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INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/24219

DOI URL: <http://dx.doi.org/10.21474/IJAR01/24219>



RESEARCH ARTICLE

CONCURRENT EARLY-ONSET PREECLAMPSIA AND OVARIAN HYPERSTIMULATION SYNDROME FOLLOWING LETROZOLE OVULATION INDUCTION IN A WOMAN WITH POLYENDOCRINE METABOLIC OVARIAN SYNDROME: A CASE REPORT

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Manuscript Info

Manuscript History

Received: 14 July 2026

Final Accepted: 16 August 2026

Published: September 2026

Key words:-

PMOS, OHSS, preeclampsia, letrozole, ovulation, case report

Abstract

Ovarian Hyperstimulation Syndrome (OHSS) and preeclampsia are well-documented complications of Assisted Reproductive Technology (ART) and ovulation induction. In patients with Polyendocrine Metabolic Ovarian Syndrome (PMOS) who are undergoing fertility treatment, these conditions may occur separately or sequentially. Their simultaneous occurrence after letrozole ovulation induction, a medication with a low OHSS is rarely documented. We report a rare case of OHSS and preeclampsia after ovulation induction with letrozole in a woman with polyendocrine metabolic ovarian syndrome.

Case summary:-A 25-year-old woman with polyendocrine metabolic ovarian syndrome conceived following letrozole ovulation induction. She presented as an emergency at 30 weeks of gestation with abdominal pain, persistent headache, elevated blood pressures, ascites and significant bilateral ovarian enlargement. She was diagnosed with moderate OHSS and severe early onset preeclampsia. Management included hospital admission, fluid balance monitoring, prophylactic anticoagulation, and antihypertensive therapy up to 34 weeks. She underwent caesarean section delivery at 34 weeks.

Conclusion:-Although very rare, moderate OHSS and early-onset preeclampsia may occur together after letrozole ovulation induction. Close monitoring, supportive care, and timely delivery can lead to optimal outcomes.

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Introduction:-

Background:-

Polyendocrine Metabolic Ovarian Syndrome (PMOS) is formerly known as polycystic ovary syndrome (PCOS). The official name change from polycystic ovary syndrome to polyendocrine metabolic ovarian syndrome (PMOS) was established in May 2026 by an international consensus of global health organizations. It is the leading cause of anovulatory infertility in reproductive age women (1). Ovulation induction increases the risk of Ovarian Hyperstimulation Syndrome (OHSS) (2). PMOS also predisposes patients to hypertensive disorders of pregnancy due to insulin resistance and vascular endothelial dysfunction (3). The coexistence of OHSS and preeclampsia is rare and challenging to manage because of this overlapping pathophysiology and clinical features(4). Ovulation

induction with letrozole has a low risk of OHSS(5)(6). However, in women with PMOS, combining letrozole with gonadotropins or Human chorionic Gonadotropin (HCG) can increase this risk(7)(8). Prior OHSS, high antral follicle count (AFC), elevated anti-Müllerian hormone (AMH), young age, and black ethnicity further increase susceptibility(9). On rare occasions, OHSS can also develop spontaneously, either during a natural conception cycle and even in the absence of pregnancy(10)(11). Letrozole is the preferred first-line agent for ovulation induction in some women with PMOS. However, rare hyper responses may occur. Cases regarding the simultaneous development of OHSS and severe preeclampsia after letrozole are remarkably scarce. We present a rare clinical case in which moderate OHSS and severe preeclampsia occurred simultaneously in a pregnant woman with underlying PMOS, following ovulation induction with letrozole alone. No other fertility medications were used.

Patient history:-

A 25-year-old woman with polyendocrine metabolic ovarian syndrome presented in 2023 with secondary amenorrhea and two years of primary infertility. Ovulation induction with clomiphene citrate in April 2025 was unsuccessful. Letrozole induction in August 2025 resulted in a missed abortion at 7 weeks. A further letrozole cycle in December 2025 resulted in a pregnancy. Pre-induction ultrasound showed bilaterally enlarged, cystic ovaries measuring 4.2cm on the left and 5.6cm on the right. Unfortunately, she missed all early antenatal visits. She presented at 30 weeks and 2 days with abdominal pain, persistent headache, and abdominal fullness. Her blood pressure was 172/112 mmHg, with a pulse of 93bpm and weighed 74 kgs. She had abdominal tenderness, guarding at the flanks but no rebound tenderness. She had ascites, 2+ pitting oedema, severe hirsutism, and acne. Pulmonary and cardiac examinations were unremarkable. Obstetric ultrasound confirmed a singleton pregnancy of 30 weeks and 4 days. The estimated fetal weight was 1520g. The umbilical Doppler PI was at the 99th percentile. Notably, both ovaries were markedly enlarged with multiple cysts (right: 11.65 cm, left: 11.85 cm) as shown in Figures 1 and figure 2 respectively. Furthermore, moderate ascites was present.



Figure 1: Right Ovary



Figure 2: Left Ovary

The haemoglobin was 14.8 g/dL. The haematocrit was 0.47L/L. Serum creatinine was 59.3 μ mol/L. Aspartate aminotransferase and Alanine aminotransferase were elevated at 78 U/L and 85 U/L respectively. Proteinuria was +++ with a random glycaemia of 7.6 mmol/L. Ovarian reserve markers, albumin and coagulation profiles were not done due to their unavailability in our laboratory.

Diagnosis and management:-

The diagnosis was concurrent moderate ovarian hyperstimulation syndrome and severe early onset preeclampsia. Bilateral ovarian cystic enlargement associated with PMOS was a differential diagnosis. We admitted her to the high-risk ward for hemodynamic stabilisation and expectant management aiming for delivery at 34 weeks. Fluid replacement was administered orally and guided by the patient's thirst. Magnesium sulphate was administered for seizure prophylaxis. We used the Pritchard protocol starting with a 14g loading dose (4g of a 20% solution intravenously and 5g in each buttock) followed by 5g of a 50% solution intramuscularly in alternate buttocks every 4 hours for 24 hours. Blood pressure was initially controlled with intravenous hydralazine 5mg then oral nifedipine 40mg twice daily. Given the high thromboembolic risk, enoxaparin 40mg subcutaneously once daily was initiated. She received dexamethasone 6 mg twice daily for 48 hours for fetal lung maturation. Intravenous paracetamol 1g was prescribed to control the abdominal pains. Urine output, fluid intake, vital signs and body weight were measured daily. Fetal biophysical profiles and umbilical artery dopplers were done twice a week. Full blood count,

liver and renal function tests were repeated after 48 hours and on day 7 post admission. Serial transabdominal ultrasound scans were done weekly to track changes in ovarian size and volume.

Over the next three weeks, haematocrit normalized, liver enzymes decreased, and urine output remained good. Nifedipine was increased to 40 mg three times daily. Methyldopa 500 mg three times daily was added to maintain a target systolic blood pressure of 130-150mmhg and a diastolic pressure of 80-100mmhg. Ovarian size did not change but ascites resolved completely. Abdominal pain persisted. She required intermittent paracetamol to control the symptoms. She remained hospitalized until 34 weeks. The dopplers and BPPs were normal. Labour was induced with oxytocin after cervical ripening with misoprostol. A caesarean section was done due to a persistent non-reassuring fetal heart rate pattern in the active phase of labour. The birth weight was 1980g. Large bilateral ovarian cysts were confirmed intraoperatively. The patient was discharged on the fifth day following delivery.

Postpartum follow up:-

The patient was seen after three weeks in the postpartum clinic. She was asymptomatic with well controlled blood pressure on nifedipine. Abdominopelvic ultrasound showed bilaterally enlarged, multicystic ovaries. Each ovary was about half the size during pregnancy but larger than at ovulation induction. The right ovary measured 6.9 cm and the left ovary measured 7.2cm as shown on Figure 3 and Figure 4 respectively. Ascites had completely resolved.



Figure 3: Left ovary



Figure 4: Right Ovary

Table 1: Summary and chronology of clinical events: -

Time	Clinical event
2023	Secondary amenorrhea and diagnosis of PMOS
April 2025	Clomiphene induction – no conception
August 2025	Letrozole ovulation induction – conception that ended in an abortion
December 2025	Letrozole ovulation induction – conception. Lost to follow up
30 weeks	Presentation with hypertension, abdominal pain, enlarged ovaries, ascites
30 – 34 weeks	Inpatient management
34 weeks	Delivery by caesarean section
3 weeks post-partum	Persistent ovarian enlargement

Discussion:-

Ovarian Hyperstimulation Syndrome (OHSS) and preeclampsia are recognised complications of assisted reproductive technology (ART) and ovulation induction (12). The royal college of obstetricians and gynaecologists classifies OHSS into mild, moderate, severe and critical categories based on clinical symptoms, ultrasound findings and haematological markers as shown below in table 1.

Table 1: Royal College of obstetricians and gynaecologists (RCOG) Classification of OHSS severity

Category	Symptoms	Ultrasound	Haematological	Fluid homeostasis
Mild	Mild abdominal pain Abdominal bloating	Ovarian size <8cm	HCT<0.40L/L	
Moderate	Moderate abdominal pain Nausea+-vomiting	Ovarian size 8-12cm Evidence of ascites	HCT <45L/L	
Severe	Clinical ascites	Ovarian size >12cm	HCT>0.45L/L	Sodium <135mmol/L

				Potassium >5mmol/L Albumin <35g/L Oliguria <30ml/h
Critical	Tense ascites Pleural effusions		HCT >0.55L/L White cell count >25000/ml	Anuria Thrombosis Acute respiratory distress

Our patient had moderate OHSS due to the moderate abdominal pain, nausea, ovarian sizes of 11cm and evidence of ascites on ultrasound scan. Although her haematocrit was 0.47L/L, she did not have other features to classify her into the severe category. Although distinct, both OHSS and preeclampsia share a common mechanism involving systemic endothelial dysfunction and abnormal vascular permeability (13). The coexistence of OHSS and preeclampsia is a diagnostic and management challenge since both may manifest with oedema, ascites, excessive weight gain, oliguria, abnormal liver and renal function tests (14). This coexistence is also a rare interaction between pro-angiogenic and anti-angiogenic pathways. OHSS is mediated by excess angiogenic vascular endothelial growth factor (VEGF) and vasoactive cytokines (15). On the other hand, preeclampsia involves the systemic release of anti-angiogenic factors like soluble fms-like tyrosine kinase-1 (sFlt-1) (16)(17). The clinical picture in this patient may demonstrate that the two distinct and opposing angiogenic pathways can operate simultaneously in separate vascular compartments. The underlying polyendocrine metabolic ovarian syndrome may be the underlying risk factor for both complications. OHSS frequently presents or worsens in early pregnancy. The late presentation in our case was likely a result of the continuous production of endogenous human chorionic gonadotrophin by the placenta maintaining hyperstimulated ovaries well into the third trimester. The patient did not attend antenatal care until the third trimester. It may be possible that other signs of OHSS were already present before her presentation at 30 weeks of gestation.

The main challenge in this dual diagnosis is balancing two opposing fluid management strategies. Moderate OHSS is managed with fluids to expand the intravascular volume and maintain renal perfusion (18). On the contrary, severe preeclampsia is managed by restricting fluid to prevent volume overload. We addressed this balance by using oral hydration instead of intravenous fluids as the patient was hemodynamically stable. We were therefore able to avoid aggressive intravenous fluid expansion and at the same time expanded the intravascular volume without the risk of fluid overload. Severe preeclampsia requires inpatient hospitalization because acute, life-threatening complications can rapidly develop. On the other hand, patients with moderate OHSS can be managed as outpatient if they are hemodynamic stable, tolerate oral intake, and can be followed up easily (19)(20). Inpatient management was preferred in this case due to the severity of the patient's preeclampsia. OHSS induces a prothrombotic state through haemoconcentration and endothelial dysfunction (21). The incidence of thrombosis has been estimated by other studies to be between 0.7% and 10% when OHSS develops (22). Enoxaparin thromboprophylaxis was administered because the patient had multiple thrombotic risk factors including pregnancy, OHSS and preeclampsia.

Severe hypertension was managed with intravenous hydralazine due to the unavailability of labetalol in our setting. We achieved long-term blood pressure control with nifedipine and methyldopa. This practice is in keeping with other standard guidelines (23). Delivery at 34 weeks of gestation was also consistent with international recommendations for stable preeclampsia with severe features (24). The elevated umbilical artery Doppler pulsatility index (PI) at the 99th percentile strongly suggested severe placental insufficiency. This was directly associated with a birth weight of 1980g and features of intrauterine growth restriction observed in the foetus. The persistence of enlarged, multicystic ovaries throughout pregnancy and well into the postpartum period may suggest that the resolution of OHSS may be a prolonged process. This is in keeping with findings reported in other previous cases and studies (25)(26).

Conclusions and Recommendations:-

The coexistence of moderate OHSS with early-onset preeclampsia is very rare. It may occur in patients with metabolic disorders like PMOS. While letrozole is generally safe for ovulation induction, some individuals may experience a hyper-response. Clinicians should suspect this dual pathology in patients with abdominal pain, hypertension, and enlarged ovaries and ascites after ovulation induction. Effective management may include individualized inpatient monitoring, strict fluid balance, tailored antihypertensive therapy, thromboembolic prophylaxis, and timely delivery among many other interventions.

Acknowledgments:-

All health professionals involved in the management of this case.

Funding Statement:-

No funding was received.

Consent for Publication:-

Institutional ethical approval was waived for the publication of this single case report. Written informed consents for the publication of this case report and accompanying images were obtained from the patient.

Author Contributions:-

Handsome Dube: Manuscript conception, data collection, manuscript preparation, analysis, drafting, revision, proof reading and submission.

Daniel Niyomufasha: Data collection, analysis, revision and proof reading.

All authors gave final approval of the version to be published.

Disclosure:-

The authors declare that there are no competing interests.

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