج– ٢٤ ژنێن تەمام دووگیان و دیار ساخلەم ب تەمەنێن هەڤسەنگ.

کارئینا ئانتی ئوکسیدانتا تەمام لناڤ سیرەم (TAC) پیڤەرێن ژیانێ یێن ئوکسیدتیڤ ستریّس یا تەڤینەکا هەڤالوکی و سیرەم 8-iso prostaglandin F2a (8-Isoprostane)، و ئێنهیبینا A ب کیتێن ELISA هاتن پیڤان.

ئەنجام: ڤەکولینێ نیشان دا کو زێدەبونەکا بەرچاڤ ل سیرەم و تەڤینەکا هەڤالوکیا 8-Isoprostane پێشنیار دکەت کو ئوکسیدتیڤ ستریّس یەك ژ سالوخەتێن گوهەرتنێن پاتوفیزیولوجیکی و زرارا syncytiorophoblast یا هەڤالوکی یە کۆ ل بەرچونێن زوو و بەرزەیا دوبارە هاتبون دیتن، کارئینانا ئانتی ئوکسیدانتێن تەمام یا سیرەم و ئینهیبینا A یا سیرەم ب شێوەیەکێ بەرچاڤ ل گروپێ بەرچوونا زوو و بەرزەیا دوبارە ل هەمبەر گروپێ کونترول ل ئاستێ خوارتر بو.

دەرئەنجام: ئوکسیدیتیڤ ستریّس ل گروپێ ژنێن ب ژدەست دانا دووگیانیا دوبارە هاتە دیتن کۆ نیشاندەرێ هەبونا رولێ وێ ل بەرچونا زوو و بەرزەیە، بتایبەت لناڤ ژنێن ب تیری یێن خوارێ ژ کارینا ئانتی ئوکسیدانتێن سیرەم و ئینهیبینا A.

الخلاصة

تأثير الإجهاد المؤكسد في الإجهاد المتكرر

الخلفية والأهداف: فقدان الحمل (الإجهاض) المتكرر هي تجربة محبطة ومؤذية جدا لكل من المريض والطبيب. حيث أنه يوجد دليل قوي يؤكد أن اإلجهاض المؤكسد له دور مؤثر لكثير من األمراض و الشيخوخة المبكرة.

الهدف من هذا البحث هو تحديد تأثير اإلجهاد المؤكسد على فقدان الحمل المتكرر من خالل تقييم حالة اإلجهاد المؤكسد على دم ومشيمة النساء مع اإلجهاض المتكرر.

طرق البحث: أجريت هذه الدراسة في كلية الطب قسم الفسلجة/ جامعة دهوك ومستشفى آزادي التعليمي. حيث تضمن البحث مجموعتان من النساء، المجموعة الأولى كانت 88 امرأة راقدة في مستشفى آزادي قسم التوليد والأمراض النسائية اللواتي تم تشخيصهن بمرض إنهاء الحمل، والتي تم تقسيمها إلى 73 مرضى لهن تاريخ الفشل والإجهاض المتكرر و15 مرضى أخرى لهن إجهاض متكرر سابق. أما المجموعة الثانية كانت 88 إمرأة، كمجموعة قياسية وتم تقسيمها إلى 3 مجاميع فرعية: أ- ثلاثون إمرأة حبلى بالعمر الحملي المتناظر. ب- ثلاثون امرأة حبلى مرضى بنفس العمر على مايبدو. ج- ٢٤ سيدة إخرى بنفس العمر وأصبحن حاملات من غير مرض.

النتائج: أظهرت زيادة ملحوظة في المصل والخلايا المشيمية ل – 8 أيزوبروستين واقترحت بأن الإحباط المؤكسد هو ميزة للتغييرات للفسلجة االمراضية وتحطيم الخلايا المشيمية التي تم رؤيتها في النساء ذات الحمل والإجهاض المتكرر. قدرة مضادات الأكسدة التامة كانت أقل من الإجهاض المتكرر بصورة هامة بمجموعة الأولي مقارنة بالمجموعة الثانية.

الاستنتاجات: وجد اإلجهاد المؤكسد في المجموعة الأولي النساء ذات الحمل والإجهاض المتكرر والذي أشار بأن له دور أساسي للإجهاض خاصة في تلك النساء ذوات مضادات الأكسدة المنخفض التركيز.