Review of: "Gestational Inflammation: Its Foetal Control and the Proper Therapeutic Approach"

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The article **"Gestational Inflammation: Its Foetal Control and the Proper Therapeutic Approach"** by Fortunato Vesce is well-structured but has several significant shortcomings that must be addressed before it can be deemed fit for publication. While the topic of gestational inflammation and its role in obstetric complications is highly pertinent to modern obstetrics, the presentation of the material, reliance on outdated references, and subjective tone hinder its scientific rigor.

The **structure** of the article is logically organized, starting with a detailed introduction to gestational inflammation and its vascular implications. For example, the opening line on page 1, *"Inflammation triggers coagulation. Gestational inflammation, with its vascular implications, is the cause of major obstetric complications…"*, sets a clear foundation for the discussion that follows, addressing complications such as miscarriage, foetal growth restriction, and preterm birth. This introductory section provides a coherent overview of the physiological role of inflammatory mediators, highlighting their dual functions in the maternal-fetal immune balance. However, as the article progresses, the structure falters. The shift to the discussion on therapeutic interventions—specifically betamethasone—occurs abruptly. On page 3, line 18, the author asserts, *"Betamethasone is the drug of choice for prevention and therapy of gestational inflammation,"* without sufficiently exploring other therapeutic alternatives or justifying this choice with recent clinical evidence. The article presents a one-sided view, focusing solely on betamethasone, while failing to discuss other established treatments like progesterone, aspirin, or immunomodulators.

The **scientific validity** of the claims made in the article is often undermined by a lack of engagement with broader, contemporary research. The description of immune mechanisms in pregnancy is generally sound, as seen in the discussion on cytokine balance in preeclampsia. For instance, on page 4, line 6, the author explains how the *"IFN-gamma/IL-6 ratio switches around the 19th week of pregnancy"*, providing a scientifically accurate and well-referenced insight into the immune shifts during gestation. However, this rigor is not consistently applied throughout the article. For example, on page 2, line 7, the statement *"Controlling gestational inflammation is primarily a foetus's job"* oversimplifies the complex interplay between maternal and foetal immune systems. This line disregards the significant role maternal health and immune function play in managing inflammation during pregnancy, an omission that weakens the overall argument. Similarly, the sweeping generalization on page 2, line 11, that *"current obstetrics does not effectively counteract gestational inflammation"* is not substantiated by sufficient evidence from clinical studies, giving the impression that the article is more opinionated than scientifically grounded.

In terms of **references**, the article heavily relies on older sources, which diminishes its relevance in the context of current

obstetric practices. While some references are pertinent, such as the citation of Saito and Sakai (2003) in discussing cytokine imbalances in preeclampsia on page 4, line 16, much of the literature cited is outdated. Several critical references, including those on the use of corticosteroids in pregnancy (e.g., page 10, line 4), are from the 1980s and 1990s, missing out on more recent findings that could either corroborate or challenge the article's arguments. The suggestion that betamethasone should be prescribed universally in cases of gestational inflammation, even in women without a history of pregnancy loss, is a particularly bold claim. However, this assertion is not backed by contemporary large-scale studies or meta-analyses that could provide a stronger empirical basis for such a recommendation. The author's reliance on older studies and lack of engagement with newer systematic reviews limit the article's ability to contribute meaningfully to the ongoing scientific debate about the best treatments for pregnancy-related inflammation.

The **relevance of the theme** is undeniable. Inflammation in pregnancy is a critical issue, with direct links to miscarriage, preterm birth, and foetal growth complications. The article addresses these concerns in detail, particularly through its exploration of cytokine regulation in pregnancy and the immune balance between the mother and the foetus, as seen on page 6, lines 10-12. However, the author's recommendation for widespread use of betamethasone (page 2, line 10) is controversial. Broadly advocating for its use in all women, including those without prior pregnancy complications, without adequately discussing the associated risks, is problematic. This advice could be seen as reckless in the absence of robust evidence from randomized controlled trials, particularly considering the potential side effects of prolonged corticosteroid use during pregnancy.

The **level of writing** is generally clear and accessible, but the tone of the article sometimes lapses into subjectivity, which detracts from the objectivity expected in academic writing. While the explanations of biological processes, such as the foetal immune system's role in modulating placental blood flow (page 3, line 8), are well-articulated, the personal tone of the article becomes problematic when the author leans too heavily on personal clinical experience. For example, on page 10, line 15, the author notes, *"I soon realized that for recurrent miscarriage, the therapy was always the same, despite its previous failures,"* introducing a subjective element that shifts the focus away from evidence-based analysis toward personal opinion. This undermines the academic neutrality required in peer-reviewed articles, where clinical experience should be framed within the context of broader empirical evidence.

As for **methodologies**, the article does not present new experimental data but offers a review of existing studies along with personal clinical observations. While the discussion of prostacyclin and thromboxane imbalance in recurrent miscarriage (page 5, lines 10-13) is well-supported by references and adds value to the discussion, the reliance on anecdotal evidence elsewhere weakens the overall methodological rigor. For instance, the extensive focus on personal clinical experience with betamethasone (page 10, line 18) is problematic, as the lack of empirical backing from large-scale trials or observational studies makes it difficult to assess the generalizability of these findings. A more robust methodological approach would involve citing randomized controlled trials that provide stronger empirical support for the claims made.

The **discussion and conclusion** sections reiterate the importance of controlling gestational inflammation, but they do so in a manner that is overly reliant on the author's personal therapeutic approach. For example, on page 11, line 7, the

author claims, *"Betamethasone is the drug of choice for prevention and therapy of gestational inflammation,"* without acknowledging alternative approaches or adequately discussing the risks associated with long-term corticosteroid use. This narrow focus on a single therapeutic option, without considering potential risks or discussing complementary treatments, limits the depth of the discussion and the article's potential impact on the field.

In conclusion, while the article contributes to an important discussion on gestational inflammation, it requires **significant revisions** before it can be considered for publication. These revisions should include:

1. **Updating the references** to include more recent studies and systematic reviews.
2. **Broadening the therapeutic discussion** to incorporate alternative treatments and approaches.
3. **Reducing the personal tone** and ensuring that claims are backed by empirical data rather than anecdotal evidence.
4. **Providing a more balanced review** of contemporary research on the subject, addressing both the strengths and limitations of current obstetric practices.

Without these revisions, the article lacks the scientific rigor necessary to meet the standards of a high-impact journal.