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Original Research Article

Clinical profile and outcome in neonates born to COVID-19 positive mothers and COVID positive children aged between 1 month to 12 years admitted in a tertiary COVID care centre: a cross sectional study

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ABSTRACT

Background: COVID-19 pandemic has caused worldwide havoc since the first case was discovered in China in December 2019. The infection has caused less severe infections and fewer deaths in children compared to adults. During the first two waves of COVID-19, the mortality rate in children has been <3% in India though more severe infections and hospitalizations were seen during the second wave. This study was undertaken at a tertiary Pediatric COVID care center during the third wave to understand the clinical, morbidity profile and outcomes in neonates born to COVID positive mothers and children who are COVID positive.
Methods: Neonates born to COVID positive mothers and children between the age group 1 month to 12 years admitted in Government general hospital, Kakinada, Andhra Pradesh from 1 January 2022 to 31 March 2022 were included in the study. Their demographic, clinical, morbidity profile, treatment details were noted and outcomes observed.
Results: All neonates were found to be RTPCR negative. 28% of neonates were born prematurely and 16% had birth asphyxia. Respiratory distress was the most presenting symptom. Death was seen in 4 newborns due to perinatal complications. More children less than 10 years required admission.15% of children were asymptomatic. Fever, cough, and running nose were the most presenting complaints. 2 children who had co-morbidities at the time of admission died.
Conclusions: The third wave of COVID-19 did not cause any significant change in morbidity and mortality in children compared to the previous two waves.

Keywords: COVID-19, Neonates, Children, Respiratory distress, Fever

INTRODUCTION

COVID-19 disease has been less severe in children causing fewer infections, severity, and deaths. The majority of affected children are asymptomatic (>70%) and in those symptomatic, the illness has been mild with <1.5% of children requiring hospitalisations.[1] This could be due to fewer Angiotensin-converting enzyme 2 receptors in children required for the adherence of the spike protein of SARS-CoV-2 and absence of significant comorbidities. UNICEF has reported 0.4% mortality in children among the 3.7 million COVID 19 deaths.[2] Severity of COVID-19 has been more in middle and lower-income countries than in high-income countries.

In India, since the first case of COVID-19 was reported on Jan 27th2020, more than 420 million people have been affected with approximately 3% prevalence in 10 years and 8 % prevalence in 11-20 years age groups in the first wave.[1] Similar figures were seen during the second wave

but there was an increase in the absolute number and children requiring hospitalizations and ICU admissions, one of the contributing factors being the Delta variant of COVID-19 which caused a more serious infection. The mortality in children was reported to be 1-2% during both the first and second waves of COVID-19. Neonatal morbidity and mortality in neonates born to COVID-positive mothers were not significantly altered due to COVID-19 infection. The direct and indirect effects of COVID-19 in neonates still need to be known. Some complications like premature births and perinatal asphyxia have been seen in mothers aaffected by COVID.

The third wave of COVID-19 was seen in India with a rise in COVID cases from December 2021 to March 2022. There were speculations that the third wave could be more severe in children owing to the factors that they were largely unvaccinated and more vulnerable unable to follow social distancing norms and mask rules.

The lack of strict restrictive measures like lockdowns, and regular attendance at school and other places is another factor. Countries like US and UK have seen an exponential increase in infections and hospitalizations among children during the third wave. This study was done to assess the clinical profile and outcome in newborns born to COVID positive mothers and children with COVID admitted to a tertiary COVID care center in South India during the third wave of COVID-19.

METHODS

A hospital-based cross-sectional study was done at a dedicated pediatric COVID center at a tertiary hospital, Government general hospital, Kakinada in East Godavari district, Andhra Pradesh from 01 January 2022 to 31 March 2022 during which COVID positive cases were reported in high numbers during the third wave.

Inclusion and exclusion criteria

All neonates born to COVID positive mothers, both intramural and extramural (mothers tested positive by Rapid antigen or RTPCR tests) and children in the age group of 1 month to 12 years who were COVID positive tested by nasopharyngeal swab RTPCR test and admitted in COVID center were included in the study.

Informed consent of the parents was taken. Those who were unwilling to participate in the study were excluded from the study.

Procedure

Demographic profile of the children like age, sex, birth weight, and gestational age of neonates and their morbidity profile was noted. Information about clinical characteristics like the presence of symptoms of fever, cough, cold, respiratory distress, vomiting, loose stools, etc, oxygen saturations at admission was taken. Requirement for oxygen, duration of hospital stay, medical treatment, and outcomes were also noted. Statistical analysis was done using SPSS 21 software.

RESULTS

The demographic, clinical characteristics, and morbidity profile of 25 neonates included in the study is depicted in (Table 1). More female newborns (56%) were admitted compared to males (44%). 7 neonates were born prematurely, less than completed 37 weeks.

All neonates tested negative for COVID by nasopharyngeal RTPCR test. Respiratory distress was the most common presenting complaint (60%). 64% of newborns had good oxygen saturations at the time of admission and most of them required minimal oxygen support. 4 neonates succumbed due to perinatal complications like severe birth asphyxia and prematurity. The mean birth weight of newborn babies is 2.47 kgs with SD of 0.63.

The demographic, clinical characteristics, and morbidity profile of the 20 COVID-positive children in this study is depicted in (Table 2). Children less than 10 years were mostly admitted with more male children admitted than female children. 55% of children acquired infection from unknown contact. Asymptomatic infection was seen in 15% of children with those children with symptoms having fever, cough, running nose, and seizures as the most presenting complaints. Very few children (5) required oxygen supplementation. 2 children who were very critical and had co-morbidities at the time of admission expired. No statistical significance was found between different age groups or gender and duration of hospital stay.

Table 1: Demographic, clinical, and morbidity profile of neonates born to COVID positive mothers.

Factors	N (%)	Factor	N (%)
Sex		**Comorbidities**	
Male	11 (44)	Meconium aspiration	07 (28)
Female	14 (56)	Prematurity	07 (28)
Gestational age (weeks)		Birth asphyxia	04 (16)
<28	1 (4)	IUGR	01 (4)
28-32	0	LGA	02 (8)
32-35	3 (12)	Neonatal jaundice	03 (12)
35-37	3 (12)	Syndromic features	02 (8)

Continued.

Factors	N (%)	Factor	N (%)
>37	18 (72)	**SpO2 at admission (%)**	
Birth weight (kg)		>95	16 (64)
<1	01 (4)	90-95	04 (16)
1-1.4	01 (4)	<90	05 (20)
1.5-2.4	6 (24)	**Duration of oxygen therapy**	
2.5-3.5	14 (56)	<24 hours	06 (24)
>3.5	03 (12)	1-3 days	11 (44)
Mean birth weight	2.476±0.6359	>3 days	01 (4)
RT-PCR		**Duration of hospital stay**	
Positive	Nil	<24 hours	03 (12)
Negative	22 (88)	1-3 days	10 (40)
Could not be tested	03 (12)	4-7 days	09 (36)
Presenting symptoms		7-14 days	02 (8)
Respiratory distress	15 (60)	>14 days	01 (4)
Fever	01 (4)	**Outcome**	
Birth asphyxia requiring resuscitation	04 (16)	Discharged	21 (84)
Sepsis	02 (8)	Death	04 (16)
Low birth weight	08 (32)		
Oxygen supplementation			
Oxygen with prongs	10 (40)		
HFNC	06 (24)		
Mechanical ventilation	04 (16)		

Table 2: Demographic, clinical, and morbidity profile of COVID positive children included in the study.

Factor	N (%)	Factors	N (%)
Age		**Comorbidity**	
1 month to 1 year	06 (30)	Congenital heart disease	01 (5)
1 to 5 years	05 (25)	Seizure disorder	01 (5)
5 to 10 years	06 (30)	Febrile seizures	01 (5)
>10 years	03 (15)	Suspected IEM	01 (5)
Mean age (years)	4.9	**SpO2 at admission**	
Median	4.0	<90%	02 (10)
Standard Deviation	4.22	90-95%	15 (75)
Sex		>95%	03 (15)
Male	11 (55)	**Oxygen supplementation**	
Female	09 (45)	Oxygen with prongs	03 (15)
Contact history		HFNC	0
Family contact	05 (25)	Mechanical ventilation	02 (10)
With suspect case	04 (20)	**Duration of oxygen therapy**	
With unknown person	11 (55)	<24 hours	0
Presenting symptoms		1-3 days	03 (15)
Asymptomatic	03 (15)	3-7 days	02 (10)
Fever	15 (75)	**Duration of hospital stay**	
Cough	06 (30)	1-3 days	09 (45)
Running nose	06 (30)	3-7 days	10 (50)
Respiratory distress	02 (10)	7-10 days	01 (5)
Fever+cough+ running nose	04 (20)	**Outcome**	
Fever+cough+running nose+respiratory distress	01 (5)	Discharged	18 (90)
Diarrhoea	02 (10)	Death	02 (10)
Vomitings	02 (10)		
Fever+diarrhoea+vomitings	01 (5)		
Seizures	09 (45)		
Shock, sepsis	01 (5)		

Table 3: Relation between age groups and duration of hospital stay.

Age group (years)		Duration of hospital stay (days)			Chi Square test		
		≤3	>3	Total	Value	Df	P value
<1	N	1	4	5	1.728	2	0.421
	%	20	80	100			
1-5	N	3	3	6			
	%	50	50	100			
>5-12	N	5	4	9			
	%	55.6	44.4	100			
Total	N	9	11	20			
	%	45	55	100			

Table 4: Relation between sex and duration of hospital stay.

Sex		Duration of hospital stay (days)			Chi Square test		
		≤3	>3	Total	Value	Df	P value
Female	N	5	4	9	0.737	1	0.653
	%	55.6	44.4	100			
Male	N	4	7	11			
	%	36.4	63.6	100			
Total	N	9	11	20			
	%	45	55	100			

DISCUSSION

Ours is a pediatric COVID care center attached to a tertiary care center, Government general hospital, Kakinada, catering to the population of East Godavari and nearby districts. As many as 132 and 81 pediatric cases including neonates were admitted and treated during the first and second waves of the COVID-19 pandemic. A total of 45 cases (25 neonates and 20 pediatric patients) were admitted during the third wave. The decrease in the number of admissions during the third wave from 01 January to 31 March, 2022, was due to less number of severe infections requiring hospitalization. Many of the diagnosed cases had mild symptoms and could be managed with supportive treatment and monitoring at home. Neonates largely acquire COVID-19 through vertical transmission and from caregivers. Contrary to previous studies Vertical transmission of COVID-19 from mothers to newborn babies has been documented in studies by Vivanti et al, Zing et al and Dong et al where the virus has been isolated from maternal placenta tissue (due to hematogenous spread), amniotic fluid and vaginal secretions and human milk.[3-5] COVID-19 infection in neonates is mild, the majority of them being asymptomatic and in those symptomatic too neonates were found to have less severe complications.

All the neonates born to COVID-positive mothers included in this study who could be tested, were negative by nasopharyngeal swab RTPCR test done within 48 hours after birth. 3 Newborn babies could not be tested because of early death due to perinatal complications. Neonatal SARS-CoV-2 infection can be confirmed by naso-pharyngeal swab RTPCR. No perinatal transmission was seen in studies by Salvatore et al, Chen et al and Dong et al.[6,7] Some Indian studies by Nanavati et al, Anand et al and a study by Kotlyar reported an incidence of 10.7%, 10.6% and 3.2 % COVID-19 infection in neonates born to COVID positive mothers.[8-10] Role of SARS-CoV-2 antibodies in diagnosis is uncertain. The possibility of a false-negative test cannot be ruled out in this study because of early testing and no-repeat testing in all babies. Only 1 neonate who had septicemia and NICU stay of more than two weeks was tested again on 20 day of life and found to be negative. 28% of neonates in this study were born prematurely. Association of COVID-19 and preterm deliveries had been shown in studies by Pereira et al, Ferrazzi et al.[11] As per the study by Zhu et al 6 out of 10 neonates were born prematurely which is much higher than seen in this study. A review by NNF COVID-19 registry shows that the prematurity rate in India is around 20.7% in COVID infected mothers.[12]

SARS-COV-2 infection in the mother causes inflammatory changes in the placenta causing placental insufficiency and hypoxemia thereby causing premature births, low birth weight, and birth asphyxia. Birth asphyxia was seen in 16% of cases and low birth weight in 28% of cases in this study. The mean birth weight was 2.4 kgs in this study. The most presenting complaint was respiratory distress seen in 60% of neonates in this study. The cause of respiratory distress in these newborns was prematurity, birth asphyxia, and meconium aspiration. Fever and gastrointestinal symptoms as seen in infected neonates in other studies were not present in this study. Similar findings were noted by NNF India COVID-19 registry. Most of the babies recovered well with supportive management like intravenous fluids, oxygen supplementation antibiotics, and phototherapy. Babies with respiratory distress improved well with oxygen

supplementation with prongs or HFNC for 1-2 days. Mechanical ventilation was needed for two very sick neonates who had severe HIE.

One baby with culture-positive sepsis needed mechanical ventilation for 1 day and was later weaned off successfully. One baby with neonatal jaundice due to AO incompatibility required exchange transfusion. 50% of babies in the present study who were stable without any complications were discharged from NICU within 3 days and shifted to the mother's side for routine care and breastfeeding as per WHO perinatal management recommendations. These babies did not report back further with any complications later. Mortality was seen in four babies, three with severe HIE, two of them having syndromic features, and one very preterm. COVID 19infection cannot be attributed to their deaths. In the pediatric age group from 1 month to 12 years, more males (55%) were admitted compared to females (45%). The mild predominance of COVID-19 infection in males was also seen in studies by Dong and Gotzinger et al.[13,14] Data from various studies on COVID-19 shows that its prevalence is higher in the age group of 5-7 years with exception of the United States where the prevalence was higher in the median age of 11 years with more cases in the 10-19 years group. In this study, the prevalence was almost similar in age groups 1month to 1 year, 1-5 years, and 5-10 years with less number of children above 10 years.

The mean age group in this study was 4.9 years. Children mostly acquire the infection from contact with an adult in the household mainly parents or siblings or by contact with a person from outside the family or an unknown subject. This study shows the presence of contact with a positive person in the family in 25% of cases. A majority (55%) acquired infection from an unknown subject with 20% of cases having a possibility of acquiring the infection from contact with a suspect case in the hospital. It has been evident that school-age children are less susceptible and less frequent drivers of SARS-CoV-19 infection. It could be due to less expression of ACE-2 and TMPRSS2 receptors in the lungs of children.[15] There is also speculation that mandatory vaccination particularly BCG and measles provide cross-protection to COVID-19 in children by an enhanced immune response against other respiratory pathogens including SARS-COV-2. A study by Manjhi et al found that those children who received the measles/MR vaccine had a less severe of COVID-19 disease as compared to those who were not vaccinated.[16]

Most of the data from studies around the world had found that children had a mild disease or asymptomatic infections with fewer critical cases and deaths due to COVID-19. Asymptomatic infection in children ranged from 4.4% to 39%. In symptomatic children fever, cough, and respiratory distress were found to be the major presenting complaints. In our study 15% of cases were asymptomatic. 75% of cases had a fever as the predominant clinical symptom followed by cough (30%), and running nose (30%) with 20% of children having all the three complaints. Seizures were also noted in 45% of cases with many children presenting as the first episode of febrile seizures or fever provoked seizures. Gastrointestinal symptoms like vomiting and diarrhoea were seen in 10% of children. Studies have shown that ICU admissions were more in the male gender and children with pre-existing medical conditions like respiratory, cardiovascular, ontological, and immunosuppressive disorders. In this study children having a pre-existing medical condition or come morbidities were very few like seizure disorder, sepsis, suspected congenital heart disease, and IEM.

Children in this study had good oxygen saturations requiring minimal or no oxygen support. Only two cases that were critical required mechanical ventilation. (10%) and had associated co-morbidities like suspected congenital heart disease and IEM. Symptomatic treatment was given in all the cases with none being treated with immune-modulators like steroids or antiviral agents like remdesivir. We had a few critical cases during the second wave of COVID-19 who had a successful outcome with treatment with steroids and remdesivir. Most of the children admitted had mild to moderate symptoms, they were discharged within one week of hospital stay (95% cases) and were advised to follow COVID appropriate measures at home. There was no statistical significance in relation to duration of hospital stay and age or gender of the children. It was mostly dependant on the severity of symptoms and presence of co-morbidities. Mortality was seen in two cases who were critical at the time of admission and had co-morbidities. The rest of the cases were discharged after recovery.

Limitations

Limitations of current study were it is a small cohort study. Neonates were not retested again for COVID infection. Some studies have shown that babies may test positive as late as twelfth or fourteenth postnatal day. Other samples like placenta, amniotic fluid, and umbilical cord were not tested to establish vertical transmission. Follow-up of COVID-positive children is needed to look for long-term complications like MIS-C which causes serious morbidity and mortality. These children could not be followed up despite repeated reminders to attend the hospital.

CONCLUSION

This study shows that in the third wave of COVID-19 children were mostly asymptomatic or mild symptoms in both neonates and children with no significant increase in morbidity and mortality when compared to the previous waves of COVID. Routine newborn care such as rooming-in and breastfeeding can be continued to all babies born to COVID positive mothers as the benefits far outweigh the risks and no significant complications

were seen in those babies in this study who were shifted to the mother's side after discharge from NICU. Long term effects of COVID-19 on neonates need to be studied. MISC in neonates has been reported in some studies. Hence all these neonates born to COVID-positive mothers need long-term follow-up to learn about other possible complications. Vaccination of all pregnant mothers for COVID-19 should be widely encouraged as studies have shown the presence of IgG antibodies in the placenta and breastmilk giving neonates protection from COVID-19. Routine vaccination of children should be strongly advocated as routine vaccines like the Measles vaccine has shown cross-protection against COVID-19 in some studies. Follow-up of all COVID infected children whether symptomatic or not is needed to look for long-term complications like MIS-C.

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