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Epidemiology and clinical spectrum of COVID19 infection in a Tunisian pediatric population

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ABSTRACT :

Objective : The objective of this study was to describe epidemiological data, symptoms profiles and management of children with confirmed COVID19 and assess risk factors of fatal issue.

Methods : the study was conducted in the pediatric COVID unit, Hedi Chaker Hospital, Sfax TUNISIA from 1st December 2020 to 31 august 2021. Children younger than 14 years old who had COVID 19 were included. Confirmed cases were detected via RT-PCR (reverse transcription polymerase chain reaction) in nasopharyngeal swab.

Results : a total of 60 children were included; 34 boys and 26 girls, median age was 22 months [12day- 14 years]. Among all patients, 29 had family contact history (48.3%) and 20 had one or more coexisting condition (33.3%). The median time from illness onset to diagnosis was 5 days (interquartile range ; 2-7 days). Four patients were asymptomatic (6.6%); the main symptoms were fever (49 cases, 81.6%) and Shortness of breath (26 cases, 43.3%). Thirty-two patients presented with gastrointestinal symptoms (53.3%). Four patients had multisystem inflammatory syndrome associated with COVID19 (6.6%). Twenty-six patients received oxygen (43.3%); among them, nine required invasive mechanical ventilation (15.0%).
Ten patient died (16.6%); the main cause of death was acute respiratory distress syndrome (5 cases, 50% of causes of mortality).

Conclusion : a high rate of severe cases and mortality were observed in our study, Moreover, 70 % of infants presents a severe form of the illness.

Key words : COVID19 infection; child; epidemiology; outcome.

INTRODUCTION :

Since the outbreak of coronavirus disease 19 (COVID19) in Yuhan CHINA in 2019, COVID19 had spread aroundthe world; The world health organization characterized the infection as pandemic on March 2020 [1]. Pediatric population is susceptible to COVID 19, and many pediatric studies has been published to characterize the full spectrum of the disease in children. The infection leads often to mild or moderate clinical presentation in children unless they have underlying comorbidities [2] In Tunisia, published data on epidemiological, clinical spectrum and outcome of children with COVID 19 is not available. We describe, here, the experience of COVID19 pediatric unit during a period of nine months.

METHODS :

A retrospective study was conducted in COVID 19 pediatric unit in Hedi Chaker Hospital , Sfax, TUNISIA, during a period of nine months (1st December 2020-31 August 2021). Children aged less than 14 years tested positive for COVID 19 by RT PCR on nasopharyngal swab were included. The RT PCR were performed in laboratory of virology Habib Bourguiba Sfax TUNISIA. We collected, epidemiological data, exposure, underlying conditions, clinical presentation, laboratory testing (blood count,

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C reactive protein, liver function, renal function), management and outcome of patients. The severity of COVID 19 was based on clinical features, laboratory testing and chest imaging as asymptomatic; mild, moderate, severe or critical. The diagnosis criteria were as follows:

Asymptomatic : without any clinical symptoms, whereas RT PCR COVID 19 is positive.

Mild : symptoms of acute upper respiratory tract infection (nasal congestion, rhinorrhea) , sore throat, cough, myalgia, digestive symptoms: vomiting, abdominal pain, diarrhea

Moderate : pneumonia , frequent fever, but not obvious hypoxemia or shortness of the breath. Chest tomography may shows lung lesions.

Severe : respiratory symptoms with dyspnea and hypoxia (oxygen saturation is less than 92%)

Critical : respiratory failure, acute respiratory distress syndrome, encephalopathy, multi-organ failure.

Children who met all criteria of Multisystem inflammatory syndrome (MIS-C) and had positive RT-PCR were included; MIS-C criteria were consistent with the WHO definition [3].

Data Collection And Statistical Analyses :

Statistical analysis was performed using IBM SPSS.25 Software. Categorical variables were expressed as numbers and percentages. The Kolmogorov–Smirnov test was used to assess the distribution of continuous variables. Normally distributed continuous variables were expressed as mean ± standard deviation (SD) and non-Gaussian continuous variables were expressed as medians and interquartile ranges (IQR). The study of the associations between variables was done by hypothesis tests. The comparison between two qualitative variables was made by the Pearson "Chi2" test when the conditions were verified otherwise the exact Fisher test was a remedy. For all tests performed, the significance threshold was set at 5%.

RESULTS :

1-1- Baseline characteristics and epidewmiology :

Sixty patients tested reverse transcription (RT-PCR) positive. The median age of all patients was 20 months (range 12 days- 14 years). Thirty-four patients were boys (SR=1.3). Among all patients, 29 had family contact history (48.3%) and 20 had one or more coexisting condition (33.3%); neurological disorders and malignancies (acute lymphoblastic leukemia, Burkitt lymphoma) were the most common coexisting conditions in 7 and 6 cases respectively. The demographic characteristics were shown in table 1.

Tableau 1 : WHO definition of MIS-C [3]

0 ≤ Age ≤19 years
AND Fever lasting ≥ 3 days
AND at least two among these symptoms: a- Rash or bilateral conjunctivitis or oral changes or peripheral extremity changes b- Hypotension or shock c- Cardiac complications (myocarditis, coronary artery abnormalities) d- Elevated D dimer e- Gastrointestinal disorders (abdominal pain, vomiting, diarrhea)
AND Laboratory evidence of inflammation (VS, C reactive protein, PCT)
And No alternative plausible diagnoses
And Positive for current or recent SARS-CoV-2 infection by RT-PCR, antibody, or antigen test; or exposure to a suspected or confirmed COVI19- case

1-2- Clinical manifestations :

The median time from symptom onset to diagnosis was 5 days (interquartile range; 2-7 days)

The most common symptoms were fever (49 cases, 81.6%), shortness of breath (26 cases, 43.3%) and vomiting (16 cases, 26.6%). Regarding the severity of clinical presentation, 4 patients (6.6%) were asymptomatic (three had malignancies and one had idiopathic bone marrow failure), 25 patients (41.6%) were diagnosed as mild or moderate and 27 patients (45%) had severe or critical cases (Table 2).

Tableau 2 : Demographic characteristics of children with COVID 19

Characteristic		Number	%
Gender	Male	34	56.6
	Female	26	43.3
Age (years)	≤ 1 year	29	48.3
	]1-5]	14	23.3
	]5-10]	7	11.6
	]10-14]	10	16.6
Underlying disease	Neurological disorder	7	11.6
	Asthma	3	5.0
	Congenital heart disease	3	5.0
	Malignancies	6	10.0
	Crohn disease	1	1.5
	Primary immunodeficiency	1	1.5
	Lupus	1	1.5
	GH deficiency	1	1.5
	Chronic renal failure	1	1.5
Exposure route	Intra-familial cases	30	50
	confirmed	29	48.3
	suspected	1	1.5
	Other confirmed contact	2	3
	Unkown	28	46.6

Table 3 represents the severity of illness by age; it reveals that %70 of infants presented a severe form of the illness (23/16). Four patients presented MIS-C associated with COVID 19.

Tableau 3 : clinical characteristics in children with COVID19

	Clinical parameters	Number	(%)
Symptoms	None	4	
Systemic	Fever	49	81.6
	Headache	4	6.6
	Weakness	8	13.3
Respiratory	Dyspnea	26	43.3
	Cough	19	31.6
	Nose obstruction and/ or rhinorrhea	11	18.3
Gastrointestinal	Vomiting	16	26.6
	Diarrhea	9	15.0
	Abdominal pain	7	11.6
Other	Seizure	3	
	Drowsiness	1	
	Loss of smell	1	
	Sore throat	1	

1-3- Laboratory findings and chest imaging :

Blood cell count was performed in 58 patients. Leukocytosis (white blood cell (WBC) count >129 /L) was observed in 15 cases (25.8%). Fourteen patients (23.3%) showed leucopenia (WBC count < 5 109/L); 16 patients (26.6%) presented neutropenia (blood neutrophil count < 1,5 109/L) and 10 (16.6%) had thrombopenia. Only 17 patients (28.3%) had elevated C reactive protein (≥ 30 mg/l) range (44- 226mg/l). Liver function tests were performed in 38 cases; alanine aminotransferase and aspartate amino transferase were both elevated in 19 cases (50%), there was no case of liver failure. Regarding renal function, blood creatinine was increased in two cases; one child had paralytic myelomeningocele and one had a known chronic kidney failure. Regarding blood coagulation function, D-dimer, was increased in 9 among 10 patients who underwent this test, maximum of D dimer was 27000 µg/L. Four patients fulfilled criteria of Mis-C associated with COVID 19 and their D dimer were respectively 1500, 1408, 1500 and 999 µg/L. Chest X ray was performed in 23 cases; it was abnormal in 17 cases (73.9%). The major observed lesion was bilateral alveolar opacities (9 cases). CT imaging was performed in 18 cases; it was normal in only one case, fifteen patients (83.3%) showed characteristic radiologic abnormalities (ground glass opacities, lesion's extension ranged from 25% to 80%) and two patients showed respectively pneumothorax and pleuro-pneumonia.

1-4- Treatment and outcome :

Glucocorticoid were administered in severe cases (19 patients) and immunoglobulins were used in 4 patients who had Mis C syndrome at the dose of 2g/kg. Oxygen support (nasal cannula, non invasive ventilation) was administrated to 26 patients according to the severity of respiratory distress and saturation. Among them, nine patients required mechanical ventilation. Twelve patients received Azithromycin.The duration of hospitalization ranged from 1 to 43 days with a mean of 8,02 days.

Ten patients were died (16.6%); the main cause of death was SDRA (6 cases) (Table 4).

Tableau 4 : severity of illness by age group.

Age group (year)	Asymptomatic (n)	Mild (n)	Moderate (n)	Severe (n,%)	Critical (n,%)	Misc-C	Total(n)
≤ 1 an	0	11	0	16 (26)	2 (3,3)	0	29
1-5 ans	2	6	0	3 (5)	0	3	14
5- 10 ans	1	2	0	3 (5)	0	1	7
11 -14 ans	1	5	1	2 (3,3)	1 (1,6)	0	10
Total (n)	4	24	1	24 (40)	3 (5)	4	60

Factors linked to fatal outcome were age ≤ 1an, dyspnea, polypnea, desaturation, SDRA and mechanic ventilation. (Table5)

Tableau 5 : Risk factors of mortality.

Characteristic		Death (Total = 10) (N, %)	p
Age	≤ 1 an (N=29)	8 (27.6)	0.03
	>1an (N=31)	2 (6.45)	
Gender	Male (N=34)	7 (20.6)	0.49
	Female (N=26)	3 (11.5)	
Underlying disease	N=20	1	
Exposure route	Confirmed or suspected contact (N=32)	5 (15.6)	1
	Unkown (N=28)	5 (17.8)	
Clinical Symptoms	Fever (N=49)/No fever (N=11)	9 (19.4)/1 (9.0)	0.76
	Headache (N=4)/No Headache (N=56)	0 (0.0)/10 (17.8)	1
	Weakness (N=8) No weakness (52)	1 (14.3)	1
	Dyspnea (N=26)/ No dyspnea (N=34)	8 (30.8)/ 2 (5.8)	0.01
	Cough (N=19)/ No cough (N=41)	4 (21.1)/ (14.6)	0.71
	Nose obstruction (N=7)	2 (28.6)	0.33
	Rhinorrhea (N=4)	1 (25.0)	0.52
	polypnea	9 (36)/1(2.9)	0.001
	Vomiting (N=16)	4 (25.0)	0.43
	Diarrhea (N=9)	2 (22.2)	0.63
	Abdominal pain (N=7)	1 (14.3)	1
Clinical form	Severe or critical (N=27)	10 (37)	<0.001
	Others (N=33)	0 (0)	
Physical examination	crackling rales (N=6)/no crackling (N=54)	3 (50)/ 7 (12.9)	0.05
	Sibilant rales (N=10)/ no sibilants (N=50)	3 (30)/ 7 (14)	0.34
	Desaturation (N=19)/No (N=41)	8 (42.1)/ 2 (4.9)	0.001
Biological characteristics	Leukocytosis (white blood cell (WBC) count >129 /L (N=15) vs <129 (N=45)	5 (33.3) 5 (11.1)	0.10
	leucopenia (WBC count < 5 109/L) (N=13)/ No leucopenia (N=44)	2 (15.4) 8 (18.2)	1
	neutropenia (blood neutrophil count < 1,5 109/L) (N=14)/ No (N=41)	2 (14.3) 8 (19.5)	1
	Thrombopenia (N=10)/ No (N=50)	3 (30)/7 (14)	0.35
	C reactive protein (≥ 30 mg/l) (N=17)/ No (N=43)	4 (23.5)/6 (13.9)	0.44
Complications	SDRA (N=5)/No SDRA (N=55)	3 (60)/7 (12.7)	0.02
	Surinfection (N=2)/ No (N=58)	1 (50)/9 (15.5)	0.28

DISCUSSION :

The most striking feature in this cohort is the high frequency of severe cases (27/60) ; several studies have reported that symptoms of COVID 19 in children are usually milder as compared with adults [4-6]. In a nationwide Chinese study enrolling 2135 child, severe and critical forms of the illness represented 5,8%, while asymptomatic; mild and moderate cases accounted 94,1% of all cases [4]. In a recent review, 2597 children with COVID 19 were collected from 24 articles; only 4,4% had severe illness and 0,9% were critically ill [6]. The high rate of severe cases in this study was observed especially in children aged less than one year and those who had underlying diseases. The proportion of severe and critical cases was 62% for the age group less than 1 year; similarly, in the Chinese study, the proportion of severe and critical cases was highest in infants aged less than one year in comparison with other age group (10,8 %) [4]. These results suggest that infants are vulnerable to COVID 19 infection. Regarding exposure history, we found that intra-familial exposure was the most cause of infection (50%) ; similarly , in a Korean study , which included 91 child with COVID-19 , the most common source of infection was household contact (63%) [7]. Of the 2597 cases included in a review, most children had exposure to household members with confirmed COVID 19 [6]. We observed slightly more boys than girls (34 vs 26) which is similar to different epidemiological studies [4,8,9], the median age of all children was 22 months; in the Chinese study, mentioned above, the median age was 7 years [4]. The median time from symptom onset to diagnosis was longer in the Chinese study (5 days versus 2 days). There is a variety of symptoms of COVID 19 in children, the major symptoms in this study were fever (81,6%), lower respiratory tract symptoms (75%) and gastrointestinal disorders (53,3%). In the review accounting 2597 cases, the clinical information from 452 children in 23 articles were analyzed; most children with COVID 19 experienced the following symptoms: fever (43,1%), cough (43,3%), sore throat (20,4%), tachycardia (16,8%), rhinorrhea (16,4%), nasal congestion (15,3%), shortness of breath (12,6%), diarrhea/vomiting (12,3%), myalgias or fatigue (5,1%) and chest pain (0,4%). Regarding laboratory findings, in the same review, the following observations were made: leukocytes were normal in 74,4%, leucocytosis in 8,8%, lymphopenia in 9,8%, Creative protein was increased in 18,8%, alanine aminotransferase and aspartate aminotransferase were increased respectively in 11,2 % and 17,3%, blood creatinine was increase in only two cases and D dimer were increased in 12,1% [6]. Chest computed tomography was recommended by the Tunisian pediatric society in highly suspected cases who had negative RT PCR COVID 19, in immunocompromised children and in severe or critical cases [10]. Similar to adults, the typical radiographic image described in the literature is parenchymal destruction expressed as ground-glass opacities and consolidation [11,12]. A high rate of deaths was noted in this study (16,6%), especially in children aged less than one year and those who had underlying diseases. In a systematic review of the literature, that included 10 articles describing a total of 2914 pediatric patients; the mortality rate of children that were hospitalized with COVID 19 was 0,18% (5/2914) [13]. In an English study, case-fatality rate in children with COVID19 was < 0,5% [14].

Our study had a limitation of the small number of children with COVID19, analytic study will be more interesting with large cohort , and may help us to find more factors linked to mortality.

No conflict of interest

List of abbreviations :

CT imaging : chest tomography imaging
GBS : Guillain Barré syndrome
MIS-C : multi-system inflammatory syndrome in children
IQR: interquartile range
IV: intravenous
PCT: procalcitonin
RT-PCR : reverse transcription polymerase chain reaction)
SDR A : Acute respiratory distress syndrome
SD : deviation standard
SR : sexratio
VS : sedimentation rate
WBC : white blood cell
WHO : world health organization

REFERENCES :

[1] Who.who director –general's statement on IHR Emergency committee on novel coronavirus (2019 n.cov). Available at https://www.who.int/dg/speeches/detail/ Accessed March 3, 2020.

[2] Lu X, Zhang L, Du H and Al. SARS-cov2 infection in children. N Engl.J.Med 2020;382 (17):1663-1665.

[3] Who/2019-Ncov/sci_brief/multisystem_syndrome_children/2020.1. checked on 3 July 2022.

[4] Dang Y, Hu Y, Qi X, and Al. Epidemiolgy of COVID19 among children in China. Pediatrics 2020,145;6:e 20200702.

[5] Cai X, Jiang H, Zhang S. Clinical manifestations and pathogen characteristics in children admitted for suspected COVID19. Front. Med. 2020; 14(6): 776-785.

[6] Cui H, Zhang T, Zheng J and al. Children with coronavirus disease 2019: a review of demographic, clinical, laboratory, and imaging features in pediatric patients. J Med virol 2020; 1-10.

[7] Han Mi S, Choi E H, Chang S H. clinical characteristics and viral RNA detection in children with coronavirus disease 2019 in the republic of Korea. JAMA Pediatr 2021; 175 (1):73-80.

[8] The novel coronavirus pneumonia emergncy response epidemiology team. The epidemiological chracteristics of an outbreak of 2019 novel coronavirus diseases (COVID19) China, 2020. China CDC weekly 2020;2(8): 113-122.

[9] Guan WJ, Ni ZY, Hu Y et al. China medical treatment expert group for COVID 19. Clinical characteristics of coronavirus disease 2019 in China. N Engl JMed 2020 ;382(18):1708-1720.

[10] INEAS – Les recommandations nationales pédiatriques et enfants COVID-19 - Novembre 2020.Checked on 3 July 2022.

[11] Li W, Cui H, Li K, Fang Y, Li Sh. Chest computed tomography in children with COVID 19 respiratory infection. Pediatr Radiol 2020;50 (6):796-799.

[12] Peng X, Guo Y, Xiao H et al . Overview of chest involvment at computed tomography in children with coronavirus disease 2019 (COVID 19). Pediatr Radiol 2021;51:222-230.

[13] Patel NA. Pediatric COVID19: Systematic review of the literature. Am J Otolaryngol 2020;41: 102573.

[14] Ladhani SN, Chowdhury ZA, Davies HG and al. COVID19 in children : analysis of the fisrt pandemic peak in England. Arch Dis Child 2020;105:1180-1185.