www.jmscr.igmpublication.org
Impact Factor 5.84
Index Copernicus Value: 83.27
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v5i6.189

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Original Research Article

Clinical Profile and Outcome of Pregnancy of Unknown Location in A Tertiary Care Centre

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Abstract
Objectives: *To study clinical profile and outcome of pregnancy of unknown location (PUL) in a tertiary care centre.*
Methods: *Study group comprised of 61 PUL cases in whom pregnancy test was positive but there was no ultrasound evidence of intrauterine (IUP) or extrauterine pregnancies (EP).Their clinical profile studied and outcome observed. Hemodynamically stable cases were followed up with serial blood human chorionic gonadotropin (betah CG) estimation and transvaginal ultrasound (TVS) until reaching the final outcome like EP, viable IUP, failed pregnancy or persistent PUL.*
Results: *Majority of patients presented with abdominal pain and vaginal bleeding. Maximum incidence was noted between 21-30 yrs of age. 57.4% of study subjects were nullipara, h/o infertility treatment was present in3.3% cases and 6.6% had previous history of EP. Out of the 61 women studied 36.1% ended up in EP, 32.8% in normal (IUP) and failing pregnancy around 31.1%. Majority required 2 values of hCG and 2TVS.*
Conclusion: *Most PULs are not aggressive but EP can be a life threatening outcome and its diagnosis is a biggest challenge. Prompt follow up with Ultrasound scanning (USS) and beta HCG is the mainstay in diagnosis and management of PUL. The help of an expert sinologist can reduce the incidence of PUL. Apelvic examination to assess the size of the uterus and delaying of USG till 7 weeks of gestation in asymptomatic women can to some extent reduce the incidence of PUL.*
Keywords: *Discriminatory zone. Gestational sac, HCG, Ectopic pregnancy.*

Introduction

The PUL is defined as the situation where the pregnancy test is positive but there are no signs of IUP, EP via TVS [(1)]. This is a descriptive term rather than a pathological entity. Up to 31% of women attending early pregnancy assessment centers have PUL though an experienced sinologist can reduce this to around 10%. Incidence of PULs in different studies range from 5-42% [(2)]. The increasing prevalence of PUL is due to easy access to urine pregnancy tests, better availability of ultrasound scans and anxiety of the women to confirm a pregnancy at the earliest.

In the first trimester about 25% of women experience vaginal bleeding. Nearly 50% of it will have abnormal outcome and 50% will continue to term [3]. Before embryonic stage a quantitative estimation of serum beta hCG and TVS is accurate method of identifying normal gestation. The discriminatory zone values commonly cited as=/>1500iu/ml when an intrauterine gestational sac (IUGS) can be seen in TVS[4]. An EP is strongly suggestive when extraovarian adnexal mass is observed without IUGS and beta hCG above discriminatory zone. In viable IUP, hCG is anticipated to double every 2 days, known as doubling time. A minimal HCG rate of increase for a normal IUP is 24 % at 1 day and 53% in 2 days. Kadar et al was the first to describe minimal rate of increase for an IUP to be 66% over 2 days[5]. Initial serum hCG value alone is not predictive of outcome in PUL. Change in hCG value over time has been used to predict outcome in PUL. Sensitivity and specificity of combining TVS and beta hCG has been reported to range from 93-100% [6].

The four possible outcomes of PUL are failing PUL, IUP, EP or persistence as PUL itself [7]. The most common is resolving pregnancy, seen in 30-60% case either IUP or EUP where without treatment, hCG levels gradually decrease to <5 IU/L. Progression to IUP can occur in upto 30-37% where there will be doubling of hCG value and appearance of intrauterine gestational sac on TVS. Diagnosis of EP by TVS is based on detection of the extra uterine gestational sac and lack of hCG doubling time. Progression to EP is seen in about (7-20%) of PUL. A single visit approach management of PUL may miss EP. Persisting PUL account 0.1- 2% cases where hCG levels do not decrease, there are no signs or symptoms of pregnancy and the location of the pregnancy cannot be identified. Most PUL are not aggressive and represent either failing intrauterine or EP which are never visualized using TVS or IUP.

The first point to be considered regarding management is hemodynamic stability. If unstable, USS done to assess presence of free fluid in pelvis which will indicate ruptured EP. If stable then management is based on serial assay of hCG and repeated TVS[8]. Clinically stable women with a PUL may be managed expectantly, as expectant management of women with PUL is safe. Earlier diagnosis of EP may improve the success of conservative treatment of unruptured EP. Even though about 15% of ectopic pregnancy resolves spontaneously, correct diagnosis of EP is essential as there is no method to differentiate the high risk group that will develop tubal pregnancy which may eventually rupture.

Objectives

- To study the clinical profile and outcome of PUL in a tertiary care centre.

Methods

This descriptive study was conducted in the Department of Obstetrics and Gynecology, TD Medical College, Alappuzha during the period January 1st 2016 to August 31st 2016. Altogether 61 cases with positive pregnancy test without USS evidence of IUP/EUP studied. All cases were admitted. The qualitative variables studied were age, parity, gestational age, past obstetric, medical and family history. General, systemic and pelvic examination done. Serial blood beta hCG was done to look for doubling time or decline. TVS with Doppler was done to detect presence or absence of gestational sac.

Statistical Analysis

Data was entered into a master sheet and necessary statistical tables were constructed. To test hypothesis, tests like Chi square test and Odds ratio were used.

Results

The majority of the patients were in the age group 21- 30 years (Table-1). About 57.4% were nullipara (Table-2). Main complaints were amenorrhoea, abdominal pain and vaginal bleeding (Table-3). Referral cases came to be

around 73.8%, 63.9% of the study subjects belonged to middle income category. Majority (50.8%) had O positive blood group. No contraception was used by 88.5% of ladies.

There was no history of infertility in96.7%.H/O previous abortion was present in 16.4 % and 83.6% did not give a history of abortion. None of the study subjects had history of pelvic inflammatory disease (PID) or tuberculosis. Previous h/o EP was present in6.6% women (Table-4). H/O previous tubal surgery was present in 1.6% cases (Table-5). 42 (68.9%) had hemoglobin level of >/= 11 gm%. Important clinical signs were abdominal tenderness, vaginal bleeding, brownish vaginal discharge, cervical motion tenderness, fornix tenderness, and presence of a mass in adnexa (Table-6).

Duration of hospital stay varied from 5-12 days. The outcome was EP in 36.1%, normal IUP in 32.8% and failing pregnancy in 31.1% (Table-7). There were no cases of persistent PUL. Two values of hCG and 2TVS could diagnose about 80% of IUP by 7days and 20% by10 days. Regarding EP, 87% was diagnosed by 2 USS and two values of hCG in 7 days. Almost all cases of failed PUL could be diagnosed with 2hCG and 1 TVS within 4-5 days. Out of the22 cases of EP, 8 cases needed surgery and others were managed by expectant or medial management.

Table -1 Age distribution

Age in years	Frequency	Percentage
< =21	11	18
21-30	40	65.6
> = 31 years	10	16.4
Total	61	100

65.6 % of the study subjects belonged to 21-30 years age group

Table-2 Parity

Parity	Frequency	Percentage
Nullipara	35	57.4
Para 1	19	31.1
Para 2	7	11.5
Total	61	100

Majority of the study subjects were nullipara.

Table-3 Presenting symptoms.

Symptom	Frequency	Percentage
Abdominal pain	24	39.3
Bleeding PV	17	27.9
Spotting PV	9	14.8
Brownish discharge PV	6	9.8
Back ache	1	1.6
Abdominal discomfort	1	1.6
Asymptomatic	3	4.9
Total	61	100

Abdominal pain &bleeding p/v were the major complaints.

Table-4. Previous history of ectopic pregnancy.

H/O Ectopic pregnancy	Frequency	Percentage
Nil	57	93.4
Medically managed	2	3.3
Managed expectantly	1	1.6
Managed surgically	1	1.6
Total	61	100

57(93.4%) of the study subjects did not have history of ectopic pregnancy.

Table -5. History of previous abdominal surgery

Abdominal surgery	Frequency	Percentage
Nil	52	85.2
Caesarean section	8	13.1
Tubal surgery	1	1.6
Total	61	100

8 (13.1%) of the study subjects gave history of previous caesarean section.

Table- 6 Clinical signs

Clinical signs	Frequency	Percentage
Bleeding PV	24	39.3
Abdominal tenderness	1	1.6
Brownish discharge	5	8.2
Cervical tenderness	1	1.6
Fornix tenderness	8	13.1
Fornix mass	8	13.1
No signs	14	23
Total	61	100

39.3% of the study subjects had bleeding PV on clinical examination.

Table- 7 Outcome of PUL

Outcome	Frequency	Percentage
Normal intra uterine pregnancy	20	32.8
Ectopic pregnancy	22	36.1
Failing pregnancy	19	31.1
Total	61	100

Ectopic pregnancy was the outcome in 36.1%.

Discussion

PUL is a condition where the pregnancy test is positive but no ultrasound indicator of IUP or EP. For those cases where TVS cannot locate pregnancy, serial blood beta hCG assays are necessary for diagnostic work up[9]. Studies showed that 8-31% cases reporting for USS assessment in early pregnancy unit may be initially classified as PUL [10]. Majority might be a resolving pregnancy where no treatment is needed and in some it can be very early IUP. Few can be ectopic which can be life threatening to the patient. Persistent PUL is extremely rare.

Maximum incidence was noted between 21-30 yrs of age being maximum period of infertility (65.6%). This age group accounts for maximum percentage of intrauterine pregnancy also[11]. Age>35 increase risk of PUL and EP (12). Out of the 61 women, 68.9% of women were housewives, 63.9% belonged to above poverty line, and 57.4% were nullipara. 3.3% had history of infertility. None of the study subjects gave history of PID or tuberculosis. Previous delivery was by caesarean section 13.1% women. History of abortion was there in 16.4% cases. Only 6.6% had previous history of EP. Previous h/o EP is a strongest risk factor for EP in future pregnancy[13]. Risk factors like previous surgeries were found to be significant. History of abortion was not found to be significant. 39.3% presented with abdominal pain as the first symptom. 39.3% subjects had vaginal bleeding. 68.9% of had haemoglobin level>/=11gm%.

A major challenge is the detection of early unruptured EP. The outcome can be successfully predicted by follow up and protocols of management have been chartered to manage the condition with minimal patient visit which involve repeated blood beta hCG estimation and repeated TVS. The reported outcome by various studies were 54-70% of women with PUL had a spontaneous resolving pregnancy[14], 30-37% of PUL turned out to be early IUP and 8.1% - 42.8% turn out to be EP [15]. Another study reported 50-70% of PUL turned out to failing pregnancies and 7-20% EP [16].

In our study duration of hospital stay varied from5-12 days. The outcome was EP in 36.1%, normal IUP in 32.8% and failing pregnancy in 31.1%. There were no cases of persistent PUL. Two values of hCG and 2 TVS diagnosed 80% of IUP by 7days and 20% IUP by10 days. Regarding EP,87% was diagnosed by 2 USS and two values of hCG in 7 days and 13%EP in 8-10 days. Almost all cases of failed PUL could be diagnosed with 2hCG values and 1 TVS within 4-5 days. Out of the 22 cases of EP 8 cases needed surgical treatment and others were managed either by expectant or medial management.

Conclusion

PUL accounts for about 8-31% of hospital admission. Fate of a PUL can be either complete resolution, developing in to viable IUP or ectopic pregnancy and few may persist as PUL. Incidence of PUL is increasing as we are doing very early USS for detection of pregnancy. By prompt follow up after admission, repeated USS and serial serum beta hCG estimation we can know the fate of PUL. This actually causes financial burden and psychological insult to the patient. A proper clinical examination can diagnose IUP and EP by assessing the uterus and adnexa so that we can delay USS to around 7 weeks of gestation and reduce the incidence of PUL. An experienced sinologist also has a role in reducing the incidence of PUL. Detection of ectopic pregnancy within the PUL group is a major challenge.

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