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Clinical profile of patients infected with suspected SARS-CoV-2 Omicron variant of concern, Tamil Nadu, India, December 2021-January 2022

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***Background & objectives*: COVID-19 cases have been rising rapidly in countries where the SARS-CoV-2 variant of concern (VOC), Omicron (B.1.1.529) has been reported. We conducted a study to describe the epidemiological and clinical characteristics and outcomes of COVID-19 patients with 'S' gene target failure (SGTF, suspected Omicron). Furthermore, their clinical outcomes with COVID-19 patients with non-SGTF (non-Omicron) were also compared.**

***Methods*: This study was conducted in Tamil Nadu, India, between December 14, 2021 and January 7, 2022 among patients who underwent reverse transcription-PCR testing for SARS-CoV-2 in four laboratories with facilities for *S* gene screening. Consecutively selected COVID-19 patients with SGTF were telephonically contacted, seven and 14 days respectively after their date of positive result to collect information on the socio-demographic characteristics, previous history of COVID-19, vaccination status and clinical course of illness along with treatment details. To compare their outcomes with non-SGTF patients, one randomly suspected non-Omicron case for every two suspected Omicron cases from the line-list were selected, matching for the date of sample collection and the testing laboratory.**

***Results*: A total of 1175 SGTF COVID-19 patients were enrolled for this study. Almost 6 per cent (n=72) reported a history of previous infection. 141 (13.5%) suspected Omicron cases were non-vaccinated, while 148 (14.2%) and 703 (67.4%) had received valid one and two doses of COVID-19 vaccines, respectively. Predominant symptoms reported included fever (n=508, 43.2%), body pain (n=275, 23.4%), running nose (n=261, 22.2%) and cough (n=249, 21.2%). Five (0.4%) of the 1175 suspected Omicron cases required oxygen supplementation as compared to ten (1.6%) of the 634 suspected non-Omicron cases. No deaths were reported among omicron suspects, whereas there were four deaths among suspected non-Omicron cases.**

***Interpretation & conclusions*: Majority of the suspected Omicron cases had a mild course of illness. The overall severity of these cases was less compared to the suspected non-Omicron cases.**

Key words B.1.1.529 - COVID-19 - epidemiology - Omicron - SARS-CoV-2 - severity - variant of concern

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The rapid upsurge of COVID-19 currently reported worldwide is primarily driven by the SARS-CoV-2 Omicron variant[1]. The World Health Organization (WHO) designated B.1.1.529 (Omicron) as a variant of concern (VOC) on November 26, 2021[2]. Omicron was first identified in South Africa in mid-November 2021 and has spread to more than 171 countries within a short span. This variant has also replaced Delta VOC in several countries[3]. In India, upsurge of COVID-19 cases were reported since the last week of December 2021[4].

Omicron has a large number of mutations, including 26-32 mutations in the spike protein[3]. It reportedly has a higher transmission advantage with a higher reproduction number compared to Delta[5], which is evident by the recent rapid increase of COVID-19 cases reported across countries[1]. Studies have documented a significant reduction in neutralization capacity against Omicron, both with convalescent sera as well as with sera of vaccinated individuals[6,7]. The risk of reinfection with Omicron variant is five times higher compared to Delta[8], and a substantial drop in vaccine effectiveness against symptomatic infection has also been observed[9]. These findings indicate immune evasion capability of the Omicron variant. *S* gene target failure (SGTF) is considered as a proxy marker to screen for this variant[3].

Recent studies have indicated mild course of illness in majority of the Omicron-infected patients[10]. The evidence about severity and hospitalization has largely been shared from countries with high levels of population immunity[3]. The seroprevalence of IgG antibodies against SARS-CoV-2 in India was 67.6 per cent during June-July 2021[11]. More than 84 million have received at least one dose, and 60 million have received two doses in India as of January 24, 2022[12]. Information about clinical severity such as the use of oxygen, mechanical ventilation and number of deaths associated with Omicron was needed from India to equip the healthcare services given the large number of cases reported due to Omicron. In this context, this study was conducted to describe the epidemiological, clinical characteristics and outcomes of SGTF COVID-19 patients (suspected Omicron) and also compare them with the clinical outcomes of non-SGTF COVID-19 patients (suspected non-Omicron).

Material & Methods

This study was conducted in Tamil Nadu between December 14, 2021 and January 7, 2022 among patients who underwent reverse transcription-polymerase chain reaction (RT-PCR) testing for SARS-CoV-2 in four laboratories equipped with facilities for *S* gene screening. Based on the results of laboratory testing, individuals positive for SARS-CoV-2 with the absence of *S* gene by RT-PCR were considered as suspected Omicron cases while individuals positive for SARS-CoV-2 with the detection of *S* gene by RT-PCR were considered as suspected non-Omicron cases. The line-list of persons undergoing COVID-19 tests in the four laboratories was shared by the State Public Health Department. The study was approved by the Institutional Ethics Committee of the ICMR-National Institute of Epidemiology, Chennai, India.

Study design: All the willing COVID-19 patients with SGTF detected by the four laboratories between December 14, 2021 to January 7, 2022 were consecutively enrolled. To compare the outcomes, we randomly selected one suspected non-Omicron case for every two suspected Omicron cases from the line-list, matching for the date of sample collection and the testing laboratory. The selected participants were telephonically contacted seven and 14 days, respectively after their date of positive result. After obtaining an informed verbal consent, trained investigators collected information from the participants in Open Data Kit (*https://getodk.org/*).

Survey procedure: During the first contact on day seven, information on the socio-demographic characteristics, previous history of COVID-19, vaccination status and clinical course of illness were collected along with treatment details. The interviewers were blinded for the SGTF status of the patient. Patients requiring supplemental oxygen during the course of illness were considered as having severe illness and remaining as mild illness. Individuals who had received two doses of COVID-19 vaccine 14 days before testing were considered as those who received valid two doses, whereas individuals who had received only one dose of COVID-19 vaccine before 21 days of testing were considered as those who received valid one dose. The patients were followed up telephonically after two weeks of positive test result to document their clinical outcomes.

Statistical analysis: Categorical variables were summarized as percentages and continuous variables as median with interquartile range (IQR), and mean with standard deviation (SD). The outcomes (severe disease defined as those who required oxygen supplementation, and death) were compared among Omicron and non-Omicron patients using Chi-square tests of significance

considering a $P<0.05$. Statistical software STATA SE version 17.0 (Stata Corp LLC, Texas, USA) were used for the analysis.

Results

Profile of suspected Omicron cases: A total of 104,544 samples were tested for COVID-19 during the study period using TaqPath™ COVID-19 RT-PCR Kit (Thermo Fisher Scientific, California, USA) to screen for *S* gene by the four laboratories. Of these, 2470 (2.4%) samples were positive for COVID-19. Among the 2470 positives, 1581 (64.1%) had *S* gene dropout and 889 (35.9%) were positive for *S* gene target.

A total of 1489 suspected Omicron cases were telephonically contacted from the line-list. Of these, 1175 (78.9%) could be interviewed and the remaining 314 participants could not be reached, did not answer the call or refused to participate in the study. The median age of the cases was 37 yr (IQR: 24-50). More than half of the cases were in the age group of 20-50 yr and 63.5 per cent were males. About half (n=579, 49.3%) underwent testing because of their symptoms, whereas 25.4 per cent (n=298) underwent group testing at workplace or residence (Table I). Nearly one-fifth (n=234) of the case patients reported as having at least one comorbidity, with diabetes (11.2%) and hypertension (9.9%) being the predominantly reported comorbidities. Other comorbidities included heart diseases (1.4%), asthma (1.2%), chronic kidney disease (0.3%) and cancer (0.2%). 141 (13.5%) suspected Omicron cases were non-vaccinated, while 148 (14.2%) and 703 (67.4%) had received valid one and two doses of COVID-19 vaccines, respectively (Table I). Almost six per cent (n=72) reported history of previous infection. Among the 703 fully vaccinated, suspected Omicron cases, the duration between receipt of the second dose and positive test result was more than 90 days in 511 (72.7%), between 61 and 90 days in 77 (11.0%), between 31 and 60 days in 71 (10.1%) and 14 and 30 days in 44 (6.3%) individuals (Table II).

Of the 1175 suspected Omicron cases, 758 (64.5%) reported to have had symptoms. Predominant symptoms reportedly included fever (n=508, 43.2%), body pain (n=275, 23.4%), running nose (n=261, 22.2%) and cough (n=249, 21.2%) (Table I). Around 46 per cent of the cases were hospitalized. The median duration of hospitalization was five days (IQR: 4-7). Five (0.4%) of the 1154 patients were given

Table I. Demographic and clinical details of suspected Omicron cases, Tamil Nadu, December 2021-January 2022 (n=1175)

Characteristics	n (% of the total)
Age (yr)	
Up to 10	23 (2.0)
11-20	186 (15.8)
21-30	229 (19.5)
31-40	244 (20.8)
41-50	204 (17.4)
51-60	181 (15.4)
Above 60	108 (9.2)
Sex	
Male	746 (63.5)
Female	429 (36.5)
Reason for testing	
Had symptoms	579 (49.3)
Contact is positive/symptomatic	169 (14.4)
Group testing at workplace/residence	298 (25.4)
Travel related	130 (11.1)
Medical reasons	51 (4.3)
Others	52 (4.4)
Comorbidity	
Yes	234 (19.9)
No	941 (80.1)
Comorbid conditions	
Diabetes	132 (11.2)
Hypertension	116 (9.9)
Heart disease	17 (1.4)
Asthma	14 (1.2)
Chronic kidney disease	4 (0.3)
Cancer	2 (0.2)
Vaccination status (n=1043)	
Unvaccinated	141 (13.5)
One dose (<21 days)	2 (0.2)
Partially vaccinated (valid one dose)	148 (14.2)
Two dose (<14 days)	41 (3.9)
Fully vaccinated (valid two doses)	703 (67.4)
Three doses	8 (0.8)
Symptom status	
Yes	758 (64.5)
No	417 (35.5)
Fever	508 (43.2)
Body pain	275 (23.4)
Running nose	261 (22.2)

Contd...

Characteristics	n (% of the total)
Cough	249 (21.2)
Sore throat	202 (17.2)
Headache	163 (13.9)
Diarrhoea	25 (2.1)
Shortness of breath	13 (1.1)

supplemental oxygen during hospitalization. No deaths were reported (Table II).

Of the five patients who required oxygen supplementation, four were above 60 yr of age and all were males. Three of the five (60%) had reported at least one comorbidity. Out of the five patients, one was non-vaccinated, one had received single valid dose of COVID-19 vaccine and three had received both the doses (valid two doses) of COVID-19 vaccine.

Comparison of clinical outcomes among suspected Omicron and suspected non-Omicron patients: 798 suspected non-Omicron patients were contacted, of whom 634 (79.4%) consented to participate in the study, whereas 164 could not be interviewed because their telephone number was either not reachable or the patient refused to participate in the study. The distribution of suspected Omicron and suspected non-Omicron patients was similar with respect to age, gender, comorbidity and vaccine status. Around two-third of the patients reported symptoms in both the groups, and fever was the most commonly reported symptom. Five (0.4%) of the 1175 suspected Omicron cases and ten (1.6%) of the 634 suspected non-Omicron cases required oxygen supplementation (P=0.010). No deaths among the suspected Omicron cases were noted whereas there were four deaths among the suspected non-Omicron cases (P=0.007).

Discussion

The present study describes the epidemiological, clinical characteristics and outcomes of 1175 SGTF COVID-19 patients (suspected Omicron) in Tamil Nadu. Nearly one-third of the suspected Omicron patients did not report any symptoms, and majority had received either one or two doses of COVID-19 vaccination. Our study findings indicate milder course of illness in majority of the suspected Omicron patients. Clinical presentation and vaccination status were similar in both suspected Omicron and non-Omicron patients. However, progression of illness and mortality was higher among suspected non-Omicron patients than the suspected Omicron patients.

The mild course of illness may be due to interplay of low virulence of the Omicron[13] and high population immunity developed as a result of vaccination and previous infection. The one-dose and two-dose coverage among adults in Tamil Nadu was 89 and 63 per cent, respectively[14], and the serosurvey conducted in July-August 2021 indicated a seroprevalence of 66.2 per cent[15].

In this study, around six per cent reported reinfection and breakthrough infection was reported in 67 per cent of suspected Omicron cases having received valid two doses of COVID-19 vaccination, indicating the immune evasion capacity of this variant. The UKHSA (UK Health Security Agency) reported 5.9 per cent reinfection among the reported cases[16]. Studies have also documented a decrease in vaccine effectiveness against symptomatic Omicron infection. However, the protection against severe disease and mortality remains high[9].

Two-third of the suspected Omicron cases were symptomatic in the present study, with fever, body pain and running nose being the predominant symptoms. Only a few had lower respiratory tract infection symptoms such as shortness of breath. This is consistent with decreased ability of the Omicron variant to replicate in lungs as observed in animal studies[17,18]. Higher rate of hospitalization observed in the study was mostly due to the initial State policy of mandatory admission of all the suspected Omicron cases, leading to close clinical monitoring of the patients, and this could have actually resulted in better outcomes. The overall severity of the suspected Omicron patients in terms of requirement of oxygen supplementation and mortality was significantly lower compared to the suspected non-Omicron cases. Our findings are comparable with the findings of studies reported from regions with high population immunity[10].

Milder course of illness might lead to lesser hospitalizations, especially critical care than as previously seen during the Delta wave. In most countries, Omicron VOC has presented as a sudden surge with high volume of infections. A rapid surge of Omicron can strain the healthcare services, and hence, the health system must be adequately prepared in terms of increasing bed capacity in the hospitals,

Table II. Comparison of profile of suspected Omicron versus non-Omicron cases from Tamil Nadu, December 2021-January 2022

Description	Suspected Omicron cases (n=1175), n (%)	Suspected non-Omicron cases (n=634), n (%)	*P*
Median age (IQR)	37 (24-50)	36 (23-49)	
Age >60 yr	108 (9.2)	63 (9.9)	0.605
Male sex	746 (63.5)	390 (61.5)	0.407
Overall comorbidity	234 (19.9)	117 (18.5)	0.454
Diabetes	132 (11.2)	82 (12.9)	
Hypertension	116 (9.9)	61 (9.6)	
Symptomatic	758 (64.5)	428 (67.5)	0.201
Fever	508 (43.2)	315 (49.7)	0.018
Cough	249 (21.2)	165 (26.0)	0.048
Sore throat	202 (17.2)	131 (20.7)	0.145
Vaccination status	n=1043	n=567	
Unvaccinated	141 (13.5)	82 (14.5)	
One dose (<21 days)	2 (0.2)	1 (0.2)	
Partially vaccinated (valid one dose)	148 (14.2)	61 (10.8)	0.094
Two dose (<14 days)	41 (3.9)	20 (3.5)	
Fully vaccinated (valid two doses)	703 (67.4)	395 (69.7)	0.821
Three doses	8 (0.8)	8 (1.4)	
	n=1175	n=674	
History of previous infection	72 (6.2)	21 (3.3)	0.215
Hospitalization	540 (46.0)	280 (44.2)	0.465
Median admission day (IQR)	5 (4-7)	6 (5-9)	
Required oxygen	5 (0.4)	10 (1.6)	0.010
Outcome-deaths	0	4 (0.6)	0.007
Duration between receipt of second dose and positive test result	n=703	n=395	
>90 days	511 (72.7)	294 (74.4)	0.721
61-90 days	77 (11.0)	35 (8.8)	
31-60 days	71 (10.1)	39 (9.8)	
14-30 days	44 (6.3)	27 (6.8)	

IQR, interquartile range

augmenting the existing capacity in quarantine centers and mobilizing human resources for clinical care of patients.

Our study had certain limitations. First, nearly 20 per cent of the suspected Omicron patients could not be contacted. This could have introduced a bias in the findings regarding the severity of infection. Second, we could not confirm the VOC using genomic sequencing studies. Instead, we considered SGTF as a surrogate of suspected Omicron infection and presence of *S* gene as a surrogate of suspected non-Omicron infection, probably Delta VOC. Third, several countries have reported the emergence of BA.2 lineage which does not have the characteristic *S* gene drop-out mutation. It is therefore likely that we might have misclassified some of the COVID-19 cases with BA.2 lineage as non-Omicron. However, more than 90 per cent of the positive samples with *S* gene drop-out sequenced at the State Public Health Laboratory during the study period were of the Omicron variant (Government of Tamil Nadu, unpublished data).

In conclusion, majority of the suspected Omicron cases had a mild course of illness. The overall severity of suspected Omicron cases was less compared to the suspected non-Omicron cases.

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***Conflicts of Interest*:** None.

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