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Clinical profile, risk factors and outcomes of pediatric COVID-19: a retrospective cohort multicentre study in Saudi Arabia

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ABSTRACT

Objective To describe the risk factors, clinical profile and outcomes of COVID-19 in the paediatric population.

Design Multicentre, retrospective observational study.

Setting Four tertiary hospitals in Saudi Arabia.

Patients We recruited 390 paediatric patients aged 0–18 years who presented from March to December 2020 and tested positive for COVID-19 on PCR.

Main outcome measures We retrospectively analysed medical records for sociodemographics, health indicators, clinical presentations, laboratory findings, clinical complications, and outcomes.

Results The mean participant age was 5.66±4.90 years, and the mean hospital stay was 2.17±3.48 days. Forty patients, mostly school-aged children (16, 40.00%; p=0.005) and children with comorbidities (25, 62.50%; p<0.001), received more than just supportive care. Complications were seen in 15 (3.9%) patients, bacterial infection being the most common (6, 40.00%). Patients presented with dyspnoea (OR 6.89; 95% CI 2.89 to 20.72), abnormal chest radiographs (OR 6.11; 95% CI 1.26 to 29.38), lethargy (OR 9.04; 95% CI 2.91 to 28.06) and elevated ferritin (OR 14.21; 95% CI 4.18 to 48.37) and D-dimer (OR 48.40; 95% CI 14.32 to 163.62), with higher odds of developing complications. The odds of paediatric intensive care unit (ICU) admission were higher for patients with dyspnoea (adjusted OR 4.66; 95% CI 1.24 to 17.50) and elevated white blood cell count (adjusted OR 3.54; 95% CI 1.02 to 12.30).

Conclusions COVID-19 complications were limited among our patients. However, dyspnoea, abnormal chest radiographs, lethargy and elevated ferritin and D-dimer were associated with an increased risk of complications. Dyspnoea, leucocytosis, comorbidities and abnormal chest radiographs at presentation increased the risk of ICU admission.

Strengths and limitations of this study

- ► The study represented the largest national multicentre cohort that followed up paediatric patients during their hospital admission.
- ► The study's retrospective design may affect its quality.
- ► Unavailability of follow-up data prevented the formation of a conclusion on the long-term effects of COVID-19 on the paediatric population.

What is already known on this topic

- ► The incidence of paediatric COVID-19 is less than 2.0%.
- ► The concept of silent carriers became known in this population because children have a milder presentation or remain asymptomatic.
- ► The complication and intensive care unit (ICU) admission rates are much lower for children than for adults.

What this study adds

- ► Risk factors like dyspnoea, abnormal chest radiographs, lethargy and elevated ferritin and D-dimer levels are associated with higher chances of developing complications in children with COVID-19.
- ► Dyspnoea and leucocytosis at presentation increased the risk of ICU admission in this population.

INTRODUCTION

By March 2020, COVID-19 was declared a pandemic by WHO.[1] This pandemic inflicted a major burden on the healthcare system, especially the intensive care units (ICUs). Initial reports on COVID-19 concentrated primarily on the adult population and included the clinical presentation and management recommendations.[2] This may have been because the pneumonia-related symptoms are more common in adults than in children.[3] The first paediatric COVID-19

case was discovered in Shenzhen, China, on 20 January 2020.[4] However, after COVID-19 screening campaigns were initiated in multiple regions worldwide, more paediatric cases were discovered, and the concept of silent carriers or patients with mild disease symptoms became known in this population.[5]

The incidence of paediatric COVID-19 (aged ≤18 years) is reportedly 0.8%–2.0% of all cases.[2 6–9] A multicentre cohort study involving 25 European countries concluded that COVID-19 could be manifested throughout the paediatric age scale.[10] In that study, Götzinger *et al* found that 7% of 582 paediatric COVID-19 cases were under 1 month old, 22% were 1–12 months old, 10% were 1–2 years old, 11% were 2–5 years old, 16% were 5–10 years old and 34% were older than 10 years. The incidence of paediatric COVID-19 in Saudi Arabia paralleled the figures found in other international reports, with a local incidence of 4%.[11 12] In one local study, most paediatric patients presented with mild symptoms.[13]

Apart from the classic symptoms of COVID-19, which include fever, cough, and shortness of breath, paediatric patients were exclusively linked to the occurrence of a unique medical phenomenon termed 'multisystem inflammatory syndrome in children' (MIS-C). MIS-C was reported in several international studies to affect critically ill children infected with SARS-CoV-2.[14 15] MIS-C was handled as a distinct entity because of its wide range of severity levels and multisystem manifestations, including gastrointestinal symptoms, rash, heart lesions and shock.[14–17] An overlap between MIS-C features and those of Kawasaki disease has been reported by several authors, although the latter usually occurs in younger children than COVID-19.[17]

Although there are numerous reports about the epidemiology, clinical presentation, laboratory and radiological findings, and outcomes of COVID-19, most are primarily based on adult populations, with variable focus on the paediatric age group. Paediatric reports on COVID-19 among Saudi population were limited by a cross-sectional design accompanied by a single-centre setting or a small sample size.[11–13 18–21] Accordingly, their findings cannot be generalised to the paediatric COVID-19 patient population.

This study aimed to identify the risk factors, initial clinical presentation and laboratory findings, and outcomes in paediatric COVID-19 patients presented to four medical centres in different regions of Saudi Arabia.

METHODS

This was a multicentre, retrospective observational study conducted in four tertiary hospitals in the Eastern, Middle and Western provinces of Saudi Arabia. The participating institutions were King Fahd Hospital of the University, Alkhobar; Johns Hopkins Aramco Healthcare, Dhahran; King Saud Medical City, Riyadh; and Dr. Soliman Fakeeh Hospital, Jeddah. Collectively, their paediatric ward capacity is 325 beds, and the paediatric ICU (PICU) capacity is 56 beds. All four hospitals were designated as COVID-19 centres at the beginning or during the study period. The study included all paediatric patients (age ≤18 years) who presented to these hospitals from May to August 2020 and were SARS-CoV-2 PCR-positive following the nationally adopted screening criteria.[22] Patients with incomplete or missing data were excluded from the study.

The retrieved data were as follows: age (infant, <1 year; toddler, 1–2 years; preschool, 3–5 years; school age, 6–11 years; adolescent, 12–18 year); sex; region (Western, Eastern and Central); admission status (admitted or not admitted); route of recruitment (emergency room (ER), paediatric ward, PICU); history of contact with COVID-19-confirmed case (yes or no); presence of comorbidities (yes or no) such as cardiac, respiratory, neurological, endocrinological, haematological, gastroenterological and other diseases; month of admission; duration of admission; presence of complications (yes or no) and the complication type; type of treatment received (supportive or other interventions, including medication and ventilation); presence of symptoms at admission (yes or no), including fever, cough, sore throat, headache, dyspnoea, rash, myalgia, rhinorrhoea and diarrhoea; laboratory blood test results at the time of presentation (normal, increased or decreased), including white cell count (WCC) and differential counts, platelet count, C reactive protein, erythrocyte sedimentation rate, ferritin, bilirubin, aspartate transaminase, alanine transaminase, creatine kinase (CPK), lactate dehydrogenase (LDH), albumin, creatinine and D-dimer; chest radiography findings (normal, unilateral consolidation, bilateral consolidations or ground glass appearance); and outcome (discharge, death).

All analyses were performed using Stata V.16 (StataCorp). We used the t-test, the χ^2 test or Fisher's exact test as appropriate for comparisons of different age groups and other study variables. Additionally, unadjusted and adjusted (for age and sex) logistic regression models estimated the odds of developing abnormal blood results and complications among study participants. Continuous values are presented as mean±SD. Categorical variables are presented as number and percentage.

Patient and public involvement

No patient involved.

RESULTS

Participants

This study included 390 patients. As seen in table 1, most participants were from the Western region (247, 63.3%), female (203, 52.1%) and infants (115, 29.5%). The participants' age was 5.66±4.90 years (0.5–18.0 years), weight was 20.46±13.17 kg (2–50 kg), and hospital stay was 2.17±3.48 days (0–18 days). Fifteen patients (3.9%) developed complications, with bacterial infection (6, 40.00%),

Table 1 Study participants sociodemographic features

	Asymptomatic*		Symptomatic		Total				
	n	%	n	%	n	%			
	294	75.4	96	24.6	390	100.0	χ^2	df	P value
Age group									
Infant (<1 year)	74	64.35	41	35.65	115	29.5			0.009†
Toddler (1–2 years)	36	90.00	4	10.00	40	10.3			
Preschool (3–5 years)	46	76.67	14	23.33	60	15.4			
School age (6–11 years)	89	80.18	22	19.82	111	28.5			
Adolescent (≥12 years)	49	76.56	15	23.44	64	16.4			
Sex									
Male	133	71.12	54	28.88	187	48.0	3.52	1	0.06
Female	161	79.3	42	20.7	203	52.1			
Region									
Western	212	85.8	35	14.2	247	63.3	89.41	2	<0.001
Eastern	65	79.27	17	20.13	82	21.0			
Central	17	27.87	44	72.13	61	15.6			
Admission status									
Not admitted	227	100.0	0	0.0	227	58.2			<0.001†
Admitted	67	41.10	96	58.90	163	41.8			
Rout									
Emergency room	227	99.6	1	0.4	228	58.5			<0.001†
Paediatric ward	64	42.38	87	57.62	151	38.7			
PICU	3	27.27	8	72.73	11	2.8			
Contact with COVID-19-positive cases									
No	92	69.70	40	30.30	132	33.9	3.48	1	0.06
Yes	202	78.3	56	21.7	258	66.2			
Comorbidity									
No	248	76.8	75	23.2	323	82.8	1.97	1	0.16
Yes	46	68.66	21	31.34	67	17.2			
Season of admission									
Spring (March–May)	37	57.81	27	42.19	64	16.4			0.001†
Summer (June–August)	248	79.2	65	20.8	313	80.3			
Autumn (September–November)	9	69.23	4	30.77	13	3.3			

*Asymptomatic or with mild symptoms at addmision
†Indicates that the p value was calculated by Fisher's exact test
PICU, paediatric intensive care unit.;

acute respiratory distress syndrome (ARDS; 2, 13.33%) and shock (2,13.33%) being most common.

Symptoms at presentation

In regard to infant particpants, 61 infants were 6 months old or younger (15.64%); 32 of these (52.46%) were male. Many of these infants had COVID-19 symptoms that required admission (29, 47.54%) and 41 (67.21%) had a history of being in contact with a COVID-19-positive case. Furthermore, 50 (81.97%) had no comorbid conditions. Of the 11 infants (18.03%) with a comorbid disease in this young infant group, three had a cardiac disease and three had a neurological disease. Thirty-nine (63.93%) had fever, 22 (36.07%) had rhinologic symptoms, 21 (34.43%) had cough, 12 (19.67%) had diarrhoea and 6 (9.84%) had lethargy. None showed a rash at presentation. In regard to other participants, fever was the most common symptom at presentatioin 269 (68.97%) espicially among older children. In addition, cough was statisycally significantly more common among adolsenct 36 (56.25%) as well as dyspnoea 19 (26.69%). Symptoms of

Table 2 Symptoms of COVID-19 at presentation according to paediatric age groups

	Infant n=115		Toddler n=40		Preschool n=60		School age n=111		Adolescent n=64				
Symptom	n	%	n	%	n	%	n	%	n	%	χ^2	df	P value
Fever													
No (n=121)	44	38.26	18	45.00	16	26.67	28	25.23	15	23.44	10.46	4	0.03
Yes (n=269)	71	61.74	22	55.00	44	73.33	83	74.77	49	76.56			
Cough													
No (n=256)	85	73.91	31	77.50	40	66.67	72	64.86	28	43.75	19.64	4	0.001
Yes (n=134)	30	26.09	9	22.50	20	33.33	39	35.14	36	56.25			
Sore throat													
No (n=307)	109	94.78	33	82.50	49	81.67	81	72.97	35	54.69	42.62	4	<0.001
Yes (n=83)	6	5.22	7	17.50	11	18.33	30	27.03	29	45.31			
Headache													
No (n=353)	112	97.39	40	100.00	56	93.33	92	82.88	53	82.81			<0.001*
Yes (n=37)	3	2.61	0	0.00	4	6.67	19	17.12	11	17.19			
Dyspnoea													
No (n=337)	102	88.70	40	100.00	55	91.67	95	85.59	45	70.31			<0.001*
Yes (n=53)	13	11.30	0	0.00	5	8.33	16	14.41	19	26.69			
Rash													
No (n=383)	115	100.00	40	100.00	58	96.67	107	96.40	63	98.44			0.17*
Yes (n=7)	0	0.00	0	00.00	2	3.33	4	3.60	1	1.56			
Myalgia													
No (n=357)	108	93.91	38	95.00	55	91.67	103	92.79	53	82.81			0.14*
Yes (n=33)	7	6.09	2	5.00	5	8.33	8	7.21	11	17.19			
Rhinorrhoea													
No (n=276)	76	66.09	29	72.50	43	71.67	87	78.38	41	64	5.80	4	0.22
Yes (n=114)	39	33.91	11	27.50	17	28.33	24	21.62	23	35.94			
Diarrhoea													
No (n=342)	100	86.96	33	82.50	51	85.00	99	89.19	59	92.19	2.89	4	0.58
Yes (n=48)	15	13.04	7	17.50	9	15.00	12	10.81	5	7.81			

Infant, <1 year; todler, 1–2 years; preschool, 3–5 years; school age, 6–11 years; adolescent, 12–18 years.
*Indicates that the p value was calculated by Fisher's exact test.

COVID-19 at presentation according to paediatric age groups are listed in table 2.

Labratory test results at presentation

Table 3 summarises the investigation results by age groups. Among the 6 months old or younger infants, abnormal D-dimer was found in four (6.56%), high ferritin in three (4.92%), elevated LDH in seven (11.48%), and abnormal lymphocyte count in 13 (21.21%); lymphocyte counts were increased and decreased in six (84.78%) and seven (15.22%) cases, respectively.

Treatments and interventions of COVID-19

As seen in table 4, most patients received supportive treatment. However, 14 received hydroxychloroquine, five received dexamethasone, and 20 received a combination of treatments. Most of the 40 children requiring more than supportive care were school-age children (16, 40%; Fisher's exact test, p=0.005), and children with preexisting comorbidities (25, 62.50%; $\chi^2(1)=62.50$, p<0.001). Complications were seen in 15 participants (3.85%) and they mainly were due to secondery infection 6 (40%). Only two patients died during the study period. One was a 1-year-old girl with a neurological disease who developed ARDS, and the other was a 10-year-old boy with no comorbidities who developed shock.

Most patients admitted to the PICU were preschool children (7/11, 63.64%; $\chi^2(5)=13.23$, p=0.02). The mean PICU stay was 8±3.44 days (3–16 days) and most patients were discharged without complications (8/11, 72.73%; $\chi^2(1)=16.79$, p<0.001). Of the 11 PICU patients, 1 received supportive care, one received dexamethasone,

Table 3 Central tendency measures (mean and SD) of laboratory investigations

Measured labratory tests				Paediatric age groups*									
				Infant n=115		Toddler n=40		Preschool n=60		School age n=111		Adolescent n=64	
Lab test	Status	Number	Unit	M	SD	M	SD	M	SD	M	SD	M	SD
WCC (n=206)	Normal	154	(x10^9/L)	10.66	5.20	10.49	4.71	8.71	5.54	9.26	5.78	7.28	4.54
	Increased	26											
	Decrease	26											
Neutrophil (n=204)	Normal	143	(x10^9/L)	3.13	2.93	4.02	3.21	4.01	3.76	5.01	4.63	4.01	3.76
	Increased	20											
	Decreased	41											
Lymphocyte (n=205)	Normal	145	(x10^9/L)	5.21	3.04	5.49	2.69	3.64	3.44	2.28	1.51	4.15	13.89
	Increased	25											
	Decreased	35											
Eosinophil (n=197)	Normal	147	(x10^9/L)	0.32	0.44	0.17	0.33	0.06	0.07	0.30	0.81	0.13	0.92
	Increased	5											
	Decreased	45											
Platelet (n=206)	Normal	176	(x10^9/L)	377.89	160.92	306.39	120.45	275.17	77.79	286.54	129.91	251.89	87.89
	Increased	21											
	Decreased	9											
ESR (n=12)	Normal	5	(mm/hr)	28.00	28.84	10.00	00.00	73.33	46.46	16.33	10.25	46	56.51
	Increased	7											
Ferritin (n=50)	Normal	30	(ng/mL)	214.88	193.69	169.83	215.45	40.57	28.00	612.15	882.75	511.69	1656.63
	Increased	18											
	Decreased	2											
Bilirubin (n=108)	Normal	86	(mg/dL)	34.60	57.74	21.06	45.33	14.42	22.46	9.80	18.64	11.93	15.50
	Increased	21											
	Decreased	1											
AST (n=111)	Normal	93	(U/L)	41.53	29.66	41.14	16.19	50.18	31.56	49.33	83.24	27.03	16.59
	Increased	18											
ALT (n=119)	Normal	111	(U/L)	25.25	25.64	20.37	6.60	21.66	24.50	19.19	17.44	14.38	14.49
	Increased	5											
LDH (n=66)	Normal	32	(U/L)	329.33	33.45	453.33	263.52	242.50	108.70	548.80	601.69	223.07	103.39
	Increased	33											
	Decreased	1											
Albumin (n=108)	Normal	100	(g/L)	30.87	14.41	38.09	12.36	30.13	18.00	29.95	18.00	23.59	18.99
	Decreased	8											
Creatines (n=154)	Normal	82	(mg/mL)	0.42	0.55	0.36	0.62	1.99	7.03	1.00	1.85	0.62	0.17
	Increased	6											
	Decreased	66											
D-dimer (n=40)	Normal	14	(µg/mL)	1.32	0.14	2.31	1.49	1.68	1.84	2.63	1.79	0.94	1.10
	Increased	26											

*Infant, <1 year; todler, 1–2 years; preschool, 3–5 years; school age, 6–11 years; adolescent, 12–18 years
ALT, alanine transaminase; AST, aspartate transaminase; ESR, erythrocyte sedimentation rate; LDH, lactate dehydrogenase; WCC, white cell count.

5 received hydroxychloroquine and 4 received a combination of dexamethasone and hydroxychloroquine.

Risk estimation of developing poor COVID-19 outcomes

After age adjustment in the logistic regression models, the odds of having elevated LDH were lower in female patients (OR 0.43; 95% CI 0.200 to 0.91) and patients with higher body weight (OR 0.90; 95% CI 0.84 to 0.97), while they were higher in patients with preexisting comorbidities (OR 5.63; 95% CI 2.67 to 11.85), increased lymphocyte count (OR 3.90; 95% CI 1.50 to 10.13) and increased platelet count (OR 5.04; 95% CI 1.80 to 14.08). No association was found between increased LDH and the presence of various symptoms at presentation.

The odds of having elevated lymphocyte count were lower in patients with fever at presentation (OR 0.23; 95% CI 0.09 to 0.55) and higher in patients with

Table 4 The distribution of COVID-19 outcomes in relation to presence of symptoms at admission

	Asymptomatic		Symptomatic		Total				
Outcome	N=294	75.38%	N=96	24.62%	N=390	100%	X^2	df	P value
Complications									
No	291	98.97	84	87.50	375	96.15	25.79	1	<0.001
Yes	3	1.02	12	12.50	15	3.84			
ARDS	0		2						
Acute cardiac injury	0		2						
Acute kidney injury	0		1						
Shock	1		1						
Secondary infections	1		5						
Other	1		2				14.12	1	<0.001
PICU admission									
No	291	98.97	88	91.66	379	97.17			
Yes	3	1.02	8	8.33	11	2.82			
Treatment recieved									
Supportive	269	91.49	81	84.37	350	89.74	3.99	1	0.046
Other interventions	25	8.50	15	15.62	40	10.25			
Ventilator	0		1						
Dexamethasone	3		2						
Hydroxychloroquine	5		9						
Combination trearment	17		3						
Mortality									
Discharged	293	99.65	95	98.95	388	99.48			0.432*
Death	1	0.34	1	1.04	2	0.51			

*P value comes from Fisher's exact test.
ARDS, acute respiratory distress syndrome; PICU, paediatric intensive care unit.

pre-existing comorbidities (OR 3.54; 95% CI 1.47 to 8.51). The odds of developing higher ferritin were lower in patients with higher body weight (OR 0.82; 95% CI 0.73 to 0.91), dyspnoea (OR 3.08; 95% CI 1.06 to 8.98) and pre-existing comorbidities (OR 15.84; 95% CI 5.38 to 46.62).

The odds of having elevated D-dimer were lower in patients with higher body weight (OR 0.85; 95% CI 0.77 to 0.92) and higher in the presence of cough (OR 2.59; 95% CI 1.13 to 5.91), dyspnoea (OR 4.29; 95% CI 1.77 to 10.42), rash (OR 11.06; 95% CI 2.31 to 52.74), fatigue and myalgia (OR 6.96; 95% CI 2.76 to 17.54) and pre-existing comorbidities (OR 12.29; 95% CI 5.14 to 29.36). The development of complications increased the odds of interventional treatment (OR 17.68; 95% CI 5.79 to 53.71). The odds of developing complications were higher in patients presenting with dyspnoea (OR 6.89; 95% CI 2.89 to 20.72), abnormal chest radiographic findings (OR 6.11; 95% CI 1.26 to 29.38), lethargy (OR 9.04; 95% CI 2.91 to 28.06), elevated initial ferritin result (OR 14.21; 95% CI 4.18 to 48.37) and elevated D-dimer (OR 48.40; 95% CI 14.32 to 163.62). The odds of PICU admission were higher for patients with dyspnoea (adjusted OR 4.66; 95% CI 1.24 to 17.50) and elevated WCC count (adjusted OR 3.54; 95% CI 1.02 to 12.30) for further results please refer to tables 5 and 6.

DISCUSSION

On 2 March 2020, the first confirmed case of paediatric COVID-19 was discovered in Saudi Arabia.[23] After reviewing the literature, this work represents the largest multicentre observational study of paediatric COVID-19, involving three major regions in the kingdom and a significant cohort size, comparable to international reports on the topic.[17] In our cohort, males and females were equally affected. We found that 29.49% participants were infants (<1 year), 10.3% were 1–2 years old, 15.4% were 3–5 years old, 28.5% were 6–11 years old and 16.4% were over 12 years old. This age structure finding is somewhat comparable to other international reports, except for the second most affected age group. It was children aged 6–11 years in our study and adolescents (>11 years) in other reports.[17] This could be because school-aged children comprised almost one-third of our study population. The observation of infants being more affected

Table 5 Summary of logistic regression models that estimate the risk of developing poor prognostic labratory findings of COVID-19

	Elevated ferritin		Elevated D dimer		Elevated LDH		Lymphocytopenia		Elevated creatinine		Decreased platelet	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Age												
≤5 years	Ref.											
6–11 years	**4.16**	**1.38,12.49**	1.59	0.61 to 4.16	1.79	0.84 to 3.81	1.76	0.76 to 4.06			0.70	0.13 to 3.59
≥12 years	2.07	0.48 to 8.89	**2.93**	**1.10 to 7.77**	0.61	0.17 to 2.16	1.14	0.43 to 3.01			0.42	0.05 to 3.57
Gender*												
Male	Ref.											
Female	0.69	0.26 to 1.79	0.87	0.39 to 1.94	**0.43**	**0.20 to 0.91**	2.08	0.96 to 4.47	5.79	0.65 to 51.07	0.84	0.22 to 3.24
Weight* (kg)	**0.82**	**0.73 to 0.91**	**0.85**	**0.77 to 0.92**	**0.90**	**0.84 to 0.97**	1.06	0.99 to 1.13	0.93	0.80 to 1.09	0.97	0.85 to 1.01
Comorbidities*												
No	Ref.											
Yes	**15.84**	**5.38 to 46.62**	**12.29**	**5.14 to 29.36**	**5.63**	**2.67 to 11.85**	0.49	0.19 to 1.25			1.28	0.31 to 5.31
Chest X-ray*												
Normal	Ref.											
Abnormal	1.62	0.54 to 4.92	**2.79**	**1.01 to 7.75**	1.79	0.77 to 4.18	1.78	0.76 to 4.16	1.12	0.15 to 8.58	1.04	0.22 to 4.94
Dyspnoea*												
No	Ref.											
Yes	**3.08**	**1.06 to 8.98**	**4.29**	**1.77 to 10.42**	2.33	0.96 to 5.62	0.61	0.22 to 1.64	0.56	0.06 to 5.15	1.23	0.24 to 6.41
Cough*												
No	Ref.											
Yes	1.77	0.67 to 4.70	**2.59**	**1.13 to 5.91**	1.96	0.94 to 4.08	1.04	0.48 to 2.24	0.35	0.04 to 3.14	1.01	0.24 to 4.23
Fever*												
No	Ref.											
Yes	0.63	0.24 to 1.70	1.43	0.56 to 3.69	0.67	0.32 to 1.40	**2.96**	**1.08 to 8.10**	**0.15**	**0.03 to 0.89**	1.64	0.33 to 8.24

Bold font indicated significant p<0.05
*Adjusted regression models for age
LDH, lactate dehydrogenase; Ref., reference.

by the disease could be due to their relatively immature immune system.[24]

Most of our patients were asymptomatic or had mild symptoms, and only around one-third of them required hospital admissions. This observation is similar to previous reports on paediatric COVID-19.[25 26]

Only 2.8% of our patients required intensive care admission. This observation was found in various international studies and confirmed that the paediatric age group had a milder degree of COVID-19 than adults.[12 20 26] In one local multicentre study of 88 COVID-19 patients, the rate of PICU admission was higher than ours (8%).[27] This could be because our national COVID-19 guidelines had been revised in May 2020, adopting a lower threshold for defining suspected COVID-19 cases qualifying for PCR screening. This change allowed the discovery of asymptomatic paediatric patients and those with mild symptoms.[22]

Compared with international reports, the percentage of our asymptomatic patients and those with mild symptoms (75.4%) was slightly lower than in two previous major metanalyses (98% and 96%).[28 29] This could be because our indicators for disease severity were based on multiple factors and not merely on the severity of symptoms. These included fever measured or subjectively reported by history, respiratory symptoms of any severity, and mild symptoms of the disease with a history of contact with a confirmed COVID-19 case.

We report a mean hospital stay of 2.17 days (1–18 days), the lowest in all local and international studies to date. A local study by Kari *et al* reported a hospital stay of 5.9 days.[20] In the UK, the average stay was 3 days.[27] A case series by Xia *et al* reported an average hospital stay of 12.9 days.[30] This difference could be due to our nationally adopted protocol involving discontinuation of isolation of confirmed mild COVID-19 cases, characterised by a passage of 10 days from the start of the symptoms, resolution of fever for at least 3 days without antipyrectic drugs, and alleviation of other symptoms.[22]

Fever was the most observed symptom (69%), followed by cough (34.3%) and rhinorrhoea (29.2%). In comparison, previous reports noted fever as the most observed symptom, ranging between 41% and 59% cases, while cough was the second most prominent symptom (37%–46%).[26–34]

Only 3.85% patients in our cohort developed complications, with the most common being bacterial infection (40.0%), ARDS (13.3%) and shock (13.3%). Furthermore,

Table 6 Summary of logistic regression models that estimate the risk of developing poor prognostic outcomes of COVID-19

	Interventional treatment		Complications		PICU admission	
	OR	95% CI	OR	95% CI	OR	95% CI
Age						
≤5 years	Ref.					
6–11 years	**2.62**	**1.21, 5.66**	1.70	0.56, 5.18	**14.40**	**1.75, 118.61**
≥12 years	**3.22**	**1.37, 7.61**	0.96	0.19, 4.73	**10.52**	**1.07, 102.99**
Gender						
Male	Ref.					
Female	0.86	0.44, 1.66	0.60	0.21, 1.72	1.50	0.43, 5.24
Weight (kg)	0.87	0.81, 0.94	**0.86**	**0.7, 0.96**	**0.90**	**0.81, 0.99**
Comorbidities						
No	Ref.					
Yes	**13.15**	**6.30, 27.47**	**6.12**	**2.14, 17.53**	**9.91**	**2.76, 35.53**
Chest X-rays						
Normal	Ref.					
Abnormal	2.14	0.94, 4.86	**6.11**	**1.30, 29.38**		
Dyspnoea						
No	Ref.					
Yes	**5.07**	**2.41, 10.67**	**6.89**	**2.29, 20.72**	**4.64**	**1.28, 16.85**
Cough						
No	Ref.					
Yes	0.84	0.41, 1.71	1.83	0.50, 6.66	1.29	0.37, 4.47
Fever						
No	Ref.					
Yes	0.84	0.41, 1.71	2.29	0.80, 6.62	0.45	0.13, 1.54
Any symptom at presentation						
No	Ref.					
Yes	**2.16**	**1.07, 4.33**	**14.31**	**3.92, 52.18**	**10.08**	**2.57, 39.52**

Bold font indicated significant p<0.05
Ref., reference.

we found that dyspnoea, abnormal chest radiographic findings, lethargy, elevated initial ferritin and elevated D-dimer were significantly associated with the development of complications in our cohort. Lymphocytopenia and increased LDH differed significance among age groups. This observation has been reported before.[35 36] The presence of dyspnoea, leucocytosis, abnormal chest radiograhic findings and comorbidities at the time of presentation was significantly associated with an increased risk for ICU admission among our cohort. In comparision, AAntúnez-Montes *et al* reported a relatively similar observation through their Multinational Latin American study involving a cohort of four hundred nine children. Preexisting medical condition, immunodeficiency, lower respiratory tract infection, gastrointestinal symptoms, abnormal radiologic changes and low socioeconomic conditions were their reported risk factors for admission to the ICU.[37]

Our reported fatality rate (0.5%) is consistent with the previously reported percentage (<2%) in other international paediatric COVID-19 studies.[10 38–40] In the UK, The International Severe Acute Respiratory and Emerging Infection Consortium study reported a fatality rate of 0.9% due to Paediatric COVID-19.[41] In another recent english study, the fatality rate in children who died of SARS-CoV-2 was 0.2 per 100 000 person years (95% Poisson CI) compared with 25.5 per 100 000 for all other causes of death.[42] In the USA, fatelity rate of paediatric COVID-19 reached 0.9%.[43] In our cohort, 99.49% patients were discharged without a negative prognosis.

Our interventional management options included the use of non-invasive ventilation, mechanical ventilation, administration of dexamethasone, hydroxychloroquine, antiviral agents or a combination of two or more of these options. Most of our cohort received supportive treatment; however, few (3.6%) received hydroxychloroquine,

dexamethasone or a combination of both. The sole reliance on supportive treatment for managing paediatric COVID-19, regardless of its severity, is well reported in the literature.[44–46] Most children requiring more than supportive management, that is, interventional management, were school-aged children (aged 6–11 years) and children with comorbid diseases. Data on the appropriate pharmacological choices for COVID-19 treatment are still under study by various institutions, and the proposed guidelines are not generalised yet for the paediatric population.[44] Cao *et al* recommended following their randomised, controlled, open-label trial for hospitalised adult patients with confirmed SARS-CoV-2 infection, stating that antiviral drugs should be reserved for patients with severe disease.[47] Furthermore, the WHO Guideline Development Group for COVID-19 drug treatments strongly recommended the use of systemic corticosteroids to treat patients with severe and critical COVID-19.[48]

Our study has some limitations, including its retrospective design that could affect the quality of such a study. Furthermore, we could not formulate a conclusion on the long-term effects of COVID-19 on the paediatric population as our follow-up period ended at discharge. One of the major strengths of our study is its being one of the largest multicentre studies that followed up paediatric patients during their hospital admission.

CONCLUSION

COVID-19 presentation in the paediatric population ranges from mild to severe disease, depending on the age group. However, most of our participants presented with mild or asymptomatic COVID-19. Furthermore, the presence of dyspnoea, abnormal chest radiographic findings, lethargy, elevated ferritin, and elevated D-dimer were associated with the development of complications among our participants. The presence of dyspnoea, leucocytosis, abnormal chest radiograhic findings and comorbidities at the time of presentation was associated with an increased probability of ICU admission.

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