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The Prevalence of Pregnancy-Associated Deaths and Related Factors in Pregnant Women During the COVID-19 Pandemic in Rasht, Iran

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Abstract

Background: Pregnant women are at an elevated risk for severe complications from COVID-19, which may exacerbate pre-existing conditions and lead to adverse outcomes.

Objectives: Given the occurrence of maternal mortality linked to pregnancy-related complications during the COVID-19 pandemic, we undertook this study to examine the incidence of pregnancy-associated deaths and the contributing factors among pregnant women.

Methods: This cross-sectional study was conducted on the data of 10 deceased pregnant women who were referred to Al-Zahra Hospital, Rasht, Iran, during the COVID-19 pandemic. Demographic and clinical data of patients were recorded. Data were analyzed using SPSS software version 22, and a significance level was considered at < 0.05.

Results: The mean age of the deceased pregnant women was 29.30 ± 5.31 years. Three patients were positive for COVID-19, and eight individuals had underlying medical conditions, with all patients admitted to the intensive care unit (ICU). The mean duration of hospitalization was 10.10 ± 5.68 days, and the mean gestational age was 31.60 ± 4 weeks. Two individuals (20%) had a history of previous miscarriage, and eight patients (80%) had low socio-economic status. Most deaths occurred during pregnancy or shortly after delivery, with pre-eclampsia complicated by COVID-19 being the leading cause (40%).

Conclusions: Our study indicated that women with pre-eclampsia were a vulnerable group at higher risk for severe COVID-19 complications that resulted in death.

Keywords: Eclampsia, Pregnancy, Pre-eclampsia, COVID-19, Pregnant Women

1. Background

The occurrence of pregnancy-associated deaths remains a significant global health concern, particularly in developing countries (1). A key global health objective within the sustainable development goals is to lower the maternal mortality ratio to fewer than 70 deaths per 100,000 live births by 2030 (2). The epidemiological landscape of pregnancy-associated deaths exhibits marked disparities across geographic regions, socioeconomic strata, and healthcare accessibility, with low- and middle-income countries bearing a disproportionate burden, accounting for most maternal deaths (3, 4).

The etiology of pregnancy-associated deaths is multifactorial, encompassing direct obstetric causes such as hemorrhage, hypertensive disorders, and sepsis, as well as indirect causes exacerbated by pregnancy, including pre-existing medical conditions and infectious diseases (5). Pregnancy-induced hypertension, particularly pre-eclampsia, is a significant contributor to maternal morbidity and mortality (6).

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These conditions are associated with increased risks of maternal complications, including cerebral hemorrhage, retinal detachment, liver hematoma/rupture, acute renal failure, disseminated intravascular coagulation (DIC), and placental abruption, potentially leading to maternal death (7). Pre-eclampsia in pregnancy is characterized by high blood pressure and proteinuria and is associated with significant maternal and fetal complications (8). Furthermore, the HELLP syndrome (hemolysis, elevated liver enzymes, and low platelet count) represents a severe manifestation of pregnancy-induced hypertensive disorders, associated with significant maternal morbidity and mortality (9).

The COVID-19 pandemic has had profound global impacts, affecting nearly every aspect of life, from public health to economies. It has particularly strained healthcare systems and highlighted disparities in healthcare access and outcomes. Vulnerable populations, including the elderly, those with pre-existing conditions, and pregnant women, have faced heightened risks of severe illness (10-13). Efforts to control the spread through vaccination, social distancing, and public health interventions have been central, while the long-term effects of the pandemic continue to shape global health and policy responses (14, 15).

2. Objectives

Research into pregnancy-associated deaths contributes valuable data to global efforts in achieving sustainable development goals. The current study investigated the prevalence of pregnancy-associated deaths and related factors in pregnant women in Rasht, Iran.

3. Methods

This cross-sectional study was conducted on data from 12,014 pregnant women, of which 12,004 resulted in successful deliveries, and 10 died due to pre-eclampsia at Al-Zahra Hospital, Rasht, Iran, from 2020 to 2023. The deceased patients' files were reviewed by an obstetrics and gynecology specialist and a clinical pharmacologist.

Data on age, underlying diseases, marital status, educational status, socioeconomic status (based on a combination of educational attainment and self-reported household income), COVID-19 infection at the time of death, intensive care unit (ICU) stay, medication, duration of hospitalization, history of previous miscarriage, gestational age, multiple gestations, type of delivery, time of death, and cause of death (pre-eclampsia, eclampsia, sepsis, HELLP syndrome, cardiac arrest, obstetric hemorrhage) were recorded. Pre-eclampsia, typically defined as new-onset hypertension (systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg) after 20 weeks of gestation accompanied by proteinuria or other end-organ dysfunction, affects approximately 10 - 15% of pregnancies globally (16). This study was reported according to STROCSS criteria (17). Data were reported as number, percentage, and mean ± standard deviation (SD). All data were analyzed in SPSS software version 22, and the significance level was set at 0.05.

4. Results

The mean age of deceased women was 29.30 ± 5.31 years (21 - 38 years), and the mean duration of hospitalization was 10.10 ± 5.68 days (1 - 20 days). The mean gestational age was 31.60 ± 4 weeks (24 - 38 weeks). According to our findings, 80% of the deceased women were married, and 50% had a diploma-level education. Notably, 80% of the women had a low socioeconomic status.

Medical history showed that 70% (n = 7) of the women did not have a history of COVID-19, but a substantial 80% (n = 8) had underlying diseases. Obesity was the most common comorbidity (40%), followed by diabetes, hypertension, and hypothyroidism (20%). Obstetric factors indicated that 80% (n = 8) had no history of miscarriage. Delivery modes were evenly split between cesarean section and vaginal delivery. The majority (90%) were singleton pregnancies. Most deaths occurred during pregnancy (50%) or after delivery (40%). The leading cause of death was pre-eclampsia complicated by COVID-19 (40%). Regarding medication use, nutritional supplements were most common (90%), while antibiotics were least used (10%) (Table 1).

5. Discussion

The most common causes of maternal mortality worldwide are hemorrhage, pre-eclampsia, and sepsis. Lack of access to medical care, comorbidities, and social determinants of health are also considered significant contributors to maternal deaths (18). The current study demonstrated a high prevalence of pre-eclampsia and eclampsia in deceased women with COVID-19 disease. Similar studies show a high rate of pre-eclampsia in hospitalized pregnant women with COVID-19 (19, 20). Algeri et al. reported that the risk of pre-eclampsia in pregnant women with COVID-19 was considered a potential threat to maternal and fetal health (20, 21). A study by Papageorghiou et al. illustrated a significant

Table 1. Demographic and Clinical Data on Pregnancy-Associated Deaths and Related Factors in Pregnant Women [a]

Variables	Values
Marital status	
Married	8 (80.0)
Divorced	2 (20.0)
Educational status	
Under diploma	3 (30.0)
Diploma	5 (50.0)
University degree	2 (20.0)
Socioeconomic status	
Low	8 (80.0)
Middle	2 (20.0)
History of COVID-19	
Yes	3 (30.0)
No	7 (70.0)
History of underlying disease	
Yes	8 (80.0)
No	2 (20.0)
Comorbidities	
Diabetes	2 (20.0)
Gastrointestinal disease	1 (10.0)
Obesity	4 (40.0)
Fatty liver disease	1 (10.0)
Minor thalassemia	1 (10.0)
Hypertension	2 (20.0)
Migraine	1 (10.0)
Hepatic cholestasis	1 (10.0)
Hepatic cholestasis	1 (10.0)
Coagulation complications	1 (10.0)
Hypo thyroiditis	2 (20.0)
Hyperthyroidism	1 (10.0)
Urinary infection	1 (10.0)
Anemia	1 (10.0)
Seasonal allergy	1 (10.0)
None	1 (10.0)
History of miscarriage	
Yes	2 (80.0)
No	8 (20.0)
Type of delivery	
Cesarean section	5 (50.0)
Vaginal delivery	5 (50.0)
Multiple gestations	
Yes	1 (10.0)
No	9 (90.0)
Time of death	
During pregnancy	5 (50.0)
After delivery	4 (40.0)
During labor	1 (10.0)
Cause of death	
Pre-eclampsia, COVID-19	4 (40.0)
Eclampsia, COVID-19	1 (10.0)
COVID-19	1 (10.0)
HELLP, COVID-19	1 (10.0)
Sepsis	1 (10.0)
Cardiac arrest	1 (10.0)
Obstetric hemorrhage	1 (10.0)
Medication	
Diabetes medications	2 (20.0)
Cardiovascular medications	4 (40.0)
Gastrointestinal medications	3 (30.0)
Nutritional supplements	9 (90.0)
Hormonal medications	3 (30.0)
Antibiotics	1 (10.0)

[a] Values are expressed as No. (%).

association between COVID-19 during pregnancy and pre-eclampsia with maternal and neonatal complications and mortality (21). They represented that COVID-19 during pregnancy is strongly associated with pre-eclampsia, especially among nulliparous women (22).

Evidence illustrated that COVID-19 infection can predispose individuals to pre-eclampsia by causing disruptions in various body systems, of which peripheral nervous system involvement and thrombotic complications were reported in pregnant women with COVID-19 (21, 23). These complications may be due to the activation of coagulation pathways and potential progression towards DIC or fibrinolysis, accompanied by increased coagulation activity due to thrombocytopenia (24). Since pregnancy is associated with increased coagulability, which can occur through increased thrombin production and increased intravascular inflammation, pregnant women with

COVID-19 may have additional risk factors for thrombosis (25, 26).

In another study it was reported that in pregnant women with COVID-19, pregnancy hypercoagulopathy could lead to increased patient mortality and faster disease progression (27). Furthermore, the physiological changes that occur in the cardiopulmonary system of pregnant women potentially increase both the risk of infection and the severity of COVID-19. Pregnancy-related changes, such as reduced lung volume, increased oxygen consumption, and impaired clearance of respiratory secretions, make pregnant women more vulnerable to respiratory pathogens like SARS-CoV-2 (28, 29).

Most COVID-19 deaths result from acute respiratory distress syndrome (ARDS), with pulmonary endothelial dysfunction playing a key role. During pregnancy, immune adaptations such as a shift from T helper 1 (Th1) to Th2 responses support fetal growth but increase susceptibility to viral infections (30). This shift can worsen COVID-19, as Th1 responses, particularly elevated interleukin-6 (IL-6), are linked to lung damage and poorer outcomes (15, 31, 32). A dominant Th2 immune response in pregnancy may reduce COVID-19 severity. However, during the pro-inflammatory states of the first and third trimesters, pregnant women are more vulnerable to severe inflammation and cytokine storms from SARS-CoV-2, potentially increasing disease severity and mortality (30, 32, 33).

Moreover, studies suggest that anxiety can trigger pre-eclampsia, and the heightened stress during the COVID-19 pandemic likely contributed to an increased incidence of pre-eclampsia through this mechanism (34).

Our findings indicated that the mean age of deceased pregnant women and the mean gestational age were 30 years and 31 weeks, respectively. Moreover, our results showed that most individuals had underlying diseases, and all were admitted to the ICU. Brown et al. reported that comorbidities and the number of comorbidities increased the rate of morbidity and mortality in pregnant women (34, 35). Studies have reported that risk factors for pre-eclampsia include primiparity, maternal age extremes, multiple gestation, obesity, history of hypertension, race, genetic predisposition, placenta previa, diabetes, and renal disease (36, 37). The immunological hypothesis suggests that impaired development of blocking antibodies against placental antigens may increase the risk of hypertensive disorders in pregnancy (38).

In the current study, most deceased pregnant women had low socioeconomic and educational status. Women in the low socioeconomic status group still experienced higher rates of inadequate prenatal care, abortion, cesarean delivery, pre-eclampsia, preterm delivery, and obstetric hemorrhage compared to those in the middle/high socioeconomic status group (39). To address the disparities observed in pregnancy outcomes among women of low socioeconomic status, healthcare authorities should implement targeted interventions aimed at improving access to comprehensive prenatal care.

5.1. Conclusions

These findings highlighted the complex interplay of medical, socioeconomic, and obstetric factors in pregnancy-associated deaths, emphasizing the need for comprehensive prenatal care and management of comorbidities, particularly in the context of the COVID-19 pandemic.

5.2. Limitations

This study provided valuable insights into maternal mortality related to pre-eclampsia; however, the cross-sectional and single-center design and small sample size of the study limited causal inferences and expansion to other populations. Additionally, certain important confounding variables — such as COVID-19 vaccination status, the specific viral variant, and the timing of infection in relation to pregnancy trimester — were not consistently or systematically documented in the medical records and therefore could not be reliably included in our analysis. As a result, there is a risk of residual confounding, which may affect the interpretation of our findings. Future prospective studies with standardized data collection are needed to more comprehensively assess these factors and their impact on pregnancy-associated mortality during the COVID-19 pandemic.

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Footnotes

Authors' Contribution: Study concept and design: K. D. and S. B.; Analysis and interpretation of data: H. H., P. M., and S. B.; Drafting of the manuscript: Z. H.; Critical revision of the manuscript for important intellectual

content: H. H., K. D., and S. B.; Statistical analysis: H. H. and P. M.

Conflict of Interests Statement: The authors declare no conflict of interest.

Data Availability: The current study's data are available from the corresponding author upon reasonable request.

Ethical Approval: This study design was approved by the Ethical Committee of Guilan University of Medical Sciences, Rasht, Iran: IR.GUMS.REC.1402.524 .

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Informed Consent: Written informed consent was obtained from the patients before participation in the study.

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