SHORT COMMUNICATION

Maternal Mortality with *SARS-COV-2* during its 4th Wave in Pakistan: The Vaccine Paradox and Pregnancy

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ABSTRACT

The goal of this study was to investigate the maternal death rate among admitted pregnant patients with *SARS-COV-2* during its 4th wave in Pakistan. It was a cross-sectional analytical study, carried on pregnant patients admitted due to COVID-19, in Sadiq Abbasi Hospital from 15th August to 15th September, 2021. Thirty-three PCR confirmed and HRCT suggestive patients were included with mean age of 28 ± 4.5 years and mean gestational age of 28.5 ± 6 weeks. Twenty-seven (81%) were non-vaccinated, 22 (66%) were admitted with severe disease, 13 (39.4%) and 11 (33.3%) were on non-invasive and invasive ventilator support, respectively. Only nine (27%) patients could continue their pregnancy. Fifteen (45%) patients had severe oligohydramnios. Twenty-two (66.7%) patients were died, all were unvaccinated. Regression analysis for maternal mortality predicted by severity and vaccination status was significant with R^2=.68, $F_{(1, 31)}$ =66.6, p <.001 CI (-.69, -.42) and R^2=.44, $F_{(1, 31)}$ = 24.8, p <.001 CI (-1.14, -.48), respectively. There was substantial mortality in the admitted and non-vaccinated pregnant patients with COVID-19.

Key Words: Pregnancy, Vaccination, Severe COVID, Maternal outcome.

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Since, the world was stricken by COVID-19 pandemic, caused by *SARS-COV-2*, it had wreaked havoc in every corner of the world. Clinical presentation varies from mild to critical illness. Risk factors had been identified for developing severe disease such as old age, diabetes and obesity. Pregnancy is found to be a risk factor for any viral or bacterial infection because of shift in cellular immunity to humoral immunity.[1] COVID-19 has bi-directional impact on pregnancy. On one hand severe and inappropriate immunogenic inflammatory response (IL-1, IL-6, TNF) in severe COVID-19, which can cause adverse pregnancy outcome *e.g.* abortion, preterm birth and pre-eclampsia and IUD in more severe cases; on the other hand, mechanical effect of gravid uterus on diaphragm compromises the functional residual lung volume and adding to severity of ARDS. In the first year of pandemic of COVID-19, maternal mortality was not high as there were few case reports on it.[2] With arrival of variants of concern (VOC), like delta variant B.1.167.2, maternal mortality showed alarming figures.[3]

Seeing pregnant and lactating women omitted from COVID vaccine trials, there is indeed a vacuum of scientific evidence to vaccinate this high risk population. Despite the fact that maternal deaths have been documented, the frequency with which this dreadful consequence happens is undetermined. So, we have designed a study at COVID dedicated hospital to see maternal and fetal outcomes in pregnant ladies admitted to hospital with COVID-19.

This observational study was conducted among pregnant patients admitted to High Dependency Unit (HDU) and Intensive Care Unit (ICU) of Sir Sadiq Abbasi Hospital, Bahawalpur from 15th August to 15th September, 2021. Patient's data were noted from electronic record and hospital charts. After approval from the Ethical Review Board, (No. 1129, dated: July 21st, 2021), 33 pregnant patients with PCR confirmed and HRCT suggestive COVID-19 infection were included in the study. Patients were divided into mild, moderate and severe cases, according to symptoms, oxygen saturation and HRCT scoring. Body mass index (BMI) of patients before getting pregnant were noted from antenatal record and divided into normal weight (18.5-24.9 Kg/m^2), overweight (25-29.9 Kg/m^2) and obese (> 30 Kg/m^2). Mode of oxygen delivery, obstetric intervention, antenatal complication developed during COVID illness, and vaccination status were also noted. Outcomes were measured in terms of maternal deaths or clinical improve-

ments; and fetal outcomes in terms of intra-uterine deaths on admission to hospital or during hospital stay, alive births and early neonatal deaths.

Data was analysed through SPSS version 20. Frequencies and percentages of categorical variables were calculated. Pearson correlation, bivariate and multiple regression analysis were applied to find out correlation and predictability of outcome by independent variables, keeping p-value <0.05 as statistically significant.

Thirty-three pregnant women with age range of 19 to 38 years, mean age of 28 ± 4.6 years were included in the study. Their mean gestational age was 28.5 ± 6 weeks and mean BMI was 25.5 ± 3.1 Kg/m^2. Frequencies of categorical variables are shown in Table I.

Table I: Frequencies of categorical variables.

Variables	*n*	%
Age		
18-30 years	25	75.8
More than 30 years	8	24.2
Gestational age		
First trimester	1	3
Second trimester	6	18.2
Third trimester	26	78.8
Obstetric history		
Primary gravid	10	30.3
Multiparous	23	69.7
Body mass index		
Normal weight	15	45.5
Overweight	17	51.5
Obese	1	3
Vaccination status		
Vaccinated	6	18.2
Non vaccinated	27	81.8
Severity of disease		
Mild illness	4	12.1
Moderate	7	21.2
Severe to critical	22	66.7
Mode of oxygen delivery		
No oxygen support	5	15.2
Non invasive ventilator	13	39.4
Invasive ventilation	11	33.3
Via face mask	4	12.1
Antenatal complications		
No complication	10	30.3
Oligohydramnios	15	45.5
PIH	6	18.2
IUD	2	6.1
Obstetric Intervention		
No intervention	19	57.6
Spontaneous delivery	2	6
C Section	10	30.3
Obstetric hysterectomy PPH	2	6.1

Twenty-two (66.7%) pregnant patients were died, all were unvaccinated and only 11 (33.3%) patients were discharged, among them six (54.5%) were fully vaccinated. Nine (27.3%) patients continued their pregnancy. Five (15.2%) delivered alive baby with good Apgar score during hospital stay, three (9.1%) babies were died in early neonatal period, and 16 (48.5%) were died in utero. Six vaccinated patients developed mild to moderate disease, clinically improved and continued

their pregnancy. Ten (30.3%) patients underwent C Sections and two (20%) out of those improved after Cesarean section; whereas, eight (80%) patients could not improve after Cesarean section and were died. Pearson correlation shows strong negative relationship among vaccination status and maternal outcome, severity of disease, antenatal complications, and fetal outcome (r=.67, p<.001), (r=.816, p<.001), (r=.49, p=.004) and (r=.47, p=.006), respectively.

The R^2 for regression equation for predicting maternal outcome from vaccination status was .44, with $F(1, 31) = 24.8$, $p<.001$. CI [-1.15, -.481].

The findings support a high death rate of 66 percent in hospitalised pregnant patients. Forty-five percent patients developed severe oligohydramnios as an ante-natal complication due to severe disease and 73.3% out of those had IUD later during hospital stay, while 6% patients had IUD on admission to hospital. These results are consistent with high rates of ante--natal complications, and bad fetal outcome in patients who need admission to hospital with COVID-19. Majority studies published in initial one year of pandemic of COVID-19 showed pregnancy to be a low risk factor for severe disease; and those who developed critical illness, had other risk factors of obesity, increase maternal age, and diabetes mellitus.[4] In this study, 75% patients were between the age group of 18-30 years, and only 3% had obese range BMI, which shows maternal age and weight to have an insignificant role for mortality. Study also does not support termination of pregnancy to relieve the pressure of gravid uterus on diaphragm in order to increase residual lung volume. As 80% patients, who underwent C section, could not survive.[5] According to CDC guidelines updated on 11th August 2021, vaccination for COVID-19 is recommended for pregnant and lactating mothers as they are more likely to get severe infection; and may become seriously ill with COVID 19. Seeing the good maternal and fetal outcome among vaccinated patients, it is need of the hour to start an effective nationwide awareness programmes for encouragement of vaccination in pregnant ladies; and myths regarding getting antenatal complications, congenital anomalies, and infertility should be omitted from the society. Post-marketing studies of several vaccines in pregnant and lactating mothers have shown their safety and immunogenicity.[6]

In summary, symptomatic and severe COVID-19 with pregnancy was associated with alarming rate of maternal mortality, ante-natal complications and poor fetal outcomes. There was good outcome in patients who were vaccinated before getting pregnant. Thus, vaccination is the only way to reduce mortality in pregnant patients and get rid of preventable tragedy. Moreover, it will be easiest to state then to be done, as a lot of rumors about vaccination are already circulating in the society. So, a mass awareness programme for both obstetricians and patients is needed to prevent further loss.

ETHICAL APPROVAL:
The study was approved by Institutional Ethical Review Board of Qauid-e-Azam Medical College, Bahawalpur, No. 1129,

dated: July 21st, 2021. Approval was taken prior to initiation of research work.

PATIENTS' CONSENT:
Informed consents had been taken from all patients; and in some cases from gaurdians to publish the data for this study.

CONFLICT OF INTEREST:
The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
JA: Conceptualisation, study design, formal analysis, interpretation and drafting of the work.
MM, QM: Data acquisition and analysis.
MA: Conceptualisation and study design.
SJ, MAM: Final approval of the work.

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