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Symptomatic prevalence of covid-19 in vaccinated and non-vaccinated population

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ABSTRACT

Background: Coronavirus disease (COVID-19) is an infectious disease caused by the SARS-CoV-2 virus. The world has witnessed havoc with the rapid emergence of COVID-19. The unpreparedness towards the pandemic caused the whole world to face severe consequences. Emerging economies like India with a population of more than 1.3 billion faced heavy toll of life due to the rapid spread of highly contagious COVID-19 and shortage of medical supplies and infrastructure. The testing, tracing, and isolation of COVID-19 positive patients helped greatly to break the chain of COVID-19 infection, this later boosted by the vaccine production and administration on a war scale by Government of India.

Aim: In this study, we have tried to understand the symptomatic effects of COVID-19 on Indian population, its prevalence, and significance. Many individuals developed symptoms like COVID-19 but tested negative for the same and vice versa. The cases of individuals not developing symptoms of COVID-19 but infected by COVID-19 act as a carrier of the virus possibly infecting other individuals unknowingly. These individuals may have weaker immunity and more submissive health conditions due to age, under surgical treatment or are infected by other chronic or acute diseases. This makes it essential to correlate and study the symptomatic incidence of COVID-19 with respect to age and vaccination status of Indian population.

Materials and Methods: This study was undertaken to determine the symptomatic prevalence of COVID-19 in vaccinated and non-vaccinated patients that were tested in our laboratory. There were 86,761 samples tested out of which 49,371 samples were positives and 37,390 were negative. The samples from different parts of India were tested between1st July 2020 and 14th November 2022, dividing the total period in 5 phases for better correlation as vaccine administration started during early 2021 primarily for health workers and till it reached common people by mid of July 2021.

Results and Discussion: The observations and statistical study have described the significance of vaccination and have given better insights about the working class of individuals between 18 and 45 years of age which were more exposed to infection. The study also identifies various parameters which aggravated and conciliated the symptoms of COVID-19. The study helps us to identify the prevalence and incidence of COVID-19 virus in Indian Population and can be beneficial in devising a better strategies in future to tackle symptomatic adversaries of any infection.

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1. Introduction

The onset of 2020 had witnessed the sudden outbreak of pandemic of deathly novel coronavirus (nCoV-2019), which is also termed as Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2).

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1.1. Structure of SARS-CoV-2 virus

SARS-CoV-2 virus is an enveloped positive single-stranded RNA virus (+ssRNA) with a genome size of 2.9 KB nucleotide RNA genome and ~100 nm in diameter along with four structural proteins, namely envelope (E), nucleocapsid (N), membrane (M), and spike (S). SARS-CoV-2 infects by binding to Angiotensin-Converting Enzyme 2 (ACE2) receptors on the host cell surface through its S-Protein.[1,2]

1.2. Symptoms

Symptoms of COVID-19 patients ranged from mild to severe. Few people had little or no symptoms where most of the people had severe illness due to COVID-19.[3] Asymptomatic patients were still a carrier and posed a threat for people who were more prone to get severe symptoms. Patients already on corticosteroids, suffering from other respiratory diseases suffered higher mortality during COVID-19.[4] People tried every household remedy and prevention method to avoid COVID-19 infection. The physical home exercise helped to improve the strength and functional capacity of the human body, especially in the older age group.[5] The world of Ayurveda was also ventured to obtain a cure for this pandemic.[6] This shows every aspect was tested by people to prevent the infection and obtain immunity against it.

1.3. India and SARS-CoV-2 virus

Starting from its emergence in zeroth patient at Wuhan, Hubei province, China, in December 2019,[7] the virus engulfed the whole world bringing it to a complete shutdown of various countries including developed countries having world class healthcare systems. The sudden fall of established healthcare systems was due to lack of preparedness and experience to deal with this unknown wave of SARS-CoV-2.

India, having more than 1.3 billion population did see a sharp rise in SARS-CoV-2 virus infection as expected.[8] Epidemiological studies also correlated the burden of COVID-19 with its implications on public health and policy making by government and non-government organisations.[9] The similar prevalence study done in states of Tamil Nadu and Andhra Pradesh showed the death due COVID-19 were more in age group between 50 and 64 years as compared to others due to the presence of other co-morbidity diseases.[10] Even, individuals in younger age groups too were more predisposed to infection. COVID-19 has caused occupational stress due to overwork and irregularities in working hours, in fact, extra work hour requirements by health workers in hospitals and testing laboratories.[11] This has added more stress to all the health care professionals across the world. Study done by Mahajan NN, 2020 clearly indicated that the vulnerability was much higher in frontline health workers as compared to the rest of the population,[12] which was the reason they were vaccinated first.[13]

Testing and tracing of SARS-CoV-2 virus infected patients was found to be the most important mechanism in order to halt its prevalence till vaccine against SARS-CoV-2 virus was discovered and made available for human administration.[14] The success of test-trace-isolate strategy and appropriate restrictions to prevent resurgence cannot be overlooked.[15] However, vaccination with COVID-19 was a prime step toward its containment. Various vaccines were produced having different features with respect to its production, mode of action and distribution but still proved to be a success.[16] Vaccination of all groups of people were found to be beneficial even in the case of pregnant women.[17] Various studies showed vaccination can induce immune responses more rapidly and greater, which could be effective in controlling SARS-CoV-2.[18]

This makes it essential to know the prevalence of COVID-19 in Indian population. Symptomatic patients of COVID-19 had to be isolated and patients suffering from other comorbidities had to be kept under special care to prevent mortality.[19] It became imperative to understand the response of Indian population towards COVID-19 infection before and after vaccination considering age as the major parameter.

In this study, we have tried to identify the prevalence of SARS-CoV-2 virus and its effect on Indian population before and after the administration of SARS-CoV-2 vaccines. Prevalence of COVID-19 and vulnerability of Indian population need to be assessed before and after vaccination.

1.4. Materials and Method

1.5. Sample collection

The oral and nasal swabs of patients were collected. The samples were collected and transported to the lab from various parts of India. Before collection of samples, the patients were given Test Requisition Form (TRF) to fill. This form captured all the information about the patients age, vaccination status, presence of symptoms and other miscellaneous details required for proper maintenance of data and consent.

1.6. RNA extraction

RNA Extraction was done using MagMAX Viral and Pathogen Nucleic Acid Isolation Kits (RUO) on KingFisher Flex instruments for automated purification.

1.6.1. Polymerase chain Reaction (PCR)

TaqPath 1-Step Multiplex Master Mix (No-ROX) is a fast, single-tube, and 4 X RT-qPCR mix that provides for sensitive, reproducible detection of up to four different

RNA/DNA targets in a single multiplex reaction was used. The real-time PCR of the RNA extracted was carried out on QuantStudio^{TM}5 machine.

1.6.2. Reliability of data

The data presented in this study was submitted to Indian Council of Medical research (ICMR), Government of India, on daily basis with patient details. The method and kit used for detection have been standardised on the lines of regulation laid by ICMR. The study also witnessed the 100% concordance of lab results with COVID-19 interlab proficiency testing for 8 times in a row and successfully cleared the norms of National Accreditation Board for Testing and Calibration Laboratories (NABL) and College of American Pathologists (CAP) during the phase of study. This rule out any possibility of error in COVID-19 detection system during the study.

2. Results

The data obtained from the testing and analysis of COVID-19 samples during the Phase I to Phase V have been presented. A total of 86,761 samples were tested and analysed for the symptomatic status of COVID-19.

1. Phase I: 1^{st} July 2020 to 31^{st} December 2020
2. Phase II: 1^{st} January 2021 to 30^{th} june 2021
3. Phase III: 1^{st} July 2021 to 31^{st} December 2021
4. Phase IV: 1^{st} January 2022 to 30^{th} june 2022
5. Phase V: 1^{st} July 2022 to 14^{th} November 2022

The data obtained for each phase is shown in the Table 1:

The data obtained was more scrutinised for the categorization of symptomatic patients tested either negative or positive to COVID-19 infection and correlated with their vaccination status and age. The incidence rate at 95% confidence interval was calculated for each group. The significance levels (P level) were calculated for each age group in accordance with their vaccination status by using analysis of variance (ANOVA).

The median incidence rate for all age groups is as described in the below table

The significance value at a threshold of $p<0.05$ was considered to correlate the symptomatic and asymptomatic positives with respect to age and vaccination status in all 5 phases.

For symptomatic COVID-19 positive patients, the P value was found to be significant for the age group between 18 and 45 (P value= 0.004), whereas it was insignificant for age groups below18 and above 45(P value 0.09 and 0.189 respectively).

The significance for asymptomatic but COVID-19 positive cases was found to be P=0.006 for the age group below 18 years. However, it was insignificant for the age groups between 18 and 45 years and above 45 years, i.e., P =0.21 and p=0.08, respectively.

3. Discussion

The main objective of identifying the incidence of symptoms in COVID-19 patients was well understood by statistical comparison.

The age group from 18 to 45 years were mainly comprised of frontline health workers and the working class people who were majorly responsible for contributing to the nation's growth. The significant relation was determined between the incidence of COVID-19 symptoms and vaccination drive. The first class of people to get administered with vaccines were the front line health workers, police, and other government and Non-government COVID-19 warriors. In these class of people, the symptomatic incidence of COVID-19 were found to decrease with the increase in COVID-19 vaccinations.

The other two age groups of below 18 and above 45 years did not show any significant symptomatic incidence with vaccination majorly due to the late vaccination and high care during the whole COVID-19 journey by every household. The exposure to the outside world was relatively less for the two said age groups than the people of the age groups between 18 and 45 years.

Asymptomatic COVID-19 patients, between all the three age groups, were contacted telephonically to understand the reason for being asymptomatic for COVID-19. The questions asked were:

1. Did you experience any minor signs of cough, cold or fever which made you to undertake a COVID-19 test?
2. Did you recently started any medication in your daily routine for some other indication or disease?
3. Did you come in contact with any known COVID-19 patient unknowingly? If yes, then for how much time and at what distance.

It was not possible to contact all the patients but we could manage to contact 50 patients from each group. However, the purpose of this studied was fulfilled because the majority of these patients gave similar answers to these questions.

1. Majority of the asymptomatic patients did not possess any symptoms for the presence of COVID-19 virus. Few did have symptoms in the form of minor muscle ache or body pain for a day. Other than this, no symptoms were found.
2. The uptake of Vitamin C tablets and immunity booster were seen in almost all asymptomatic patients. Many asymptomatic patients of above 45 years were on high blood pressure and diabetic medication. Female asymptomatic patients were found to be on multivitamin and calcium tablets.
   These medications may have contributed in lessening the symptoms of COVID-19 in these patients.
3. Very few patients from the age group 18 to 45 years that were COVID-19 positive for more than one time,

Table 1: Describes the total count of positive and negative samples analysed for each phase.

Phase	Asymptomatic		Symptomatic		Total sample count
	Negative	Positive	Negative	Positive	
I	4122	460	1658	6643	12883
II	6113	202	4975	12310	23600
III	10719	20	16	1356	12111
IV	13375	26	20	6396	19817
V	14315	19	1	4015	18350

Table 2: Represents the incidence rates of symptomatic and asymptomatic COVID-19 patients of all age groups at 95% Confidence interval.

		Below 18			Age between 19 and 45			Age above 45		
		Unvaccinated	Single Dose	Vaccinated	Unvaccinated	Single Dose	Vaccinated	Unvaccinated	Single dose	Vaccinated
Phase 1	Symptomatic	5.4	0	0	7.39	0	0	11.42	0	0
	Asymptomatic	1.8	0	0	0.41	0	0	0.46	0	0
Phase 2	Symptomatic	12.6	0.34	0	15.94	0.017	0	16.11	0.03	0.004
	Asymptomatic	1.9	0	0	0.02	0	0	0.58	0	0
Phase 3	Symptomatic	2.3	0.011	0.023	1.35	0.081	0.13	1.66	0.04	20
	Asymptomatic	0.46	0	0	0.019	0	0	0.02	0	0
Phase 4	Symptomatic	6.5	0.011	16	7.65	0.015	1.45	6.18	0.016	0.61
	Asymptomatic	0.34	0	0	0.033	0	0	0.03	0	0
Phase 5	Symptomatic	8.7	0	9	4.61	0.023	0.78	2.96	0	0.3
	Asymptomatic	0.46	0	0	0.03	0	0	0	0	0

Table 3: Describes the median incidence rate of each group of COVID-19 patients.

		Unvaccinated	Single dose	Vaccinated
Below 18 year age group	Symptomatic	6.5%(95% CI, 2.32%-11.87%)	0.011%(95% CI, 0%-0.35%)	4.51%(95% CI, 0%-18.59)
	Asymptomatic	0.46%(95% CI, 0%-1.97%)	0	0
Age group between 18 and 45	Symptomatic	7.39%(95% CI, 0.66%-14.11%)	0.02%(95% CI, 0.0%-0.084%)	0.45%(95% CI, 0.0%-1.65%)
	Asymptomatic	0.03%(95% CI, 0%-0.31%)	0	0
Age group above 45 years	Symptomatic	6.18%(95% CI, 0.17%-15.17%)	0.023%(95% CI, 0%-0.048)	0.45%(95% CI, 0%-15.6%)
	Asymptomatic	0.03%(95% CI, 0%-0.56%)	0	0

had no COVID-19 symptoms the second time they were infected but had symptoms in their first infection.

In order to understand the scope of symptomatic patient's pre and post vaccination, these patients were contacted similarly like asymptomatic patients and following questions were asked during the call:

1. What were the type of symptoms you had?
2. Severity of your symptoms and whether hospitalisation was needed during the infection
3. Was there presence of any other disease along with COVID-19 infection?
4. What was the time taken for recovery from COVID-19 infection?
5. Presence of any medication in their daily routine taking for some other disease?

From the above conversations, it was clear that the severity of symptoms were more in patients without any vaccination. The unevenness and difficulty in breathing caused many patients to get hospitalised. Before the vaccination drive started, the condition of symptomatic patients were found to be more severe specifically during the second wave. There was significant increase in oxygen demand and hospital beds during the second wave.

The single dose or completely vaccinated symptomatic patients had normal flu-like symptoms such as cold, fever, and body ache with no severity.

The recovery rate of vaccinated patients were better than non-vaccinated patients. Before vaccine administration, the

positive patients took around 10 to 18 days to turn negative for COVID-19 whereas the vaccinated patients turned negative in less than 10 days. This is in concordance with the study done by Lewis N,2022.[20]

Few patients did postpone their surgeries due to infection with COVID-19 but symptoms were controlled by proper medication.

This shows that the vaccination drive proved to be a boon in able to control the severity of COVID-19 infection in India. The timely and speedy vaccination drive not only contained the pandemic but was instrumental in bringing normality back in nation, as also suggested by.[21]

Now we are standing at the phase where COVID-19 is slowly becoming past. The world is getting normal, mask-free and moving back to development race. This gives immense peace but a lesson to learn that a full proof strategy needs to be devised by every nation to deal with any future challenges in health care depending on its social, political, geographical and economical needs.

India has successfully defended the challenge of COVID-19 pandemic. The strategy of testing, tracing and isolation of positives followed by speedy vaccination drive helped us as a nation to overcome the pandemic. The study helped us to understand the importance of vaccination in alleviating the symptoms in Indian population.

4. Future Prospects

The study majorly deals with the data obtained through RT-PCR data for positive and negative patients. The antibody level study can give more insight about the bodily immune response towards COVID-19 and intervention by other medications or therapies or clinical condition of any other disorders. The limitation of testing population without eliminating the untested COVID-19 patients can be ruled out by antibody based studies by detecting IgG antibodies produced before and after vaccination in response of COVID-19 infection.

However, to bring a holistic insight of the prevalence and disposal of population towards symptoms ranging from mild to severe was successfully determined by this study.

5. Conflict of Interest

The authors declare that they have no conflict of interests.

6. Source of Funding

None.

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