Lockdown with a Price: The impact of the COVID-19 Pandemic on Prenatal Care and Perinatal Outcomes in a Tertiary Care Center

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ABSTRACT **Background:** The World Health Organization classified coronavirus disease-19 (COVID-19) as a pandemic and recommends strict restrictions regarding most aspects of daily activities.

Objectives: To evaluate whether the pandemic has changed the prenatal care and pregnancy outcome in pregnant women without COVID-19.

Methods: The authors conducted a cross-sectional study to describe changes in outpatient clinic visits and to compare the rates of cesarean and instrumental deliveries between two periods of time: March–April 2020 (during the COVID-19 outbreak) with March–April of the preceding year, 2019.

Results: During the COVID-19 outbreak, visits to obstetric triage, gynecologic triage, high-risk clinic, and ultrasound unit decreased by 36.4%, 34.7%, 32.8%, and 18.1%, respectively. The medical center experienced a 17.8% drop in the total number of births (610 births) compared with March and April 2019 (742 births). During the outbreak women were more likely to be nulliparous (33.3% vs. 27.6%, $P = 0.02$) and present with hypertensive disorders during pregnancy (7.5% vs. 4%, $P = 0.005$) or gestational diabetes (13% vs. 10%, $P = 0.03$). More epidural analgesia was used (83.1% vs. 77.1%, $P = 0.006$). There were more operative vaginal deliveries during the outbreak (16.7% vs. 6.8%, $P = 0.01$). All other maternal and neonatal outcomes were comparable between the two periods.

Conclusions: The medical facility experienced a major decline in all aspects of the routine obstetrics activities during the time of the pandemic. The higher rate of operative vaginal deliveries among nulliparous may be associated with the pandemic effect on the rate of high-risk patients.

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KEY WORDS: coronavirus disease-19 (COVID-19), lockdown, outcomes, pandemic, pregnancy

The first outbreak of coronavirus disease-19 (COVID-19) started during December 2019 in Wuhan, China. Shortly thereafter, the World Health Organization classified COVID-19 as a pandemic and recommended strict restrictions regarding most aspects of daily activities including work, social life, leisure time, and healthcare [1].

As soon as the pandemic was identified, hospitals and ambulatory care facilities planned prevention and control strategies to reduce transmission of COVID-19 to patients and healthcare workers [1]. Although their goal was to reduce the impact on emergency departments and hospital bed capacity in addition to maximizing the efficiency of healthcare personnel with regard to COVID-19 cases, it also created a challenge for hospitals to establish non-COVID 19 medical priorities. Evidence is emerging on the dramatic decline of the number of patients with serious medical conditions, such as strokes and myocardial infarction, arriving at hospitals since the beginning of the COVID-19 pandemic [2-4]. This deferral has already resulted in increased morbidity and mortality among cardiac, neurologic, and oncologic patients, and may also jeopardize the safety of patients in the future [5,6].

Limited data are available about how COVID-19 affects the behavior, prenatal care, and outcomes of pregnant women without the disease. Most obstetrics and gynecology organizations have issued guidance regarding prenatal care for low- and high-risk women during the COVID-19 outbreak. Some of the suggestions include reducing the number of in-person visits by using telehealth, altering the timing of visits, grouping screening tests, restricting accompanied visitors, and scheduling maternal and fetal assessment appointments when relevant [7-10].

Following the restrictions imposed by the Ministry of Health, we noticed a drop in the number of prenatal visits and admissions to our obstetrics and gynecology department. We therefore decided to characterize this change and to assess whether this drop, similar to other disciplines, had any adverse effect on the maternal and fetal outcomes.

PATIENTS AND METHODS

This cross-sectional study was conducted at a large tertiary referral center. The hospital opened a dedicated inpatient ward for receiving patients, including pregnant women, who had been diagnosed with the COVID-19. However, no pregnant women who were diagnosed with COVID-19 were included in our study. Preparations included the formation of a distinct staff for this department as well as the establishment of a set of procedures to ensure safe and comprehensive isolation, in accordance with the strict requirements defined by the Ministry of Health [11]. Our obstetrics and gynecology department provides care to approximately 15,000 patients annually, and includes nearly 5500 births. The study was approved by the hospital's research ethics board (REB-0172-20).

Demographic and clinical data were retrieved from the combined maternal and fetal medical records, and included antenatal, intrapartum, and postpartum characteristics. All registered visits to our obstetrics and gynecology department during two distinct time periods were eligible for the study: March–April 2019 was defined as period I and March–April 2020 (throughout the peak COVID-19 outbreak) was defined as period II.

During the outbreak, all personnel working in the triage areas were protected from the virus by wearing a face mask, screen shield, and disposable medical gown. In the triage, every woman was asked about respiratory symptoms, fever, and any close contact with COVID-19 cases. Women were told to continue ongoing home care or were sent to a regular labor ward or to a designated labor ward if COVID-19 was suspected.

The primary objective of this study was to describe changes in outpatient clinic visits and to compare the rates of cesarean and instrumental deliveries between study period I (March–April 2019) and period II (March–April 2020). The secondary goal was to compare other maternal and neonatal outcomes during the peak COVID-19 outbreak to the same period of the preceding year. To reduce personal contact and to protect as many medical staff members as possible, the only difference in care during the COVID-19 outbreak was that we switched to 12-hours shifts followed by 24-hours of rest. Perinatal outcomes were only analyzed in women who ultimately gave birth at our institution. Maternal outcome data included demographic data, medical data, and maternal and fetal outcome. Estimated blood loss of > 500 ml during a vaginal delivery and more than 1000 ml during a cesarean delivery were used to define postpartum hemorrhage. Clinical criteria for chorioamnionitis were maternal fever with two or more of the following symptoms: maternal tachycardia, fetal tachycardia, leukocytosis, uterine tenderness, and malodorous amniotic fluid. Neonatal outcomes included shoulder dystocia, Apgar scores at 1 and 5 minutes, umbilical artery cord pH, admission to the neonatal intensive care unit, and intrauterine fetal death.

Table 1. Demographic and clinical characteristics of the study groups

	Period I (March–April 2019) (n=742)	Period II (March–April 2020) (n=610)	*P* value
Maternal age, years, mean ± SD	30.6 ± 5.2	30.8 ± 4.9	0.4
Nulliparous, n (%)	205 (27.6)	203 (33.3)	0.02
Hypertensive disorders, n (%)*	30 (4)	46 (7.5)	0.005
Gestational diabetes, n (%)	74 (10)	83 (13)	0.03
PROM, n (%)	124 (16.7)	126 (20.7)	0.06
Induction of labor, n (%)	187 (25.2)	133 (21.8)	0.14
Epidural analgesia, n (%)	572 (77.1)	507 (83.1)	0.006
Gestational age at delivery, weeks, mean ± SD	39.2 ± 1.6	39.1 ± 1.5	0.05
Preterm birth < 37 weeks gestation, n (%)	48 (6.5)	39 (6.4)	0.96
Preterm birth < 32 weeks gestation, n (%)	3 (0.4)	1 (0.2)	0.63
Birth weight at delivery, grams, mean ± SD	3261.8 ± 500	3273.5 ± 483	0.7

*Preeclampsia or pregnancy induced hypertension
P < 0.05 was considered significant
n = number, PROM = pre-labor rupture of membranes, SD = standard deviation

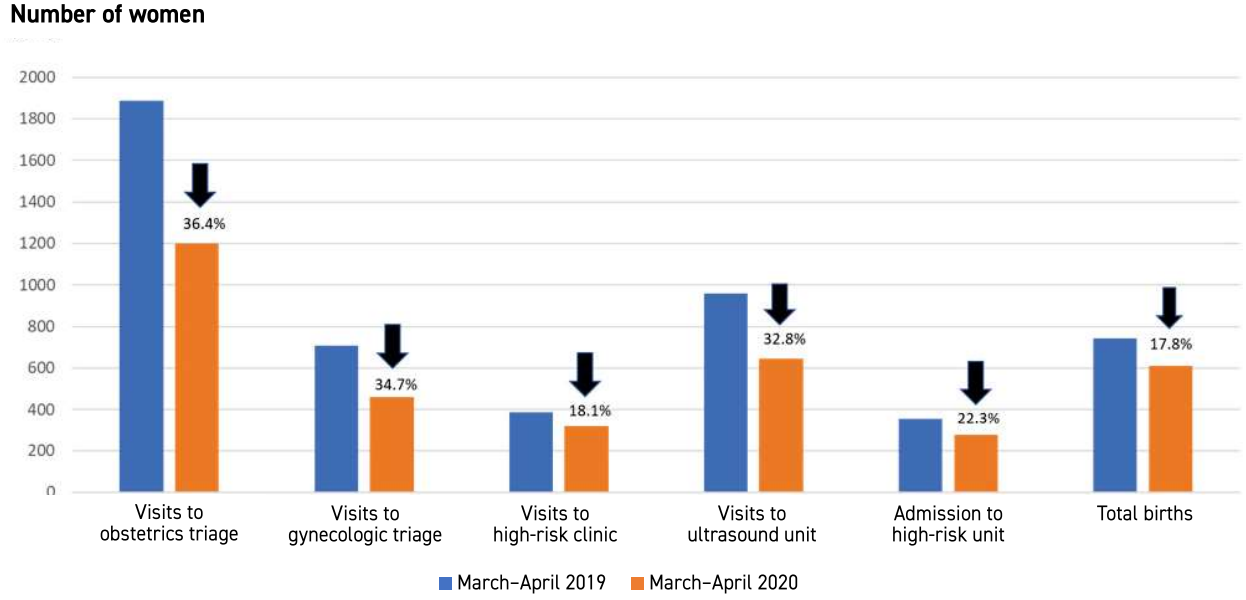
STATISTICAL ANALYSIS

No power calculations were computed for this cross-sectional study. Descriptive statistics were reported as mean ± standard deviation for continuous variables and as numbers (percentages) for categorical variables. Univariate analyses were performed using Chi-square and *t*-test or Mann–Whitney U test to compare the groups on maternal and neonatal outcomes. The threshold of statistical significance was $P < 0.05$. Statistical analyses were performed using IBM Statistical Package for the Social Sciences statistics software, version 25 (SPSS, IBM Corp, Armonk, NY, USA).

RESULTS

During the early months of the COVID-19 pandemic, the number of visits and admissions to our obstetrics and gynecology department declined significantly [Figure 1]. Visits to obstetric triage, gynecologic triage, high-risk clinic, and ultrasound unit, as well as the total number of deliveries decreased by 36.4%, 34.7%, 32.8%,18.1%, and 17.8%, respectively. The total number of admissions to high-risk unit also declined by 22.3%. Twenty pregnant women were tested for the virus due to high suspicion and all were ultimately proved negative.

Figure 1. Comparison of the number of visits and admissions to our obstetrics and gynecology divisions between two periods of time: before and during COVID-19 outbreak



Baseline demographic and clinical characteristics of the study groups are presented in Table 1. Pregnant women were more likely to be nulliparous (33.3% vs. 27.6%, $P = 0.02$), to present with hypertensive disorders of pregnancy (7.5% vs. 4%, $P = 0.005$) or gestational diabetes (13% vs. 10%, $P = 0.03$), and to use epidural analgesia (83.1% vs. 77.1%, $P = 0.006$) during period II compared with period I.

Table 2 shows comparisons of maternal and neonatal outcome variables between the two groups. The rate of cesarean deliveries, including of emergency cesarean deliveries, was not different between the two periods: 22.1% (164/742) in period I vs. 24.1% (147/610) in period II, $P = 0.39$. Rates of operative vaginal deliveries were overall similar in both groups; however, there were more operative vaginal deliveries among nulliparous women during period II than during period I (16.7% vs. 6.8%, $P = 0.01$). A sub-analysis of the common indications for operative vaginal deliveries (non-reassuring fetal heart rate, prolonged second stage, maternal exhaustion) showed that prolonged second stage was significantly more common in period II than in period I: 14.3% (2/14) in period I vs. 52.9% (18/34) in period II, $P = 0.01$. All other maternal and neonatal outcomes were similar between the two periods.

DISCUSSION

During the first months of the outbreak of the coronavirus disease, we noticed a dramatic decrease in the number of visits and admissions into our obstetrics and gynecology department. Women who attended their visits were more likely to be nulliparous, high-risk patients, who presented with hypertensive disorders of pregnancy or gestational diabetes and used more epidural analgesia during labor. We also observed a higher rate of operative vaginal deliveries among nulliparous women. No differences were demonstrated in any of the other perinatal outcomes.

As the COVID-19 pandemic continued, many pregnant women were uncertain about the impact of the outbreak on their pregnancy outcome. Pregnancy by itself constitutes a state of relative immunosuppression [12,13], and recent data suggest that pregnant women have increased susceptibility to contract the disease as well as to increased morbidity [8].

We did not expect the number of childbirths, which reflect the number of pregnancies that began several months earlier, to drop during the pandemic period. In our opinion, by being a referral center for patients with COVID-19, women preferred to reduce the risk of acquiring the virus by choosing to give birth in a non-COVID-19 medical center. We speculate that women who gave birth elsewhere were more likely to be low-risk patients and multiparous, which left us with a relative higher number of high-risk and nulliparous women. Another possible explanation for the increased number of women with hypertensive disorders of pregnancy and gestational diabetes may be the stress associated with the COVID-19 lockdown.

The stress that pregnant women experienced during the COVID-19 lockdown could instigate a cascade of endocrinological and immunological alterations that affect the delicate equilibrium needed to maintain a normal pregnancy and give

Table 2. Comparison of maternal and neonatal outcomes between two periods of time: before and during COVID-19 outbreak

	Period I (March–April 2019) (n=742)	Period II (March–April 2020) (n=610)	*P* value
Maternal outcomes			
Cesarean delivery, n (%) Emergency, n (%) In nulliparous, n (%)	164 (22.1) 105 (14.2) 45 (22)	147 (24.1) 71 (11.6) 48 (23.6)	0.39 0.17 0.68
Operative vaginal delivery, n (%) In nulliparous, n (%)	46 (6.2) 14/205 (6.8)	44 (7.2) 34/203 (16.7)	0.46 0.01
PPH, n (%) Blood transfusion, n (%) Third- and fourth-degree laceration, n (%)	38 (5.1) 18 (2.4) 2 (0.3)	32 (5.2) 19 (3.1) 1 (0.2)	0.92 0.44 0.68
Chorioamnionitis, n (%)	16 (2.2)	17 (2.8)	0.46
Neonatal outcomes			
Apgar score at 1 minute, mode Apgar score at 1 minute < 7, n (%) Apgar score at 5 minutes, mode Apgar score at 5 minutes < 7, n (%)	9 29 (3.9) 10 5 (0.7)	9 23 (3.8) 10 3 (0.5)	0.86 0.9 0.76 0.66
Shoulder dystocia, n (%)	4 (0.5)	1 (0.2)	0.26
Arterial cord pH < 7.0, n (%)	0	0	1
Admission to NICU, n (%) IUFD, n (%)	59 (8) 3 (0.4)	49 (8) 2 (0.33)	0.95 0.81

P < 0.05 was considered significant

n = number, IUFD = intrauterine fetal death, NICU = neonatal intensive care unit, PPH = postpartum hemorrhage

rise to the development of coexisting pregnancy complications. It was postulated that the high maternal cortisol levels could be correlated to reduced T-lymphocyte sensitivity to glucocorticoids. This acquired form of steroid resistance could be associated with a higher release of pro-inflammatory cytokines (TNF-α and IL-6) and hypothalamic–pituitary–adrenal axis dysregulation, leading to endothelial dysfunction and consequent preeclampsia development [14]. Similarly, excessive activity of circulating cortisol is a possible contributor to increased insulin resistance, a typical feature in the pathogenesis of gestational diabetes [15,16].

Nulliparity is a known risk factor for operative vaginal delivery [17]. Yet, we noticed an increase in the rate of vacuum assisted births during the initial months of the outbreak among nulliparous women. The increase in the rate of vacuum assisted births during the COVID-19 pandemic may be the consequence of a combination of well-known risk factor for operative deliveries, high-risk nulliparous women, and prolonged second stage [18,19]. In addition, although the effect of neuraxial analgesia on the second stage of labor is inconsistent [20,21], we assume that the higher rate of epidural analgesia use during period II also contributed to the higher rate of operative deliveries during period II. Fortunately, we did not observe a higher rate of maternal or fetal complications secondary to the procedure.

LIMITATIONS AND STRENGTHS

This cross-sectional study has limitations. For example, we postulated that, at least in part, COVID-19 was the main reason for the decline in number of hospital visits and births, but there might be other explanations for the decline that we were not able to explore. As the aim of our study was to describe the perinatal care and outcomes during the two periods of time, some other variables, such as the indications for cesarean delivery and distinction between the types of gestational diabetes and the types of hypertensive disorders, were not fully evaluated in the current study. Evaluating these additional parameters would add little to this aim. In addition, the small number of vacuum assisted deliveries prevented us from performing multivariate analysis that could have shed some more light regarding the causes for our observations. Also, no data are available regarding the women who did not deliver at our institution or their pregnancy outcome. The major strengths of this study include the relatively large number of deliveries and our ability to describe maternal and neonatal outcomes in two consecutive months during the COVID-19 outbreak compared to the same period in the preceding year.

CONCLUSIONS

During the COVID-19 outbreak a decline in all obstetrics and gynecology visits in general, and specifically in births, was noted. This decline resulted in higher risk women attending labor

and delivery wards. Hospitals and caregivers should be aware that higher risk women may attend labor and delivery wards during the time of the pandemic.

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Capsule

Distinct synovial tissue macrophage subsets regulate inflammation and remission in rheumatoid arthritis

Immune-regulatory mechanisms of drug-free remission in rheumatoid arthritis (RA) are unknown. **Alivernini** and co-authors hypothesized that synovial tissue macrophages (STM), which persist in remission, contribute to joint homeostasis. The authors used single-cell transcriptomics to profile 32,000 STMs and identified phenotypic changes in patients with early/active RA, treatment-refractory/active RA and RA in sustained remission. Each clinical state was characterized by different frequencies of nine discrete phenotypic clusters within four distinct STM subpopulations with diverse homeostatic, regulatory and inflammatory functions. This cellular atlas, combined with deep-phenotypic, spatial and functional analyses of synovial biopsy fluorescent activated cell sorted STMs, revealed two STM subpopulations (MerTKposTREM2high and MerTKposLYVE1pos) with unique remission transcriptomic signatures enriched in negative regulators of inflammation. These STMs were potent producers of inflammation-resolving lipid mediators and induced the repair response of synovial fibroblasts in vitro. A low proportion of MerTKpos STMs in remission was associated with increased risk of disease flare after treatment cessation. Therapeutic modulation of MerTKpos STM subpopulations could therefore be a potential treatment strategy for RA.

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