Characteristics and Outcome of Hospitalized Children with COVID-19: A Single Center Experience

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Abstract

Objectives: Are to describe the clinical, and laboratory features of patients hospitalized with COVID-19 and to compare some of these parameters between patients with and without MIS-C.

Methods: A cross sectional study, undertaken over a 10 months period from 1st of march to 31 of December 2020 at child's central teaching hospital in Baghdad city , Iraq.

Results: In total, 80 children hospitalized with a diagnosis of COVID-19. The mean age of the patients was 6.05±5.1years.60% were male and 46.35% had no comorbidities . Different types of malignancies were the most common comorbidity accounting for 22.5% of the patients. A history of contact with infected person was reported in 27.5% of the patients. Chest X-ray revealed that 52.5% of the patients had normal findings. 11.25% developed multi systemic inflammatory syndrome. Only two hematological abnormalities were significant in pediatric COVID-19 cases for development of MIS-C which is elevated NLR and CRP. In this study, there were no deaths linked to COVID-19 admission..

Conclusions : The majority of children admitted to the hospital with confirmed COVID-19 have a mild course and a good outcome. malignancy is the commonest comorbidity associated with COVID-19 admissions. Elevated Neutrophil: lymphocyte ratio and CRP are independently associated with development of MIS-C in pediatric COVID-19.

Keywords: *Children, Coronaviruses , COVID-19 .*

Introduction

SARS-CoV-2, the novel coronavirus that causes the disease COVID-19, first presented in December 2019 in Wuhan City, China, and on January 30, 2020 was declared a public health emergency of international concern, as it spread quickly around the globe through human-to-human transmission [1]. In Iraq the first case was reported on February 24th, 2020 [2] .since that time more than 1,139,373 cases reported [3].

Despite the global spread, clinical patterns of COVID-19 remain largely unclear, particularly among children[4]. Many studies show that pediatric COVID-19 has a milder course than adult COVID-19, that children have a better prognosis, and that deaths are exceedingly rare [5]. On other hand, Since April 2020, the number of children and young people who have presented with a hyperinflammatory illness involving many organs and mimicking Kawasaki disease shock syndrome has increased. The United Kingdom, the United States, and the World Health Organization have used several labels for this presentation, including multisystem inflammatory syndrome in children (MIS-C) and pediatric inflammatory multisystem syndrome temporally linked with SARS-CoV-2 infection. [6].

Until far, neither the WHO nor the US Centers for Disease Control and Prevention (CDC) have recommended any specific treatment for children. The goal of treatment for children with COVID-19 is to prevent organ failure, acute respiratory distress syndrome(ARDS), and hospital-acquired infections. To achieve this, supportive care is commonly used, which includes enough hydration, calorie intake, and ventilator support. (7).

The goal of this study is to describe the clinical and laboratory characteristics of pediatric COVID-19 patients who are hospitalized, as well as to compare those parameters between those who are hospitalized with and without MIS-C.

Materials and Methods

A cross sectional study, conducted over a period of 10 months from 1st of march 2020 to 31 of December 2020 at child's central teaching hospital in Baghdad city in Iraq.

Data was collected after obtaining consent and ethical approval from the patient's parents and family members, who were explicitly told about the study's goal. The information was gathered through a questionnaire created by the researcher. The questionnaire was verified for inconsistencies in data quality and secret coding.

80 children <16 years old with laboratory-confirmed COVID-19 and admitted to the child's central teaching hospital were included in the study.

All children included in the study had a thorough medical history and physical examination. The results of laboratory and radiographic tests, as well as patient management and outcomes, were gathered.

In our study, A COVID-19 case was diagnosed based on positive test for SARS-CoV-2 infection by a positive real-time reverse transcription polymerase chain reaction test of a specimen using deep nasopharyngeal swab.

A temperature equal or more than 38.0°C was considered as fever. Normal levels of hematological indices including absolute neutrophil count, absolute lymphocyte counts and platelets count and subsequently neutrophil lymphocyte ratio (NLR) and platelet lymphocyte ratio (PLR) determined based on normal values for age. Multisystem Inflammatory Syndrome in Children (MIS-C) was defined according to CDC criteria[8]

Statistical Analysis

Statistical analyses were performed by using SPSS software version 25.0 (SPSS, Chicago). Continuous data were subjected to normality test (Shapiro Wilk test), Data with normally distribution were presented as mean and standard deviation, and analyzed with Student t-test. Data with non-normal distribution were presented as median and range and analyzed with Mann Whitney U test. Categorical variables were expressed as number and percentage and analyzed with Chi-square test. Receiver operating characteristic curve (ROC) was used to evaluate the prognostic value of NLR and CRP in predicting MIS-C. A p- value less than 0.05 was considered to indicate a statistically significant difference.

Results

Demographic Characteristics of the Patients:

This study included 80 children with COVID-19. The mean age of the patients was 6.05±5.1years (range <1-16years). The age group 1-3 years was the most frequent accounting for 37.5% followed by age group 8-11 years (23.75%) and 12-16 years (15%). Infants constituted (11.25%) of the cases . Males had a preponderance over females (60% versus 40%). The residency of about one-fourth of the patients were urban. About half of the patients had no comorbidity at presentation. Different types of malignancies were the most common comorbidity accounting for 22.5% of the patients, while asthma was reported in 15% of the patients. A history of contact with infected person was reported in 27.5% of the patients. The mean hospital

stay was 3.15±1.94 days. Chest X-ray revealed that 52.5% of the patients had normal findings. The most common lesion was diffuse haziness of the lung accounting for 26.25% of the patients followed by lung infiltration (11.25%) and finally patchy lesion (10%). Ten patients (12.5%) required O_2 therapy, while 9 patients (11.25%) developed multi systemic inflammatory syndrome (Table 1).

Table 1: Demographic and clinical characteristics of the patients (n=80)

Variables	Values
Age, years <1 1-3 4-7 8-11 12-16 Mean±SD Range	 9(11.25%) 30(37.5%) 10(12.5%) 19(23.75%) 12(15%) 6.05±5.1 16 days-16 years
Gender Male Female	 48(60%) 32(40%)
Residence Urban Rural	 61 (76.25%) 19(23.75%)
Comorbidity No comorbidity Malignancy Asthma Cerebral palsy Others	 37(46.35%) 18(22.5%) 12(15%) 4(5%) 4(5%)
Contact with infected person Yes No	 22(27.5%) 58(72.5%)
Hospital stays, days Mean±SD Range	 3.15±1.94 1-9

Cont... **Table 1: Demographic and clinical characteristics of the patients (n=80)**

Radiological Findings(chest x ray)	
Normal	42(52.5%)
Haziness	21(26.25%)
Bilateral Infiltration	9(11.25%)
Patchy lesion	8(10%)
Need for O2 therapy	
Yes	10 (12.5%)
No	70(87.5%)
Multisystemic inflammatory syndrome	
Yes	9(11.25%)
No	71(88.75%)

Presenting Symptoms

Nineteen patients (23.75%) were asymptomatic at presentation. So far, fever was the most common presenting symptom reported in 47.5% of the patients followed by cough (21.25%), SOB (20%) and vomiting (16.25%). Less common presentation included diarrhea (8.75%), rash (7.5%) loos of appetite (5%) headache (3.75%) and conjunctivitis (3.75%) ,loss of taste and smell was not seen in any case (Table 2).

Table 2: Presenting symptoms

Presenting symptoms	Frequency (%)
Asymptomatic	19(23.75%)
Fever	38(47.5%)
Cough	17(21.25%)
SOB	16(20%)
Vomiting	13(16.25%)
Edema of hands and feet	9(11.25%)
Diarrhea	7(8.75%)
Rash	6(7.5%)
Loss of appetite	4(5%)
Headache	3(3.75%)
Conjunctivitis	3(3.75%)

A patient can have more than one presenting symptoms

Hematological Indices

The mean WBC, neutrophil, lymphocyte and platelet count was $8.77\pm5.96\times10^3$/ml, $6.26\pm4.52\times10^3$/ml, $2.1\pm1.55\times10^3$/ml and $284.19\pm107.85\times10^3$/ml, respectively. On the other hand, mean NLR was 4.83 ± 7.1, while PLR was 241.05 ± 320.2. The mean CRP concentration was 40.71 ± 60.4 mg/L (Table 3).

Table 3: Hematological indices (n=80)

Variables	Values
Total WBC $\times10^3$/ml Mean±SD Range	8.77±5.96 1.07-23.8
Neutrophil$\times10^3$/ml Mean±SD Range	6.26±4.52 0.75-18.9
Lymphocyte$\times10^3$/ml Mean±SD Range	2.1±1.55 0.2-7.0
Platelets$\times10^3$/ml Mean±SD Range	284.19±107.85 41.0-515
NLR Mean±SD Range	4.83±7.1 0.24-44.0
PLR Mean±SD Range	241.05±320.2 7.32-2050
CRP, mg/L Mean±SD Range	40.71±60.4 0-168

Admission Diagnosis

So far, pneumonia was the most common diagnostic entity encountered in 51.25% of the patients. Fever without a source came next with 21 patients (26.25%) followed by gastroenteritis (13.75%), seizure (12.5%) and Kawasaki (7.5%) as shown in table 4.

Table 4: Diagnosis at admission (n=80)

Diagnosis	Frequency (%)
Pneumonia	41(51.25%)
Fever without focus	21(26.25%)
Gastroenteritis	11(13.75%)
Febrile Seizure	10(12.5%)
Kawasaki	6(7.5%)
Histiocytosis	1(1.25%)

Some patients had more than one diagnosis

Association of demographic and Clinical characteristics with MIS-C

Four factors were found to be significantly associated with development of MIS-C. Most patients (60%) with no MIS-C had **no comorbidity** compared to 10% of those who develop MIS-C, with a significant difference. The mean **hospital stay** among patients with MIS-C was 5.44±2.92 days which was significantly longer than those without MIS-C (2.86±1.58). The **median NLR** in patients with MIS-C was 6.21(range=0.24-44.0) which was significantly higher than that without MIS-C (median = 2.25, range=0.5-39). Finally, in patients who developed MIS-C, the **median of CRP** was 112.0 mg/L (range= 0-168 mg/L) compared with 32.0 mg/L (0-128 mg/L) in those without MIS-C, with a significant difference (Table 5).

Table 5: Association of demographic characteristics with patients' outcome

Variables	No MIS-C (n=70)	With MIS-C (n=10)	p-value
Age, years mean±SD	6.1±4.28	5.67±4.32	0.777†
Gender Male Female	44(62.86%) 26(37.14%)	4(40%) 6(60%)	0.168‡
Residence Urban Rural	54(77.14%) 16(22.86%)	4(40%) 6(60%)	620‡

***Cont...* Table 5: Association of demographic characteristics with patients' outcome**

Comorbidity			
No comorbidity	42(60%)	1(10%)	**0.003‡**
Malignancy	14(20%)	4(40%)	0.157
Asthma	9(12.86%)	3(3%)	0.156
Cerebral palsy	3(4.39%)	1(10%)	0.438
Others	3(4.29%)	1(10%)	0.438
History of contact			
Yes	51(72.9%)	7(70%)	0.850‡
No	19(27.1%)	3(30%)	
Hospital stays, days			
Mean±SD	2.86±1.58	5.44±2.92	**<0.001†**
Need for O$_2$ therapy			
Yes	63(90%)	7(70%)	0.074
No	7(10%)	3(30%)	
Total WBC ×10^3/ml			
Median (range)	7.7(1.07-23.8)	9.05(4.3-21.9)	0.235‡
Neutrophil×10^3/ml			
Median (range)	6.4(0.75-18.9)	6.65(1.4-18.3)	0.085‡
Lymphocyte×10^3/ml			
Median (range)	1.6(0.2-7.0)	1.35(0.2-5.9)	0.393‡
Platelets×10^3/ml			
Median (range)	288(41-515)	247(166-515)	0.344‡
NLR			
Median (range)	2.25(0.5-39.0)	6.21(0.24-44.0)	**0.013‡**
PLR			
Median (range)	175.34(7.32-2050)	162.2(4.68-218.3)	0.454‡
CRP, mg/L			
Median (range)	32.0 (0-128)	112.0(0-168)	**0.038‡**

† Student t-test, ‡ Chi square test, ‡ Mann Whitney U test

Prognostic Value of NLR and CRP

Receiver operating characteristic (ROC) curve was used to find out the cut off value of NLR and CRP in predicting MIS-C. **For NLR**, the area under the curve (AUC) was 0.827, 95%CI=0.670-0.984, p=0.006. The sensitivity and specificity of the test at cut off value of NLR= 3.34 were 71% and 82%, respectively. **For CRP**, the AUC was 0.748, 95%CI=0.512-0.984, p=0.039. The sensitivity and specificity of the test at cut off value of CRP= 101.7 mg/L were 71% and 89%, respectively (Figure 1).
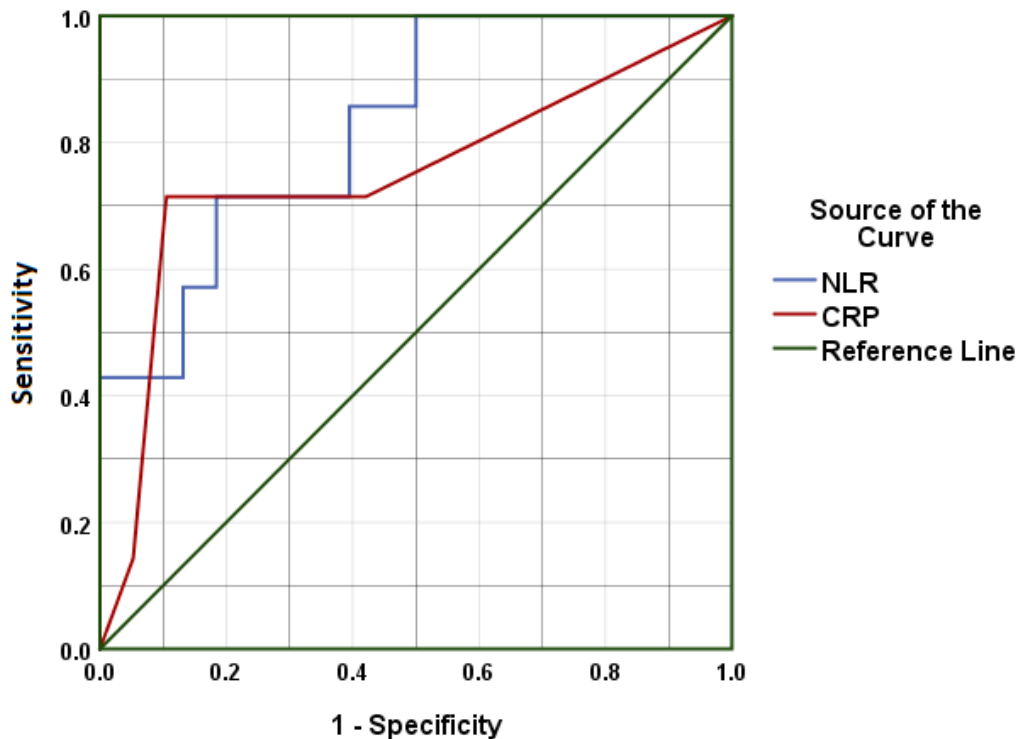
Figure 1: Receiver operating characteristic curve for NLR and CRP in predicting development of MIS-C in children with COVID-19

Antimicrobials were used in all cases (100%) and oxygen need was seen in 50% of study cohort. COVID-19 investigational treatments were not administered to any case in study cohort. intravenous immunoglobulin was given to the cases with MIS-C for suspected Kawasaki disease . During the study period no mortality was documented in the study cohort.

Discusion

Despite the rising incidence of COVID-19 cases in children, little is known about their clinical and analytical features. In contrast to adults with COVID-19, studies demonstrate that changes in leukocyte indices are mainly inconsistent in children. As a result, leukocyte indices do not appear to be accurate indicators of illness severity in children (9). We are conducting this research to better understand the clinical and laboratory features hospitalized COVID 19 cases in pediatric age group, and more critically, to find a valid disease severity predictive biomarker..

In the current study, the mean age of the patients was 6.05±5.1 years (range <1-16years), lower than what's is found by Lu X et al [10] and Dong Y et al [11]. male were predominant this agree with Dong et al who reported that 56.6% of the patients in their study were boys[4].

In this study, only 27.5 percent of cases had a positive history of contact with a confirmed case of COVID-19, which is significantly lower than the 70 percent of patients in other studies conducted in China, Saudi Arabia, and Oman.[12,13,14]. This may be attributed to the lack of accurate and frequent testing and most importantly documentation, all these could have led to the underestimation of reported cases.

Pediatric patients with COVID-19 in this study were more likely to have underlying comorbidities (53.75%), this percentage is more than what has been described in other studies for example 39% by DeBiasi et al [15] . however, Shekerdemian et al found

that underlying comorbid conditions were present in 83 percent of the patients with COVID19 who had admitted to intensive care unit [16].

Different types of malignancy were the most common comorbidity in this study accounting for 50%. this is much higher than what found by DeBiasi et al (1%) and While other studies the most common comorbidity was sickle cell anemia in Al Yazidi et al [14], asthma in DeBiasi et al [15]. sickle cell not seen in any case in our study this is probably because other hospital in Baghdad city is concerned with sickled children.

Fever was the most common presenting symptom in children hospitalized with COVID-19 in the current study; this was similar to results reported by Al Yazidi et al [14], Qiu et al [17], Derespina et al [18].

The most common Initial syndromic diagnoses in our study was pneumonia, this agree with result by Lu x et al study at Wuhan Children's Hospital located in Wuhan, the epidemic center of this novel infection who found that pneumonia was diagnosed in 64.9% of children with COVID 19 infection [19].

The complete blood count revealed no significant changes in children hospitalized with COVID-19 in this study, which is consistent with findings by Henry et al [9].In terms of inflammatory markers, Children with COVID-19 rarely exhibit high inflammatory markers, according to Al Yazidi et al [14] and Liguoro et al [20], which is consistent with the findings of this study. However, Kainth et al[21] , Zachariah et al[22] have linked elevated inflammatory markers to severe illness in children.[22] .

Half of patients in our study had normal findings on chest radiograph, which is similar to what Liguoro et al found , that only 50% of children with confirmed COVID-19 had chest X-ray abnormalities , this could be attributed to milder involvement by the disease so chest X-ray may fail to identify typical lesions, and it is primarily used in the neonatal period and infancy [20] .

All the patients in the current study received antibiotic empirically, which could be explained by physician's worries about COVID-19 's potential severity and risk of co-infection with other viruses or bacteria. antibiotic use in children with COVID-19 has been shown to range from 19.4% to 100.0% by Wang et al [23],while al Yazidi et al found that Antimicrobials were used in 68% of children admitted with COVID- 19 [14].

In our analysis, nine patients (11.25 percent) had a diagnosis of MIS-C, which was defined as a severe COVID 19 presentation with unknown pathogenesis [24]. Patients with MIS-C have greater comorbidity, according to our findings. Harman et al similarly found a link between underlying comorbidities and severe COVID-19 [25] .

longer stay at hospital was found in patients with MIS-C about 5.44±2.92 days, likewise, Sinaei R et al [26] in case series of children with MIS-C in Iran reported that the average length of PICU stay for MIS-C cases was 6 days.

Regarding laboratory result two factors was found to be significant in children who develop MIS-C which was the NLR and CRP. This goes with results found in a case series by Feldstein LR et al showed that patients with MIS-C had higher neutrophil to lymphocyte ratio and C-reactive protein level [27]. Also agree with Zachariah et al in a case series done at New York City who found that patient with severe disease had significantly higher C-reactive protein.

This could be of benefit since those are simple, rapid tests, of low cost and widely available at ER and can be used as an early signal for development of MIS-C.

Finally, the outcome for all children in this study was favorable, with no reported mortality, which was similar to result by Al Yazidi et al.

Conclusions

Mild course and favorable outcome signify the

majority of pediatric cases of COVID 19 Malignancy is the commonest comorbidity associated with COVID-19 admissions. Elevated NLR and CRP are independently associated with development of MIS-C in COVID-19 among children.

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