

Preeclampsia and the COVID-19 pandemic

Mesut Önal^{1*}, İlknur Çınar Dura¹

¹ Ondokuz Mayıs University Faculty of Medicine, Department of Obstetrics and Gynecology, Samsun, TR

* Corresponding Author: Mesut Önal E-mail: drmesut.onal@gmail.com

ABSTRACT

Objective: The novel coronavirus pandemic (COVID-19) has deteriorating effects on vulnerable populations, including pregnant women. Previous studies suggested increased adverse pregnancy outcomes like preeclampsia in this population, but the results are inconclusive. Therefore, this study evaluated the changes in adverse pregnancy outcomes, primarily preeclampsia, among pregnant women in the Black Sea region in Turkey.

Material and Methods: This study included all deliveries between April 1st, 2018, and December 31st, 2019, as the pre-pandemic cohort and between April 1st, 2020, and December 31st, 2021, as the pandemic cohort. The primary objective of the study was to compare the preeclampsia rates.

Results: A total of 4379 patients were included, 2000 in pre-pandemic and 2379 in pandemic cohorts. The preeclampsia rate in the pre-pandemic cohort (11.0%) was similar to the pandemic cohort (9.7%) ($p=0.16$), likewise, the mean baby weights were also similar between cohorts ($p=0.32$).

Conclusion: The preeclampsia rates in the pre-pandemic period did not change significantly during the pandemic. However, this was based on observational data, which needs further evaluation and confirmation in controlled studies.

Keywords: COVID-19, pandemic, preeclampsia, pregnancy outcomes, Turkey.

INTRODUCTION

Preeclampsia is a common pregnancy complication characterized by new-onset hypertension and new-onset proteinuria and affects about 5% to 7% of pregnant women worldwide (1). As more evidence becomes available, the classical definition of preeclampsia is evolving. For example, professional associations are now recommending that a diagnosis of preeclampsia can be made even if proteinuria is not present, especially in cases where multiple systems are involved (2). The previous well-known definition of preeclampsia was the occurrence of hypertension and proteinuria after 20 weeks of gestation in a previously normotensive patient, but the 2013 task force of the American College of Obstetrics and Gynecology (ACOG) revised this to include severe features of the disease with or without proteinuria (3, 4). The mainstays of pathogenesis are abnormal placentation and the release of antiangiogenic markers that result in endothelial dysfunction, vasoconstriction, and immune dysregulation (5).

More recently, during the SARS-CoV-2 pandemic, endothelial dysfunction and related damage were hypothesized as a potential pathological mechanism that might be responsible for the association between COVID-19 and preeclampsia (6). The endothelial dysfunction and damage have been extensively evaluated in COVID-19 patients. Many studies in the abundant literature on COVID-19 reported their role in the pathogenesis using laboratory and autopsy data (7).

However, there is no consensus on this association, and it still needs further assessment. Epidemiological studies are essential in this regard to evaluate the possible associations between COVID-19 and preeclampsia, which should then shed light on further clinical and laboratory studies. To the best of our knowledge, no previous epidemiological research assessed pregnancies complicated with preeclampsia during the COVID-19 pandemic in Turkey. Therefore, considering this clinical entity's importance and the preliminary evidence suggesting an association between COVID-19 and preeclampsia, we conducted a cross-sectional study to compare the preeclampsia outcomes among our patient cohorts before and during the COVID-19 pandemic.

Research Article

Received 02-02-2023

Accepted 12-02-2023

Available Online: 14-02-2023

Published 28-02-2023

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MATERIAL and METHODS

This study was conducted in the Obstetrics and Gynecology Department of the OndokuzMayis University, Faculty of Medicine, as a cross-sectional and retrospective analysis of patient records. The study group included all pregnant women between 18 to 45 years of age and admitted for delivery between April 1st, 2018, and December 31st, 2019, as the pre-pandemic cohort, and all patients between April 1st, 2020 to December 31st, 2022, as the pandemic cohort.

The primary outcome of this study was to evaluate and compare the preeclampsia rates between the pre-pandemic and pandemic periods. Secondary objectives included comparing the babies' birth weight and other demographic and clinical parameters between cohorts.

The local ethical committee approved the study protocol on 09/02/2022, approval number 2022/55.

Statistical Analyses: Descriptive statistics were presented using mean and standard deviation for continuous variables and frequency and percent for categorical variables. Independent groups were compared using the Student t and chi-square tests, respectively. A p-value <0.05 was considered statistically significant. All analyses were made using SPSS 28 (IBM Inc., Armonk, NY, USA).

RESULTS

A total of 4379 patients with a mean age of 29.5 ± 5.8 years were included in the study. The pre-pandemic cohort included 2000 women, and the pandemic cohort included 2379.

Regarding the primary and secondary outcomes of the study (Table 1), the overall preeclampsia rate was 10.3% in all deliveries. The comparisons between study cohorts showed that the preeclampsia rate in the pre-pandemic cohort (11.0%) was not statistically significantly different than the pandemic cohort (9.7%) ($p=0.16$). Likewise, the mean baby weight was 2814 ± 796 grams in all deliveries, and the mean baby weights were similar between cohorts ($p=0.32$).

The comparisons between COVID-19 positive and negative patients in the pandemic cohort revealed a preeclampsia rate of 10.1% among COVID-19 positive cases and 9.7% among negative cases, which were statistically not different ($p=0.89$). However, comparing patients with and without preeclampsia showed that the ages of preeclampsia cases were higher than those of preeclampsia ($p=0.005$).

DISCUSSION

This study evaluated whether preeclampsia rates or mean birth weights of babies have changed during the SARS-CoV-2 pandemic among our patients. To assess this, we included all pregnant women admitted to our department for delivery during equal timeframes before and after the declaration of the COVID-19 pandemic on March 11th, 2020. The analyses revealed that preeclampsia rates were similar, which were 11% and 9.7% in the pre-pandemic and pandemic periods, and there was no significant change regarding the birth weights of babies. However, preeclampsia was seen among pregnant women at higher ages.

The COVID-19 pandemic has been our century's most critical public health problem, affecting billions worldwide, causing more than 600 million confirmed cases and 6.5 million casualties as of October 2022 (8). The previous evidence from the SARS-CoV and MERS-CoV infections that also affected a significant proportion of the world population suggested increased mortality and morbidities among pregnant women (9, 10), which was also indicated for the novel SARS-CoV-2 pandemic due to the immune and physiological changes during the pregnancy period (11). Comprehensive assessment of data from pregnancy follow-up databases and the meta-analyses of these detailed studies showed that confirmed COVID-19 infections among pregnant women were related to increased rates of preterm births, premature rupture of membranes, fetal vascular abnormalities, and malperfusion (12).

However, the data on the changes in preeclampsia rates during pregnancy is inconclusive. From a pathophysiological perspective, COVID-19 shares similar characteristics with preeclampsia, such as hypertension, altered thrombocyte functions, and immune changes, which are also common findings in preeclampsia. Thus, a detailed assessment of pregnant women with these symptoms and COVID-19 infection is crucial to exclude and diagnose preeclampsia since this discrimination should direct the management of the pregnancy. A previous prospective observational study by Mendosa et al. reported that pregnant women with COVID-19 may present with similar clinical findings to preeclampsia but lack the other clinical or biochemical markers like uterine artery pulsatility index and angiogenic factors like soluble FMS-like tyrosine kinase-1/placental growth factor (13). However, these reports are generally observational and should be interpreted cautiously by keeping the potential shortcomings and biases introduced by the uncontrolled study designs (14).

Table 1. Preeclampsia rates and baby weights in the cohorts

	All Patients (N=4379) Mean±SD / n (%)	Pre-Pandemic (n=2000) Mean±SD / n (%)	Pandemic (n=2379) Mean±SD / n (%)	p
Preeclampsia	449 (10.3)	219 (11.0)	230 (9.7)	0.16
Baby weight (gr)	2814±796	2802.7±803.3	2826±788.3	0.32

In contrast to the general acceptance of the increased preeclampsia-like symptoms but not the actual preeclampsia rates among pregnancies complicated with COVID-19, some studies reported that COVID-19 is strongly associated with preeclampsia. For example, Papageorgiou et al. evaluated the associations between COVID-19 during pregnancy and a diagnosis of preeclampsia and found a strong association between these two, particularly among nulliparous women, regardless of any previous risk factors (6). Similar results were also reported by Wei et al. (15) and Jamieson and Rasmussen (16), who reported that COVID-19 might be associated with an increased risk of preeclampsia.

As noted in the studies discussed above and others in the literature on the relationship between COVID-19 and pregnancy outcomes, there appears to be a tendency towards either a possible association or a lack of association between the two. Our results in this study support that preeclampsia risk was not changed during the pandemic. However, this should be interpreted very cautiously. Since we conducted only a chart review of records and did not include control groups, the outcomes are only observational and should not be treated as conclusive. When attempting to infer the relationship between COVID-19 and preeclampsia, it is important to consider various factors such as the vaccination status of patients, the timing of the COVID-19 diagnosis and the onset of preeclampsia symptoms, biochemical and clinical markers that support the diagnosis of preeclampsia, and any other clinical determinants that may influence the association between the two conditions. But, these clinical data were not available during our analyses. So, these shortcomings were also the limitations of this study. Thus, these results should be regarded as only preliminary findings that may suggest unique relationships among our patients, which should be evaluated in further controlled studies that may elucidate these unexpected outcomes.

CONCLUSION

The results of this study suggest that the preeclampsia rates observed in the pre-pandemic period among our patients did not change significantly during the pandemic. However, this was based on observational data, which needs further evaluation and confirmation in controlled studies.

Acknowledgments: None

Conflict of interest: The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. This research did not receive and a specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author Contributions: MÖ, İÇD: Study conceptualization, protocol planning, clinical data collection, clinical data analysis and supervision. **MÖ:** manuscript writing/editing.

Ethical approval: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and/or with the Helsinki Declaration of 1964 and later versions. Informed consent or substitute for it was obtained from all patients for being included in the study. Ethics committee approval dated 03.08.2022 and numbered 2022/537 was obtained from Mersin University Ethics Committee before starting the study

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