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Demographic profile of COVID-19 positive mothers & their outcome in government Rajaji hospital, Madurai, Tamilnadu – A cross sectional Study

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ABSTRACT

Background: COVID-19 is a new pandemic disease. This disease course and its effect on pregnancy is little known due to limited available data. The objective of this study was to describe the demographic profile of COVID-19 positive mothers admitted in Government Rajaji hospital, Madurai in terms of time, place and person and to assess the general and pregnancy outcome of study population.

Methods: This cross-sectional study was done among 381 COVID-19 positive mothers* admitted during March 22 – August 31, 2020 in dedicated COVID-19 hospital, Madurai. Data was collected using Case Investigation Form (CIF) as a part of Rapid Response Team*(RRT) by Community Medicine* Department and analysed using SPSS version 21. Descriptive statistics done; Chi-square test & Fischer exact test was done to find out association between patient profile and outcomes.

Results: Out of 381, 154 (40.4%) belonged to 21–25 years, 192 (50.4%) to rural area, 318 (83.5%) to 3rd trimester,189 (49.6%) Primi gravida. 125 (32.8%) were symptomatic and 153 (80.8%) had at least one co-morbidity. Death as general outcome was 3 (0.8%), all of them were referred cases and had comorbidity like GDM/PIH. 10 (2.62%) had abortion or perinatal death, 14 (3.77%) had preterm delivery, 99 (25.98%) babies were born small for gestational age. Increased maternal age had more death but was not statistically significant; All symptomatic mothers ($p = 0.000$),1st & 2nd trimester ($p = 0.000$) mothers had statistically significant poor pregnancy outcome*.

Conclusion: COVID positive mothers with increased age, symptomatic, 1st & 2nd trimester were significantly associated with poor outcome, requires special attention. Early referral must be emphasized to mitigate maternal death.

1. Introduction

Coronavirus disease (COVID-19) is now dominating the lives of everyone globally and its history is being re-written constantly. On December 31, 2019, The World Health Organization (WHO) country Office was notified of pneumonia cases of unknown etiology from Wuhan City, Hubei province of China.[1] WHO closely monitored the situation for further outbreak. By the end of January 2020, COVID-19 spread to 20 other countries from China and hence WHO declared this disease as Public Health Emergency of International Concern (PHEIC).[2] By the same time, India also contracted its index case of coronavirus, imported from China.[3] On March 11, 2020 more than 1,18,000 cases were detected in 114 countries and 4291 people died due to this disease, after which WHO declared COVID-19 as pandemic.[4]

In order to curtail the spread of COVID-19, many countries announced their lockdown and other containment measures like travel restrictions, quarantine etc. India announced its 14- hour voluntary public curfew on March 22, 2020 followed by complete nationwide lockdown from March 24 - May 31, 2020.[5] But once Unlock started from June 2020 there was a huge surge.[6] Due to multifactorial reasons, each Indian state experienced peak during different times.[7] Tamil Nadu was at its peak during mid-July – August 2, 020.[8] As on Aug 31, 2020, there were 52,379 cases in Tamil Nadu and 14,279 cases in Madurai.[9]

COVID19 affected everyone irrespective of age. However, the impact

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of COVID-19 on pregnant women has drawn much attention regarding maternal morbidity, mortality, and perinatal outcomes. Also, during lockdown period, pregnant mothers would have experienced difficult in access to healthcare due to movement restriction, lack of transport etc.,.[10] Pregnancy, a unique immunological state faces great challenges in establishing and maintaining tolerance to the allogeneic fetus while preserving the ability for protection against microbial challenges. There is ample evidence that systemic maternal viral infections can also affect pregnancy. Previous studies have shown that SARS, MERS infection during pregnancy can lead to high rates of spontaneous abortion, premature birth, and intrauterine growth restriction etc.[11] There is limited data and research done regarding maternal and perinatal outcome in COVID19 affected women globally, done in developed & developing countries.[12,13] In order to gain more knowledge of COVID19 outcomes in pregnancy and for better understanding of this newly emerging disease this descriptive cross-sectional study was done. The objective of this study was to describe the demographic profile of COVID-19 positive mothers admitted in Government Rajaji hospital, Madurai in terms of time, place and person and to assess the general and pregnancy outcome of the study population.

2. Materials & Methods

This was a descriptive cross-sectional study conducted at Government Rajaji Hospital (GRH) & Medical College, Madurai, which provides tertiary care to more than 20 million people in South Tamil Nadu. During COVID-19 pandemic, since 1st week of April 2020, all the COVID-19 patients were being treated at 4-storeyed, 400-bedded dedicated COVID-19 wing while pregnant and postnatal mothers were given special care with a separate floor.[14]

All the COVID-19 positive mothers admitted and treated at GRH, Madurai from March 22 – August 31, 2020 were taken as study participants. About 400 COVID-19 positive mothers were admitted during this period. After excluding the non-responders & patients who gave incomplete information, the total participants included in the study were 381.

As a part of COVID-19 pandemic preparedness, Rapid Response Team (RRT), under the leadership of Head of the Department & Dean, Madurai Medical College, was initiated as per guidelines of ICMR since March 2020.[15] Case Investigation Form (CIF)[16] designed by National Centre for Disease Control (NCDC) was used to collect details of COVID-19 patients admitted in the hospital. CIF included the following details – I) Sociodemographic details including age, gender, place of residence, district and contact number, II) Clinical information including onset of symptoms, date of admission, symptoms like fever, cough, general weakness, sore throat, breathlessness, diarrhoea, nausea/vomiting, running nose and associated co-morbidities like Diabetes, Hypertension, Heart disease etc. COVID-19 positive line list, confirmed by RtPCR(Reverse transcriptase Polymerase Chain Reaction) was obtained from GRH Control Room on daily basis and separate list was maintained for COVID-19 affected pregnant & postnatal mothers. Contact numbers of COVID-19 positive mothers were taken from that list and after informed oral consent, patients were interviewed through telephone by the investigator. Those who didn't attend the phone call for the 1st time were called again after a gap of 2 days for consecutive 3 times. Patients who didn't attend the phone call or who gave incomplete information were excluded from the study. Parturition details (Labour Natural/LSCS, alive/still birth/abortion, term/preterm, birth weight of baby) were collected from the registers maintained by Department of Obstetrics and Gynaecology, GRH. Discharge details were collected from COVID-19 control room for all admitted COVID-19 positive mothers. All the babies born to COVID-19 positive mothers admitted at our hospital were tested for COVID-19. The test performed was RtPCR.All the collected data was entered in google spread sheet for analysis.

Both general outcome and pregnancy outcome were studied at the time of discharge. General outcomes included discharge and expiry of COVID-19 affected mothers. Pregnancy outcome studied were preterm, abortion, still birth and small for gestational age. Mothers with any one of these outcomes was classified under poor pregnancy outcome and the rest were classified under good pregnancy outcome. Mothers who had abortion and still birth were classified as having dead babies and rest of them were classified as having alive babies. Preterm baby was defined as baby delivered before 37 weeks of gestation. Abortion was defined as spontaneous or induced termination of pregnancy before fetal viability. Still birth was defined as baby who died after 28 weeks of pregnancy but before or during birth. Small for gestational age (SGA) was defined as birth weight of less than 10th percentile for gestational age. Gestational Diabetes Mellitus was defined as carbohydrate intolerance resulting in hyperglycemia of variable severity with onset or first recognition during pregnancy. Pregnancy Induced Hypertension was defined as systolic BP of$\geq$140 mmHg od diastolic BP of$\geq$90 on 2 occasions at-least 15 min apart on same arm. Data entered in Google spread sheet was analysed using SPSS version 21. Continuous variables were expressed in mean and standard deviation and categorical variables were expressed in numbers and percentage. Chi Square test & Fischer exact test was used to find the association between the various maternal characteristics and outcome variables. Ethical clearance was obtained from Institutional Ethical Committee before the commencement of this study.

3. Results

The overall mean age of our study population was 25.98 years (S.D $\pm$ 4.35). The minimum age was 18 years and the maximum age was 50 years among the COVID-19 positive mothers admitted in our hospital.

Table 1 shows the demographic and obstetric details of our study population. Most of the COVID-19 positive mothers admitted belonged to age group 21–25 years (N = 154,40.4%). Both rural (N = 192,50.4%) and urban (N = 189,49.6%) residing women were admitted in equal proportions since it was the only government COVID-19 specialty hospital nearby. Majority of the patients belonged to Madurai district (N = 340,89.2%) and referral cases (N = 41,10.76%) were admitted from surrounding districts. There were 189 (49.6%) mothers admitted in their 1st gravida; Most of the COVID-19 positive mothers admitted belonged to 3rd trimester (N = 318,83.5%). Around 125 (32.8%) COVID-19 positive mothers admitted in our hospital had symptoms and 153 (40.2%) mothers had comorbidity.

Fig. 1 describes the symptom profile of our study population depicting fever (N = 70,56%) as the most common symptom. Among symptomatic COVID-19 positive mothers, 101 (80.8%) had single

Table 1
Sociodemographic and obstretic details of the STUDY POPULATION (N = 381).

Characteristics	Frequency (N = 381)	Percentage % (95 %C·I) (100%)
Age in years: < 20	36	9.4 (6.71–12.84)
21–25	154	40.4 (35.45–45.54)
26–30	148	38.8 (33.92–43.94)
31–35	32	8.4 (5.82–11.65)
>36	11	2.9 (1.45–5.11)
Setting: Rural	192	50.4 (45.26–55.53)
Urban	189	49.6 (44.47–54.74)
District: MADURAI	340	89.2 (85.69–92.17)
OTHER DISTRICTS	41	10.76 (7.83–14.31)
Gravida: Primigravida	189	49.6 (44.47–54.74)
2nd gravida	179	47.0 (41.88–52.13)
3rd gravida	13	3.4 (1.83–5.76)
Trimester: I	7	1.8 (0.74–3.75)
II	18	4.7 (2.82–7.36)
III	318	83.5 (79.35–87.05)
POST PARTUM	38	10.0 (7.15–13.43)
Symptoms: Present	125	32.8 (28.11–37.77)
Absent	256	67.2 (62.23–71.89)
Comorbidity: Present	153	40.2 (35.2–45.27)
Absent	228	59.8 (54.73–64.80)

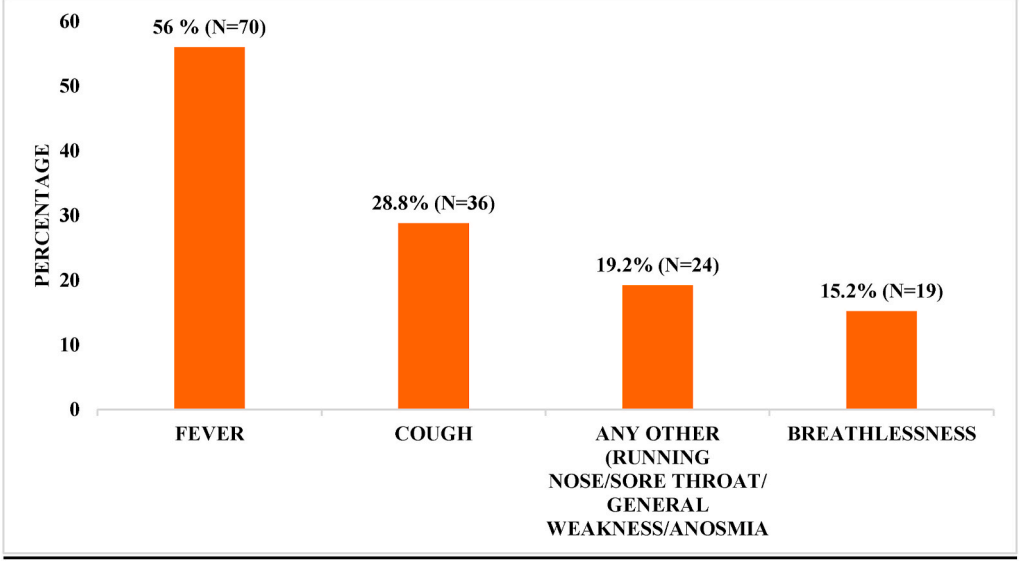

Fig. 1. Symptom distribution of the study population (N = 125).

symptom while 24 (19.2%) had more than 1 symptoms.

Fig. 2 shows the comorbidity status of the study population. Pregnancy Induced Hypertension (N = 49,32%) was reported the highest followed by Hypothyroidism (N = 47,30.72%), Gestational Diabetes Mellitus (N = 39,25.5%) and others. About 136 (88.8%) of the study population with comorbidity had at least one comorbidity while 17 (11.2%) had more than 1 comorbidity.

Table 2 shows the outcome status of our study population. **General Outcome:** Out of the 381 COVID-19 positive mothers admitted, 378 (99.2%) were discharged and 3 (0.8%) expired at the time of discharge. Among the discharged mothers, 28 (7.41%) were antenatal mothers and 350 (92.6%) were postnatal mothers. The 1st death was a 50-year-old 3rd gravida, initially asymptomatic at the time of admission later developed breathlessness, known case of Type 2 diabetes mellitus under insulin. She delivered alive preterm twins and subsequently admitted in Intensive Care Unit. She died after 3 days of admission and cause of death was COVID19 pneumonia/Acute Respiratory Distress Syndrome. The 2nd death was a 34-year-old primi, who came with complaints of fever and cough, a known case of Pregnancy Induced Hypertension and Type 2 diabetes mellitus, delivered preterm twins by caesarean section. She developed breathlessness and went to sudden cardiorespiratory arrest within 24 h of admission. The cause of death was COVID19 pneumonia/acute respiratory distress syndrome. The 3rd death was a 28-year-old 2nd gravida, came with complaints of fever and cough, known case of pregnancy induced hypertension and anemia, later developed breathlessness at the 3rd day of admission and went to sudden cardiorespiratory arrest. The cause of death was COVID19 pneumonia/Acute Respiratory Distress Syndrome. Among the 3 death patients, 2 were symptomatic and 1 was asymptomatic. All of them had at least one comorbidity, presented to the hospital at their 3rd trimester and delivered their babies through caesarean section. Two expired patients delivered preterm twins while alive mother delivered term baby.

Pregnancy Outcome: Out of 353 births that occurred to COVID-19 positive mothers admitted in our hospital, 343 (97.2%) were alive and 10 (2.8%) were dead. Among the 343 alive babies, 329 (96%) were term and 14 (4%) were preterm; 125 (35.4%) were born by labor natural and 218 (61.7%) by LSCS. Around 99 (25.98%) babies were born small for gestational age. 10 (2.8%) babies born to COVID-19 positive mothers

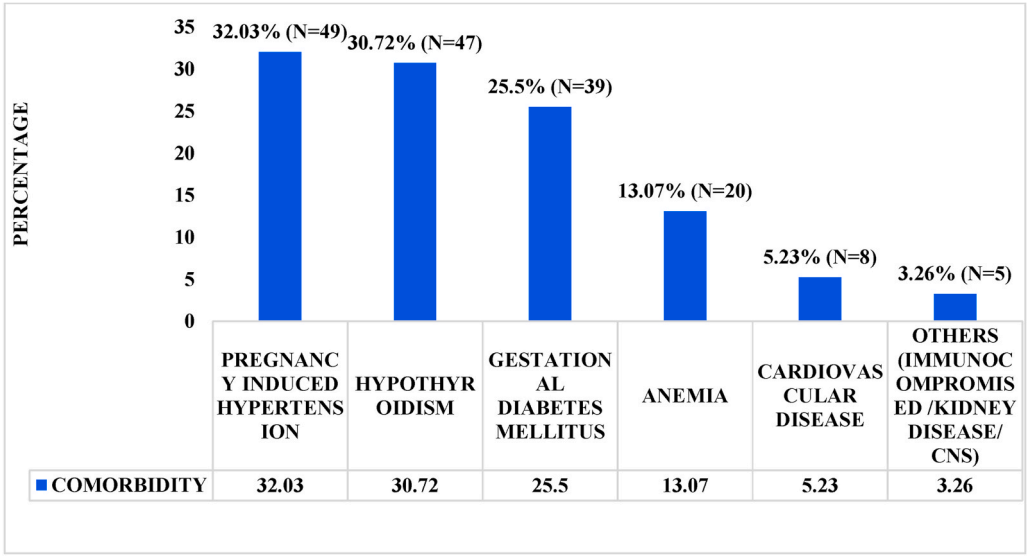

Fig. 2. Comorbidity distribution of study population (N = 153).

Table 2
Outcome status of the Study population (N = 381).

Characteristic	Frequency (N)	Percentage % (95% C·I)
COVID outcome		
Expired	3	0.8 (0.16–2.28)
Discharged	378	99.2 (97.72–99.84)
Total	381	100
Pregnancy outcome (n=381)		
Not born (antenatal at time of discharge)	28	7.35 (4.94–10.45)
Abortion	5	1.31 (0.43–3.04)
Still birth	5	1.31 (0.43–3.04)
Preterm	14	3.67 (2.02–6.09)
Term	329	86.35 (82.49–89.64)
Small for gestational age (SGA)	99	25.98 (21.65–30.70)
Birth weight (N = 348)		
<1.5 Kgs	5	1.44 (0.47–3.32)
1.6–2.49 Kgs	113	32.5 (27.58–37.67)
2.5–3.5 Kgs	228	65.52 (60.26–70.50)
>3.6 Kgs	2	0.57 (0.07–2.06)
TOTAL	348	100

expired. 5 (50%) of them were abortions and 5 (50%) of them were still birth. Out of 10 mothers with expired babies, 9 (90%) were symptomatic and 3 (30%) had comorbidity. It was also found that 5 (50%) of the COVID-19 positive mothers during their 1st trimester had abortion while 4 (40%) of the 2nd trimester mothers had either abortion or still birth and 1 (10%) mother had still birth during her 3rd trimester. Most of the COVID-19 mothers were referred to GRH and they were mostly asymptomatic for COVID-19. They tested positive while routine screening before delivery. Most of them were not in obstetric emergency needing immediate medical attention at the time of admission. They were admitted mainly for isolation and observation. Therefore, logistic issue might have not been involved in poor pregnancy outcomes. Fig. 3 shows the pregnancy outcome of study population. No neonate were tested positive for COVID-19 born to COVID-19 positive mothers.

Tables 3 and 4 shows the association between various factors with COVID-19 outcome and pregnancy outcome. COVID-19 death was more among increased age group, compared to younger age group but it was

Table 3
Association between maternal characteristics and COVID19 outcome of our study population (N = 381).

Characteristic	COVID outcome			Pearson's Chi Square test	Fischer exact test P value
	Death (n = 3)	Discharged (n = 378)	Total (n=381)		
Age Group: < 30 years	1 (0.3)	337 (99.7)	338 (100)	4.526	0.0694
>30 years	2 (4.6)	41 (95.4)	43 (100)		
Setting: Rural	2 (1.04)	190 (98.9)	192 (100)	0.00018	0.9999
Urban	1 (0.5)	188 (99.5)	189 (100)		
Gravida: Primi gravida	1 (0.5)	188 (99.5)	189 (100)	0.514	0.7734
2nd gravida	2 (1.2)	177 (98.8)	179 (100)		
3rd gravida	0 (0)	13 (100)	13(100)		
Trimester: I	0 (0)	7(100)	7 (100)	0.5991	0.8966
II	0 (0)	18 (100)	18(100)		
III	3 (0.94)	315 (99.05)	318 (100)		
Postpartum	0 (0)	38 (100)	38 (100)		
Symptoms: Yes	2 (1.62)	123 (98.4)	125 (100)	0.4054	0.5034
No	1 (0.4)	255 (99.6)	256 (100)		
Comorbidity: Yes	3 (1.96)	150 (98.03)	153 (100)	2.346	0.1280
No	0 (0)	228 (100)	228 (100)		

$p < 0.05$ = significant*.

not statistically significant. Maternal COVID-19 symptoms were significantly associated with expiry of the baby. It showed that symptomatic mothers with fever were more prone to deliver an expired baby than mothers without fever which was statistically significant**.** COVID-19 positive mothers at their early trimester (I&II) had more risk of having expired baby than late trimester mothers, which was also statistically significant. Similarly, COVID19 positive mothers with comorbidity had the chance of being symptomatic and this association was also

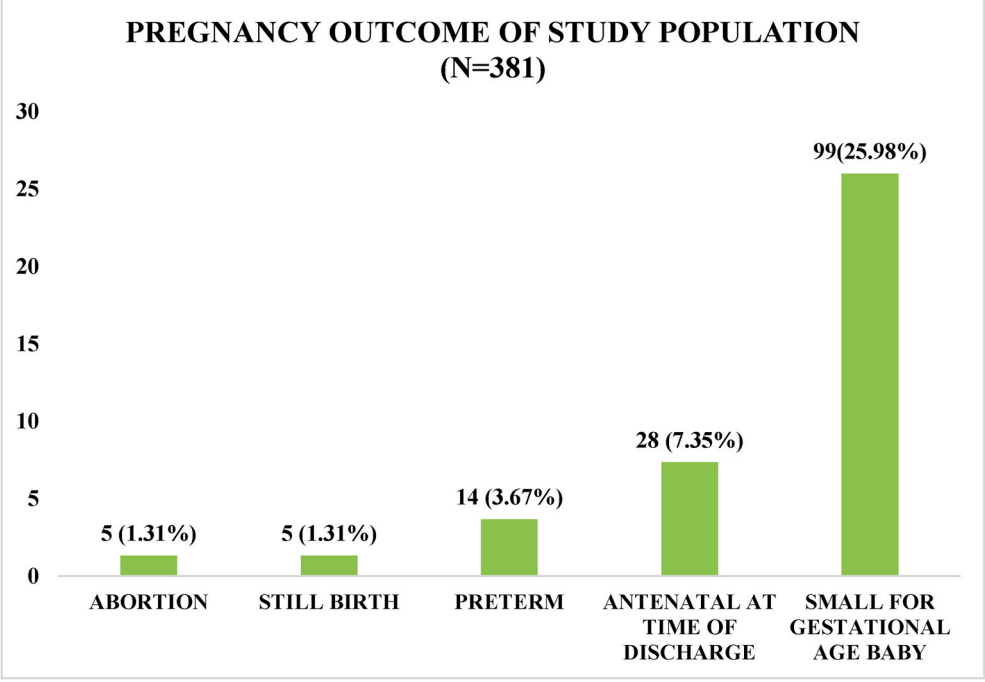

Fig. 3. Pregnancy outcome of the study population (N = 381).

Table 4
Association between maternal characteristics and pregnancy outcome of our study population (N = 381).

Characteristic	Pregnancy outcome			Pearson's Chi Square/	Fischer exact test P value
	Baby Dead (n = 10)	Baby Alive (n = 371)	Total (n = 381)		
Age Group: < 30 years	9 (2.7)	329 (97.3)	338 (100)	0.1415	0.9999
>30 years	1 (2.3)	42 (97.7)	43 (100)		
Setting: Rural	5 (26.5)	187 (73.5)	192 (100)	0.087	0.9999
Urban	5 (2.6)	184 (97.4)	189 (100)		
Gravida: Primi gravida	8 (4.2)	181 (95.8)	189 (100)	3.854	0.1456
2nd gravida	2 (1.1)	177 (98.9)	179 (100)		
3rd gravida	0 (0)	13 (100)	13 (100)		
Trimester: I	5 (71.4)	2 (28.6)	7 (100)	164.4	<0.00000001*
II	4 (22.2)	14 (77.8)	18 (100)		
III	1 (0.4)	317 (99.6)	318 (100)		
Postpartum	0 (0)	38 (100)	38 (100)		
Symptoms: Yes	9 (7.2)	116 (92.8)	125 (100)	12.69	0.00051*
No	1 (0.4)	255 (99.6)	256 (100)		
Comorbidity: Yes	3 (2)	150 (98)	153 (100)	0.1137	0.7526
No	7 (3)	221 (97)	228 (100)		

$p < 0.05$ = significant*.

statistically significant.

4. Discussion

Pregnant women are more prone to develop severe illness after respiratory viral infection.[17] Also, previous studies show that SARS CoV and MERS-CoV were associated with adverse clinical effects in mothers and newborn.[18,19] Initial studies of COVID-19 during pregnancy did not address any serious maternal or neonatal complications.[20–23] But as time goes, many studies regarding pregnancy outcome in COVID19 were researched in depth with minimal effect on the fetus.[12,24]

The overall mean age of our study population was 25.98 (S.D ± 4.35) and median maternal was 26 years (Interquartile range [IQR] 23–29) which was similar to Indian study done by Bachani et al.[13] and lower than the systematic review done by Anna Nunzia Della et al. with median of 30 years (interquartile range [IQR], 27.5–33).[25] Studies by G. Kayem et al.[26] and Brandt JS et al.[27] stated that advanced maternal age is a risk factor for COVID19 outcome during pregnancy. In our study also death among COVID-19 positive mothers greater than 30 years of age was higher than their counterparts but it was not statistically significant. Both rural (50.4%) and urban (49.6%) residing women were admitted in equal proportions since it was the only government COVID19 specialty hospital nearby. The reason behind this equal strength of rural and urban patients may be due to the fact that most of the antenatal mothers would have been diverted to our tertiary care hospital from their primary health centers as a part of safety measure during lockdown period. Majority of the patients belonged to Madurai district (89.2%). Most of the admitted COVID19 positive mothers were 1st gravida (49.6%) and belonged to 3rd trimester (83.5%). It should be noted that the higher hospitalization rate in 3rd trimester might be due to intensive screening nearing expected date of delivery.

Anna et al.[25] showed that around 69% admitted mothers were symptomatic but in our study only 32.8% were symptomatic at the time of admission. Around 67.2% were asymptomatic in our study when compared to findings of Brandt JS et al.[27] saying that 61.1% were asymptomatic. This rings an alarm that asymptomatic patients may be a large burden in our society if not tested properly. The public health threat that this poses both for the transmission in the greater community and for the risk to healthcare providers—highlights the importance of universal testing for COVID-19 on labor and delivery. Also, our study says that pregnant women with at least 1 comorbidity were more prone to be symptomatic. In our study, among the 125 symptomatic patients admitted, predominantly presented with fever (N = 70, 56%) & cough (N = 36, 28.8%). Several other studies also had similar findings. Bachani et al.[13] states that 45 (78.9%) pregnant women had low grade fever, cough and diarrhoea. Anna et al. states that 17 (48%)pregnant women presented with fever at hospital admission and 16 (46%) women indicated dry cough (either alone or associated with any other symptom).[25] Huang et al. reported that the early symptoms of pregnant mothers admitted with COVID19 were fever, cough, dyspnea and fatigue.[28] Study by Liu et al. also stated that fever and cough were the most common symptoms in patients with COVID-19 [29]. In our study, 7 (5.6%) patients in postpartum had fever which was less than other studies which reported 8 (23%) patients with fever in the postpartum period.[25] In our study, 40.2% of COVID19 positive mothers had any one comorbidity similar to the findings from UK Cohort study.[24] Pregnancy Induced Hypertension (31.37%) was the commonest comorbidity found among the study population but study by Mullins et al.[12] done from UK pregnancy registry showed that Gestational Diabetes Mellitus (9.7%) was most common comorbidity recorded. Study by Bachani et al.[13] showed anemia, hypertension disorder and thrombocytopenia as common comorbidity.

In our study most of the admitted COVID19 mothers delivered by caesarean section (61.7%). Our general hospital statistics showed caesarean rate in COVID-19 negative mothers was lower (40.6%). A cohort study conducted at UK showed 59% of COVID19 mothers delivered by caesarean section.[24] According to NFHS-4 [30], Tamil Nadu showed a caesarean rate of 26.3%births occurred in public health facility. Most of these caesarean deliveries occurred as a precautionary step due to SARS Co–V 2 infection. But as a matter of fact, by analysing the available literature till date, the clinical outcome was generally favourable for both mothers and their new-born.

Among the 381 COVID-19 mothers, 378 (99.2%) were discharged and 3 (0.8%) expired. Similarly Indian study by Bachani et al.[13] showed 3 maternal mortalities. Systematic review regarding pregnancy and COVID outcome[31] states that studies showed that outcome of death due to COVID-19 was minimal but significant. So special attention is needed for all COVID19 positive mothers. A study conducted at UK showed preterm delivery of 12%.[24] Another study by Brandt JS et al.[27] also stated that the risk of preterm deliveries was higher among the COVID19 cases compared to the controls. But on the contrary our study findings show that 96% of babies were born at term and only 4% babies were born preterm and 99 (25.98%) babies were small for gestational age. Our hospital statistics showed that 2.9% babies were preterm and 23.72% were small for gestational age born to COVID-19 negative mothers. This study will form a base for future studies to find out risk factors associated with prematurity and small for gestational age among neonates born to COVID-19 mothers.

Our study shows that out of 353 babies born at time of discharge to COVID-19 positive mothers, 343 (97.2%) were alive and 10 (2.8%) were dead (either aborted or spontaneous expelled). But study by Bachani et al.[13] showed no neonatal mortality. In our study, no neonate tested positive for COVID-19 but Bachani et al.[13] showed 5 neonates tested COVID-19 positive. Particularly 1st and 2nd trimester COVID19 positive mothers had more risk of baby being dead and this association was statistically significant. Organogenesis occurs during the 1st & 2nd

trimester which may lead to exposure of fetus to virus causing negative pregnancy outcome. Our study also showed that if the COVID positive mothers were symptomatic, the chance of baby being dead was more than asymptomatic and this association also was statistically significant. This shows that COVID-19 may be severe in symptomatic. This finding, while preliminary, suggests that early fetal loss could be a complication in COVID19 positive mothers, and hence symptomatic mothers need more attention.

4.1. Strength & weakness

The main strength is that this study was conducted using standard questionnaire prepared by National Centre for Disease Control, in order to minimize reporting bias. Apart from the general population, special focus on pregnant women regarding effects of this newly emerging disease is the need of the hour. The limitation is that this study was conducted at a single centre and no control group was allotted to compare the risk factors associated with pregnancy outcomes. Further knowledge on this disease effects on pregnancy needs more research in depth.

5. Conclusion

It would be fruitful to pursue further research on COVID-19 outcomes focusing pregnancy in order to help the policy makers in making decisions regarding screening and other necessary actions. As time progress, this newly emerging disease may become more virulent on vulnerable population, especially antenatal and postnatal women. Studies regarding vertical transmission is needed for further clarity. Hence, Early detection and intervention of COVID19 may reduce potential obstetric complications such as pregnancy loss, maternal death, preterm delivery and may be beneficial for improving maternal outcome. Since the effects of this disease is uncertain, long term follow up studies on maternal and fetal outcome must be encouraged.

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Data integrity

Dataset is under the control of our institution, but it can be provided through proper channel upon requisition to corresponding author.

Submission declaration

This work is not published previously or considered for publication. Publication is approved by all authors and by responsible authorities where work has been carried out. If accepted it will not be published elsewhere in the same form without written consent of copyright holder.

Declaration of competing interest

None

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