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Original Research Paper

Paediatrics

CLINICAL CHARACTERISTICS AND LABORATORY PROFILE OF CHILDREN WITH COVID-19: AN OBSERVATIONAL STUDY

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ABSTRACT

Background: The Novel Corona virus (COVID-19) becomes a pandemic and continues to effect large population all over the world. The aim of this study is to describe the clinical and laboratory profile of children with COVID- 19 in India.

Method: A total of 71 pediatric COVID positive cases are included and their Epidemiological, clinical, laboratory, and radiological characteristics and treatment and outcomes data were obtained with data collection forms from electronic medical records and history given by patients admitted in S.M.S. Medical College Jaipur India. Patients were tested for COVID-19 by real time reverse transcription polymerase chain reaction (RT-PCR) assay.

Results: In this study the boy to girl ratio being 1.3:1. The mean age was 12 year. Out of 71 children 12 were Symptomatic (16%) and 59(84%) were Asymptomatic, the most common symptom at onset of illness was fever (15.49%) followed by respiratory distress (7.04%). Cough, diarrhea and pain abdomen were found in (4.2%) followed by headache, cyanosis, vomiting and hepatomegaly and convulsion in (1.4%) children. Lymphopenia occurred in 46 (64%) children, relatively neutrophillia found in 5 children. All critical cases have Thrombocytopenia, deranged RFT and elevated CRP. BCG vaccine was received by 97.2%. 8 Symptomatic and 3 asymptomatic children showing bilateral patchy airspace consolidation mostly at periphery of lungs, Peribronchial thickening and ground glass opacity in their chest X-ray film

Conclusion: The Asymptomatic cases and mean age is different form studies of other countries. Gastrointestinal symptom may be the initial presentation and it may be more fatal.

KEYWORDS : Children, Clinical Characteristics, Clinical Profile, Corona Virus, COVID-19, Laboratory Finding

INTRODUCTION

In December 2019, an epidemic caused by Severe Acute Respiratory Syndrome Corona virus-2 (SARS-CoV-2) infection has occurred in Wuhan, Hubei Province, China, and it had quickly spread from Wuhan to the other areas in China and abroad[1, 2, 3, 4]. World Health Organization named this novel corona virus disease, COVID-19 and declared it pandemic on 11th march 2020. In India COVID-19 total cases till today were around 80,000 out of these cases 2700 were died. India became the 11th country affected by this epidemic .In Rajasthan total no. of cases were around 3000 and 77 deaths.

Corona viruses are included in the family *Coronaviridae*, order *Nidovirales* .[5] Corona viruses are enveloped, single-stranded, zoonotic RNA viruses. They can infect many animals like bats, camel, livestock, and birds , in which it may cause serious respiratory, enteric, cardiovascular and neurologic disease.[6,7] In humans, CoVs mostly cause respiratory and gastrointestinal symptoms ranging from the common cold to more severe disease such as bronchitis, pneumonia, severe acute respiratory distress syndrome (ARDS), coagulopathy, multi-organ failure and death.[8,9] Human corona viruses (HCoVs) have also been associated with exacerbations of chronic obstructive pulmonary disease,[10] cystic fibrosis[11] and asthma[12,13]. There are four subtypes of CoVs as *Alphacoronaviruses* and *Betacoronaviruses* (inbats,rodents, human) and *Gammacoronaviruses* and *Deltacoronaviruses* (in birds).[14,15,16] . This virus is capable of rapid mutation and recombination leading to novel CoVs .In year 2002 in china it emerged as severe acute respiratory syndrome corona virus (SARS-CoV) transmitted from civet cats or bats to humans.[17,18,19] Another novel CoVs emerged in Saudi Arabia in 2012, Middle East respiratory syndrome corona virus (MERS-CoV), which is transmitted from dromedary camels to humans.[20,21] in 2019 novel CoV (SARS-CoV-2), which originated in ,China and is currently causing outbreaks globally, is a novel *Betacoronavirus* belonging to the lineage B or subgenus sarbecovirus, which includes SARS-CoV.[22] Sequencing shows that the genome is most closely related 87%–89% nucleotide identity to the bat SARS-related CoV found in Chinese horseshoe bats (bat-SL-CoVZC45).[22,23] . A local seafood and animal market was identified as a potential source. Symptomatic and asymptomatic humans infected with SARS-CoV-2 from whom the virus can spread to others through respiratory droplets or direct contact.[22] From Wuhan city SARS-CoV-2 has spread to other Chinese cities and became a global pandemic. The virus enters respiratory epithelial cells by attaching to angiotensin converting enzyme-2 (ACE-2) via S-protein; ACE-2 is also a receptor for SARS-CoV-1[24]. Cellular entry is facilitated by proteolytic cleavage of ACE-2 by transmembrane serine protease-2[25]. Affinity of SARSCoV-2 for ACE-2 is approximately 10–20 times higher than SARS-CoV-1, which could explain higher infectivity of SARS-CoV-2. ACE-2 is found on apical membranes of nasal, oral, nasopharyngeal and oropharyngeal mucosal epithelium, alveolar epithelium, endothelial cells of blood vessels and heart, renal tubules,

and enterocytes in small intestine[26]. CD-147 (target for antibody, Meplazumab) and glucose regulated protein-78 are newly described receptors of SARSCoV-2 for cellular entry[27,28].

The closest RNA sequence is that of Bat corona virus, hence are thought to be primary source. Phylogenitically 2 strains are found, L type – accounting for 70% of cases and were found in early days of spread in china and S type- accounting for 30% cases. The possibility of COVID should be considered in patients with fever and respiratory tract symptoms with epidemiologic risk factors. Compared to adults, the number of reported pediatric patients is limited[29,30]. Mortality rate among diagnosed case (case fatality rate) has a variable range, true overall mortality rate is uncertain as the total no of cases including undiagnosed persons with milder illness is unknown.

The Aim & Objectives of the study is to assess the Age distribution, Clinical and laboratory profile and treatment Outcome of Children with COVID- 19 admitted in SMS Medical College & Hospital, Jaipur.

MATERIALS AND METHOD

Present study is observational study carried out in SMS Medical College &Attach hospital, Jaipur. All COVID-19 conformed children in the age range of 0- 18 year admitted in J.K Loan / SMS Hospital from 4th April to 4th May were included in this study. Detail history of every patient was taken including – medical history, epidemiological history, underlying diseases, clinical symptoms were assessed. Clinical examination, laboratory data and radiological characteristics were obtained.

Data collection- The medical records of patients were analyzed. Epidemiological, clinical, laboratory, and radiological characteristics and treatment and outcomes data were obtained with data collection forms from electronic medical records and history given by patients. All data were reviewed included demographic data, medical history, exposure history, underlying co morbidities, symptoms, signs, laboratory findings; chest X ray, and treatment measures (antiviral therapy, Anti-retroviral therapy, anti-malarial therapy, respiratory support) and BCG vaccination status. Real-Time Reverse Transcription Polymerase Chain Reaction (RT-PCR) Assay was done for Throat swab samples were collected for extracting from patients suspected of having COVID-19 infection.

Observation

Table No. 1 Demographic and Epidemiological Profile of Patients with COVID-19

S.No	Characteristics		No. of cases	Percentage
1	Gender	Male	40	57%
		Female	31	43%
2	Age Group			
		Neonate	1	1%
		1- 6 month	1	1%
		6 Month to 3 year	6	9%
		3 - 6 year	5	7%
		6 -10 year	24	34%
		More than 10 year	34	48%
3	Epidemiological History			
		Travel History	0	0%
		Contact Within Family	70	99%
		Unknown	1	1%

Table No. 2 Symptom Wise Distribution of COVID 19 Cases (n=71)

S.No.	Symptomatic/Asymptomatic	No. of Cases	Percentage
1	Symptomatic	12	16%
2	Asymptomatic	59	84%
3	Grand total	71	100%

Table No.3 Clinical Presentation of COVID 19 Symptomatic Cases (n= 12)

S.No.	Symptom	Present in No. of cases	Percentage	Percentage of total 71 cases
1	Fever	11	91.6%	15.49%
2	Respiratory Distress	5	41.6%	7.04 %
3	Abdominal Pain	3	25%	4.2%
4	Cough	3	25%	4.2%
5	Diarrhea	3	25%	4.2%
6	Edema	1	8.3%	1.4%
7	Headache	1	8.3%	1.4%
8	Cynosis	1	8.3%	1.4%
9	Vomiting	1	8.35%	1.4%
10	Convulsion	1	8.3%	1.4%

Table No.4 Selected Laboratory Parameters of COVID 19 cases (n=71)

S.No.	Lab Parameter	Increased	Decreased	Normal
1	WBC	3	5	63
2	Lymphocytes	0	46	25
3	Relative Neutrophil Count	5	6	60
4	Platelets	2	7	62
5	Urea	3	0	68
6	Creatinine	1	0	70
7	SGOT	6	0	65
8	SGPT	3	0	68
9	PT-INR	2	0	69
10	CRP	2	0	69
11	Sodium	0	0	71
12	Potasium	0	0	71
13	Chloride	49	0	22

Table No. 5 Status of BCG Vaccine in COVID-19 Admitted Cases (n=71)

S.No.	BCG Vaccine	No. of Cases	Percentage
1	Yes	69	97.2%
2	No	1	1.4%
3	Not Known	1	1.4%

Table No. 6 Status of outcome of COVID 19 Cases Admitted (n=71)

S.No.	Status of COVID 19	No. of Cases	Percentage
1	Discharged/ Recovered	68	95.7%
2	Death	3	4.3%
3	Grand Total	71	100%
	Place of Admission		
1	Wards	66	93%
2	ICU	5	7%
	On oxygen support	2	2.8%
	on Ventilator support	3	4.2%
3	Grand Total	71	100%

RESULT

1. Demographic and Epidemiological Profile

A total of 71 patients with COVID-19 were included in the study. There were 40 (57%) males and 31 (43%) female with the boy to girl ratio being 1.3:1 (table no.1). The mean age was 12 year , children aged > 10 year was 34 (48%), 6-10 year 24 (34%), 3-6 year 5 (7%), 6 month- 3 year 7(9%) and lees than 6 month only one patient (1%) respectively one neonate found affected in

this study (Table no.1). 70 patients had a definite history of contact only one patient did not have such history. 90% of affected children were from the Ramganj area of jaipur which was a epicenter of the jaipur city. All the children became infected by the contact within family (Table no.1).

2. Clinical characteristics

Table no. 2 showing that out of 71 children 12 were Symptomatic (16%) and 59 (84%) were Asymptomatic having no symptom of COVID-19. Out of the 12 children the most common symptom at onset of illness was fever (11, 15.49%) followed by respiratory distress (5, 7.04 %). Cough, diarrhea and pain abdomen were found in 3 (4.2%) followed by headache, cyanosis, vomiting and hepatomegaly in 1(1.4%) children. Convulsion was found in only one (1.4%) children.

3. Laboratory Parameter

Table no.3 showing the selected laboratory parameter of all 71 children admitted in the hospital with COVID-19 positive. These test revealed that white blood cell counts were normal in 63 cases and decreased in 5 cases, 3 children shows an increased level of WBC counts. Lymphopenia occurred in 46 children, 25 have normal lymphocyte count no children have increased lymphocyte counts. Relatively neutrophillia found in 5 children, normal in 60 and 6 children having neutrophill counts below normal. Thrombocytopenia found in 7 children, 62 children have normal platelet counts and 2 children shows increase platelet count also. Urea creatinine increased in 3 and 1 children respectively. Liver enzyme SGOT and SGPT are elevated in 6 and 3 children rest having normal value. CRP level was increased in two children. The electrolyte study show that sodium and potassium were normal in range in all the cases but chloride level was found elevated in 49 children. PTINR was found raised in 2 children.

4. BCG Vaccine Status

Out of total 71 children 69 (97.2%) received BCG Vaccines, One child was not immunized by BCG and one child BCG Vaccination status was not known. (Table no.5)

5. Treatment and Outcome

All the children were admitted in SMS Medical College & Hospital , most of the children 66 (93%) were admitted in general ward only ,5 (7%) of total patient were shifted to ICU (Table no.6) .All the symptomatic patients (12) received HydroxyChloroquine . 3 patients became critical and require ventilator support (Table no.6) and one of them receive HCQ and only one dose of anti viral Ritonavir plus Lupinavir, one patients received HCQ and one newborn do not receive either HCQ or antiviral because of short duration of stay in the hospital. out of 71 patients 68 were recovered or discharged except for 3 critical cases who did not survive (Table no.6)

DISCUSSION

This study included 71 Covid- 19 positive cases with the median age being 12 year which is older than reported by Xia et al[31] (2year) ,Fang et al[32], Liu et al[33] (3 years) and. ,Cai et al[34] ,Wang et al[35] , Jiang et el[36](7 year). This may be due to high prevalence of viral infection in India in children below 6year and there may be some cross immunity with other family of corona virus / other virus and novel COVID- 19. The male to female ratio was 1.3:1 in this study similar ratio was found in study conducted by Xia et al ,Jiang et al and Fang et al (1.27:1) ,but female are more commonly affected in study conducted by Wang et al.(1:1.1). Total 1100 positive Cases and 44 death in jaipur city out of that 106 case were belong to pediatric age group that is 10% of total cases, admitted in different hospital of jaipur city were higher than the study conducted in china by Wu Z et al[37]., they reported total 44672 cases out of which only 2.2% are below age of 19 years. We included 71 cases out of 106 which were admitted in SMS Medical College. In this study out of 71 children 59 were Asymptomatic (84%) and 12 (16%) Symptomatic children 7 (9% of total) had milder disease, only 5 (7%) children required ICU care and 3(4.2%) patients died. Asymptomatic cases and mortality both are higher in this study as compare to Xia et al (10% asymptomatic, no mortality) and Wang et al study where the asymptomatic cases are 23% and Mortality 0% in pediatric age group and 4.3% in adult cases. This study reported that 7% cases require ICU care that is similar to study conducted by Fang Zheng (8%). The difference in mortality and more Asymptomatic cases may be due to difference in the geographical and Environmental condition or may be due to genetic mutation in the virus and may be due to high coverage of BCG vaccine. In a randomized trial, BCG vaccination was associated with reduced viremia with experimental attenuated yellow virus strain infection and epigenetic changes in monocytes[38]. IL-1 response up regulation correlated with reduction of viremia[39]. BCG vaccination has been associated with decrease in acute upper respiratory infection (URI) in elders and decreased mortality in under-5 children . Following BCG vaccination in adults, there is enhanced pattern recognition receptors expression in monocytes and elevation of Th1 and Th17 immune response to non-mycobacterial stimulation, up to 1 y following vaccination[40]. The most common symptom was fever found in 11 (15.4% of total cases) patients, followed by respiratory distress in 5 patients (7% of total cases) and cough in 3 cases (4% of total cases) as initial presentation in this study which was in contrast to Fang et al study where fever was most common symptom in 13out of 25 children (52%), followed by cough in 11(44%) children. Wang et al, noted fever in 65% cough in 45% cases, Xia et al also recognized fever in 60%, cough in 65%. In this study Gastrointestinal symptom were present as pain abdomen and diarrhea in 3 cases (4% of total) and vomiting in1 case(1.4%) which are lesser than studies of Fang et al (diarrhea 12%, abdominal pain and vomiting in 8% of cases),Wang et al, and Xia et al ,also reported GI Symptom in 10% and 15% children respectively. All the three cases who were died were admitted in the hospital with fever and gastrointestinal symptom (pain abdomen, diarrhea, vomiting) as a initial presentation later on they develop respiratory distress, renal failure and MODS were similar to the finding of Wang et al. reported that 10.1% of COVID-19 patients initially presented with diarrhea and nausea 1 to 2 days before the development of fever and dyspnea. The reason for this phenomenon might be related to the distribution of receptors and the transmission, COVID-19 infects the host via the receptor ACE2 [40,41]. ACE2 is abundantly expressed in alveolar type I and type II epithelial cells and small intestinal epithelial cells. This suggests that SARS-CoV-2 might infect patients not only through the respiratory tract in the form of air droplets, but also through the digestive tract. Normally Children do not pay much attention to hand hygiene so the likelihood of infection through the digestive tract by contact or fecal–oral transmission is likely to be significantly greater for children than for adults, and gastrointestinal symptoms as the initial presentation may be more common in children. In this study leukocyte count were normal in 63 (88%) cases decrease in 5 (7%)and increase in 3 (4.2%)cases supporting the study of Wang et al who detected 83% cases with normal leukocyte count . Leukocytosis is noted in a minority of COVID cases and appears due to bacterial super infection. Lymphopenia is noted in 46 (64%) cases and normal in 25(35%) cases, Lippi et al[42], reported that 35 to 75 % of patients develop lymphopenia and it is more severe in critical patients, it is due to defective immune response to the virus. This may be due to some geographical variability, viral genomic mutation and the immunological response to the virus by different races of human. Thrombocytopenia found in 7(10%) cases. 2 (2.8%) cases showing thrombocytosis . Lippi et al[42] also found that thrombocytopenia is a marker of consumption coagulopaty in critical patient of COVID- 19, we also noted that all 3 critical cases have thrombocytopenia. Out of the total 71 cases 8 symptomatic and 3 asymptomatic

children which were showing bilateral patchy airspace consolidation mostly at periphery of lungs, Peri bronchial thickening and ground glass opacity in their chest X-ray film. Tu hsuan chang[43] et al also found that out of 55 children 14 (27%) having completely normal CT scans despite having Covid infection 16(31%) having patchy consolidation and 25 having ground glass opacity. Chan et al and Jiang et al also reported two children who were Asymptomatic but having ground glass opacity in chest CT scan similarly we also noted 3 cases having abnormal CXR but they were Asymptomatic.

CONCLUSION

This study showed that in spite of Covid-19 positive the Asymptomatic cases are more and having more epidemiological risk to the society so they should be isolated or quarantined. In children not only the respiratory symptom are the initial presentation but gastrointestinal symptom may be the initial presentation and it may be more fatal. Lymphopenia and Thrombocytopenia and deranged coagulation profile show some correlation with critical illness.

LIMITATIONS

It is a different disease so the detail case description and clinical courses are limited and most of the children were Asymptomatic so the long term outcome and further follow-up should be needed. Risk factor and protective factor for Covid-19 in children are still unknown.

CONFLICT OF INTEREST

None of the authors have conflict of interest.

ABBREVIATIONS -

BCG- Bacille Calmette- Guerin, **SGOT**- Serum Glutamic Oxaloacetic Transaminase, **SGPT**- Serum Glutamic- Pyruvic Transaminase, **CRP**- C reactive protein, **PTINR**- Prothrombin Time and International Normalized Ratio

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