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## REVIEWER'S REPORT

**Manuscript No.:** IJAR-53568 Date: 26/08/2025

Title: Hormonal Contraception and Breast Cancer Risk: Balancing Benefits and Vigilance

**Recommendation:**
✓ Accept as it is .....
Accept after minor revision.....
Accept after major revision .....
Do not accept (*Reasons below*) .....

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

Reviewer Name: Dr. S. K. Nath Date: 26/08/2025

**Reviewer's Comment for Publication:**
The paper effectively balances current evidence on the modest, reversible increase in breast cancer risk associated with hormonal contraception, emphasizing that this risk is influenced by factors such as duration, hormonal formulation, and genetic predispositions. It underscores the importance of personalized counseling, especially for women with high genetic risk (e.g., BRCA mutations), and advocates for integrating emerging epigenetic biomarkers to tailor contraceptive choices in the future. While the evidence base supports the continued use of hormonal contraceptives in most women, clinicians should carefully weigh individual risk factors and involve patients in shared decision-making.

***Reviewer's Comment / Report***

**Strengths**

1. **Comprehensive Literature Review:** The paper synthesizes data from multiple large-scale epidemiological studies, meta-analyses, and systematic reviews, providing a broad overview of current evidence.
2. **Focus on Genetic Factors:** It emphasizes the differential impact of hormonal contraception on women with genetic mutations, particularly BRCA1 and BRCA2, which is crucial for personalized medicine.
3. **Discussion on Duration and Type of Use:** The article highlights how risk varies with duration of contraceptive use and hormone composition, providing practical insights for clinicians and patients.
4. **Integration of Epigenetics:** It explores future perspectives involving epigenetic markers (like DNA methylation), advocating for personalized contraceptive strategies based on biological signatures.
5. **Reassures Low Absolute Risk:** The paper contextualizes the modest increase in risk, especially noting that for most women, the absolute risk remains low, supporting informed decision-making.

**Weaknesses**

1. **Limited Data on Long-term Follow-Up:** Although the paper mentions risk diminishes after discontinuation, long-term prospective data are limited, and ongoing studies could provide more definitive conclusions.
2. **Heterogeneity of Studies Cited:** Variability in study designs, populations, and hormonal formulations may complicate the interpretation of pooled results, which the paper acknowledges but could analyze more critically.
3. **Insufficient Focus on Ethnic and Population Diversity:** Most cited studies are from specific regions (e.g., Swedish or Western cohorts), and the impact on diverse populations is less explored.

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4. **Emerging Perspectives Are Theoretical:** The discussion on biomarkers and epigenetics is forward-looking but not yet applicable in clinical practice, which might oversell the near-term relevance.
5. **Limited Discussion on Non-Hormonal Alternatives:** The focus is predominantly on hormonal methods; a comparative analysis including non-hormonal options would add value.