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Research Article

Adverse Birth Outcomes and Associated Factors among Women with COVID-19 admitted at Eka-Kotebe General Hospital: Retrospective Chart Review

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ABSTRACT

Background: The COVID-19 pandemic has been a global health crisis since its first detection in China in December 2019. The number of people affected by COVID-19 is immense, causing staggering mortality and morbidity figures. Pregnant and recently pregnant women with COVID- 19 attending or admitted to the hospitals are more likely to develop severe illness compared to non-pregnant women of reproductive age. Data from MERS, SARS-CoV-1, and COVID-19 suggest that infection in pregnancy is associated with a high prevalence of preterm birth, stillbirth and other birth outcomes.

Objective: To assess adverse birth outcomes and associated factors among pregnant women with COVID-19 admitted at Eka Kotebe General Hospital, Addis Ababa, Ethiopia, from March 2020 to February 2022.

Methods: A retrospective chart review study was conducted on pregnant women admitted to Eka Kotebe General Hospital from March 2020 to March 2022. A structured data collection tool was used to collect all the necessary data from the patient's medical records. The association between adverse birth and determinant variables was analyzed using Binary Logistic Regression. The adequacy of the final model was assessed using the Hosmer and Lemeshow goodness of fit test and the final model fitted the data well p-value=0.355).

Results: A total of 208 pregnant women with positive COVID-19 who had delivered in the study area were included in this study. Pregnancy Associated Hypertension (CI 95% 2.386, 22.360, p-value=0.000) and Severe COVID-19 (AOR 3.840 (CI 95% 1.517, 9.722, p-value=0.005) were found to be significantly associated with adverse birth outcomes in women with COVID-19.

Conclusion: This study emphasizes the importance of providing adequate attention to pregnant women with COVID-19 in order to detect severity signs earlier. Furthermore, women with COVID-19 and pregnancy-related hypertension should be given special attention in order to avoid unfavourable birth outcomes.

Keywords: Birth outcome, COVID-19, Retrospective chart review, Ethiopia, Logistic regression.

BACKGROUND

The COVID-19 pandemic has been a global health crisis since its first detection in China in December 2019. The number of people affected by COVID-19 is immense, causing astonishing mortality and morbidity figures. Pregnant women make up a significant proportion of the vulnerable groups of people. As it is well-known

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pregnancy results in major immunological and physical changes that would potentially make susceptibility to COVID-19 and other respiratory pathogens higher [1-3].

Even though existing evidence suggests intrauterine vertical transmission is unlikely, the maternal infection and inflammation that occurred in response to COVID- 19 might affect the developing fetus, and even postnatal life. Also, it is concerning to have COVID-19 in pregnancy because of the potential effect it could have on the fetus or the neonate [4,5].

Infection during pregnancy is associated with severe disease and adverse neonatal outcomes, including an increased risk of miscarriage, fetal growth restriction, and preterm birth, according to MERS and SARS data. Infection with SARS-CoV-2 during pregnancy has also been linked to an increased risk of preterm birth, stillbirth, caesarean section, preeclampsia, and NICU admission when compared to non-COVID pregnancies. However, all adverse effects require further investigation to confirm their association with the virus [6-9].

In general, data on COVID-19, particularly among pregnant women and their birth outcomes is scarce in low and middle-income countries, including Ethiopia. To our knowledge, there is no study on Birth outcome and associated factors among COVID-19 positive women in our study area. Thus, this study is conducted to fill this information gap and generate baseline information about COVID-19 and Birth outcomes.

METHODS

The study was conducted at Eka Kotebe General Hospital from April 1–April 30, 2022. As of March 12, 2022 the hospital has admitted 6439 COVID-19 confirmed patients of which 260 were pregnant women. The study design was retrospective chart review. The study was conducted on pregnant women with COVID-19 who gave birth within the given study period. Pregnant women with gestational age <28 weeks and/or whose charts were lost or lacked dependent variables recorded in the chart were excluded.

Sample size determination was made using a single population proportion formula with p of 50% was used (as there was no study on this subject in our country), with a 95% confidence interval. After small population correction was done and chart loss of 15% was assumed the final sample size became 179. However, because the pregnant women admitted were small in number, all charts were reviewed.

Dependent Variable was adverse birth outcome with categories of Present (Unfavorable Outcome) or Absent (Favourable Outcome). Independent Variables were Maternal Characteristics, Pregnancy-associated conditions, Underlying illness, Gestational Week, Socio-demographic factors, Mode of Delivery, COVID-19 Related factors (Symptoms and Severity levels).

Operational definitions

Adverse birth outcome

The occurrence of Low Birth Weight, preterm delivery, low Apgar score at first and fifth minutes after birth, or severe neonatal conditions including fetal death [10].

COVID-19 severity classification

Mild: Patients with uncomplicated upper respiratory tract viral infection may have symptoms such as fever, fatigue, and cough with or without sputum production, anorexia, malaise, muscle pain, sore throat, nasal congestion, headache, diarrhea, nausea and vomiting, loss of smell or taste [11].

Moderate: Moderate illness is defined as evidence of lower respiratory disease during clinical assessment or imaging, with SpO2 ≥94% on room air [11].

Severe: Patients with COVID-19 are considered to have severe illness if they have SpO2 <94% on room air, PaO2/FiO2 <300 mm Hg, a respiratory rate >30 breaths/min, or lung infiltrates >50% [11].

Critical: Respiratory failure, septic shock, and/or multiple organ dysfunctions (MOD) or failure (MOF) and in need of invasive or special management [11].

Data collection tools techniques, data management and analysis plan

A data abstraction tool that consists of all the variables was developed and used to collect data. The extracted data were coded, entered into Epi-Info version 7.2.1.0, cleaned, stored, and exported to SPSS version 20.0 software for analysis. Categorical covariates were summarized using frequencies and percentages and numerical variables were summarized with a mean value. A Chi-square test/Fischer's exact test was run to compare the underlying characteristics of the patients based on disease severity. A statistically significant difference was detected for variables with a P-value of ≤0.05. The presence of multi-collinearity was checked for the independent variables fit on the final model and the VIF result ranges from 1.001 to 1.006 showing that there is no multi-collinearity issue in the final model. The association between adverse birth outcome and determinant variables were analyzed using Binary Logistic Regression. Univariate analysis was done a 25% level of significance to screen out independent variables used in the multivariable Binary Logistic regression model. The adequacy of the final model was assessed using the Hosmer and Leme show goodness of fit test and the final model fitted the data well p-value=0.355). For the Binary Logistic regression, a 95% confidence interval for AOR was calculated and variables with p-value ≤ 0.05 were considered as statistically associated with adverse birth outcome.

RESULTS

Maternal socio-demographic and clinical characteristics

A total of 208 pregnant women with positive COVID-19 who had delivered in the study area were included in this study. Their age ranged from 18 to 38 years with a mean age of 29 years. Only 3 patients were aged less than 20. Seventy-three percent were multigravida of the women were multigravida accounting for 73.1% (152) of the patients. About 6.8% (14) of women had other concomitant medical illnesses including DM, RVI, Asthma, and other illnesses (Table 1).

Over 3/4 of the patients (165) had term deliveries, while 1/5th (39) had preterm deliveries. More than half of the patients had at least one pregnancy-related condition. Previous C/S scar, which was present in 14.9% of the patients, was the most common pregnancy-related condition identified in this study.

The clinical presentation of the patients was with signs and symptoms in 76.4% of the study population. The most common symptoms were Cough, Shortness of breath, Fever, and Fatigue,

Table 1. Maternal Socio-demographic and clinical characteristics.

Variable		Percentage	Frequency (n=208)
Age	**Min:18**	**Max:38**	**Mean: 28.89**
	<= 34	91.3%	190
	> 34	8.7%	18
Parity	Primigravida	26.9%	56
	Multigravida	73.1%	152
Comorbid illness	Yes	6.7 %	14
	No	93.3%	194
Duration of pregnancy	Early Preterm (28 - 32weeks)	1.9%	4
	Mid to late preterm (33 - 36 weeks)	16.8%	35
	Term (37 - 41 weeks)	79.3%	165
	Post Term (> 42 weeks)	1.9%	4
Pregnancy related conditions	Yes	55.3%	115
	No	44.7%	93
Previous C/S	Yes	48.6%	101
	No	51.4%	107
Bad obstetric history	Yes	2.4%	5
	No	97.6%	203
PIH	Yes	9.1%	19
	No	90.9%	189

Table 2. COVID-19 related clinical characteristics.

		Percentage	Frequency (n=208)
Presenting symptoms	Asymptomatic	23.6%	49
	Cough	65.9%	137
	Fever	35.6%	74
	Anosmia	4.8%	10
	SOB	36.1%	75
	Fatigue	22.1%	46
	Myalgia	12.5%	26
	Arthralgia	10.6%	22
	Other Symptoms	2.4%	5
COVID-19 severity	Asymptomatic	20.2%	42
	Mild	50.5%	105
	Moderate	11.1%	23
	Severe	11.5%	24
	Critical	6.7%	14

which were present in 65.9% (137), 36.1% (75), 35.6% (74), and 22.1% (46) of patients respectively. Myalgia, arthralgia, and anosmia were the other less common symptoms.

COVID-19 severity

Regarding the COVID-19 severity, the majority of the patients have either asymptomatic or mild illnesses (Table 2). The most common COVID-19 severity was mild illness in the study population followed by an asymptomatic presentation. The proportion of patients with severe or critical COVID-19 was 16.7% (35) (Figure 1).

Birth outcome

Vaginal delivery was the most common mode of delivery, accounting for 65.7% of all deliveries (136). Cesarean Section accounts for 33.3% (69) of the deliveries. In terms of pregnancy outcome, 4.8% (10) of cases had stillbirths, with the remaining live births (Table 3).

COVID-19 severity and adverse birth outcome

As depicted above the total number of patients with non-severe COVID-19 was 172 and the number of patients with a severe form was 36. Among these 47 patients had at least one of the adverse birth outcomes which included LBW, Preterm delivery, Abnormal 1st & 5th minute Apgar score, and stillbirth. Among patients with a severe form of COVID-1, 9 the percentage of adverse birth outcomes was 50% (Table 4). In contrast, there were only 18.8% of patients with non-severe COVID-19 illness developed adverse birth outcomes.

On the other hand, the percentage of LBW was 34.2% and 11.8% in patients in the severe group and non-severe group respectively. In addition, the proportions of stillbirth were 21.1 % and 1.2% respectively.

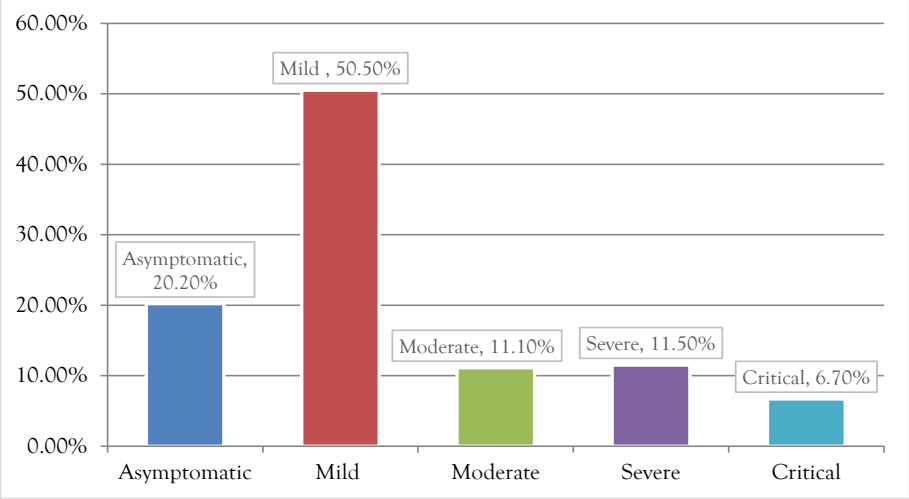

Figure1. Categorization of pregnant women based on COVID- 19 Severity.

Table 3. Birth Outcome and Mode of Delivery.

		Variables	Frequency	Percent
Mode of delivery		Vaginal Delivery	138	66.3%
		Cesarean Section	70	33.7%
		Early Preterm (28 - 32 weeks)	4	1.9%
		Mid to late preterm (33 - 36 weeks)	35	16.8%
		Term (37 - 41 weeks)	165	79.3%
		Post Term (> 42 weeks)	4	1.9%
Stillbirth or Not		Alive	198	95.2%
		Dead	10	4.8%
Birth weight		Min: 1kg	Max: 4.7kg	Mean: 3.07kg
		NBW	160	76.9%
		LBW	33	15.9%
		Big baby	15	7.2%
APGAR score	1st min	Normal	175	84.1%
		Abnormal	33	15.9%
	5th min	Normal	191	91.8%
		Abnormal	17	8.2%
Adverse Birth Outcome		Yes	51	24.5%
		No	157	75.5%

Table 4. Adverse Birth outcomes according to the COVID-19 level of severity.

Factors		COVID-19 Severity			
		Non-Severe (n=172)	Severe (n=36)	Chi square	p-value
Adverse Birth Outcome	No	138 (81.2%)	19 (50.0%)	16.31	<0.000
	Yes	32 (18.8%)	19 (50.0%)		
Birth weight	NBW	137 (80.6%)	23 (60.5%)	10.131	0.003
	LBW	20 (11.8%)	13 (34.2%)		
	Macrosomia	13 (7.6%)	2 (5.3%)		
1st min APGAR score	Normal	152 (89.4%)	23 (60.5%)	19.413	<0.000
	Abnormal	18 (10.6)	15 (39.5%)		
5th min APGAR score	Normal	165 (97.1%)	26 (68.4. %)	33.938	<0.000
	Abnormal	5 (2.9%)	12 (31.6%)		
Still birth or Not	Alive	168 (98.8%)	30 (78.9%)	26.811	<0.000
	Dead	2 (1.2%)	8 (21.1%)		
Gestational Age	Term	143 (84.1%)	22(57.9%)	14.323	<0.000
	Preterm	23 (13.5%)	16 (43.1%)		
	Post term	4 (2.4%)	0 (0%)		

Table 5. Factors associated with Adverse Birth outcome.

Factors		Adverse Birth Outcome		COR	p-value	AOR	p-value
		No	Yes				
Age	< = 34	146	44	1			
	>34	11	7	2.112 (0.772, 5.773)	0.145	1.807 (0.560. 5.834)	0.322
Parity	Primigravida	39	17	1			
	Multigravida	118	34	0.661 (.333, 1.312)	0.237	0.538 (0.240, 1.206)	0.132
Pregnancy Associated Hypertension	No	150	39	1		1	
	Yes	7	12	6.593 (2.434,17.860)	0.000	7.304 (2.386, 22.360)	<0.000*
Comorbidity	No	150	44	1		1	
	Yes	7	7	3.409 (1.135, 10.244)	0.029	2.418 (0.711, 8.227)	0.158
Asymptomatic	No	116	43	1		1	
	Yes	41	8	0.526 (0.229, 1.213)	0.132	1.460 (0.332, 6.422)	0.616
Cough	No	57	14	1		1	
	Yes	100	37	1.506 (0.751, 3.021)	0.248	0.743 (0.235, 2.355)	0.614
Fever	No	109	25	1		1	
	Yes	48	26	2.362 (1.238, 4.504)	0.009	1.419 (0.622, 3.239)	0.405
Fatigue	No	130	32	1		1	
	Yes	27	19	2.859 (1.416, 5.774)	0.003	2.091 (0.897, 4.876)	0.088
Shortness of Breath	No	109	24	1		1	
	Yes	48	27	2.555 (1.339, 4.875)	0.004	1.655 (0.701, 3.907)	0.251
Severity	Non-Severe	138	32	1		1	
	Severe	19	19	4.312 (2.051, 9.067)	0.000	**3.840 (1.517, 9.722)**	**0.005***

In this study, the percentage of preterm deliveries was 43.1% in the severe group and 13.5% in the non-severe group. In the former group of patients, there were no post-term deliveries.

Factors associated with adverse birth outcome

In this study factors which could possibly affect the Birth outcome were assessed through Binary logistic regression analysis methods. Univariate analysis at 25% level of significance was conducted and Maternal age, Parity, Comorbidity, Being Asymptomatic, Cough, Shortness of Breath, Fatigue, Fever, COVID-19 Severity, Pregnancy Associated Hypertension condition were found to be associated with Adverse Birth outcome.

On the multivariable logistic regression, after adjusting for other covariates, Pregnancy associated Hypertension, and COVID-19 Severity were found to be significantly associated with Adverse Birth Outcome at 5% level of significance (Table 5).

Pregnant women with severe to critical COVID-19 disease were about 7 times more likely (AOR 7.304 (CI 95% 2.386, 22.360) to have adverse birth outcome compared to those with non-severe disease.

Pregnant women with COVID-19 disease who also had pregnancy induced hypertension were around 4 times more likely (AOR 3.840 (CI 95% 1.517, 9.722) to have adverse birth outcome compared to those who didn't have pregnancy induced hypertension.

Discussion

One of the associated factors identified in this study was hypertensive disorders in pregnancy. According to a meta-analysis assessment of seventeen researches, the overall pooled prevalence of hypertensive disorders in pregnancy in Ethiopia was 6.07% (12). The prevalence of hypertension related to pregnancy is increased in this study, with a rate of 9.1%. Two large scale studies: INTERCOVID, a large, longitudinal, prospective, multinational observational study and a study done in eastern Asia among COVID-19 positive pregnant women: reported an 8.1% and 8.2% rate of preeclampsia respectively. The increased prevalence of preeclampsia that was seen among mothers with COVID-19 infection might be ascribed to misdiagnosis, as COVID-19 and preeclampsia have coincidental medical features [13-15].

In this study, majority (84.2%) of the women with pregnancy associated hypertension had non-severe COVID-19. Pregnancy associated Hypertension in this study also has an increased Odds Ratio 95% confidence interval 1.799, 19.150), compared to other studies done in preeclampsia without COVID-19, and COVID-19 with preeclampsia (risk ratio, 2.16; 95% confidence interval, 1.63-2.86; risk ratio, 2.53; 95% confidence interval, 1.44-4.45; and risk ratio, 2.84; 95% confidence interval, 1.67-4.82, respectively). Preterm birth, severe perinatal morbidity and mortality are all independently and cumulatively related to both diseases. Women

with pregnancy associated hypertension should be thought of as a particularly sensitive population in terms of the hazards brought on by COVID-19 [14].

The prevalence of preterm delivery in this study's patients was 20.8%. This was similar to European and Chines studies which reported similar rates which were 19% and 17% respectively. In contrast American studies showed relatively lower prevalence of preterm deliveries which was 12%. But multiple systematic reviews which included large groups of patients have consistently demonstrated the higher prevalence of preterm deliveries in COVID-19 patients. The most common explanation given for this is the increased rate of cesarean deliveries in this population group for the reasons mentioned above [16,17].

In this study the proportion of preterm deliveries was relatively higher in the severe to critical illness groups as compared to the other group of patients. This could also be explained by the above mentioned reasons. These groups of patients are at higher risk for fetal distress, maternal deterioration and advanced clinical care which makes them likely to undergo early termination of pregnancy through cesarean section.

In this study the proportion of LBW babies born was 15.9%. This was similar to a study which was done to investigate pregnant and neonatal outcome. This is higher than a pre-COVID -19 prevalence of 10% (18). The prevalence of LBW in Ethiopian setting ranged from 6 to 21 %. The lowest prevalence of LBW was in Addis Ababa which is around 8.66% (19). Considering this factor, the prevalence of LBW is high in our study population. The possible explanations for this occurrence include the higher prevalence of preterm deliveries in this population and possible direct effect of the COVID-19 virus on fetal growth. The later postulation came from the association of SARS virus infection with LBW in infected patients [18-20].

The other adverse birth outcome which was assessed in this study was the prevalence of stillbirth in this population group. The result of this study indicated that there is 4.8% prevalence of stillbirth in this population group. In contrast to this study's findings PregCOVID-19 Living Systematic Review found no association between COVID-19 and stillbirth. Globally the prevalence of still birth is estimated to be less than 2%. In Ethiopia there is variability across region but the pooled national prevalence is 7.1%. Interpreting the result by these facts, it can be concluded that there is association between Severe COVID-19 and Adverse birth outcome in this study. However, this result should be interpreted with caution as some studies done in USA indicated that there is significant difference of prevalence of still birth between delta variant period and pre-delta variant period [21-23].

However, when the prevalence of stillbirth is compared in severe groups with non-severe groups we can see that the former group has higher prevalence of 21.1% vs 1.2 % in the latter group. A data from the UK Obstetric Surveillance System national cohort study indicated also that there is increased prevalence of stillbirths in severe COVID-19 as compared to mild to moderate COVID-19. This could be due to the above-mentioned other complications associated with COVID-19 infection and also the possible placental infection by the virus itself [24,25].

CONCLUSION

The findings of this study indicate that COVID-19 in pregnancy has association with adverse birth outcomes like preterm deliveries, low birth weight, stillbirth and abnormal APGAR scores more pronounced in the severe to critical illness groups and in women with Pregnancy associated Hypertension.

RECOMMENDATION

This study highlights the need for adequate attention for pregnant women with COVID-19 in order to pick severity signs earlier. Additionally, particular attention should be given to women who have COVID-19 and pregnancy-related hypertension in order to prevent unfavorable birth outcomes. Based on the results further studies to assess the relatively very high prevalence of still birth in patients with severe to critical COVID-19 group need to be done and also implement policies to mitigate dreaded birth outcomes.

Limitation and Strength of the study

Given the small number of deliveries, it will be challenging to generalize the study's findings. Additionally, because the study was retrospective, it was difficult to evaluate neonates' conditions after delivery, and the results only have an impact on outcomes for the early postpartum period.

Ethiopia and other low- and middle-income nations lack research on the topic; therefore this study can be utilized to emphasize early detection and intervention of COVID-19, which may lessen potential obstetrical consequences.

Acronyms and Abbreviations

BOH: Bad Obstetrics History; C/S: Cesarean Section; COVID -19: Coronavirus disease 2019; LBW: Low Birth Weight; LMIC: Low- and Middle-Income Countries; MERS: Middle East Respiratory Syndrome; NBW: Normal Birth Weight; SARS: Severe Acute Respiratory Syndrome; SARS-CoV-1: Severe Acute Respiratory Syndrome Coronavirus 1; WHO: World Health Organization

DECLARATIONS

Ethics approval and consent to participate

The study was conducted after obtaining ethical clearance from GAMBY medical and business college IRB and Eka Kotebe general hospital. Medical record numbers were used for the data collection and personal identifiers of the patients were not used in the research report. Access to the collected information was limited to the principal investigator and confidentiality was maintained throughout the project.

CONSENT FOR PUBLICATION

Not applicable

AVAILABILITY OF DATA AND MATERIALS

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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AUTHOR'S CONTRIBUTIONS

LSM contributed on the conceptualization, conducted the literature review, formulated the study design, performed the statistical

analysis and drafted the initial manuscript. ECB contributed to the literature review, conceptualization and analysis. MTN contributed on literature review, research design and drafted data extraction sheet, EWA and TGH contributed to the conception, revised data extraction sheet, collected patient data, reviewed and interpreted the data, and revised the manuscript.

All authors read and approved the final submitted paper

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