

Clinical Profile, Maternal and Perinatal Outcome in Sars-Cov2 Infection in Pregnancy

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Abstract

Introduction: Coronavirus disease (COVID-19) is an infectious disease caused by the SARS-CoV-2 virus. Maternal physiological adaptations in pregnancy, and the physiological state of relative immune suppression, place pregnant women at increased risk of infection [1,2]. The present study is important due to the tremendous impact Covid 19 has on people at large, especially expectant mothers. In our study, we collected information on pregnant women with confirmed SARS-CoV-2 infection.

Aim and Objective:

- 1) To estimate clinical features, maternal and perinatal outcome of Covid 19, during first, second and third wave of covid pandemic
- 2) To compare the Obstetric outcome in first and second wave with third wave.
- 3) To estimate vertical transmission to new born child in this institution as evidenced by test positivity.

Method: Retrospective observational study was designed to examine the clinical characteristics and outcome of covid positive pregnancies admitted in our institution.

Result: In our study of 266 pregnant women with covid, it was noticed that the mean age of the patients was found to be 27.55 years with a standard deviation of ± 4.99 years. 55.64% of cases belonged to category B1, 33.08% in B2 and 11.28% in C. 2nd wave had more patients in category C. Gestational diabetes complicated 28.95% and hypertension in 17.29% of study population. Inflammatory markers were more elevated in 2nd and 3rd wave. There was a total maternal death of 11 patients. Out of this, 10 was (91%) due to covid pneumonia and ARDS. Breast feeding was given for 88.7% of the babies and for 88% of the babies rooming in was practiced. Only 2.6% of the babies turned positive within a week.

Conclusion: Our study shows that expectant mothers were more severely affected in the second wave. Maternal mortality was associated with increased maternal age (> 35 years), raised CRP levels (> 75 mg/L) and higher D dimer levels (> 3000 ng/ml) and is found to be statistically significant. There is no evidence to show any vertical transmission of the disease as only 2.1% of the neonates (7nos) were affected within a week.

Keywords: Covid 19 and Pregnancy, Maternal mortality, Covid symptoms, Coronavirus

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Introduction

Since the beginning of the pandemic, literature has been pouring in. Initially we didn't have much data regarding how pregnancy is going to be affected, whether pregnancy increases the risk of getting infection. There was also scientific enquiry about any particular obstetric complications are at increased risk of getting infected or increased disease severity. There was also concern about transmission to the fetus and newborn.

According to RCOG guidelines [3] which was published initially in the course of the pandemic and then revised multiple times, pregnancy is not a risk factor for getting the infection. Almost 2/3rd of women with the disease will be asymptomatic. Pregnant women are more likely to get admitted to hospitals and ICU. Risk factors for worsening of the disease include ethnic minority background, BMI more than 25, co morbidities like diabetes and hypertension, elderly women over 35 years age. Delta variant was more severe than alpha variant. Omicron variant is less severe but more infectious, but still likely to be have adverse outcomes in women and new born especially for unvaccinated mothers. Higher rates of perinatal mental disorders including anxiety has been observed. There is more chance for preterm labor, small for gestational age, and stillbirth. Congenital anomalies are not found to be increased and vertical transmission is uncommon.

In an early retrospective cohort study published in June 2020 by R San Juan *et al*, they categorized women based on symptoms, Chest X ray finding, liver enzymes, CRP and thus mode of delivery were decided and C section rates were as low as 10% [4]

In a study from Kannur, Kerala, pregnancy did not seem to worsen the course and progress of the disease and fetal outcome is not worsened [5]. Another study from the same institution showed increased C section rates. New born transmission risk is increased in vaginal delivery, breast feeding and rooming in [6]. In this study the rate of C section was 52.28%, and 1.43% turned positive.

In a scoping review by Kotlar *et al* [7] pregnant women are at increased risk of getting severe symptoms and getting hospitalized and admitted in ICUs. Intrauterine, vertical and breast milk transmission were unlikely.

In another study by Cassarco *et al* [8], although vertical transmission is less, new born babies were adversely affected due to prematurity. Women underwent caesarean section due to severe disease and that resulted in iatrogenic prematurity.

In a study from India by Mahajan *et al* [9], more admission and death rates in pregnancy was observed in second wave. Preterm birth and still birth were not significantly raised.

In a retrospective study from Kerala [10], anxiety and depression are more in pregnant women with Covid 19. Another study from the same institution involving 856 pregnant women observed increased prevalence of diabetes in pregnancy in severe disease and was associated with adverse outcomes in both mothers and new born [11]

Materials and Methods

Type of Study: Retrospective observational study

Period of Study: 1-4-2022 to 31-10-2022

Study Setting: Govt. Medical College, Kottayam

Sample size: 266 patients

Study Population: Mothers admitted with SARS CoV 2 infection during pregnancy

Inclusion Criteria: All women with SARS CoV 2 infection in pregnancy and within 42 days postpartum admitted to Department of O&G, GMCH, Kottayam

Exclusion Criteria: Women not consenting to undergo telephonic interview were excluded

Clinical data was entered in excel sheet and was analyzed using SPSS16 software. Qualitative data is expressed in frequency and percentages. The association of independent variables to maternal mortality was analyzed using Chi square test and odds ratio also was calculated

Operative definitions

Results

According to Government of Kerala guidelines [12], a confirmed case is defined as a person with laboratory diagnosis of SARS CoV 2 infection irrespective of clinical symptoms. The cases have been categorized to A, B and C with mild, moderate or severe. As pregnancy is a risk factor, pregnant women with infection falls into category B even if they have no symptoms. For better risk identification and management of cases, Kerala Federation of Obstetrics and Gynecology has further divided category B into B1 and B2 depending on whether they have symptoms or risk factors [13]. Women with no symptoms or risk factors belong to category B1, and those with mild symptoms and or risk factors belonged to B2. Those with severe disease are categorized into C.

The occurrence of first second and third waves of Covid pandemic is derived by referring Government of Kerala dashboard on Covid 19 [14]. Accordingly, First wave falls between 1st April 2020 to 18th March 2021. Second wave falls between 19th March 2021 to 27th December 2021. The third wave started from 28th December 2021.

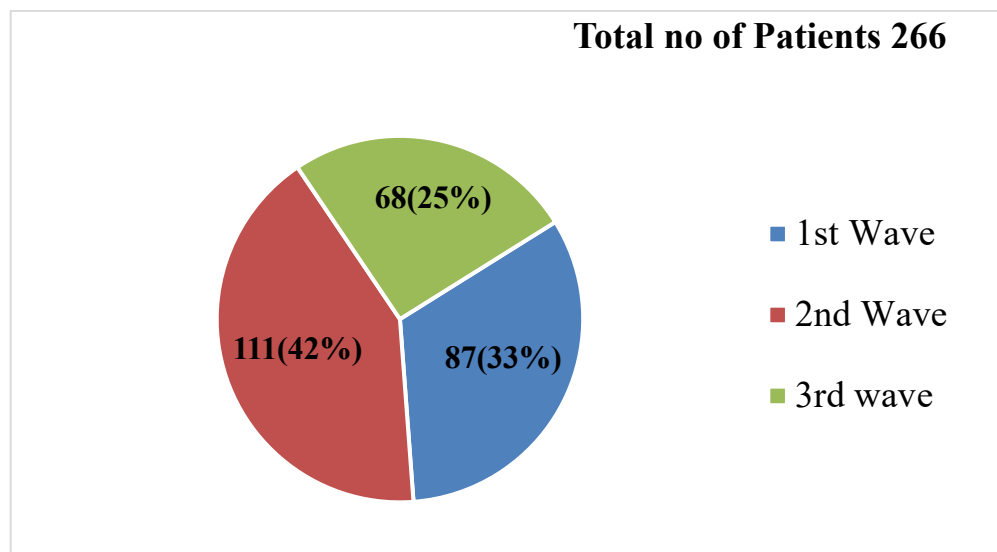


Figure 1

Table 1: Clinical profile of the patients admitted during each wave with their percentage

Variables of covid +ve patients	1ST WAVE		2ND WAVE		3RD WAVE		TOTAL	
Obstetric score								
Primi	12	13.79%	46	41.44%	29	42.65%	87	32.71%
Multi	75	86.21%	65	58.56%	39	57.35%	179	67.29%
Gestational Age								
< 28 weeks	10	11.49%	15	13.51%	2	2.94%	27	10.15%
28 to 34 weeks	11	12.64%	16	14.41%	18	26.47%	45	16.92%
≥ 34 weeks	66	75.86%	80	72.07%	48	70.59%	194	72.93%
Vaccination status								
At least one	0	0.00%	24	23.76%	24	35.29%	48	18.82%
Diabetes	25	28.74%	35	31.53%	17	25.00%	77	28.95%
Anemia	13	14.94%	7	6.31%	3	4.41%	20	7.52%
Hypothyroidism	15	17.24%	17	15.32%	8	11.76%	40	15.04%
Asthma	4	4.60%	2	1.80%	1	1.47%	7	2.63%
Hypertension	15	17.24%	17	15.32%	14	20.59%	46	17.29%

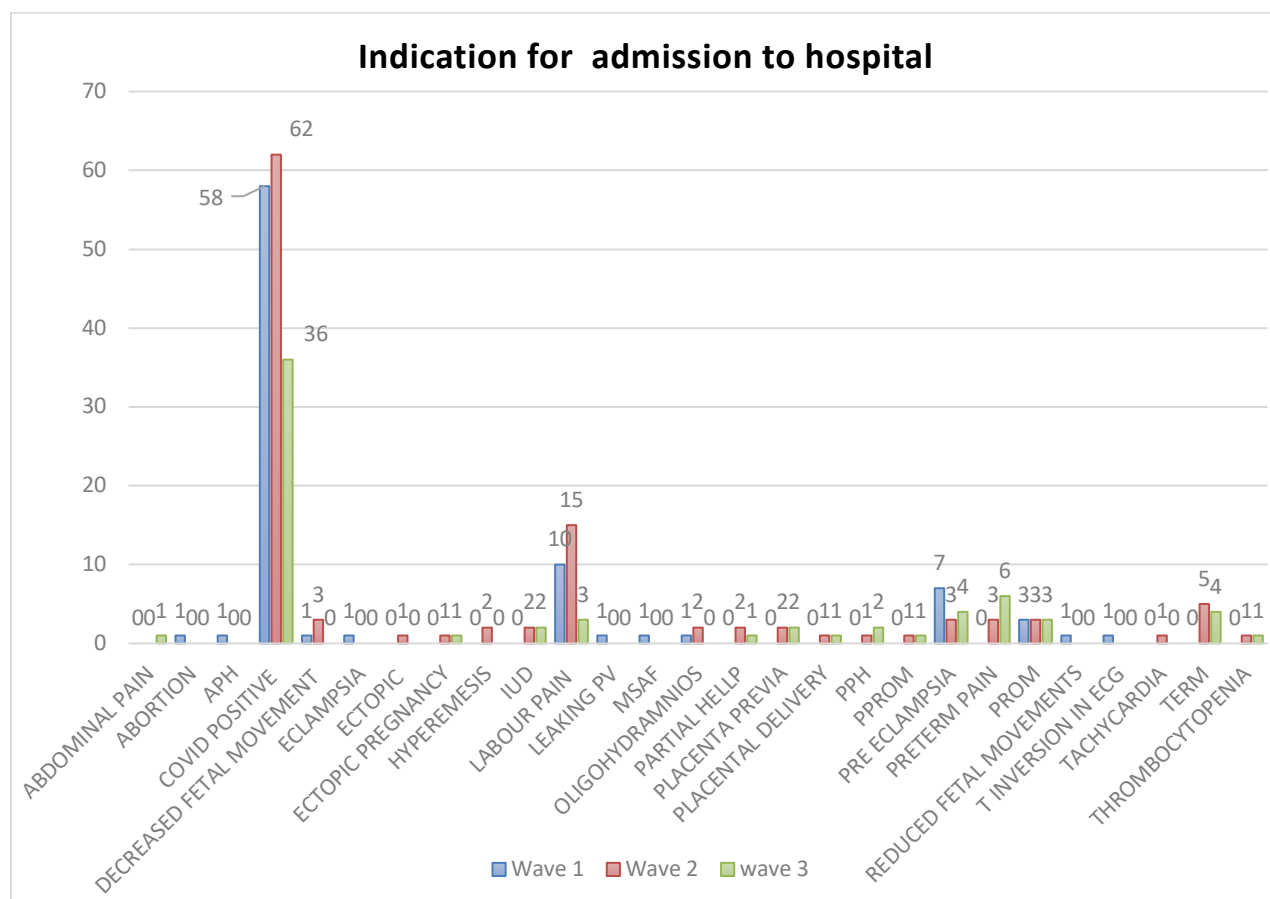


Figure 2: Main reasons for admission during each wave

Table 2: Patient distribution in each wave

Patient category	1ST WAVE		2ND WAVE		3RD WAVE		TOTAL	
B1	50	57.47%	53	47.75%	45	66.18%	148	55.64%
B2	34	39.08%	37	33.33%	17	25.00%	88	33.08%
C	3	3.45%	21	18.92%	6	8.82%	30	11.28%
	87	100%	111	100%	68	100%	266	100%

Table 3: Blood investigation results during the 3 waves.

Blood investigations	1ST WAVE		2ND WAVE		3RD WAVE		TOTAL	
CRP Level								
<3mg/L	71	81.6%	21	18.9%	11	16.2%	103	38.7%
3mg to 10mg/L	4	4.6%	37	33.3%	27	39.7%	68	25.6%
10.1 mg to 100mg/L	11	12.6%	52	46.8%	30	44.1%	93	35.0%
>100mg/L	1	1.1%	1	0.9%	0	0.0%	2	0.8%
D Dimer								
<500ng/ml	79	90.8%	18	16.2%	8	11.8%	105	39.5%
500 to 1000 ng/ml	2	2.3%	11	9.9%	7	10.3%	20	7.5%
1000 to 2000ng/ml	2	2.3%	41	36.9%	28	41.2%	71	26.7%
2000 to 4000ng/ml	2	2.3%	23	20.7%	15	22.1%	40	15.0%
> 4000ng/ml	2	2.3%	18	16.2%	10	14.7%	30	11.3%
FERRITIN								
<11µg/L	0	0.0%	3	2.7%	2	2.9%	5	1.9%
11µg to 307µg/L	86	98.9%	101	91.0%	63	92.6%	250	94.0%
>307µg/L	1	1.1%	7	6.3%	3	4.4%	11	4.1%

Table 4: Treatment data

Treatments	1ST WAVE		2ND WAVE		3RD WAVE		TOTAL	
Medicine								
Remdesivir	3	3%	28	25%	10	15%	41	15%
Tocilizumab	0	0%	22	20%	4	6%	26	10%
Dexamethasone/Methyl Prednisolone	12	14%	38	34%	14	21%	64	24%
Tamiflu	15	17%	23	21%	9	13%	47	18%
Non-Invasive Ventilation	3	3%	20	18%	4	6%	27	10%
Invasive Ventilation	2	2%	10	9%	1	1%	13	5%

Table 5: Labor and delivery data

Parameter	1st wave	% of total delivery in the wave	2nd wave	% of total delivery in the wave	3rd wave	% of total delivery in the wave	Total	% of total covid delivery
Term	68	82.90%	49	65.30%	35	74.40%	152	74.50%
Preterm	14	17.10%	26	34.70%	12	25.60%	52	25.50%
Vaginal	37	45.10%	35	46.70%	24	51.10%	96	47.10%
C section	45	54.90%	40	53.30%	23	48.90%	108	52.90%
Primary C section	30	36.60%	33	44%	15	31.90%	78	38.20%
Clear liquor	73	89%	71	94.60%	43	91.50%	187	91.70%
Meconium stained liquor	9	11%	4	5.40%	4	8.50%	17	8.30%

Table 6: Clinical profile of maternal deaths

Parameter	Value	percentage
Age group		
Less than 30	2	18.18
30-35	3	27.27
More than 35	6	54.55
Mean age , SD	33.55 ±5.25	
Mode of delivery		
VAGINAL	3	27.27
CS	6	54.54
Before delivery	2	18.18
Diabetes	5	45.5
Hypertension	4	36.4
Hypothyroidism	3	27.27
CRP		
Less than 10	0	
11-75	4	36.4
76-100	6	54.54
More than 100	1	9.1
D dimer		
Less than 3000	3	27.27
More than 3000	8	72.73
Mean CRP	71.8	
Mean D dimer	7295	
Cause of death		
ARDS	10	90.9
Pulmonary embolism	1	9.1

Table 7: Factors associated with maternal mortality rate

Factor	N (%) n=11	p	Odds Ratio (95% CI)
Age above 35	6(54.5%)	<0.001	16.8(4.65-60.71)
Preterm	8(72.7%)	0.02	4.41(1.14-17.05)
Caesarean Section	8(72.7%)	0.31	1.02(0.98-1.08)
D-dimer>3000	7(63.6%)	<0.001	7.2(2.02-25.46)
C Reactive Protein>75	7(63.6%)	<0.001	18.53(5.03-68.27)
Diabetes	5(45.5%)	0.27	1.96(0.58-6.62)
Hypertension	4(36.4%)	0.09	2.89(0.81-10.34)
Hypothyroidism	3(27.3%)	0.25	2.21(0.56-8.71)

There was significant association maternal age>35 ,preterm, d-dimer>3000 and CRP>75 with maternal mortality as p value was <0.05 as shown in the table.

Table 8: Neonatal outcome

Baby outcomes	1ST WAVE		2ND WAVE		3RD WAVE		TOTAL	
Baby Weight								
<2.5kg	29	33.00%	31	27.70%	16	24.20%	76	28.60%
2.5 to 4kg	58	65.90%	80	71.40%	50	75.80%	188	70.70%
>4kg	1	1.10%	1	0.90%	0	0.00%	2	0.80%
Baby apgar								
<7	4	4.50%	2	1.80%	2	3.00%	8	3.00%
7 to 10	84	95.50%	110	98.20%	64	97.00%	258	97.00%
Whether turned +ve								
Yes	4	4.50%	0	0.00%	3	4.50%	7	2.60%
Oxygen								
Yes	3	3.40%	1	0.90%	0	0.00%	4	1.50%
Surfactant								
Yes	2	2.30%	1	0.90%	0	0.00%	3	1.10%
Breast feeding								
Yes	79	89.80%	99	88.40%	58	87.90%	236	88.70%
Rooming in								
Yes	83	94.30%	96	85.70%	55	83.30%	234	88.00%

Discussion

In our study of 266 covid positive expectant mothers, the mean age of the study population was found to be 27.29 years. It was noted that 33% (87 patients) got admitted in the 1st wave, 42% (111 patients) in the second wave and 25% (68 patients) in the third wave. More number of patients were admitted during the 2nd wave when compared to first or third wave. In all 3 waves multigravidas were more affected than primi gravidas. Out of this, highest number of primi were affected in the third wave (42.65%) as compared to first and second.

With regards to gestational age, it was noted that more than 70% of the pregnant women were affected after 34 weeks in all three waves. No one was vaccinated during the first wave. However, this was 23.76% during the 2nd wave and 35.29% during the 3rd wave.

Reason for admission varied across all waves. It was noted that a good number of pregnant women got admitted as they turned covid positive with symptoms. It was 66.67 % of admissions in first wave, 55.86% in

second wave and 52.94% in third wave. There were some patients who came with labor pain and later turned out to be covid positive. Other reasons were, preterm labor, PROM (pre-labor rupture of membranes), preeclampsia and also as they got near term for safe confinement.

57.47% of women belonged to Category B1 in 1st wave as compared to 47.75% in 2nd and 66.18 % in 3rd wave. 39.08% of women belonged to Category B2 in 1st wave, 33.33% in 2nd and 25% in 3rd wave. 3.4% of women fell on Category C with severe disease in 1st wave as compared to 18.92% in 2nd and 8.82% in 3rd wave. This shows that second wave was more severe with more sick patients when compared to other waves.

Gestational diabetes was higher in the 2nd wave (31.53%) compared to 1st and 3rd and it is high when compared to general prevalence of the same 4-18% [15]. Hypertension complicated about 15.04% of covid positive pregnant women as opposed to general prevalence of 8-10% [16]. More number of anemic patients were during the

1st wave 14.94%. Women with hypothyroidism and bronchial asthma were 15.04% and 2.63% respectively in the study.

In blood investigations, inflammatory markers were studied. C-reactive protein (CRP) elevation was found only in 13.7% of women in first wave. During second wave 47.7% and during third wave, 44.1 % women had raised CRP. This shows that second and third wave had more inflammatory changes in pregnant women

D dimer was normal in 90.8% of women in first wave and elevated only in 9.2%. During second wave, it was elevated in 83.8% and in third wave, it was 88.2%. A very high value of more than 4000 was seen in 2.3% in first wave, 16.2% in second wave, and 14.7% in third wave.

There was a total of 11 maternal deaths, 1 in 1st wave, and 10 in second wave. No maternal life was lost in 3rd wave. Cause of death was acute respiratory distress syndrome (ARDS) in 10 cases (91%) and pulmonary thromboembolism in 1 case (9%). The mean age of women who died was 33.55 years with a standard deviation of ± 5.25 . 54.55% of death were over 35 years. Diabetes complicated in about 45.5% of these women. Hypertension and hypothyroidism complicated about 36.4% and 27.27% of them. D dimer value was elevated more than 3000 ng/ml in 72.7% of these women and CRP value of more than 75mg/l was seen in 63.64%. There was significant association maternal age > 35, d-dimer > 3000ng/ml and CRP > 75mg/l with maternal mortality with p value < 0.05. Statistical association could not be established in complications like diabetes and hypertension even though the values are seemingly high.

Remdesivir was given in 3% in 1st wave, 25% in 2nd wave and 15% in 3rd wave. Women were treated with tocilizumab in 0%, 20% and 6% in 1st, 2nd and 3rd waves respectively. Women were treated with steroids 14%, 34%, & 21% in 1st, 2nd and

3rd waves respectively. Noninvasive ventilation was given in 3%, 18% & 6% in 1st, 2nd and 3rd wave and invasive ventilation in 2%, 9% & 1% in 1st, 2nd and 3rd wave. Remdesivir, tocilizumab and steroids were more used in second wave when compared to other waves and so are noninvasive and invasive ventilation showing that women were more affected during second wave.

Throughout all waves, 52.90 % underwent C section, with a high primary CS rate of 38.20%. This is similar to study by Nambiar *et al* [6]. The reason for the increased rate may be due to a lower threshold for CS in positive cases and C section done in Category C cases for persistent desaturation. More women delivered preterm by either route with a high 25.5% of total covid deliveries which is high when compared to national general prevalence of 12.9% [17]. This may be due to both covid as well as iatrogenic.

Liquor was meconium stained in 8.3%. Baby weight was between 2.5 and 4kg in 70.70% of the cases. Birth weight less than 2.5 kg was found more with first wave (33.0%) followed by second wave (27.70%) and 3rd wave (24.2%). Baby Apgar was between 7 to 10 in 95% of the cases in all three waves. Apgar less than 7 was found in 4.5% in 1st, 1.8% in 2nd and 3.0% in 3rd wave. Oxygen administration was needed only for 4 babies (1.5%). Surfactant was necessary in 3 babies (1.1%). 88.7% of the babies were breast fed and for 88% of the babies rooming in was practiced. Still only 2.6% of the babies turned positive within a week as opposed to 1.4% in a study done at Kerala [6].

Limitations

One of the limitations of this study was that, there were incomplete documentation in some case records. Such cases were excluded from this study. Secondly, a comparison with non-covid data would have been interesting, but was not considered, as it was not part of our objective. However this limitations have

not affected our present work and the outcome can be relied upon as a referral study.

Conclusion

In this observational study, it was seen that pregnant women were more severely affected in the second wave. Maternal mortality was associated with increased maternal age (> 35 years), raised CRP levels (> 75mg/L) and higher D dimer levels (> 3000 ng/ml) and is found to be statistically significant. Even though, Comorbidities like diabetes, hypertension, bronchial asthma, and hypothyroidism were observed in maternal mortality, they were not statistically significant. Also there is no evidence to show any vertical transmission of the disease as only 2.1% of the neonates (7nos) were affected within a week.

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Declarations

Ethical approval : The study was approved by the institutional ethical committee IRB 16/2022

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