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Original Article

Miscarriage Trends and Blood Group Associations During the COVID-19 Pandemic: A Comparative Study in Ramsar, Iran

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Abstract

Background: The COVID-19 pandemic has placed significant physiological, physical, and psychological burdens on populations worldwide. Childbearing, as a fundamental aspect of human life, can be negatively affected during such crises. This study aimed to evaluate the impact of the COVID-19 pandemic on miscarriage rates and to investigate the potential association between spontaneous abortions and maternal blood groups. **Materials and Methods:** A retrospective analytical cross-sectional study was conducted using 8,613 hospital records from two healthcare centers in Ramsar and Tonekabon, Iran. Miscarriage rates were analyzed relative to total delivery requests during the pre-pandemic (2017–2019) and pandemic (2020–2022) periods. In the second phase, unexplained spontaneous abortions were examined in relation to maternal ABO and the Rhesus factor (Rh) blood groups across both periods. **Results:** The analysis revealed a significant increase in miscarriage rates during the pandemic, despite a general decline in delivery requests. In the study sample, blood group distribution was A: 29.86%, B: 21.53%, O: 43.06%, and AB: 5.56%, while 9.72% were Rh-negative and 90.28% Rh-positive. Although abortions appeared more common in certain blood groups (notably B and O), statistical analysis showed no significant association between miscarriage and maternal individual blood types before or during the pandemic. **Conclusions:** The findings suggest that physiological and psychological stressors during the pandemic may have contributed to increased miscarriage rates. Health systems should implement integrated strategies, including mental health support and enhanced prenatal care, to reduce adverse pregnancy outcomes during pandemics or similar crises.

Keywords: *Abortion, COVID-19, pandemics, pregnancy complications, psychological distress, reproductive health*

Introduction

Successful pregnancy and childbirth are central to family life, relying heavily on the mother's holistic health, which encompasses physical, mental, genetic, and sociocultural factors that collectively determine pregnancy outcomes.[1,2] Miscarriage, the loss of a pregnancy before 20 weeks of gestation, is a deeply distressing event that can lead to considerable physical and emotional suffering for the mother and may also precipitate significant strain within the family unit.[1,3,4] While it is crucial to identify infectious, non-infectious, and environmental factors influencing pregnancy outcomes,[5,6] a substantial proportion of spontaneous miscarriages occur without an identifiable maternal or fetal cause. This indicates that as-yet-unexplored psychological or biological factors may contribute significantly and merit further investigation.

The COVID-19 pandemic introduced a unique combination of risk factors that may have increased the likelihood of pregnancy loss. Directly, SARS-CoV-2 infection was associated with an increased risk of miscarriage, potentially through placental inflammation that impairs fetal development.[7] Indirectly, the pandemic generated widespread psychological distress, with pregnant women, already a vulnerable group, experiencing heightened levels of anxiety, depression, and fear.[8-10] This stress is a recognized major risk factor for miscarriage, potentially by stimulating natural killer cells.[11,12] Concurrently, physiological changes during pregnancy, such as immune suppression, may increase susceptibility to viral complications.[13,14]

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Beyond these environmental stressors, the role of individual biological characteristics remains less clear. While parental blood incompatibility is an established risk factor,[15] limited and conflicting evidence exists regarding the association between a mother's specific blood type and her risk of spontaneous miscarriage,[16-18] creating a significant gap in the literature.

This study aims to address these gaps by examining the multifaceted risks of miscarriage during the COVID-19 pandemic. This period was marked by extraordinary physical and psychological challenges.[19,20] Accordingly, this study investigates whether the prevailing environmental conditions during the pandemic influenced miscarriage rates within the population. The primary objective was to evaluate changes in miscarriage rates during the COVID-19 pandemic compared to the pre-pandemic period among women in Ramsar and Tonekabon, Iran. A secondary objective was to explore the potential association between unexplained spontaneous miscarriages and maternal ABO/Rh blood groups. Recognizing the role of individual patient characteristics in disease susceptibility,[21] this study aims to shed light on the possible relationship between maternal blood type and miscarriage incidence, contributing to a clearer understanding of this underexplored area.

Ultimately, the study aimed to provide evidence to inform health system planning and management during public health emergencies such as pandemics, particularly concerning maternal health, it also sought to identify factors linked to spontaneous miscarriages to guide preventive and supportive strategies for pregnant women in future crises.

Materials and Methods

This retrospective analytical cross-sectional study was conducted using hospital records from two healthcare centers, Imam Sajjad Hospital in Ramsar and Shahid Rajai Hospital in Tonekabon, Mazandaran, Iran, while ensuring the confidentiality of patient information. The study was conducted in two stages. In the first stage, total miscarriage rates were analyzed relative to the number of deliveries during two periods: Before the COVID-19 pandemic (March 2017 to February 2019) and during the pandemic (March 2020 to February 2022). Based on these results, the second stage focused on spontaneous miscarriages of unknown cause, examining their potential association with maternal blood type. The study protocol received ethical approval from the Mazandaran University of Medical Sciences Ethics Committee (IR.MAZUMS.RIB.REC.1401.072). Patient confidentiality was strictly maintained throughout the study, and none of the participants were enrolled in concurrent randomized clinical trials.

In the first phase, medical records of 8,613 pregnant women aged 18–35 years were reviewed, encompassing both live births and miscarriage outcomes. Miscarriage was defined as pregnancy loss before 20 weeks of gestation, calculated from the last menstrual period (LMP). All recorded miscarriages, regardless of cause, were included. Data were collected using standardized checklists capturing demographic details and pregnancy outcomes.

The second phase of the study was to investigate the association between spontaneous miscarriages of unknown cause and maternal ABO/Rh blood groups during and before the pandemic in both hospitals. The study included pregnant women aged 18–35 years who, based on laboratory tests, paraclinical evidence, and medical history from their records, had experienced spontaneous miscarriages without an identifiable maternal or fetal cause. To ensure accuracy and minimize potential bias, strict exclusion criteria were applied: Women with a history of infectious diseases, recurrent miscarriages, ovarian disorders, multiple pregnancies (e.g. twins, triplets), or fetal abnormalities were excluded from the study. Initially, 400 miscarriages were considered, of which 144 women met the criteria for complete spontaneous abortion and were included in the final analysis. The final sample size for blood group analysis was calculated assuming a 35% miscarriage prevalence, with a statistical power of 80% and a type I error rate of 5%. Accordingly, 144 cases were randomly selected: 72 from the pre-epidemic period and 72 from the epidemic period. Information on maternal ABO and Rh blood groups was collected from medical records and analyzed to assess any association with miscarriage in the two study periods.

Data analysis was performed using Prism and SPSS (IBM, version 17). Descriptive statistics were presented as means and standard deviations for quantitative variables. The Kolmogorov-Smirnov test was used to assess data distribution normality. For group comparisons, independent t-tests and Chi-square tests were employed. Statistical significance was set at $p < 0.05$, linear correlation analysis was also performed to explore potential predictors of miscarriage.

Ethical considerations

The study protocol was approved by the Ethics Committee of Mazandaran University of Medical Sciences (IR.MAZUMS.RIB.REC.1401.072). Confidentiality of patient data was strictly maintained, and no participants were involved in concurrent randomized clinical trials.

Results

Demographic analysis of the 8,613 reviewed cases showed that, in the pre-COVID-19 period (2017–2019), 4,309 records were documented, including 3,288 live births and 812 miscarriages. During the COVID-19 pandemic (2020–2022), hospital attendance decreased to 3,492 cases, with 2,877 resulting in live births and 615 in miscarriages [Table 1].

Statistical analysis showed a significant increase in miscarriage rates, despite a decrease in overall childbirths during the pandemic ($p = 0.031$) [Figure 1].

Blood group and Rh factor distributions were compared in 144 mothers with spontaneous miscarriages, including 72 cases before and 72 during the COVID-19 pandemic. Among the 144 participants, blood group distribution was: A = 43 (29.86%), B = 31 (21.53%), O = 62 (43.06%), and AB = 8 (5.56%). For Rh factor, 14 women (9.72%) were Rh-negative and 130 (90.27%) were Rh-positive. Blood group distribution differed between the two periods. Before the pandemic, the proportions were: A = 35.62%, B = 17.81%, O = 38.36%, and AB = 8.22%. During the pandemic, the corresponding proportions were: A = 23.94%, B = 25.35%, O = 47.89%, and AB = 2.82%.

The correlation coefficient test was used to examine the relationship between categorical variables, specifically maternal ABO and Rh blood groups, and the incidence of miscarriages. The results showed that both variables had *p* values below the 0.05 threshold (ABO blood groups: 0.038; Rh alleles: 0.025), indicating a statistically significant association with miscarriage rates. In other words, miscarriage frequency varied across maternal blood types and Rh alleles, suggesting these biological factors may influence miscarriage outcomes [Table 2]. The results suggest that, during the pandemic, spontaneous miscarriage rates decreased among women with blood groups A and AB, while increasing among those with blood groups B and O. However, Chi-square analysis at the 0.05 significance level showed no statistically significant association between individual blood groups and spontaneous miscarriage when comparing the pandemic and pre-pandemic periods [Figure 2a], indicating that the observed fluctuations may reflect random variation rather than a consistent pandemic-related effect.

Regarding the Rh factor, 93.15% of mothers with spontaneous miscarriages were Rh-positive and 6.85% were Rh-negative before the pandemic. During the pandemic, the distribution shifted to 87.32% Rh-positive and 12.68% Rh-negative [Figure 2b]. Statistical analysis ($p = 0.272$) indicated no significant association between the Rh factor and spontaneous miscarriage in relation to the COVID-19 pandemic.

Discussion

The findings of this study revealed a significant increase in miscarriage rates during the COVID-19 pandemic, despite a concurrent decline in overall childbirths. This paradox highlights the complex interplay between biological, psychological, and social factors influencing pregnancy outcomes. Such results are particularly important because they suggest that, in addition to infection-related risks, indirect consequences of the pandemic, such as restricted access to healthcare facilities, heightened psychological stress, may have exerted a stronger influence on reproductive health.[22] These findings provide novel evidence from an Iranian population, adding valuable insight to the global understanding of how pandemics can affect reproductive outcomes. By highlighting the rise in miscarriage rates during COVID-19, this study emphasizes the need for health systems to consider both direct and indirect pandemic-related impacts on maternal health.

Previous studies have reported inconsistent findings concerning the direct physiological effects of COVID-19 on pregnancy. Some early investigations suggested increased risks of cesarean section, preterm birth, stillbirth, and neonatal complications among symptomatic COVID-19-positive mothers.[17,23] In contrast, a Swedish prospective cohort study demonstrated no significant rise in fetal mortality among mothers infected with COVID-19.[24] Such discrepancies are likely to reflect differences in study design, sample size, population characteristics, and the criteria used to define pregnancy outcomes. These inconsistencies emphasize the multifactorial nature of miscarriage, wherein biological vulnerability may intersect with psychosocial stressors to determine outcomes.[12] Clinically, this suggests that while infection control remains important, psychosocial support may be equally critical in safeguarding maternal health during crises.

Psychological distress, including anxiety and depression, has long been linked to an increased risk of miscarriage.[25,26] Alterations in neurochemicals, including serotonin, dopamine,

Table 1: Demographic characteristics of reviewed cases before and during the COVID-19 pandemic, including total cases, live births, and miscarriages

Period	Total Cases	Live Births	Miscarriages
Pre-COVID-19 (2017-2019)	4309	3288	812
COVID-19 Pandemic (2020–2022)	3492	2877	615
Total	8613	6165	1427

Table 2: Results of the correlation coefficient test for the association between all blood groups and Rh alleles with number of miscarriages

Variable	*n*	Statistical Test χ^2	Degrees of Freedom	*p*
Blood Groups	144	9.028	3	0.038
Rh Alleles	144	7.236	1	0.025

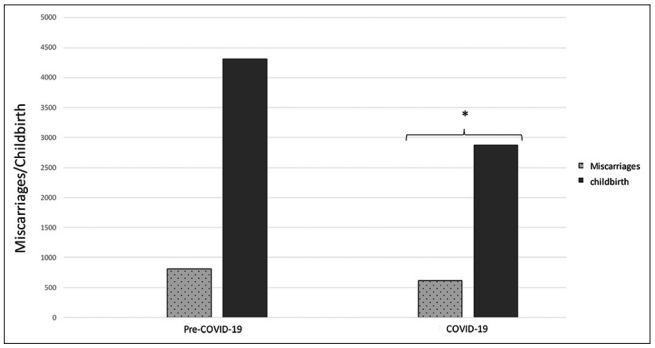


Figure 1: Comparison of the ratio of abortions to births before and during the COVID-19 period. Statistical analysis revealed that, although the number of women presenting for childbirth decreased during the COVID-19 period, the miscarriage-to-birth ratio showed a significant increase ($p \leq 0.005$)

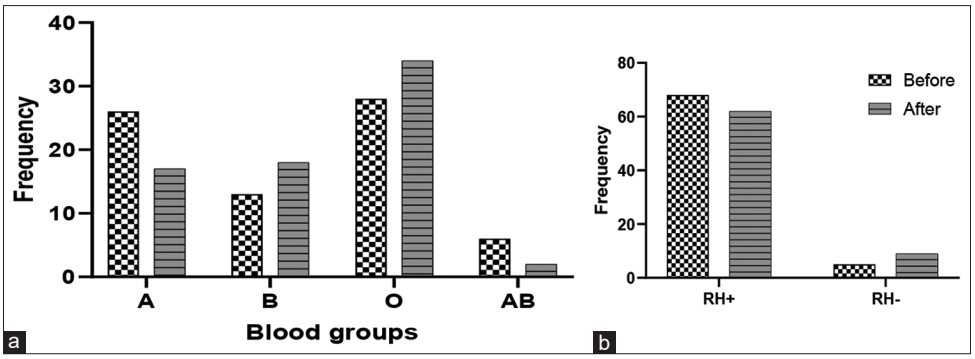


Figure 2: Comparison of blood group and Rh factor distribution among mothers with spontaneous miscarriages before and during the COVID-19 pandemic. While changes were observed in the distribution of blood groups A, B, O, and AB (a), along with a modest rise in Rh-negative cases during the pandemic. (b), statistical analysis revealed no significant associations between individual blood groups, Rh cases, and the rate of miscarriages ($p > 0.05$)

and γ-Amino butyric acid (GABA), have been suggested as potential mediators affecting pregnancy outcomes.[27,28] However, research indicates that psychological factors alone are insufficient to account for most cases of miscarriage.[29] For example, an Italian study found no significant change in miscarriage rates before versus during the pandemic, highlighting that such outcomes may be highly context-dependent, shaped by cultural, healthcare, and social factors.[30] This suggests that while stress may contribute to miscarriage risk, it likely acts alongside other biological and environmental factors rather than serving as the sole cause.[31] Future studies should explore the combined psychological, biological, and social factors influencing miscarriage to clarify their interrelated effect.

Additional findings from this study highlighted the potential role of maternal biological factors, specifically ABO blood groups and Rh status, in miscarriage outcomes. While overall analyses indicated significant associations with miscarriage rates, comparisons of individual blood groups and Rh status between the pre-pandemic and pandemic periods revealed no statistically significant differences. Associations between miscarriage and maternal blood type have been reported in some studies, whereas others have found no significant relationship, highlighting the inconsistency in existing evidence.[32,33] These inconsistencies are likely due to variations in population genetics, regional diversity, and differences in study design and methodology.[30] Given the complexity of the blood group system, with over 600 alleles and 27 serologically defined blood group systems,[29,34] it is plausible that certain subgroups remain underexplored, which may contribute to the inconsistent findings in previous research These results highlight the need for more comprehensive molecular and genetic investigations to better understand the biological factors contributing to miscarriage risk.

Overall, the results of this study suggest that public health crises, such as the COVID-19 pandemic, can adversely affect pregnancy outcomes through a combination of physiological and psychological factors. The observed rise in miscarriage rates, despite a concurrent decline in overall childbirths, suggests that psychosocial stressors and reduced access to healthcare may have had a greater impact on pregnancy outcomes than the direct effects of COVID-19 infection in the study population. However, further research is needed to explore the underlying causal mechanisms and clarify the relative contributions of these factors. Importantly, these findings emphasize the need to view maternal health holistically, integrating both medical and psychological perspectives, particularly during public health crises. However, the study was limited by its sample size and observational design, which may affect the generalizability of the findings. Future research should consider these limitations and focus on longitudinal and multicenter studies, as well as molecular and genetic investigations, to provide more accurate and comprehensive insights into miscarriage risk factors.

During the COVID-19 pandemic, some patients avoided visiting hospitals and public centers and continued their medical care in private clinics and dispensaries, and sometimes at home, which affected the statistical population. Therefore, it is better for health centers and consultants to follow up on patients' conditions and manage the situation in times of crisis through non-face-to-face means, such as phone calls.

Conclusion

This study highlights the importance of reproductive health surveillance and the provision of psychological support for pregnant women during public health crises. Policymakers and healthcare providers should implement proactive strategies, such as integrating mental health services into antenatal care and ensuring uninterrupted access to reproductive healthcare during crises. Future research should use longitudinal, multicenter designs to better clarify the interplay between infection, psychological stress, and biological factors, such as maternal blood group, in influencing miscarriage risk. Such studies will be crucial in developing evidence-based interventions to safeguard maternal and fetal health in future emergencies.

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Conflicts of interest

Nothing to declare.

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