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Case Report

Ruptured ectopic pregnancy with negative serum beta-human chorionic gonadotropin: a case report and literature review

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ABSTRACT

A negative urine pregnancy test is commonly used in emergency settings to exclude pregnancy; however, this assumption can be misleading and may delay critical diagnoses. We present a rare case of a ruptured ectopic pregnancy in a 30-year-old female with a serum beta-human chorionic gonadotropin (hCG) level of only 4 IU/l, falsely suggesting the absence of pregnancy. The patient presented with sudden-onset lower abdominal pain, presyncope, and hemodynamic instability. On arrival, she was hypotensive and tachycardic, with clinical and ultrasound findings consistent with massive hemoperitoneum of more than three litres of blood. Despite an initial negative pregnancy test, the patient required emergent laparotomy and right salpingectomy for a ruptured ectopic pregnancy. The patient was resuscitated with blood products and stabilised postoperatively in the intensive care unit before being discharged. This case highlights the limitations of beta-hCG testing in diagnosing ectopic pregnancy, emphasising that low or undetectable levels do not exclude the condition. A comprehensive literature review identified fourteen similar cases of ruptured ectopic pregnancy with negative or low serum beta-hCG levels, illustrating the diagnostic challenges associated with such presentations. Whilst serial beta-hCG monitoring remains a valuable tool, this case underscores the importance of clinical suspicion and point-of-care imaging, particularly transvaginal ultrasound (TVUS), as the primary modality for detecting ectopic pregnancies. Early recognition and intervention are crucial to reducing morbidity and mortality.

Keywords: Ruptured ectopic pregnancy, False-negative beta-hCG, Hemoperitoneum, Emergency laparotomy, Point-of-care ultrasound

INTRODUCTION

Ectopic pregnancy is a life-threatening condition in which a fertilised egg implants outside the uterus, most commonly in the fallopian tube. It remains a leading cause of maternal morbidity and mortality.[1] An ectopic pregnancy presents initially with colicky abdominal or pelvic pain localised to one side and may become generalised once the fallopian tube ruptures. Other associated symptoms include vaginal bleeding, presyncope, syncope, vomiting and shoulder tip pain.[2] Ectopic pregnancy should be considered in all females of reproductive age. Globally, the incidence of ectopic pregnancy ranges from 1-2% of all pregnancies, with a higher prevalence observed in women under the age of 25, or with previous tubal surgery, in vitro fertilisation, pelvic inflammatory disease or previous ectopic pregnancies.[3,4] If left untreated, ruptured ectopic pregnancy accounts for approximately 2.7% of all pregnancy-related deaths, primarily due to significant haemorrhage associated with rupture.[5] Despite advances in diagnostic modalities, approximately 10% of women with ectopic pregnancy have no identifiable risk factors, making universal screening for symptoms crucial.[6]

The introduction of high-resolution transvaginal ultrasound (TVUS) and serial beta-hCG measurements has led to earlier diagnoses and reduced morbidity. However, false-negative pregnancy tests, particularly when beta-hCG levels are below 20 IU/l, continue to pose a significant diagnostic challenge.[7] The use of point-of-care ultrasound (POCUS) in emergency settings has been shown to significantly improve early detection rates, allowing for timely intervention before rupture occurs.[8]

This report presents the rare case of ruptured ectopic pregnancy with a negative urine pregnancy test and low serum beta-hCG, emphasising the need for clinical suspicion, bedside imaging, and timely intervention.

CASE REPORT

A 30-year-old female with no significant past obstetric history presented to the emergency department with sudden onset sharp right iliac fossa and suprapubic abdominal pain, presyncope, nausea and one episode of vomiting. She reported a normal bowel movement the previous day and denied fever, dysuria, vaginal bleeding, or recent illness.

On arrival, she was hypotensive (BP 77/50 mmHg) and tachycardic (HR 107 bpm). Initial examination revealed voluntary guarding in the right iliac fossa with tenderness but no signs of peritonism. A bedside point-of-care ultrasound (FAST scan) showed significant free fluid in the abdomen, raising suspicion of hemoperitoneum. Laboratory investigations revealed a haemoglobin drop from 11.7 g/dl to 7.7 g/dl over a few hours, leucocytosis (WCC 16), and a beta-hCG level of 4 IU/l, which was falsely reassuring. Despite the negative pregnancy test, the presence of hemoperitoneum warranted immediate surgical intervention.

The patient was resuscitated with intravenous fluids and blood products, including six units of packed red blood cells, four units of cryoprecipitate, and two units of fresh frozen plasma. Due to ongoing haemodynamic instability, an emergency laparotomy was performed.

Intraoperative findings confirmed a ruptured right tubal ectopic pregnancy with massive hemoperitoneum of more than three litres of blood. A right salpingectomy was performed, and both ovaries were found to be intact. The uterus and left fallopian tube appeared normal. The patient was stabilised postoperatively in the intensive care unit and was later discharged with a plan for follow-up in the gynaecology clinic.

DISCUSSION

A comprehensive literature review was conducted using databases including PubMed, Scopus, Embase, and Web of Science to identify studies reporting ectopic pregnancy with negative beta-hCG from infinity to January 2025.

The search strategy included the following MeSH terms and keywords: "ectopic pregnancy", "ruptured ectopic pregnancy", "negative beta-hCG", "false negative pregnancy test", "hemoperitoneum", and "emergency management".

Inclusion criteria

Articles published in peer-reviewed journals, reported ruptured ectopic pregnancy with negative or low beta-hCG (<20 IU/l), provided clinical, diagnostic, and management details, and available in English.

Exclusion criteria

Studies with incomplete patient data, non-English articles without available translations, studies focusing only on non-surgical management, and duplicate publications.

A data extraction form was used to ensure consistency in collecting clinical details, diagnostic workup, and management strategies across studies. The relevant cases were summarised in a table format.

A total of fourteen case reports of ruptured ectopic pregnancies with negative beta-hCG were identified in the literature. These cases demonstrate that ectopic pregnancies can present with undetectable or low beta-hCG levels, posing a significant diagnostic challenge. The reported cases vary in presentation, with some patients experiencing severe pain, syncope, and hemoperitoneum, while others had atypical symptoms such as dysuria or mild abdominal discomfort. These cases highlight the variability in beta-hCG production, with some pregnancies exhibiting fluctuating levels while others present with undetectable beta-hCG throughout. TVUS remains the gold standard diagnostic tool, with nearly all cases demonstrating an adnexal mass, free fluid, or hemoperitoneum on imaging. In all reported cases, laparoscopy or laparotomy was necessary for definitive management, with salpingectomy being the most frequently performed procedure.

Ectopic pregnancy remains a significant cause of maternal morbidity and mortality, particularly when rupture occurs due to delayed or missed diagnosis.[23] The reliance on beta-hCG testing in the emergency setting presents a major diagnostic limitation, as evidenced by the increasing number of cases reporting ruptured ectopic pregnancies despite negative or low serum beta-hCG levels.[6] Approximately 1% of ectopic pregnancies present with a negative urine pregnancy test, and in some instances, serum beta-hCG can remain below the diagnostic threshold.[7] This presents a considerable challenge to emergency physicians, who may inadvertently rule out pregnancy in women presenting with acute abdominal pain, potentially delaying life-saving intervention.

Several pathophysiological mechanisms have been proposed to explain why some ectopic pregnancies

produce little or no detectable beta-hCG, namely poor trophoblastic implantation; impaired beta-hCG synthesis, and variations in metabolic clearance. Trophoblastic degeneration due to poor implantation in the fallopian tube can lead to decreased hormone production, resulting in undetectable beta-hCG levels.[3] Additionally, cases with a small number of chorionic villi may not produce sufficient beta-hCG to be measured using standard assays.[4] Another possibility is the enhanced clearance of beta-hCG from circulation, which has been hypothesised to contribute to falsely reassuring test results.[5] The hook effect, in which high concentrations of beta-core fragment (βcf-hCG) interfere with immunoassay detection, has also been reported as a potential contributor to false-negative pregnancy tests.[8] This highlights the limitations of solely relying on biochemical testing in ectopic pregnancy diagnosis.

Given these diagnostic pitfalls, clinical judgment remains critical when evaluating women of reproductive age who present with acute abdominal pain and hemodynamic instability. In such cases, TVUS remains the most reliable diagnostic tool, particularly when an adnexal mass, hemoperitoneum, or the absence of an intrauterine pregnancy (IUP) is noted.[23] The literature supports the high predictive value of TVUS in ectopic pregnancy diagnosis, with studies demonstrating a positive predictive value of 96.3% when a tubal ring or free fluid is visualised.[7] In this regard, clinicians must maintain a high index of suspicion and prioritise imaging when beta-hCG results are inconclusive or potentially misleading.

Table 1: Summary of cases of ruptured ectopic pregnancies with negative beta-hCG.

Study	Age (years)	β-hCG (IU/l)	Clinical presentation	Diagnostic workup	Management and outcome
Lee and Lamaro, 2009[9]	25	4	Abdominal pain, syncope	TVUS: hemoperitoneum	Emergency laparotomy
Pabon et al, 2011[10]	34	6	Pelvic pain, hemoperitoneum	TVUS: no IUP, free fluid	Emergency surgery
Nishijima et al, 2005[11]	32	1.84	Hypotension, no vaginal bleeding	TVUS: adnexal mass	Laparoscopy, salpingectomy
Kalinski and Guss, 2002[12]	44	7	Acute rupture, shock	TVUS: free fluid, no IUP	Laparotomy, salpingectomy
Brennan et al, 2000[13]	23, 28	<25	Severe pain, negative urine test	TVUS: no IUP	Surgery
Grynberg et al, 2009[14]	26	0	Negative urine and serum tests	TVUS: adnexal mass	Exploratory surgery
Daniilidis et al, 2014[15]	36	13	Hypovolemic shock	TVUS: hemoperitoneum	Laparotomy, salpingectomy
Kopelman et al, 2021[16]	23	<5	Syncope, hemoperitoneum	TVUS and CT: right adnexal mass	Salpingectomy
Sheele et al, 2016[17]	35	10	Abdominal pain, declining β-hCG	TVUS: free fluid, no IUP	Laparoscopy, salpingectomy
Talebian et al, 2024[18]	31	2.08	Acute rupture, hemodynamic instability	TVUS: complex adnexal mass	Laparotomy, blood transfusion
Fejgin et al, 1986[19]	30	0	Ovarian pregnancy with rupture	TVUS: ovarian mass	Emergency surgery
Hochner-Celnikier et al, 1992[20]	28	Undetectable	Ruptured ectopic pregnancy	TVUS: free fluid	Laparoscopy, salpingectomy
Maccato et al, 1993[21]	27	<5	Nausea, mild pain	TVUS: No IUP, free fluid	Laparoscopy, conservative treatment
Lonky and Sauer, 1987[22]	33	<5	Shock, massive hemorrhage	TVUS: free fluid	Laparotomy, salpingectomy

Management of ruptured ectopic pregnancy largely depends on the patient's hemodynamic status at presentation. In stable patients, treatment options include medical management with methotrexate, or surgical management with salpingostomy or salpingectomy.[2] Expectant management is rare. Overall, surgical management is more effective than methotrexate in successfully treating ectopic pregnancy. In hemodynamically unstable patients, immediate resuscitation with intravenous fluids and blood products is warranted, followed by emergent surgical intervention.[6] As evidenced in this case and previous literature, laparotomy or laparoscopy remains the gold standard for managing ruptured ectopic pregnancies.[3] Laparoscopic

salpingectomy is the preferred approach in hemodynamically stable patients, while laparotomy is often necessary in cases with extensive hemoperitoneum or profound shock.[4]

The importance of serial beta-hCG monitoring should not be overlooked, particularly in cases where initial levels are low but ectopic pregnancy remains a differential diagnosis. Serial beta-hCG testing, combined with a comprehensive clinical assessment and serial ultrasonography, can help detect abnormal doubling times, which are often indicative of an ectopic pregnancy.[5] However, as demonstrated in this case, reliance on beta-hCG alone is not sufficient, and ultrasound should always be performed in patients presenting with symptoms suggestive of ectopic pregnancy.[8]

Ultimately, this case report and the reviewed literature highlight the critical need for a multimodal diagnostic approach that incorporates clinical assessment, serial beta-hCG measurement, and ultrasound imaging to identify patients presenting with an ectopic pregnancy.

CONCLUSION

This case report highlights the rare presentation of a 30-year-old G0P0 female presenting with a ruptured right tubal ectopic pregnancy with massive hemoperitoneum despite negative beta-hCG. It demonstrates the diagnostic dilemma associated with negative beta-hCG and reinforces the importance of maintaining a high index of suspicion in women of reproductive age presenting with acute abdominal pain.

Recommendations

Timely identification of an ectopic pregnancy is imperative to reduce maternal mortality and morbidity. Clinicians should incorporate a thorough history and examination findings with serial beta-hCG measurements and point-of-care imaging, particularly transvaginal ultrasound, for early detection of ectopic pregnancies.

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