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Analysis of COVID - 19 and Mucormycosis Infection in Vaccinated and Unvaccinated Individuals: A Cross-Sectional Study

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Abstract

Introduction

Ongoing Coronavirus-19 pandemic unprecedentedly led to health crisis in population all across the globe. Even though the advent of vaccine has brought the spread of infection under control, shortage in vaccine supply, surge in breakthrough infections and associated mucormycosis in immunosuppressed individuals posed a potential threat. Therefore, our study was focused to know the incidence and the clinical outcome of COVID-19 with accompanying mucormycosis in both vaccinated and unvaccinated people.

Materials and Methods

The study was a cross-sectional analysis undertaken in Respiratory Medicine department for a period of four months. Symptomatic COVID-19 patients who were hospitalized and tested positive by reverse transcription polymerase chain reaction were enrolled in the study. Details of age, gender, co-morbidities, vaccination status and high resolution

computed tomography chest findings were taken into account. In COVID-19 associated with mucormycosis, glycosylated haemoglobin value, dose and duration of steroid therapy and clinical severity of COVID-19 were also noted. Clinical outcome for all the cases were analysed. Statistical analysis of the data collected was done with SPSS™ 17.

Results

There were 134 cases, in which 84 cases (63%) and 50 cases (37%) belonged to vaccinated and unvaccinated group respectively. Isolated COVID-19 infection was noted in 102 cases (76%) and COVID-19 with mucormycosis in 32 cases (24%). Diabetes mellitus, high value of HbA1c and steroid therapy were shown to be predisposing factors for development of mucormycosis in COVID-19 positive patients. High proportion of unvaccinated individuals 18 cases (60%) died due to isolated COVID-19 infection compared to 12 cases (16.6%) of vaccinated individuals and the difference of 43.4% was found to be statistically significant.

Conclusion

Complete vaccination which offers maximum protection against COVID-19 related deaths is mandatory especially in elderly population with underlying illness and concomitant mucormycosis.

Keywords

Reverse Transcription Polymerase Chain Reaction (RT-PCR), High Resolution Computed Tomography (HRCT), Glycosylated haemoglobin (HbA1c), Coronavirus-19 (COVID-19)

Introduction

Coronavirus disease-19 (COVID-19) caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) became a major pandemic in 21st century resulting in dramatic loss of human life globally including India. The first incident of this life-threatening disease began at Wuhan city of China in December 2019 and since then it rapidly spread across the world.[1] In India, COVID-19 infected millions of people following its first outbreak reported on 30th January 2020 in Kerala.[2] To control the spread of infection World Health Organisation (WHO) imposed a stringent lockdown all over the world as early as March 2020 with quarantine polices. To combat the potential threat of the pandemic, the pharmaceutical companies from all over the continents started to develop effective vaccines in mid of 2020. In India, Central Drugs and Standard Committee approved COVID-19 vaccines to be prepared by Serum institute of India and Bharat Biotect Limited which were Covishield and Covaxin respectively.[3] The mass vaccination program was initiated on 16th January 2021 targeting frontline health care workers, followed by civilians older than 45 years of age with accompanying co morbidities.[4]The Indian government on 1st May 2021 announced vaccination for all people above 18 years of age.[4]Due to shortage of vaccine supply and negligence in social distancing, breakthrough Covid-19 infections began to flare up.[5]In midst of this pandemic crisis, accompanying co-morbidities and immunosuppression following high dose and prolonged steroid treatment for COVID-19, patients became susceptible to mucormycosis fungal infection.[6] We aim to know the incidence of COVID-19 infections and concomitant mucormycosis in vaccinated group (partial and complete vaccination) and unvaccinated group and also the clinical outcome in both the groups.

Materials and Methods

This was a cross-sectional study carried out for a period of four months from April 2021 to July 2021 in the department of Respiratory Medicine at Tertiary care

hospital, New Delhi. The study population comprises of 134 symptomatic COVID-19 patients admitted in COVID wards of Respiratory department and tested positive by RT-PCR of nasopharyngeal swab. For all the patients in addition to age and gender, the other details taken into account were clinical features, pre-existing illness, vaccination history, the time interval between vaccination and the manifestations of COVID-19 symptoms. People who received first dose of vaccine came under partial vaccination group. Two weeks following second dose of vaccine came under complete vaccination group. The breakthrough infection is defined as infection occurring 14 days after receiving second dose of the vaccine. [5]The severity score of HRCT chest in COVID-19 patients who presented with triad of fever, cough and dyspnoea was also noted. The 25-point severity score was graded as mild (less than 8), moderate (9 to 15) and severe (more than 15). In dual infection of COVID-19 and mucormycosis, HbA1c value and the dose and duration of steroid treatment was documented during their hospital stay. The clinical severity of COVID-19 patients prior to the development of mucormycosis was also noted which according to Indian Council of Medical Research (ICMR) guidelines is categorised as mild (more than 94% SpO2), moderate (90% to 93% SpO2) and severe (less than 90% SpO2). All patients were followed up for a period of thirty days to know their clinical outcome. Data was collected with the help of a proforma and managed in Microsoft Excel. All the statistical analysis was done with SPSS™ 17. The study obtained clearance from the Ethical committee of the institute.

Results

In a total of 134 patients, 84 (63%) of them have been vaccinated in which 72 cases (72/134, 54%) and 12 cases (12/134, 9%) came under partial and complete vaccinated groups respectively. In the rest 50 cases (37%) patients belonged to unvaccinated group (Figure-1). From the total, dual infection of COVID-19 and mucormycosis was noted in 32 cases (32/134, 24%) and isolated COVID-19 infection in 102 cases (102/134, 76%). The patient's age varied between 20 to 80 years with a median age of 48 years. Females were 48 (36%) and males were 86 (64%).

In vaccinated group, dual infection of COVID-19 and mucormycosis was seen in 12 cases (12/84, 14%) in which 10 cases and two cases received partial and complete vaccination respectively. While only COVID-19 infection was seen in 72 cases (72/84, 86%) in which 62 cases and 10 cases had partial and complete vaccination respectively. In unvaccinated group, dual infection and COVID-19 infection was noted in 20 cases (20/50, 40%) and 30 cases (30/50, 60%) respectively (Figure-2).

In dual infection category, in vaccinated group the mean time interval between COVID-19 symptoms and onset of mucormycosis was 19 days while in unvaccinated group it was 15 days. The clinical severity of COVID-19 patients prior to the occurrence of mucormycosis was mild in eight cases (8/32, 25%) and moderate in 24 cases (24/32, 75%). In all moderate clinical severity cases a cumulative dose of 520mg of intravenous methyl prednisolone was given. The average duration of steroid therapy was 15days along with nasal oxygen support. In this category, co-morbidities were seen in 28 cases (28/32, 87.5%) and not present in four cases (4/32, 12.5%). Diabetes mellitus was present in all the 28 cases (87.5%). It was associated with hypertension, coronary artery disease and cirrhosis in ten, four and two cases respectively. The common site for mucormycosis was nose and sinus (30/32, 94%) followed by rhino-sino-orbit (16/32, 50%)

and maxillary sinus (2/32, 6.25%). The glycosylated haemoglobin value in all the 32 cases was above 7% (Table-1,2). The recovery from dual infection was seen in 26 cases (26/32, 81.25%) and in six cases (6/32, 18.75%) who were above 60 years of age with underlying pre-existing illness and moderate clinical severity died due to COVID-19 pneumonia, sepsis, acute respiratory distress syndrome and multi-organ failure. Of the six cases, two received partial vaccination and four were unvaccinated.

In COVID-19 infection category, the mean time interval between partial and complete vaccination with that of COVID-19 symptoms was found to be 18 days and 32 days respectively. The common clinical presentation was triad of fever, cough and dyspnoea which was present in 84 cases (84/102, 82%). In all these cases HRCT chest showed mild, moderate and severe severity score in 40 cases (40/84, 48%), 30 cases (30/84, 36%) and 14 cases (14/84, 16%) respectively. A combination of fever and sore throat was seen in 16 cases (16/102, 16%) followed by fever and loose stools in two cases (2/102, 2%). Co-morbidities were present in 76 cases (76/102, 75%) and not seen in 26 cases (26/102, 25%). Hypertension was present in all 76 cases. It was associated with diabetes mellitus, pulmonary tuberculosis, bronchial asthma, malignancy and hypothyroidism in twenty eight, ten, eight, six and four cases respectively. Two cases each of chronic kidney disease and coronary artery diseases were also noted. The recovery from COVID-19 infection was seen in 72 cases (72/102, 71%) and in 30 cases (30/102, 29%) patients died due to pneumonia, sepsis, acute respiratory distress syndrome and multi-organ failure. Out of 30 mortality cases, 12 (12/30, 40%) and 18 (18/30, 60%) cases belonged to partial vaccinated and unvaccinated group respectively. From these 30 patients, 28 of them were above 55 years (28/30, 93%) and two of them were below 40 years of age (2/30, 7%) who belonged to unvaccinated group.

In complete vaccinated group no mortality was seen. The overall clinical outcome in partial vaccinated group, recovery cases were 58 (58/72, 81%) and mortality cases were 14 (14/72, 19%). In unvaccinated group, recovery cases and mortality cases were 28 (28/50, 56%) and 22 (22/50, 44%) respectively. (Table 3)

The association between dual infection and outcome was not statistically significant with p value of 0.815 while that between COVID-19 infection and outcome was statistically significant with p value of 0.000012.(Table 4,5)

Figure 1: Distribution of cases in vaccinated (partial and complete) and unvaccinated group

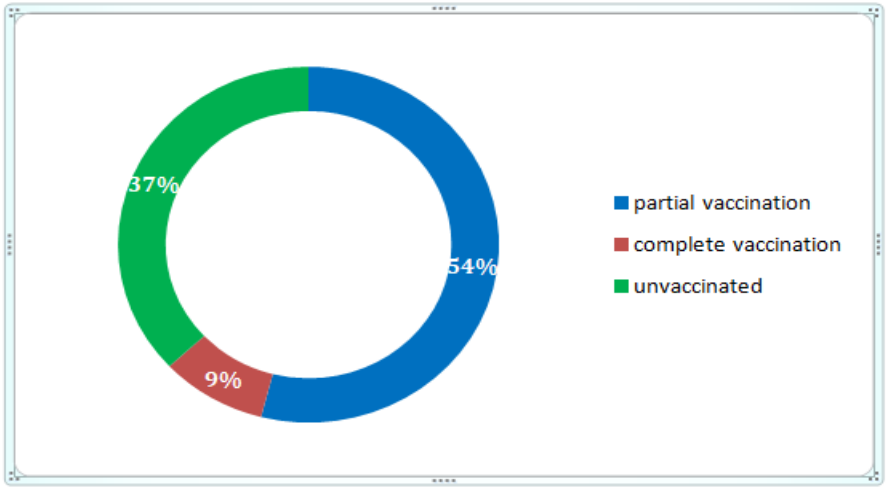

Figure 2: Distribution of dual infection and COVID-19 in vaccinated (partial and complete) and unvaccinated group

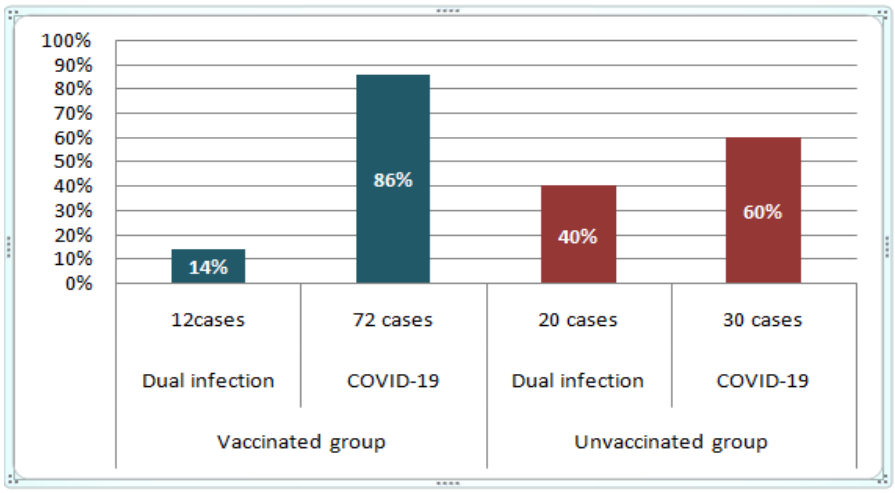

Table 1: Details of Dual Infection in Vaccinated (partial and complete) group

S. No	Age (years)	Sex	Vaccine doses	Co-morbiditie s	It b/w vaccine & C-19 (days)	I b/w C-19 & MU (days)	Site of MU	HbA1c (%)	Outcome
1	48	Male	I	DM	11	22	Left RS	7.8	Re
2	38	Male	I	DM	13	18	Left RSO	11.2	Re
3	61	Male	I	DM,HTN	10	16	Right RSO	11.3	E
4	53	Female	II	DM, HTN	26	21	Right RSO	8.3	Re
5	66	Male	I	DM	10	18	Right RS	10.9	Re
6	26	Female	I	Nil	12	19	Right RSO	7.2	Re
7	64	Male	I	DM,HTN	11	16	Right RSO	11.3	E
8	39	Male	I	DM	19	17	Left RSO	11.2	Re
9	56	Female	II	DM, HTN	28	23	Right RSO	8.3	Re
10	62	Male	I	DM	16	19	Right RS	10.9	Re
11	28	Female	I	Nil	12	22	Right RSO	7.2	Re
12	45	Male	I	DM	14	19	Left RS	7.8	Re

Note: First-I, Second-II, It- Interval, b/w-Between, COVID-19-C-19, MU-Mucormycosis, R-Rhino, S-Sino, O-Orbital, Re-Recovered, E-Expired, DM-Diabetes mellitus, HTN-Hypertension

Table 2: Details of Dual Infection in Unvaccinated group

S. No	Age (years)	Sex	Co-morbidities	It b/w C-19 & MU (days)	Site of MU	HbA1c (%)	Outcome
1	45	Female	DM	12	Bilateral RSO	7.6	Re
2	48	Male	DM	16	Right M	7.8	Re
3	48	Male	DM, HTN, C	14	Right RSO	10.8	Re
4	21	Male	Nil	15	Bilateral RS	7.1	Re
5	62	Female	DM, HTN	11	Left RS	8.8	Re
6	42	Male	DM	21	Left RS	8.2	Re
7	61	Male	DM, CAD	13	Right RSO	10.2	E
8	72	Female	DM, CAD	12	Bilateral RS	11.8	E
9	58	Male	DM, HTN	17	Left RS	11.3	Re
10	62	Male	DM	17	Right RSO	9.6	Re
11	44	Male	DM	19	Right M	7.8	Re
12	65	Female	DM, HTN	14	Left RS	8.8	Re
13	73	Female	DM, CAD	11	Bilateral RS	11.8	E
14	22	Male	Nil	22	Bilateral RS	7.1	Re
15	47	Female	DM	15	Bilateral RSO	7.6	Re
16	64	Male	DM	18	Right RSO	9.6	Re
17	40	Male	DM	21	Left RS	8.2	Re
18	48	Male	DM, HTN, C	14	Right RSO	10.8	Re
19	55	Male	DM, HTN	12	Left RS	11.3	Re
20	63	Male	DM, CAD	11	Right RSO	10.2	E

Note: It-Interval, b/w-Between, COVID-19-C-19, MU-Mucormycosis, R-Rhino, S-Sino, O-Orbital, M-Maxillary sinus, Re-Recovered, E-Expired, DM-Diabetes mellitus, HTN-Hypertension, CAD-Coronary artery diseases, C-Cirrhosis

Table 3: Clinical outcome in vaccinated (partial and complete) and unvaccinated group

Group	Dual infection (Number of cases)		Covid-19 infection (Number of cases)		Total
Outcome	Recovery	Death	Recovery	Death	
Partial Vaccinated	08 (30.7%)	02(33.3%)	50(69.4%)	12(40%)	72 (53.7%)
Complete Vaccinated	02 (7.6)	0	10(13.8%)	0	12(8.9%)
Unvaccinated	16 (61.5%)	04(66.6%)	12(16.6%)	18(60%)	50 (37.3%)
Total	26 (100%)	06(100%)	72(100%)	30(100%)	134(100%)

Table 4: Association between dual infection and outcome

Group	Death	Recovery	Total
Unvaccinated	04(20%)	16(80%)	20(100%)
Vaccinated (Partial and complete)	02(16.6%)	10 (83.3%)	12(100%)
Total	06(18.75%)	26(81.25%)	32(100%)

Table 5: Association between COVID-19 infection and outcome

Group	Death	Recovery	Total
Unvaccinated	18(60%)	12(40%)	30(100%)
Vaccinated (Partial and complete)	12(16.6%)	60 (83.3%)	72(100%)
Total	30(29.4%)	72(70.5%)	102(100%)

Discussion

COVID-19 infection, a zoonotic disease not only had an enormous impact on health of people but also caused social and economic disruption worldwide. On 11th March 2020, WHO proclaimed this communicable disease as a pandemic all across the world.[1] The term COVID-19 and SARS-CoV-2 were officially coined by WHO and International Committee on Taxonomy of Viruses respectively on 11th February 2020.[7]

The vaccination campaigns in India commenced on 16th January 2020 to bring the spread of this contagious infection under control. To vaccinate the Indian population of 1.39 billion was a huge challenge for the government. As stated by the Delhi government on 31st July 2021, Delhi with a population of 1.5 crore above 18years of age, complete vaccination was seen in 26 lakh people which was less compared to those who were partially vaccinated which was 48 lakh people with still 76 lakh people being unvaccinated.[8] In our study too completely vaccinated patients were less compared to those who were partially vaccinated. The reason for not being completely vaccinated was due to shortage of vaccine supply as stated by the government.[9] It was also due to COVID-19 infection that occurred in people who had taken their first dose and who did not follow social distancing norms as observed in our study. There were 50 patients in our study who did not choose to get vaccinated. This is because these patients were scared of the side effects and complications encountered following vaccination.[10] There is no vaccine which offers 100% protection from any disease leading to breakthrough infections as seen in our study. According to the statement released by ICMR on 21st April 2021, 2 to 4 per 10,000 got infected with COVID-19 after vaccinations in India [5]. The breakthrough infections may be because of COVID variants bypassing the immunity provided by the vaccine, lack of social distancing norms and also ability of the vaccinated population to spread the diseases.[11] The symptomatic breakthrough infections seen in our study was 14.2% (12/84) which was comparable with the study done by Kanika T et al where it was 13.3% (15/113).[5] In another study done by Moriah B et al breakthrough infection documented was 2.6% (39/1497) which was low compared to our study.[12]

In COVID-19 infection category the most common clinical presentation was fever followed by cough and dyspnoea. This was consistent with the study done by Margherita M et al.[13] Sore throat and loose motion seen in our cases were also documented in a study done by Kanika T et al.[5] The mean interval between complete vaccination and onset of COVID-19

symptoms in our study was 32 days which was consistent with the study done by Kanika T et al and Moriah B et al where the mean were 34.8 days and 39 days respectively.[5,12] The co morbidities seen in our study was also observed in the study done by Margherita M et al with hypertension being the most common one in both the studies.[13] The HRCT chest severity score was mild in most of the cases followed by moderate and severe severity scores in our study. This correlated with the study done by Ghufran A S et al.[14]

In recent years the prevalence of Mucormycosis in India was 0.14 per 1000 and was found out to be higher when compared globally which was 0.005 to 1.7 per million population.[15] The use of high dose of steroids as a supportive treatment with pre-existing illness has increased the susceptibility of opportunistic fungal infection in COVID-19 positive patients. Singh AK et al stated 82 cases of mucormycosis in COVID-19 positive patients were reported from India and we report 32 cases from Respiratory department.[15] Cases of dual infection were well documented in studies done by Drashti J. P et al , Mrittika S et al and Ravani SA et al as with our study.[6,16,17] Diabetes mellitus was seen as the common pre-existing illness in 87.5% of the dual infection cases along with high HbA1c levels in our study which is consistent with the studies done by Singh AK et al, Mrittika S et al and Ravani SA et al.[15,16,17] In unvaccinated group the mean time interval between the COVID-19 symptoms and onset of mucormycosis noted in our study was comparable with that of the Mrittika S et al study.[16]In our study the treatment of COVID-19 infection with steroids was found to be a risk factor for the development of mucormycosis which was compatible with the study done by Singh AK et al.[15] The commonest site in our study was rhino-sinus region which was consistent with the data presented by Singh AK et al.[15]

The median age of our study population was 48 years with men being affected more than women. This correlated with the study done by Kanika T et al, Brown CM et al and Ghufran A S et al. [5,11,14]

In a study done by ICMR, the incidence of COVID-19 infection following first dose of vaccine was comparatively more than following complete vaccination.[18] Similar observation was noted in our study.

In a study done in Delhi by All India Institute of Medical Sciences and ICMR , zero and 0.4% mortality was reported respectively following breakthrough infection which was comparable with our study in complete vaccination group.[19,20]A study conducted in UK, reported 21.5% (113/526) of mortality cases following first dose of COVID-19 vaccine which correlated with our study.[21] According to a study conducted by ICMR, mortality rates is seen more in unvaccinated population than in those who are partially vaccinated.[22] Similar finding was observed in our study also.

Conclusion

COVID-19 pandemic had shown higher mortality rates in unvaccinated population compared to vaccinated group. In midst of this crisis, a surge in mucormycosis in COVID-19 positive cases was noted with risk factors being underlying diabetes mellitus, high HbA1c value and steroid therapy. The commonest site of mucormycosis was rhino-sinus region. Hypertension was the common co-morbidity in isolated COVID-19 patients. The incidence of breakthrough infections following complete vaccination was 14.2% and all the patients showed complete recovery with no mortality. Hence two doses of COVID-19 vaccine

which offers 95 % of protection against COVID-19 related mortality is mandatory along with social distancing norms to combat the serious threats of ongoing pandemic.[22]

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