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Case Series

Paediatrics Section

Outcome of COVID-19 Positive Neonate Born to Mothers with SARS-CoV-2 Infection: A Case Series

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ABSTRACT

Coronavirus Disease 2019 (COVID-19) the disease caused by the novel coronavirus, has led to an unprecedented global pandemic affecting people of all ages. In this case series, all COVID-19 positive neonates (≤28 days of life) born to mothers with Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) infection were selected from tertiary care hospital, in Central India from March 2020 to September 2020. There were 15 neonates affected by SARS-CoV-2 infection. In this case series, authors found that out of 15 neonates, 5 were male and 10 were female. Main symptoms were fever, shortness of breath, poor feeding and others (like-abdomen distension, vomiting) but, often these neonates did not showed other symptoms during stay in designated COVID-19 Neonatal Intensive Care Unit (NICU) with no mortality found in this case series. COVID-19 positive neonates showed a good prognosis, with low rate of severe complications and without any mortality. Treatment was mostly symptomatic or supportive. Most of the neonates tested positive for SARS-CoV-2 were asymptomatic or had mild disease.

Keywords: Coronavirus disease 2019, Nasopharyngeal swab, Severe acute respiratory syndrome coronavirus, Vertical transmission

INTRODUCTION

The COVID-19 pneumonia was firstly reported in Wuhan, China, in December 2019. The disease had a rapid spread all over the world becoming an international public health emergency [1]. Emergence of 2019-nCoV has attracted global attention, and World Health Organization (WHO) has declared the COVID-19 a Public Health Emergency of International Concern (PHEIC). Immune profile and physiological changes in newborns immediately after birth may predispose them for infection and may attribute to high risk for COVID-19 related complications [2]. Also, the possibility of SARS-CoV-2 vertical transmission from mothers to foetuses does exist [3-5]. Studies have predominantly described benign course in neonates [6-8]. However, there have been some case reports suggesting adverse outcome in SARS-CoV-2 infected neonates [9]. There is meagre data with respect to SARS-CoV-2 infected neonate.

The information and knowledge of SARS-CoV-2 infections in neonates are still evolving with increasing reports of COVID-19 in pregnant women and neonates from India. In view of diversity in clinical profile, available data from China, Europe and US cannot be generalised to other population in world. There is a meagre data regarding clinical manifestations, clinical courses and prognosis of SARS-CoV-2 infected neonates. Authors hereby, report a case series on clinical, biochemical profile and outcome of COVID-19 positive neonate born to mothers with SARS-CoV-2 infection.

CASE SERIES

This was a case series, retrospective analysis of SARS-CoV-2 infected neonates born to COVID-19 mothers who admitted and delivered at Indira Gandhi Medical College, Nagpur, Central India from March 2020 to September 2020 which is registered Tertiary Care Hospital of National Registry of Pregnant women with COVID-19 in India. The ethical approval was obtained for the same from IGMC Ethics Committee (Reg. No. ECR/485/Inst/MH/2013/RR-20 and IGGMC/Pharmacology/IEC/475/2020 on dated 20/11/2020).

The nasopharyngeal swab specimens of neonate exposed to SARS-CoV-2 positive mother was sent to the local VDRL Lab which is authorised by Indian Council of Medical Research (ICMR), where the SARS-CoV-2 RNA (Ribonucleic Acid) was detected by real-time Reverse Transcription-Polymerase Chain Reaction (RT-PCR) at 24 hours and 5th day of life of neonates. All COVID-19 positive neonates (≤28 days of life) born

to mothers with confirmed SARS-CoV-2 infection were included in analysis. The diagnosis and management of newborn with or at risk of COVID-19 in accordance with guidelines provided by American Academy of Paediatrics (AAP), National Neonatology Forum of India (NNF) and Indian Academy of Paediatrics (IAP) [10-12].

The information about SARS-CoV-2 infected neonates was retrieved from case record form from Medical Record Department (MRD). The data was extracted considering outcome variables as gestational age, sex, birth weight, clinical features, laboratory findings, chest X-ray images, treatment, duration in NICU and their outcomes in terms of morbidity and mortality. The data was entered in Excel sheet, was tabulated and analysed further.

Fifteen neonates were reported to have SARS-CoV-2 infection. Out of 15 neonates, 5 were male and 10 were female. The mean gestational age was found 38.06±0.70 weeks and 1 neonate born before 37 weeks of gestation and 14 were born after 37 weeks of gestation. Amongst them, 12 were Appropriate for Gestational Age (AGA) and 3 were Small for Gestational Age (SGA). The mean birth weight was recorded as 2946±640 gm and 5 babies were low birth weight (<2500 gm) and 10 babies were >2500.

Clinical Manifestations

Asymptomatic neonates were clinically normal and stable taking feeds well. Three neonates were symptomatic and 12 neonates were asymptomatic. Symptomatic neonates treated according to their symptoms as per the protocol developed at Institutional level as per ICMR guidelines [13].

Protocol included neonates who were symptomatic/sick and were born to a mother with suspected or proven SARS-CoV-2 infection should be managed in isolation NICU. This area should be separate from the regular NICU. This isolation facility should preferably have single closed rooms. Isolation NICU should have adequate ventilation. The treating doctors, nursing and other support staff working in these isolation NICU should be separate from the ones who are working in regular NICU. The staff should be given adequate supplies of PPE. The staff also must be trained for safe use and disposal of PPE. Respiratory support for neonates with suspected/proven SARS-CoV-2 infection is guided by principles of lung protective strategy including use of non invasive ventilation. Treatment was according to symptoms and sign of neonates.

Case no- 4,7 and 8 were symptomatic in which case number 4 had initial symptoms of poor feeding, lethargy and fever. During the course of hospital stay, patient started deteriorating and developed respiratory distress. Chest X-ray showed no evidence of pneumonia. On serial, Complete Blood Count (CBC) monitoring showed decreased platelet count, increased White Blood Cells (WBC) count and initially C-Reactive Protein (CRP) was negative suggestive of sepsis. This case patient required Continuous Positive Airway Pressure (CPAP) for 5 days, intravenous antibiotics were started according to blood and umbilical tip culture sensitivity reports for 14 days and also platelets and fresh frozen plasma were given to patient. Gradually patient started improving; weaning off from CPAP to O_2 by nasal prongs at the rate of 2 litre/min. Feeds were started via nasogastric tube; initially in small quantity which increased progressively as feeds were tolerated by patient. On 7th day of life,O_2 was removed and saturation was maintained. Overall patient improved clinically, stable and well. Ultrasonography of abdomen and pelvis within normal and Neurosonography (NSG) was also normal. On discharge, patient was taking feeds very well with weight gain and called for follow-up for Otoacoustic Emission (OAE), Retinopathy of Prematurity (ROP) and routine vaccination.

Case no. 7 patient complained of fever which had occurred on 3rd day of life. All required investigations were done and symptomatic treatment was given to the patient as per the protocol. Protocol and feeding was established simultaneously. No other clinical symptoms were developed during the hospital stay. On discharge, patient was taking feeds properly. Patient was called for follow-up in neonatology clinic.

Case no. 8 patient showed abdomen distention and started vomiting which was greenish in colour. On clinical examination, abdomen was distended and shiny with initially sluggish bowel sound which were absent after 24 hours. All routine and necessary investigations were done. Ultrasonography of abdomen and pelvis, and standing abdomen X-ray showed signs of intestinal obstruction. Patient was kept Nil By Mouth (NBM) and i.v. fluids and antibiotics were started. Patient was referred to Government Medical College and Hospital for further management by Paediatric Surgery Department. On enquiry, patient was managed conservatively and his health was improved and was discharged on day 8.

All other 12 asymptomatic neonates were taking feeds properly and no other symptoms were developed during the hospital stay. All asymptomatic neonates were discharged for home care with mother or parents (if mother is unwell) with appropriate precautions and recalled for follow-up in neonatology clinic [Table/Fig-1,2].

Case No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Gestational age (Mean age=38.06 wk) and SD=0.7039	38 wk	38 wk	39 wk	38 wk	39 wk	38 wk	38 wk	39 wk	38 wk	38 wk	38 wk	38 wk	38 wk	36 wk	38 wk
Sex	Female	Female	Male	Male	Female	Male	Male	Female	Female	Female	Female	Female	Female	Male	Female
Birth weight (Mean=2946 gm) and (SD=640.08).	3900 gms	2930 gms	2200 gms	2000 gms	2400 gms	2750 gms	3000 gms	2500 gms	2600 gms	3500 gms	2800 gms	3200 gms	2750 gms	1800 gms	1960 gms
APGAR score															
1 min															
5 min	8	8	8	8	9	8	8	8	9	8	8	8	8	8	8
(Mean=8 and 9)	8	8	8	9	8	9	9	8	9	9	9	8	8	8	9
AGA/SGA	AGA	AGA	AGA	SGA	AGA	AGA	AGA	AGA	AGA	AGA	AGA	AGA	AGA	SGA	SGA
Clinical features	Asympt omatic	Asympt omatic	Asympt omatic	Sympt omatic poor feeding, lethargy, fever and shortness of breath	Asympt omatic	Asympt omatic	Sympt omatic fever	Symptomatic abdomen distension and vomiting	Asympt omatic	Asympt omatic	Asympt omatic	Asympt omatic	Asympt omatic	Asympt omatic	Asympt omatic
COVID-19 NICU stay	No	No	No	Yes	No	No	Yes	Yes	No	No	No	No	No	No	No
Transfusion H/o	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No
Complications	No	No	No	Sepsis and respiratory distress	No	No	No	No	No	No	No	No	No	No	No
Outcome	Dis charge	DAMA (Called follow-up after 5 day)	Dis-charge	Dis-charge	Dis-charge	DAMA (Called follow-up after 5 day)	Dis-charge	Refer to GMCH super speciality for further M/n and discharge on 08 day of life	Dis-charge	Dis-charge	Dis-charge	Dis-charge	Dis-charge	Dis-charge	Dis-charge

[Table/Fig-1]: Demographic characteristic, clinical features and outcome of COVID-19 positive neonates born to mothers with confirmed SARS-CoV-2 infection.
DAMA: Discharge against medical advice; SD: Standard deviation; SGA: Small for gestational age; AGA: Appropriate for gestational age; M/n: Management

Case No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Haemoglobin (Hb) (g/dL)	14.5	15.6	17.7	15.8,14.5, 14.4, 13.4, 11.6, 10.7 (Serial CBC done)	19.5	17.3	14.6	16.7	18.9	17.7	18.7	14.8	16.3	17.1	16.4
WBC (x 10^3/ µL)	11630	17090	12700	19450, 29840, 9300, 21700, 19800 (Respectively)	15500	17000	19280	26200	10540	20600	27700	21210	3075	10200	10710
PLT (x 10^3/ µL)	3.93 Lac	2.93 Lac	2.56 Lac	2.07 Lac,15000, 12000, 38000, 1.06 Lac (Respectively)	1.27 Lac	1.97 Lac	2.25 Lac	1.70 Lac	2.95 Lac	1.04 Lac	1.99 Lac	2.57 Lac	2.62 Lac	2.89 Lac	2.63 Lac

CRP (mg/dL)	Negative	Negative	Negative	Negative, Positive and Negative (Respectively)	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative
Chest X-ray	Not done	Not done	Not done	Normal	Not done	Normal	Normal	Abdomen X-ray it also shows sign of intestinal obstruction	Not done	Not done	Not done	Not done	Not done	Not done	Not done
LFT	Not done	Not done	Not done	Normal	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done
KFT	Not done	Not done	Not done	Normal	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done
Blood culture	Not done	Not done	Not done	Candida Alb. growth seen	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done
Ferritin (ng/mL)	Not done	Not done	Not done	533	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done
D-dimer (µg/mL)	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done
Procalcitonin (mg/mL)	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done	Not done
USG	Not done	Not done	Not done	Abdomen and pelvis- normal neuro sonography-normal	Not done	Not done	Not done	Abdomen and pelvis suggest intestinal obstruction	Not done	Not done	Not done	Not done	Not done	Not done	Not done
Nasopharyngeal swab 1st (More than 12h i.e., on 1 day)	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive
2nd (More than 120h i.e., on 5 day)	Negative	Not done (Called follow-up after 5 day)	Negative	Negative	Negative	Not done (called follow-up after 5 day)	Negative	Negative (Managed conservatively at GMCH super specialty and discharge	Negative	Negative	Negative	Negative	Negative	Negative	Negative
Others	–	–	–	1-Umbilical tip culture-Pseudomonas growth seen 2-Urine culture -No Growth seen.	–	–	–	Standing Abdomen X-ray suggest Intestinal obstruction	–	–	–	–	–	–	–

[Table/Fig-2]: Investigation of COVID-19 positive neonates.
PLT: Platelet; CRP: C-reactive protein; LFT: Liver function test; KFT: Kidney function test

DISCUSSION

In this case series, signs and symptoms of COVID-19 positive neonates was less serious compared to adults. Main symptoms were poor feeding, lethargy, fever, shortness of breath abdomen distension and vomiting however, these newborns did not showed other symptoms or developed new symptoms during COVID-19 NICU stay.

Present case series demonstrated almost similar findings as mentioned in [Table/Fig-3] [9,14-24]. Systematic review by Dhir SK et al., states that in India, most COVID-19 positive neonates found were symptomatic and required intensive care. Gale C et.al., in London UK by a prospective national cohort study using active surveillance showed that 66 neonates were mildly affected, with two cases of severe disease [14,24]. Case reports by Kulkarni R et al., Alzamora MC et al., Vivanti AJ et al., Sisman J et al., reported symptomatic neonate [9,18,22,23]; whereas Mehta H et al., and Dumiriu D et al., showed asymptomatic neonates [19,20]. Case series by Kalamdani P et al., Anand P et al., Nanavati R et al., and Zeng L et al., found most of the neonates were asymptomatic and thrive on breast feeding [15-17,21].

Sr. No.	Author	Place	Outcome
1	Dhir SK et al., [14] (June 2020)	Chandigarh, India	By systematic review found, most COVID-19 positive neonates were symptomatic and required intensive care.
2	Kulkarni R et al., [9] (July 2020)	Pune, India	01 Symptomatic
3	Kalamdani P et al., [15] (Oct 2020)	Mumbai, India	Mostly asymptomatic (12 asymptomatic and thrive on breast feeding)
4	Anand P et al., [16] (Feb 2021)	New Delhi, India	Mostly asymptomatic (5 asymptomatic and 02 symptomatic)
5	Nanavati R et al., [17] (Jun 2021)	Mumbai, India	Mostly asymptomatic (14 asymptomatic and 07 asymptomatic)
6	Alzamora MC et al., [18] (April 2020)	USA	01 Symptomatic
7	Mehta H et al., [19] (May 2020)	USA	01 Asymptomatic
8	Dumitriu D et al., [20] (June 2020)	New york	02 Asymptomatic
9	Zeng L et al., [21] (Jul 2020)	Wuhan china	Mostly asymptomatic (03 Symptomatic and 33 Asymptomatic)
10	Vivanti AJ et al., [22] (Jul 2020)	France	01 Symptomatic
11	Sisman J et al., [23] (Sept 2020)	Dallas, Texas	01 Symptomatic
12	Gale C et al., [24] (Nov 2020)	London, UK	By a prospective national cohort study using active surveillance shows that 66 Neonates were mildly affected, with 2 cases of severe disease.
13	Present Case Series (March 2020-Sept 2020)	Nagpur, India	Mostly asymptomatic (03 Symptomatic and 12 Asymptomatic)

[Table/Fig-3]: Various published case reports and case series outcome [9,14-24].

Limitation(s)

However, as the present case series had the small number of cases, a large sample is required to come into any firm conclusion. Also, this was an observational retrospective case series in which authors had looked at the clinical and pathological status in neonates. Authors hereby, did not evaluate the presence of virus in amniotic fluid, cord blood, or placental tissue which might had clarified pathogenesis in neonates. In present study, follow-up of patients for a longer duration had not reported.

CONCLUSION(S)

COVID-19 positive neonates show a good prognosis, with low rate of severe complications and without any mortality. Treatments were symptomatic or supportive. Most of the neonates tested positive for SARS-CoV-2, were asymptomatic or had mild disease. Authors had not commented on vertical transmission so, it remains unproven, and horizontal transmission is the most probably source of infection in neonates. Hence, this case series finding were inconclusive about vertical transmission of SARS-CoV-2 from mothers with COVID-19 to their neonates.

Author contribution: The CB and MS had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: CB, MS Acquisition of data: MS, BT Analysis, or interpretation of data: All authors, Drafting of the manuscript: CB, MS, Statistical analysis: CB, MS and LD.

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