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### Letter to the Editor

## Beyond the Usual Suspects: A Genetic Perspective on Toxoplasmosis-Related Recurrent Abortion and IL-18

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### Dear Editor-in-Chief

The research article by Fadhil and Saheb, Single Nucleotide Polymorphism (SNP) of IL-18 (*Rs1946519*) in Recurrent Aborted Iraqi Women and Its Association with Toxoplasmosis, (1) offers a significant contribution to our understanding of the complex interplay between genetics, immune function, and reproductive health outcomes. Specifically, the study investigates the role of a SNP in the IL-18 gene (*rs1946519*) and its association with recurrent abortion in Iraqi women, a population with a unique cultural and epidemiological context. This research is particularly valuable as it examines this relationship within the context of toxoplasmosis, a significant infectious agent known to impact pregnancy outcomes.

The study's central finding, a significant association between specific genotypes of the IL-18 SNP (*rs1946519*) and the risk of recurrent abortion in the presence of toxoplasmosis, provides compelling evidence for the involvement of genetic factors in this complex condition. Notably, the CC genotype appears to offer some level of protection against recurrent abortion, while the presence of the A allele seems to increase the risk. These findings suggest a direct influence of this genetic variation on an individual's susceptibility or resistance to the detrimental effects of *Toxoplasma gondii* infection during pregnancy. While previous researches (2, 3) have explored the role of this SNP in various inflammatory conditions, including recurrent abortion, this



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study significantly expands our understanding by examining its association with toxoplasmosis in a specific and understudied population.

Furthermore, the study observed notable differences in serum levels of IL-18, a crucial cytokine involved in immune responses, across different genotypes and study groups. This finding strongly suggests that the IL-18 SNP not only acts as a genetic marker but also exerts a functional effect on the expression and regulation of IL-18 itself. This, in turn, likely influences the strength and effectiveness of the immune response during pregnancy. Specifically, lower serum IL-18 levels observed in women carrying the AA and AC genotypes may indicate a less robust inflammatory response to *T. gondii* infection, potentially increasing the risk of pregnancy loss. These findings underscore the importance of moving towards a more personalized approach to reproductive healthcare, where genetic factors are considered alongside other risk factors.

From a public health perspective, this research has several critical implications. Firstly, it highlights the need to acknowledge the significant role of genetic predisposition in the prevention and management of recurrent abortion. While environmental and lifestyle factors are undoubtedly important, this study emphasizes that genetic susceptibility can substantially contribute to the risk of adverse pregnancy outcomes. This knowledge can inform public health strategies by enabling the identification of women at higher risk for toxoplasmosis-related recurrent abortion through targeted screening programs. Increased public awareness campaigns regarding toxoplasmosis prevention, including food safety and hygiene practices, are crucial for all women of childbearing age, particularly in regions with high rates of infection.

Secondly, the study advocates for the development of personalized interventions based on individual genetic profiles. Given the potential association between the A allele and a

dysregulated immune response to *T. gondii*, future research should focus on developing therapeutic strategies that can modulate this response. This may involve exploring novel immunotherapies or other targeted approaches to mitigate the negative effects of the A allele.

Thirdly, the findings emphasize the importance of comprehensive maternal health programs that incorporate screening for infectious diseases, such as toxoplasmosis, and potentially integrate genetic testing, particularly for high-risk populations. These programs should provide access to quality prenatal care, implement systematic screening for *T. gondii* infection, and offer comprehensive counseling on safe food handling and hygiene practices. It is crucial to consider the unique cultural and social contexts of different populations when designing such programs. The study did not explicitly investigate how cultural practices might influence an individual's risk of toxoplasmosis infection. Further research is necessary to understand these factors better to develop more effective and culturally appropriate public health interventions.

Finally, this research serves as a strong foundation for further investigation. Large-scale studies are needed to validate these findings in diverse populations and to further elucidate the underlying mechanisms by which the IL-18 SNP influences IL-18 expression and function. Longitudinal studies and multi-omic approaches, which integrate data from various levels of biological organization, can provide a more comprehensive understanding of the complex interplay between genetic, immunological, and environmental factors in recurrent abortion. Furthermore, future research should explore the potential interactions between the identified SNP, environmental factors (such as diet, stress, and occupational hazards), and other genetic factors that may contribute to the risk of recurrent abortion.

This study, while valuable, has some limitations. The authors did not explicitly investigate the specific exposure or infection status of the study participants for *T. gondii*. Incorporating this information

into future studies will be crucial for a more comprehensive understanding of the relationship between the SNP, toxoplasmosis infection, and recurrent abortion. Additionally, the cross-sectional study design limits the ability to draw definitive conclusions about causality. Longitudinal studies are needed to track the progression of recurrent abortion and the influence of genetic factors over time.

The study provides valuable insights into the role of an IL-18 gene polymorphism in recurrent abortion, particularly within the context of toxoplasmosis infection. The findings have significant implications for public health, highlighting the need for population-level screening, targeted interventions, and comprehensive maternal health programs. Further research is essential to translate these findings into effective clinical and public health practices, ultimately improving maternal and reproductive health outcomes for women worldwide.

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### **Conflict of Interest**

The authors declare that there is no conflict of interests.

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