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Research Article

Clinical Course and Disease`s Outcome Aspects of COVID-19 Pediatric Patients in Ibn Al-Khateeb Isolation Hospital

Abbas Oweid Oleiw[1], Kholod Dhaher Habib[1*], Kadhim Abed Mohammed[1], Oday Yassen Abbas[1], Zainab Ali Jaber[2]

1- Fatima Al Zahra Administrative Hospital, Baghdad, Iraq.
2- College of Medicine, University of Baghdad, Baghdad, Iraq.
* corresponding to: kholod_hib60@yahoo.com

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ABSTRACT

Background: Corona virus disease 2019 (COVID-19) is a communicable disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It was first identified in December 2019 in Wuhan, China, and has since spread globally, leading to an ongoing pandemic.

Aim of study: to review the clinical, lab investigation and imaging techniques, in pediatric age group affected COVID-19 to help medical experts better understand and supply timely diagnosis and treatment.

Subjects and methods: this study is a retrospective descriptive clinical study. The medical records of patients were analyzed. Information's recorded include demographic data, exposure history, symptoms, signs, laboratory findings, chest x- ray, and chest computed tomographic (CT) scans. Data were obtained with data collection forms from paper medical records.

Results: there were 76 COVID-19 pediatric patients, 46.1% of those patients were within the age group 6 -10 years. The female to male ratio was 1:1, and 92.1% of them were living within the urbane area. About 60.5% of patients were pupils. Seventy-one (93.4%) patients of them had no comorbidity. Twenty (26.3%) patients were asymptomatic. Regarding the duration of hospital stay, 39(51.31) patients had <7 days. All of the patients were nonsmokers. All patients had recovered and discharged from hospital after 2 negative real technique-polymerase chain reaction (RT-PCR) tests, no death was reported. Only 16(21.1%) patients had severe symptoms.

Conclusions: the most common symptoms were fever, Cough, Loss of appetite, Shortness of breath & Fatigue. There was a statistically significant association between white blood cells counts, neutrophil number, Chest X-Ray results, with case severity and a statistically significant association between form of treatment in patients who received Oxygen, Oseltamivir, Azithromycin, Paracetamol, Dexamethasone, and case severity.

Introduction

Pneumonia of unknown cause detected within the city of Wuhan in Hubei province (China) was first reported to the world Health Organization (WHO) Office in China on 31st December 2019(1). A novel coronavirus, firstly named 2019-nCoV, was isolated from human airway epithelial cells (2), the WHO named the disease officially, coronavirus disease 2019 (COVID-19), since then, it's become a pandemic. (3)

A small number of pediatric patients were affected with COVID 19. They present with fever, cough and breathing difficulties, and in many cases GIT symptoms. Although children often have mild symptoms, they could be potential agents of transmission. (4)
Individual presenting symptom, sign, laboratory test, or radiological finding couldn't predict a diagnosis of COVID-19 accurately. At the time of testing, one-fifth had asymptomatic infections; about two-thirds had just one symptom. (5,6)
Sensitivity rates of CXR in adults vary from 25 - 69 %. Sensitivity rates for CT–scans are higher. Yicheng Fang. et al, reported that sensitivity of CT for COVID-19 infection was 98% when compared to PCR sensitivity of 71% ($p < .001$) (7).

In pediatric population, radiological manifestations seem to be less marked. Most of the publications regarding children are based on CT and a large number of them failed to show abnormalities on initial studies (7,8). Opacities were detected in up to 50% of CXR and 25% manifested with the standard pattern of multifocal ground-glass opacities (GGOs). Chest x- ray was good in describing consolidations, normal x-rays and (GGOs). Imaging techniques have a role within the management of Pediatric population with known or suspected COVID-19, especially in those with moderate or severe symptoms or with underlying risk factors (9).
Pediatric population has been less studied than adult population and prompt diagnosis is challenging because of asymptomatic or mild episodes, so we decided to review the clinical, lab investigation and imaging techniques, in pediatric patients of COVID-19.

Subjects and methods

A retrospective descriptive clinical study, there were 76 confirmed hospitalized cases of COVID-19 between 24th February and August 24th, 2020 in Ibn Al khateeb isolation hospital, had been included in this study. Patients enrolled during this study were diagnosed by a positive PCR test for COVID-19 and treatment plan for the new coronavirus infection formulated by Iraqi ministry of health had been tried (10,11).

The initial treatment protocol adopted by Ministry of Health in Iraq March 1, 2020:

Severity	Finding	Protocol
Mild	No pneumonia in the CT scan	Conservative treatment No specific medication
Moderate	Pneumonia in the CT scan	Oseltamivir 75 mg BID for 5 days Hydroxychloroquine (400mg BID first day then 200mg BID for 5 days)
Severe	Pneumonia in the CT scan with multi-organ failure	Oseltamivir 75 mg BID for 5 days Hydroxychloroquine (400mg BID first day then 200mg BID for 5 days) Kaletra (Lopinavir-Ritonavir) (200/ 50 mg) 2 tablets PO BID 5 days
Critical	Indicated for ICU admission	Oseltamivir 75 mg BID for 5 days Hydroxychloroquine (400mg BID first day then 200mg BID for 5 days) Kaletra (Lopinavir-Ritonavir (200/ 50 mg) 2 tablets PO BID 5 days Ribavirin

The treatment protocol was approved by the committee of Covid-19 virus, this protocol was primary and to be updated according to the new studies and evidences all over the world.
The addition of Azithromycin was considered after the 1st week as part of therapy especially for the younger age group

Cases Definition, inclusion and exclusion criteria:

All the patients of pediatric age groups (1 day- 15 years),{these are the limits of age group for admission to the pediatric words in Iraq according to the instruction of Al-Rusafa Health Directorate },who were diagnosed as COVID-19 and admitted to Ibn Al-Khateeb hospital and had a certain outcome during the period of the study were included. COVID-19 cases diagnosis was done consistent with clinical guidelines set by the world Health Organization on 28 January 2020 and 13 March 2020, clinical management of severe acute respiratory infection when novel corona virus (nCOV- 2019) infection is suspected. Specimens were collected from the upper respiratory tract (URT) as nasopharyngeal and oropharyngeal swabs and nCOV- 2019 testing was done by polymerase chain reaction (PCR) (12). Patients above 15 years were excluded.

The present study is a retrospective descriptive clinical study. The medical records of patients were analyzed. Information`s recorded include demographic data (age, sex, occupation, and smoking history), exposure history, symptoms, signs (fever, dry cough, and tiredness, other symptoms that are less common like aches and pains, nasal congestion, headache, conjunctivitis, sore throat, diarrhea, loss of taste or smell or a rash on skin or discoloration of fingers or toes), laboratory findings, chest x- ray, and chest computed tomographic (CT) scans.
Data were obtained with data collection forms from paper medical records. The date of disease onset was defined as the day when the symptom was noticed.

Diagnostic criteria for case severity:

- Mild: patients with symptoms meeting the criteria for COVID-19 without presence of viral pneumonia or hypoxia.
- Moderate: Pneumonia in Child: with clinical signs of non-severe pneumonia (cough or difficulty breathing + fast breathing and/or chest in drawing) and no signs of severe pneumonia.
- Severe: Severe pneumonia in Child with clinical signs of pneumonia (cough or difficulty in breathing) + a minimum of one among the following: Central cyanosis or SpO2 < 90%; severe respiratory distress (e.g. fast breathing, grunting, very severe chest in drawing); general danger sign: inability to breastfeed or drink, lethargy or unconsciousness, or convulsions.

Fast breathing is categorized as follows : < 2 months has ≥ 60 breaths/min; 2–11 months has ≥ 50 breaths/min; 1–5 years has ≥ 40 breaths/min.

- Critical: respiratory failure and mechanical ventilation is required; shock; and complicated with other organ failure requiring RCU care. (13)

Throat swab, nasopharyngeal swab, and blood sample, specimens were collected from patients with suspicion of COVID-19. The COVID-19 was confirmed by PCR.

Blood samples: white blood cells (WBC), differential white blood cell count normal pediatric values vary according to age groups, it ranges from 9-30 cell (x 103/µL) at birth to 4.5-12.5 cell (x 103/µL) at 15 years (14).

A white blood cell counts below 3,000 cells considered low WBC. Reduced Lymphocyte number meets a count of less than 3,000 lymphocytes per microliter of blood in children. Normal total neutrophil count is 1.500-6.500 cells per microliter of blood. (15)

C-reactive protein (CRP) blood test spots inflammation or infection within the body. "The finding of low eosinophil count and elevated CRP can effectively help in assignment suspected COVID-19 patients from other patients attending the fever clinic with COVID-19-like initial symptoms". (16)

Platelet count: a standard platelet count ranges from 150,000 to 450,000 platelets per microliter of blood. Thrombocytosis is having more than 450,000 platelets while thrombocytopenia is having less than 150,000.

Comorbidity includes (diabetes mellitus, heart disease, asthma, renal disease) & treatment includes (hydroxychloroquine, Oseltamivir (Tamiflu), Lopinavir-Ritonavir (kaletra), azithromycin, bronchodilators, antipyretics, corticosteroids, mechanical ventilator, oxygen and others).

Outcome: All patients who received treatment completed a planned therapy, the majority 63(82.9%) received azithromycin starting with a single dose of 10 mg/kg/day on the first day, followed by doses of 5 mg/kg per day for the following 4 days, antipyretic if axillary body temperature ≥37.5 C, other treatment options were added consistent with pediatrician judgment. The outcome of COVID-19 patients was either recovered / discharged or death. To mention that the patient is recovered, (RT-PCR) tests results were collected at the end of the treatment, nasopharyngeal and throat specimens were obtained from patients by using specific kits by a professional health-staff and sent to the Central Public Health Laboratory in Baghdad for RT-PCR testing. The patient wasn't discharged until two PCR-tests were negative at least 24 hours apart, according to the WHO interim guidance, 13 March 2020, clinical management of severe acute respiratory tract infection. The frequency of specimen selection may rely upon local circumstances, but should be done at least every 2 - 4 days until there are two negative consecutive results, at least 24 hours apart in a clinically recovered patient. (12).

Statistical analysis

The statistical analysis was performed using statistical package for social science (SPSS-21). The Chi-square and fisher's exact probability tests were used. A P value of ≤ 0.05 was considered significance.

Ethical approval:

Ethical approval was obtained from Al-Rusafa Health Directorate Scientific and Ethical Review Committee, Ministry of Health, Iraq. Verbal approval was obtained from the Ibn- Al Khateeb Isolation Hospital administration with a clarification on the purpose of the research before the research was started.

Results

There were 76 pediatric patients, 46.1% of these patients were in the age group in 6 -10 years. The female to male ratio was 1:1, and 92.1% of them were living in the urban area.

About 46(60.5%) of patients were pupils. Seventy-one (93.4%) patients of them had no comorbidity. Twenty (26.3%) patients were asymptomatic. Regarding the duration of hospital stay, 39(51.31%) patients had <7 days. All of the patients were nonsmokers.

All patients had recovered and discharged from hospital after 2 negative PCR tests, no death was reported. Only 16(21.1%) patients had severe symptoms. Twenty (26.3%) of COVID-19 patients in the study had no signs and symptoms, but were contacts of a positive case. They were investigated and when their test result was positive, they were admitted to hospital for quarantine. Table1.

The blood investigation showed that thirty-five (46.1%) patients had positive CRP test and 65 (85.5%) patients had normal WBC count, and 65(85.5%) patients had normal total neutrophil counts. About 47(61.8%) patients had lymphopenia; with lymphocyte count of less than 3,000 lymphocytes per microliter of blood. Regarding the platelet count 65(85.5%) patients had normal count (150,000 - 450,000 per microliter of blood).

There was no statistically significant association between (gender, age), and COVID-19 patients' outcome. There was statistically significant association between WBC count, neutrophil number, Chest X-Ray results, and comorbidity), with case severity. There were 48(63.15%) patients had clear chest x- ray on examination, and 28(36.84%) patients had Ground glass appearance on chest x ray, there was statistically significant association between result of chest x-ray, and case severity, p value (0.00). Table2.

The most common symptoms were fever 45(59.21%) patients, Cough 43(56.57%) patients, Loss of appetite 18(23.68%) patients, Shortness of breath & Fatigue 15(19.73%) patients. There was statistically significant association between symptoms like (fever, cough, loss of appetite, Shortness of breath & Fatigue, Sore throat) and case severity. Table3.

Most patients received Tamiflu 53(69.73%), Azithromycin 63(82.89%) and tonics 51(67.1%) even the asymptomatic patients, only 4 patients received Dexamethasone. There was statistically significant association between type of treatment in patients who received Oxygen, Tamiflu, Azithromycin, Paracetamol, Dexamethasone, and case severity as shown in table 4.

Table 1: sociodemographic and clinical characteristics of the studied population

		Frequency	%
Age	< 1 year	5	6.6
	1 to 5 years	19	25.0
	6 to 10 years	35	46.1
	11 to 15 years	17	22.4
Sex	Male	38	50.0
	Female	38	50.0
Categories of body weight in kg	Below 10 kg	4	5.3
	10 to 20 kg	19	25.0
	21 to 40 kg	28	36.8
	Above 40 kg	25	32.9
Residency	Urban	70	92.1
	Rural	6	7.9
Did they develop symptoms?	Yes	56	73.7
	No	20	26.3
What job do they have?	Infant	5	6.6
	Child	24	31.6
	Pupil	46	60.5
	Housewife	1	1.3
Duration of hospital stay in days	<7 days	39	51.31
	8-14 days	31	40.78
	>14 days	6	7.89
Comorbidity	Obesity	0	0.0
	Diabetes mellitus	0	0.0
	Congenital heart disease	0	0.0
	Asthma	4	5.3
	Renal disease	0	0.0
	Urinary tract infection	1	1.3
	None	71	93.4
	recovered	76	100
Patients' outcomes	Dead	0	0.0
	Asymptomatic	20	26.3
Case severity	Mild	15	19.7
	Moderate	25	32.9
	Severe	16	21.1
	Critical	0	0.0
Total		76	100.0

Table 2: characteristics of the studied population

		Case severity				Total	P value
		Asymptomatic	Mild	Moderate	Severe		
Age	< 1 year	1	1	2	1	5	0.532
	1 to 5 years	4	7	6	2	19	
	6 to 10 years	11	4	13	7	35	
	11 to 15 years	4	3	4	6	17	
Comorbidity	asthma	0	0	0	4	4	0.003
	UTI	0	1	0	0	1	
	none	20	15	25	12	72	
Gender	Male	7	9	13	9	38	0.442
	Female	13	6	12	7	38	
C Reactive Protein	Positive	5	6	15	9	35	0.093
	Negative	15	9	10	7	41	
	Below 3,000	9	1	1	0	11	
WBC count	3,000 - 10,000	11	14	24	16	65	0.000
	More than 10,000	0	0	0	0	0	
Neutrophil number	Below 1,500	9	1	1	0	11	0.000
	1,500 - 6,500	11	14	24	16	65	
	More than 6,500	0	0	0	0	0	
Lymphocyte number	Below 3,000	12	11	13	11	47	0.332
	3,000 - 5,000	8	3	12	5	28	
	More than 5,000	0	1	0	0	1	
Platelet number	Below 150,000	2	4	3	2	11	0.572
	150,000 - 450,000	18	11	22	14	65	
	More than 450,000	0	0	0	0	0	
PCR for COVID-19	Positive	20	15	25	16	76	-----
	Negative	0	0	0	0	0	
Chest X-Ray	Clear	20	10	15	3	48	0.000
	Ground glass	0	5	10	13	28	
	Consolidation	0	0	0	0	0	
	Pulmonary hypertension	0	0	0	0	0	
Total		20	15	25	16	76	

Table 3: Symptoms and case severity

	Case severity				Total	P value
	Asymptomatic	Mild	Moderate	Severe		
Asymptomatic	20	0	0	0	20	0.000
Fever below 38c	0	6	11	1	18	0.000
Fever above 38c	0	2	10	15	27	
Total fever	0	8	21	16	45	0.000
Cough	0	9	19	15	43	0.000
Loss of appetite	0	0	11	7	18	0.000
Fatigue	0	1	7	7	15	0.002
Shortness of breath	0	0	1	14	15	0.000
Coughing up sputum	0	0	0	2	2	0.079

	Case severity				Total	P
Muscle aches and pain	0	0	1	0	1	1.000
Diarrhea	0	2	3	1	6	0.383
Nasal congestion	0	1	1	2	4	0.387
Headache	0	0	2	3	5	0.093
Conjunctivitis	0	0	0	0	0	----
Sore throat	0	0	4	7	11	0.000
Loss of taste or smell	0	1	2	0	3	0.405
Skin rash	0	0	0	0	0	----
Discoloration of fingers or toes	0	0	0	0	0	----
Abdominal pain	0	0	3	0	3	0.143
Constipation	0	0	1	0	1	1.000
Vomiting	0	0	2	0	2	0.440
Fit	0	0	0	1	1	0.408
Epistaxis	0	0	0	2	2	0.079
Total	20	15	25	16	76	

Table 4: Treatment and case severity

	Asymptomatic	Mild	Moderate	Severe	Total	P value
Oxygen	0	0	6	6	12	0.001
CPAP	0	0	0	0	0	----
Ventilator	0	0	0	0	0	----
Hydroxychloroquine	0	1	2	2	5	0.460
Oseltamivir	6	13	22	12	53	0.000
Azithromycin	9	15	24	15	63	0.000
Flagyl	0	1	3	0	4	0.234
Paracetamol (Antipyrol)	3	8	17	11	39	0.001
Tonics	18	8	16	9	51	0.056
Buscopan	0	0	2	1	3	0.609
IV fluid	0	0	3	1	4	0.319
Novomit	0	0	1	0	1	1.000
Ceftriaxone	0	0	2	1	3	0.609
Clexane (Enoxaparin sodium)	0	0	0	2	2	0.079
Dexamethasone (Decadron)	0	0	0	4	4	0.002
Solvodin (Bromhexine)	0	0	0	3	3	0.079
Kaletra (lopinavir/ritonavir)	0	0	0	2	2	0.079
Total	20	15	25	16	76	

Discussion

The study showed that children are at a lower risk of developing COVID-19 and have a milder disease than adults; this result was constant with other studies (17-20), since all patients recovered with no complication and no death was reported.

Regarding severity of cases we found that 26.3% of patients were asymptomatic, 19.75% of patients had mild symptoms, and only 21.1% of patients had severe symptoms, while Dong Y., et al, early study of pediatric patients with COVID-19 infection reported that children develop a comparatively mild disease course with 83% of confirmed cases presenting with mild to moderate infection, with a further 13% being asymptomatic, and only 3% presenting with severe and critical illness, (19). We found that the percent of sever cases in our study was high compared with other studies (10, 19, 20), this result because most of asymptomatic or mild pediatric cases were treated locally at the pediatric hospitals in Baghdad and other provinces except the moderate to severe cases which were referred to Ibn Al Khateeb hospital.

Many studies have established pre-existing comorbidities as risk factors for severe COVID-19 infection in adults (21) but we don't know the association between childhood comorbidities and COVID-19 outcomes. While systematic reviews and meta-analyses examining COVID-19 in pediatric patients are published (22), these reports didn't evaluate the risk of severe COVID-19 infection specifically in children with pre-existing conditions, but in our study, we found that there was statistically significant association between case severity and comorbidity (asthma).

We found that the most common symptoms were fever, Cough, Loss of appetite, Shortness of breath & Fatigue, this result had been reached by many studies like Zhou F, et al, (17), and Ding Y, et al. (16) .

Up to date there is no Iraqi national guideline for treatment of pediatric age group of COVID-19 patients, we try to give Azithromycin instead of Hydroxychloroquine in children below age of 14 years because we were afraid of the side effect of Hydroxychloroquine on children especially hemolytic anemia in G6PD patients, retinopathy and permanent vision loss (23). But we use (Hydroxychloroquine in addition to Azithromycin for 5 days) to treat 5 patients who were 14-15 years old and their body weight >40 kilograms, no complication was found after this mode of treatment given to patients.

Azithromycin had been tried by other clinical trials (24,25), and their results were in benefit of early use of Azithromycin in COVID-19 patients, but some other clinical trials reached a conclusion "that In patients with severe COVID-19, adding azithromycin to standard of care treatment (which included hydroxychloroquine) did not improve clinical outcomes", and their findings do not support the routine use of azithromycin in combination with hydroxychloroquine in patients with severe COVID-19.(26)

Azithromycin used in treatment of COVID-19 patients due to its antiviral effects presumably result from interfering with receptor mediated binding, viral lysosomal escape, intracellular cell signaling pathways and enhancing type I and III interferon expression. "It's immunomodulatory effects may mitigate excessive inflammation

and benefit tissue repair" (27), for this reasons it was used in clinical trials.

There was statistically significant association between form of treatment in patients who received Oxygen, Oseltamivir, Azithromycin, Paracetamol, Dexamethasone, and case severity, this was in contrast with Chao, J. Y.,(28), they found that no statistically significant association between the above treatment and the case severity , and they use Remdesivir for critical patients.

There was statistically significant association between number of WBC, neutrophil number, and Chest X-Ray results, with case severity; this was consistent with Chao, J. Y., et al. (28)

It was found that the clinical symptoms of children are mild, perhaps because of a less pronounced inflammatory response, and that the occurrence of symptoms appears to inversely correlate with age, which was consistent with Du W, et al. (29-30)

Conclusion

The most common symptoms were fever, Cough, Loss of appetite, Shortness of breath & Fatigue. There was statistically significant association between numbers of WBC, neutrophil number, Chest X-Ray results, with case severity. There was statistically significant association between form of treatment in patients who received Oxygen, Oseltamivir, Azithromycin, Paracetamol, Dexamethasone, and case severity.

Recommendation

Efforts must be combined to find a national action plan to treat COVID-19 pediatric patients.

Carrying out more comprehensive and broader studies in all parts of Iraq to determine an action plan for diagnosing pediatric COVID patients, determining the clinical signs and lab results that help in diagnosing pediatric COVID patients.

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