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Evaluation of Clinical Presentations of Covid -19 in Pediatric Patients in the Child Central Teaching Hospital

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ABSTRACT

Background: The coronavirus belongs to a family of viruses that may cause various symptoms such as pneumonia, fever and breathing difficulty. These viruses are common in animals worldwide, but very few cases have been known to affect humans.

AIM of the study: To increase the awareness of different patterns of symptoms and signs of covid -19 in children.

Methods: this is prospective study of patients those admitted to the child central teaching hospital and confirmed covid 19 infection by real time polymerase chain reaction from twentieth of march 2020 to the first of April 2021. patients sex, age, symptoms, signs, duration of the symptoms before the admission to the hospital crowdedness, their status of vaccination in particular BCG vaccine, Investigations (white cell count, chest Xray) and the fate of those patients. Patients with chronic diseases also included. The study group had a postive contact with confirmed covid-19 relatives that either living with them or had visited them.

Results: one handered twenty patients with confirmed covid-19 infection admitted to (central teaching hospital for pediatrics) during the study period, noticed that there was 58 male (48%) and 62 females (52%), patients had different age groups, most affected age group was 1-5 years 34 patient (28%) and 5-10 years (28%) also. The most common signs and symptoms were fever 78 patient (65%), malaise 50 patient (41%), Cough 45 patient (37%), dyspnea 37 patient (30%) and frequent bowel motion 38 patient (31%). Sign and symptom found to be significantly related to either death or admission to the respiratory care unit like cyanosis (4.2% p-value 0.0001), Fever (65% p-value 0.03), disturbed level of consciousness (2.5% p-value 0.035), frequent bowel motion (31.7% p-value 0.045). Ten patients (8%) needed respiratory support, About two third of patient (62%) lives in a crowded environment and (62.5%) reported that they had contacts with confirmed COVID 19 infected patients. Twenty nine patient (24.2%) those with COVID-19 virus infection had comorbid conditions. The result of chest Xray of 63 patient (52.2%) with ground glass appearance, Consolidation was found to be the most related chest x-ray finding related to death and respiratory care unit admission about (14.2% p-value 0.0001). There were two peaks of signs and symptoms like (fever, malaise and vomiting) during the summer months especially August followed by a higher peak in the winter months especially January. Frequent bowel motion peak was in the winter months especially January and February.

Conclusion: The infection had two peaks during the year. Females slightly more than males. Fever, malaise, cough, shortness of breath and frequent bowel motion were the prevalent symptoms. duration of the occurance of the signs and the symptoms mainly 3 days. About two thirds live in crowded areas and with contact to infected patient. The children have mild symptoms with highly recovery rate. Only minority of patients was admitted to respiratory care unit for ventilatory support.

Introduction

The coronavirus belongs to a family of viruses that may cause various symptoms such as pneumonia, fever and breathing difficulty [1]. These viruses are common in animals worldwide, but very few cases have been known to affect humans. The World Health Organization (WHO) used the term 2019 novel coronavirus to refer to a coronavirus that affected the lower respiratory tract of patients with pneumonia in Wuhan, China on 29 December 2019 [2,3,4]. The WHO announced that the official name of the 2019 novel coronavirus is coronavirus disease (COVID-19) [4].

In response to the outbreak, the Chinese Center for Disease Control and Prevention dispatched a rapid response team to accompany health authorities of Hubei province and Wuhan city to conduct epidemiological and etiological investigations.

Pathophysiology

Severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) infection is characterized by an initial cytokine storm that can result in acute respiratory distress syndrome and macrophage activation syndrome. This initial phase is then followed by a period of immune dysregulation, which is the major cause of sepsis-related fatalities. [5]

Differences between adult and pediatric disease are likely the result of changes within both immune function and the angiotensin-converting enzyme (ACE) 2 receptor, used by the virus to enter type II pneumocytes in the lung. Decreases in ACE2 seen in animal models of aging result in changes in neutrophil influx and resultant lung injury. Thus, immunosenescence and changes in inflammatory responses with age likely account for the different spectrum and severity of disease in children versus adults and, furthermore, in neonates versus older children. The profound lymphopenia seen in patients with COVID-19 is likely the result of T lymphocyte infection and death that occurs as SARS CoV-2 infects these cells. (6)

As the infection progresses, with acceleration in viral replication and epithelial-endothelial injury, the inflammatory response is accentuated. Interstitial mononuclear inflammatory infiltrates and edema followed by hyaline membrane formation occurs leading to acute respiratory distress syndrome (ARDS). These changes may be visible as ground glass opacities on a CT scan. Further injury to the endothelial tissues results in microthrombi formation and can lead to thrombotic complications such as pulmonary embolism, venous thrombosis, and thrombotic arterial complications as seen in severely ill patients. These complications have been seen more in adult than in pediatric patients, although they have been reported in the latter as well. Secondary sepsis in these individuals further contributes to the severity of the illness.

Physical examination

The significant number of children with SARS-CoV-2 infection who are asymptomatic but the children with confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection had the most common signs and symptoms like cough sore throat and fever. Other signs and symptoms included the following: Diarrhea, Fatigue, Rhinorrhea, Vomiting, Nasal congestion and Tachypnea. [4]

We know now that gastrointestinal manifestations often accompany the initial presentation with fever. These commonly include abdominal pain, diarrhea, and/or vomiting. Neurologic manifestations have also been described.

The overall mortality rate low[37] In general, symptoms are less pronounced in children when compared with adults [3], children with SARS-CoV-2 infection who are at risk for severe disease include those with underlying conditions (eg, congenital heart disease, bronchial pulmonary hypoplasia, respiratory tract anomaly, abnormal hemoglobin level, or severe malnutrition) and

those with immune deficiency or immunocompromised status (eg, as a result of long-term immunosuppressant use). [11]

The following conditions indicate a greater likelihood of severe disease:

- Dyspnea: Respiration rate of >50 breaths/min in children aged 2-12 months; >40 breaths/min in children aged 1-5 years; >30 breaths/min in patients older than 5 years old (after excluding the effects of fever and crying).
- Persistent high fever for 3-5 days.
- Poor mental response, lethargy, disturbance of consciousness, and other changes of consciousness.
- Abnormally increased levels of enzymes, such as myocardial and liver enzymes and lactate dehydrogenase.
- Chest imaging findings indicating bilateral or multi-lobe infiltration, pleural effusion, or rapid progression of conditions during a very brief period.
- Age younger than 3 months.
- pediatric inpatients with COVID-19 infection were co-infected with other pathogens like bacteria andviruses, including influenza viruses A and B, mycoplasma, respiratory syncytial virus, and cytomegalovirus. [12]

SARS CoV-2 Infection in Neonates

Early evidence has shown low rates of peripartum severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission and uncertainty concerning in utero viral transmission. To date there does not seem to be any conclusive evidence indicating vertical transmission of COVID-19 from infected pregnant mothers to their neonates, [13] though some cases have been suspected.

Neonates can be infected by SARS-CoV-2 after birth because of their immature immune systems, they are vulnerable to serious respiratory viral infections. SARS-CoV-2 may be able to cause severe disease in neonates. A recent review of neonates born to mothers with perinatal confirmed COVID-19 infection showed that severe maternal disease can lead to fetal distress, premature delivery, and other adverse outcomes. [14]

SARS-CoV-2 infection during pregnancy is associated with aidverse outcomes in neonates. Like higher rates of respiratory disorders, hyperbilirubinemia, and admission for neonatal care in infants born to mothers who tested positive for SARS-CoV-2.

Workup Laboratory studies

Early in the course of the disease, the white blood cell count is normal or decreased, and the lymphocyte count is decreased. The majority of patients have normal neutrophil counts.

The children who underwent nucleic acid testing for common respiratory pathogens showed co-infection with pathogens other than SARS-CoV-2.

Finally the children had reverse transcription– polymerase chain reaction (RT-PCR) analysis of fecal specimens demonstrated the prolonged existence of SARS-CoV-2 RNA.

Levels of liver and muscle enzymes and myoglobin are increased in some children. Many

patients have elevated C-reactive protein (CRP) levels and erythrocyte sedimentation rates. In severe cases, patients have high D-dimer levels and progressively decreasing lymphocyte counts. [12]

Children and adolescents with confirmed COVID-19 had high levels of CRP and procalcitonin (PCT) levels. [17] Because PCT values can increase significantly in systemic bacterial infections and sepsis, higher levels are strongly suggestive of bacterial co-infection in patients with COVID-19. [18]

Imaging studies

Common chest radiograph findings in children with COVID-19 pneumonia include bilaterally distributed peripheral and subpleural ground-glass opacities and consolidation. Nonspecific findings include the following [19] :

- Unilateral ground-glass opacities and consolidation
- Bilateral peribronchial thickening and peribronchial opacities
- Multifocal or diffuse ground-glass opacities and consolidation without specific distribution

common abnormality seen on computed tomography (CT) of the chest in children with COVID-19 is ground-glass opacity and nodules, which are usually bilateral. [4] Other CT findings include the following:

- Local patchy shadowing
- Bilateral patchy shadowing
- Interstitial abnormalities

Chest CT findings in children with COVID-19 are similar to those seen in adults. [13] Pleural effusion is rare.

METHODS

This is prospective study of patients that admitted to the Child Central Teaching Hospital those with confirmed covid 19 infection by real time PCR from 20th of March 2020 to the 1st of April 2021. Information collected according to sex and age started from neonatal period to 18 years. The age subdivided in to < 1 month, 1 month -1 year, 1-5 year, 5-10 years and >10 years, symptoms and signs of the patients include fever, malaise, sore throat, cough, dyspnea, cyanosis, FBM, vomiting, headahe, seizure, DLOC and skin rash associated with the duration of their symptoms before the admission to the hospital. The distribution of different symptoms and signs around the months of the entire year of collecting this data also recorded. We had used laboratory analysis and imaging represented by PCR, white blood cell count and chest Xray for all the patient in this study. we put in consideration the fate of the patients if they had compelete recovery or death and if they admitted to the ward or admitted to RCU and needed ventilatory support.

Crowdedness was included in the quetionare paper according to Eurostat criteria :

- One room for the householeld.
- One room per couple in the householeld.
- One room for each persom aged 18 and more.
- One room for single pairs of same gender aged between 12-17yr.
- One room per pair of children under 12 years (20).

The status of vaccination in particular BCG vaccine and the patients with chronic diseases those with positive PCR covid -19 virus infection were included in this study like asthma, DM, ALL, AML, RF, NHL and RMS.

Also patients with contact with sick covid-19 relatives were recorded. The data was coded and each questionaire assigned using statistical package for social sciences version 26 with help of specialist statistician. data presentd in a simple measures of frequency, percentage, standard deviation and range (minimum – maximum).The significance of the difference in different percentages (qualtitave data) was tested using Pearson Chi – square test.

Statistical significance was considered whenever the P- value was equal to or less than 0.05.

RESULTS

Of the 120 patients with confirmed covid-19 infection admitted to (Child Central Teaching Hospital) during the study period, noticed that there was 58 male (48%) and 62 females (52%).

Patients had different age groups, 2 patients (1.5%) were less than 28 days, 19 patient (15.8%) were from 1mo.-1 year, 34 patient (28.3%) were from 1-5 years, 34 patient (28.3%) were from 5-10 years and older than 10 years were 31 patient (25.8%)

About 75 patient (62%) live in a crowded environment. Also those who had COVID-19 virus infection with comorbid conditions were 29 patient (24.2%) the most frequent leukemia, lymphoma, solid tumors, respiratory, renal and diabetes melitus.

Eighty patients (66%) reported a contact with confirmed COVID 19 patients as shown in (Table 1).

Demographic characteristics			Number (N = 120)	%
Age	< 28 days		2	1.6
	1month - 1 year		19	15.8
	1-5 years		34	28.3
	5-10 years		34	28.3
	> 10 years		31	25.8
Sex	Male		58	48.3
	Female		62	51.7
Crowded area	No		45	37.5
	Yes		75	62.5
Chronic disease	No		91	75.8
	Yes	ALL	13	10.8
		Asthma	6	5.0
		AML	4	3.3
		CRF	3	2.5
		RMS	1	8
		DM	1	8
		NHL	1	8
Contact with +ve PCR covid-19 pt.	No		40	33.3
	Yes		80	66.7

Table 2 shows the most common signs and symptoms starting from fever 78 patients (65%), malaise 50 patients (41%), Cough 45 patients (37%), FBM 38 patients (31 %), dyspnea 37 patients (30%), vomiting 35 patients (29%), sore throat 28 patients (23%) and finally skin rash 12 patients (10 %).

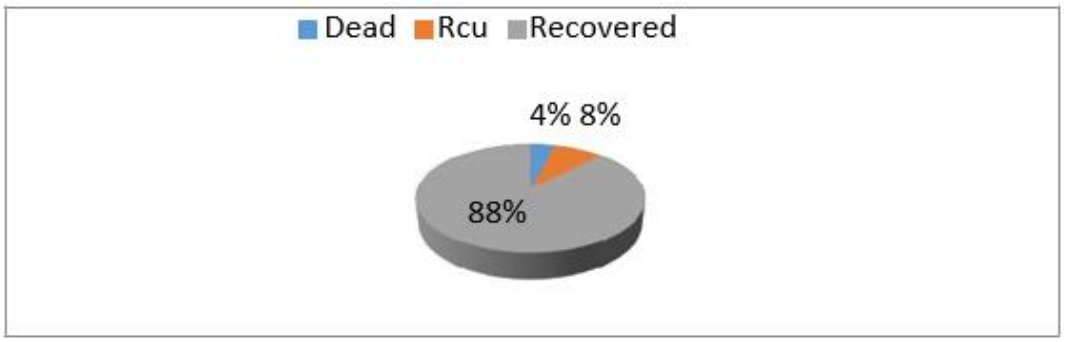
About 63 pt. (52.5%) Had ground glass appearance, 40 pt. (33.3%) of them had a normal chest x-ray and chest x-ray with consolidation 17pt. (14.2%) as shown in (Table 2).

Table 2 Most prevalent presentations and chest x-ray finding of patients at ER (n=120)

The presentation of participants		N = 120	%
Fever		78	65.0
Malaise		50	41.7
Cough		45	37.5
FBM		38	31.7
Dyspnea		37	30.8
Vomiting		35	29.2
Sore throat		28	23.3
Skin rash		12	10.0
Headache		11	9.2
Seizure		5	4.2
Cyanosis		5	4.2
DLOC		3	2.5
Chest X-Rays	Ground.glass	63	52.5
	Normal	40	33.3
	Consolidation	17	14.2

Most of the patients included in this study had high rate of recovery about 105 patients (87.5).

Ten patients (8%) of the total 120 patient needed respiratory support : high flow O2 (4 patient). CPAP (4 patient) and (2 patient) had been intubated in the intensive care unit. Five patients only died (4%) as shown in (Fig2)



Out of 120 patients who were admitted to the emergency more than one sign and symptom found to be significantly related to either death or admission to the RCU (Cyanosis, Fever, DLOC, FBM) as the p-value was (0.0001, 0.03, 0.035 and 0.045) respectively.

Consolidation was found to be the most related chest x-ray finding related to death or RCU admission (p-value 0.0001) followed by ground glass appearance.

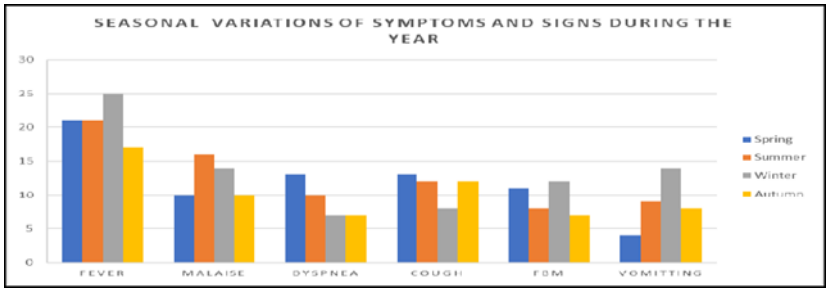
As shown in Table 3

Variable		Fate of pt			Total	P-value
		Dead n. 5/120	Rcu n.10/120	Recovered		
Age group	< 28 days	0	0	2	2	0.08
	1 mo.- 1 year	3	2	14	19	
	1-5 years	2	1	31	34	
	5-10 years	0	4	30	34	
	> 10 years	0	3	28	31	
Sex	Male	2	2	54	58	0.153
	Female	3	8	51	62	
chronic disease	No Chronic Disease	4	8	79	91	0.996
	ALL	1	1	11	13	
	AML	0	0	4	4	
	CRF	0	0	3	3	
	Asthma	0	1	5	6	
	DM	0	0	1	1	
	NHL	0	0	1	1	
	RMS	0	0	1	1	
Crowd	No	2	4	39	45	0.977
	Yes	3	6	66	75	
BCG vaccine	No	0	6	37	43	0.917
	Yes	3	6	68	77	
Signs and Symptoms	Fever	5	4	69	78	**0.03***
	Malaise	3	3	44	50	0.534
	Cough	4	5	36	45	0.083
	FBM	4	4	30	38	**0.045***
	Dyspnea	3	4	30	37	0.267
	Vomiting	1	5	29	35	0.297
	Sorethroat	0	1	27	28	0.241
	Skin rash	0	1	11	12	0.748
	Headache	0	1	10	11	0.768
	Seizure	0	0	5	5	0.689
	Cyanosis	3	0	2	5	**0.0001***
	DLOC	1	0	2	3	**0.035***
duration of symptoms before admission	2 days	2	2	29	33	0.452
	3 days	0	5	49	54	
	4 days	0	1	10	11	
Chest xray	Ground glass	2	5	56	63	**0.0001***
	Normal	0	0	40	40	
	Consolidation	3	5	9	17	
White blood cell count	Lymphopenia	2	4	73	79	0.157
	Neutrophilia	1	4	18	23	
	Normal	2	2	14	18	

According to this study, we found that the distribution of the sign and symptoms during the period of the study as follows:

There was a two peak for (Fever, Malaise, Vomiting) during the summer months especially August followed by a higher peak in the winter months especially January.

On the other hand, the FBM and peak was in winter months especially January and February as shown in (Fig3)



DISCUSSION

This study observe that male was slightly less than female (58 patient 48% to 62 patient 52%) and this result was in disagreement with other similar epidemiological studies done in Saudi Arabia by Ali Alsuheel Asseri et al [21] reported that more boys than girls (56% vs 44%) affected with COVID-19. Another study by Lara S. Shekerdemian et al [22] show 25/48 male and 23/48 female age was (52% to 48%). While Eva W. Cheung et al [91] mentioned that 8/17 male patients was less than 9/17 female patient (47% to 53%) in their study, and this discrepancy in the result

might be due to the sample size of the studies.

Neonates less than 28 days represent 2 pt. (1.5%), infants from 1month to one year represent 19 patient (15.8%) most pediatric ward admissions were 1–10 years of age (68 patients represent 56.6%). result as described by Yuanyuan Dong et al [23] were close to our study results.

According to this study, more than two-thirds of the participants (91 patient) was free from comorbidity and this was going on with the result mentioned by Vibhu Parcha et al [24] in his study that 8,297 didn't have comorbidity factors among 12306 patients. acute lymphocytic leukemia was the most comorbidity found in this study which was 13 pt. (10.8%) followed by asthma 6 patients (5%) and CRF pt. 2.5%, Vibhu Parcha et al [93] mentioned that respiratory problems including asthma were found in about 2.9% of the children, hematological conditions about 0.5% and renal problems were only 0.3%, which is not similar to our study results that maybe related to a different sample size.

The most common sign and symptoms in the study was fever in 78 patient. (65%) of the patients followed by malaise and cough and this result going on with the finding of Tang et al [25] that fever and cough were the dominant symptoms in pediatric patients, of which the frequencies were lower compared with adults (55.49–78.49%), and this was also the same result concluded by Olivia V Swann et al [26] that the most common presenting symptoms were fever, cough.

occurred in about one-third of the participants 37 patient (30%) in the study and this was against the finding of Bingbing Li et al [27] study as it reported that shortness of breath occurs in more than two-thirds of critically admitted patients. And this difference might be due to that the patients were mild to moderate symptoms were included in our study.

compared to study by Bingbing Li et al that he cinsidered the shortness of breath was the main finding in critically admitted children in his results.

Frequent bowel motion and vomiting was reported in 38 patient around 30% of our patients, which is in line with a study done in France by Nadia Nathan et al [28] that about one-third of the admitted children presented with diarrhea and vomiting.

Twelve patients with skin rash (10%) this finding also was similar to study done by Ali- Asseri et al (89), he mentioned also that about 9 pt. of 79 pt. (10.1%) had skin rash might related to MIS-C.

Seizure 4.2%, DLOC 2.5% and headache 9.2% were reported in our study sample this is also reported by Mao et al (98) he found other neurological diseases in pt. with covid 19 infection like gullain barre syndrome, periphral neuropathy and stroke.

The radiological finding in this study concluded that about one-third of the patients had normal radiological findings while glass ground appearance was found to be in about 52% (63 patient) and this result was close to the finding reported by Susan C. Shelmerdine et al [29] that about 34% of the children had normal radiological finding while 62% had a ground-glass appearance and the reason for the differences might be due to that the differences in the sensitivity between CXR we used in our study and CT that used in the other study.

This study found that the percentage of the pediatrics that need admission to the RCU was about 10 patients (8%), five patients (4%) died, and this result was in disagreement with the result mentioned by Olivia V Swann et al [25] as he found that the percentage of critical cases that need admission to the ICU was 116/632patient(18%) while the death rate was 6 patients 1%, while in brazil Arnaldo Prata-Barbosa et al [30] mentioned that the rate of critical cases need admission to the ICU was 14of 79patient (18%) among pediatric patients while the death rate was about 2 patients (3%), this discrepancy might be because of the differences in the facilities available during the pandemic in addition to the awareness of the community to the sign and symptoms of

moderate and severe infection that need to seek medical assistant as fast as possible to prevent deterioration of the patient's condition.

According to the study, cyanosis was the most associated sign related to the severity of COVID 19 infection and this result was going on with the result mentioned by Tiago H. de Souza et al [31] as he reported that about 145 patients (36.9%) of children had cyanosis due to pneumonia in severe infection with COVID 19.The study mentioned that FBM was associated with the severity of COVID 19 and this result was compatible with the result mentioned by Mubbasheer Ahmed et al [32]. Abdominal pain/diarrhea (73·8%) of the severe cases of COVID 19 infection. An association was found between DLOC with the severity of the illness and this finding was the same result reported by Wael Ibrahim [33] that the CNS manifestation including DLOC was associated with a severe course of infection with COVID 19 in children.There was a statistical association between consolidation and ground glass radiological finding by CXR and the severity of the infection that need admission to the RCU or ended with death and this result was close to the finding of Susan C. Shelmerdine et al [28] mentioned that chest CT imaging findings in children with COVID-19 are frequently mild, with lower lobes most commonly affected, demonstrating patchy ground-glass opacification or, less frequently, areas of consolidation. Chest CT imaging should be reserved for severe cases or for identifying alternative diagnoses.Also an association between Lymphopenia and the critical situation of the participants and this result was against the conclusion mentioned by Ali Alsuheel Asseri et al [20] that critical care patients have greater white cell counts, and inflammatory markers are still higher in PICU admitted patients, but the difference is not statistically significant (data are not shown). And the difference might be due to that about 29 patient (25%) of the participants in our study had chronic comorbidity factors and on chemotherapy that might affect the account of white blood cells in their body.

Conclusion

The infection had two peaks during the year one on august and the other in january. WE noticed tha female slightly more than males in the age category of 1-5 yrs and 5-10 yrs.ALSO About two thirds live in crowded areas and with contact to infected patient. This study observed that the children have milder symptoms with high recovery rate. Fever,malaise, cough, shortness of breath and FBM were the prevalent presentations. Skin rash observed in some patients that had COVID-19 infection.

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