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Original Research Article

A study on outcome of pregnancy of unknown location

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ABSTRACT

Background: Pregnancies of unknown location (PUL) are becoming more common as women presenting to early pregnancy assessment units when a pregnancy test comes positive but there is no evidence of an intrauterine pregnancy. The objective of the present retrospective study was to find out the outcome of women with pregnancy of unknown location presenting to a tertiary hospital in Northern Ireland.
Methods: This retrospective analytic study used medical record data between July 2019 and December 2021 from the Altnagelvin Area Hospital of Northern Ireland. TVUS was considered to diagnose the PUL and thereafter beta-human chorionic gonadotrophin (β-hCG) level was monitored as per institutional protocol. Expectant management was carried out until the pregnancy outcome was finalised. Using Statistical package for social sciences (SPSS) version 26, all collected data were analysed using the multinomial logistic regression.
Results: For the analysis among the 63 participants, 25.4% were primi gravida and 38.1% presented with 4-5 weeks of gestation. Pain abdomen and vaginal bleeding was represented by 20.6% and 52.4% respectively. Confirmed ectopic pregnancy was observed among 4.8% and was surgically managed. Also, persistent PUL was 7.9% and these cases were successfully managed by Methotrexate.
Conclusions: The large proportion will be biochemical pregnancy or intrauterine pregnancies, with a tiny fraction of ectopic pregnancies. Early detection of ectopic pregnancy is most challenging part among the women presented with PUL category.

Keywords: PUL, Ectopic pregnancy, Pregnancy of unknown location, Biochemical pregnancy, Transvaginal sonography

INTRODUCTION

Whenever a woman has a positive pregnancy test but no intra- or extra-uterine pregnancy is visible on transvaginal sonography, she is classified as having a pregnancy of unknown location (PUL). PUL is a term that describes a woman who does have a positive pregnancy test but still no pregnancy could be seen on transvaginal ultrasonography (TVUS).[1] The occurrence of PUL at centres specialising in early gestational review ranges from 8% to 10% and is primarily determined by the accuracy of the ultrasound scan conducted, that is determined by the examiner's perspective and the extent of precision of the machine in use.[2,3] Biochemical pregnancy is the most evident manifestation (44-69%), and 7-20% of women will be diagnosed with Ectopic Pregnancy (EP). A compromise must be struck between late EP diagnosis and overtreatment of potential IUP. Late detection of EP can

result in higher morbidity and death, as well as affecting the woman's future fertility. Determining serum beta-human chorionic gonadotrophin (β-hCG) hormone and TVUS predicts the PUL outcome.[4] Sole value of β-hCG to predict outcome in a PUL is of inadequate.[5] The notion of collective TVUS with serum β-hCG using prejudiced precinct has been extensively gauged.[6]

This retrospective study was envisioned to determine the pregnancy of unknown location PUL and its outcome. Additionally, it was intended to recognize its connotation with age and clinical features.

METHODS

The research approach was a single-centred retrospective hospital study from Altnagelvin Area Hospital of Northern Ireland. Data was acquired from database of medical records, ultrasound and biochemistry between July 2019 and December 2021 reviewing on cases diagnosed as PUL. All 63 patients came with 4-13 weeks gestation, lower abdominal pain and/or bleeding. The patients undergone investigations for β-hCG and TVUS. TVUS facilitated to exclude IUP, free fluid in cul-de-sac and adnexal mass, including EP. Clinical outcomes were defined under 4 viable categories i.e. Confirmed Ectopic Pregnancy, Presumed Ectopic Pregnancy, Miscarriage and Intrauterine Viable Pregnancy. TVS was the basis for defining PUL and women with positive pregnancy and assumed initial pregnancy complications were scrutinized by TVUS to find the site and possibility of pregnancy. Pregnancies that were not cited by TVS, the β-hCG taken from blood samples determined the presence. PUL was managed in accordance with the EPAU protocol. The patients were monitored and tracked for serial β-hCG and TVUS while waiting for the concluding diagnosis was established as a failing PUL, an intrauterine pregnancy (IUP) or an ectopic pregnancy. Treatment was completed with Methotrexate subsequently excluding contraindications. Surgical managing was well thought-out in haemodynamically unstable patients, unsuccessful to medical management or with EP underwent laparoscopy or laparotomy, and salpingostomy or salpingectomy bestowing to the medical evaluation.

Data were prepared and analysed over the SPSS version 26. Means and standard deviations were considered for continuous variables. Frequencies and percentages were calculated for categorical variables. Chi-square test was applied for univariate analysis of all the parameters. $P<0.05$ was considered as the level of significance.

RESULTS

The data analysed from 63 patients showed their mean age (years) 29.6±6.522 SD (range 18-43 years), majority 31 (49.2%) and 23 (36.6%) belonged to the age group of 21-30 and 31-40 years respectively. Patients' parity showed 19 (30.2%) were nulliparous and the rest 44 (69.8%) were multiparous. The 16 (25.4%) of patients presented with primi-gravida and rest where mostly 47 (74.6%) patients were multi gravida. Most patients presenting with 4-5 weeks of gestation were 24 (38.1%) followed by 6-7 weeks of gestation by 17 (27%) patients.

Patients presenting with symptoms of lower abdominal pain, vaginal bleeding and both (bleeding and pain) were documented to be 13 (20.6%), 33 (52.4%) and 17 (27%) respectively. patients having >5 mm incidental endometrium thickness among them 15 were obese. On the other hand, PUL outcome depicted 44 (69.8%) was failed PUL, followed by 11 (17.5%) intra uterine viable pregnancy.

Confirmed ectopic pregnancy was observed among 3 (4.8%) along with persistent PUL among 5 (7.9%) patients. Detailed frequency distribution for number of β-hCG and TVUS examinations undergone by the patients for PUL outcome determination are also shown in the Table 1. Five patients with persistent PUL endured therapeutic management with Methotrexate after ruling out ectopic pregnancy. Whereas, 3 patients with ectopic pregnancy underwent surgical management.

Table 1: Frequency and percentage distribution of variables (n=63).

Variables		Frequency	%
Maternal age (years)	≤20	5	7.9
	21-30	31	49.2
	31-40	23	36.6
	≥40	4	6.3
Gravida	Primi	16	25.4
	2	24	38.1
	3	14	22.2
	4	9	14.3
Parity	Nulli	19	30.2
	1	24	38.1
	2	14	22.2
	3	6	9.5
Period of gestation (weeks)	4-5	24	38.1
	6-7	17	27.0

Continued.

Variables		Frequency	%
	8-9	15	23.8
	≥10	7	11.1
Previous ectopic pregnancy	No	53	84.1
	Yes	10	15.1
Presenting symptoms	Lower abdominal pain	13	20.6
	Vaginal bleeding	33	52.4
	Pain and bleeding	17	27.0
Outcome	Failed PUL	44	69.8
	Intrauterine viable pregnancy	11	17.5
	Persistent PUL	5	7.9
	Confirmed ectopic pregnancy	3	4.8
No. of β-hCG	1	18	28.6
	2	17	27.0
	3	16	25.4
	4	4	6.3
	5	4	6.3
	6	3	4.8
	7	1	1.6
No. of TVUS	1	31	49.2
	2	19	30.2
	3	8	12.7
	4	5	7.9

Table 2: Multinomial logistic regression (n=63).

Effect	Model Fitting Criteria -2 Log Likelihood of Reduced Model	Likelihood ratio Tests		
		Chi-square	df	Sig.
Intercept	47.157[a]	.000	0	.
No. of βhCG	53.125[b]	5.969	3	0.113
No. of TVUS	56.816[b]	9.659	3	0.022
Gestational Age	83.994	36.837	18	0.006
Gravida	49.323	2.167	9	0.989
Parity	66.466	19.310	9	0.023
Previous ectopic pregnancy	48.037[b]	.881	3	0.830

A multinomial logistic regression model was fitted to know the effects of gestational age, gravida, parity, previous ectopic pregnancy, no. of β-hCG and no. of ultrasound on PUL outcome. Pearson chi-square statistic 49.998 (p=1.000) indicates that the model does fit the data well.

The chi-squared ratio test on the fitted model information yielded a value of 63.657 (p=0.035), indicating a good model fit. Satisfactory values were also obtained for the pseudo R-squared (Cox and Snell: 0.636, Nagelkerke: 0.761).

The likelihood ratio tests for the effects of the model and the partials in table shows that the independent variables no. of TVUS, gestational age and parity are statistically significant. Whereas, no. of β-hCG, gravida and previous ectopic pregnancy were non-significant.

DISCUSSION

PUL occurs when a confirmed pregnancy check is obtained but a TVUS does not reveal intrauterine or ectopic pregnancy, nor does it reveal the retaining of conception materials.[7] The prevalence of PUL at facilities specialising in the monitoring of early pregnancy is from 8% to 10% and is mostly determined by the precision of the TVUS done, which is determined by the investigator's competence and the instrument's precision.[2] The International Consensus on Ultrasound in Obstetrics and Gynecology established that earlier stage pregnancy facilities should aim for a PUL rate of less than 15%.[3] TVUS is the most effective means of determining the position of a pregnancy in its early stages. One experiment was carried out in London at a unit that specialised in early pregnancy revealed that TVUS correctly detected the pregnancy location in 91.3 % patients.[9]

PUL is not a diagnosis, and the patient should be monitored until a conclusive diagnosis can be made.[10] In PUL follow-ups, β-hCG is the most commonly employed biomarker. A single β-hCG serum dose cannot be used to forecast the outcome of a PUL; rather, it is utilised to determine if the obtained value is above or below the discriminating zone. The discriminating zone, also known as the discriminatory value, is the level of serum β-hCG at which an intrauterine gestational sac should be evident on TVUS.[11] When employing TVUS, most providers currently consider a discriminating zone between 1,500 and 2,000/2,500 mIU/ml of hCG.[12] An EP should be considered when the β-hCG level is well above the discrimination region and no intrauterine pregnancy is seen on TVUS; nevertheless, even if the TVUS does not show an IUP and the β-hCG level is above the discrimination region, it is feasible to have a feasible IUP. Embryos with heart activity have been seen in the follow-up of conceptions in which the embryonic sac wasn't really evident on TVUS and β-hCG levels were above 2,000 mIU/mL across numerous reports.[13-15] According to a finding, the discriminant level of β-hCG ought to be 3,510 mIU/mL to have a 99% chance of seeing an intrauterine gestational sac using TVUS.[14] Repeated β-hCG measurements are the most popular means for monitoring a PUL.

Women with PUL who have few or no symptoms and are at risk of EP can get expectant care with a 48-hour follow-up. Improved clinical prediction of PUL end outcome may reduce the number of outpatient visits and lessen the time it takes for some patients to receive a definitive diagnosis. Patients who are at risk for EP necessitate prompt and precise detection, as a delayed diagnosis can result in higher morbidity and mortality. Timely treatment, on the other hand, may be unneeded and may even impair early IUP. Repeated tests should indeed be balanced against the danger of EP and its comorbidities, as repeated checking might lead to false positive outcomes.[16]

In the present research, individuals who reported with vaginal bleeding and/or abdominal pain in the first trimester were being diagnosed with PUL. Some of these individuals were treated in outpatient clinics based on their symptoms, EP history, β-hCG level, and follow-up compliance. To monitor the result of PUL, these patients were contacted every 48 hours for β-hCG and weekly for TVS. Patients who required admission due to their symptoms, prior history, or β-hCG levels were treated accordingly. First most likely consequence is a failed PUL (44–69%) that resolves on its own.[17,18] Failed PUL showed of 69.8 percent in the current investigation, which can be substantiated with outcomes of other reports. Because of its small size, early IUP may not be apparent on TVUS, leading to a diagnosis of PUL. After an initial diagnosis of PUL, 30-37% of individuals develop IUP, according to several studies.[6] Following early assessment of PUL, a finding of 17.5% was recorded in the current study for IUP. According to numerous researches, 8.1-42.8% of PUL individuals have an EP result. When the confirmation of EP was reflected on the imaging of an adnexal mass instead of the lack of an intrauterine sac on TVUS, lower rates (8-14%) were obtained in specialty detection centres.[5] In the current study, 9.3 percent of patients were found for being EP after being diagnosed with PUL. Persistent PUL is a condition that affects about 2% of PUL patients, but this study found 4.8% participants having persistent PUL. Other methods of diagnosis, such as serum progesterone, tumour markers, and mathematical models, were not used in this investigation. These techniques have been demonstrated to improve PUL diagnosis and anticipate prognosis.[19]

CONCLUSION

PUL isn't really a finding, and thus the subject should indeed be monitored for a conclusive diagnosis can be made. Despite the fact that there is agreement on the criteria and classification of PUL, there are no universally approved standards for PUL follow-up examinations, which causes tension and repeated tests till a verdict is determined. Because no strategy for predicting the clinical benefit of PUL is totally true, symptomless PUL should always be treated cautiously. It is recommended that β-hCG and TVUS tests be repeated till the pregnancy is reliably detected or treatment is required. If an ectopic pregnancy is detected, it should always be treated as per institutional norms. Women who have experienced a 'presumptive' total miscarriage must be treated like they've had a PUL. Women with symptomless persistent PUL should seek medical assistance. Diagnostic and treatment protocols of management should be developed and used by early prenatal monitoring facilities. PUL typically resolves spontaneously, conservative care results in fewer unneeded interventions; the challenge is recognising that what kinds does not.

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