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Original Research Article

Clinical features and outcomes of COVID-19 patients previously vaccinated with COVID vaccine

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ABSTRACT

Background: With countries facing multiple waves of COVID-19 disease throughout the world it is the need of the hour to vaccinate individuals to protect against the deadly virus. Vaccination has shown noteworthy results with reduction in cases, however despite of vaccination many individuals have been infected with SARS-CoV-2 virus. Aims and objectives were to compare the outcomes of COVID-19 positive individuals who have previously received at least one dose of COVID-19 vaccine with unvaccinated individuals and to study the demographic and clinical features in COVID-19 patients who have previously received at least one dose of COVID-19 vaccine.
Methods: This prospective, observational single-center study considered adults patients from April to May 2021 who were diagnosed with COVID 19 infection by RT-PCR technique or Rapid Antigen Test. The sample size for the study was 3076, out of which 2969 were unvaccinated and 107 were vaccinated. Necessary clinical data were collected and selected subjects were followed up until discharge or death. Statistical analysis was carried out using SPSS version 24.
Results: Out of 3076 patients, 2002 (65.08%) were males and 1074 (34.92%) were females. There were 2969 individuals (96.52%) who were unvaccinated and 107 (3.48%) individuals who had received at least one dose any of the COVID 19 vaccines. Among the unvaccinated individuals, 895 (30.1%) succumbed to death and 2074 (69.9%) were discharged. Among the vaccinated individuals 19 (17.8%) succumbed to death and 88 (82.2%) were discharged (Odds ratio-0.5002) (CI-0.3029 to 0.8265).
Conclusions: Vaccination decreases the severity and mortality of the disease. Genetic variants might have a key role and further studies regarding the variants of SARS-CoV-2 is needed.

Keywords: COVID-19 vaccine, Covishield, Covaxin, Variants of concern, Variants of interest

INTRODUCTION

COVID-19 infection first being detected as a cluster of pneumonia from Wuhan, China in December 2019, was later declared to be a pandemic by the World Health Organization (WHO) on 11 March 2020.The pandemic has caused huge devastating impact on the entire globe. The pandemic has disrupted healthcare system and economy of many developed and developing nations. As per WHO till 10th June 2021 there have been 174 million confirmed cases of COVID-19 including 3.7 million deaths.[1] India itself has detected 29.2 million confirmed cases of COVID-19 including 359,676 deaths as of 10 June 2021. The recovery rate being around 98.78 % and 1.21 % of the cases succumbed due to COVID-19.[2] India which had seen a decline of COVID-19 cases in January and February 2021 witnessed a huge spike in cases from mid-March 2021 onwards. The second wave in India has led to

considerable morbidity and mortality. Coronaviruses are enveloped, positive sense single-stranded RNA viruses with glycoprotein spike on the surface. The glycoprotein spike mediates receptor binding and cell entry during infection. Coronaviruses encode four major structural proteins, namely, spike, membrane, envelope, and nucleocapsid. The spike protein binds to the angiotensin-converting enzyme 2 (ACE2), a protein receptor presents on the surface of human cells that mediates entrance of the virus into the human cells. SARS-CoV-2 invades the lung parenchyma and causes severe interstitial inflammation of the lungs.[3]

The clinical presentation of COVID-19 infection ranges from asymptomatic to severe respiratory failure. The most common symptoms at the onset of illness include fever, cough, fatigue, sore throat, myalgia and breathlessness. Other atypical symptoms include loss of taste, loss of smell, anorexia, nausea, vomiting and diarrhoea.[4] Genetic variants of SARS-CoV-2 have been emerging and circulating around the world throughout the COVID-19 pandemic[5].WHO as on June 15th 2021 has identified 4 Variants of Concern (VOCs) and 6 Variants of Interest (VOIs) of the SARS-CoV-2 virus. WHO variants first identified in South Africa (known as 20H/501Y or B.1.351), Brazil (P.1), and the UK (B.1.1.7) are circulating in India, alongside a newly identified distinct Indian variant (B.1.617) which is named as the delta variant.[6] The variants themselves might have been the cause of an increased proportion of cases and the reason for multiple waves of the pandemic. Also causing significant reduction in vaccine effectiveness, a disproportionately high number of vaccine breakthrough cases, or very low vaccine-induced protection against severe disease.

Vaccine development

To combat the spread of COVID-19 there has been a worldwide initiation to develop vaccines against the deadly virus. As of June 15th, 2021 a total of 287 COVID - 19 vaccine candidates have been developed, with 102 in clinical phase and 185 in preclinical phase. Vaccines are being developed using various approaches such as conventional whole virus vaccines (live attenuated or inactivated vaccines), recombinant protein-based vaccines (protein subunit vaccines, virus-like particles), viral vector vaccines, and nucleic acid vaccines (DNA- and mRNA-based vaccines).[7] WHO has listed 8 vaccines in its Emergency Use Listing (EUL) as of June 3 2021.

Vaccination drive in India

India began its vaccination drive from 16th January, 2021 onwards, vaccinating the healthcare and other frontline workers initially. The next phase began from March 1 onwards where all residents above 60 years and individuals with one or more qualifying comorbidities above 45 years were eligible. From April 1st all residents above 45 years were eligible. From May 1st onwards all adults older than 18 years became eligible for vaccination. Covishield vaccine (ChAdOx1_nCoV-19) manufactured by Serum Institute of India and Covaxin manufactured by Bharat Biotech Limited were granted emergency use authorization by the central drugs standard control organization (CDSCO) in India. Sputnik-V has been granted Emergency Use Authorization (EUA) in the month of April 2021. Covishield is a recombinant ChAdOx1 adenoviral vector encoding the Spike protein antigen of the SARS-CoV-2 virus whereas Covaxin is an inactivated vaccine developed using Whole-Virion Inactivated Vero Cell derived platform technology. As of 8th June 2021, a total of 2,154,075,098 vaccine doses have been administered in India.[2] While the debate around the efficacy of vaccine continues, there have been case reports of breakthrough infection despite receiving covid vaccine. The present study intends to study the clinical features and laboratory findings in COVID-19 positive patients who have previously received either one or two doses of any COVID vaccine.

METHODS

The cross-sectional study was conducted from April to May 2021 in hospitals affiliated to Bangalore medical college and research institute. The sample size for the study was 3076, out of which 2969 were unvaccinated and 107 were vaccinated.

Inclusion criteria

Patient willing to give informed consent, Age more than 18 years and Patients who were diagnosed with COVID - 19 infection by RT-PCR or Rapid Antigen test were included.

Exclusion criteria

The study excluded patients <18 years of age and patients not willing to give informed consent were excluded.

Case record format along with follow-up chart was used to collect the demographic data, clinical features of the disease and the vaccine received. Demographic and clinical data such as age, sex, symptoms, comorbidities (diabetes, hypertension, ischemic heart disease etc), vaccine received, number of doses received and days since last vaccine dose received was collected. Individuals were considered partially vaccinated if they had taken at least one dose of vaccine, two weeks prior to being detected covid positive. Individuals were considered completely vaccinated if they had taken both doses of vaccine, and the second dose being taken two weeks prior to being detected covid positive. Laboratory parameters of the patients such as complete blood count, c-reactive protein, serum lactate dehydrogenase, serum ferritin, d-dimer, and fibrinogen were collected. All patients were followed up until discharge or death. Patients were classified into mild, moderate and severe disease category as per the clinical management protocol released by the Ministry of Health and Family Welfare, Government of India.[8]

Mild disease

Patients with uncomplicated upper respiratory tract infection, may have mild symptoms such as fever, cough, sore throat, nasal congestion, malaise, headache without evidence of breathlessness or hypoxia (normal saturation).

Moderate disease

Pneumonia with no signs of severe disease with presence of clinical features of dyspnea and or hypoxia, fever, cough, including SpO_2<94% (range 90-94%) on room air, respiratory rate more or equal to 24 per minute.

Severe disease

Clinical signs of pneumonia plus one of the following: respiratory rate >30 breaths/min, severe respiratory distress, SpO2 <90% on room air.

Statistical analysis

SPSS (Statistical Package for Social Sciences) version 24 was used to perform the statistical analysis.

Continuous variables were expressed as means and standard deviation and categorical variables were presented as counts and percentages. Different parameters were compared between the groups using t-test for continuous and chi-square test for categorical data.

RESULTS

The study included 3,076 participants who were diagnosed positive for COVID-19 infection and were admitted to Victoria hospital, a tertiary care hospital affiliated to Bangalore medical college and research institute. Out of the 3,076 patients, 2,002 (65.08%) were males and 1,074 (34.92%) were females.

There were 2,969 individuals (96.52%) who were unvaccinated and 107 (3.48%) individuals who had received at least one dose any of the COVID-19 vaccines. Age, sex, severity and outcome wise distribution of individuals is shown in (Table 1).

Among the unvaccinated individuals 213 (7.2 %) had mild disease, 1,201 (40.5%) had moderate disease and 1,555 (52.4%) had severe covid pneumonia. Among the vaccinated individuals 45 (42.1%) had mild disease, 38 (35.5%) had moderate disease and 24 (22.4%) had severe covid pneumonia. On comparing the two groups, it was found that severity of the disease was significantly higher in the unvaccinated individuals, whereas, majority of vaccinated individuals had mild disease. Mortality was higher in the 45-59 years and >60 years age groups. Out of the total 914 deaths, 42.23% of the individuals belonged to the ≥60 years age group and 37.42% of the individuals belonged to 45-59 years age group (Table 2).

Of the 2,969 unvaccinated individuals, 895 (30.1%) succumbed to death and 2,074 (69.9%) were discharged. Among the 107 vaccinated individuals, 19 (17.8%) succumbed to death and 88 (82.2%) were discharged. To find out the risk of death among vaccinated individuals when compared to unvaccinated individuals' Odds ratio was used.

An odds ratio of 0.5003 (CI-0.3029 to 0.8265) indicating vaccinated individuals had lesser risk of death when compared to unvaccinated individuals was obtained (p=0.0069) (Table 3).

Table 1: Demographic, clinical severity and outcome of covid positive cases among vaccinated and unvaccinated individuals (n=3076).

Parameters		Total COVID positive patients N (%)		P value
		Unvaccinated (n=2969)	Vaccinated (n=107)	
Age group (years)	18-29	264 (8.9)	38 (35.5)	<0.001
	30-44	828 (27.9)	12 (11.2)	
	45-59	1000 (33.7)	36 (33.6)	
	≥60	877 (29.5)	21 (19.6)	
Sex	Female	1029 (34.7)	45 (42.1)	0.122
	Male	1940 (65.3)	62 (57.9)	
Severity	Mild	213 (7.2)	45 (42.1)	0.005
	Moderate	1201 (40.5)	38 (35.5)	
	Severe	1555 (52.4)	24 (22.4)	
Outcome	Death	895 (30.1)	19 (17.8)	0.0069
	Discharge	2074 (69.9)	88 (82.2)	

Clinical profile among the individuals who were vaccinated was also analyzed. Among the 107 individuals, 71 (66.36%) received first dose of vaccine and 36 (33.64%) had received second dose. 25 (23.4%) individuals had received COVAXIN and the remaining 82 (76.6%) individuals had received Covishield vaccine.

Table 2: Age wise distribution and outcome of COVID positive cases among vaccinated and unvaccinated individuals.

Vaccination status	Age (years)	Outcome N (%)		Total N (%)	Mean±SD
		Death	Discharge		
Unvaccinated	18-29	21 (0.68)	243 (7.9)	264 (8.58)	50.42±15.42
	30-44	164 (5.33)	664 (21.59)	828 (26.92)	
	45-59	332 (10.79)	668 (21.72)	1000 (32.51)	
	≥60	378 (12.29)	499 (16.22)	877 (28.51)	
Vaccinated	18-29	0 (0)	38 (1.24)	38 (1.24)	44.64±17.97
	30-44	1 (0.03)	11 (0.36)	12 (0.39)	
	45-59	10 (0.33)	26 (0.85)	36 (1.17)	
	≥60	8 (0.26)	13 (0.42)	21 (0.68)	
Total	18-29	21 (0.68)	281 (9.14)	302 (9.82)	50.22±15.44
	30-44	165 (5.36)	675 (21.94)	840 (27.31)	
	45-59	342 (11.12)	694 (22.56)	1036 (33.68)	
	≥60	386 (12.55)	512 (16.64)	898 (29.19)	
	Total	914 (29.71)	2162 (70.29)	3076 (100)	

Table 3: Comparison of death outcome in COVID positive cases among vaccinated and unvaccinated individuals.

Total COVID positive patients (n=3076)		Unvaccinated (n=2969)	Vaccinated (n=107)	P value	Odds ratio	95% CI
		N (%)				
Outcome	**Death**	895 (30.1)	19 (17.8)	0.0069	0.5003	0.3029-0.8265
	Discharge	2074 (69.9)	88 (82.2)			

Table 4: Clinical profile in vaccinated individuals and comparison among completely vaccinated and partially vaccinated individuals.

Parameters		Vaccination status N (%)		Total N (%)	P value
		Partially vaccinated	Completely vaccinated		
Vaccine received	Covaxin	20 (28.2)	5 (13.9)	25 (23.4)	0.146
	Covishield	51 (71.8)	31 (86.1)	82 (76.6)	
Age group (years)	18-29	16 (22.5)	22 (61.1)	38 (35.5)	0.001
	30-44	8 (11.3)	3 (8.3)	11 (10.3)	
	45-59	30 (42.3)	6 (16.7)	36 (33.6)	
	>60	17 (23.9)	5 (13.9)	22 (20.6)	
Length of hospitalization (weeks)	<1	30 (42.3)	15 (41.7)	45 (42.1)	0.597
	1-2	33 (46.5)	19 (52.8)	52 (48.6)	
	>2	8 (11.3)	2 (5.6)	10 (9.3)	
Disease category	Mild	22 (31.0)	23 (63.9)	45 (42.1)	0.003
	Moderate	32 (45.1)	6 (16.7)	38 (35.5)	
	Severe	17 (23.9)	7 (19.4)	24 (22.4)	
Outcome	Death	13 (18.3)	6 (16.7)	19 (17.8)	1.000
	Discharge	58 (81.7)	30 (83.3)	88 (82.2)	
Sex	Female	31 (43.7)	14 (38.9)	45 (42.1)	0.683
	Male	40 (56.3)	22 (61.1)	62 (57.9)	

It is significant to note that the percentage of mild disease is higher in vaccine completed group when compared with partially vaccinated group (p= 0.003) (Table 4). However, there is no significant difference in mortality in completely vaccinated and partially vaccinated group. Among the vaccinated individuals 42.1% had less than 1 week of hospitalization. The median time between receipt of the first dose and the positive test was 35 days (interquartile range, 22 to 46). The median time between receipt of the second dose and the positive test was 39 days (interquartile range, 27 to 53). Diabetes was the most common comorbid condition in the vaccinated individuals (28.04%), followed by hypertension (17.76%). Fever was the most common clinical presentation (71.03%) followed by cough (65.42%) and myalgia (42.06%) among the vaccinated individuals (Table 5).

DISCUSSION

The present study shows that vaccination significantly reduces the severity as well as mortality associated with COVID-19 infection.

The study also demonstrates that breakthrough infection despite vaccination is possible. Emergence of variants of COVID-19 virus is of serious concern and will be a challenge in the coming days even after development of vaccines. In a cohort study conducted by Hacisuleyman et al a group of 417 individuals who were administered two doses of the vaccine were examined. The study discovered that after vaccination, two individuals experienced breakthrough infections. The symptoms observed in both patients were mild. Upon analyzing the virus sequences, it was revealed that the variant viruses detected in these patients held potential clinical significance. One woman exhibited the E484K mutation, while both patients had three mutations (T95I, del142-144, and D614G).[9]

A study conducted by Garcia-Beltran WF focused on a cohort of 99 individuals who were administered either one or two full doses of the BNT162b2 or mRNA-1273 vaccines. The objective was to evaluate the neutralization potential of their sera against SARS-CoV-2 pseudoviruses carrying spike proteins found in circulating strains. The study revealed that while neutralization remained largely effective against numerous variants, there was a significant decrease in neutralization against variants containing the K417N/T, E484K, and N501Y RBD mutations, namely, the P.1 and B.1.351 variants, even among fully vaccinated individuals. Individuals who had received only a single recent dose of the vaccine exhibited lower neutralization titers overall and did not demonstrate detectable neutralization against B.1.351 variants in the assays. The study emphasized that the BNT162b2 and mRNA-1273 vaccines only partially cross-neutralize novel variants.[10] In a pivotal efficacy trial conducted by Polack FP et al, individuals aged 16 years and above were randomly assigned in a 1:1 ratio to receive two doses of either placebo or the BNT162b2 vaccine, with a 21-day interval between doses.

Among the participants who received BNT162b2, there were 8 cases of Covid-19 that occurred at least 7 days after the second dose. The study concluded that the BNT162b2 vaccine provided 95% protection against COVID-19. However, in our current study, we observed that 107 individuals developed COVID-19 despite being vaccinated, suggesting that vaccination may not provide complete effectiveness in preventing the disease, potentially due to the emergence of new variants.[11]

In an ongoing blinded, randomized, controlled trial conducted by Folegatti et al in three countries, it was concluded that the ChAdOx1 nCoV-19 vaccine demonstrated an efficacy of 70.4% after the administration of two doses. Within the trial, there were ten cases of COVID-19 that required hospitalization among the vaccinated individuals. Among those cases, two were classified as severe COVID-19, including one fatal outcome. However, in our study, we observed a total of 19 deaths despite individuals being vaccinated. Notably, six of those deaths occurred in individuals who had received two doses of the vaccine. [12]

In a multicenter, double-blinded, randomized, controlled trial conducted by Madhi et al the safety and efficacy of the ChAdOx1 nCoV-19 vaccine were assessed. The study found that serum samples obtained from vaccine recipients exhibited greater resistance to the B.1.351 variant in both pseudovirus and live-virus neutralization assays compared to samples from placebo recipients. However, despite these findings, the study concluded that a two-dose regimen of the ChAdOx1 nCoV-19 vaccine did not provide protection against mild-to-moderate Covid-19 caused by the B.1.351 variant.[13]

According to a study by Rana et al a total of 506 healthcare workers tested positive for the COVID-19 virus despite receiving vaccination. Among a group of 7,170 healthcare workers who had received at least one dose of the vaccine, 184 individuals tested positive. Additionally, among 3,650 healthcare workers who had received the second dose of the ChAdOx1 nCoV-19 vaccine, 72 individuals tested positive for COVID-19.[14]

The aforementioned studies indicate the possibility of breakthrough infections even after vaccination. However, they consistently highlight that the severity of infection and the risk of death are significantly lower among vaccinated individuals in comparison to those who remain unvaccinated.

Limitations

In current present study the genetic analysis of the SARS-CoV-2 virus strains which caused the infection was not determined. Estimation of antibody levels among the vaccinated individuals would have given a better information about the immunogenicity of the vaccines.

CONCLUSION

Breakthrough infections might pose a newer challenge worldwide. Vaccination might decrease the severity of the disease as well as death outcomes. However, mortality despite of vaccination, have been found as per the study but on comparison with unvaccinated group there is significant low risk of mortality among vaccinated individuals. Genetic variants might have a key role in breakthrough infections and further studies regarding the variants of SARS-CoV-2 are needed in vaccinated individuals who develop COVID-19 despite vaccination.

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