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A STUDY ON DEMOGRAPHIC AND CLINICAL STATUS OF COVID 19 INFECTIONS IN CENTRAL INDIA DURING THIRD WAVE.

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ABSTRACT **Background:** India had experienced three waves of COVID 19 infection with a huge number of cases and death since its appearance in January 2020. **Objective:** In the present study, the percent positivity of non-hospitalized COVID-19 cases were analysed during third wave (December 2021-March 2022) and age, gender, vaccination and clinical status were compared. **Method:** A total of 17567 cases were referred/walked-in to the Sampurna Sodani Diagnostics Clinic, Indore, India. Real time PCR tests targeting ORF1ab, N gene and S gene for COVID 19 were performed in nasopharyngeal and oropharyngeal specimens. Statistical significance was set at $p< 0.05$. **Result:** Of the tested samples, 40.01% (95% CI 36 – 45.4; 4101/10082) males and 39.10% (95% CI 36 – 45.4 ;2927/7485) females were positive. Most of the infected patients were vaccinated (73.5%, 5169/7028), as most of the adult population get vaccination by the Government of India. The ratio between symptomatic and asymptomatic patients among the vaccinated group is 1.4:1, and 2.5:1 among unvaccinated groups. Among unvaccinated adult COVID 19 positive cases, 46.70% male and 47.39 % female were symptomatic whereas asymptomatic cases were 33.09% male and 30.70% females. Among 444 positive samples, S gene were tested and detected among 311 patients; of which 52.02% were vaccinated and 18.02% were non-vaccinated. S gene dropout was observed in 21.4% vaccinated and 8.56% non-vaccinated patients. **Conclusions:** This study will through light on the demographic, clinical and vaccination status of non-hospitalized covid-19 positive patients during third wave as limited reports are available from Central India for this.

KEYWORDS : COVID 19, third wave, vaccination status.

INTRODUCTION

India's first wave of SARS-CoV-2 infection began in late January 2020 and lasted for about nine months with 11 million cases and 0.157 million deaths [1]. This was relatively mild compared to the second wave that followed, from mid-February 2021 onwards, and exhibiting a more explosive spread across the country. A major factor driving this second wave was the emergence of more-infectious variants of SARS-CoV-2 B.1.617.2 (Delta variant). There was increasing speculation about the potential of a third wave of SARS-CoV-2 infection in India. At the same time Covid 19 mass vaccination among all the age groups except children also geared up during this phase. It was thought that there would be an end to the number of positive covid cases but the new cases increased exponentially and on 19 January 2022, India reported around 317,000 new COVID-19 cases [2]. Third wave of covid began in the last week of November 2021 with the emergence of new variant covid 19 Omicron B.1.1.529, first detected in South Africa's Gauteng [3]. As of 15 December 2021, the OMICRON variant has already popped up in around 77 countries with the majority of the cases from the United Kingdom, South Africa, and the United States [4]. The variant was introduced into India by people traveling from foreign countries. The union health ministry, Govt. of India, declared the first Omicron case on December 02, 2021 and expanded in India with increasing daily infections [2]. People are not admitted in hospital for COVID-19 symptoms but for long COVID or post COVID complications [5].

In the light of above background, the present study was planned to know percentage of the covid positive cases as well as emergence of new virus variant omicron in the sample during third wave of infections among both vaccinated (symptomatic and asymptomatic) and unvaccinated (symptomatic and asymptomatic) population at our diagnostic centre in Indore, India during Dec 2021- March 2022.

Materials and methods:

Study design, setting, and period:

The study included suspected or referred covid-19 cases at Sampurna Sodani Diagnostic Clinic, Madhya Pradesh, India from Dec 1, 2021-March 31, 2022. The demographic details, clinical history, risk factors (travel history, comorbidities) and vaccination status were recorded for every case in specimen referral form (SRF), ICMR (Indian Council of Medical Research), India. Sample collection date, sample testing date, PCR kit used, patients contacts and test results were also recorded and updated on ICMR portal. The data was submitted to the Government of India centralized database. Sample collection and testing of COVID19 RTPCR was approved by National Accreditation Board for Testing and Calibration Laboratories (NABL).

Sample collection:

Nasopharyngeal and Oropharyngeal samples were collected from the upper respiratory tract for early detection and covid-19 diagnosis [6]. All the samples were collected in Viral transport media (Hi-media) at the collection area, maintaining the precautions and transported with 3-layer packing in refrigerated conditions to Molecular Biology laboratory. RT-PCR kits approved by ICMR were used in the study. Of the total tested samples, 10082 were males & 7485 were females. These data are not individually identifiable.

RNA Extraction

RNA was extracted from 200 µl of collected samples using Zybio automation extraction kit on automated extraction system (Zybio, China). The extracted RNA was stored at -80°C in aliquots.

Reverse transcription Polymerase Chain Reaction (RT-PCR)

RTPCR was performed using Covipath RT-PCR COVID 19 kit on Real time PCR Instrument, Quantstudio 5 (Thermofisher, USA), targeting ORF 1ab gene and nucleoprotein N gene as previously described [6].

Taq path Covid-19 CE-IVD RT PCR kit

We also performed Real time PCR using Taq path Covid-19 CE-IVD RT PCR kit for S-gene target as a source deletion for S-gene as a drop out [7]. The European CDC and US FDA have noted this pattern of detection for early detection of B.1.1.7 as a screening test for Omicron. The TaqPath covid-19 multiplex assay contains three primer probes sets targeting SARS-CoV-2 ORF1-ab, S gene and N gene. The Real time PCR for Taq Path Covid-19 was programmed according to kit manual [7].

Results were entered immediately upon their availability into the

ICMR portal and shared with the district/state surveillance teams to facilitate immediate tracing of contacts.

Statistical analysis: Statistical comparisons between two groups were made using the 't' test and chi square $\chi 2$ test. Statistical significance was set at $p< 0.05$. All calculations were made using the Graphpad Prizm software (GraphPad Software, Inc.). The study was approved by the Institutional ethical committee.

RESULTS:

The present study is a descriptive analysis of the nasal and oropharyngeal swabs referred from non-hospitalised patients for COVID-19 testing between December 1, 2021 and March 31, 2022 at our Diagnostic Centre.

To understand the dynamics of SARS-CoV-2 transmission during the third wave, data were analysed from the ICMR portal. Monthly distribution of COVID-19 cases among both genders were analyzed according to vaccine and clinical status (Table 1). Of the total 17567 suspected cases, 7028 (40%) were identified as laboratory-confirmed COVID-19-positive cases (Table 1). The month of January 2022 recorded the highest number of positive cases (5952/7028); 84.7% positive samples were from this month. The gender distribution of 7028 COVID 19 cases during the study period of third wave (December 2021-March 2022) revealed an almost equal dominance of male (40.68%; CI 35.995–45.405) (4101/10082) and female (39.10%; CI 34.3 – 43.6%) (2927/7485). Amongst the 7028 COVID 19 positive cases, 5169 (73.5%) were vaccinated, as most of the adult population (>18 years) received complete vaccination by Government of India. The ratio between symptomatic and asymptomatic patients among the vaccinated group is 1.4:1, but the same ratio among unvaccinated groups is 2.5:1; both cases symptomatic cases were significantly higher than reported asymptomatic individuals ($p<0.001$). Clinical status of non-vaccinated COVID 19 patients revealed that the percentage of asymptomatic cases among male and female in the age group of less than 18 years were 27.29% (155/568) and 28.25% (124/439) respectively, whereas among symptomatic group the percent positivity in male was 33.68%(163/484) and 25.59%(119/465) in females (Fig 1). Among unvaccinated adult (>18 years of age) COVID 19 positive cases, symptoms were recorded from 46.70% male (530/1135) and 47.39 % female (517/1091) whereas symptoms not reported from 33.09% (185/559) male and 30.70% (66/215) females.

S gene detection screening test was performed on request of consultant Doctors. Out of 444 tested positive samples, S gene was detected among 311 patients; of which 52.02% (231/311) were vaccinated cases and 18.02% (80/311) were non-vaccinated cases. S gene dropout was observed in 133 cases; 21.4% (95/133) were vaccinated and 8.56% (38/133) were non-vaccinated patients (Table 2). Symptomatic to asymptomatic ratio was less than one in all the cases. Omicron suspected cases were further sent to government authority for further gene sequencing analysis.

DISCUSSION:

Omicron variant of SARS-CoV-2 or B.1.1.529 was reported from South Africa on 24th November 2021 and spread rapidly to several parts of the world [6]. The variant was introduced into India by people traveling from foreign countries. The union health ministry, Govt. of India, declared the first Omicron case on December 02, 2021 and expanded in India with increasing daily infections [7]. Our study describes the epidemiology of SARS-CoV-2 infections among non-hospitalised cases during the omicron third wave in Central India. In this study period from December 2021 to March 2022, 40% (7028/17567) non-hospitalised patients were positive for COVID 19 (Table 1). The Omicron predominant third wave reported higher percent positivity unlike the first wave and second wave, where percent positivity was 31.28%-31.8% and 27.89-37.56% respectively [6]. Lower severity and high viral loads were also associated with the Omicron variant of COVID 19 compared to Delta strain [3]. Till January 10, 2022, Omicron variant of COVID 19 became community transmission in India [8]. ICMR, Government of India guidelines COVID 19 testing for symptomatic and co-morbid patients [9].

In our study, the highest number of cases were recorded in the month of January 2022, correlating well with the peak of the third wave in India (Table 1). In India, adult vaccination (>18 years of age) programme under Government of India was started from May 01, 2021. During the study period, most of the adult population 7.9 to 9.9 billion of population (57.4%-71.7% of total population) were already vaccinated. The vaccination status was studied among reported symptomatic and asymptomatic cases in both genders (Table 1). Our data report higher symptomatic cases than the asymptomatic ones in both vaccinated and unvaccinated groups (Table 1); however the ratio of symptomatic and asymptomatic cases among unvaccinated groups is much higher as compared to the vaccinated group (2.5:1 vs 1.42:1). Several studies confirmed that though two doses of vaccines provided limited to negligible protection against symptomatic disease caused by the omicron variant but remain effective in reducing severity and rate of hospitalization [10,11]. In our study also, all the vaccinated symptomatic patients reported mild symptoms like fever, cough, sore throat. Patients were not admitted in the hospital at the study time point, though post hospitalization status and duration of illness were not recorded to compare the vaccine efficacy.

In Omicron B.1.1.529 strains, as the S gene is heavily mutated, some of the primers may lead to results indicating absence of the S gene (called as S gene drop out or S-gene target failure SGTF). SGTF along with the detection of other viral genes could be used for screening of Omicron [7]. However, for confirmation of the omicron variant genomic sequencing is required. One of the three sub lineages of Omicron BA.2 does not contain His 69_Val70 del and is not identified by SGTF [1]. BA.2 lineage became a substantial fraction in India till January 10, 2022 and lacked S gene dropout. In our study, 444 samples were tested for the detection of the 'S' gene; of them 326 were vaccinated. S gene were detected in 311 patients and SGTF were reported from 133 patients (Table 2). Lower cases of SGTF might be due to the fact that some samples may belong to BA.2 lineage. Positive samples were sent for sequencing confirmation, though results of individual samples were not declared.

Limitation

The present study was conducted among non-hospitalised cases at that specific time point. Post testing status and coinfection, if any, of the patients were not included in this study.

CONCLUSION

The finding of the study demonstrates that, during the third wave of COVID19 pandemic in Madhya Pradesh, India, SARS COV 2 infection occurred in both symptomatic and asymptomatic individuals among non-hospitalised cases. In our studies both vaccinated and non-vaccinated individuals were affected by SARS-COV2 in the third wave though symptomatic cases were much lower in vaccinated group. On July 11, 2022 INSACOG, Government of India reported cases of Omicron sublineages BA.2, BA.2.38 BA.4 and BA.5 variants of SARS-CoV-2 [12,13]. However, the variants have not been associated with increased disease severity or increased hospitalization. Constant vigilance on COVID 19 strains and vaccination will help to combat the disease. The government has revised and updated some of the key policies related to COVID-19 testing, isolation, contact tracing, treatment guidelines, and hospital discharge [12]. Individuals need to follow COVID19 appropriate behaviour to prevent further waves of COVID 19 with new variants.

Table 1: Monthly distribution of COVID 19 cases among vaccinated and non-vaccinated group during the study period (December 2021-March 2022). The highest number of cases 5952 were reported on January 2022. Most of the cases were vaccinated as most of the population above 18 years were fully vaccinated in India.

				Male			Vaccinated		Non-vaccinated	
Month	Total tested	Total positive	% positivity	Sample tested	Sample positive	% Positivity	Symptomatic	Asymptomatic	Symptomatic	Asymptomatic
Dec-21	3000	55	1.83	1644	31	1.89	9	9	10	3
Jan-22	10553	5952	56.40	6105	3572	58.51	1560	1114	601	297

Feb-22	2937	868	29.55	1690	484	28.64	217	149	79	39
Mar-22	1077	26	2.41	643	14	2.18	5	5	3	1
Total	17567	7028	40.01	10082	4101	40.68	1791	1277	693	340
Percent Positivity							43.7	31.1	16.9	8.3
Ratio							1.4		2.04	
p value							p<0.001			
				Female			Vaccinated	Non-vaccinated		
				Sample tested	Sample positive	% Positivity	Symptomatic	Asymptomatic	Symptomatic	Asymptomatic
				1356	24	1.77	7	9	7	1
				4448	2507	56.36	1073	730	547	157
				1247	384	30.79	163	110	79	32
				434	12	2.76	3	6	3	0
Total				7485	2927	39.10	1246	855	636	190
Percent Positivity							42.6	29.2	21.7	6.5
Ratio							1.46		3.35	
p value							p<0.001			

Table 2: S gene status of COVID19 cases. Clinical status were categorized according to the vaccination status.

	S gene detected				S gene not detected					
	Vaccinated		Non-vaccinated		Vaccinated				Non-vaccinated	
	Symptomatic	Asymptomatic	Symptomatic	Asymptomatic	Symptomatic		Asymptomatic		Symptomatic	Asymptomatic
	86	145	16	64	30		65		9	29
Total	231		80		95				38	
Total	311				133					
Total	444									

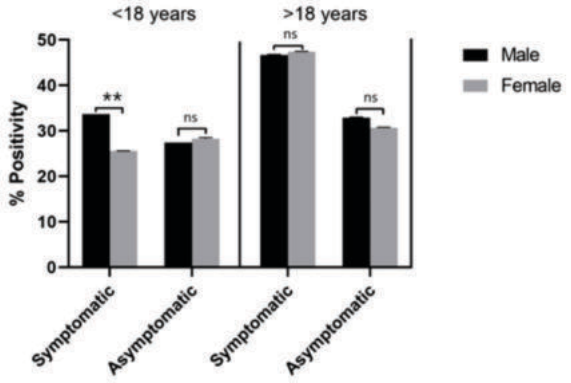

Fig 1: Clinical status of non-vaccinated COVID-19 cases among children (<18 years of age) and adults (>18 years of age). Significant difference (p<0.001) was not observed among both genders in adults. In children, symptomatic patients were significantly higher (p<0.001) in male as compared to female.

Declarations:

Competing interests: The authors declare that they have no competing interests.

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