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HISTOPATHOLOGICAL ANALYSIS OF ENDOMETRIAL BIOPSIES FROM WOMEN WITH ABNORMAL UTERINE BLEEDING

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ABSTRACT

Background: Histopathological evaluation of endometrial samples is essential in the diagnosing of abnormal uterine bleeding. The abnormal bleeding can be caused by a wide variety of disorders and it is one of the commonest complaints leading to endometrial sampling. This study was carried out to assess the patterns of endometrial histological findings in women with abnormal uterine bleeding (AUB) and to correlate these findings with clinical features. Materials and Methods: One thousand and nine hundred fifty six patients with diagnosis of abnormal uterine bleeding underwent endometrial sampling in Duhok city during a period extended from January 2013 to December 2014. The slides stained with Hematoxylin and Eosin stain were studied. Results: The predominant endometrial histopathological finding was pregnancy related lesion (Retained products of conception) 403 cases (20.6%) followed by secretory endometrium 363 cases (18.5%). Malignant lesions were more common in patients aged 40 years and more and they were comprised 9 cases (0.4%) of all cases. Endometritis was least finding 29 cases (1.8%) followed by endometrial carcinoma 9 cases (0.4%). Conclusions: Histopathological examination of endometrium should be done in women presenting with abnormal uterine bleeding to rule out neoplastic and non neoplastic specially the retained products of conception hyperplasia and malignant lesions. Around 40% of endometrial biopsy reaveled absence of pathological findings which reflects the high icidence of extrauterine causes of abnormal uterine bleeding. Pregnancy related lesions were the highest among organic findings which highlight the needs for more perinatal care.

KEYWORDS: Endometrium hyperplasia, abnormal uterine bleeding, proliferative and secretory endometrium.

INTRODUCTION

Abnormal uterine bleeding (AUB) is considered one of the most common problems in gynecology and expanse from a pattern observed during a normal menstrual cycle or after menopause (Zeeba et al. 2013).

Initial evaluation for abnormal uterine bleeding is by endometrial sampling which is mostly obtained by dilatation and curettage. It is an easy and cost effective procedure for detecting the underlying

pathologies and other few lesions will escape the detections (Sher et al. 2003).

Endometrial sampling should be considered in women over 35 years with menorrhagia (Heavy menstrual bleeding= HMB), women between the age 18 and 35 years with AUB who have risk factors for endometrial malignancy or if AUB does not response to medical management (ACOG Practice Bulletin. 2001)

Histopathological examination of the submitted endometrial sample provides a tissue diagnosis for causes of abnormal vaginal bleeding which may be due to structural or functional causes (Muzzafar et al. 2005). Common structural causes include myometrial tumors, endometrial polyps, endometrial hyperplasia, endometrial carcinoma and complications of pregnancy (Ely et al. 2006). The large group of functional disorders called as Dysfunctional uterine bleeding (DUB) can only be diagnosed after exclusion of structural, iatrogenic, psychological and systemic disorders by various diagnostic techniques (Albers et al. 2004, Morano et al. 2003)

Aims Of Study:

1. To determine the endometrial pathologies and their frequencies in patients presenting with AUB

2. To correlate the underlying causes of AUB in women with various age groups.

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MATERIALS AND METHODS

The study was conducted in the Central Laboratory/Directorate of Health, Duhok-Iraq, and specimens were retrieved from histopathology lab in Duhok during a period extended from January 2013 to December 2014. The paraffin embedded blocks (PEBs) of the patients containing the tissues were selected. Sections from the PEBs where obtained in a 4 microns thickness and to perform the Hematoxyline and eosin stain**.** Data were analyzed by using the statistical package for social science (SPSS) version 21. One way analysis of variance (one way ANOVA) was used to show whether there is a significant difference between the means of three groups of normal cyclic endometrium, abortion and other pathological findings and then used to show whether there is a significant difference between the mean age of the three group.

RESULTS

During a period of 2 years from January 2013 – December 2014, 1956 female patients were included in the study with median age of 37.1 years (range 15- 88 years). The main finding of endometrial curettage was retained products of conception (403 cases= 20.6%) which reflect the high incidence of abortion in this locality. While the least diagnosis was endometrial carcinoma (9 cases= 0.40%). Inadequate curettage was seen in (40 cases= 2%). Endometrial polyps were found in (58 cases= 3.00%). Chronic endometritis was detected in 1.80%. Disordered proliferative endometrium and hormone imbalance effect were (227 cases= 11.6%), (172 cases= 8.80 %) of endometrial biopsies respectively. All the pathologies assessed in present study are shown in (Table-1) with their mean age. The p value 0.001 was statistically significant which mean the old ages are more susceptible to different endometrial pathological changes; mainly endometrial polyp, hyperplasia and carcinoma than the younger, who were showed RPOC (Retained Products Of Conception) and normal cyclic endometrium (Includes proliferative, secretory and menstrual phase) (Table-2). Among all pathologies included in the study 790 cases (40.4%) of the cases revealed normal cyclic endometrium, which is statistically significant (Table-3). Regarding the main presentation and indication for endometrial biopsy; Menorrhagia was the main feature followed by irregular vaginal bleeding (Table-4). Hydatidiform mole pregnancies were (79 cases= 4.00%); with mean age 28.8 years. They include partial mole (20 cases=24.5%) and complete mole (59cases= 75.5%) (Table-5; figure 3). The endometrial cancer cases includes choriocarcinoma (2 cases= 22.2%) and adenocarcinoma (7cases= 77.8%) (Table-6; figures 4 & 5).

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Table (1): Histopathologic distribution of endometrail biopsies.

Pathology	No. Of cases	(%)	Mean age= Years
RPOC	403	20.60%	32.0
Secretory	363	18.55%	37.0
Proliferative	316	16.20%	36.4
Disordered proliferative phase	227	11.60%	41.6
Hormone imbalance effect	172	8.80%	39.3
Menstrual phase	111	5.55%	40.0
In active endometrium	92	4.70%	46.5
Hydatidiform mole	79	4.00%	29.0
Inadequate	40	2.00%	39.7
Endometrial polyp	58	3.00%	44.7
Endometrial hyperplasia	57	2.80%	41.0
Chronic endometritis	29	1.80%	36.6
Endometrial carcinoma	9	0.40%	46.7
Total	1956	100%	37.1

RPOC: Retained Products Of Conception

Table (2): Three main groups of endmetrial biopsies with their mean age.

Histological findings	No. Of cases = %	Mean age	P-Value
RPOC	403= 20.6%	32.0	0.001
Normal cyclic endometrium (unremarkable)	790= 40.4%	37.8	
Different pathological findings	763= 39.0%	40.5	
Total	1956	37.1	

Table (3): Distribution of normal and abnormal endometrial findings

Histological findings	No. Of cases	N0.= %	P-Value
Normal cyclic endometrium (unremarkable)			
Secretory phase	363	790= 40.4%	
Proliferative phase	316		
Menstrual phase	111		
Pathological findings			
RPOC	403		0.001
Disordered proliferative phase	227		
Hormone imbalance effect	172		
In active endometrium	92	1126= 57.6%	
Hydatidiform mole	79		
Endometrial polyp	58		
Endometrial hyperplasia	57		
Chronic endometritis	29		
Endometrial carcinoma	9		
Inadequate	40	40= 2.0%	
Total	1956	1956= 100%	

RPOC: Retained Products of Conception.

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Table (4): Clinical presentation of the pateints and indication of endometrial biopsies

Main presentation	No.	%
Menorrhagia HMB	1644	84.0
Irregular vaginal bleeding	129	6.60
Endometrial polyp	89	4.55
Infertility with AUB	49	2.55
Dysmenorrhea	30	1.55
Oligomenorrhea and amenorrhea	6	0.30
Missed IUCD with AUB	4	0.20
other	5	0.25
Total	1956	100

Table (5): Types of hydatidiform mole

Types of hydatiform mole	(no.= 79) %	Mean age= years
Partial mole	24.5%	26.8
Complete mole	75.5%	29.6
Total	100%	28.8

Table (6): Types of endometrial carcinoma

Types of endometrial carcinoma	(no.= 9) %	Mean age= years
Choriocarcinoma	2= 22.2%	40
Adenocarcinoma	7= 77.8%	53.2
Total	9= 100%	46.7

DISCUSSION

Normal menstruation is a result of normal cyclic hormonal changes and it is defined as the bleeding from secretory endometrium – associated with an ovulatory cycle – not exceeding a length of 5-7 days with amount of 30-80 ml. Any bleeding not fulfilling these criteria is referred to as an abnormal uterine bleeding which cyclic or in continous form (Rosai. 2010).

Abnormal uterine bleeding is a commonly encountered gynecological problems and it includes both dysfunctional uterine bleeding (DUB) and bleeding from structural causes like leiomyomas, endometrial polyps, endometrial carcinoma, and pregnancy complications. In DUB no organic cause is detected and endometrial curettage (Biopsy) plays an important role in excluding organic uterine disorders (Albers et al. 2004, Johnson et al.1999).

Evaluation of the histological examination of the submitted endometrial tissue revealed various patterns and we found the most common histopathological pattern was retained products of conception 20.6% which could indicate high incidence of abortion, followed by secretory endometrium.

In this study organic causes were more than 57.6% as compared with no pathological findings in 40.4% of cases, whereas the inadequate biopsies represent 2% and this shows similarities to other study by Nadia et al. 2013, 61.8% organic causes, 33.5% non organic causes and 4.6% was inadequate.

While organic causes were reported lesser in other study 27% (Sharma et al. 2014).

Disordered proliferative endometrium is common in the perimenopausal years because of anovulatory cycles. It refers to a proliferative phase endometrium that does not seem appropriate for any one time in the menstrual cycle (Saraswathi et al. 2011). In this study disordered proliferative endometrium was recorded to be 11.6% and this was in disagreement with 5.7% reported in Jairajpuri et al. 2013). This may be due to effect of exogenous hormon. Regarding the hyperplasia (figures 1 & 2) it was constituted 2.80% patients with mean age 41. These figures are similar to other studies (Reed et al. 2009, Lerner et al. 1996, Wentz et al. 1974 and Mughal. et al. 1997), but different from other (Sharma et al. 2014)

Endometrial carcinoma is the most distressing cause of abnormal vaginal bleeding. In the current

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study it was 0.4% of the total and this shows agreement to some study 0.3% (Jairajpuri et al. 2013) and disagreement to other studies 2.1% (Nadia et al. 2013).

Regarding molar pregnancy which constitutes 4% of the total cases. Most of the patients in this study were in their second and third decades of life, the maximum reproductive period, it was difficult to calculate the incidence of hydatidiform mole in relation to different age and parity groups because the data of maternal age and parity for all the mothers delivered during the same period of time was not available. However, some studies showed an increase in the incidence of HM with falling maternal age below 20 years,(Fukunga et al. 1995, Baghsawe et al. 1983) while others report an increased risk in patients over 35 years(La Vacchia et al. 1984, Abdulaziz et al. 2000). Early marriage and early pregnancy are usual in women our locality.

CONCLUSIONS

Endometrial sampling and biopsy is an important diagnostic procedure in evaluation of AUB. Endometrial causes of uterine bleeding are age related where pregnancy related lesions were around age 30 years while hyperplasia and carcinoma were above age of 40 years. Around 40% of endometrial biopsy revealed absence of pathological findings which reflects the high incidence of extra uterine causes of AUB while abortion related causes was the frequent finding and it is one of the most common problems faced by gynecologists which indicated the high importance of further study and evaluation regarding the causes and perinatal care. Correct diagnosis of the possible causes; plays an important role in the management and follow-up of A

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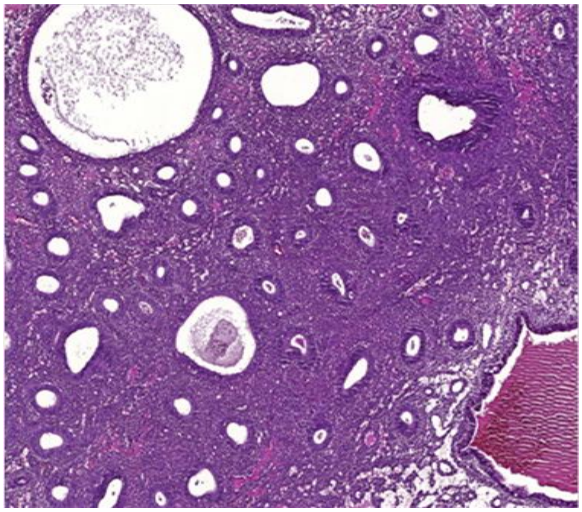

Fig. (1): Simple endometrial hyperplasia (H&E x40)

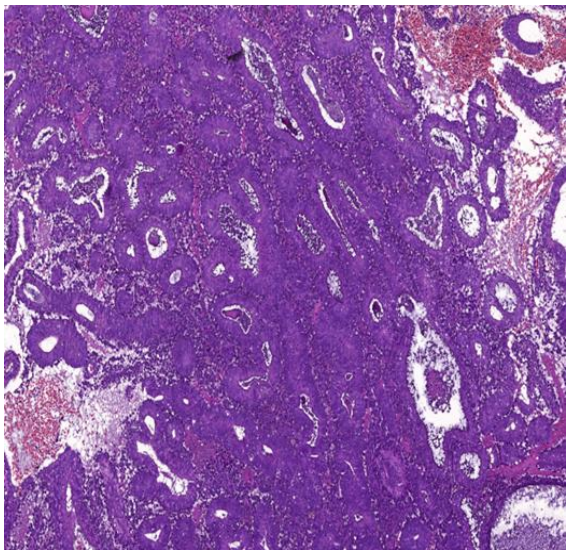

Fig. (2): Atypical endoemtrial hyperplasia showing glandular crowding, multilayering of lining epithelium, hyperchromatic nuclei and note the mitoses (H&E x40)

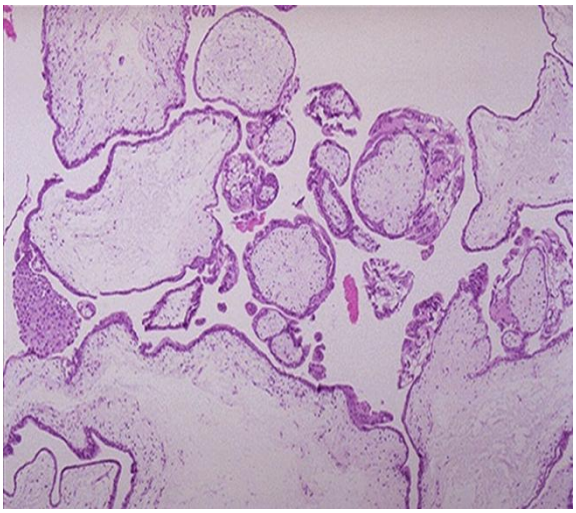

Fig. (3): Hydatidiform Mole – Complete (H&E x40)

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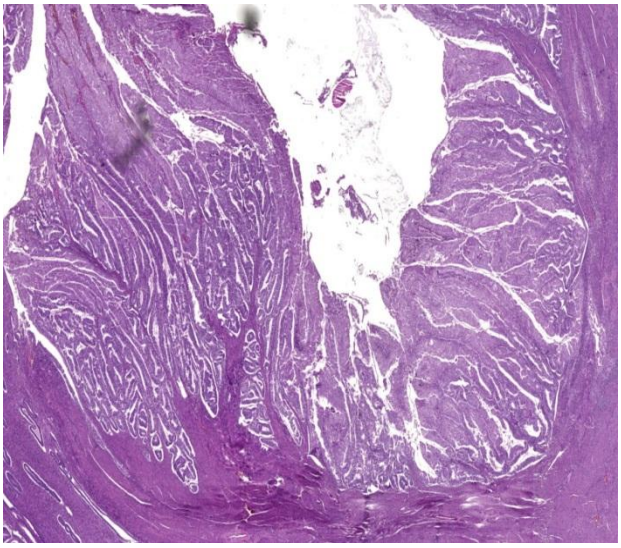

Fig. (4): Hysterectomy: Endometrial carcinoma (grade I), shows villoglandular pattern. Note the back to back glands with absence of stroma (H & E X40)

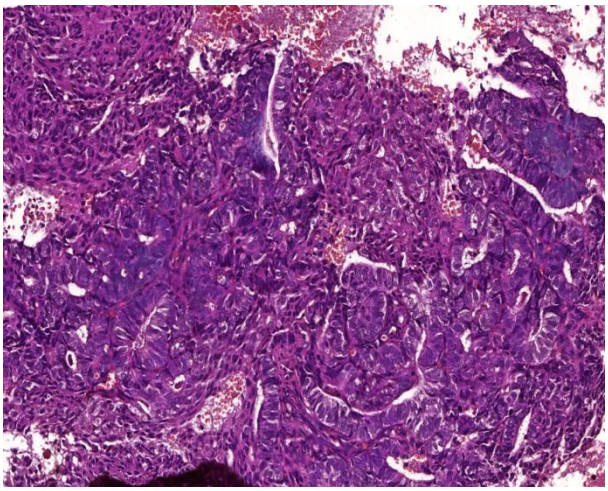

Fig. (5): Section of endometrial carcinoma (grade II). It shows preserved glandular differentiation with an area of sheet of neoplastic cells. There are dysplastic changes; hyperchromasia, increased N/C ration and nuclear pleomorphism (H&E X400)

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پوختە
پاشین: هەڵسەنگاندنێن هێستوپاتولوژی بۆ نموونەیێن ناڤپۆشا مالبچویکی ئێکە ژ پێنگاڤێن سەرەکی لدەمێ پشکنین و ڤەکۆلینا خوین بەربوونا مالبچویکی یا نەسروشتی. خوینبەربوونا مالبچویکی ژ ئەنجامێ گەلەك نەخۆشیێن جوداجودا پەیدابیت و ئێکە ژ گازندەیێن بەربەلاڤ کو نەخۆش نەچاردبیت نموونە ژ ناڤپۆشا مالبچویکێ وێ بهێـتە وەرگرتن.
مەرەم ژ ئەنجامدانا ڤێ ڤەکولینێ ئەوبوو ژ پێخەمەت هەڵسەنگاندنا شێوازێ ڤەدیتنێن هێستوپاتولوژی یێن ناڤپۆشا مالبچویکی ل دەف وان ئافرەتێن تووشی خوین بەربوونا مالبچویکی یا نەسروشتی بووین، هەردیسان ژبۆ هەڤبەرکرنا ڤان ڤەدیتنێن هێستوپاتولوژی دگەل نیشانێن کلینیکی.
کەرەستە و ڕێکێن کاری: ژبۆ ئەنجامدانا ڤێ ڤەکۆلینێ نموونە ژ **1956** نەخوشان هاتنە وەرگرتن دگەل پشکنینا خوین بەربوونا مالبچویکی یا نەسروشتی و وەرگرتنا نموونەیان ژ ناڤپۆشا مالبچویکی. ئەڤ ڤەکۆلینە ل باژێرێ دهوکێ دناڤبەرا ماوێ کانونا دوێ یا سالا **2013** هەتا کانونا ئێکێ یا سالا **2014** هاتە ئەنجامدان. پشتی ئەو سلایدێن هاتینە ئامادەکرن ب هەردوو بۆیاغێن هیماتوکسیلین و ئیوسین هاتنە بۆیاغکرن و پاشی هاتنە خواندن.
ئەنجام: ڤەدیتنا هێستوپاتولوژی یا ناڤپۆشا مالبچویکی یا هەرە بەرەلاڤ، برینا پەیوەندی ب دووگیانێ ڤە هەی (بەرهەمێن بەرمایکا دووگیانیێ) بوو ل دەڤ **403** حالەتان ب ڕێژا **(20.6%)** هاتە تومارکرن، ل دویڤدا ڤەڕێژێن ناڤپۆشا مالبچویکی کو ل دەڤ **363** حالەتان ب ڕێژا **(18.5%)** هاتە تومارکرن. برینێن وەرەمێن پیس پتر ل دەف وان نەخۆشان هەبوون یێن ژیێ وان ژ **40** سالان بوری کو بتنێ **9** حالەت ب ڕێژا**(0.4%)** هاتنە تومارکرن. هەودانێن ناڤپۆشا مالبچویکی ژ کێمترین ڤەدیتن بوو کو بتنێ لدەڤ **29** حالەتان ب ڕێژا**(1.8%)** هاتنە تومارکرن و ل دویڤدا پەنجەشێرا ناڤپۆشا مالبچویکی ل دەڤ **9** حالەتان ب ڕێژا **(0.4%)** هاتە توماکرن.
دەرئەنجام: دڤێ ڤەکولینێ دا بۆمە دیاردبیت کو پێدڤیە پشکنینێن هێستوپاتولوژی ب شێوەیەکی گشتی بۆ هەمی وان ئافرەتان بهێنە ئەنجامدان یێن تووشی خوین بەربوونا مالبچویکی یا نەسروشتی دبن ژ پێخەمەت دەرئێخستنا بەرمایکێن نە وەرەمی ب تایبەت بەرهەمێن بەرمایکێن دوگیانیێ و مەزنبوونا شانەیان و برینێن پەنجەشێرێ.
نێزیکی **40%** ژ بایوپسیێن ناڤپۆشا مالبچویکی دیاربوو کو پشکنینێن هێستوپاتولوژی بۆ نەهاتینە ئەنجامدان کو ئەڤەژی ڕەنگڤەدانێ دکەتە سەر بلندبوونا حالەتێن دەرڤەی ناڤپۆشا مالبوچیکی یێن خوین بەربوونا مالبوچیکی یێن نەسروشتی. برینێن پەیوەندی ب دووگیانیێ ڤە هەی ژ حالەتێن هەرە بەربەلاڤ بوون ل دەڤ ڤەدیتنێن ئەندامی و ئەڤەژی ئاماژی بۆ هندێ کو ئەو پێدڤی ب چاڤدێریەکا باشترن ل دەمێ دووگیانیێ.

الخلاصة
معلومات أساسية: تقييم بطانة الرحم عينات نسيجية ضروري لتشخيص نزيف الرحم غير طبيعي. يمكن أن يكون سبب النزيف الشاذ طائفة واسعة من الاضطرابات وأنها واحدة من الشكاوى الأكثر شيوعاً مما يؤدي إلى أخذ العينات بطانة الرحم. هذه الدراسة أجريت لتقييم أنماط النتائج النسيجي بطانة الرحم في النساء مع نزيف الرحم غير طبيعي **(AUB)** وربط هذه النتائج مع المظاهر السريرية. المواد والطرق: ألف وتسعمائة وستة وخمسون حالة من المرضى لديها تشخيص نزيف الرحم غير طبيعي خضعت العينات بطانة الرحم في مدينة دهوك خلال فترة تمتد من كانون الثاني/يناير **2013** إلى كانون الأول/ديسمبر **2014**. وجرت دراسة الشرائح مصبغة باستعمال الهيماتوكسيلين والأيوسين. النتائج: تم

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إيجاد نسيجية بطانة الرحم الغالبة الحمل المتصلة بآفة احتفاظ الرحم بأحشاء الحمل (**Retained products of conception**) **403** حالات **(20.6** في المائة**)** تليها بطانة الرحم افرازية الحالات **363 (18.5%).** الآفات الخبيثة كانت أكثر شيوعاً في المرضى الذين تتراوح أعمارهم بين **40** سنة وأكثر وكانت تتألف **9** حالات **(0.4** في المائة**)** من جميع الحالات**.** التهاب بطانة الرحم كانت حالات **29** وكانت أقل الحالات **(1.8** في المائة**)** تليها حالات سرطان بطانة الرحم **9 (0.4** في المائة**).** الاستنتاجات**:** دراسة نسيجية لبطانة الرحم ينبغي أن يتم في المرأة التي تعاني من نزيف رحمي غير طبيعي وإلى استبعاد الحالات الورمية والغير الورمية خصوصا المحتفظ باحشاء الحمل والتضخم والآفات الخبيثة. حوالي **40%** من الخزعات لبطانة الرحم كانت خالية من النتائج المرضية والتي تعكس نسبة عالية لأسباب النزيف الرحمي غير طبيعي من امراض خاج الرحم**.** الحالات المرتبطة بالحمل كانت الأعلى بين نتائج العضوية التي تسلط الضوء على الحاجة إلى المزيد من الرعاية قبل الولادة**.**