Original Article

Clinical profile and in-hospital outcomes of COVID-19 among adolescents at a tertiary care hospital in India

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ABSTRACT

Introduction: We aimed to describe the clinical profile and risk factors for severe disease in adolescents hospitalised with coronavirus disease 2019 (COVID-19). **Methods:** A retrospective analysis of an admitted cohort of COVID-19 patients was performed at a tertiary hospital in North India. Adolescents aged 12–18 years who were hospitalised during the first wave (March–December, 2020) and the second wave (March–June, 2021) were included. Data on the demographic details, clinical presentation, laboratory parameters, disease severity at admission, treatments received, and in-hospital outcomes were retrieved. **Results:** The study included 197 adolescents with a median [inter-quartile range (IQR)] age of 15 (13–17) years, of whom 117 (59.4%) were male. Among these, 170 (86.3%) were admitted during the first wave. Underlying co-morbidities were present in nine (4.6%) patients. A total of 60 (30.9%) patients were asymptomatic. In the severity grading, 148 (84.6%) had mild, 16 (9.1%) had moderate, and 11 (6.3%) had severe disease. Fever (14.9%) and cough (14.9%) were the most commonly encountered symptoms. The median (IQR) duration of hospital stay was 10 (8–13) days, and six (3.1%) patients died in the hospital. **Conclusion:** Adolescents admitted with COVID-19 had predominantly asymptomatic or mild disease, and the mortality rate was 3.1%.

KEY WORDS: Adolescent, clinical profile, COVID-19, risk factor

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic has severely affected every aspect of human life and health, including physical, social, behavioral, and psychological well-being. Globally, it has affected 288 million people and caused more than 5.4 million deaths as of now.[1] Approximately 20% of adult COVID-19 patients require hospitalisation, 5% become critically ill, and between 2 and 5% may die.[1] Although children constitute a relatively small proportion of the hospitalised COVID-19 cases with relatively lower severity and mortality, there has been a surge in the number of cases in children with the progression of the pandemic.[2]

Various vaccines have been developed to counteract COVID-19, but till now, the vaccines available in India are restricted for use among adults (aged 18 years and above) only. However, from 3 January 2022 onwards, adolescents between 15 and 18 years of age will be given the Covaxin

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vaccine, as per the latest government guidelines.[3] India has the largest adolescent population in the world of approximately 253 million, and every fifth person is between 10 and 19 years. Adolescents in the age group of 12–18 years have already suffered because of closures of schools during the lockdowns, hampering their educational, emotional, and social development.[4] Worryingly, reports suggest that adolescents are also susceptible to developing severe COVID-19 illness.[5]

Although there have been multiple studies involving adults and children below 12 years of age,[6] the clinical characterisation and course of COVID-19 in the 12–18 age adolescent group are still not well defined.

Furthermore, there are limited studies assessing risk factors for severe disease, particularly from developing countries. This study aimed to describe the clinical profile and in-hospital outcomes of adolescents hospitalised with COVID-19 in a tertiary care teaching hospital from India.

MATERIALS AND METHODS

Study population
We performed a retrospective analysis on a cohort of patients admitted at a dedicated COVID-19 tertiary care hospital in North India. We retrieved the clinical data of adolescents aged 12–18 years hospitalised with severe acute respiratory symptom coronavirus 2 (SARS-CoV-2) during the first (March 2020 to December 2020) and second (March 2021 to June 2021) waves of the COVID-19 pandemic in India. Patients with a positive reverse transcription polymerase chain reaction or a cartridge-based nucleic acid amplification test (CBNAAT) for SARS-CoV-2 from secretions of the upper or lower respiratory tract were eligible for inclusion in the study. Tests for SARS-CoV-2 were performed as per the Indian Council of Medical Research (ICMR) guidelines.[7] Besides, all hospitalised patients were tested for SARS-CoV-2 as per the institutional policy. Initially, all cases of COVID-19 were being hospitalised; however, from July 2020, the Government of India recommended home isolation for patients who were asymptomatic or mildly symptomatic without any co-morbidity. Consequently, only moderate to severe cases, adolescents with co-morbidities, and those for whom home isolation was not feasible were hospitalised. We excluded home-isolated patients from our study.

Data collection
We extracted data from the electronic records of patients regarding demographic details; clinical features including the nature, duration, and severity of symptoms; various laboratory parameters; and patients' in-hospital outcomes (discharge or death). The patients were treated according to the institutional protocols. In most cases, treatment was supportive, and specific medications were used on a case-to-case basis.[8] Outcome measures included

descriptive statistics related to demographic, clinical, and laboratory parameters in the patients. We classified disease severity as per World Health Organisation (WHO) guidelines: Patients were deemed to have severe disease if SpO_2 was less than 90% or the respiratory rate was greater than 30 per minute, moderate disease if there were symptoms of pneumonia (fever, cough, tachypnea, and breathlessness) with SpO_2 greater than 90%, and mild disease if there were no symptoms or signs of pneumonia or hypoxemia.[9] The study protocol was approved by the institute ethics committee (IEC).

Statistical analysis
Data were analysed using Stata v14 (StataCorp LP, College Station, TX). Categorical data were reported as percentage (%). Continuous parameters were reported as mean (standard deviation, SD) if data were normally distributed or median (interquartile range, IQR) if data had a skewed distribution. The patients were classified into two groups to assess risk factors for disease severity: The first group included asymptomatic and mild illness, and the second group included moderate and severe illness. Clinical and laboratory parameters were compared among both groups using bivariate analysis. Means were compared using Student's t-test, and medians were compared using Mann–Whitney test. A *P* value of less than 0.05 was considered as significant.

RESULTS

Demography
We enrolled a total of 197 adolescents aged 12–18 years in the study. The median (IQR) age was 15 (13–17) years with 117 (59.4%) males. Among them, 170 (86.3%) were enrolled during the first wave and 27 (13.7%) were enrolled during the second wave of the COVID-19 pandemic in India. The most common co-morbidities were malignancy (n = 8), auto-immune disease (n = 4), diabetes mellitus (n = 2), asthma (n = 2), chronic kidney disease (n = 2), and hypertension (n = 1).

Clinical features
Among the enrolled patients, 60 (30.9%) were asymptomatic at hospital admission. Among the symptomatic patients, 148 (84.6%) had mild, 16 (9.1%) had moderate, and 11 (6.3%) had severe disease. The most common symptoms were fever (14.9%), cough (14.9%), myalgia (11.5%), fatigue (10.4%), nasal symptoms (8.8%), dyspnoea (6.2%), and diarrhoea (2.6%). The median (IQR) duration of symptoms at presentation was 3 (2–5) days. Table 1 summarises the laboratory investigations in included patients with the proportion of patients having abnormal values. Common laboratory abnormalities included high ferritin (34.9% of the patients), low haemoglobin (30.1%), a low total leukocyte count (21.1%), a low platelet count (19.3%), high serum glutamic oxaloacetic transaminase (SGPT) (16.8%), high D-dimer (15.5%), a high neutrophil lymphocyte ratio (NLR) (15.1%), high

Table 1: Laboratory parameters in adolescents infected with SARS-CoV-2

Laboratory parameter (data available)	Abnormal Values	Proportion of children having abnormal values, *n* (%)
Haemoglobin (Hb), g/dl (*n*=176)	Hb <11.5	53 (30.1)
	Hb <7.0	8 (4.6)
Total leucocyte counts (TLC)/mm³ (*n*=175)	TLC <4000	37 (21.1)
	TLC >12000	4 (2.3)
NLR (*n*=172)	NLR >3	26 (15.1)
Platelet counts/mm³ (*n*=176)	Platelets <150 000	34 (19.3)
Urea, mg/dl (*n*=176)	Urea >40	9 (5.1)
Creatinine, mg/dl (*n*=176)	Creatinine >0.9	6 (3.4)
Total bilirubin, mg/dl (*n*=176)	Bilirubin >1	25 (14.2)
SGOT, IU/dl (*n*=173)	SGOT >45	26 (15.0)
SGPT, IU/dl (*n*=173)	SGPT >45	29 (16.8)
Serum albumin, g/dl (*n*=174)	Albumin <3.5	9 (5.2)
Ferritin, ng/ml (*n*=89)	Ferritin >60	31 (34.8)
C-reactive protein (CRP), mg/L (*n*=121)	CRP >6	11 (9.1)
Fibrinogen, mg/dl (*n*=108)	Fibrinogen >400	10 (9.3)
D-dimer, ng/ml (*n*=116)	D-dimer >500	18 (15.5)

SARS-CoV-2, severe acute respiratory syndrome coronavirus-2; IQR, interquartile range; SD, standard deviation; NLR, neutrophil lymphocyte ratio; SGOT, serum glutamic oxaloacetic transaminase; SGPT, serum glutamic pyruvic transaminase

Table 2: Treatment received in adolescents infected with SARS-CoV-2

Nature of treatment (data available)	Number (%) of children, received the treatment
Antipyretics (*n*=177)	126 (71.2)
Anti-histamines (*n*=177)	112 (63.3)
Oral Vitamin C (*n*=177)	173 (97.9)
Teicoplanin (*n*=175)	7 (4.0)
Dalteparin (*n*=175)	18 (10.3)
Remdesivir (*n*=59)	10 (16.9)
Steroid (*n*=58)	14 (24.1)
Tocilizumab (*n*=177)	1 (0.6)
Oxygen (*n*=177)	13 (7.3)
NIV/HFNC (*n*=177)	5 (2.8)
Intubation (*n*=171)	4 (2.3)

SARS-CoV-2, severe acute respiratory syndrome coronavirus-2; NIV, non-invasive ventilation; HFNC, high-flow nasal cannula

serum glutamic pyruvic transaminase (SGOT) (15.0%), and high total bilirubin (14.2%).

Treatment and in-hospital outcomes

The majority of symptomatic patients received supportive therapy. Asymptomatic patients did not receive any treatment. Some patients received additional therapies, as shown in Table 2. Comparison between asymptomatic/mild vs moderate/severe cases in shown in Table 3. The most commonly used drugs were oral vitamin C, antipyretics, and anti-histamines. Fourteen patients received steroids, and 13 patients received oxygen. The median (IQR) duration of hospital stay was 10 (8–13) days. The majority of the patients survived; six (3.1%) patients died. Among the six deaths, four occurred in the first wave, two were females, two had co-morbidities (one each with malignancy and hypertension), and five had severe disease.

DISCUSSION

In this retrospective analysis of a prospectively enrolled cohort from a dedicated COVID-19 hospital in North India, we described the clinical and laboratory profiles of 197 adolescents aged 12–18 years hospitalised with COVID-19 infection. A large proportion of the subjects were asymptomatic or had mild disease at hospital admission.

Fever and cough were the most commonly encountered symptoms in our patients. Previously, a multi-centre study of adolescents with COVID-19 in Italy reported fever (82.1%) to be the most common symptom.[10] Similarly, a systematic review of studies enrolling children with COVID-19 found fever and cough to be the most common symptoms.[11] In contrast, other studies conducted in Chinese and American children with COVID-19 reported fever to be less common (36–56%) compared with cough or pharyngitis.[12-14] Although there are no previous Indian studies describing clinical features of COVID-19 among adolescents, fever and cough have been reported to be the most common symptoms of Indian COVID-19 patients in both the under-12 years age group (6) and in adults.[15]

In a previous Indian multi-centre study conducted among children under the age of 12 years hospitalised with COVID-19, the most common laboratory abnormalities included lymphopenia, thrombocytopenia, low alkaline phosphatase, and high ferritin.[6] We observed similar findings in adolescents aged 12–18 years. Additionally, we found raised D-dimer levels in a substantial proportion. Although the effects of SARS-CoV on hematopoiesis are still being explored, it has been proposed that the virus-mediated infection leads to consumption of T-lymphocytes, particularly the CD4 and CD8 T-cells, thereby leading to lymphopenia.[16] For thrombocytopenia, a proposed mechanism is virus-mediated endothelial damage leading to platelet activation and micro-thrombus formation in the pulmonary vasculature, which in turn leads to platelet consumption.[17] Meanwhile, higher serum ferritin levels have been found to be associated with severe pulmonary involvement, independent of age and gender.[18] D-dimer is an indicator of activation of the coagulation cascade and the fibrinolytic system. This activation of the coagulation cascade is postulated to be because of the viremia, accentuated cytokine levels, infection, and organ dysfunction.[19]

We observed a relatively low in-hospital mortality rate (3.1%) in our cohort. This is in concurrence with other studies which observed low mortality in younger age groups (2) with mortality gradually increasing with age.[20] An analysis of 5574 patients of all age groups admitted in our hospital in the first wave showed 2.5% mortality.[21] This mortality rate of our adolescent patients can be attributed to a lower concomitant co-morbidity, better immune response, and lesser exposure in adolescents in comparison to adults and the geriatric population.[22]

Table 3: Clinical features for asymptomatic/mild vs moderate/severe cases of COVID-19 in adolescents

Characteristics (data available)	Asymptomatic/Mild (*n*=148; 84.6%)	Moderate/Severe (*n*=27; 15.4%)	*P*
Age (years) (*n*=175)*	16 (14-17)	15 (13-17)	0.02**
Gender, male: female (*n*=175)	87:61	13:14	0.30
Wave, first: second (*n*=175)	132:16	17:10	<0.001**
Co-morbidities			
Diabetes mellitus (*n*=175)	1 (0.7)	1 (3.7)	0.17
Hypertension (*n*=175)	1 (0.7)	0	0.67
Asthma (*n*=175)	2 (1.4)	0	0.54
Chronic kidney disease (*n*=44)	2 (6.7)	0	0.32
Auto-immune disorder (*n*=41)	4 (13.3)	0 (0.0)	0.20
Haematological malignancy (*n*=40)	2 (6.9)	0 (0.0)	0.37
Solid organ malignancy (*n*=45)	1 (3.5)	4 (25.0)	0.03**
Duration of symptoms in days (*n*=119)*	3 (2-5)	4 (3-7)	0.03**
Symptoms			
Fever (*n*=172)	21 (14.3)	7 (28.0)	0.09
Nasal symptoms (*n*=172)	14 (9.5)	3 (12.0)	0.70
Cough (*n*=172)	22 (14.9)	6 (24.0)	0.26
Dyspnoea (*n*=172)	9 (6.1)	3 (12.0)	0.29
Fatigue (*n*=172)	14 (9.5)	5 (20.0)	0.12
Myalgia (*n*=172)	17 (11.6)	4 (16.0)	0.53
Diarrhoea (*n*=172)	4 (2.7)	1 (4.0)	0.72
Haemoglobin (Hb), g/dl (*n*=160)#	12.7 (0.2)	10.3 (0.6)	<0.001**
Total leucocyte counts/mm^3 (*n*=157)*	5390 (4095-6490)	5600 (4300-7650)	0.47
NLR (*n*=154)*	1.3 (1.0-2.1)	1.3 (1.1-2.1)	0.35
Platelet counts/mm^3 (*n*=160)*	238000 (174000-305000)	217000 (158000-293000)	0.79
Urea, mg/dl (*n*=160)*	19 (14-24)	19 (15-26)	0.76
Creatinine, mg/dl (*n*=160)*	0.6 (0.5-0.7)	0.5 (0.4-0.7)	0.20
Total bilirubin, mg/dl (*n*=160)*	0.6 (0.4-0.8)	0.6 (0.4-0.8)	0.80
SGOT, IU/dl (*n*=157)*	28 (23-34)	32 (24-46)	0.17
SGPT, IU/dl (*n*=157)*	22 (15-34)	24 (16-45)	0.31
Serum albumin, g/dl (*n*=158)#	4.4 (0.1)	4.1 (0.2)	0.01**
Ferritin, ng/ml (*n*=83)*	36 (21-93)	30 (18-183)	0.23
C-reactive protein, mg/dl (*n*=111)*	0.09 (0.01-0.68)	0.20 (0.02-3.16)	0.01**
Fibrinogen, mg/dl (*n*=98)*	284 (251-326)	270 (230-315)	0.88
D-dimer, ng/ml (*n*=107)*	95 (64-213)	115 (71-464)	0.01**
Antipyretics (*n*=173)	96 (65.8)	26 (96.3)	0.01**
Anti-histamines (*n*=173)	84 (57.5)	24 (88.9)	0.01**
Oral Vitamin C (*n*=173)	142 (97.3)	27 (100)	0.38
Teicoplanin (*n*=172)	1 (0.7)	6 (22.2)	<0.001**
Dalteparin (*n*=172)	6 (4.1)	12 (44.4)	<0.001**
Remdesivir (*n*=58)	3 (7.5)	7 (38.9)	0.01**
Steroid (*n*=57)	5 (12.8)	7 (38.9)	0.01**
Tocilizumab, *n* (%) (*n*=174)	0 (0.0)	1 (3.7)	0.02**
Oxygen (*n*=174)	2 (1.4)	11 (40.7)	<0.001**
NIV/HFNC (*n*=173)	1 (0.7)	4 (14.8)	<0.001**
Intubation (*n*=168)	0 (0.0)	4 (14.8)	<0.001**
Duration of hospital stay, days (*n*=175)*	10 (8-13)	10 (8-12)	0.84
Outcome (*n*=175)			
Survived	147 (99.3)	22 (81.5)	<0.001**
Died	1 (0.7)	5 (18.5)	<0.001**

All values expressed as frequency (%), mean (SD)#, or median (IQR)*; **P<0.05. IQR, interquartile range; NLR, neutrophil lymphocyte ratio; SGOT, serum glutamic oxaloacetic transaminase; SGPT, serum glutamic pyruvic transaminase; NIV, non-invasive ventilation; HFNC, high-flow nasal cannula

The strength of this study is that it is one of the largest single-centre studies on COVID-19 in the adolescent age group in India, covering both the waves of the pandemic. Second, a comprehensive clinical and laboratory spectrum was recorded and analysed. Inflammatory markers in the adolescent age group had been rarely reported. However, this study has some limitations. Because this is a retrospective record review, the treatment details of remdesivir and steroid use had not been included in the hospital record for a large number of patients in the first wave (before October 2020). Furthermore, laboratory tests were performed mostly in patients with greater severity of illness, which may lead to over-estimation of laboratory abnormalities in this study compared to community-based studies or studies enrolling both hospitalised and non-hospitalised patients of similar demography.

In conclusion, we found that among adolescents admitted because of COVID, the majority had asymptomatic and mild illness and the mortality rate was 3.1%.

Availability of data and materials

The data would be made available by the authors on specific request keeping patient confidentiality in view.

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