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CHARACTERISTICS AND RISK FACTORS OF POST-VACCINATION COVID-19 ON INDONESIAN ADULTS: A CROSS-SECTIONAL STUDY

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Abstrak

Pandemi COVID-19 telah mendorong berbagai negara untuk melaksanakan vaksinasi sebagai upaya untuk membatasi penyebarannya. Meskipun vaksin telah didistribusikan, kasus COVID-19 masih terus dilaporkan. Penelitian ini bertujuan untuk mengidentifikasi faktor risiko yang mempengaruhi kejadian dan keparahan COVID-19 pasca-vaksinasi pada warga negara Indonesia dan menjelaskan karakteristiknya. Penelitian deskriptif ini dilakukan dari Januari hingga Maret 2022 dengan menggunakan desain penelitian potong lintang. Populasi penelitian terdiri dari warga negara Indonesia yang telah menerima vaksin COVID-19 dan terinfeksi setelahnya. Data dikumpulkan melalui kuesioner online. Peserta diklasifikasikan berdasarkan jumlah dan jenis vaksin yang diterima serta keparahan manifestasinya. Dari 623 warga negara Indonesia, 111 (18%) mengalami COVID-19 pasca-vaksinasi. Gejala ringan ditemukan pada 72% peserta dan 12% peserta bersifat asimtomatik. Manifestasi paling umum adalah anosmia (72%), diikuti oleh demam (55%). Seluruh peserta dengan gejala sedang dan berat menerima vaksin virus inaktif. Manifestasi berat ditemukan pada peserta dengan kelebihan berat badan atau obesitas, diabetes, penyakit jantung, dan penyakit autoimun. Dosis ketiga vaksin berkaitan dengan gejala ringan atau tidak ada gejala. Penelitian kami merekomendasikan pemberian dosis tambahan khususnya untuk populasi berisiko.

Kata Kunci: COVID-19, Vaksin, Manifestasi Klinis, Indonesia, Komorbiditas

Abstract

The COVID-19 pandemic has prompted various countries to carry out vaccinations as an effort to limit its spread. Despite the distribution of vaccines, COVID-19 cases are still being reported. This study aims to identify the risk factors that influence the occurrence and severity of post-vaccination COVID-19 in Indonesian citizens and describe its characteristics. This descriptive study was conducted from January to March 2022 using cross-sectional research design. The study population comprised of Indonesian citizens who have received COVID-19 vaccines and were infected afterwards. Data were collected through online questionnaires. Participants were classified based on the number and types of vaccine received and severity of manifestation. Of 623 Indonesian citizens, 111 (18%) experienced post-vaccination COVID-19. Mild symptoms were found in 72% participants and 12% participants were asymptomatic. The most common manifestation was anosmia (72%), followed by fever (55%). The entire participants with moderate and severe symptoms received the inactivated virus vaccine. Severe manifestations were found in participants with overweight or obesity, diabetes, heart disease, and autoimmune disease. Third dose of vaccination was related to mild or no symptoms. Our study recommends an administration of additional doses especially for at-risk populations.

Keywords**:** *COVID-19, Vaccines, Clinical Manifestation, Indonesia, Comorbidity*

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INTRODUCTION

Towards the end of December 2019, several cases of Pneumonia were reported in Wuhan, China, which was later identified as coronavirus disease 2019 (COVID-19) (Anand et al., 2021). In less than three months, the spread of COVID-19 has reached 114 countries and caused more than 400,000 deaths worldwide (Park, 2020). World Health Organization (WHO) has announced various guidance to limit the spread of COVID-19, however right now, millions of people are still vulnerable to infection as herd immunity has not been formed (Zhang et al., 2021). As the rate of morbidity and mortality soars, countries are racing to find an effective and wide-scaled breakthrough to reach an endpoint for the pandemic, that is vaccines (*Rethinking Herd Immunity and the Covid-19 Response End Game*, 2021).

Despite the very short period of development, numerous studies have proven the efficacy of vaccines in providing protection against SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) infection. This evidence was followed by the global urge to administer vaccines. Unfortunately, almost a year after the distribution of vaccines, a high number of COVID-19 cases and mortality is still reported across the globe, including in Indonesia (Septiani & Mulyana, 2023). The surge of cases and the obscure outcome of vaccine protection may point to the foreign nature and manifestations of SARS-CoV-2 infection. Identifying the risk factors such as the demographics or medical profile factors in vaccinated post-COVID-19 patients may offer a notable assessment for the development of further public health policies and strategies.

Considering the potential of vaccine in putting the COVID-19 cases to a halt, this study was conducted to uncover and assess all the pivotal data including the characteristics and risk factors for post-vaccination COVID-19, with the hope of advancing vaccine development, health policies, and eventually towards the COVID-19 mitigation in Indonesia.

METHOD

Study Design

This study is an observational descriptive study of demography and clinical data from Indonesian citizens who have received COVID-19 vaccinations using a cross-sectional design.

Study Population and Data Collection

The study population comprised of Indonesian-based citizens (> 18 years) who have received the COVID-19 vaccine and agreed to fill out the online questionnaires. Sampling was carried out from January to March 2022 using a consecutive sampling technique. Data regarding the patients' demographic, vaccines received, as well as the number and clinical manifestations of COVID-19 were collected.

Study Variables

The variables of this study were the number of post-vaccination COVID-19 cases; the type and number of vaccine doses received; COVID-19 risk factors including age, Body Mass Index (BMI), and comorbid of COVID-19; as well as the symptoms and severity of COVID-19. Demographic data presented were age, sex, domicile, and occupation.

Data Management

Descriptive statistics were used to present and summarize the data. Patients were classified into several groups based on their age, the number and type of vaccines received, and the severity of COVID-19 manifestations.

RESULTS AND DISCUSSION

The total respondents who filled out the questionnaire were 653 people. A total of eight respondents were excluded because they were under the age of 18 and there were 22 respondents excluded because they did not fill out the questionnaire thoroughly. In total, there were 623 respondents included as a sample in this study.

Discussion

Participants Demographics

This study showed that 91% (n=570) participants were adults and predominantly female who live on the Java Island (90.9%). This is in line with the domicile distribution of the Indonesian population which is currently concentrated on the Java Island and the dominance of the female sex compared to men on the Java Island.[6] Table 1 summarizes the demographic characteristics of the study participants.

Demographics of Post-Vaccination COVID-19 Participants

Out of 623 Indonesian citizens, 111 (17.8%) people still experience COVID-19 after the vaccine. Compared to the neighboring country

which has a similar demographic pattern, Indonesia has an almost identical percentage of cases as India, which reached 16.8% of vaccinated study participants (Tyagi et al., 2021).

Second dose of vaccination has already been administered to most of the respondents (68%) at the time they were infected. Consistent with this finding, data from the Indonesia Ministry of Health showed that the second vaccine coverage has reached 56.52% of the population as of February 2022, when the peak of COVID-19 cases occurred. (Organization, 2021), In addition, there were short dosing interval between first and second vaccination, hence there was a greater potential for infection after the second vaccine administration.

Inactivated virus vaccines such as Sinovac and Sinopharm were the predominant vaccination type received by the participants (93%). The mean age of participants in this study was 35 years (SD 10.2) with a median of 32 years. This is in accordance with data from the Ministry of Health which revealed that the highest COVID-19 cases were in the 31 – 45 years age group. Detailed presentation of the data are summarized in Table 2.

Clinical Manifestation of Post-Vaccination COVID-19

Anosmia was the most common symptom (71%) found in this study which is similar to other studies which show that the most common manifestations are associated with the upper respiratory system such as nasal congestion, rhinorrhea, or cough (Table 3) (Peghin et al., 2022) (A. G. D. of Health, 2022). Systemic manifestations have been encountered in most of the individuals. A total of 61 people (55%) had fever, 42 people (38%) felt tired, and there were two people who experienced chest pain. This finding is consistent with the data from the Ministry of Health which states that 40.7% of COVID-19 patients have a history of fever, which is the most frequent manifestation after cough ("Situasi Virus Corona," 2022). In our study, very few participants suffered from gastrointestinal symptoms such as diarrhea, nausea, or vomiting, which was similar to the study by Chau NVV et al., that showed that only 8% of participants experienced nausea (Chau et al., 2021).

Five participants (5%) were still experiencing COVID-19 symptoms after four weeks. Based on the National Institute for Health and Care Excellence (NICE) guidelines, this manifestation is categorized as long covid. Our findings showed that all participants with long covid had systemic symptoms such as fever or myalgia and one person has hypertension. Another study that examined long covid stated that vaccination did not provide a significant protective effect against long covid, albeit the vaccines given (Taquet et al., 2022).

Three people (3%) had symptoms of COVID-19 for more than 12 weeks. These manifestations are defined as the post-COVID-19 syndrome. Based on the symptoms experienced, two out of the three people experienced anosmia, increased heart rate, and severe COVID-19 symptoms. One person has multiple comorbidities, namely cardiovascular and autoimmune disease. In accordance with this result, a study by Peghin et al., reported that one of the common symptoms of the post-COVID-19 syndrome is anosmia (Peghin et al., 2022).

Risk Factors of Post-Vaccination COVID-19

Several risk factors mentioned in our study were age, sex, nutritional status, medical conditions, and duration of interval between last vaccine dosing and exposure of the disease, which are written in Table 4. The interval between the last vaccine administration and the time of COVID-19 exposure can predict whether the antibodies level is adequate to prevent infection or not. The duration of interval can affect both the formation, as well as the fading of the antibodies.

One study revealed that adequate antibodies sufficient to impede an infection formed approximately 14 days after the second dose (A. G. D. of Health, 2022). In contrast, various researches have reported a progressive and significant decrease of antibody profile during the third month after the second dose. The vaccine efficacy decreased from 96% during the second month to 84% at fourth to seventh month (*Waning Immunity after the BNT162b2 Vaccine in Israel*, 2022). Along with this fact, 15% participants in our study were infected less than two weeks after receiving the vaccine and as many as 31% participants tested positive for COVID-19 after three months from the last dose administered, when there was already a decrease in the antibody profile, while 20% of participants were infected after six months, when the decrease of the antibodies was significant enough to allow a serious manifestation (*Waning Immunity after the BNT162b2 Vaccine in Israel*, 2022). From the participants who tested positive between 2-12 weeks after infection, seven individuals (18.4%)

had comorbidities such as asthma and heart disease and 22 people (58%) had overweight or obese nutritional status. This finding indicates an underlying risk factor for infection and severe manifestation although the interval between the last vaccination and the time of exposure was perceived as sufficient for antibody formation. In total, 66% participants of our study were estimated to have inadequate immune systems to avert the infection.

The majority of post-vaccination COVID-19 participants in this study were adults. There were only four respondents aged more than 60 years and categorized as an elderly which differs from other studies who found that the majority of post-vaccine subjects were elderly (Butt et al., 2021). These conflicting results can be secondary to the method of data collection we used in this study. To achieve a wide variety of clinical and profile characteristics, we used an online questionnaire which can be distributed easily and vastly, but may be difficult to access for the elderly. Consequently, the number of participants in the elderly group is far lesser than the adults age group. Data from this study revealed that none of the participants in the elderly group was asymptomatic. Two people had mild symptoms and two others experienced complications such as shortness of breath and required hospitalization.

The impact of obesity as risk factor for COVID-19 is prominently showed in our study, similar to other studies which showed obesity as an independent risk factor for severe manifestations (Simonnet et al., 2020). Observed from the nutritional status, a total of 59 participants (54%) in this study were overweight or obese. Severe manifestations were experienced by five people with overweight nutritional status (72%) and six people with moderate symptoms (54%). Antibody titers were found to be higher in obese patients, which may be a result of the high production of cytokines from adipose cells in obese patients (Soffer et al., 2021).

In this study, there were 12 participants (11%) who had comorbidities. A total of three people (25%) with comorbid had severe manifestations of COVID-19 and one of them had multiple comorbidities. The most common medical condition found in this study was Asthma, followed by Diabetes in four participants and Hypertension in three subjects. Various evidences have shown the role of vaccination in suppressing the poor prognosis of COVID-19 in patients with underlying medical conditions.

Severity of Post-Vaccination COVID-19 based on Vaccine Types and Number of Doses Administered

After vaccination in Indonesia, one of the mutations of SARS-CoV-2, the Omicron variant, caused a spike in COVID-19 cases in February 2022. The efficacy of the Sinovac vaccine, which is classified as an inactivated virus vaccine, has been found to decrease when infected with the Omicron variant. (“Sinovac Vaccine Efficacy against Omicron Increases Following MRNA Booster, Yale Study Finds,” 2022), (“Can Sinovac Protect Indonesia from the Omicron Wave?,” 2022). This may be one of the risk factors for post-vaccination infection for participants in this study, where the majority of respondents received inactivated viral vaccines. Our data showed that there were 18 people (16%) who had received the second dose of inactivated virus vaccine but still experienced moderate and severe manifestations such as shortness of breath (Table 5). The efficacy of the inactivated viral vaccine will increase when additional doses of the mRNA vaccine are given. In this study, out of the 277 respondents who had received the third dose, there were only three people (1%) who experienced COVID-19 and none of them experienced either moderate or severe symptoms. This finding supports every study that reveal three doses of vaccination can increase the neutralizing ability of SARS-CoV-2 (Walls et al., 2022). Moderna and Pfizer vaccines, which are mRNA vaccines, were found to have good effectiveness in preventing the need for hospitalization of COVID-19 patients. This protective role was still prominent in preventing variants of concern of SARS-CoV-2. Data from this study presented that out of 20 recipients of the mRNA vaccine, only two participants (10%) developed COVID-19 after receiving the mRNA vaccine, and all of them had mild or asymptomatic symptoms. Observing from the number of doses received, there were 15 recipients of the first dose (57.6%) and 55 recipients of the second dose (75%) of the inactivated virus vaccine who experienced mild symptoms such as cough, dizziness, and fever. All recipients of the non-replicating viral vector vaccine had mild symptoms. Complications from COVID-19 were found to be much lower than in individuals who had received the vaccine. This conclusion supports current studies which stated that the risk of symptomatic and severe COVID-19 will decrease with increasing vaccination doses (Balachandran et al., 2022).

CONCLUSION

This research concluded that 18% of Indonesian citizens experienced COVID 19 after vaccination. As many as 72% of participants had mild symptoms, 10% had moderate symptoms, 6% had severe symptoms, and 12% were asymptomatic. There are five participants who experienced long covid and three participants who suffered from post-COVID-19 syndrome. All participants with moderate and severe symptoms received the inactivated virus vaccine. On the other hand, recipients of non-replicated vector and mRNA vaccines only suffered from mild symptoms or were asymptomatic. Participants who received three doses of vaccine only experienced mild or asymptomatic symptoms. Five participants with overweight and obesity, one participant with diabetes, one participant with heart disease, and one participant with autoimmune disease had severe COVID-19 manifestations. Further study with a longer research duration and a wider variety of samples is needed in order to give a better representation of post-vaccination COVID-19 cases in Indonesia. In addition, further research is needed to analyze other risk factors that have not been studied in this study, such as the practice of health protocols and lifestyle. Additional doses of COVID-19 vaccine are associated with a better prognosis, therefore our study recommends an administration of additional doses especially for at-risk populations.

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