

Original Research Article

Clinicopathological profile and outcome of COVID-19 infection among children and newborn admitted to a dedicated COVID hospital in West Bengal, India

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ABSTRACT

Background: Aim of the study was to assess the clinicopathological profile and outcome of COVID 19 infection in children and newborn in a dedicated COVID tertiary care center.

Methods: A retrospective study of a cohort of 105 children (1 month-12 years.) and 128 newborns admitted from 7th July to 7th August 2020. All the admitted children were COVID 19 positive and newborns were delivered from mother with COVID positive status. We collected data from medical records regarding epidemiology, clinical features, comorbidities, investigational report, treatment and outcome of the study population.

Results: The median age of 105 children was 3 years with IQR (11 months-6 years) with almost equal sex distribution with higher disease prevalence and severity in younger age group. The mean duration of stay is 10.11 days (SD: 4.93). 35 (33.3%) children were asymptomatic, whereas 53 (50.5%) mildly symptomatic, 8 (7.6%) moderate disease severity, 9 (8.6%) critically ill at time of admission. Fever (57%) and Cough (23.8%) commonest symptoms. Hyper inflammatory syndrome was a new challenge in COVID affected children as well as concomitant infections like Dengue, Scrub and enteric fever, 38 (56%) children had comorbidities and 14 (13.3%) required PICU admission with 4 (3.8%) children. 42 out of 128 neonates became positive being born from 128 COVID positive mother and the rate of longitudinal transmission was more in outborn babies. None of the newborns tested swab positive within 48hrs of life and the preterm and LBW babies were relatively less infected. Most of the neonates were asymptomatic (84%) and we recorded zero death among COVID positive newborn.

Conclusions: In the absence of comorbidities and concurrent infections, COVID 19 is relatively benign in Indian children.

Keywords: COVID 19, Neonates, Outcome, PIMS-TS, RT-PCR

INTRODUCTION

Almost 100 years after the deadliest pandemic Spanish Flu (1918) the mankind faced a new pandemic named COVID 19 since the end of December 2019 which had its outbreak from Wuhan province of China.¹ COVID 19 is a predominantly respiratory illness with massive

transmissibility and unpredictable lethality affecting all age groups, caused by a novel corona virus which was named by WHO as SARS-CoV-2 and subsequently they declared COVID 19 disease as a Global pandemic on 11th March 2020.² Surprisingly the disease was benign in children and newborns at the early part of pandemic but of late, Multisystem Inflammatory Syndrome in children

(MIS-C) temporally associated with COVID 19 infection sets a new challenge to pediatrician. Our study aimed at exploring the epidemiological characteristics and clinical outcome with investigational findings of COVID 19 infection with a cohort of 105 children and 128 newborns admitted at a tertiary care center dedicated for Covid care.

METHODS

We conducted a retrospective study in a COVID referral hospital at Kolkata among all admitted children and newborns in the Department of Pediatric Medicine and Neonatology between the time span of 7th May to 7th August 2020. Approval from Institutional Ethics Committee obtained and informed consent from parents taken to conduct the study. Children from one month to 12 years who were admitted and tested COVID 19 positive by RT-PCR/CBNAAT/.

Antibody test were included in the study. We included newborns both delivered in our institute (Inborn) as well as referred from other centers (Outborn) but essentially their mothers were tested COVID 19 positive either 14 days prior delivery or 28 days postpartum. Inborn babies after birth had a compulsory swab test (RT-PCR) within 24 hours of their life irrespective of mother's COVID 19 severity and if found negative a repeat swab after 48 hours conducted.

A two consecutive negative reports required to stamp them COVID 19 negative and the baby being send to mother but kept under observation of any newly onset illness, when we again send a repeat swab. In the absence of maternal illness Covid positive newborns were roomed in with their mother and in case of maternal sickness they were shifted to Covid positive nursery. Referred babies both asymptomatic and sick, were admitted only with history of being delivered from a Covid positive mother or acquired COVID infection in neonatal phase.

We collected data on epidemiology, clinical characteristics, laboratory findings, comorbidities, management and outcome of our study population from medical records and filled up the predesigned proforma. Admitted children were classified as, per ICMR guidelines a) asymptomatic, who were without any clinical symptoms but COVID 19 positive, b) mild severity, who were with features of acute upper respiratory tract infection but without signs of Pneumonia on chest imaging, c) moderate severity, who were with documented Pneumonia but no sign of severe disease and d) severe variety who were with septic shock, ARDS.³

Symptomatic analysis done and plotted in chart. We recorded fever, cough, cold, sore throat, respiratory distress, skin manifestations in master chart. For diagnosis of Hyperinflammatory Syndrome/ PIMS-TS we followed diagnostic criteria published by WHO.⁴ Laboratory workup was done in all patients which includes routine investigations but inflammatory markers

like D-Dimer, LDH, Ferritin and Procalcitonin only in symptomatic group. Chest X-ray done only in symptomatic cases. Patients being treated as per ICMR guidelines and followed institutional discharge policy. For newborns similar methodology followed by exploring medical record sheet, data collected and put on pre-designed chart.

Statistical analysis

It was done using SSPS software version 26. Data were expressed in terms of frequency and percentage. Mean, median and interquartile range (IQR) was calculated for various parameters. Also significant association between symptom grade and pediatric age, duration of stay, outcome was evaluated using chi square test. Same method was applied for neonates.

RESULTS

The median age of 105 children admitted was 36 months with IQR (11 month-6 years) having almost equal sex distribution between male 59 (56.2%) and female 46 (43.8%) with a mean duration of hospital stay of 10.11 days and a history of positive household contact was among 80 (76.2%) children. Most of the children were asymptomatic 35 (33.3%) or mildly symptomatic 53 (50.5%) with 8 (7.6%) children having moderate severity and 9 (8.6%) had critically illness.

We found 14 (13.3%) children required PICU admission of which 5 (4.8%) were shifted to ventilator. Among the symptomatic group, Fever was the commonest clinical presenting symptoms found in 60 (57.1%) children, followed by cough 25 (23.8%), respiratory distress 22 (23.8%), convulsion 21 (20%), skin manifestation 11 (10%), diarrhea 9 (8.6%). Cough was mostly dry cough not associated with wheeze. We found 4 (3.8%) children satisfied the criteria of PIMS-TS of which the youngest one was 3 months presented with features of classical Kawasaki disease with coronary artery dilatation on Echocardiography and was RT-PCR positive for Covid19.⁵

The rest 3 children with MIS-C were positive to COVID 19 antibody and all showed characteristic skin manifestations, eye signs, GI manifestations but not sign for classical Kawasaki disease. We recorded 7 (6.7%) children suffered shock of which 2 children with MIS-C, had myocardial dysfunction with normal coronary artery on Echocardiography and raised Pro-BNP. A total of 38 (56%) children with COVID 19 infection got admitted with comorbidities and Malignancy 14 (13%) being the commonest one followed by CKD 6 (5.7%) CHD 7 (6.7%) CNS disease 9 (8.6%). We found 9 (8.5%) children had concomitant locally endemic infections along with COVID 19, which were Scrub Typhus (5), Dengue fever (2) and Enteric fever (2). We noted 14 (20%) children in symptomatic group with abnormal Chest X-ray findings of which 5 (4.8%) children

diagnosed isolated Pneumonia cases. Over the span of three months, 4 (3.8%) COVID 19 positive children died of which one diagnosed as COVID Pneumonia, and the rest 3 death were associated with additional risk factors like Dengue fever, Leukemia and Complex heart disease (Table 1).

We found the disease was more prevalent as well more severe in younger age group (<5years) compared to higher age group (5-12 years) and infants being the most affected (30.5%), (Table 3). The mean hemoglobin among pediatric study population was 10.68 gm% (SD=1.45). There was a predominance of Leucocytosis (Mean: 16255±5302 SD) and Thrombocytosis (Mean 313145±141235 SD) with raised CRP (Mean 49.13±36 SD). Inflammatory markers D-Dimer, LDH, Procalcitonin were raised in 4 (3.8%), 14 (13.3%) and 9 (8.6%) children respectively. We treated most children conservatively, HCQS/antiviral not used, Steroids given in 9 (8.6%) children and all 4 PIMS -TS children treated by IVIg±steroids (Table 2).

Out of total 128 newborns admitted we had 63 (49%) inborn and 65 (51%) outborn with almost equal sex distribution (M: F=67:61). 42 neonates were tested positive (RT PCR) being delivered from 128 COVID 19 positive mother, so an overall disease transmissibility of 32% (both Inborn and Outborn) recorded and the transmission was more among outborn babies (OB: IB=22:10). Disease transmission rate was somewhat low among low birth weight (25%) and preterm babies (3%) compared to term (29%) and (23%) normal/higher birth weight babies.

Among inborn babies we found no significant difference in disease transmission on mode of delivery but among Outborn babies vaginal delivery born babies were more affected compared to LUCS (VD:LUCS 30:13.8) born neonates (Table 4). Day 3 was the minimum age when we detected swab positive among newborns. Most of the neonates were asymptomatic (84%) and we practiced rooming in most cases (70%). Newborns were discharged along with the mother's release from Obstetrics department.

A total of 20 (15.6%) neonates of the neonatal cohort went ill and shifted to NICU of which 6 (4.6%) neonates were COVID 19 positive and rest 14 (10.9%) were swab negative. Concomitant diseases we found were Birth asphyxia (n=5) and sepsis (n=15) which was present in both COVID positive and negative group. Thermal instability, food intolerance, convulsion and respiratory distress were the commonest clinical findings. Abnormal Chest X-ray was found in 10 neonates out of which 4 (3.12%) were swab positive and they were diagnosed as isolated COVID Pneumonia. CRP was raised in most of the sick neonates (n=16/20) with a routine blood picture not greatly affected by COVID 19 infection. Finally 5 (3.9%) newborns required mechanical ventilation and 2 newborn died, both were Covid negative of which one

died due to complex heart disease and other due to sepsis. Thus we recorded a zero Covid death among neonates.

Table 1: Epidemiological and clinical profile of children with covid-19 (n=105).

Variable	Categories	Frequency (%)
Duration of stay	<7 days	25 (23.8)
	>14 days	14 (13.3)
	7-14 days	66 (62.9)
Age in months	<12	32 (30.5)
	13-60	41 (39)
	>60	32 (30.5)
Sex	Female	46 (43.8)
	Male	59 (56.2)
Family members affected	Yes	80 (76.2)
	No	25 (23.8)
Symptoms/ Sign	Fever	60 (57.1)
	Cough/cold	25 (23.8)
	Dyspnea	22 (21)
	CNS/convulsion	21 (20)
	Diarrhoea	9 (8.6)
	Sore throat	8 (7.6)
	Headache/body-ache	5 (4.8)
	PIMS	4 (3.8)
	Skin Manifestation	11 (10)
	Shock	7 (6.7)
	Comorbid conditions	Malignancy
CNS Malformation		9 (8.6)
Cong Heart disease		7 (6.7)
Chronic kidney disease		6 (5.7)
GI comorbidity		5 (4.8)
Infection-scrub		5 (4.8)
Chronic lung disease		2 (1.9)
Symptom grade	Asymptomatic	35 (33.3)
	Mild	53 (50.5)
	Moderate	8 (7.6)
	Severe	9 (8.6)
CXR/CT scan	Infective changes	14 (20)
Blood C/S	Positive	4 (3.8)
D Dimer	Rised (>1)	4 (3.8)
Procalcitonin	Positive (>2)	9 (8.6)
LDH	Raised (>45)	14 (13.3)
Management	Anttibiotics	53 (50.5)
	Steroids	9 (8.6)
	IVIg	4 (3.8)
PICU admission		14 (13.3)
Oxygen Supplementation		13 (12.4)
Mechanical ventilation		5 (4.8)
Outcome	Death	4 (3.8)
	Discharge	101 (96.2)

Table 2: Laboratory investigation of children with COVID-19 infection.

Values	Duration of stay	Age in months	HB (g/dl)	TLC (/cmm.)	TPC (/cmm.)	CRP (mg/dl)	FERRITIN (mic/L)	
Mean	10.11	48.07	10.68	16255.14	313145.52	49.13	147.75	
Median	10	36	11	10000	320000	32	145	
Std. Deviation	4.935	41.558	1.458	53022.882	141235.89	36.036	35.62	
Minimum	2	1	6	2160	2000	7	90	
Maximum	33	144	13	552000	864500	144	400	
Percentile s	Q1	8	11	10	7580	238000	20	120
	Q3	12	72	12	14000	359500	76.5	162.5

Table 3: Correlation of symptom grade with other parameters.

Parameters		Symptom grade				Total	Chi Square	P-value	
		Asymptomatic	Mild	Moderate	Severe				
Duration of stay	<7 days	Count (%)	6 (17.1%)	14 (26.4%)	2 (25%)	3 (33.3%)	25 (23.8%)	4.6	0.6
	7-14 days	Count (%)	26 (74.3%)	32 (60.4%)	4 (50%)	4 (44.4%)	66 (62.9%)		
	>14 days	Count (%)	3 (8.6%)	7 (13.2%)	2 (25%)	2 (22.2%)	14 (13.3%)		
Age in months	<12	Count (%)	11 (31.4%)	14 (26.4%)	3 (37.5%)	4 (44.4%)	32 (30.5%)	4.4	0.6
	13-60	Count (%)	14 (40%)	19 (35.8%)	4 (50%)	4 (44.4%)	41 (39%)		
	>60	Count (%)	10 (28.6%)	20 (37.7%)	1 (12.5%)	1 (11.1%)	32 (30.5%)		
Outcome	Alive	Count (%)	35 (100%)	53 (100%)	8 (100%)	5 (55.6%)	101 (96.2%)	44	0
	Dead	Count (%)	0 (0%)	0 (0%)	0 (0%)	4 (44.4%)	4 (3.8%)		

Table 4: Epidemiological and clinical profile of neonates (n=128).

Variable		Inborn		Chi square	P value	Outborn		Chi square	P value
		RTPCR				RTPCR			
		Positive	Negative			Positive	Negative		
Age in days	≤ 7	12 (19.05%)	39 (61.9%)	1.42	0.49	28 (43.08%)	35 (53.85%)	3.32	0.35
	8-14	1 (1.59%)	10 (15.87%)			0 (0%)	1 (1.54%)		
	>14	0 (0%)	1 (1.59%)			1 (1.54%)	0 (0%)		
Sex	Male	5 (7.94%)	24 (38.1%)	0.38	0.54	15 (26.79%)	23 (41.07%)	0.98	0.32
	Female	8 (12.7%)	26 (41.27%)			14 (25%)	13 (23.21%)		
Birth weight	LBW	2 (3.17%)	20 (31.75%)	2.75	0.1	10 (15.38%)	15 (23.08%)	0.35	0.55
	Normal	11 (17.46%)	30 (47.62%)			19 (29.23%)	21 (32.31%)		
Gest age	Preterm	1 (1.59%)	14 (22.22%)	2.35	0.13	3 (4.62%)	9 (13.85%)	2.29	0.13
	Term	12 (19.05%)	36 (57.14%)			26 (40%)	27 (41.54%)		
Delivery mode	Vaginal Delivery	5 (7.94%)	18 (28.57%)	0.03	0.87	20 (30.77%)	18 (27.69%)	2.38	0.12
	LSCS	8 (12.7%)	32 (50.79%)			9 (13.85%)	18 (27.69%)		
Feeding/nutrition	EBF	6 (9.52%)	20 (31.75%)	2.76	0.43	14 (21.54%)	17 (26.15%)	1.59	0.66
	IVF	0 (0%)	7 (11.11%)			0 (0%)	1 (1.54%)		
	KSF	7 (11.11%)	21 (33.33%)			14 (21.54%)	15 (23.08%)		
	OGF	0 (0%)	2 (3.17%)			1 (1.54%)	3 (4.62%)		
Rooming in		8 (28.6%)	20 (71.4%)	1.94	0.16	22 (53.7%)	19 (46.3%)	3.68	0.06
Antibiotics given		1 (10.0%)	9 (90.0%)	0.82	0.37	3 (50.0%)	3 (50.0%)	0.08	0.78
Oxygen supplementation		0 (0%)	5 (100%)	1.41	0.24	1 (33.3%)	2 (66.7%)	0.16	0.69
NICU admission		1 (8.3%)	11 (91.7%)	1.37	0.24	4 (6%)	4 (6%)	0.11	0.74
Mechanical ventilation		0 (0%)	1 (100%)	0.26	0.61	1 (25.0%)	3 (75.0%)	0.66	0.42
Outcome	Alive	13 (20.63%)	49 (77.78%)	0.26	0.61	29 (44.62%)	35 (53.85%)	0.82	0.37
	Dead	0 (0%)	1 (1.59%)			0 (0%)	1 (1.54%)		

Table 5: Clinical profile and lab investigation of sick neonates.

Parameter		COVID-19 Positive sick newborn (n=6)	COVID-19 Negative sick newborn (n=14)
Respiratory distress		4	6
Thermal instability		5	8
Cyanosis		4	4
Feed intolerance		6	9
Convulsion		Nil	3
Total leucocyte count (per cmm.)	Range	10700-21460	4800-14700
	Median	18600	10860
Lymphocyte count (per cmm.)	Range	1080-3700	1200-8800
	Median	2600	6400
Platelet count (per cmm.)	Range	2,10,000-3,20,000	1,20,000-2,80,000
	Median	290000	178000
CRP raised		6	10
Blood culture positive		Nil	3
Chest Xray (pneumonia)		4	6
Birth asphyxia		2	3
Sepsis		6	9

DISCUSSION

India is at the mid stage of COVID 19 pandemic and the surge of pediatric and newborn patients started couple of months back with the onset of rapidly spreading adult infection. That's why till date very few publications are there on Indian children. In a study by Sarangi et al, (N=50) conducted at Pune Maharashtra which is the most affected state in India, found the median age of hospitalized pediatric population was 6 years, which is close to the value of 7 years (median age) in another study by Dong et al conducted in China (N=2143).^{6,7}

However the median age value is 3 years in our study, which is less in comparison to their studies, probably due to their inclusion of more number of children of higher age group (till 18 years) whereas we included children till 12 years due to our hospital admission policy. Both the studies found almost equal male, female distribution which is identical to our study. Dong et al found that younger children particularly infants were more vulnerable to Covid 19 infection, which is similar to our findings, as 73 (69%) children of our cohort belong to less than 5 years age group and of them most were infants 32 (30.5%).

The disease is more severe in younger age group as we got 88% of moderate to severely affected children were from less than 5 years age group (Table 3) compared to 12% of elderly children. Sarangi et al reported about 90% of their COVID 19 infected children had a positive history of household contact, which is comparable with our study findings of 76.2% positive household contact. They also reported 58% children with COVID 19 infection is asymptomatic while 40% had mild symptoms,

more or less similar to our findings of 33.3% asymptomatic and 50.5% mildly symptomatic.⁶

However Dong et al found 4.4% asymptomatic, 50.9% mildly symptomatic, but a large number with moderate severity illness, which was 38.8%. This could be due to the majority of their children were from Hubei province close to the epicenter of pandemic and also they conducted the study at the early part of pandemic when the lethality of SARS-CoV-2 virus was maximum, which they also mentioned in their research article that from late February 2020 they noticed a decline in pediatric cases.⁷ We recorded 7.6% children were with moderate severity infection, of which 8.6% was critically ill. Whereas we got 38% children admitted with comorbidities, Sarangi et al found only 2% children with additional comorbidities.

Harman et al found 8 (41%) COVID 19 positive children admitted with comorbidities in King's College Hospital, London, UK, between February 25, 2020 and April 28, 2020 and they were mostly Cerebral Palsy, and Prematurity with single cases of Wilson's disease and dilated cardiomyopathy.⁸ Our findings on comorbidities were different, like Malignancy being the commonest comorbidity along with renal disease, congenital heart diseases as well as CNS diseases like cerebral palsy, epileptic encephalopathy. In another multicentric study at North America by Shekerdeman et al found that 50% of the admitted COVID 19 positive children at several PICUs of city had comorbidities. 39% children do required mechanical ventilation with 2 (4%) children died and 5 (11%) were critically ill till study was published.⁹

We recorded a total death of 4 (3.8%) children of which one died from COVID pneumonia, and of the rest three deaths were associated with comorbidities, like

Leukemia, CHD and the last one associated with Dengue Hemorrhagic Fever. We also got COVID patients with concomitant infections like Dengue fever, Scrub Typhus, Enteric fever which altered their clinical course. All the Covid positive children with Scrub Typhus and Enteric fever survived but there was a death with a Dengue positive child. We treated most of the COVID 19 infected children conservatively and antibiotics required in 50.5% cases.

We didn't used HCQS or any antiviral medications. Steroids was used in 8.6% children mostly in children with shock, multisystem inflammatory syndrome and Covid pneumonia. IVIg gave good response in all PIMS-TS children and patients with raised D Dimer got Low molecular weight heparin. Bhat et al observed that by 13th May 2002 more than 300 cases of PIMS-TS were reported in Europe and North America, but not a single case in India till then.¹¹ As the pandemic consolidates more and more cases of MIS-C getting reported from several parts of country, one such recent article published by Jain S et al from Mumbai, India of a cluster of 23 multisystem inflammatory patients related to COVID 19 infection from four tertiary hospitals.¹⁰

They used steroids (96%) and IVIg in 65% cases with an excellent recovery and reported one death only. Riphagen et al reported a cluster of 8 children all admitted with Hyperinflammatory shock following COVID 19 infection, whereas we got 2 similar cases and the rest Shock presentation were due to Dengue and Sepsis.¹²

We got no evidence of vertical transmission of COVID-19 from mother to newborn as swab positive among newborns were recorded from Day 3 onwards, however we don't have the facility of conducting RT-PCR of amniotic fluids, which is another direct evidence of vertical transmission. We recorded at institution level (Inborn) maternal to neonate disease transmissibility 20% in comparison to 8% in western literature.¹⁵

We noted a lower incidence of disease transmission both in Preterm (3%) and Low birth weight (25%) babies compared to term (29%) and normal birth weight babies (23%) which was probably due to high alertness and careful Parenting for LBW and preterm babies from Zeng et al in Wuhan, China found 3 neonates affected with Covid 19 being delivered from 33 Covid19 positive mothers of which 1 (3%) was preterm and rest were healthy term baby.¹⁴ All of their 3 babies (100%) were symptomatic whereas here in our study population 6 (4.6%) neonates with Covid positive status, were symptomatic.

Strength

The strength of our study is a relatively larger cohort of 105 children and 128 neonates in a dedicated Covid hospital and being a referral center we got a mixed

demography of a larger area. We included only Covid positive cases in our study to reduce biasness.

Limitations

There are limitations, like a larger sample size required to validate our findings. Being in mid stage of pandemic we couldn't cover the diversified presentations and unprecedented outcome of the disease with mutational changes of the virus from day to day. More number of PIMS are getting reported at the plateau phase of pandemic which we couldn't report in our study.

CONCLUSION

Children of all age groups can be affected but it's the younger age group are mostly and more severely affected by COVID 19 infection. Overall the disease carries less mortality in pediatric population and like adults comorbidities and concomitant infections could alter disease outcome. Of late PIMS-TS a new challenge for pediatrician which is more common in elderly children, however it had a good prognosis with immunosuppressive therapy. Newborns had good outcome with COVID19 infection, so breast feeding should be continued as well as rooming with mother should be practiced following COVID prevention protocol.

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