

Frequency of Outcomes of patients with Pregnancy of unknown location at a tertiary care hospital

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ABSTRACT

Background: A pregnancy of unknown location (PUL) is said to occur when empty uterus is seen on a Transvaginal Scan in a female with a positive pregnancy test with absence of signs of an intrauterine pregnancy (IUP) or an ectopic pregnancy.

Aim: To determine the frequency of outcomes of patients with pregnancy of unknown location at a tertiary care hospital.

Methods: The study was carried out at Department of Obstetrics & Gynecology, Lady Willingdon hospital, Lahore. It was a Descriptive case series conducted from 2021 to May 2022. 160 subjects meeting the inclusion criteria were enrolled in the study. A thorough history was obtained and levels of serum Beta-HCG recorded. Serum beta HCG levels of 25IU/L represented a positive pregnancy test. The follow up consisted of monitoring serum beta HCG levels after 48 hours and evaluation of findings of transvaginal ultrasound. The females were followed till they were placed in the category of failing PUL, an intrauterine pregnancy or an ectopic pregnancy. Data was collected from women categorized as having a PUL.

Results: In this trial, of 160 cases, it was seen that 109(68.13%) had amenorrhea whereas 51(31.87%) had bleeding at the time of presentation. Frequency of outcomes of patients with pregnancy of unknown location showed that 75(46.88%) had failing PUL, 19(11.87%) had ectopic pregnancy, 15(9.38%) had persistent PUL and 51(31.87%) had intrauterine pregnancy.

Conclusion: Failing PUL was the leading entity in cases of pregnancy of unknown location followed by ectopic pregnancy and persistent PUL. However, this data is primary and needs validation through some other local trials.

Keywords: Pregnancy of unknown location, outcome, failing PUL, ectopic pregnancy, persistent PUL

INTRODUCTION

Pregnancy of unknown location (PUL) is defined as occurring in a woman who has positive pregnancy test, but pregnancy cannot be seen sonographically¹. It is seen 8-10% of patients². PUL may turn out either to be an Intrauterine pregnancy (IUP), Failing PUL (F-PUL), Ectopic pregnancy (EP) and or a Persistent PUL (P-PUL)³. Most common outcome is a Failing pregnancy of unknown location which occurs in 44- 69% and 7-20% will later come out to be Ectopic pregnancy (EP). A balance has to be struck between late diagnosis of ectopic pregnancy and aggressive treatment of possible intrauterine pregnancy. Late diagnosis of ectopic pregnancy may result in more morbidity, mortality and has the potential to compromise future fertility of the female.

In many women with PUL, common presentation is that of lower abdominal pain or vaginal bleeding. The number of early pregnancies initially considered to be PUL within a unit has been seen to vary between 8% and 42%, although there is interobserver in locating the gestational sac between the operators⁴.

Prediction of fate of PUL can be made by use of serum beta-human chorionic gonadotropin hormone and ultrasound⁵. Discriminatory zone is the level of the level of b-chg. above which gestational sac is to be seen on USG. It has a sensitivity nearing 100%. With the help of high resolution transvaginal ultrasonography, the discriminatory levels of serum beta human chorionic gonadotropin hormone are seen to be around 1000-2400 I.U/L.⁶⁻⁷ In a study conducted by Ameer N, et al and colleagues, it was seen that in cases of PUL, 71.6% patients presenting with amenorrhoea, 50% had bleeding and 50% presented with pain. Almost half of the patients had failing pregnancy of unknown location and one third had intrauterine pregnancy⁸.

In a study done by Zubair S the mean serum beta HCG level was 1446±1079.63IU/L. Furthermore 6% of patients were diagnosed with pregnancy of unknown location (PUL). There were significant differences between the occurrences of different pregnancy sequel ($p=0.001$)⁹.

Thida W and colleagues in their study, found PUL cases rate as 9% out of all the PUL patients, half were of failing pregnancy. PUL patients that one tenth of the patients that ended in ectopic pregnancy had features like intrauterine pregnancy. Those ending up in IUP, one fifth had variable levels of Bhcg¹⁰.

In a study by Shanti Sri and colleagues, majority presented with bleeding amongst cases of PUL. Outcome was failing pregnancy in most of cases¹¹.

The rationale of this study is that the rate of PUL among women varies between 5 and 42% and is increasing with creation of increasing number of early pregnancy units,¹² and limited local data is available, so I have designed this study to determine the frequency of outcomes of patients with pregnancy of unknown location at our hospital. This would help us in generating local data so that it could prove useful in designing the best treatment modality for the patients¹³.

The objective of the study was to determine the frequency of outcomes of patients with pregnancy of unknown location at a tertiary care hospital.

Operational Definitions:

PUL – Pregnancy of unknown location: It is defined as failure to visualize an intrauterine pregnancy on transvaginal scan in a female with a positive pregnancy test with no evidence of retained products of conception and no visualization of extra uterine pregnancy.

Ectopic pregnancy: It is a definite extra-uterine mass seen on TVS. On follow up a heterogeneous mass is visualized in the adnexal region near the ovary, a mass having a hyper echogenic ring encompassing the gestational sac or the presence of embryo with or without a heartbeat in the adnexa along with raised serum beta human chorionic gonadotropins levels.

Failing pregnancy (FPUL): A FPUL was said to be occurring in a woman having a negative pregnancy test a fortnight after her initial consultation.

Persistent PUL: In a female with PUL if more than three levels of serial serum human chorionic gonadotropin (HCG) showed a variation of less than 15%, pregnancy location remains questionable on TVS, it was considered persistent.

Miscarriage: It was diagnosed on ultrasound having a mean gestational sac diameter of more than 25mm with absence of other structures and subsequently failed in the first instance.

Viable IUP: A VIUP is the presence of an intrauterine gestational sac having an embryo with a heartbeat present on ultrasonography.

Non-viable IUP: A NVIUP is a pregnancy that gets confirmation as intrauterine but then subsequently miscarries and meets criteria for a miscarriage.

PATIENTS & METHODS

This study was conducted at Department of Obstetrics &

Received on 07-06-2022

Accepted on 17-08-2022

Gynecology Lady Willingdon Hospital, Lahore. It was a Descriptive case series conducted from Nov 2021 to May 2022. Non-probability consecutive sampling was done. Sample size was calculated using WHO sample size calculator with expected prevalence of ectopic pregnancy in PUL patients, $P=9.3\%$, Confidence level= 95% , Absolute precision = 4.5% , ending up in a sample size of 160. All patients between 18 to 40 years meeting the operational definition of PUL were included in the study. Those having Intrauterine pregnancy, adnexal mass considered to be ectopic, free fluid in cul-de-sac on the initial scan, presence of retained products of conception seen through the speculum and hemodynamic ally unstable patient and those having an acute abdomen were excluded from the study.

After the approval from the Ethical Review Board and informed consent, 160 patients conforming to the operational definitions and the inclusion criteria were enrolled in the study. A thorough history was taken and salient features noted along with levels of serum b-HCG. Serum beta HCG levels of 25IU/L was considered a positive pregnancy test. Beta HCG levels were repeated after 48 hours according to study protocol. Monitoring consisted of measurement of serum beta HCG levels every 48 hours and making note of TVS findings. Followed up was carried out until the final diagnosis was made. It could be of a failing PUL, an intrauterine pregnancy or an ectopic pregnancy. Data collection was made from women classified as having a PUL. Females with a positive pregnancy test and early pregnancy complications were subjected to transvaginal ultrasound for knowing the the location and viability of pregnancy. Patients were followed by serum b-chg. and TVS. The discriminatory zone for the b-chg. was placed at 1500IU/L . TVS helped to rule out IUP, free fluid in pouch of Douglas and adnexal mass, including ectopic pregnancy (EP). A Performa was designed in which relevant patient information was recorded. All participants were followed by clinical evaluation, serial b-hCG and TVS twice weekly to monitor the outcome.

The data was analyzed using SPSS version 20. Frequency and percentage was calculated for qualitative variables including gender, parity, amenorrhea, bleeding on presentation, and outcomes of PUL. For the quantitative variables like age, and serum b-HCG value, mean \pm SD was calculated. Effect modifiers like age, BMI and parity were stratified to find out the effect of these on the outcome, through chi square ($p < 0.05$ was considered significant). Post stratification chi square test was applied taking p value < 0.05 as significant.

RESULTS

Age distribution indicates that $89(55.63\%)$ were between 18-30 years of age whereas $71(44.37\%)$ were between 31-40 years of age, mean \pm SD was calculated as 30.23 ± 4.37 years (Table 1). Parity distribution shows that $139(86.88\%)$ were between 1-3 parity whereas $21(13.12\%)$ had >3 parity, mean \pm SD was calculated as 2.66 ± 0.94 parity. (Table 2) Mean BMI of the patients was done, it shows that 30.89 ± 2.84 (Table 3). Frequency of amenorrhea and bleeding on presentation shows that $109(68.13\%)$ had amenorrhea whereas $51(31.87\%)$ had bleeding on presentation (Table 4). Frequency of outcomes of patients with pregnancy of unknown location shows that $75(46.88\%)$ had failing of PUL, $19(11.87\%)$ had ectopic pregnancy, $15(9.38\%)$ had persistent PUL and $51(31.87\%)$ had intrauterine pregnancy (Table 5). Effect modifiers like age. Parity and BMI were stratified to find out their effect on the outcome, through chi square ($p < 0.05$ was considered significant). Post stratification chi square test was applied taking p value ≤ 0.05 as significant (Tables 6-9).

Table 1: Age distribution

Age(in years)	n	%age
18-30	89	55.63
31-40	71	44.37
Total	160	100
Mean \pm SD	30.23 \pm 4.37	

Table 2: Parity distribution (n=160)

Parity	n	%age
1-3	139	86.88
>3	21	13.12
Total	160	100
Mean \pm SD	2.66 \pm 0.94	

Table 3: Mean BMI of the patients(n=160)

BMI	Mean	SD
	30.89	2.84

Table 4: Frequency of amenorrhea and bleeding on presentation(n=160)

Variable	n	%age
Amenorrhea	109	68.13
Bleeding	51	31.87
Total	160	100

Table 5: Frequency of outcomes of patients with pregnancy of unknown location (n=160)

Outcome	n	%age
Failing PUL	75	46.88
Ectopic pregnancy	19	11.87
Persistent PUL	15	9.38
Intrauterine Pregnancy	51	31.87
Total	160	100

Table 6: Mean serum HCG value(n=160)

Serum hCG	Mean	SD
	1456.86	134.011

Table 7: Stratification with regards to age

Outcome	Age in years		P value
	18-30 (n=89)	31-40(n=71)	
Failing PUL(n=75)			
Yes	40	35	0.58
No	49	36	
Ectopic pregnancy(n=19)			
Yes	13	6	0.23
No	76	65	
Persistent PUL(n=15)			
Yes	9	6	0.72
No	80	65	
Intrauterine Pregnancy (n=51)			
Yes	27	24	0.64
No	62	47	

Table 8: Stratification with regards to BMI

Outcome	Age in years		P value
	Upto 30 (n=86)	>30 (n=74)	
Failing PUL(n=75)			
Yes	43	32	0.39
No	43	42	
Ectopic pregnancy(n=19)			
Yes	11	8	0.69
No	75	66	
Persistent PUL(n=15)			
Yes	7	8	0.56
No	79	66	
Intrauterine Pregnancy (n=51)			
Yes	25	26	0.41
No	61	48	

Table 9: Stratification with regards to parity

Outcome	Parity		P value
	1-3 (n=139)	>3(21)	
Failing PUL(n=75)			
Yes	68	7	0.18
No	71	14	
Ectopic pregnancy(n=19)			
Yes	16	3	0.71
No	123	18	
Persistent PUL(n=15)			
Yes	12	3	0.40
No	127	18	
Intrauterine Pregnancy (n=51)			
Yes	43	8	0.51
No	96	13	

DISCUSSION

A pregnancy of unknown location is considered to be present when, in a female with a positive pregnancy test, an empty uterus is visualized on transvaginal ultrasound scan (TVS), with no signs of an extra uterine (ectopic) pregnancy. The prediction about clinical course of PUL can be made by measurement of serum beta- human chorionic gonadotropin (b-hCG) hormone and ultrasonography (USG). The concept of combined USG with serum b-hCG using discriminatory zone has been widely studied.

The rate of PUL in women presenting in early pregnancy units varies ranges from 5 to, 42% and is on the rise with establishment of early pregnancy units, however, limited local data is available. This study was designed to determine the frequency of outcomes of patients with pregnancy of unknown location at our tertiary care hospital. If patient is aerodynamically stable, PUL should be managed expectantly till the final outcome is known.

In this trial of 160 cases, 89(55.63%) of the patients were between 18-30 years of age whereas 71(44.37%) were between 31-40 years of age, mean±SD was calculated as 30.23±4.37 years, frequency of amenorrhoea and bleeding on presentation shows that 109(68.13%) had amenorrhoea whereas 51(31.87%) had bleeding on presentation. Frequency of outcomes of patients with pregnancy of unknown location at a tertiary care hospital shows that 75(46.88%) had failing of PUL, 19(11.87%) had ectopic pregnancy, 15(9.38%) had persistent PUL and 51(31.87%) had intrauterine pregnancy.

In a study conducted by Ameer N, et al and colleagues, it was seen that in cases of PUL, 71.6% patients presenting with amenorrhoea, 50% had bleeding and 50% presented with pain. Almost half of the patients had failing pregnancy of unknown location and one third had intrauterine pregnancy⁸.

In a study done by Zubair S the mean serum beta HCG level was 1446±1079.63IU/L. Furthermore 6% of patients were diagnosed with pregnancy of unknown location (PUL). There were significant differences between the occurrences of different pregnancy sequel ($p=0.001$)⁹.

Thida W and colleagues in their study, found PUL cases rate as 9% out of all the PUL patients, half were of failing pregnancy. PUL patients that one tenth of the patients that ended in ectopic pregnancy had features like intrauterine pregnancy. Those ending up in IUP, one fifth had variable levels of Bhcg¹⁰.

Shanti Sri A, et al reported that in his study on PUL, 10.42% were patients with early pregnancy, 11.6% patients with PUL; 92.85% with amenorrhoea, 87.5% with bleeding and 69.64% presented with pain. Outcome was failing pregnancy 48.83%, 36.04% had intrauterine pregnancy, 9.3% converted to ectopic pregnancy while 5.81% had persistent pregnancy of unknown location¹¹.

In a study by Lee Young and others¹² in those having a clinical suspicion of EP, one fifth were diagnosed to be PULs the most common outcome was that of miscarriage. A large number of women (42%) needed a repeat examination. They inferred that PUL has continued to be a challenging entity. Around 10% of cases of EP end up in an intervention.

The international society of ultrasound in obstetrics and Gynecology says that early pregnancy units should work towards keeping a PUL rate a less than 15%^{13,14}. The current values

recommended for discriminatory zone range from 1000–2400iu/15,16. Expectant management of PUL has been found to be safe for most of asymptomatic women who are hemodynamic ally stable.

CONCLUSION

We concluded that failing PUL was the leading outcome of unknown location followed by ectopic pregnancy and persistent PUL. However, our data is primary and needs validation through some other local trials.

Conflict of interest: Nil

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