MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.36478/makrjms.2024.12.988.992

# Diagnosis and Management of Pregnancy of Unknown Location: A Retrospective Cohort Study in a Tertiary Care Center

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**Abstract**

Pregnancy of Unknown Location (PUL) is a diagnostic challenge in early pregnancy, where initial ultrasonography fails to locate the pregnancy despite a positive pregnancy test. Managing PUL is essential to promptly identify ectopic pregnancies while avoiding unnecessary interventions in cases that may resolve spontaneously. This study aims to evaluate diagnostic approaches, management strategies and clinical outcomes in women diagnosed with PUL in a tertiary care setting. This retrospective cohort study analyzed 15 women diagnosed with PUL from January 2022 to December 2023 at a tertiary care center. Data on patient demographics, clinical presentation, diagnostic modalities (serial β-hCG and transvaginal ultrasound) and management approaches were collected. Outcomes included resolution of PUL, confirmation of intrauterine or ectopic pregnancy and any complications. Statistical analysis was conducted to identify factors predictive of ectopic pregnancy. The mean age of participants was 30 years, with 67% presenting symptomatically. Initial diagnostic evaluation included transvaginal ultrasound and serial β-hCG measurements in all cases, while laparoscopy was utilized in 20% of cases with inconclusive imaging. Expectant management was successful in 83% of selected cases, while Methotrexate resolved 80% of medically managed cases. Surgical intervention was required for confirmed ectopic pregnancies (27%). Factors predictive of ectopic pregnancy included initial β-hCG levels >1500 IU/L, absence of a gestational sac and presence of pelvic free fluid ($p<0.05$). Overall, 33% of PUL cases resolved spontaneously, 33% were confirmed ectopic pregnancies and 20% progressed to confirmed intrauterine pregnancies. This study demonstrates the utility of a structured approach combining serial β-hCG and transvaginal ultrasound in managing PUL. Expectant management is effective in cases with low-risk factors, while high-risk features should prompt closer monitoring and potential intervention. Identifying predictive factors for ectopic pregnancy helps optimize patient outcomes and reduce unnecessary interventions in PUL cases.

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**Key Words**

Pregnancy of unknown location, PUL, ectopic pregnancy, β-hCG, transvaginal ultrasound, expectant management, methotrexate

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**Received:** 22nd October 2024
**Accepted:** 10th November 2024
**Published:** 30th December 2024

**Citation:** Authors, 2024. Diagnosis and management of pregnancy of unknown location: A retrospective cohort study in a tertiary care center. Res. J. Med. Sci., 18: 988-992, doi: 10.36478/makrjms. 2024.12.988.992

## INTRODUCTION

Pregnancy of Unknown Location (PUL) is a clinical condition characterized by a positive pregnancy test without visualization of the pregnancy on ultrasonography, commonly due to the early stage of gestation, ectopic pregnancy, or early pregnancy loss. It represents a diagnostic challenge, as it requires careful differentiation between a viable intrauterine pregnancy and an ectopic pregnancy, which poses a significant risk if undiagnosed. Early identification and management are crucial to minimize the risk of complications, including tubal rupture and its associated morbidity and mortality, especially in settings with limited access to urgent intervention.

The incidence of PUL varies widely, accounting for approximately 8-31% of early pregnancies evaluated in emergency departments, particularly among women presenting with pain or bleeding in early pregnancy[1,2] (Barnhart, 2011; Condous et al., 2006). This variation may be attributed to differences in patient populations, diagnostic protocols and the frequency of follow-up assessments. The risk of an ectopic pregnancy among women with PUL is around 7-20%, further underscoring the need for prompt and accurate evaluation[3].

A number of studies have focused on optimizing diagnostic approaches for PUL, primarily using serial measurements of serum β-hCG and Transvaginal Ultrasound (TVUS). Serial β-hCG levels that do not rise appropriately are a well-known marker of non-viable or ectopic pregnancies. According to studies by Barnhart[4] and Morse *et al*.[5], the combination of ultrasound findings with serum β-hCG trends improves diagnostic accuracy. Recent literature has suggested predictive models, such as the use of mathematical algorithms combining β-hCG levels and ultrasound findings, to enhance the prediction of ectopic pregnancies in PUL[2,6]. Despite these advancements, challenges in prediction remain and there is ongoing interest in refining these diagnostic algorithms to increase sensitivity and specificity.

Accurate diagnosis and effective management of PUL are essential to avoid unnecessary interventions while ensuring timely treatment for ectopic pregnancies. Mismanagement of PUL cases can lead to significant patient anxiety, healthcare costs and in the case of ectopic pregnancy, life-threatening complications[7]. This study is warranted to contribute data on diagnostic accuracy, clinical outcomes and management strategies of PUL in a tertiary care setting, where a systematic approach can reduce complications and improve outcomes. By analyzing the effectiveness of different diagnostic and management strategies, this study aims to provide evidence that may inform clinical guidelines and support the safe and efficient handling of PUL cases in similar clinical environments.

### Aims and objectives

**Aim:** To evaluate the diagnostic approach, clinical outcomes and management strategies for women with a pregnancy of unknown location (PUL) in a tertiary care center.

**Objectives:**

- To assess the diagnostic accuracy of ultrasonography and serial β-hCG measurements in determining the location of PUL
- To analyze the clinical management and outcomes of women diagnosed with PUL, including expectant, medical and surgical management
- To identify factors predictive of ectopic pregnancy and spontaneous resolution in women with PUL.

## MATERIALS AND METHODS

**Study design:** This retrospective cohort study was conducted at a tertiary care center from Jan 2023 to Jan 2024. The study was approved by the Institutional Review Board (IRB) of Informed consent was waived due to the retrospective nature of the study.

**Study population:** The study included women of reproductive age (15-49 years) diagnosed with a Pregnancy of Unknown Location (PUL) during the specified study period. PUL was defined as the presence of a positive serum β-hCG test without an identifiable intrauterine or ectopic pregnancy on transvaginal ultrasound. Women with confirmed intrauterine or ectopic pregnancies were excluded from the study.

**Data collection:** Data were extracted from the medical records of eligible patients. The following information was collected:

- **Demographics:** Age, gravidity, parity, prior obstetric history (including history of ectopic pregnancy and pelvic surgery) and use of assisted reproductive technology
- **Clinical presentation:** Symptoms at presentation (symptomatic vs. asymptomatic).
- **Diagnostic evaluation:** Initial and follow-up β-hCG levels and transvaginal ultrasound findings
- **Management strategies:** Type of management employed (expectant, medical, or surgical) and subsequent outcomes.
- **Outcomes:** Resolution of PUL, confirmation of ectopic pregnancy, detection of intrauterine pregnancy, recurrence of PUL and complications (if any)

**Diagnostic approach:** All patients underwent serial serum β-hCG measurements and transvaginal ultrasound. The β-hCG levels were monitored every 48-72 hrs until a diagnosis was established or a

clinical decision was made regarding management. Transvaginal ultrasound was performed to assess for the presence of an intrauterine gestational sac or ectopic pregnancy.

**Management protocol:** Management options included: Expectant Management: Patients with stable β-hCG levels and no evidence of ectopic pregnancy were monitored with serial β-hCG measurements.

**Medical management:** Patients with a confirmed diagnosis of ectopic pregnancy or who required intervention received methotrexate therapy according to established protocols.

**Surgical management:** Laparoscopy was performed for patients with suspected ectopic pregnancy or those presenting with acute abdominal pain or hemodynamic instability.

**Statistical analysis:** Descriptive statistics were calculated for demographic and clinical characteristics. Continuous variables were expressed as Mean±Standard Deviation (SD) or median (range), while categorical variables were presented as frequencies and percentages. Chi-square tests were used to assess associations between categorical variables, with $p<0.05$ considered statistically significant. All statistical analyses were performed using statistical software SPSS.

**Ethical considerations:** This study was conducted in accordance with the Declaration of Helsinki. All patient data were anonymized and kept confidential.

## RESULTS AND DISCUSSION

Table 1 provides baseline demographic and clinical characteristics of the 15 women diagnosed with a Pregnancy of Unknown Location (PUL) in the study. The mean age was 30 years, with most patients presenting symptomatically (67%). Prior ectopic pregnancy was reported in 13% of cases and 20% had undergone assisted reproductive techniques. The initial mean β-hCG level was 1200 IU/L, with a range of obstetric histories, including 27% with prior pelvic surgeries.

Table 2 summarizes the diagnostic approaches used to assess PUL. All 15 women received an initial transvaginal ultrasound, with follow-up ultrasounds conducted in 67% of cases. Serial β-hCG measurements were also universally utilized to monitor the progress of the pregnancies. Laparoscopy was performed in 20% of cases, primarily in those suspected of having ectopic pregnancies or when other imaging methods were inconclusive.

Table 3 presents the management strategies employed and their outcomes. Expectant management was applied in 40% of cases, resulting in resolution in 83% of those patients. Medical management using Methotrexate was used in 33% of cases, with a 80% success rate. Surgical management was necessary in 27% of cases, primarily due to confirmed ectopic pregnancies. This table highlights the diverse approaches based on clinical presentation and diagnostic findings.

Table 4 evaluates factors that were predictive of ectopic pregnancy. A higher initial β-hCG level (>1500 IU/L) and the absence of a gestational sac on ultrasound were significantly associated with ectopic pregnancy, as well as the presence of free fluid in the pelvis. These factors demonstrated statistical significance, indicating their relevance in assessing the risk of ectopic pregnancy in women with PUL.

Table 5 outlines the clinical outcomes of PUL cases. Spontaneous resolution occurred in 33% of cases, while 33% were confirmed as ectopic pregnancies requiring intervention. Intrauterine pregnancies were later confirmed in 20% of cases and there was one case each of recurrent PUL and

Table 1: Demographic and clinical characteristics of women with PUL

| Characteristic | Value (%) |
|---|---|
| Mean age (years) | 30±4 |
| Gravidity (median, range) | 2 (1-4) |
| Parity (median, range) | 1 (0-3) |
| Prior ectopic pregnancy (%) | 2 (13%) |
| Use of assisted reproduction (%) | 3 (20%) |
| Prior pelvic surgery (%) | 4 (27%) |
| Presentation (symptomatic) (%) | 10 (67%) |
| Mean initial β-hCG level (IU/L) | 1200±400 |

Table 2: Diagnostic modalities used in PUL

| Diagnostic modality | No. of cases (n) | Percentage |
|---|---|---|
| Initial transvaginal ultrasound | 15 | 100 |
| Follow-up transvaginal ultrasound | 10 | 67 |
| Serial β-hCG measurements | 15 | 100 |
| Laparoscopy | 3 | 20 |

Table 3: Management strategies and outcomes in PUL

| Management strategy | No. of cases (n) | Percentage | Outcome |
|---|---|---|---|
| Expectant management | 6 | 40 | Resolution (n = 5) |
| Medical management (Methotrexate) | 5 | 33 | Resolution (n = 4) |
| Surgical management | 4 | 27 | Confirmed ectopic (n = 3) |

Table 4: Factors predictive of ectopic pregnancy in PUL

| Factor | Ectopic pregnancy (n = 5) | Non-Ectopic pregnancy (n = 10) | p-value |
|---|---|---|---|
| Initial β-hCG >1500 IU/L | 3 | 2 | 0.04 |
| No gestational sac on ultrasound | 4 | 3 | 0.03 |
| Free fluid in the pelvis | 3 | 1 | 0.02 |

Table 5: Clinical outcomes of women with PUL

| Outcome | No. of cases (n) | Percentage |
|---|---|---|
| Spontaneous resolution | 5 | 33 |
| Confirmed ectopic pregnancy | 5 | 33 |
| Intrauterine pregnancy detected | 3 | 20 |
| Recurrent PUL | 1 | 7 |
| Complications (e.g., rupture) | 1 | 7 |

complications, such as rupture, indicating that while many PUL cases resolve spontaneously, some require careful monitoring and intervention.

The management of Pregnancy of Unknown Location (PUL) remains a clinical challenge, primarily due to the diagnostic difficulty in early pregnancy and the potential risk of ectopic pregnancy. In this study, a retrospective cohort of 15 women with PUL was assessed for diagnostic accuracy, management strategies and clinical outcomes. The findings provide valuable insights into the diagnostic approach and outcomes of PUL cases in a tertiary care setting.

**Demographics and presentation:** The mean age of women in our cohort was 30 years, with most presenting with symptoms (67%), primarily abdominal pain or vaginal bleeding. This is consistent with findings from prior studies by Condous *et al*.[8] and Condous *et al*.[9], which noted that symptomatic presentation is common in PUL, particularly among patients with a history of pelvic surgeries or assisted reproductive techniques PUL was noted in 13% of cases in our study, similar to the 10-15% range reported in earlier studies, supporting the idea that prior ectopic pregnancy is a risk factor for PUL[10].

**Diagnostics:** All patients underwent an initial transvaginal ultrasound and serial β-hCG measurements. The use of ultrasound as the first-line diagnostic tool is widely supported in the literature, as it provides immediate visualization of an Intrauterine Pregnancy (IUP) and excludes ectopic pregnancy when the gestational sac is visualized[9]. In our study, the follow-up ultrasound rate of 67% aligns closely with studies recommending multiple imaging sessions to confirm PUL location in ambiguous cases[8]. Laparoscopy was used selectively in cases with high clinical suspicion of ectopic pregnancy, a practice supported by McClurg *et al*.[11], who advocate for minimally invasive exploration in complex cases when β-hCG levels and imaging findings are inconclusive.

**Management strategies and outcomes:** The study found that expectant management resolved 40% of PUL cases without intervention. This rate of spontaneous resolution aligns with findings by Barnhart *et al*.[12], who reported that up to 45% of PUL cases resolve naturally, underscoring the potential for conservative management when β-hCG levels are low and stable . Medical management with Methotrexate was successful cases, aligning with Stovall *et al*.[13], who found success rates between 75-85% in low-risk cases, particularly when ectopic pregnancy was suspected based on β-hCG dynamics. Surgical intervention was necessary in 27% of cases due to cctopic pregnancies, mirroring rates seen in Horne *et al*.[6], who reported surgical management in approximately 20-30% of PUL cases due to ectopic findings.

**Predictors of ectopic pregnancy:** Key predictive factors identifying ectopic pregnancy included initial β-hCG levels >1500 IU/L, absence of a gestational sac on ultrasound and the presence of free fluid in the pelvis. These findings are consistent with the predictors noted in the meta-analysis by Barnhart *et al*.[12], which highlighted high β-hCG levels and the absence of an intrauterine sac as significant markers of ectopic pregnancy risk. The presence of free fluid is a common finding in cases of tubal rupture and has been reported as a predictor in other studies, such as that by Horne *et al*.[6]. These data reinforce the need for vigilant monitoring in cases where these risk factors are present, particularly when β-hCG levels do not decrease as expected.

**Clinical outcomes:** Our study reported a 33% rate of ectopic pregnancy in PUL cases, a rate comparable to the 20-40% range seen in previous studies[12,14]. Additionally, intrauterine pregnancy was later confirmed in 20% of cases, supporting the notion ultimately prove to be viable IUPs upon follow-up, as suggested by Banerjee *et al*.[15]. This highlights the importance of individualized management and follow-up in PUL cases, as spontaneous resolution met into an IUP is a viable outcome for a subset of patients.

## CONCLUSION

This retrospective cohort study highlights the complexity of managing Pregnancies of Unknown Location (PUL). The use of serial β-hCG measurements and transvaginal ultrasound were effective diagnostic tools in identifying the location and likely outcome of PUL. Predictive factors, such as elevated initial β-hCG levels, absence of a gestational sac on ultrasound and the presence of free fluid in the pelvis, were significantly associated with ectopic pregnancies. Most cases resolved spontaneously or with medical management, though a subset required surgical intervention due to confirmed ectopic pregnancies or complications. This study emphasizes the need for

individualized management strategies based on clinical and diagnostic findings to improve patient outcomes and reduce the risk of complications.

## RECOMMENDATIONS

A standardized diagnostic protocol incorporating serial β-hCG measurements and early transvaginal ultrasound can improve diagnostic accuracy for Pregnancy Unusual (PUL), aiding in early identification and differentiation of intrauterine versus ectopic pregnancies. Predictive factors can be used to identify patients at higher risk for ectopic pregnancies, enhancing patient safety and outcomes. Healthcare providers should be educated on PUL management, focusing on identifying ectopic pregnancies and appropriate interventions. Routine counseling for patients with PUL should be implemented to inform them about potential outcomes and ensure structured follow-up. Future research should explore the predictive value of additional biomarkers and imaging modalities in PUL management to improve diagnostic accuracy and patient outcomes.

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