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# The Impact of Vaccination Status on the Severity of Pain Syndrome in COVID-19 Patients

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**ABSTRACT**

COVID-19 has a lot of different symptoms, and pain syndrome is one of them. Getting a COVID-19 vaccine cut down on illnesses with symptoms and/or high viral loads. The study's goal is to find out how bad the pain syndrome is in people who have been vaccinated against COVID-19 and people who have not been immunized. A cross-sectional observational study was done on 304 COVID-19 patients from September 2021 to April 2023. The patients' ages ranged from 18 to 65. After they gave written permission, the people who took part in the study were given an electronic form with 20 questions. The study subjects were split into 5 groups based on their vaccine status: those who had not been vaccinated, those who had been partially vaccinated (≥ 14 days after dose 1 or < 14 days after dose 2), those who had been fully vaccinated (≥ 14 days after dose 2), those who had been vaccinated after the third dose, and those who had been vaccinated after the fourth dose. All subjects, vaccinated and not vaccinated, had pain syndrome symptoms, and there were no significant differences (P>0.05). A lot of people who weren't protected (40.2% of them) reported severe pain. In the group that got the fourth dose, however, it was not found at all (0%). It was (29.7%), (38.7%), and (39.1%) in the groups that had been partly vaccinated, fully vaccinated, and given the third dose of the vaccine, in that order. In conclusion, pain syndrome was found in all COVID-19 patients. The pain was much worse in patients who had not been vaccinated, but not in those who had gotten the fourth dose of the vaccine.

**KEYWORDS:** COVID-19, vaccination, pain syndrome, Headache, Myalgia.

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## INTRODUCTION

Coronavirus Disease 2019 (COVID-19) is a very bad virus that has spread around the world since December 2019. The patients may have flu-like symptoms or even find it impossible to breathe (Ouassou et al., 2020). SARS-CoV-2 was found in the cerebrospinal fluid of some cases, which suggested that it might be a neuroinvasive virus. SARS-CoV-2 was also found in the brains of some patients whose RT-PCR tests came back negative (Paniz-Mondolfi et al., 2020; Freij et al., 2020). You can have acute pain, like a sore throat, or systemic pain, like a headache, myalgia, nerve pain, or arthralgia. The pain could be caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) or by the body's immune system reacting to the virus (Berger, 2020; Guadarrama-Ortiz et al., 2020). A cytokine storm linked to SARS–CoV may also play a role in the development of myalgia, headaches, and arthralgia (Mangalmurti and Hunter, 2020).

Myalgia, high CK levels in the blood, and rhabdomyolysis are signs that about one-third of patients have virus-associated myositis (Fan et al., 2006; Wang et al., 2004; Chen et al., 2005; Tsai et al., 2004). An early side effect that can happen to 10–15% of COVID-19 patients is arthralgia (Hoong et al., 2021). People who have COVID-19 often get headaches. This is because the virus enters the nasal cavity and damages

endothelial cells. This causes vasoconstrictor and oxidative stress on the trigeminal nerve, which in turn causes headaches (Bolay et al., 2020; Varga et al., 2020). Several COVID-19 vaccines were given Emergency Use Listing or Emergency Use Authorization (EUL or EUA) by regulatory officials and WHO during the COVID-19 pandemic based on results from randomized controlled trials that showed the vaccines worked (Bio, 2021). The mRNA (BNT162b2) COVID-19 vaccine is given twice, with 4 to 8 weeks between each dose (30 µg, 0.3 ml). After 4 to 6 months, the first extra dose is given. The second extra dose is given 4 to 6 months after the first one, mostly to people who don't have strong immune systems.

You can get a vaccine against different types of viruses, but after two doses, the Omicron version is less effective against severe and mild disease than the Delta variant, and its effectiveness wears off faster (World Health Organization, 2021). To get the ChAdOx1-S vaccine, you should get two intramuscular shots, one of 0.5ml each, 8 to 12 weeks apart. A extra dose may be given 4 to 6 months later, with people who are immune-compromised getting it first (World Health Organization, 2022). The way that vaccine might work to fight the virus is by boosting the immune system, which then stops the virus from replicating and gets rid of virus-infected cells (Ferdinands et al., 2021). Giving older people either the BNT162b2 or ChAdOx1-S COVID-19 vaccine lowers the number of people who get sick with the disease and makes it less severe (Bernal et al., 2021). We did this study to look at pain condition in COVID-19 patients and see if the level of pain changed depending on whether the patient had a vaccine in Al-Rayan Colleges, Al-Madinah.

## METHODS

304 COVID-19 patients were part of this historical cross-sectional observational study. The people who took part were between the ages of 18 and 65. In the years September 2021 to April 2023, the study took place at AL-Rayan Colleges in AL-Madinah, KSA. Using reverse transcription-polymerase chain reaction (RT-PCR) on oropharyngeal and nasal swab samples proved that COVID-19 was indeed present. The sample size was estimated by Open Epi (http://www.openepi.com) based on how common pain syndrome is in COVID-19 patients (Oguz-Akarsu et al., 2022). We got the information from an electronic form that was a verified questionnaire with 20 items. After they signed the consent form, the study subjects were sent the questionnaire by email.

People were asked about their age, gender, job, smoking habits, history of chronic diseases, COVID vaccination, the start and length of their COVID infection, their vaccination status at infection, the time between their infection and their last vaccination dose, their need to be hospitalized, their treatment with oxygen therapy or ventilation, and the presence and severity of neuropathic pain, myalgia, polyarthralgia, and headaches. The pain scale (Wong and Whaley, 1986) was used to figure out how bad the pain was. The poll had a question about neuropathic pain, which is what the International Association for the Study of Pain (Raja et al., 2020) calls a pain syndrome. Patients whose vaccination status wasn't clear (less than 14 days after dose 1) or who had a chronic musculoskeletal problem or chronic pain syndrome before getting COVID-19 were not included. People who took part in the study were split into five groups based on their vaccine status: not vaccinated, partially vaccinated (≥14 days after dose one or <14 days after dose 2), fully vaccinated (≥14 days after dose 2), 3rd dose vaccinated, and 4th dose vaccinated (Thompson et al., 2021).

## STATISTICS METHODS

SPSS version 20 was used to do statistics analysis on the data. The Chi-square test was used to show qualitative data as numbers and percentages. A P number less than 0.05 was thought to be significant.

## RESULTS

Out of the 304 people who took part in the study, 230 (75.7%) were women. The age group is from 18 to 65. It was significantly (P< 0.05) more painful for women (39.1% of them) than for men (27% of them). It was not significantly worse (P>0.05) for people with chronic diseases (40%) than for other patients (35.1%). It wasn't significantly different (P>0.05) in how bad the pain was for smokers (31.6%) and nonsmokers (31.7%). Pain that was very bad was slightly higher (P>0.05) in older patients (58–65 years old) (44.4%).

There were no significant differences (P> 0.05) between the patients who had one or more signs of pain syndrome. Myalgia happened to 74.7% of people who were not vaccinated and to 82.8 % of people who were partly vaccinated. In the fully vaccinated group, myalgia was reported in 80% of people, but it went down in the 3rd dose vaccine group (72.5%) and the 4th dose vaccine group (44.4%). Headaches were seen in 85.1% of people who were not vaccinated and 90.6% of people who were partly vaccinated. It was 85.3% of people who had been fully vaccinated. It was 84.1% in the 3rd dose vaccine group and 66.7% in the 4th dose vaccine group. Neuropathic pain happened to 24.1% of people who were not vaccinated, 32.8% of people who were partly vaccinated, 29.3% of people who were fully vaccinated, and 30.4% of people who got the third dose of the vaccine. While the group that got the fourth dose of the vaccine had the lowest percentage (11.1%; see Table 1) (Figure 1).

**Table 1. Pain symptoms in the study groups**.

| Vaccine status | Pain symptom | | | | Total 304 |
|---|---|---|---|---|---|
| | Myalgia | Headache | Neuropathic Pain | Polyarthralgia | |
| Non-vaccinated | 65<br>74.7% | 74<br>85.1% | 21<br>24.1% | 57<br>65.5% | 87 |
| Partially vaccinated | 53<br>82.8% | 58<br>90.6% | 21<br>32.8% | 42<br>65.6% | 64 |
| Fully vaccine | 60<br>80% | 64<br>85.3% | 22<br>29.3% | 47<br>62.7% | 75 |
| 3rd dose vaccine | 50<br>72.5% | 58<br>84.1% | 21<br>30.4% | 39<br>56.5% | 69 |
| 4th dose vaccine | 4<br>44.4% | 6<br>66.7% | 1<br>11.1% | 2<br>22.2% | 9 |
| P value | 0.099 | 0.397 | 0.576 | 0.104 | |

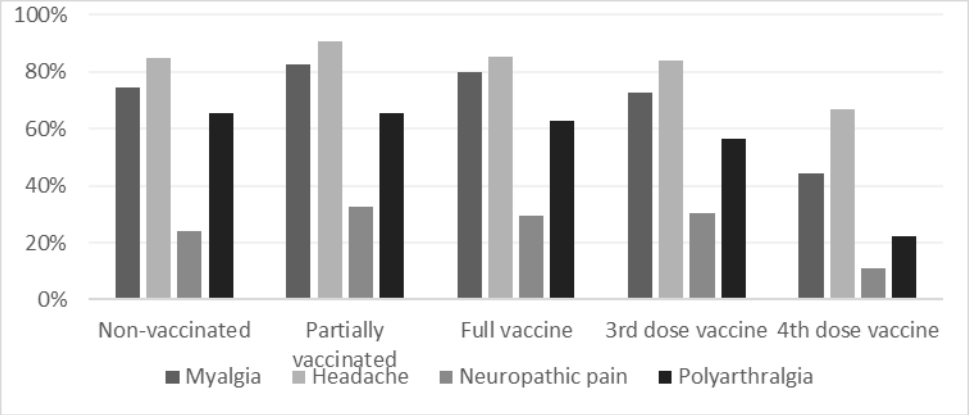


**Figure 1 Pain symptoms, myalgia, headache, neuropathic pain, and polyarthralgia were observed in all study participants with insignificant differences.**

The level of pain is significantly different (P<0.05) between all groups. People who weren't vaccinated had a lot of severe pain (40.2% of them), but no one in the 4th dose vaccine group did. It was 29.7% in the partially vaccinated group, 38.7% in the fully vaccinated group, and 39.1% in the third dose-vaccinated group (Table 2) (Figure 2).

**Table 2 Pain severity in study groups.**

| Vaccination status | Pain severity | | | | | P-value |
|---|---|---|---|---|---|---|
| | No pain | Mild | Moderate | Severe | Total | |
| Non- vaccinated<br>% | 9<br>10.3% | 10<br>11.5% | 33<br>37.9% | 35*<br>40.2% | 87<br>100% | |
| Partially- vaccinated<br>% | 2<br>1.3% | 14<br>21.9% | 29<br>45.3% | 19*<br>29.7% | 64<br>100% | |
| Fully vaccinated<br>% | 3<br>4% | 17<br>22.7% | 26<br>34.7% | 29*<br>38.7% | 75<br>100% | |
| 3rd dose vaccine<br>% | 11<br>15.9% | 16<br>23.2% | 15<br>21.7% | 27*<br>39.1% | 69<br>100% | |
| 4th dose vaccine<br>% | 4<br>44.4% | 5<br>55.6% | 0<br>0% | 0*<br>0% | 9<br>100% | <0.05 |

*P < 0.05

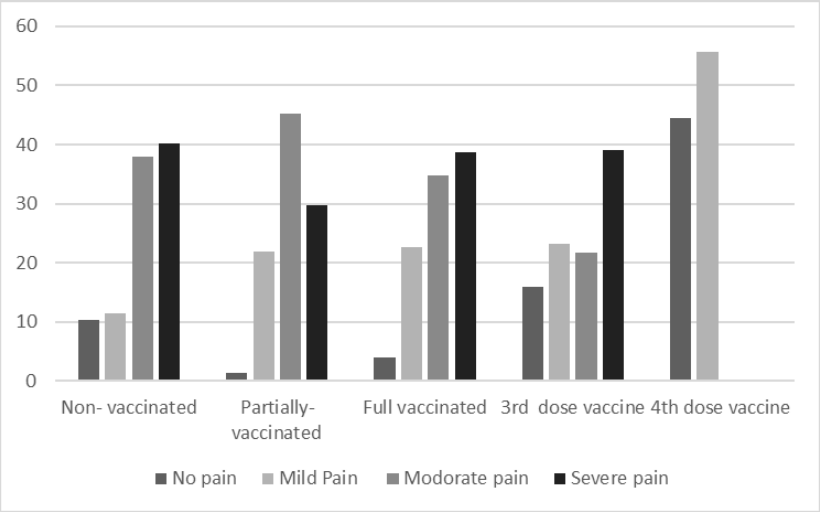


**Figure 2. Pain severity differs significantly among all study groups. It was highest in non-vaccinated patients.**

## DISCUSSION

The purpose of this study was to test the pain condition in COVID-19 patients and see if the level of pain could change depending on their vaccine status. All of the people who took part had pain syndrome signs, such as myalgia, headaches, neuropathic pain, and arthralgia. Musculoskeletal symptoms were seen in 88 (30%) of the 294 COVID-19 patients who were admitted in a study that showed similar results. 37.5% of this sign was myalgia, which was the worst kind; 5.7% was arthralgia; 6.8% was new-onset backache; and 50% was overall body ache (Hoong et al., 2021). Out of 222 COVID-19 patients who were studied in another study, 159 (71.6%) had at least one pain syndrome sign. On the other hand, 109 (49.1%) of the patients had headaches, 55 (24.8%) had nerve pain, and 30 (13.5%) had polyarthralgia (Oguz-Akarsu et al., 2022). In this study, older participants and people with long-term illnesses had slightly worse pain than younger subjects.

A study that looked back at 167,500 people found similar results: having multiple health problems and being older were linked to a higher chance of COVID severity (Ge et al., 2021). Pain severity was significantly higher in women than in men, which is different from another study that found a link between pain severity and gender (Jena et al., 2022). It's possible that these results are because more women than men took part in this study. In the same way, fewer male volunteers explain why smoker patients' pain isn't that bad. In earlier studies (He et al., 2022; Gülsen et al., 2020), it was found that smoking was linked to worsening COVID illness pain. According to Tran et al. (2023), the COVID-19 vaccine should make the illness less severe and last less time. All of the people in the study reported having pain syndrome, but the level of pain was significantly different between the groups. People who weren't protected were more likely to be in severe pain.

But it wasn't found in the group that got the fourth shot of the vaccine. These results are similar to those of a prospective cohort study that looked at 204 people to compare how well the COVID-19 vaccine worked on people who had been vaccinated and people who had not been vaccinated. The mean viral RNA load and the risk of feverish symptoms were lower in people who had been vaccinated (fully or partly) than in people who had not been vaccinated. Also, vaccinated patients were more likely to have shorter sickness times than unvaccinated patients (Thompson et al., 2021). Another study thought that the COVID-19 vaccine would no longer help lessen the seriousness of the disease after 1 to 6 months of full vaccination. It worked 20–30% less well against infections and disease symptoms after six months (Feikin et al., 2022).

There was a lot of serious pain in the fully vaccinated and third dose-vaccinated groups. This could be because of the different types of vaccines and the time after vaccination that affects how well they work. A study that looked into how well the COVID-19 vaccine protected against serious infections showed this to be true. Three doses of the inactivated SARS-CoV-2 vaccine were more effective than two doses at protecting against serious COVID-19. However, the three doses of the mRNA COVID-19 vaccine were less effective (Ng et al., 2022). Also, getting infected with COVID-19 variants may make the vaccine less effective over time. Andrews et al. (2022) found that the ChAdOx1-S vaccine lost 44.3% of its effectiveness against symptomatic COVID-19 with the delta version three months after the second dose, while the BNT162b2 vaccine lost 66.3% of its effectiveness.

Another study also showed that the third dose of the vaccine loses some of its usefulness over time. When people got two or three doses of the mRNA vaccine, it worked less well during the Omicron period than during the Delta variant phase. The success against COVID-19-related visits to the emergency room or urgent care center (ED/UC) and hospitalizations was 87% and 91% after two months, but it dropped to 66% and 78% by the fourth month (Ferdinands et al., 2022). Several things are

wrong with this study. We did not look into the things that affect how well a vaccine works after it has been given, like time, protection level, and vaccine product.

This study didn't say whether the third dose was an extra dose for people with weak immune systems or a booster dose after the first two doses were finished in people with strong immune systems. That could make the vaccine less effective against very bad pain. It wasn't possible to get genetic information about the virus, which is needed to find variants that might change how well the vaccine works. These points need to be looked at in more study with a bigger sample size. Even though COVID-19 seems to be leaving the world, after striking for years and killing millions of people, it should be studied thoroughly for twice as long to find out what it does and stop other attacks from happening.

## CONCLUSION AND RECOMMENDATIONS

All COVID-19 patients had a pain syndrome, but the pain was much worse in those who had not been vaccinated and not at all in those who had gotten the fourth dose of the vaccine. More research is needed to find out what factors affect how well a vaccine works against COVID-19 intensity.

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