

REVIEWER'S REPORT

Manuscript No.: IJAR-59213

Title:, Early-Onset Preeclampsia and Ovarian Hyperstimulation Syndrome following ovulation induction in a woman with Polyendocrine Metabolic Ovarian Syndrome: A Case Report,

Recommendation:

Accept as it is

Accept after minor revision.....

Accept after major revision ...YES...

Do not accept (*Reasons below*)

Rating	Excel.	Good	Fair	Poor
Originality		✓		
Techn. Quality			✓	
Clarity			✓	
Significance		✓		

Reviewer's ID: JPR-094

Detailed Reviewer's Report

Reviewer Report

1. Overall assessment

This case report describes a clinically unusual coexistence of moderate ovarian hyperstimulation syndrome (OHSS) and severe early-onset preeclampsia in a pregnancy conceived after letrozole ovulation induction, with persistent bilateral ovarian enlargement extending into the postpartum period.

The case has potential publication value because OHSS is generally associated more strongly with gonadotropin-based ovarian stimulation/ART, whereas the manuscript describes a severe clinical picture following **letrozole monotherapy**. The coexistence of OHSS, severe preeclampsia, ascites, markedly enlarged multicystic ovaries, and subsequent fetal growth restriction makes the case clinically interesting.

However, in its current form, the manuscript has **substantial scientific, diagnostic, chronological, and editorial weaknesses**. I would recommend **major revision before publication**.

REVIEWER'S REPORT**2. Strengths****A. Clinically unusual presentation**

The most important strength is the unusual combination of:

- pregnancy following ovulation induction with letrozole;
- markedly enlarged bilateral ovaries;
- ascites;
- OHSS;
- severe early-onset hypertension/preeclampsia;
- fetal growth restriction/abnormal umbilical artery Doppler;
- persistence of ovarian enlargement postpartum.

This combination provides a potentially useful clinical learning point.

B. Detailed clinical course

The manuscript provides useful clinical information, including:

- gestational age at presentation;
- blood pressure;
- ovarian measurements;
- ascites;
- liver enzymes;
- hematocrit;
- proteinuria;
- fetal weight;
- Doppler findings;
- medications;
- duration of hospitalization;
- mode and timing of delivery;
- postpartum ovarian measurements.

This makes the case more clinically informative than a very brief case report.

REVIEWER'S REPORT**C. Serial ovarian imaging is valuable**

The comparison between ovarian dimensions before ovulation induction, at presentation, and postpartum is potentially one of the strongest elements of the report.

The persistence of enlarged multicystic ovaries at three weeks postpartum is particularly interesting and could be emphasized more strongly.

D. Management dilemma is clinically relevant

The manuscript appropriately identifies the difficulty of managing simultaneous OHSS and severe preeclampsia because fluid management can be challenging.

The authors' description of an oral-hydration strategy rather than aggressive intravenous fluid administration is potentially useful, provided that the rationale is supported by appropriate guidelines and the patient's volume status is clearly documented.

E. Appropriate clinical outcome reporting

The manuscript reports maternal and neonatal outcomes and includes postpartum follow-up. This strengthens the case-report format.

F. Current terminology

The manuscript uses the recently introduced term **polyendocrine metabolic ovarian syndrome (PMOS)**. The terminology is legitimate as of 2026: the global consensus proposing PMOS as the new name for PCOS was published online May 12, 2026, and in *The Lancet* in June 2026.

3. Major weaknesses***A. The diagnosis of OHSS needs much stronger justification***

This is the **most important scientific concern**.

The manuscript states that the patient had "moderate OHSS," but the diagnostic criteria are not adequately demonstrated.

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The authors should explicitly explain:

1. Why this represents OHSS rather than ovarian enlargement associated with the underlying ovarian disorder.
2. Which accepted OHSS classification was used.
3. Why it was classified as **moderate** rather than severe OHSS.
4. Whether there was hemoconcentration.
5. Whether there was oliguria.
6. Whether there were electrolyte abnormalities.
7. Whether renal impairment was present.
8. Whether there was pleural effusion.
9. Whether there was thromboembolism.
10. Whether the ovarian enlargement represented hyperstimulation or pre-existing enlarged polycystic ovaries.

This is particularly important because the patient already had enlarged cystic ovaries **before conception**.

The manuscript states that the ovaries measured 4.2 and 5.6 cm before induction, then 11.65 and 11.85 cm at 30 weeks. This is suggestive of substantial enlargement, but the authors need to establish why the enlargement should be attributed specifically to OHSS.

4. The distinction between OHSS and enlarged ovaries due to PMOS/PCOS needs clarification

This is closely related to the previous concern.

The manuscript appears to assume:

enlarged ovaries + ascites + pregnancy = OHSS.

That is not sufficient.

The authors should provide a clearer differential diagnosis, including:

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- OHSS;
- spontaneous OHSS;
- ovarian hyperstimulation associated with pregnancy;
- bilateral ovarian cystic enlargement associated with PMOS/PCOS;
- ovarian tumors/neoplasms;
- ovarian torsion;
- ovarian theca-lutein cysts;
- multiple corpus luteum cysts.

A particularly important question is whether the patient received **only letrozole**, or whether hCG, gonadotropins, progesterone, or any other fertility medication was administered.

The manuscript currently says "letrozole monotherapy," but this needs to be explicitly documented.

5. The timing of OHSS is unusual and requires a much stronger explanation

The patient developed the reported syndrome at approximately **30 weeks' gestation**.

This is extremely important to the novelty of the case.

The authors should clearly distinguish:

- early OHSS;
- late OHSS;
- spontaneous OHSS;
- pregnancy-associated OHSS.

The discussion should explain the possible mechanism for **late/persistent OHSS after letrozole ovulation induction**.

The manuscript mentions VEGF and angiogenic mechanisms, but the argument remains largely theoretical.

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If available, the authors should report:

- serum β -hCG;
- estradiol;
- AMH;
- ovarian reserve markers;
- relevant endocrine investigations;
- albumin;
- electrolytes;
- coagulation profile;
- renal function;
- LDH;
- uric acid.

If these were not measured, the manuscript should explicitly state this rather than implying that the mechanism was demonstrated.

6. The diagnosis of preeclampsia needs to be presented according to accepted diagnostic criteria

The patient clearly had severe hypertension and proteinuria, but the manuscript should explicitly document the diagnostic criteria.

For example:

- BP $\geq$ 160/110 mmHg;
- proteinuria;
- elevated transaminases;
- fetal growth restriction;
- abnormal umbilical artery Doppler.

The authors should specify which guideline was used to classify the condition as **preeclampsia with severe features**.

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The phrase "severe early-onset pre-eclampsia" should be standardized throughout the manuscript.

7. There is a potentially important inconsistency regarding renal function

The manuscript states:

"Serum creatinine was 59.3 mmol/l"

This is almost certainly a **unit error**.

Creatinine is normally reported in:

- $\mu\text{mol/L}$, or
- mg/dL .

If the intended value was **59.3 $\mu\text{mol/L}$** , this should be corrected.

This is important because renal function is central to both OHSS severity assessment and severe preeclampsia assessment.

8. The magnesium sulfate regimen needs clarification

The manuscript states:

"14 g loading dose followed by 5 g intramuscularly every 4 hours"

This needs verification and clarification.

The authors should specify:

- whether the 14-g loading dose was IV/IM;
- whether the regimen was based on a particular national/institutional protocol;
- why this particular regimen was selected.

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Because this is a clinical case report, unusual dosing should not be left unexplained.

9. The fluid-management discussion is potentially overstated

The manuscript says:

"oral-hydration-first strategy"

and concludes that this avoided risk to the patient.

The authors should be cautious here.

A single case cannot establish that this strategy is safe or superior.

The manuscript should instead say that oral hydration was used in this particular hemodynamically stable patient, with close monitoring.

Avoid language suggesting that this case validates a treatment strategy.

10. Enoxaparin requires more explanation

The authors state that enoxaparin was "crucial" to prevent thromboembolism.

That wording is too strong for a case report.

It would be more scientifically appropriate to state that thromboprophylaxis was administered because the patient had multiple thrombotic risk factors, including:

- pregnancy;
- OHSS;
- preeclampsia;
- hospitalization;
- reduced mobility.

The authors should also state whether there was any actual evidence of thrombosis.

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11. The manuscript overstates the relationship between PMOS and the two complications

The statement that:

"Her underlying Polyendocrine Metabolic Ovarian Syndrome provided a baseline predisposition to both complications."

is plausible but **not demonstrated by this case**.

PMOS is associated with increased risks of pregnancy complications, including hypertensive disorders and fetal growth abnormalities, but the case does not demonstrate that PMOS caused the OHSS.

The recent literature supports an association between PMOS and pregnancy complications, including preeclampsia and fetal growth restriction, but that should not be converted into a causal claim for this individual patient.

I recommend changing causal language to **"may have contributed to"** or **"may represent an underlying risk factor."**

12. Reference 9 appears inappropriate

This is a major editorial/scientific problem.

Reference 9 is:

"The effect of cognitive behavioral therapy on disease recovery and medication adherence in first-episode schizophrenia patient."

This has **no apparent relevance** to the claim immediately preceding it concerning OHSS risk factors.

This reference should be removed and replaced with the correct source supporting:

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- prior OHSS;
- high AFC;
- elevated AMH;
- young age;
- ethnicity;
- OHSS risk.

This error may significantly undermine reviewer confidence in the reference list.

13. Reference 2 appears mismatched to the clinical intervention

The manuscript cites an **ESHRE** guideline on ovarian stimulation for IVF/ICSI when discussing ovulation induction.

The authors should ensure that references specifically support **letrozole ovulation induction in anovulatory women/PMOS**, rather than relying primarily on IVF/ICSI stimulation guidelines.

14. The title needs reconsideration

The current title is:

"Early-Onset Preeclampsia and Ovarian Hyperstimulation Syndrome following ovulation induction in a woman with Polyendocrine Metabolic Ovarian Syndrome"

The title is reasonable, but it may imply a causal relationship between letrozole and OHSS.

A more cautious title would be:

"Concurrent early-onset preeclampsia and ovarian hyperstimulation syndrome following letrozole ovulation induction in a woman with polyendocrine metabolic ovarian syndrome: a case report"

This makes the clinical association clear without claiming causality.

REVIEWER'S REPORT**15. The manuscript needs substantial language editing**

There are numerous grammatical, typographical, and formatting problems, for example:

- "womanwith"
- "preeclampsiais"
- "Letrozoleis"
- "moderateOHSS"
- "Weadmitted"
- "Ove the nextthree weeks"
- "Shewas"
- "dopplersand"
- "hypertensionwas"
- "unavailabilityof"
- "manged"
- "followup"
- "core existence of OHSS"

These should be corrected throughout.

There are also inconsistent uses of:

- OHSS;
- pre-eclampsia/preeclampsia;
- PMOS;
- fetal growth restriction/IUGR;
- Doppler/BPP terminology.

A professional English-language medical edit is strongly recommended.

16. Ethical statement requires correction

The manuscript says:

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"Ethical Clearance: Not applicable"

but subsequently states that written informed consent for publication was obtained.

The journal's case-report policy should be followed exactly.

If institutional ethical approval was not required, the authors should state this clearly, for example:

"Institutional ethical approval was waived/not required for publication of this single case report. Written informed consent for publication was obtained from the patient."

However, this should only be stated if it accurately reflects the institution's policy.

17. The figures need stronger presentation

The ovarian ultrasound images are potentially important, but the manuscript should provide:

- gestational age at imaging;
- laterality;
- ovarian dimensions;
- imaging modality;
- relevant ultrasound findings;
- arrows/labels identifying ovaries and cystic structures;
- adequate image resolution.

The postpartum images should similarly identify the three-week postpartum time point.

18. The case timeline should be presented as a table or figure

This would substantially improve the manuscript.

For example:

Time

Clinical event

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Time	Clinical event
2023	Secondary amenorrhea/infertility
Apr 2025	Clomiphene induction
Aug 2025	Letrozole → pregnancy → miscarriage
Dec 2025	Letrozole → conception
30+2 weeks	Presentation with hypertension, ascites, enlarged ovaries
30–34 weeks	Inpatient management
34 weeks	Delivery
3 weeks postpartum	Persistent ovarian enlargement

This would make the clinical sequence much easier to understand.

19. Key points / novelty

The manuscript's strongest **key points** are:

1. **OHSS can occur following letrozole-based ovulation induction**, although it is generally considered a low-risk intervention for OHSS.
2. **Marked ovarian enlargement and ascites can persist into the third trimester and postpartum period.**
3. **OHSS and severe preeclampsia can create overlapping clinical features**, complicating diagnosis and fluid management.
4. The combination of **OHSS + early-onset preeclampsia + fetal growth restriction** represents an unusual clinical constellation.
5. The case emphasizes the importance of **serial ovarian imaging and maternal fluid/hematologic monitoring** in selected patients with significant ovarian enlargement.

The authors should focus the paper around these points rather than making broad claims about PMOS causing OHSS.

REVIEWER'S REPORT**20. Significance****Potential significance: moderate to high**

The case has potential significance because it raises an uncommon diagnostic and management problem.

The most interesting aspect is **not simply that the patient had OHSS and preeclampsia**. Rather, the potentially publishable observation is the combination of:

letrozole ovulation induction → pregnancy → persistent marked bilateral ovarian enlargement/ascites → OHSS-like syndrome in the third trimester → simultaneous severe early-onset preeclampsia → fetal growth restriction → persistent ovarian enlargement postpartum.

However, the significance will depend heavily on whether the authors can establish that the ovarian findings truly meet accepted criteria for OHSS rather than representing persistent polycystic/multicystic ovarian morphology.

21. Recommended major revisions before publication

I would ask the authors to address the following **before the manuscript can be considered further**:

Essential revisions

1. **Provide explicit diagnostic criteria for OHSS.**
2. Explain why this is OHSS rather than ovarian enlargement associated with PMOS.
3. State exactly which fertility medications were administered.
4. Clarify whether **hCG or gonadotropins were ever given**.
5. Provide a clear timeline.
6. Correct the creatinine unit.
7. Reassess the magnesium sulfate regimen and explain the protocol.
8. Reassess the statement that enoxaparin was "crucial."
9. Remove/revise causal statements linking PMOS directly to OHSS.
10. Correct reference 9.

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11. Verify every reference against the statement it supports.
12. Clarify the diagnosis/classification of preeclampsia.
13. Explain the unusually late presentation/persistence of OHSS.
14. Expand the differential diagnosis of bilateral ovarian enlargement.
15. Provide institutional ethics information.
16. Professionally edit the manuscript for English and formatting.
17. Improve figure legends and image labeling.
18. Add a clinical timeline.
19. Avoid presenting the oral-hydration approach as a validated treatment strategy based on one case.
20. Moderate the conclusion so that it reflects the limitations of a single case report.

22. Reviewer recommendation**Recommendation: MAJOR REVISION**

Rationale: The case has a potentially valuable and unusual clinical presentation, and the combination of late pregnancy OHSS, severe early-onset preeclampsia, and persistent ovarian enlargement following letrozole ovulation induction could be of interest to clinicians in reproductive medicine and obstetrics.

However, the manuscript currently has important weaknesses in **diagnostic substantiation, causal interpretation, clinical terminology, treatment description, reference accuracy, and presentation**. In particular, the authors must convincingly demonstrate that the ovarian enlargement and ascites represent OHSS and not simply persistent/multicystic ovarian enlargement associated with the underlying disorder.

If these issues are adequately addressed, the case could become a useful case report.

Suggested editorial decision:

Major Revision — reconsider after substantial scientific and language revision.

One additional point is worth emphasizing: the manuscript's use of **PMOS** is not inherently problematic in a September 2026 submission, because the terminology was formally introduced

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through the 2026 global consensus publication. But because this terminology is very new, the authors should introduce it explicitly as “**polyendocrine metabolic ovarian syndrome (PMOS)**, formerly known as **polycystic ovary syndrome (PCOS)**” at first mention and explain the transition in terminology.