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COVID-19 and Pregnancy: Factors Associated with the Occurrence of COVID-19 during Pregnancy, Maternal and Perinatal Outcome in Two Referral Hospitals in the City of Douala, Cameroon

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Abstract

Introduction: The Coronavirus pandemic was responsible for an unprecedented health crisis that shook the world with its high contagiousness and lethality. Its impact on maternal and fetal health places pregnant women at high risk. The aim of our study was to determine the factors associated with the occurrence of COVID-19 in pregnant women, and the maternal and perinatal outcomes of infected patients. **Methodology:** This was a case-control study involving 42 cases matched to 42 controls recruited from two public and tertiary hospitals in the cities of Yaoundé and Douala over a period from November 31 to May 31, 2024. Cases were defined as deliveries or records of COVID-19 deliveries confirmed positive by reverse transcription polymerase chain reaction (RT-PCR) or by a COVID-19 rapid diagnostic test (Covid-RDT). Controls were defined as deliveries or records of deliveries negative to the same test. They were matched by the hospital. Non-consenting births and unusable records were excluded. The data collected were recorded on a pre-established, pretexted data sheet examining sociodemographic, clinical characteristics and maternal and perinatal outcomes which were then analyzed using SPSS version 23.0 software. **Results:** After multivariate analysis, the independent sociodemographic factors were: belonging to the [30 - 40] age group (OR: 4.4; P = 0.010), being married (OR: 8.1; P = 0.030); being unemployed (OR: 3; P = 0.040). Independent clinical factors were: being in the third trimester of pregnancy (OR: 1.1; P = 0.017), being diabetic (OR: 5; P = 0.033) and being obese

(OR: 11.5; P = 0.043). Independent factors associated with maternal outcome were: caesarean section (OR: 10; P = 0.001); admission to intensive care (OR: 30.7; P = 0.013); $SO_2 \leq 94\%$ (OR: 11.7; P = 0.033); HR > 100 (OR: 15.5; P = 0.001). Independent factors associated with perinatal outcome were: weight < 2500 (OR: 12; P = 0.039); APGAR score (OR: 15; P = 0.030). **Conclusion:** The factors associated with the occurrence of COVID-19 in pregnant women are multiple, and maternal outcome depends on its condition on admission, and has a significant impact on perinatal health, including mode of delivery. Emphasis must be placed on prevention and optimal management of these associated factors.

Keywords

COVID-19, Pregnant Woman, Comorbidity, Maternal Outcome, Perinatal Outcome

1. Introduction

The SARS-COV-2 disease (severe acute respiratory syndrome coronavirus-2) outbroke in December 2019 in patients with severe pneumonia. The virus then quickly spread to over 180 countries worldwide, causing nearly 7,000,000 cases and 400,000 deaths six months later, by June 8, 2020. In Cameroon, a study conducted in Douala found a prevalence of 6% among women [1]-[6]. Initially, data on pregnant women with SARS-COV-2 were limited, and comparisons were made with known information regarding other types of pneumonia. Pneumonia is a significant cause of morbidity and mortality in pregnant women [7]. Patients with pneumonia are also at higher risk for premature rupture of membranes, preterm delivery, in utero fetal death, intrauterine growth retardation, and neonatal deaths [8]. Some studies had highlighted adverse outcomes including miscarriages and preterm deliveries, but without comparison to unexposed patients [9]. Beyond the potential severity of the maternal infection, there are concerns about fetal outcomes and neonatal status. Pregnant women are thus a group requiring special attention due to their vulnerability to severe forms. Therefore, we decided to conduct a case-control study to determine the factors associated with the occurrence of COVID-19 in pregnant women and the maternal and perinatal outcomes in two hospitals in the cities of Douala and Yaoundé.

2. Methodology

We conducted a case-control study with both prospective and retrospective data collection at the Gyneco-Obstetric and Pediatric Hospital of Douala (HGOPED) and the Gyneco-Obstetric and Pediatric Hospital of Yaoundé (HGOPY), both first-category hospitals. The study period spanned four years, from May 2020 to May 2024.

Included in the study were, for the case group, women who had given birth or

birth records of those confirmed positive for COVID-19 by reverse transcription polymerase chain reaction (RT-PCR) or by a COVID-19 rapid diagnostic test (RDT-COVID). For the control group, included were women who had given birth or birth records confirmed negative for COVID-19 by RT-PCR or RDT-COVID. Unusable records and non-consenting women were excluded. Matching was done according to the study location, with one case for each control.

Data were collected, recorded, and analyzed using the SPSS (Statistical Package for Social Sciences) software, version 23.0. The results were illustrated using Microsoft Office Word 2019 and represented in tables and figures.

The variables studied included sociodemographic, clinical, and obstetric variables, as well as maternal and perinatal outcome variables such as mode of delivery, APGAR score, birth weight, transfer to NICU, maternal and newborn survival outcomes, mode of admission, length of hospital stay, and mode of management. Quantitative variables were expressed as means with standard deviations, and qualitative variables were expressed as counts and percentages. A p-value of <0.05 was considered statistically significant both before and after logistic regression. The search for associated factors was conducted using the chi-square test or Fisher's exact test. The measure of association used was the Odds ratio.

3. Results

A total of 84 patients were included, comprising 42 cases and 42 controls. The average age of the cases was 32.1 ± 4.9 years, with ages ranging from 20 to 42 years, while the average age of the controls was 30.6 ± 5.5 years, with ages ranging from 18 to 39 years.

3.1. Sociodemographic Characteristics Associated with COVID-19

Age and marital status

In our study population, pregnant women with COVID-19 had an average age of 32.1, ranging from 20 to 42 years. Those not affected by COVID-19 had an average age of 30.6, ranging from 18 to 39 years. Age and marital status were associated with the occurrence of COVID-19. Belonging to the age group [30 - 40) or being married significantly increased the risk of COVID-19 by 2.3 and 5.6 times (P = 0.01 and 0.005, respectively), whereas being single reduced it (P = 0.005).

3.2. Clinical Characteristics Associated

1) Gestational term and parity

The third trimester of pregnancy was associated with a high risk of COVID-19, parity was not (Table 1).

2) Co-mobordities

Diabetes, HIV and obesity were significantly associated with the occurrence of COVID-19 (Table 2).

Table 1. Association between gestational term, parity, and the occurrence of COVID-19.

	F.E COVID-19	F.E non COVID-19		
Variables	**n = 42 (%)**	**n = 42 (%)**	**OR (IC 95%)**	**P-value**
Trimester of pregnancy				
T1	8 (0.6 - 3.2)	14 (33.3)	0.5 (0.2 - 1.3)	0.136
T2	12 (28.6)	15 (35.7)	1.6 (0.6 - 4.4)	0.321
T3	22 (52.4)	13 (31.0)	2.5 (1.01 - 6.0)	**0.028**
Parity				
Large multiparous	2 (408)	2 (4.8)	1.4 (0.2 - 12.2)	0.736
Multiparous	5 (11.9)	10 (23.8)	0.7 (0.2 - 2.8)	0.641
Nulliparous	4 (9.5)	2 (4.8)	2.1 (0.7 - 6.2)	0.171
Pausiparous	22 (52.4)	15 (35.7)	2.9 (0.4 - 4.3)	0.637
Primiparous	9 (21.4)	13 (31.0)	0.7 (0.2 - 2.3)	0.558

Table 2. Association between comorbidities and COVID-19 in pregnant women.

	F.E COVID-19	F.E non COVID-19		
Variables	**n = 42 (%)**	**n = 42 (%)**	**OR (IC 95%)**	**P-value**
Comorbidities				
Asthma	2 (4.5)	1 (2.4)	2.9 (0.2 - 42.6)	0.435
Diabetes	8 (19.0)	2 (4.8)	4.7 (1.1 - 23.7)	**0.029**
Hepatitis B	2 (4.8)	1 (2.4)	2.7 (0.2 - 31.5)	0.433
HIV	6 (14.3)	1 (2.4)	6.8 (1.7 - 59.5)	**0.048**
HTA	3 (7.1)	6 (14.3)	0.5 (0.1 - 2.5)	0.418
Obesity	6 (14.3)	1 (2.4)	6.8 (1.1 - 59.5)	**0.048**

3.3. Maternal and Perinatal Outcomes Associated with the Occurrence of COVID-19 in Pregnant Women

3.3.1. Maternal Outcome

Out of 42 pregnant women with COVID-19, 13 had died (31.0%) and 29 were alive (69.0%).

1) Factors associated with maternal outcome according to functional signs dyspnoea, cough and fever significantly increased the risk by a factor of 10, 3.8 and 16.4 respectively (Table 3).

2) Factors associated with maternal outcome according to functional signs Oxygen saturation < 94, Temperature > 38.5 and HR > 100 increased significantly by 16.5 (Table 4).

Table 3. Association between functional signs and maternal outcome in pregnant women with COVID-19.

Variables	Died (n = 12)	Alive (n = 30)	OR (IC 95%)	P-value
Functional signs				
Dyspnea				
Yes	10 (83.3)	10 (33.3)	10.0 (1.8 - 54.6)	**0.003**
No	2 (16.7)	20 (66.7)	0.1 (0.01 - 0.5)	**0.003**
Asthenia				
Yes	10 (83.3)	17 (56.7)	3.8 (0.7 - 20.5)	0.413
No	2 (16.7)	13 (43.3)	0.3 (0.5 - 2.8)	0.613
Cough				
Yes	8 (66.7)	7 (23.3)	6.5 (1.5 - 28.5)	**0.008**
No	4 (33.3)	23 (76.7)	0.2 (0.04 - 0.7)	**0.008**
Fever				
Yes	10 (83.3)	7 (23.3)	16.4 (2.9 - 93.4)	**<0.001**
No	2 (16.7)	23 (76.7)	0.06 (0.01 - 0.3)	**<0.001**
Arthralgia				
Yes	7 (58.3)	15 (50.0)	1.4 (0.4 - 5.4)	0.625
No	5 (41.7)	15 (50.0)	0.7 (0.2 - 2.7)	0.625
Ageusia				
Yes	7 (58.3)	20 (66.7)	0.7 (0.2 - 2.8)	0.611
No	5 (41.7)	10 (33.3)	1.4 (0.4 - 5.6)	0.611

Table 4. Association between vital parameters and maternal outcome in COVID-19 pregnant women.

Variables	Died (n = 12)	Alive (n = 30)	OR (IC 95%)	P-value
Vital parameters				
Oxygen saturation (SaO_2)				
≤94%	1 (8.3)	12 (40.0)	16.5 (1.9 - 145.0)	**0.002**
>94%	11 (91.7)	18 (60.0)	0.06 (0.01 - 0.53)	**0.002**
Heart rate (HR)				
<70	0 (0.0)	5 (16.7)	0	0.132
70 - 100	1 (8.3)	11(36.7)	0.2 (0.02 - 0.4)	**0.034**
>100	11 (91.7)	14 (46.7)	12.5 (1.4 - 110.1)	**0.007**

Continued

Respiratory rate (RF)				
16 - 20	2 (16.7)	9 (30.0)	2.8 (0.2 - 27)	0.410
>20	0 (0.0)	21 (70.0)	0	0.210
Temperature				
≤37.5	2 (16.7)	2 (6.7)	2.8 (0.3 - 22.6)	0.319
37.5 - 38.5	3 (25.0)	22 (73.3)	0.1 (0.03 - 0.6)	**0.004**
>38.5	7 (58.3)	6 (20.0)	6.0 (1.3 - 24.0)	**0.015**

3) According to comorbidities

We found a significant association between the presence of comorbidities and maternal outcomes. The risk is increased by 11.5 and 17.5 times, with P = 0.003.

4) According to the mode of admission and management

Emergency admission and intensive care management increased the risk of unfavourable maternal outcomes by 6.7 and 25.7 times, respectively. Referral and outpatient management reduced this risk (Table 5).

5) According to mode of admission , management

Table 5. Association between mode of admission and maternal outcome of COVID-19 in pregnant women.

Variables	Died (n = 12)	Alive (n = 30)	OR (IC 95%)	P-value
Admission method				
Emergency	9 (75.0)	10 (33.3)	6.0 (1.3 - 27.2)	**0.014**
Referred	3 (25.0)	20 (66.7)	0.2 (0.04 - 0.8)	**0.014**
Support mode				
Intensive care	11 (91.7)	9 (30.0)	25.7 (2.8 - 229.6)	**0.004**
Ambulatory	1 (8.3)	21 (70.0)	0.04 (0.01 - 0.4)	**0.004**

3.3.2. Perinatal Outcome

1) According to mode of delivery

We found a significant association between the mode of delivery and perinatal outcome. The risk is increased by 5 times with P = 0.021.

2) According to birth weight, APGAR score at birth, initial emergency care

Weight < 2500 g, APGAR < 7 and NICU management increased the risk by 37.7, 31.5 and 6.3 times. Length of hospitalisation was not associated (Table 6).

3) According to perinatal complications

We found 57.2% (22) of premature babies, 50% of newborns had been admitted to the NICU, 22.5% of newborns had respiratory distress at birth and 42.9% (Table 7).

Table 6. Association between management, length of hospital stay, and perinatal outcome in pregnant women with COVID-19.

Variables	Died (n = 13)	Alive (n = 29)	OR (IC 95%)	P-value
Birth weight				
<2500				
Yes	12 (92.3)	7 (24.1)	37.7 (4.1 - 343.8)	**<0.001**
No	1 (7.7)	22 (75.9)	0.03 (0.003 - 0.3)	**<0.001**
[2500 - 3000]				
Yes	1 (7.7)	6 (20.7)	0.3 (0.034 - 3.0)	0.296
No	12 (92.3)	23 (79.3)	3.1 (0.3 - 29.1)	0.296
[3000 - 3500]				
Yes	0 (0.0)	11 (37.9)	0	**0.010**
No	13 (100.0)	18 (62.1)	1.7 (1.3 - 2.3)	**0.010**
[3500 - 4000]				
Yes	0 (0.0)	4 (13.8)	0	0.159
No	13 (100.0)	25 (86.2)	1.5 (1.2 - 1.9)	0.159
≥ 4000				
Yes	0 (0.0)	1 (1.4)	0	0.498
No	13 (100.0)	28 (96.6)	1.4 (1.1 - 1.8)	0.498
APGAR score				
≤7	12 (92.3)	8 (26.7)	31.5 (3.5 - 283)	**<0.001**
>7	1 (7.7)	21 (70.0)	0.03 (0.004 - 0.3)	**<0.001**
Support				
Intensive care	10 (76.9)	10 (34.5)	6.3 (14 - 28.4)	**0.011**
Ambulatory	3 (23.1)	19 (65.5)	0.2 (0.03 - 0.7)	**0.011**
Length of hospitalization				
0 - 7 days	4 (30.8)	7 (24.1)	1.4 (0.3 - 6.0)	0.651
>7 days	9 (69.2)	22 (75.9)	0.7 (0.2 - 3.1)	0.651

Table 7. Distribution according to perinatal complications.

Variables	No. (n = 42)	Pourcentage (%)
Prematurity	24	57.2
Neonatal respiratory distress	21	50.0
Neonatal infection	18	42.9
NICU admission	19	22.5

3.4. Factors Associated with Maternal and Perinatal Outcomes

After multivariate analysis using the logistic regression method we found that having a vaginal birth, being managed as an outpatient, having a $SO_2 > 94\%$, a HR > 100, an APGAR score > 7 and a birth weight ≥ 2500 g significantly reduced the risk of adverse maternal and perinatal outcomes while having a caesarean section, being unemployed, intensive care, dyspnoea, $SO_2 < 94\%$, HR > 100, birth weight < 2500 g, APGAR score < 7 were the independent factors favouring adverse maternal and perinatal outcomes (Table 8).

Table 8. Multivariate analysis of maternal and perinatal outcomes.

Variables	Died	Alive	OR (IC 95%)	P-value
Maternal outcome				
Mode of delivery				
Caesarean sections	9 (75.0)	9 (30.0)	10 (2.5 - 32.1)	**0.001**
Basic channel	3 (25.0)	21 (70.0)	0.2 (0.01 - 0.7)	**0.001**
Support mode				
Intensive care	11 (91.7)	9 (30.0)	30.7 (2.8 - 229.6)	**0.013**
Ambulatory	1 (8.3)	21 (70.0)	0.05 (0.01 - 0.7)	**0.013**
Functional signs				
Dyspnea	10 (83.3)	10 (33.3)	60.4 (2.4 - 150.6)	**0.018**
Oxygen saturation (SaO_2)				
≤ 94%	1 (8.3)	12 (40.0)	11.7 (1.2 - 113.2)	**0.033**
> 94%	11 (91.7)	18 (60.0)	0.058 (0.001 - 0.5)	**0.015**
Heart rate (HR)				
70 - 100	1 (8.3)	11(36.7)	0.3 (0.02 - 0.5)	**0.042**
>100	11 (91.7)	14 (46.7)	15.5 (2.4 - 120.1)	**0.001**
Perinatal outcome				
Birth weight				
<2500	12 (92.3)	7 (24.1)	12.0 (1.1 - 127.4)	**0.039**
[3000 - 3500]	1 (7.6)	11 (37.9)	0.11 (0.01 - 0.4)	**0.042**
APGAR score				
≤7	12 (92.3)	8 (26.7)	15 (1.3 - 50.3)	**0.030**
>7	1 (7.7)	21 (70.0)	0.4 (0.07 - 0.8)	**0.044**

4. Discussion

In our study, we found a significant association between maternal age and the

occurrence of COVID-19 in pregnant women. Being aged between 30 and 40 years significantly increased the risk of developing COVID-19 by more than two times, with a p-value of 0.010. Our result is similar to that of several authors who found that women over 35 years old had a higher incidence of severe COVID-19, with increased risks of hospitalization and severe complications [10]. Their hypothesis is that advanced maternal age is a risk factor for adverse outcomes of COVID-19 during pregnancy, highlighting the need to proactively monitor and manage this at-risk population [10]. Other authors did not find a correlation between age ≥ 35 years and the occurrence of COVID-19, suggesting the probable role of other age-related factors. Similarly, being married increased the risk of developing a severe form of COVID-19 by five times, with a p-value of 0.005. A hypothesis mentioned by A. Floride *et al.* in France found that the severity of COVID-19 significantly impacted the mental health of married pregnant women through anxiety, distress, stress, loneliness, and isolation, which were faced by women with COVID. Excluding fathers from pregnancy and childbirth follow-ups significantly impacted mental health, thereby increasing the risk of miscarriages, premature births, and stillbirths.

The existence of comorbidities such as diabetes and obesity was associated with the occurrence of COVID-19 in our study population. Being diabetic, obese, and in the third trimester of pregnancy significantly increased the risk of developing severe forms of COVID-19 in pregnant women by more than 2, 4, and 6 times. A study by Kayem *et al.* already found that women with critical forms of COVID-19 had high rates of comorbidities such as diabetes, obesity, hypertension, and advanced maternal age (>35 years), which was confirmed by the study of M. Knight *et al.* in 2020, who found that maternal age > 35 years, being overweight, obesity, and pre-existing comorbidities were associated with SARS-COV-2 admission during pregnancy [11]. Chantal Botterman in France found that pregnant women in their third trimester were more at risk of developing severe forms of COVID-19 [12]. Recent literature describes the third trimester as a theoretical risk factor for COVID-19 for both the mother and the fetus [13]. However, these results differ from those of A. Diouf *et al.* in Senegal and Lyu *et al.* in China, who found no correlation between the trimester of pregnancy, highlighting other factors.

Maternal outcomes were correlated with the mode of admission, delivery, and management. Emergency admissions, cesarean sections, and intensive care, as indirect reflections of severity, predicted unfavorable maternal outcomes. Unexpectedly, referrals improved maternal outcomes, as did vaginal deliveries, reflecting a less alarming clinical situation. Our results are consistent with several previous studies, notably by Knight *et al.* and Allotey *et al.*, who found that the management of COVID-19 positive pregnant women in an intensive care unit increased the risk of developing severe complications such as preeclampsia, premature rupture of membranes, cesarean deliveries, and high rates of obstetric complications. They also found that repeated cesarean sections, especially those

performed in emergencies, were associated with an increased risk of maternal complications such as severe hemorrhages, postoperative infections, and death [14]. However, systematic reviews and meta-analyses, contrary to our study, have highlighted great heterogeneity and a lack of solid evidence for certain cesarean deliveries and managements, suggesting that results may vary significantly between populations and contexts studied [15].

As expected, all signs of severity were detrimental to maternal outcomes. The factors increased the risk of unfavorable maternal outcomes by 16.5, 12.5, and 8 times, with p-values of ($P = 0.002$, $P = 0.007$, and $P = 0.018$), respectively. These results are similar to those of Breslin *et al.* and Philadelphian *et al.*, who found that dyspnea, a respiratory rate (RR) > 30 breaths per minute, and an oxygen saturation (SO_2) < 93% were severity factors of COVID-19 that led to severe complications such as respiratory distress, admissions to intensive care, the need for ventilation, and severe obstetric complications [11]. Similarly, Allotey *et al.* and Knight *et al.* found that pregnant women with saturation levels below 95% had an increased risk of severe complications and mortality [16]. This can be explained by the pathophysiological mechanisms related to hypoxemia, which reduces tissue oxygenation, leading to severe complications.

Maternal deaths occurred in 12.9% of cases and were mainly among patients admitted to intensive care. Admission to intensive care was associated with certain severity factors; however, our result is lower than that found in the United Kingdom by Knight *et al.* in 2020, which reported a 30% maternal death rate in intensive care [17], but different from the zero deaths reported by Zaigham *et al.* [18], Li *et al.* [19], and Yangli *et al.* [20] in Sweden and China. The level of hospital infrastructure in these countries seems to explain their results.

The study by Papageorghiou *et al.* on "the impact of COVID-19 on maternal and perinatal outcomes" reveals that unfavorable perinatal outcomes, such as premature birth, neonatal respiratory distress, and newborn admission to the intensive care unit, are more frequent among newborns of mothers who were COVID-19 positive at the time of birth, particularly those with severe comorbidities. Similarly, Knight *et al.* found that obesity and diabetes were associated with unfavorable perinatal outcomes with the occurrence of neonatal complications. Our results are in agreement with the data from the literature.

Contrary to the study by Schwartz *et al.*, birth weight, Apgar score, and mode of management were significantly associated with perinatal outcomes in our study, and being managed in intensive care increased the risk of unfavorable perinatal outcomes by more than 37, 31, and 6 times, with respective P-values of $P < 0.001$, $P < 0.001$, and $P = 0.001$. Our results are similar to those of Knight *et al.* in 2020, who found that pregnant women with COVID-19 had an increased risk of giving birth to low birth weight newborns, with about 12% of these newborns having a birth weight below 2500 g, compared to 7% in the general population. Vivanty *et al.* in 2020 found that newborns of mothers with COVID-19 had a higher incidence of low birth weight and prematurity, attributing this to an increase in emergency

cesarean sections due to the deterioration of the maternal condition. However, current studies indicate that COVID-19 infection does not directly affect birth weight or Apgar score; these may instead be consequences of preterm birth induced by the mother's deteriorating condition. Additionally, studies conducted at different times during the pandemic may show varying results due to viral variants and the hypothesis of acquired immunity over time.

Neonatal deaths were found in 13% of cases, with fetal prematurity being the main etiology (52.4%). This result is higher than the 22.8% of deaths reported by Ngalamé *et al.* at the Gyneco-Obstetric and Pediatric Hospital of Douala and those obtained by Li *et al.* and Dahan *et al.* in China, who found no neonatal asphyxia or deaths. The hypothesis regarding the level of technical facilities in countries like China, as well as better management of positive cases, might explain this.

5. Conclusion

At the end of our study, we note that the sociodemographic and clinical factors associated with the occurrence of COVID-19 in pregnant women are maternal age greater than 35 years, marital status, diabetes, obesity, and the third trimester of pregnancy. Maternal and perinatal outcomes are associated with the mode of delivery, the Apgar score at birth, birth weight, and care in intensive care units.

6. Study Limitations and Recommendations

Given the small sample size of our study, we recommend that the scientific community conduct this research with a larger sample size.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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