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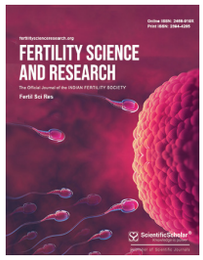

Original Article *Gynaecology*

Impacts of COVID-19 on Perinatal Mortality in Hungary

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ABSTRACT

Objectives: The first 2019 coronavirus disease (COVID-19) outbreak occurred in Hungary on 4 March 2020. This severe respiratory illness is characterised by high fever, cough, breathing difficulties, muscle pain, diarrhoea, and vomiting. It poses serious risks to pregnant women and their fetuses. Fetal losses increased in several countries during the COVID-19 pandemic, with the delta variant of severe acute respiratory syndrome coronavirus 2 causing the greatest increases in miscarriages. This study was conducted to assess the effects of the COVID-19 pandemic on pregnancy outcomes in Hungary.

Material and Methods: Data on abortions, stillbirths, and early and mid-term pregnancy losses in Hungary during the period of 1 January 2018 to 31 December 2021 were analysed retrospectively. Data are presented as numbers with percentages and rates per 1,000 births. Poisson values for the incidence rates were calculated. Incidence estimates are provided with 95% confidence intervals. Event rates were compared between time points using proportions and chi-squared tests.

Results: Stillbirth and spontaneous and voluntary abortion rates in Hungary showed decreasing trends during all four COVID-19 waves examined, but these differences were not significant.

Conclusion: A decline in fetal mortality in Hungary was observed during the study period, and COVID-19 did not significantly affect this trend.

Keywords: COVID-19, Teratogen effect, Abortion, Foetal loss

INTRODUCTION

The 2019 coronavirus disease (COVID-19) is a respiratory illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] The first COVID-19 cases were detected in December 2019 in Wuhan, China, and the World Health Organization declared the ensuing global COVID-19 outbreak a pandemic on 11 March 2020.[2] By the end of 2020, several SARS-CoV-2 variants had appeared (alpha, beta, gamma, and delta) and spread to diverse countries. The first reports of a SARS-CoV-2 omicron variant emerged from Botswana and South Africa in November 2021.[3]

SARS-CoV-2 is disseminated by close contact and droplet infection. Symptoms are very similar to those of other pneumonia types: high fever, headache, dry cough, sore throat, breathing difficulty,

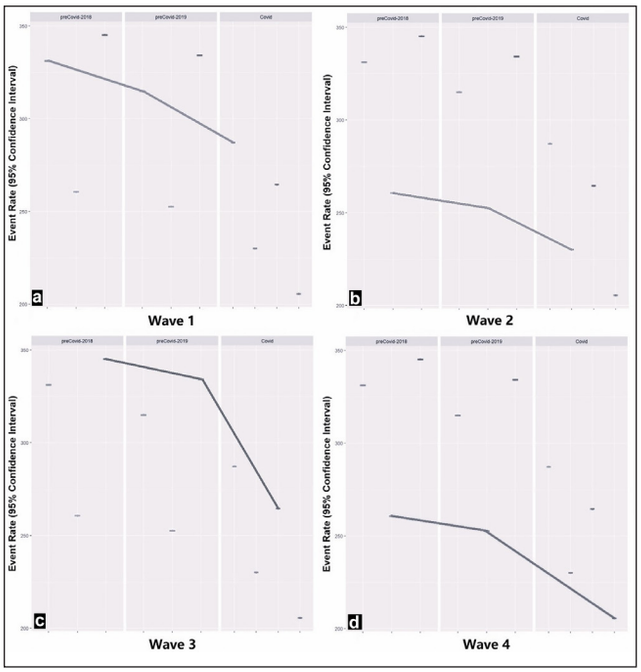

Figure 1: (a–d) Poisson trends in voluntary abortions per 1,000 births during the four COVID-19 waves compared with equivalent pre-COVID-19 periods. Incidences are shown with 95% CIs. Data were obtained from Hungary's Central Statistical Office.

muscle aches, vomiting, and diarrhoea. In addition, an increasing number of people have reported total or partial loss of smell and taste during the course of the disease.[4]

Pregnant women and their fetuses are at a high risk of the potentially harmful effects of COVID-19, and extra care is needed to protect them. The immune system is partially compromised during pregnancy, increasing the risk of disease and even fetal death. Blood coagulation factor activity is increased in many pregnancies, increasing the risk of blood coagulation disorders. The blockage of blood flow to the fetus by a thrombus deprives the fetus of oxygen and nutrients.[5] The incidence of pregnancy-related thromboembolic events has been significantly higher after the appearance of the SARS-CoV-2 infection than it was in 2018 and 2019.[6]

COVID-19 can cause serious complications in pregnant women. The delta SARS-CoV-2 variant is the most dangerous, as it can attack not only lung cells but also placental cells, potentially leading to fetal death. Pathologists in the United States first detected this variant in an inflamed placenta.[7]

The COVID-19 pandemic reached Hungary on 4 March 2020, and relatively limited data and research results from the country are available. The current study was conducted to examine the impacts of COVID-19 on fetal mortality in Hungary, overall and during each of the four pandemic waves. We hypothesised that the number and rate of fetal deaths in Hungary would be significantly higher during the four COVID-19 waves than in the pre-COVID-19 period due to the disease.

Table 1: Data on pregnancy and its outcomes in Hungary, 1 January 2018–31 December 2021.

Year	Pregnancies	Live births	Voluntary abortions	Pregnancy losses
2018	132,968	89,807	26,941	16,220
2019	131,473	89,193	25,783	16,497
2020	131,539	92,338	23,901	15,300
2021	129,491	93,039	21,907	14,545

Data were obtained from Hungary's Central Statistical Office.

Brief summary

The 2019 coronavirus disease did not increase fetal death rates in Hungary.

MATERIAL AND METHODS

Study Population and Data Collection

This retrospective analysis was conducted using perinatal data (abortion, stillbirth, and livebirth rates) for the period of 1 January 2018–31 December 2021 made available by the Hungarian Central Statistical Office (*Központi Statisztikai Hivatal*) in the summer of 2022. Statistics were not available before the summer of 2022, so these results are the first to be published.

The target population were embryos and fetuses born in Hungary between 1 January 2018 and 31 December 2021. The total number of data items in the sample was 525,471 (n = 525,471).

The sample comprised 525,471 embryos and fetuses, so that's the total number of pregnancies established. The number of live births during the study was 364,377; the number of abortions was 98,532; and the number of stillbirths was 62,562. Data on the number of pregnancies in Hungary between 1 January 2018 and 31 December 2021 are presented in Table 1.

The Ethics Board of the University of Pecs, Hungary, approved the study.

Data Analysis

The data were grouped according to the four COVID-19 waves (March–June 2020, September–December 2020, February–May 2021, and September–December 2021, respectively) and compared with equivalent pre-COVID-19 periods in 2018 and 2019. In the examination of pregnancy losses, the early, mid-term, and late periods were defined by spontaneous abortions (i.e., miscarriages) occurring before the 12th week of gestation, fetal deaths occurring between

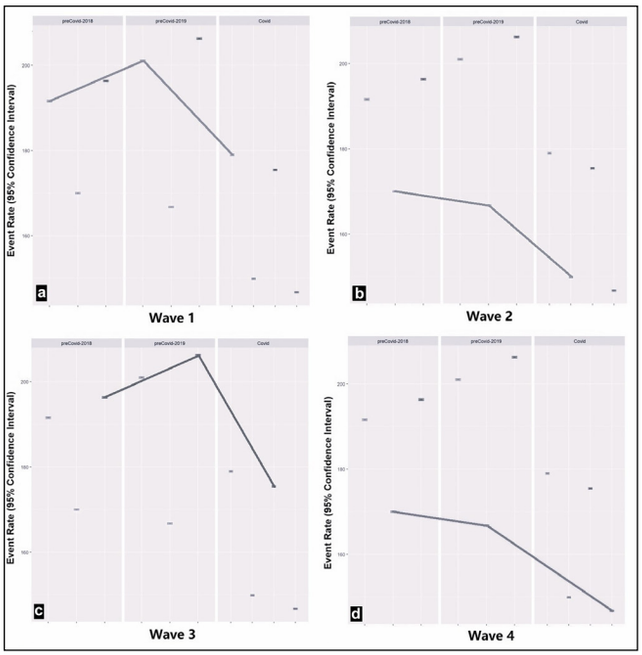

Figure 2: (a–d) Poisson trends in total pregnancy losses per 1,000 births during the four COVID-19 waves compared with equivalent pre-COVID-19 periods. Incidences are shown with 95% CIs. Data were obtained from Hungary's Central Statistical Office.

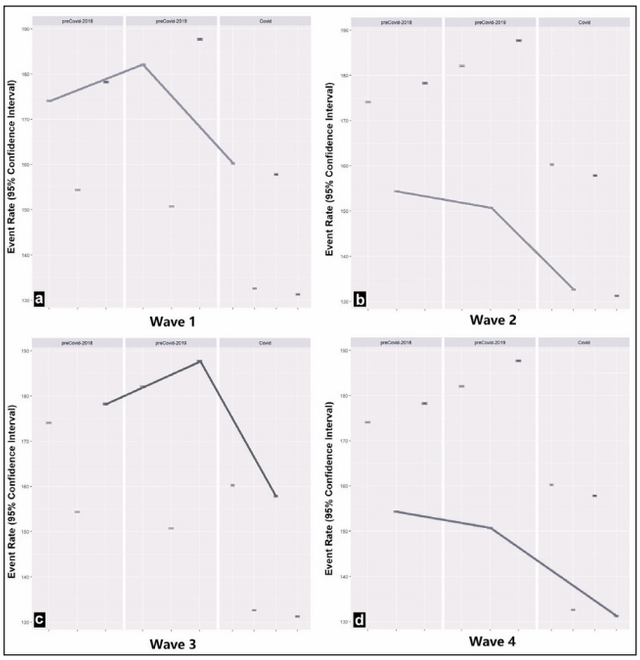

Figure 3: (a–d) Poisson trends in early pregnancy losses per 1,000 births during the four COVID-19 waves compared with equivalent pre-COVID-19 periods. Incidences are shown with 95% CIs. Data were obtained from Hungary's Central Statistical Office.

12 and 24 gestational weeks, and stillbirths occurring after the 24th week of gestation, respectively.

Statistical analyses were performed with R software (R Core Team 2021; R Foundation for Statistical Computing, Vienna, Austria). Data are presented as numbers with percentages and rates per 1,000 births. Poisson values for the incidence rates were calculated. Incidence estimates are provided with 95% confidence intervals. Event rates were compared between time points using proportions and chi-squared tests. The significance threshold was set to $p < 0.05$.

RESULTS

The sample comprised 525,471 embryos and fetuses. Poisson trend analysis revealed decreases of 1.1–1.4% in voluntary abortion rates in Hungary during the four observed COVID-19 waves relative to equivalent pre-COVID-19 periods, but these differences were not significant [Table 1 and Figure 1]. Similarly, total and early pregnancy loss rates were 1.1% lower during the four COVID-19 waves than during equivalent pre-COVID-19 periods, but these differences were not significant [Table 1, Figures 2 and 3].

DISCUSSION

This study revealed decreasing trends in pregnancy losses during all four COVID-19 waves in Hungary, likely as a result of pregnant women's increased attention to healthy lifestyle practices during the pandemic period. During this period, the public in Hungary was regularly advised to wash their hands frequently, avoid busy places, disinfect, and increase their intake of vitamins, especially vitamins C and D, which made women's bodies more resistant and supported their immune systems. Compulsory indoor mask use was introduced nationally on 21 September 2020, during the second wave of the pandemic, which may have protected pregnant women from COVID-19 and other droplet-transmitted infections. Furthermore, the government ordered closures during pandemic waves, resulting in the cancellation of events and a dramatic reduction in the number of personal contacts. Many women worked at home and thereby also avoided or reduced stress-inducing factors.[8] The reduction in voluntary abortion rates during all four COVID-19 waves may reflect pregnant women's fear of SARS-CoV-2 infection while visiting the hospital for an abortion.

Similar to our findings, studies conducted in other countries have revealed no significant association between the COVID-19 pandemic and fetal mortality rates.[9–11] In a summary of the symptoms, treatments, and pregnancy outcomes of Chinese pregnant women with COVID-19, Wang and colleagues[9] showed that the disease was not fatal, and most pregnant women with SARS-CoV-2 infection were asymptomatic. The infection did not increase the risk

of other infections or more severe pregnancy complications. Plotzker and colleagues[10] found no evidence that the severity of maternal COVID-19 contracted in the second and third trimesters of pregnancy contributed to pregnancy loss in California, but their case series was small, and the authors noted the need for further research on the perinatal impact of the disease. Magnus and colleagues[11] observed a modest decline in the number of spontaneous abortions but no significant change in the pregnancy loss rate in Sweden (n = 449,347), Denmark (n = 290,857), or Norway (n = 261,057) during the COVID-19 pandemic.[11] Romanis and colleagues[12] reported a decrease in the number of abortions during the COVID-19 pandemic, reflecting the further limitation of access and the inability of many women to terminate unwanted pregnancies for prolonged periods, even in countries in which abortion is legal (Austria, Tunisia, and some states in the United States). Pilecco and colleagues found that existing problems were magnified and that reproductive rights, such as women's access to legal abortion, were limited during the pandemic in Latin America.[13]

As this study was retrospective, it may have been affected by missing data. In addition, given the recent emergence of COVID-19, we do not yet have sufficient data to support robust conclusions about the perinatal effects of the COVID-19 pandemic.

In the following study, we were only focusing on seropositivity and perinatal outcome, and the collection of data about comorbidities was beyond our reach. One can consider this as a limitation of the current study.

In our study, vaccination status was not examined due to data protection. This is a limitation of our study. However, it is also possible that perinatal mortality was reduced during the third and fourth waves of COVID-19 due to the impact of the vaccination.

One advantage of our study, on the other hand, is that the nature of data release in Hungary could be processed relatively quickly. This study was innovative because no similar study has analysed the perinatal mortality in Hungary because of SARS-CoV-2 infection.

Our results from this study do not specifically discuss the severity of COVID-19 infection in pregnant women; we were focusing on seropositive results. To reveal the potential correlation between COVID-19 severity and perinatal outcomes might be achieved in a follow-up study.

CONCLUSION

COVID-19 did not significantly affect pregnancy outcomes in Hungary, as it did in some other countries. The observed declining trends are consistent with those seen in the years before the pandemic. As we do not yet have sufficiently strong evidence that COVID-19 does not cause perinatal complications, we advise continued research on this matter. The results of this study could form the foundation for longer-term prospective research to establish the prenatal effects of COVID-19 clearly.

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Authors' Contributions

S. Szalai: Project development, data collection, manuscript writing. N. Farkas: Statistical analysis. B. Veszpremi: Data collection. J. Bodis: Manuscript editing. K. Kovacs: Manuscript editing. B. Farkas: Project development, data analysis, manuscript editing.

Ethical approval

The research/study was approved by the Ethics Board of the University of Pecs, Hungary, with approval number 32725773, dated 22 May 2024.

Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Nil.

Conflicts of interest

There are no Conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The author(s) confirm that there was no use of Artificial Intelligence (AI)-Assisted Technology for assisting in the writing or editing of the manuscript and no images were manipulated using the AI.

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