Fetomaternl Outcome of Pregnancy with COVID-19: An Observational Study in Tertiary Care Hospitals of Pakistan

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ABSTRACT
Background: The new corona virus first appeared in Wuhan, China in December 2019 and has since spread around the world to other countries. The World Health Organization believes that this new CoV-19 epidemic is a public health emergency of international concern (PHEIC) on January 30, 2020Worldwide. The mortality rate of this viral infection ranges from 2% in Pakistan to 14.4% in Italy. Lympopenia, elevated transminase, proteinuria, increased LDH, and C-reactive protein levels are all common laboratory findings in the early stages of the disease. Covid patients have experienced a variety of complications, including extreme pneumonia, ARDS, heart defects, sepsis and septic shock, and respiratory tract super infection.
Methodology: This retrospective observational research study was carried out at the Gynecology Unit of Mardan Medical Complex, Mardan and Combined Military Hospital, Risalpur for 06 months duration from April 2020 to September 2020. In a pre-constructed data collection form, biochemical and radiological parameters of medical history, test results, symptoms, pregnancy, and neonatal outcomes were noted. Patients treated in an outpatient setting were not included in the study.
Results: There were 121 patients in total, with mean age of 27 having standard deviation ± 5, having range 19-40 years. 48.3% pregnant women reported their first pregnancy (primigravida), 51.3% of SARS-CoV-2 were in their 3rd trimester while 34.7% were in their 35-40 weeks of gestational age. Common complications are gestational hypertension (PIH) (16 cases), hypothyroidism (14 cases) and gestational diabetes (GDM) 9 cases. More than half (53%) of patients are asymptomatic. Common symptoms are cough (22%) and fever (11%). The incidence of multiple organ failure was 2% as shown in table 01. Lymphopenia was common (84%). A CT scan of 24 patients showed bilateral invasion.
Conclusion: COVID-19 has a negative impact on the foetus, according to our results. Although pregnant women do not seem to be more vulnerable to COVID-19 complications than non-pregnant adults, previous research has suggested that pregnant women could be at higher risk for negative pregnancy outcomes such as preterm birth, foetal pain and respiration, symptoms, and LBW in a newborn baby.
Keywords: Corona virus, COVID-19, Pregnancy, Outcome.

INTRODUCTION
SARS CoV2 is a single-stranded RNA virus, belonging to a corona virus group, known to cause severe acute respiratory illness in humans. High transfer rates and low pathogenicity are two traits that differentiate them from other family members (SARS-CoV and MERS-CoV) (1). The new corona virus first appeared in Wuhan, China in December 2019 and has since spread around the world to other countries (2). The World Health Organization believes that this new CoV-19 epidemic is a public health emergency of international concern (PHEIC) on January 30, 2020 (3). Worldwide, the mortality rate of this viral infection ranges from 2% in Pakistan to 14.4% in Italy (4).
COVID-19 signs are mild in the majority of SARS-CoV-2 infections. Men may be at greater risk for disease than women, and the elderly and patients with comorbidities such as cardiovascular disease, respiratory disease, and diabetes are at higher risk for severity and death. (5,6). Lymphopenia, elevated transminase, presence of excess protein in urine (proteinuria), increased level of Lactate Dehydrogenase (LDH), and level of C-reactive protein are all common laboratory findings in the early stages of the disease. Covid patients have experienced a variety of complications, including extreme pneumonia, ARDS, heart defects, sepsis and septic shock, and respiratory tract super infection (7).
The prevalence of placenta previa is reported to be 3-5 times per 1,000 people and it is statistically increasing worldwide due to risk factors for inflammation. (8) In Pakistan, the prevalence rate was 3.5%, while the proportion of women born by caesarean section rose to 65%. (9) In the past, sensitivity to the urea ratio has been observed more frequently, mainly due to the high rate of cesarean section and the unconventional late age of the pregnant mother (10). The reason for placental control is unclear, but some threats may indicate its prevalence, such as cesarean section, high mothers, increasing age and previous miscarriages. (11)
Because the immune system is less aggressive during pregnancy, the mother's body does not genetically attack other embryos. As a result, pregnant women are susceptible to various infections, including viral diseases. In addition, several physiological changes during pregnancy, such as airway swelling, increased respiratory secretions...
and oxygen demand, increased diaphragmatic and decreased functional function, are factors that have so far worsened the obstetric prognosis in pregnant women suffering from viral pneumonia. Literature reports. Limited data published in China on COVID-19 showed the worst birth outcomes, including preterm birth and mortality at birth during multiple pregnancies (12). There is anxiety among pregnant women, and our limited ability to answer questions affects women’s health in some way. Due to the lack of guidelines regarding the effects of SARS-CoV-2 on pregnancy, clinical medical records of patients with pregnancy SARS-CoV-2 are collected and reported to the third HMC treatment center for further evaluation and management. This research looked at the outcomes of foetal mothers in COVID-19-positive pregnant women.

METHODOLOGY
This retrospective observational research study was carried out at the Gynecology unit of Mardan Medical Complex, Mardan and Combined Military Hospital, Risalpur for 6 months duration from April 2020 to September 2020 after receiving ethical approval from the Research and Ethics Committee of the hospitals. A total of 121 pregnant women and their infants were treated with SARS CoV-2 RNA identified by RT PCR. Patients treated in an outpatient setting were not included in the study. In a pre-constructed data collection form, biochemical and radiological parameters of medical history, test results, symptoms, pregnancy, and neonatal outcomes were registered. Analyze your data using SPSS version 20.

RESULTS
There were 121 patients in total, with mean age of 28 having standard deviation ± 7, having range 17-42 years. 48.3 percent pregnant women reported their first pregnancy (primigravida), 51.3% of SARS-CoV-2 were in their 3rd trimester while 34.7% were in their 17-35 years of gestational age. Common complications are gestational hypertension (PIH) (16 cases), hypothyroidism (14 cases) and gestational diabetes (GDM) 9 cases.

<table>
<thead>
<tr>
<th>General characteristics</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age 27 years (range 19-40)</td>
<td>-</td>
</tr>
<tr>
<td>Nulliparous</td>
<td>48.3</td>
</tr>
<tr>
<td>Multiparous</td>
<td>51.7</td>
</tr>
<tr>
<td>Sign and symptoms</td>
<td>53</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>22</td>
</tr>
</tbody>
</table>

Fever | 11 |
Shortness of breath | 4 |
Anosmia | 3 |
Multi-organ failure | 2 |
Fever, headache, severe pneumonia | 3 |
Hemoptysis | 2 |

More than half (53%) of patients are asymptomatic. Common symptoms are cough (22%) and fever (11%). The incidence of multiple organ failure was 2% as shown in table 01. Lymphopenia was common (84%). A CT scan of 24 patients showed bilateral invasion.

Most common was mild to moderate disease in about 92.6% of patients while in about 7.4% patients there were only severe disease. In about 5 patients due to critical disease required mechanical ventilation. Patients suffered from a serious illness before giving birth and received mechanical ventilation after giving birth. Patients with mild to moderate form of diseases (92.6%) received treatment in corona ward while severe patients (7.4%) received treatment in Intensive care unit (ICU).

All of the patients (100%) were given zinc, vitamin C, and vitamin D supplements, as well as Sodium Ceftriaxone and metronidazole covers, Cefixime, and Tab. Metronidazole is given to all caesarean section patients. Azithromycin, moxifloxacin, and colistin are some of the other antibiotics used in severe diseases. Methylprednisolone, Inj. remdesivir and Inj. Use tocilizumab. 36 (29.6%) patients with low molecular weight heparin to prevent thrombosis and Tab. Rebroxaben was used in 6 (7.4%) severe patients after delivery. In 30 patients, ivermectin was used as a tablet (24.7%). There was no difference in results between those who received ivermectin care and those who did not. In the report, 106 out of 121 women (87.65%) were discharged, with seven of them suffering from moderate or severe disease. There was only one death: that of the mother. In the sample population, there were three spontaneous abortions. In the study, 78 (64.2%) of 121 patients gave birth. A Caesarean section was performed on 63 (80.8 percent), a hysterectomy was performed on 3 (2.4 percent), and a regular vaginal delivery was performed on 12 (15.3 percent). A total of 12 (15.3%) patients had an abortion. A hysterectomy was performed for chronic hypertension with combination HELLP syndrome and pre-eclampsia (PE). Indications for cesarean section are anterior cesarean section (31), fetal depression (9), preterm labor (4), eclampsia (5), severe PE (3), HELLP syndrome (3), cervix condition (3). Current pregnancy 39 (32.09%).

<table>
<thead>
<tr>
<th>Maternal outcome</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild to moderate disease</td>
<td>112</td>
<td>92.6</td>
</tr>
<tr>
<td>Severe disease</td>
<td>9</td>
<td>7.4</td>
</tr>
<tr>
<td>Delivered</td>
<td>78</td>
<td>64.2</td>
</tr>
<tr>
<td>Discharged</td>
<td>106</td>
<td>87.7</td>
</tr>
<tr>
<td>Ongoing pregnancy</td>
<td>39</td>
<td>32.1</td>
</tr>
<tr>
<td>Maternal death</td>
<td>2</td>
<td>1.2</td>
</tr>
</tbody>
</table>

The SARS-CoV-2 test was performed with a neonatal pharyngeal swab, and 6 were positive. There were 70 births, 4 endometrial deaths and 3 neonatal deaths. Neonatal death was caused in more premature infants as shown in Table 3. The mean length of continuity was 13.3 (standard deviation ± 6.5) (range 6–31) days. The average number of days it took to start breastfeeding was 13.5 (SD ± 6.44) (range 5–25).
**DISCUSSION**

Physiologic changes occur in pregnant women’s different body systems like immune, cardiopulmonary and coagulation thus made them more prone to infection. Some research studies reported no exacerbations of Covid pneumonia or any kind of CT scan features in Covid infected pregnant women. (13). Results of one of previous study on pregnant Covid infected woman patient symptoms and laboratory findings concluded fever (68%) and cough(34%) as common symptoms while increase level of C-reactive protein(70%) and lymphopenia(59%) were common laboratory findings. (14). In comparison to above studies results, our study patients reported cough(22%) and fever(11%) only while most of the patients had lymphopenia(84%) while only 7.6% patients were done with CT scan.

**Maternal and fetal outcomes:** Many researches in china was done on pregnant women having Covid infection. One of the case series study done on three pregnant women having covid positive PCR test reports gave birth to one preterm low birthweighted(LBW) baby while two normal babies (15). Another study of same perspective reported low birthweight baby(LBW) healthy baby in Covid positive 30 weeks pregnant women (16). In comparison of our study results with previous studies, 15.8% of pregnant Covid positive patients reported preterm deliveries.

Study of Liu et. Al done on 13 covid positive pregnant reported positive PCR test results in two women before 28 weeks while rest of eleven patients got infection after 28 weeks. Among these thirteen Covid positive pregnant women ten patients had caesarean sections, five of which were emergency caesarean sections, three patients had Foetal depression while only one had premature fluid rupture and one have still to born (17). In our study, 49.1 percent were infected in the third trimester, 52 patients were born in the study period, six were seriously ill and received intensive treatment, 3 were artificially ventilated, and one was died during study period.

Chen H et al. identified two cases of foetal distress, four cases of preterm birth (1 case of maternal preeclampsia, one case of PROM, and two cases with a history of caesarean section or stillbirth dead) and two cases of LBW in their study (with maternal preeclampsia) There was one case of PROM among nine pregnant women who had a positive Covid test (18). Another previous study done on 17 pregnant Covid positive women reported premature birth of 3 babies (19). Results of previous study reported death of neonate in Covid positive severely ill pregnant woman and the reason of death identified was uterine asphyxia(20). In comparison of our study results with above mentioned studies, six cases of foetal distress, three cases of IUD were identified while in eight cases there were termination of pregnancy earlier.

There were multiple negative pregnancy outcome in study carried out by Zhu H. et al on nine pregnant women with Covid positive clinical signs and symptoms in these nine women started in different time frames like in four pregnant women these symptoms started nbefore delivery, while on the day of delivery two of women got infected and three women got infection after delivery. Among these nine pregnant covid infected women gave birth to six premature babies and two babies were of SGA (small gestational age) (21).

N. Li and colleagues compared case-control study of 16 pregnant women with confirmed COVID-19 pneumonia and 18 pregnant women with suspected COVID-19 pneumonia who give birth in the third trimester in two cohort studies in 2019 and 2020 (22).

An estimated 70% of cases in both groups had other maternal complications (primary GDM, preeclampsia, hypothyroidism), a much higher proportion than in the control group (33%). In three confirmed cases there were ceased periods among which two were because of PROM and one was because of bleeding from placenta and three suspected cases (16.9 percent, one because of preeclampsia / preeclampsia and one because of placenta previa). This represents 5.8% of the control community. PIH, hypothyroidism and GDM were the most common comorbidities with 13.58%, 11.11% and 7.40% respectively in our research.

**Delivery:** The majority of caesareans were administered 24/28 (85.7%), 19/24 (79%) emergency caesareans, and 4/24 limited caesareans in a prospective follow-up report (16.6 percent) (23). Pathological CTG, birth failure, and PROM are all reasons for a caesarean section (birth failure, maternal needs and severe sepsis). two case-control studies by Zhang L. et al. performed during pandemic in China, comparing the pregnancy results of sixteen covid positive patients among which one was severe and 45 uninfected women, all of whom were delivered by caesarean section (24). The amount of blood lost during the procedure did not vary significantly, according to the researchers. In our study there were more caesarean

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### Table III. Pregnancy and neonatal outcome of patients with COVID-19 (N=121)

<table>
<thead>
<tr>
<th>Pregnancy and neonatal outcome</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delivery</td>
<td>78</td>
<td>64.2</td>
</tr>
<tr>
<td>Normal vaginal delivery (NVD)</td>
<td>12</td>
<td>15.1</td>
</tr>
<tr>
<td>Caesarean section</td>
<td>63</td>
<td>80.8</td>
</tr>
<tr>
<td>Hysterectomy</td>
<td>3</td>
<td>2.4</td>
</tr>
<tr>
<td>Abortion</td>
<td>4</td>
<td>3.7</td>
</tr>
<tr>
<td>Live birth</td>
<td>70</td>
<td>90.4</td>
</tr>
<tr>
<td>Preterm birth</td>
<td>12</td>
<td>15.4</td>
</tr>
<tr>
<td>Neonatal death</td>
<td>3</td>
<td>3.8</td>
</tr>
<tr>
<td>Neonatal COVID infection</td>
<td>6</td>
<td>7.6</td>
</tr>
</tbody>
</table>

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section as compared to normal vaginal delivery with 64.2% C-section and 15.14% normal vaginal delivery (NVD).

**Neonatal outcome:** Shortness of breath in six patients, fever in two patients and thrombocytopenia with impaired liver function in two patients were among the clinical symptoms identified by Zhu H. et al. In his study which he carried out on six newborns with a paediatric critical illness score (PCIS) of less than 90. There was one case of illness (n = 1) and one case of vomiting (n = 1). Four newborns had gastrointestinal signs such as bloating, milk rejection, food aversion, and gastric bleeding, while seven had imaging anomalies (infection, n = 4, neonatal respiratory distress syndrome, n = 2, and pneumothorax, n = 1). 8 days after birth, the baby experienced failure of many body systems and organs and diffuse clotting in between vessels, and died 9 days later after receiving a blood transfusion (21). In our study, only 6 cases were found to be positive for RT-PCR. A very premature birth resulted in 3 newborns. The rest is fine.

**CONCLUSION**
COVID-19 has a negative impact on the fetus, according to our results. Although pregnant women do not seem to be more vulnerable to COVID-19 complications than non-pregnant adults, previous research has suggested that pregnant women could be at higher risk for negative pregnancy outcomes such as preterm birth, foetal pain and respiration, symptoms, and LBW in a newborn baby. More clinical research studies are needed to direct the true impact of Covid pandemic on Fetomaternal outcomes, as well as to direct the most effective gynecologist’s recommendations. Only a multi-faceted evaluation of current virus features, epidemiology, disease immunopathology, future preventive and treatment methods, and awareness of current clinical findings may help determine the exact impact of Covid infection before, during as well as after pregnancy.

**REFERENCES**