COVID-19 (SARS CoV-2) Post-Vaccination Infection among Healthcare Professionals

Dr. Bhagyashree Sudhakar Joshi,

PhD (HA), MBA (HCS), MSc. (Nsg.) and Dr. Sujata Bhaskar Sawant, PhD (Nsg.), MSc. (Nsg) 705, F wing, Saptasur, DSK Vishwa, Dhayri, Pune, Maharashtra – 411041, India Email of corresponding author: *drbhagyashreejoshi[at]hotmail.com*

Abstract: <u>Introduction</u>: In spite of vaccination, incidences of COVID-19 (SARS CoV-2) infections are being reported in partially and fully vaccinated Healthcare Workers (HCWs) all over the world. <u>Objective of the study</u>: To explore the COVID-19 Post vaccination infection among healthcare workers. <u>Methodology and Results</u>: We performed literature search in Google scholar, Research gate, and PubMed databases for articles on the subject from January 2021 to December 2021. Only twenty studies matched the criteria and were included for this review. Data was extracted on study duration, design, settings, population / samples, vaccination status, post vaccination infection, average day of post vaccination infection, symptoms, comorbidities etc. <u>Conclusion</u>: COVID-19 pandemic showed that every country and every individual was vulnerable and no one was safe. Health care workers were at greater risk of developing Covid-19 (SARS CoV-2) infection in spite of their vaccination status. Although studies have reported that vaccine helps to decrease the severity of the condition. More research studies and time is needed to understand "the vaccine as a whole" and its effectiveness in terms of immunity development and side effects. Although vaccinated it is also important to maintain the health by healthy diet, exercises, proper lifestyle, and taking due precautions as needed.

Keywords: Breakthrough infections, COVID-19 (SARS-CoV-2), COVID-19 vaccine, Health care workers, post vaccination infection, vaccine breakthrough

1. Introduction

COVID-19 stands for coronavirus disease of 2019. COVID-19 caused by severe acute respiratory corona virus 2 (SARS-CoV-2) infection which was started from end of the year 2019. World Health Organization declared that as 'pandemic' in March, 2020. It was thought that COVID-19 battle could be conquered with the vaccine. Hence, from January, 2021 phase wise vaccination programmes were introduced all over the world. During this pandemic, healthcare workers (HCWs) were constantly exposed to patients tested positive for COVID-19 (SARS-CoV-2) infection and were still required to take care of these patients; hence at the risk of acquiring COVID-19 (SARS-CoV-2) infection. As a result, priority was given to vaccinate HCWs to protect them and ensure the continuity of healthcare services without any disruption.

However, in spite of vaccination, numbers of infections are being reported in partially and fully vaccinated people by positive RTPCR (Reverse transcription polymerase chain reaction) test and symptoms of COVID-19 (SARS-CoV-2) infection. (1) Thus, post-vaccination infection became a major concern around the world. Media and people reported need for better understanding of the COVID-19 infection, virus characteristics and mutations, durability of immunity after vaccination, concerns about post-vaccination infection and re-infection. Hence, assessment of infection following immunization is of particular interest in this study, especially in the context of SARS-CoV-2 vaccine. This study tried to shed light on the same from healthcare workers perspective.

Objective of the study: To explore the COVID-19 Post-vaccination infection among health care workers.

2. Methodology

We performed literature search in Google scholar, Research gate, and PubMed databases for articles from January 2021 to December 2021, for studies evaluating post-vaccination infection, break-through infection and covid-19 vaccine effectiveness. We also reviewed the reference lists of retrieved articles and hand searched studies that were matching inclusion criteria. Total 111 studies were screened for titles and abstracts to assess whether they met inclusion criteria. Finally only twenty studies matched the criteria and were included for this review. Data was extracted on study duration, design, settings, population /samples, vaccination status, infection after vaccination, average day of postvaccination infection, symptoms, comorbidities etc.

3. Results

Total 20 studies are included in this review (2–21). All 20 studies were conducted during six months period from December 2020 till May 2021. These studies were from various geographical areas of the world including one study each from Brazil (18), Israel (7), Nepal (16), Netharlands (15), Pakistan (10), and Saudi Arabia (6). Two studies each were from Quatar (4, 5) and United States (3, 17). Three studies from Italy (9, 14, 19) and six studies from India (2, 8, 12, 13, 20, 21). This review has also included one systematic review (11) which consisted of 16 studies: 6 studies from United States, 3 studies from Italy, 3 from United kingdom, 2 from Israel, 1 from Spain, and 1 from Ireland.

One of them was a case report (9), one was case control parallel cohort (19), one mentioned observational study (15), and one was systematic review and meta analysis (11). Three studies used cross sectional survey (13, 16, 18), four were retrospective studies (2-4, 21) and six were

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prospective studies (6–8, 10, 14, 17). Other three studies did not report any design of the study. (5, 12, 20)

During this pandemic, number of countries developed vaccines to fight the battle against COVID-19. In this review we observed that eight different vaccines were used namely (Pfizer-BioNTech), (Moderna--mRNA1273 BNT162b2 vaccine), Ad26. CoV2. S (Janssen/Johnson & Johnson), AstraZeneca, ChAdOx1 nCoV-19 Covishield, Covaxin, Coronavac, and Sino-pharm Vaccine. Four studies used BNT162b2 (Pfizer-BioNTech) (6, 7, 9, 14), two studies used BNT162b2 (Pfizer-BioNTech) and (Moderna-mRNA1273) (5, 17), four studies used BNT162b2 (Pfizer-BioNTech), (Moderna--mRNA1273 vaccine) and Ad26. CoV2. S (Janssen/Johnson & Johnson) (3, 4, 11, 15), two studies used ChAdOx1 nCoV-19 Covishield (8, 16), one study used ChAdOx1 nCoV-19 Covishield and Coronavac (18), five studies used ChAdOx1 nCoV-19 Covishield and Covaxin (2, 12, 13, 20, 21), and one study used Sino-pharm Vaccine (10). Systematic review (11) reported BNT162b2 (Pfizer-BioNTech), (Moderna--mRNA1273 vaccine), Ad26. CoV2. S (Janssen/Johnson & Johnson), and AstraZeneca in their study.

Thirteen studies (2–4, 6, 8–11, 13, 17, 19–21) reported number of HCWs after first and second dose. One study did not report vaccination dose (18). Six studies (5, 7, 12, 14– 16) reported only second dose of vaccination.

Only three studies (2, 4, 12) reported time interval between first and second dose of vaccine. One study (2) used Covishield and Covaxin vaccine and reported interval between two doses as 4 to 12 weeks, another study (12) used the same vaccine but reported median interval between the first and second dose as 30 days. Another study (4) reported for Pfizer/BioNTech and for Moderna (mRNA-1273) vaccine interval between two doses were 21 and 28 days respectively.

The "Post-vaccination infection" phrase has been interpreted / described differently by different authors like symptomatic/ asymptomatic infection, adverse events, adverse effects, breakthrough infection, post vaccination infection, vaccine-associated enhancement disease (VAED) etc. Symptoms representing these phrases were similar. Hence for this study we have combined all these terms under one phrase i. e. "post-vaccination infection". Post-vaccination infection after both-the first and the second dose was reported in only eleven studies. (2, 4, 6, 8–10, 13, 17, 19–21) Duration of developing post vaccination infection was between 1 to 111 days.

In few studies, samples had positive RT-PCR test but were asymptomatic. Acharya et al divided symptoms under three headings: mild, moderate and severe based on respiratory parameters like respiratory rate and SpO_2 levels. (2) Trunfio et al (19) reported mild flu without systemic involvement (cough, rhinorrhea, pharyngitis, and headache) and moderate SARS-CoV-2 infection (fever, arthromyalgia, asthenia/malaise, cough, pharyngitis, loss of smell/taste). Maroof et al (10) reported mild, moderate disease. Mild presentation was considered as fever, loss of smell and / or taste, mild or no cough; Moderate disease was considered as

lower respiratory tract illness on imaging or clinical assessment with $SpO_2 \ge 94\%$ on room air. Kale et al (8) mentioned mild for symptoms like fever, body ache, cough, headache, diarrhea, or vomiting. Whereas Loconsole et al (9) reported mild infection as asthenia, low-grade fever. Three authors (6, 12, 15) mentioned "mild and moderate" but did not define the criteria. Few authors (10, 14, 15, 21) have categorized Post-vaccination infection (PVI) under systemic and local symptoms or mentioned as symptomatic / asymptomatic PVIs.

Post vaccination infection-symptoms reported were: fever (4, 6-10, 12-15, 19, 20), cough (4, 6-10, 12, 14, 15, 19, 20), headache (4, 6, 8, 14, 15, 17, 19), rhinorrehea (4, 6, 12, 17, 19), rhinitis (14), rhinosinusitis (15), dyspnoea (4, 6, 7, 12, 14, 15, 19), diarrhoea (4, 8, 14, 19, 20), myalgia (4, 7, 12, 15), arthromyalgia (19), loss of smell (4, 7, 10, 19, 20), loss of taste (4, 7, 10, 19, 20), sore throat (4, 6, 12, 20), anosmia (9, 12, 14, 15), malaise (6, 13, 19), fatigue (7, 17), nausea (14, 19), vomiting (8, 19), ageusia (9, 14), arthralgia (14, 15), asthenia (14, 19), pharyngitis (15, 19), weakness (7), bodyache (8), pharyngodynia (14), pneumonia (14), peripheral neuropathy (15), otitis (15), sinusitis (15), O/G dysfunction (19), and coryza (9).

Majority of HCWs who had post vaccination infection reported at least one co-morbidity or chronic illness (5, 12, 13, 15, 17) . Comorbidities reported were: Hypertension, Diabetes, Cardiovascular disease (MI, Stroke, CHF), Thyroid related diseases (Hyperthyroidism, Hypothyroidism), Chronic lung disease (Asthma, COPD), Hematological disease. Rheumatoid Arthritis. Hyperlipidemia, Chronic liver disease, Cancer, Chronic kidney disease, Immune-compromised status, Autoimmune conditions, Psychological distress etc.

4. Discussion

COVID-19 pandemic showed that every country and every individual was vulnerable and no one was safe. During Covid-19 pandemic caring infected people caused a significant burden and threat to physical and mental health of healthcare professionals. Although personal protective measures and social distancing policy was mandatory in the hospital settings while caring and interacting with active cases of COVID-19; healthcare professionals were and still are at greater risk of acquiring infections because of direct exposure to and contact with the infected patients. Hence, on priority basis early vaccination for healthcare professionals was chosen to safeguard them and to ensure uninterrupted care for patients during this pandemic.

During Covid-19 pandemic, number of countries rapidly developed vaccine to fight SARS-CoV-2 virus. During the period from January 2021 till May 2021 mass vaccination campaign for healthcare workers was initiated all over the world. Numbers of vaccines were developed all over the world. All these vaccines claimed vaccine effectiveness in clinical trials. Vaccine effectiveness in terms of postvaccination infection in real life situations was and is still not clearly known.

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In the past, numbers of years were invested to develop vaccine against various infectious diseases. According to "John Hopkins University and Medicine", (22) vaccine development process is longer, ranging between 5 to 10 years or more, to make sure that the vaccine is found to be safe and effective in clinical trials before utilizing it for masses. However, during Covid-19 pandemic, vaccines were produced at very rapid rate and in large numbers. According to the U. S. Food and Drug Administration (FDA) (23) "There is no predetermined timeline for vaccine Typically, the better the development. scientific understanding of a pathogen and the disease it causes, the more efficient is the vaccine development. " In case of Covid-19 virus, scientists need more time to understand the Covid-19 virus mutation, their characteristics and effects on human life; to develop vaccine which will be effective against all variants of Covid-19 viruses.

It was observed that World Health Organization and various Governments emphasized repeatedly that two doses of vaccine are necessary and have been thought to be effective to protect the individual from Covid-19 disease. In the beginning, shorter duration between two doses was planned but later on government authorities extended the duration between two doses in order to cover the entire population of their countries. There were no published research studies supporting this extension of time duration between two doses of vaccination. Trunfio et al stated that "Several countries are extending the interval between vaccine doses to maximize initial nationwide coverage, but data on long-term effectiveness of modified administration schedules as well as early effectiveness of first doses are lacking." (19)

There was gap of almost one year between the disease breakout in the world and the availability of vaccine for actual immunization. Scholars think that the HCWs who were dealing with these cases must have developed herd immunity; but data on assessment of herd immunity of individuals before the vaccination is lacking.

Immune system being extremely complex is still not well understood. Individual responses to any disease condition differ significantly. How immune system responds to COVID disease and COVID vaccine is yet not clear. Number of studies have reported antibody titre in vaccinated individuals (1). It is believed that an individual having antibodies is fully protected against the disease. In contrast, some people do not develop the disease in spite of low antibody titres. (1) It is interesting to explore why some people develop the disease and others do not or in other words why some individuals developed infection after vaccination and others did not? Maclean et al. report that "antibody levels are not static and are expected to wane, with the kinetics of the waning process varying across different vaccines and dosing schedules". (1), ^{pg2} Emerging evidence shows that the risk of infection increases in the months following vaccination. Additionally virus mutations and emerging Covid virus variants such as Alpha (B.1.1.7; 501Y. V1), Beta (B.1.351; 501Y. V2), Gamma (B.1.1.28.1; 501Y. V3; P.1), Delta (B.1.617.2), Kappa (B.1.617.1), Omicron etc raise a concern regarding efficacy of a vaccine to give protection against all variants of COVID-19 virus. COVID vaccine does not give lifelong protection as vaccinated individuals have reported post-vaccine infection. Current literature also reported even after the vaccination people had positive Covid reports or positive RT-PCR test results every time when tested. Clinical picture and immunological response to Covid-19 in vaccinated individuals is still not clear. Marrof et al stated that no vaccine is 100% effective against all strains of COVID-19. (10) Likewise Akhrass et al (4) reported that authorized vaccines are not 100% effective at preventing symptomatic and asymptomatic infections. Virus is going to mutate as its natural tendency and characteristic. Pouquet et al expressed concern related to duration of protection after vaccination and how many dosages required for developing the immunity. (24) Additionally, it is not clear how many days are required to develop the immunity. (11, 17) Vaccination does not necessarily mean that the individual has developed the immunity against the particular disease.

Literature reported that although HCWs were vaccinated they used personal protective equipments and followed precautionary measures, but still developed post-vaccination infection. Number of reasons reported in the studies why HCWs were infected after vaccination were: 1) exposure to Covid-19 SARS-CoV-2 due to cross-infection from either a patient, family members (e. g. infected spouse) or colleagues. (4-8, 11, 15) No one wear mask at home; additionally exposure to viral load in confined places like home adds to the risk. High density household settings are reported potential high risk of viral transmission despite the vaccination status. (15) 2) Marra et al also reported that an asymptomatic individual may be a carrier of COVID-19 (SARS-CoV-2) disease. (11) 3) False sense of protection after vaccination resulting in non-adherence of personal protective measures while caring for the positive cases. (6, 21) 4) waining of immunity. (15) Apart from these other multiple risk factors are not only associated with higher risk of SARS CoV-2 but any infection and result in poor clinical outcome in infected persons. These risk factors include old age, smoking, overall poor health condition, poor individual immunity and associated comorbidities. In the current study, we observe that many authors reported one or more comorbidities in post-vaccination infection cases. (5, 12, 13, 15, 17) Although vaccinated still we need to take proper precautions, healthy diet, exercises, and maintain healthy lifestyle.

5. Conclusion

COVID-19 pandemic showed that every country and every individual was vulnerable in this pandemic and no one was safe. HCWs were at greater risk of developing Covid-19 (SARS CoV-2) infection in spite of their vaccination status. Although studies have reported that vaccine help to decrease the severity of the condition, this review reports it is too early to confirm this. More research studies and time is needed to understand vaccine as a whole and its effectiveness in terms of immunity development and side effects. Although vaccinated it is equally important to maintain the health by healthy diet, exercises, proper lifestyle, and taking proper precautions when needed.

Conflict of interest: No conflict of interest

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Author's contribution

Dr. Bhagyashree Joshi and Dr. Sujata Sawant: Conception, Design, Acquisition of data, Analysis and interpretation of data.

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