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A Retrospective Study Of Ectopic Pregnancy.

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ABSTRACT

The ectopic pregnancy (EP) is a well known risky and life-threatening situation taking place in 1-2 % of all pregnancies. The most frequent ectopic implantation site is the fallopian tubes, the other sites are representing 10% of EPs happen in the cervix, myometrium, ovaries, interstitial fragment of the tube, in a scar of cesarean section or any where inside the abdomen. A retrospective cross sectional study was carried out on EPs admitted to the department of Obstetrics and Gynecology at Al-Mosul Teaching Hospital. Cases who are admitted as suspected ectopic and complete their management were involved in the study. We enrolled (167) cases amongst (29828) mature pregnancies admitted at the same period of time. The data obtained include the incidence of EPs during three years period, distribution of EP according to age, seasonal variation, site, etiological factors, contraception, clinical features, duration of amenorrhea and diagnostic aids. Execl software 2010 was used to calculate ratios. The overall incidence of three years is 0.55%, mostly 58.68% in the (20-29) years age group, dominates in Autumn season (40.11%), the commonest site of EP was tubal (97%) and the commonest site in the tube was ampullary (56.28%), and the right side affected more in (55.08%). Primigravida 25.74%, the history of infertility 20.35% and history of abortion16.76%. Abdominal pain, vaginal spotting, pain on cervix movement and lower abdominal tenderness are in ratios of 88.75%, 78.75%, 72.5% and 63.75% respectively. The common diagnostic tool is ultrasound with pregnancy test (36.25%). Our work confirm the increasing incidence of EP and tubal pregnancies are the most frequent.

Keywords: ectopic pregnancy, Incidence, retrospective review

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INTRODUCTION

Ectopic pregnancy (EP) is the consequence of implantation and maturation of the fertilized ova outside the endometrial cavity, which eventually ends in the death of the fetus. Without timely diagnosis and management, the EP can become a life threatening condition.[1] It is refer to the Greek word "ektopos," meaning out of place, referring to the blasto-cyst implantation outside the endometrial cavity with over 95.5% implanting in the Fallopian tube, where the fetus or embryo is absent or stops growing.[2,3]

Hence, it is a vital reason of maternal morbidity and mortality in the pregnancy during the first trimester; accounting for almost 10% of all maternal deaths.[4]

Incidence: EP is a nearly pregnancy serious complication. In low income countries it is a main cause of maternal mortality, although exact incidence rates are unknown, due to frequent misdiagnosis. For the same reason case fatality rates are also not without bias, but reported between 1 and 3%.[5] In high-income countries, early diagnosis can often be made using ultrasound and serum human chorionic gonadotropin level.[6]Among the Europeans and North Americans, the incidence of EP has tripled over the last 30 years.[7] It is frequent in developing countries due to the high rates of pelvic infections, unsafe abortions, and puerperal sepsis.[8,9]

Location: The location of EP varies, but the most frequent site is the salpengian tube, predominantly the ampullary segment. Implantation of the fertilized ova apart from the fallopian tube, whether in the cervix, ovary, myometrium, abdominal cavity, interstitial (i.e., intramuscular/ proximal portion of fallopian tube) or coincidentally with an intrauterine pregnancy occurs in less than 10 % of the EPs.[10] The coexistence of a intrauterine normal pregnancy together with pregnancy in any of these previous sites known as Heterotopic pregnancy (HP). The Cornual type of EPs are those implanted in a horn of an atypical uterus (i.e., unicornuate, bicornuate, didelphys or septate uteri); these do not uniformly require intervention and will not be included in this review.[11]

Etiology: The main risk factors of EP are different in various countries due to different cultural and social characteristics. Determination of main risk factors of EP leads to a rapid diagnosis and an upgrading in the strategies for avoidance.[12] Although several patients may not have any risk factor and yet develop EP.[13] In theory, anything that delays the migration of the embryo to the endometrial cavity could prompts women to EP. Reported important etiological factors for EP include pelvic inflammatory disease (PID), post-abortal sepsis, puerperal sepsis, previous EP, previous pelvic surgery and the uses of contraceptive device.[14] Presence of history of infertility and congenital defects of fallopian tubes consider also as other risk factors. Retrograde embryo migration into diseased tubes is believed to be the main cause of EP among women undergoing in-vitro fertilization and embryo transfer.[15]

Symptoms and signs: The clinical feature of an EP is inconsistent with pelvic or abdominal pains in almost all cases. The symptoms could be acute, like a short period of amenorrhea (5-8 weeks), irregular scanty vaginal bleeding of dark blood with abdominal and shoulder pain. Secondary amenorrhea and abnormal vaginal bleeding; dizziness, and/or syncope are present and represent advanced stages of intra-peritoneal hemorrhage following rupture.[16,17] Ruptured EP leads to the acute onset of abdominal pains and cardiovascular collapse, and without prompt intervention, can invariably lead to death.[17] The chronic symptoms including those recovered from the preceding attacks of acute pain, amenorrhea, vaginal bleeding, dysuria, lower abdominal pain, the frequency of micturition or retention of urine and rectal tenesmus.[18]

Diagnosis: The most common diagnostic tool used in the detection of early EP is serial (β-hCG) measurement. In early pregnancy, the level of β-hCG should be twofold roughly every 48 hours. After a miscarriage, it drops quite rapidly. If it rises gradually or continues around the same level over this time, this can mean a pregnancy is failing or EP. A single serum measurement of β-hCG concentration may not show the location of the gestational sac.[19,20] In the US this is combined with an aggressive strategy of interference by uterine curettage to differentiate a non-viable intrauterine pregnancy (IUP) from an EP. Trans-abdominal scanning by non-specialists is still widely used in emergency room assessment in the US. A different approach has been taken in Europe where Early Pregnancy Assessment Units (EPAU)'s have been initiate to provide a specialist assessment. The ideal option for the first-line diagnosis of a woman who is symptomatic in the first trimester is transvaginal ultrasound scanning (TVS).[21] In cases of suspected EP, serial hCG measurement may be combined with an extended period of observation and follow-up scanning after an interval of a week or more.[21] Serum

progesterone concentration lower than 15 ng/ml may be valuable in chosen patients if the diagnosis is doubtful after checking β-hCG level and transvaginal sonography has been performed.[22] Laparoscopy is now rarely indicated unless a woman is symptomatic or hemodynamically unstable.[23] Combined transvaginal ultrasonography and serial quantitative β-hCG measurements are approximately 96% sensitive and 97 % specific for diagnosing EP.[24]

Treatment: Rupture of EP will determining whether the pregnant can be surgically managed or not.[17] The treatment option affected by clinical state, a reproductive wish of the patient, site of the ectopic gestation, as well as the facilities available.[7] However, surgical treatment still remains the norm due to the challenge of deplorable diagnostic tools, inadequate capability to deal with emergencies and consequential burden of increased both maternal morbidity and mortality with consequent reproductive failure.[25,26] Expectant management is effective in 47% to 82% in managing EP. A good candidate for expectant management has a β-hCG rank lower than 1,000 mIU/mL (1,000 IU/L) and declining, an ectopic mass less than 3 cm, no fetal heartbeat, and has agreed to comply with follow-up requirements.[27,28] Methotrexate drug is one of the folic acid antagonists. Methotrexate acts by deactivateing the dihydrofolate reductase enzyme, which reduces tetrahydrofolate levels (a cofactor for deoxyribonucleic acid and ribonucleic acid synthesis), thereby disrupting rapidly dividing trophoblastic cells.[29] The therapy includes regimens of either single dose or multiple dose had an overall 89% crude success rate. The methotrexate's side effects consist of bone marrow suppression, elevated liver enzymes, rash, alopecia, stomatitis, nausea, and diarrhea. The time to the resolution of the EP is 3-7 weeks after the therapy. Other therapeutic agents include hyperosmolar glucose, prostaglandins, and mifepristone.[30] Although laparotomy with salpingectomy, or salpingo-oophorectomy surgery, and the total abdominal hysterectomy done as surgical intervention, the laparoscopy with salpingostomy, without fallopian tube removal, has become the preferred method of surgical treatment.[31]

Aim: To review the incidence, locations, etiology, symptoms and signs, methods of diagnosis and types of treatment.

MATERIAL AND METHOD

A retrospective cross sectional study was carried out on ectopic pregnancies admitted to the department of Obstetrics and Gynecology at Al-Mosul Teaching Hospital. Cases who are admitted as suspected ectopic and whose symptoms subsided later and cases of suspected where the patient took her own discharge before completion of management not involved in the study.

Confirmed ectopic cases who received treatment at this department totaled (167) cases amongst (29828) mature pregnancies admitted at the same period of time. The information obtained include the incidence of ectopic pregnancies during three years period, distribution of EP according to age, seasonal variation, site, etiological factors, contraceptions, clinical features, the duration of amenorrhea and diagnostic aids. Execl software 2010 was used to calculate ratios.

RESULTS

The incidence of EP during three years period

The incidence of EP were distributed during three years period in the manner shown in table (1) and appear as a steady rise in the incidence was noted from 1989 onward.

Table (1): The incidence of EP during three years period.

year	No. of mature pregnancy	No. of EP	The incidence of EP
1989	9276	43	0.46
1990	10117	55	0.54
1991	10435	69	0.66

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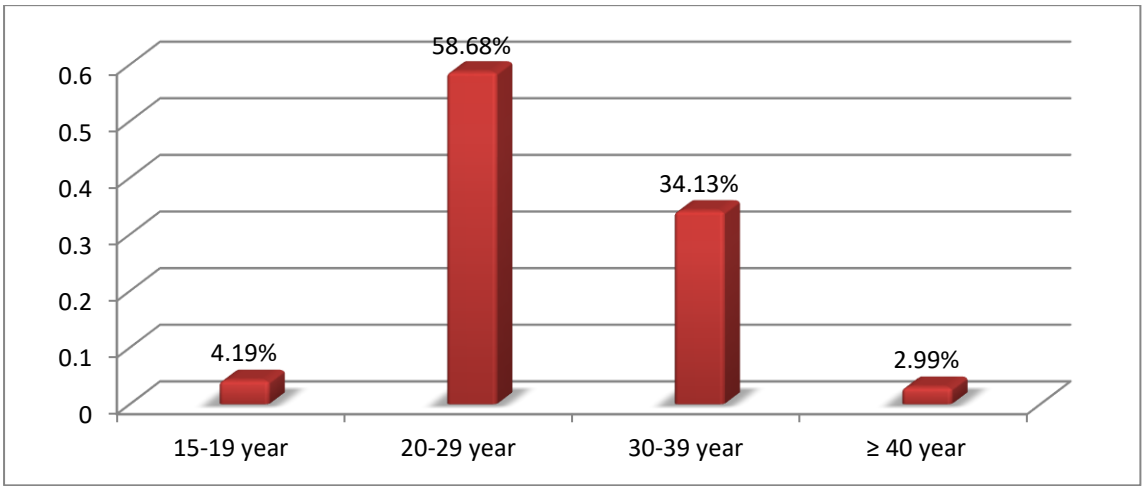
Distribution of EP according to age

The EP was commonest in patients at peak reproductive period (20-29) years, being 98 out of 167 cases (58.68%), followed by patients between (30-39) years of age (57 cases, 34.13%) as it shown in figure (1), also it was comparatively rare in extreme reproductive periods, only 5 cases (2.99%) over the age of 40 and 7 cases (4.19%) in young teenagers.

Figure (1): distribution of EP according to age.



Distribution of EP according to seasonal variation

There was a considerable disparity in the incidence of EP and the season of the year, this finding was constant throughout the three years study. The highest incidence was noted during the Autumn season (67 cases, 40.11%), notably towards the end of the season. There was a sharp decline during the winter season (35 cases, 20.95%). The level rises slightly in the spring season (41 cases, 24.55%), but noted to be at its lowest in the summer (24 cases, 14.37%).

The incidence compared to mature pregnancies was found to be as high as (0.94%) in the Autumn, dropping to (0.29%) in Summer.

Table (2): Distribution of EP according to seasonal variation

Cases	Seasons			
	Autumn	Winter	Spring	Summer
No. of EP	67	35	41	42
No. of deliveries	7122	7093	7446	8167
Total EP (%)	40.11%	20.95%	24.55%	14.37%
EP/mature pregnancy (%)	0.94%	0.49%	0.55%	0.29%

Distribution of EP in relation to the site

At operation, the commonest site of EP was tubal (97%) and the commonest site in the tube was ampullary (56.28%), Isthmus (31.13%), Fimbria (9.58%), Ovarian pregnancy and the corneal site (1.19%), Rudimentary horn (0.59%) this clear in the Figure 2-a.

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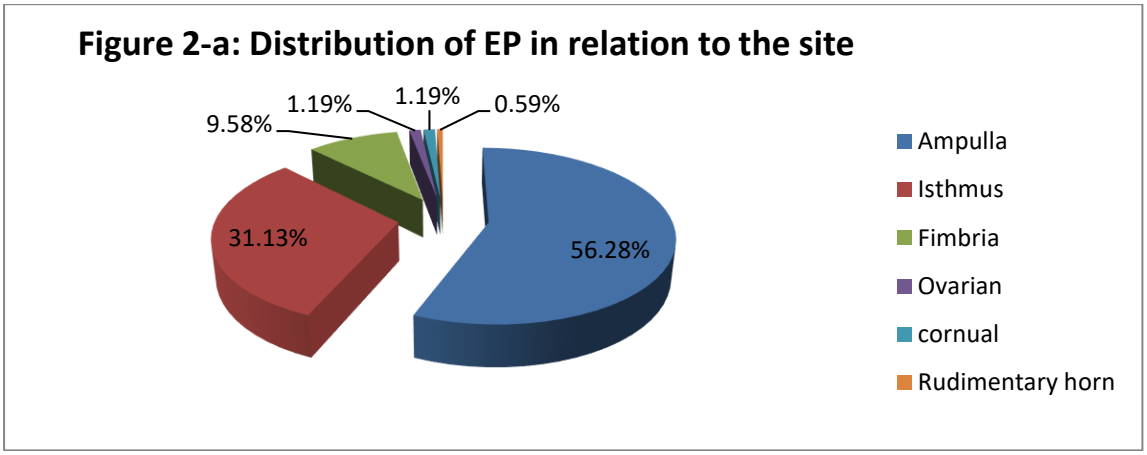
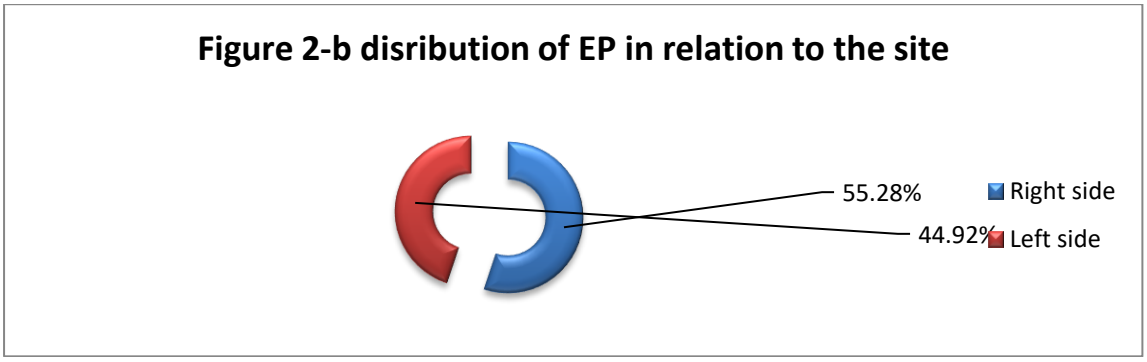
Figure (2-a): Distribution of EP in relation to the site



While the Figure 2-b illustrates that the EP was more common on the right side (55.08%) than the left (44.91%).

Figure (2-b): Distribution of EP in relation to the site



Incidence of EP in relation to etiology

History of infertility whether primary or secondary was a fairly common feature in the patients. Amongst the 167 cases examined, there were (34 cases, 20.35%) patients who had a history of infertility out of these patients only (9 cases, 5.38%) were receiving various kinds of fertility drugs.

There were (43 cases, 25.74%) Primigravida patients and the rest (124 cases, 74.25%) were of a parity between (1-10).

History of recurrent pelvic infection was present in (13 cases, 7.78%). There were 28 cases (16.76%) with history of abortion ranging from (1-4). There was one patient with history of previous EP 0.59%.

History of previous surgical abdominal operations was detected in 18 cases (10.77%). Appendectomy 9 cases, myomectomy 3 cases, and each of cholecystectomy, tubal surgery and ovarian cystectomy 2 cases.

Table (4): Incidence of EP in relation to etiology

Etiologies		cases	%
History of infertility		34	20.35%
Primigravida		43	25.74%
History of recurrent pelvic infection		13	7.78%
History of abortion		28	16.76%
History of previous EP		1	0.59%
History of previous surgical abdominal	Appendectomy	9	5.38%

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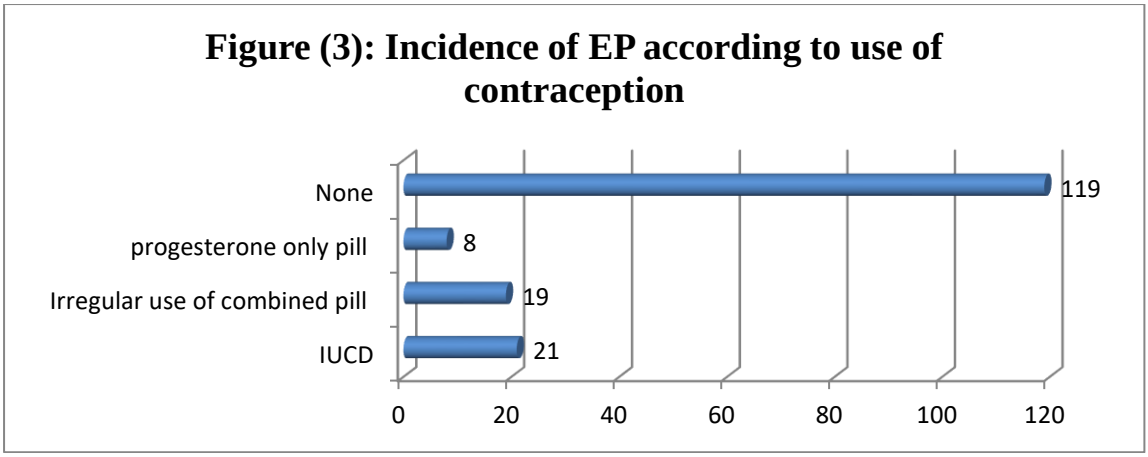
operations	Myomectomy	3	1.79%
	Cholecystectomy	2	1.19%
	tubal surgery	2	1.19%
	ovarian cystectomy	2	1.19%

Incidence of EP according to use of contraception

The incidence of IUCD users in this study was found to be 12.57%, while 19 cases were found to be using the combined pill randomly. Very few patients (8 cases) admitted to use progesterone only pill as a method of contraception 4.79%, while the majority (119 cases) had not used any contraceptions 71.25%.

Figure (3): Incidence of EP according to use of contraception

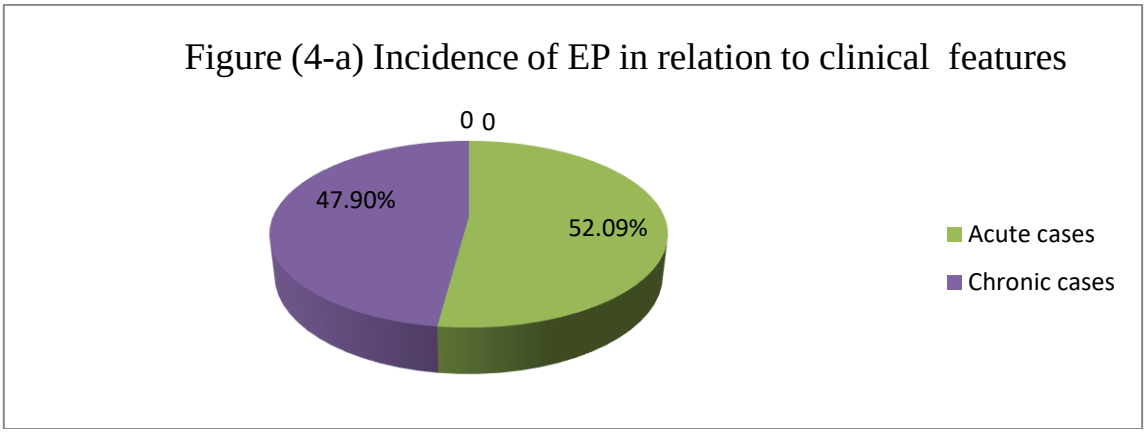


Incidence of EP in relation to clinical features:

Figure (4): Incidence of EP in relation to clinical features

The number of patients with acute ruptured EP was 87 patients representing 52.09% . most of them were in a collapsed state as shown in figure (4-a).

Figure (4-a): Incidence of EP in relation to clinical features



The figure (4-b) demonstrates that the number of patients with chronic EP was 80 cases (47.90%) of those, abdominal pain was the most frequent symptoms in 71 cases (88.75%), with some degree of vaginal spotting or bleeding in 63 cases (78.75%).

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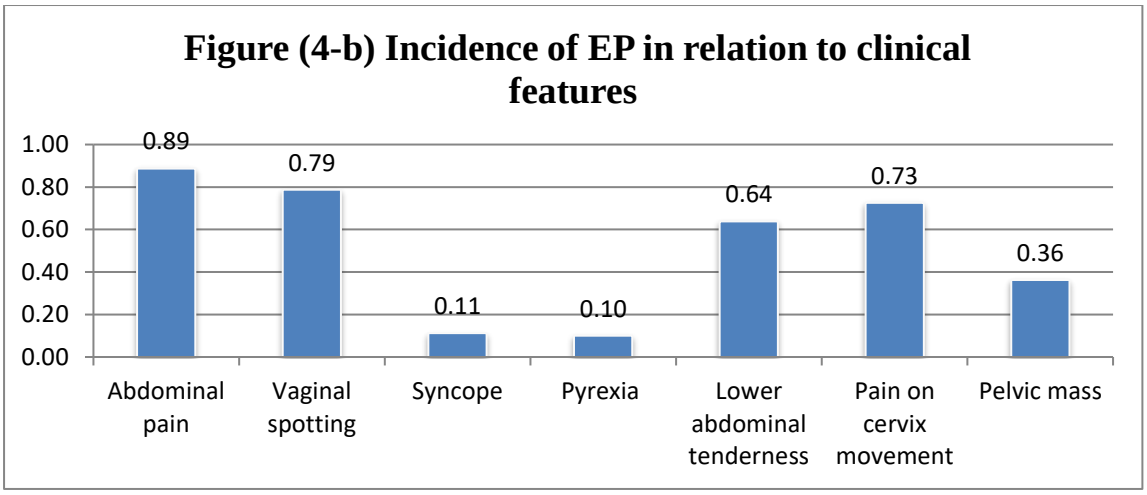
Feeling of faintness in 9 cases (11.25%), most of them were in stable general condition. Pyrexia developed in 8 cases (10%) lower abdominal tenderness and muscle guarding were present in 51 cases (63.75%).Pain on movement of cervix was observed in 58 cases (72.5%).A pelvic mass or fullness was palpable in 29 cases (36.25%).

Figure (4-b): Incidence of EP in relation to clinical features

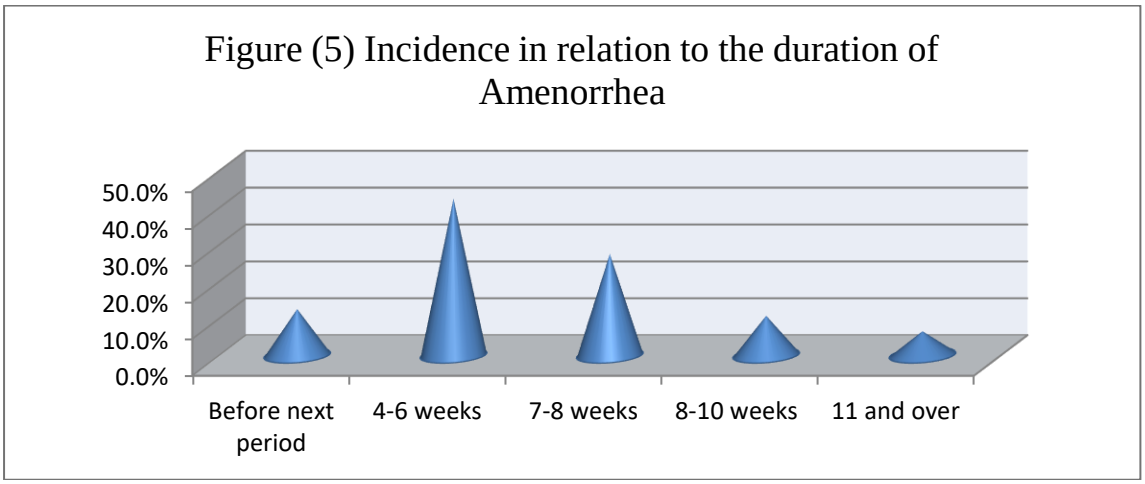


Incidence in relation to the duration of Amenorrhea:

The period of amenorrhea varied from (4-12) weeks and never more than 12 weeks amenorrhea in the studied group. There was a significant number of patients 21 cases (12.57%). Whose next period was not due before they presented with ruptured EP. But the commonest duration of amenorrhea was (4-6) weeks being 71 cases (42.51%), followed by period of (7-8) weeks 46 cases (27.54%).

The incidence of EP in patient with history of (8-10) weeks amenorrhea was 18 cases (10.77%).

The smallest number of patients was understandably those with period of amenorrhea exceeding 10 weeks 11 cases (6.58%).



Incidence of EP in relation to the diagnostic aids:

Because of the large incidence of acute EP that were admitted 87 cases (52.09%) and the urgency for laparotomy, the clinical features were usually the only guideline in the diagnosis together with history of amenorrhea, therefore the number of patient who underwent any type of investigation was few when the presentation was acute.

It can be seen that the highest number of cases were diagnosed by ultrasound with pregnancy test (absence of an intrauterine gestation sac, presence of an adnexial mass, and presence of cui-de-sac fluid, with +ve pregnancy test in 29 cases (46.25%). The diagnosis was made by laparoscopy in 23 patients (29.75%). Ultrasound alone used in diagnosis of 15 patients (18.75%). Culdocentesis was the least common diagnostic procedure being used in 13 cases (16.25%).

Table (4): Incidence of EP in relation to the diagnostic aids

Diagnostic aids	No. of patients	Percentage
Ultrasound +pregnancy test	29	36.25%
Laparoscopy	23	28.75%
Ultrasound	15	18.75%
Culdocentesis	13	16.25%

DISCUSSION

This work aimed to evaluate the incidence of EP in a major hospital and study the trend in the incidence and discuss the various associated factors in the area served by Al-Mosul Teaching Hospital.

The overall incidence of EP was found to be 0.55% of all deliveries admitted over three years period (1989-1991), this is parallel to a study done in North America climbed from less than 0.50 % of all pregnancies in 1970 to 2% in 1992.[33,34] In this study the incidence rises from 0.46% in 1989 to become 0.66% in 1991.The same results obtained in northern Europe between 1976 and 1993, the incidence boosted from 11.2 to 18.8 per 1,000 pregnancies, and in 1989 the number of admissions to US hospitals for EP increased from 17,800 in 1970 to 88,400.[35,36]Al-Turki[37] reported that there is an increasing rate of EP in Arabian countries like the Kingdom of Saudi Arabia. Simultaneously, Calderon *et al*.[38] noticed that the EP rate was 11.2 per 1000 pregnancies recorded in California from 1999 to 2000. Although study done by Farquhar 2005[39] suggested that the incidence of EP is increased among patients over 35year of age, our study show contrary observations as 58.68% of patients belonged to age interval of (20-29) and increasing with advanced age. Similar results showed that the majority of patients 61.1% was below the age of 30 years.[37] Furthermore, previous studies which found that the risk of EP increases with advancing maternal age.[40,41] This is could be due to possible scarring of the tube from PID and altering in the tubal function that delay the ovum transport and tubal implantation. The relation of seasonal variation was very clear in our study with the peak of EP occurred in the Autumn, reaching a maximal incidence of 0.94% of all deliveries. The explanation for this is difficult with no published data about relation to season. The commonest site of EP as observed in this study is the fallopian tube 97% of cases, ampullary was 56.28%, Isthmus 31.13% and Fimbria 9.58%, this agrees with report from some Nigerian studies.[7,42]. A study in France reported 95.5% tubal EP.[43] This is consistent with most Nigerian studies.[7,44] In a similar French study, the ampulla was reported as the commonest site with 70% of cases; followed by isthmus (12%) and Fimbria 11.1%.[42,45] The right sided fallopian tube was included in 62.1% of all the tubal EP in a Nigerian work, while the tube in the left side was affected in 33.5% of cases. Similarly, the right and left fallopian tubes were respectively affected in 54.6% and 34.9% in Benin City,[46] and 69.4% and 30.6% in Nnewi.[7] this corresponding to our data 55.28% in right side and 44.92% in the left, which may be related to frequent ovulation that occur in the right one Elderly Primigravida remains a high risk pregnancy and the incidence is high.[47]Also in a retrospective study of all cases of EP admitted and managed at Ebonyi State University Teaching Hospital (EBSUTH) over a 10year period (June 1, 2002 to May 31, 2012) the finding was 32.68% of cases was Primigravida.[48] These was in compliance with ours 25.74%. In some other Nigerian health institutions, low parity was found to constitute a high risk group.[49,50] Also patients evaluated for an EP at the university hospital of Pennsylvania have history of Primigravida of 50.98% .[51] The correlation between previous infertility and the occurrence of EP has been well documented.[52,53] Infertility may be cause by tubal damage resulting from prior EP and/or surgical treatment. Tubal damage can disturb the passage of the zygote through the fallopian tube and into the uterine cavity, and thus predisposes women to another EP.[54,55] This correlation appear in this study up to 20.35% of cases. In our work, history of recurrent pelvic infection was present in 7.78%. that is analogous to outcome of the retrospective descriptive study which conducted from May 2002 till April 2004 at Madina maternity and children hospital in Saudi Arabia that figured as 10% of recorded EP.[56] Although several studies have reported a strong association between prior PID and EP.[57-59], Samantha *et al*[51] found no significant difference between the groups in terms of gonorrhea, Chlamydia, or PID,

either historically or at the time of diagnosis, the possible explanation is the discrepancy in the diagnosis of PID may occur. EP have a high incidence of recurrent EP.[60] Moreover, JOSHUA's study[61] show significant association of previous EP with recurrence by OR=8.3 and confidence interval ranging from 6.0 to 11.5. While the outcomes of current study show that just one female had history of previous EP representing 0.59% of the incidence. In a case-control study[51] involving three hundred six women with single EPs and 61 women with recurrent EPs. The history of prior spontaneous abortion was 13.04% and history of prior elective abortion 17.9%, that simulate our finding regarding the abortion as a risk factor for EP in 16.76% of the study sample. Concerning the use of IUCD, the current study point up that 12.57% of EP had use IUCD, The increasing rates of EP among IUCD users was believed to be associated with several factors. First, the presence of the IUCD inside the uterus may cause irritation of fallopian tubes and prevent the ova from going into the uterus. Second, the IUCD can only prevent intrauterine pregnancy, not EP. Third, bacteria brought in through IUCD insertion may cause Fallopian tube infection, which increases the risk of EP. This risk among IUCD users is 2.94-4.5 times that in nonusers.[62] and 4-5 fold increased risk of a subsequent EP.[40,63] While in an another study no evidence proposed that the currently available IUCDs cause PID, the explanation for the mistaken association of IUCDs with EP may be that when an IUCD is present, EP occurs more often than intrauterine pregnancy.[64] Among women using the "progesterone-only" form of oral contraceptive, 4.79% of EP was noted, suggesting interruption in ovum transport through the tube since it is affected by estrogen and progesterone, which consistent with the findings of study done in Nigeria showing relation by 4%.[65] EP most commonly diagnosed from the 6th to 9th week of gestation; most pregnant present with nonspecific complaints.[66] The symptom triad consisting of mild vaginal spotting of blood in the pregnancy (first trimester) with dull pelvic pain, and secondary amenorrhea may indicate EP but can also arise in a normal pregnancy or as an outcome of early miscarriage. Further suggestive manifestations consist of abdominal pain that radiating to the shoulder(s) region, guarding of abdomen or an acute abdomen pain on displacement of the vaginal portion of the cervix.[67,68] In the current study abdominal pain was 88.75%, spotting 78.75%, pain on cervix movement 72.5%, and abdominal pain 63.75%. Similarly in a retrospective study, the results were; abdominal pain 80.0%, amenorrhea 79.0%, vaginal bleeding 65.4%, fainting attack/dizziness 37.1% and shock 10.2%. The amenorrhea ≤7 weeks duration represent 53.2% of cases and 8–12 weeks represent 45.9%.[69] The figure was larger than that of our work in which amenorrhea 4-6 weeks represented 42.51% of cases. Other study showed that 100% of EP had amenorrhea, abdominal pain in was present in 82% of patients, 62 % of patients had vomiting and 74 % had per vaginal bleeding.[70] The problem of EP is essentially a diagnostic one. The diagnosis of tubal pregnancy can be done with considerable degree of accuracy if the clinician has a significant indicator of suspicion for it. In the present work, the ultrasound with pregnancy test represent 36.25% of cases.

The β-hCG levels aid in understanding ultrasound findings. In a normal intrauterine pregnancy, these levels would increase by at least 53% every two days, peaking at a level greater than 100,000 mIu/ml (100,000 IU/l).[71,72] β -hCG levels alone cannot differentiate between ectopic and intrauterine pregnancy, and serial β-hCG levels that do not increase appropriately in a woman with suspected EP are only 36% sensitive and approximately 65% specific for detection of EP.[73] Laparoscopy used in the diagnosis and identification of EP for many years. Since the first excision of a tubal pregnancy through a laparoscope by Manhes and Bruhat in 1980,[74] it has been used with increasing frequency in the diagnosis and surgical treatment of EP, which represent 28.75% of cases in our study. Culdocentesis was the least common diagnostic procedure being used in 16.25% of cases. Results of Culdocentesis will be positive in more than 90% of ruptured EPs. A positive test results when the aspirated non clotting blood that accumulated in the Cul-de sac was more than 0.5 ml. The presence of fibrinolytic proteins in the peritoneal fluid prevent clotting of blood aspirated from the abdominal cavity from be in. Non-clotting blood is also aspirated in more than 60% of unruptured EP; intermittent episodes of small-volume bleeding can lead to pooling of blood in the cul-de-sac, without development of peritoneal signs.[75]

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