Original Article

Characteristics and outcomes of 231 COVID-19 cases admitted at a tertiary facility in India: An observational cohort study

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Abstract

Background: Ongoing pandemic because of COVID-19 has spread across countries, with varied clinical features and severity. Awareness of clinical course among asymptomatic and symptomatology in symptomatic cases is essential for patients' management as well as optimal utilization of health services (in resource limited settings) based on clinical status and risk factors. This study aimed to describe the clinical characteristics and outcomes of patients admitted with COVID-19 illness in the initial phase of the pandemic in India. **Methods:** It was an observational study. Patients aged 18 years or more, with confirmed SARS-CoV-2 infection, asymptomatic or mildly ill, were included. Patients with moderate-severe disease at admission or incomplete clinical symptomatology records were excluded. Data regarding demography, comorbidities, clinical features and course, treatment, results of SARS-CoV-2 RT-PCR, chest radiographs, and laboratory parameters were obtained retrospectively from hospital records. The outcome was noted in terms of course, patients discharged, still admitted (at the time of the study), or death. **Results:** Out of 231 cases, most were males (78.3%) with a mean age of 39.8 years. Comorbidities were present in 21.2% of patients, diabetes mellitus and hypertension being the most common. The most common symptoms were dry cough (81, 35%), fever (64, 27.7%), sore throat (36, 15.6%); asymptomatic infection noted in 108 (46.8%) patients. The presence of comorbidities was an independent predictor of symptomatic disease (OR-2.66; 95%CI 1.08–6.53, $P = 0.03$). None of the patients progressed to moderate-severe COVID-19, and there were no deaths. **Conclusions:** A large proportion of patients remained asymptomatic whereas those with comorbidities were more likely to be symptomatic. Most with mild disease had a stable disease course, barring few complication in those with comorbidities. The pandemic continues to grow as large number of asymptomatic cases may go undiagnosed.

Keywords: Asymptomatic, characteristics, COVID-19, outcomes

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Introduction

The COVID-19 pandemic because of SARS-CoV-2 infection emerged toward the end of 2019, and since then, it has spread across the globe. The coronavirus disease 2019 (COVID-19)

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pandemic has been raging across different geographies. The first case of COVID-19 from India was reported on January 30, 2020, from Kerala. The cases in India began rising in the latter half of March. A wide range of morbidity and mortality rates has been reported from various settings, with case fatality rates ranging from 1.8 to 15%.[1,2] This variation can be explained by the age and comorbidity profile of the affected population, testing criteria, and admission criteria, besides other factors.[3–5] Furthermore, SARS CoV-2 infection is mainly transmitted through respiratory droplets or direct, indirect, or close contact.[6] Airborne transmission is documented to occur during aerosol-generating procedures. Cases with symptoms such as cough (aerosol-generating) are infective. Controversies, however, exist to date regarding the transmission of the virus from asymptomatic or pre-symptomatic patients.[7] Understanding asymptomatic transmission is critical from a pandemic control strategy point of view.

Primary care physicians form an important bridging link between patients from less or inaccessible areas or low socioeconomic status. Primary care physicians attend most patients with minor symptoms and ailments at primary healthcare setups, since they are the first link to health care, based on their clinical assessment, and patients are referred to an appropriate level of health care. It is, therefore, very essential to understand the clinical course and outcome, risk factors for progression, and severity in asymptomatic or pre-symptomatic or mild cases to guide triage and referral of asymptomatic/mild patients to healthcare facilities with basic monitoring facilities as in COVID care centers or tertiary care hospitals. Overall, it will help to ensure adequate adherence to national policy for pandemic control and effective human resources utilization without compromising patients' management.

To have a complete understanding of the spectrum of illness, the severity of the disease, and outcomes, studies are required, including confirmed patients with mild illness and asymptomatic close contacts of positive cases, besides the moderate to severe cases that require hospitalization. The Indian authorities enforced lockdown early in the course of the pandemic, that is, on March 25. Large scale testing and contact tracing were carried out. All patients were admitted irrespective of symptomatology, and their close contacts were admitted in isolation facilities and tested for SARS-CoV-2. This initial phase presented a unique opportunity to elucidate the disease profile and outcomes among patients presenting with mild symptoms and those diagnosed on contact tracing. This study was designed to study the clinical characteristics and outcomes, including progression to moderate-severe disease among patients with mild COVID-19.

Methods

Study design and setting

This retrospective study was conducted in COVID-19 facilities at AIIMS, New Delhi, among patients admitted between 20th March and 30th April 2020. It is a tertiary care teaching hospital wherein facilities for the management of COVID-19 patients were created. Isolation facilities were designed to manage patients with mild illness, and a dedicated COVID ICU was created to cater to patients with moderate to severe disease. Patients presenting to the facility included those with varying degrees of disease severity and asymptomatic close contacts of a large congregation, wherein several positive cases were reported. Approved by Institutional ethical committee. Approved on 23 April 2020.

Procedures

The clinical case records of all admitted patients with laboratory-confirmed COVID-19 were screened for eligibility. The diagnosis was confirmed by real-time reverse-transcriptase- polymerase-chain-reaction (RT-PCR) for detecting SARS CoV-2 on the specimens obtained from nasal and throat swabs. Patients of age more than 18 years and asymptomatic/mild illness at presentation were included. Patients with incomplete records of clinical symptomatology were excluded. Patients were classified as having the mild disease if they presented with uncomplicated upper respiratory tract viral infection with non-specific symptoms such as fever, fatigue, cough, etc., or features of pneumonia but no signs of severe pneumonia and no need for supplemental oxygen.[8]

Data regarding the demographic profile, comorbidities, clinical features, laboratory parameters, hospital course, and treatment outcomes were noted. The daily symptom screen included fever, cough, sore throat, shortness of breath, expectoration, rhinorrhoea, myalgia, fatigue, loose stools, chest pain, anorexia, loss of taste, and loss of smell and other symptoms as given by the patients. Patients who did not have any symptoms related to COVID-19 at admission or during the hospital course were considered asymptomatic. Details of results of RT-PCR for SARS-CoV-2 were done at baseline, and day 14 was obtained retrospectively from the hospital records. Chest radiographs (wherever available) and available laboratory parameters were assessed for any abnormality. Patients were managed as per the national guidelines.[9] In clinical deterioration, the protocol was to shift patients to a high dependency unit (HDU)/intensive care unit (ICU) for further management.

Patients were considered dischargeable after two negative SARS-COV-2 RT PCR reports (at least 24 h apart), performed after at least 7 days of last positive test results. The outcome was noted in terms of the number of patients discharged, patients still admitted (at the time of the study), or death. The permission for the study was obtained from the Institute Ethics Committee (IECPG/166/23.4.2020).

Statistical analysis

Data were analyzed using STATA 13·0 and presented as mean (standard deviation)/median (interquartile range) and frequency percentage. Shapiro–Wilk's test assessed the normality of data. We used logistic regression analysis to determine independent predictors for symptomatic illness and RT-PCR

negativity at 14 days. *P* value < 0·05 was considered statistically significant.

Results

The study was conducted in the initial part of the pandemic when patients, irrespective of the severity of symptomatology, were admitted. A total of 335 laboratory-confirmed COVID-19 patients were admitted to the facility in the study period. 231 cases were included after applying the inclusion and exclusion criteria [Figure 1].

The majority were males comprising 78.4% of the cohort with a mean age of 39.8 years (range 18–73 years) [Table 1]. Most patients (205, 88.7%) had a definitive history of contact with a suspected or confirmed case. A significant proportion of the patients (49, 21.2%) had one or more chronic diseases, including diabetes mellitus, hypertension, cardiovascular or cerebrovascular disease, chronic lung disease including asthma/chronic obstructive pulmonary disease/tuberculosis or chronic liver disease. Diabetes mellitus (28, 12.1%) and hypertension (19, 8.2%) were the most common comorbidities noted.

Symptoms specific to COVID-19 were present in 123 (53.2%) of the patients; whereas 108 (46.7%) patients remained asymptomatic. The median duration of symptoms was 3 days (IQR 2–5.5). Among symptomatic, the most common symptoms included dry cough (81, 65.8%), fever (64, 52%), sore throat (36, 29.2%), and shortness of breath (24, 19.5%) [Figure 2]. The most common presentation among symptomatic patients was with dry cough alone (27, 11.7%). Other common presenting features were fever, fever with dry cough, fever with cough, and shortness of breath [Figure 3]. The laboratory abnormalities included anemia in 12·2%, leukopenia in 4.8%, and lymphocytopenia (< 1500 cells/mm3) in 11.2% of the patients.

The demographic and laboratory parameters are compared between symptomatic and asymptomatic patients in Table 2. The presence of comorbidities emerged as an independent predictor of symptomatic disease with an odds ratio of 2.66 (95% CI 1.08–6·53, *P* = 0.03) on logistic regression analysis. RT-PCR for SARS-CoV-2 was positive in 14.5% (26/179) of patients at the end of 2 weeks. Table 3 shows the comparison of various demographic, clinical, and laboratory parameters among these two groups of patients, wherein no statistically significant differences were noted.

Among the 231 cases, none progressed to moderate-severe disease during hospitalization. Four patients (1.7%) required shifting to the ward unit to manage comorbidities, including angina,[1] ureteric colic,[1] and glycemic control.[2] Overall, 8.1% (4/49) patients with comorbidities required uptriaging. There were no deaths in this cohort. At the time of writing this manuscript, 172 (74.5%) patients have been discharged, and 59 (25.5%) are still admitted.
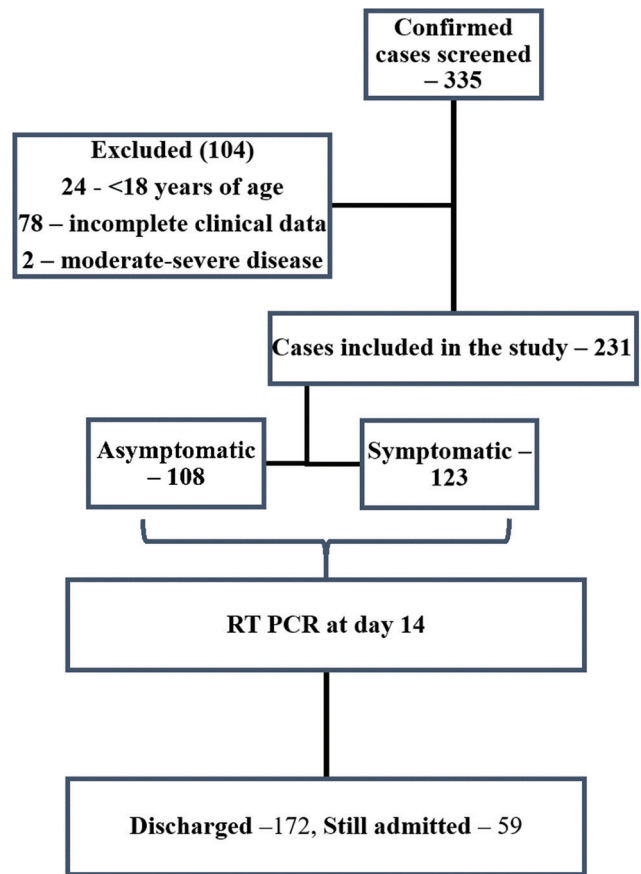

Figure 1: Study flow diagram

Table 1: Baseline characteristics of COVID-19 patients (*n*=231)	
Characteristic	***n* (%)**
Age* (in yrs)	39.8±13.6
Age category	
18-40 yrs	125 (54.1)
41-60 yrs	90 (38.9)
>60 yrs	16 (6.9)
Gender (female)	50 (21.6)
History of contact	205 (88.7)
Comorbidities	49 (21.2)
Diabetes Mellitus	28 (12.1)
Hypertension	19 (8.2)

*Mean±Standard deviation

Discussion

In this retrospective study, 231 admitted patients with asymptomatic infection or mild illness were recruited. The mean age was 40 years, and one-fifth had some comorbidities. Cough (65.8%) and fever (52%) were the most common features among symptomatic cases. A large proportion of patients (46.7%) remained asymptomatic throughout infection; patients with comorbidities were more likely to be symptomatic. None of the admitted patients progressed to moderate-severe disease.

Table 2: Demographic and laboratory parameters among symptomatic and asymptomatic patients (*n*=231)					
Characteristic	Asymptomatic (*n*=108)	Symptomatic (*n*=123)	P	Odds ratio	P
Age category					
18-40 yrs	62	63	0.06	0.63-1.9	0.74
41-60 yrs	43	47			
>60 yrs	3	13			
Gender (female)	18	32	0.08	0.25-2.44	0.67
Comorbidities	13	36	0.001	2.66 (1.08-6.53)	0.03
Hemoglobin	13.8±1.7	13.5±1.8	0.17	0.73-1.23	0.69
Total leucocyte count	8452±2576	7429±2346	0.005	0.99-1.00	0.05
Absolute lymphocyte count	2377±687	2223±695	0.15	0.33-2.88	0.97
CRP	0.13 (0.08-0.26)	0.29 (0.05-1.87)	0.80	-	-
Ferritin	23 (14.8-59.8)	126 (19.9-240)	0.08	-	-

*Hemogram available for 188, CRP for 24, Ferritin for 20 patients

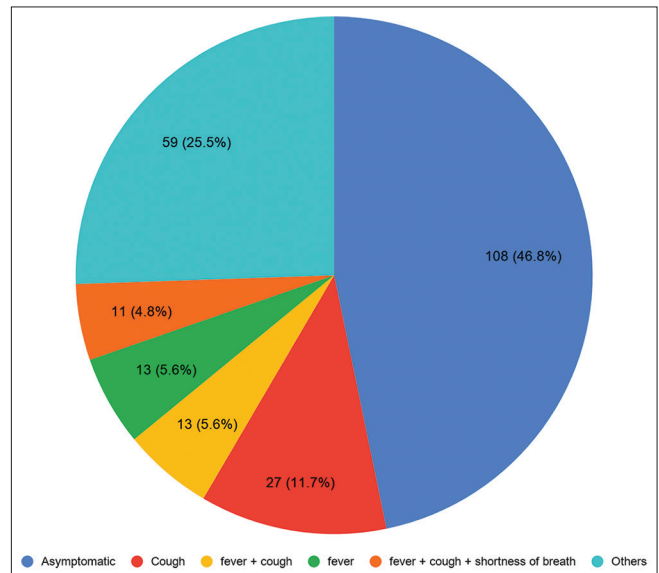| Table 3: Demographic and laboratory parameters among RT-PCR positive and negative patients at the end of 2 weeks (*n*=179)					
Characteristic	RT-PCR positive (*n*=26)	RT-PCR negative (*n*=153)	P	Odds ratio	P
Age category					
18-40 yrs	13	81	0.77	0.52-2.31	0.80
41-60 yrs	11	61			
>60 yrs	2	11			
Gender (female)	6	19	0.14	0.10-1.61	0.20
Comorbidities	5	30	0.96	0.20-2.78	0.67
Symptomatic	12	72	0.93	0.43-2.55	0.9
Received HCQ	6	29	0.62	0.41-4.02	0.65
Hemoglobin	13.6±1.9	13.8±1.5	0.59	0.77-1.46	0.7
Lymphopenia (<1500/mm^3)	2	12	0.97	0.17-6.22	0.97
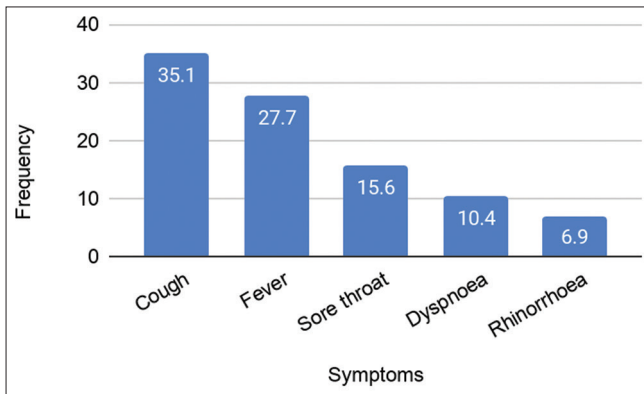
Figure 2: Common symptoms among COVID-19 patients (*n* = 231)

Figure 3: Symptomatology among COVID-19 patients (*n* = 231)

The cohort we recruited is younger than most studies[3,4,10–12] but similar in a few reported studies.[13,14] It is an important context to interpret the results because increasing age and associated comorbidities are well-known risk factors for disease severity and outcomes.[4,11,15–17] About one-fifth of our patients had comorbidities, which is higher than reported among mild cases in the same age-group from Europe[13]; however, it is closer to the reports among higher age groups from other regions.[10] Similar findings were noted in other Indian cohorts.[18,19] This probably reflects the increased burden of noncommunicable diseases in the Indian population.[20]

The studies on symptomatology are varied across geographies. Fever and cough are reported as the most common symptoms

reported across various countries.[10,15,21,22] In our study, cough and fever were the commonest symptoms, with the former being more common. It has important implications because patients with a mild cough and no fever may ignore their signs and not seek medical attention. Furthermore, the frequency of these symptoms was much lower than reported in other studies. A study from China reported that the reported frequencies of

fever and cough were reported as 88% and 68%, respectively, whereas, in the United States, it was 94% and 88%.[10,22] In an Indian study of 522 cases, fever was the most common symptom, followed by cough and shortness of breath.[19] In another Indian study, including 197 confirmed cases, where most patients were symptomatic, the most common being shortness of breath, cough, and fever, in that order.[18] This data is in stark contrast to 35% (cough) and 28% (fever) seen in the present study. It may be related to the diagnostic strategy and admission criteria, which is variable across countries. This study was carried out in the early days of the pandemic in India when large scale surveillance, testing, and contact tracing was carried out. All patients were admitted irrespective of symptomatology, and their close contacts were admitted in isolation facilities and tested for SARS-CoV-2. This presented a unique chance to study the disease course in all infected patients irrespective of symptomatology.

A significant proportion of our patients were asymptomatic throughout admission. The literature on asymptomatic infections is sparse at present. This is likely because these patients would not seek medical care or may have been treated at home as the healthcare system in most countries is overwhelmed because of a large number of patients with a moderate-severe disease requiring hospitalization. The proportion of diagnosed asymptomatic infections reported are between 1 and 19.8%.[23–27] The initial reports from China gave a frequency of 1%, whereas a much higher proportion at 19.8% was reported from the Republic of Korea.[23,28] The asymptomatic ratio among evacuated Japanese nationals from China is estimated at 30.8%.[26] This variation is because of the different strategies of surveillance and testing adopted in various settings. Our findings are similar to another reported study from India, although on smaller sample size.[14] However, this finding was in contrast to a study from south India, where only 22% of patients were asymptomatic.[18] Furthermore, asymptomatic infections were more likely among patients with comorbidities with an odds ratio of 2.66. This is consistent with another report of silent infections among young adults without comorbidities.[27] The finding of 47% asymptomatic infections in the present study has a bearing on pandemic control strategies.

There is sparse literature on disease course and progression to severe disease among patients with mild disease and asymptomatic infection. In a study from Korea, out-of-hospital cohort treatment of COVID-19 patients with mild symptoms reported disease worsening in 2.3%. Patients with severe illness and underlying chronic severe medical conditions were excluded.[29] In our study, none of the patients had disease progression to moderate-severe disease. Uptriaging was required in 1.7% of the patients because of the worsening of the underlying comorbidities. This data is reassuring for country-wide primary physicians that COVID-19 patients with mild disease or asymptomatic infections, particularly those without risk factors, can be managed at basic health services with careful daily monitoring of clinical status (symptoms – excessive cough, shortness of breath; signs – tachypnea, low oxygen saturation) as in COVID care centers. As a result, it will help in reducing the burden of patients at a particular healthcare level and leading to optimum utilization of healthcare facilities in resource-limited settings facing the COVID-19 pandemic.

This study has several limitations. First, there is sparse literature on mild cases. Our patients were younger than other reported studies, so direct comparison of clinical manifestations and disease progression is to be done cautiously. However, our patients had a significant burden of comorbidities for their age, which is a considerable risk factor for severe disease. Secondly, this being a retrospective study, there are inherent limitations. Daily symptom screen data was lacking in many cases leading to their exclusion; laboratory data was incomplete, particularly concerning markers like serum ferritin levels and C-reactive protein. Thirdly, there was a selection bias owing to aggressive contact tracing and admission of close contacts for testing. This resulted in a large number of asymptomatic patients being recruited for the study. Nevertheless, this is one of the large reports of clinical manifestations and disease course among admitted patients with mild COVID-19, reported from our country to the best of our knowledge. The data will be useful for policymakers.

Conclusion

A significant proportion of patients were asymptomatic throughout the infection; however, the remaining patients were symptomatic with mild illness. Patients with comorbidities were more likely to be symptomatic. Most patients had an uneventful course of hospitalization, barring few complications in those with comorbidities. Management of co-existing conditions is an integral part of COVID management.

Key Message

1. It is one of the large case studies conducted during the initial phase of the pandemic in India concerning the characteristics and outcomes of COVID-19
2. This study highlights the relatively high proportion of cases with asymptomatic or mild diseases
3. High burden of asymptomatic cases emphasizes the importance of contact tracing as a key component of pandemic control strategy
4. For resource-limited countries, asymptomatic and mildly ill without co-morbidities can be managed with basic healthcare services as in COVID care centers with linkage to tertiary care centers.

Conflicts of interest

There are no conflicts of interest.

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