ORIGINAL ARTICLE

COVID-19 COINFECTION AND VACCINATION PROFILE AMONGST PEOPLE WITH HIV/AIDS (PWHA) IN INDONESIA

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ABSTRACT

Introduction

COVID-19 pandemic that has been occurred for more than two years yields a huge impact for PWHA population. Due to their immunocompromised status, PWHA have greater risk of being coinfected with COVID-19. COVID-19 vaccine as a preventive way of SARS CoV-2 virus transmission has been administered for the PWHA, however the epidemiological studies remain limited.

Method

This was the first cross-sectional study in Indonesia, analysing COVID-19 coinfection and vaccination coverage in the PWHA population. A total of 307 PWHA who came to the HIV Clinic, Hasan Sadikin General Hospital were included in this study. The data regarding social history, HIV medical history, comorbidity, as well as COVID-19 coinfection and vaccination was obtained from both anamnesis and medical record. The patients` sera were obtained for IgG and IgM SARS CoV-2 rapid test analyses. Analyses were conducted using SPSS version 20, utilising Chi-square test for descriptive analysis.

Results

Three-hundred and seven PWHA from the total of 1971 patients in the HIV clinic during June 2021 – November 2021 period were included. The median age of the patient was 37 (35 – 38) years. Men dominated the PWHA population (230 people, 75%) with male have sex with male as the key population (100 people, 32.4%). On average, the PWHA were on the stadium I HIV (298 people, 96.4%), with 24.3% (75 people) had pulmonary TB coinfection and 7.1% (22 people) had extrapulmonary TB coinfection. Majority of the patients have CD4 > 200 (20.4%) and undetected viral load (13.9%). The patients consumed antiretroviral therapy daily (305 people, 98.7%). There were 13.6% (48 people) of PWHA with COVID-19 coinfection history. First-dose vaccination has been administered within 78.6% (246 people) PWHA, whereas there were 59.5% (188 people) PWHA who received second-dose vaccination. Rapid tests showed positive IgG SARS CoV-2 in 55% (170 people) PWHA, nevertheless IgM SARS CoV-2 was detected in 1.9% (6 people) PWHA. There was 61.3% seroconversion of the SARS CoV-2 IgG antibody following COVID-19 first-dose vaccination (p-value <0.05).

Discussion

Immunocompromised status of the PWHA renders the population towards vulnerability of having secondary infection. The COVID-19 infection risk in the PWHA population is somewhat similar to the general population. First-dose vaccination coverage in the PWHA impressively surpassed the national coverage target (>70%), though in the beginning of the pandemic there was hesitancy to complete the vaccination. Vaccination was significantly associated with seroconversion towards IgG SARS CoV-2 antibody in the PWHA population.

Conclusion

This was the first epidemiological study regarding COVID-19 coinfection and vaccination in the PWHA population in Indonesia. COVID-19 vaccination is recommended for the PWHA population.

Keywords: Antibody, COVID-19, HIV, PWHA, Vaccine

ABSTRAK

Latar Belakang

Pandemi COVID-19 yang telah terjadi lebih dari 2 tahun memberikan dampak besar bagi populasi orang dengan HIV/AIDS (ODHA). ODHA berisiko tinggi terinfeksi COVID-19 diakibatkan status imunokompromais. Vaksin COVID-19 sebagai metode pencegahan transmisi virus SARS CoV-2 telah diberikan pada populasi ODHA, namun studi epidemiologi terkait vaksinasi masih terbatas.

Metode

Studi ini merupakan studi potong lintang pertama di Indonesia, menganalisis koinfeksi COVID-19 dan cakupan vaksinasi pada populasi ODHA. Sebanyak 307 ODHA yang berobat di klinik HIV, Rumah Sakit Hasan Sadikin diinklusi dalam penelitian. Data terkait riwayat sosial, riwayat HIV, komorbid, koinfeksi COVID-19 dan vaksinasi diperoleh dari anamnesis dan rekam medis. Serum pasien diambil untuk pemeriksaan rapid test IgG dan IgM SARS CoV-2. Analisis statistik dilakukan menggunakan SPSS versi 20, dengan uji Chi-square untuk analisis deskriptif.

Hasil

Tiga ratus tujuh pasien ODHA dari total 1971 pasien di klinik HIV selama periode Juni – November 2021 diinklusi dalam studi ini. Median usia pasien adalah 37 (35 – 38) tahun. Laki-laki mendominasi populasi ODHA (230 orang, 75%) dengan populasi kunci laki-laki seks laki-laki (LSL) (100 orang, 32.4%). Rata-rata pasien ODHA dalam kondisi stadium I HIV (298 orang, 96.4%), dengan 24.3% (75 orang) mengalami koinfeksi TB paru dan 7.1% (22 orang) mengalami koinfeksi TB ekstrapulmonal. Sebagian besar pasien memiliki CD4 > 200 (20.4%) dan viral load tidak terdeteksi (13.9%). Pasien konsumsi terapi antiretroviral rutin (305 orang, 98.7%). Terdapat 13.6% (48 orang) ODHA dengan riwayat koinfeksi COVID-19. Vaksinasi dosis pertama telah diberikan pada 78.6% (246 orang) ODHA, dimana 59.5% (188 orang) ODHA mendapat vaksinasi kedua. Rapid test menunjukkan hasil IgG SARS CoV-2 positif pada 55% (170 orang) ODHA, sedangkan IgM SARS CoV-2 terdeteksi pada 1.9% (6 orang) ODHA. Terdapat 61.3% serokonversi antibodi IgG SARS CoV-2 setelah vaksinasi COVID-19 dosis pertama (p-value <0.05).

Pembahasan

Status imunokompromais ODHA membuat populasi tersebut rentan mengalami infeksi sekunder. Risiko infeksi COVID-19 pada ODHA serupa dengan populasi umum. Cakupan vaksinasi dosis pertama pada populasi ODHA melebihi target nasional (>70%), walau di awal pandemi terdapat keraguan untuk melengkapi vaksinasi. Vaksinasi berasosiasi signifikan dengan serokonversi antibodi IgG SARS CoV-2 pada populasi ODHA.

Simpulan

Studi ini adalah studi epidemiologi pertama terkait koinfeksi dan vaksinasi COVID-19 pada populasi ODHA di Indonesia. Vaksinasi COVID-19 direkomendasikan untuk populasi ODHA.

Kata kunci: Antibodi, COVID-19, HIV, ODHA, Vaksin

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INTRODUCTION

COVID-19 pandemic creates major impact for every human being, particularly the immunocompromised population. People with HIV AIDS (PWHA) are one of the immunocompromised populations who are at-risk to have COVID-19 coinfection, renders them into a more complicated disease state. In the beginning of the pandemic, there were many PWHA with COVID-19 coinfection [1]. The unavailability of the vaccine at that time led to an increased rate of PWHA mortality due to SARS CoV-2 coinfection [2]. The discovery of COVID-19 vaccines was an outstanding breakthrough amidst the pandemic [3]. However, there was hesitancy to administer the vaccines to the PWHA population [4]. In Indonesia, in the early phase of COVID-19 pandemic, the government initially recommended the vaccine administration if the PWHA had CD4 > 200, however they revised the recommendation in March 2021, stated that every PWHA with stable condition and on routine ARV treatment are recommended to be vaccinated [5]. Unfortunately, there were limited epidemiological studies about COVID-19 coinfection and vaccination in the PWHA population in the early phase of pandemic. To this date, the data were not available yet in Indonesia. Thus, this research was a preliminary study conducted to yield epidemiological data about COVID-19 coinfection and vaccination amongst PWHA in Indonesia. We also evaluated the serological SARS-CoV-2 profiles, which strengthen the recommendation of COVID-19 vaccination for the PWHA population.

METHOD

STUDY DESIGN AND PARTICIPANTS

We used cross-sectional study design at the HIV Clinic, Hasan Sadikin General Hospital, Bandung, Indonesia. Total sampling was utilised, of which there were 307 patients who participated in this study during June to November 2021. Patients aged 18 years and older with confirmed HIV-AIDS diagnosis in outpatient setting were included in the study. We collected the baseline and HIV data, as well as the COVID-19 coinfection and vaccination status, by doing history-taking and chart review. The data was then stored in the SPSS database, of which we did analyses regarding the baseline characteristics, HIV status, and COVID-19 coinfection, as well as vaccination, status of the patients.

DATA COLLECTION

Baseline characteristics included gender, date of birth, education level, marital status, HIV disease state (stadium, duration of HIV infection, mode of HIV acquistion as well as identifying key populations, opportunistic infection, latest CD4 level, latest viral load level, ARV treatment regiment) were obtained by history-taking and chart review. COVID-19 coinfection and vaccination, both were recently added questions, were asked directly to the participants during their outpatient visit. First and second-dose vaccination history were included. However, we did not do further qualitative question to the participants who did not complete their first or second-dose COVID-19 vaccination.

SERUM IMMUNOGLOBULIN M AND G LEVELS AGAINST SARS-COV-2 RAPID TEST

The patients` sera were obtained for serological analyses: IgG and IgM SARS CoV-2. We used the Standard Q COVID-19 IgM/IgG Plus Test (SD Biosensor, Korea) reagen to observe the serological COVID-19 profiles of the PWHA population in our study. It was a rapid chromatographic immunoassay for the qualitative immunoglobulin (Ig) M and IgG SARS-CoV-2 virus from the sera of the patients. The serum samples were analysed using the manufacturer`s instructions, which have been described elsewhere [6]. The antibody was classified as positive if the indicator turned into red line following sensitisation of the sample with the antigen, and classified as negative if the indicator remained unchanged.

STATISTICAL ANALYSIS

We used the SPSS statistic software to analyse the descriptive data. Mean was utilised if the data were normally distributed. However, if the data distribution were not normal, we chose the median of the data. We

compared the serological profile with the first-dose COVID-19 vaccination to observe the seroconversion of IgG profile following vaccination. *Chi-square* test was used for the comparison, with a 2-sided *p-value* of <.05 was considered as statistically significant.

ETHICS

This study was reviewed and approved by the institutional review board of the Faculty of Medicine, Universitas Padjadjaran (ethical number 410/UN6.KEP/EC/2021).

RESULTS

CHARACTERISTICS OF PWHA IN INDONESIA

Three-hundred and seven PWHA from the total of 1971 patients in the HIV clinic during June 2021 – September 2021 period were included. The complete baseline data were presented in the **Table 1** on the next page. The median age of the patient was 37 (35 – 38) years. As depicted in **Figure 1**, men dominated the PWHA population (230 people, 75%) with male have sex with male as the key population (100 people, 32.4%). On average, the PWHA were on the stadium I HIV (298 people, 94%), with 24.3% (75 people) had pulmonary TB coinfection and 7.1% (22 people) had extrapulmonary TB coinfection. Majority of the patients have CD4 > 200 (20.4%) and undetected viral load (13.9%). The patients consumed antiretroviral therapy daily (305 people, 98.7%).

Table 1. Baseline Characteristics of the PWHA Population

Characteristics	All Patients (N = 307 patients)
Age (median, years)	37 (35 – 38)
Gender (N, %)	
Male	230, 75%
Female	77, 25%
Education level (N, %)	
Elementary school	7, 2,2%
Junior high school	23, 7.3%
Senior high school	156, 51%
Bachelor degree	52, 16%
Master degree	6, 2%
Key Population (N, %)	
Male have sex with male	100, 32%
Heterosexual (unprotected sexual activity)	75, 24%
IV drug users	65, 21%
Health-care workers	3, 1%
Others	64, 21%
Duration of HIV infection (median, years)	3 (3 – 6 years)
HIV Stadium (N, %)	
Stadium I	298, 94%
Stadium II	4, 2%
Stadium III	2, 1%
Stadium IV	3, 3%
CD4 Level (cells/uL)	
<200	17, 5%
>200	63, 20%
N/A	229, 75%
Viral Load Level (copies/mL)	
Not detected	43, 15%
<1000	16, 5%
>1000	4, 2%
N/A	246, 78%
Tuberculosis as an opportunitistic infection (N, %)	
Pulmonary TB	75, 23%
Extrapulmonary TB	22, 7%

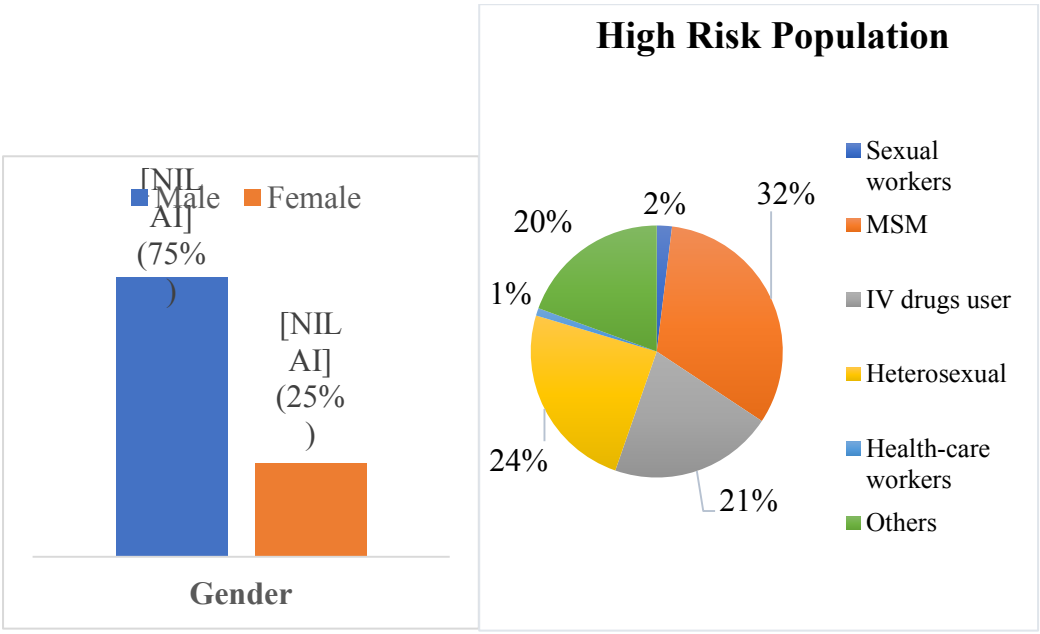

Figure 1. Gender and High Risk Population Distribution of the PWHA Population

INCIDENCE OF COVID-19 IN PWHA

There were 13.6% (48 people) of PWHA with COVID-19 coinfection history. First-dose vaccination has been administered within 78.6% (246 people) PWHA, whereas there were 59.5% (188 people) PWHA who received second-dose vaccination. The graphs were illustrated in **Figure 2** and **Figure 3.**

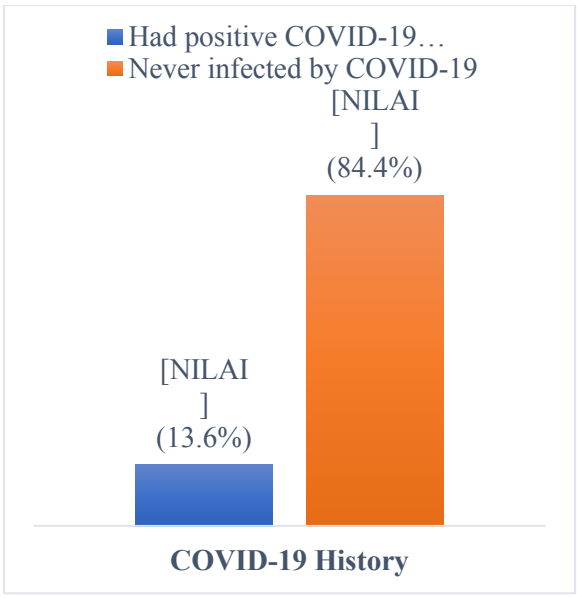

Figure 2. COVID-19 Coinfection History in the PWHA Population

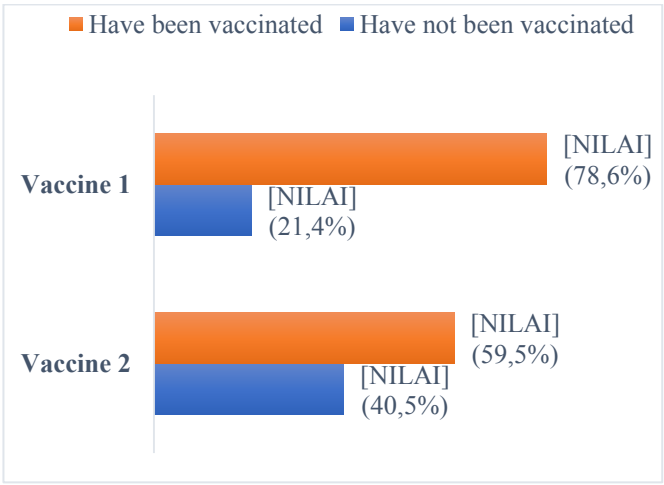

Figure 3. COVID-19 Vaccination Status of the PWHA Population

SEROLOGICAL TEST RESULTS FOR COVID-19 IN PWHA

Rapid tests showed positive IgG SARS CoV-2 in 55% (170 people) PWHA, nevertheless IgM SARS CoV-2 was detected

in 1.9% (6 people) PWHA, as depicted in the **Figure 4**.

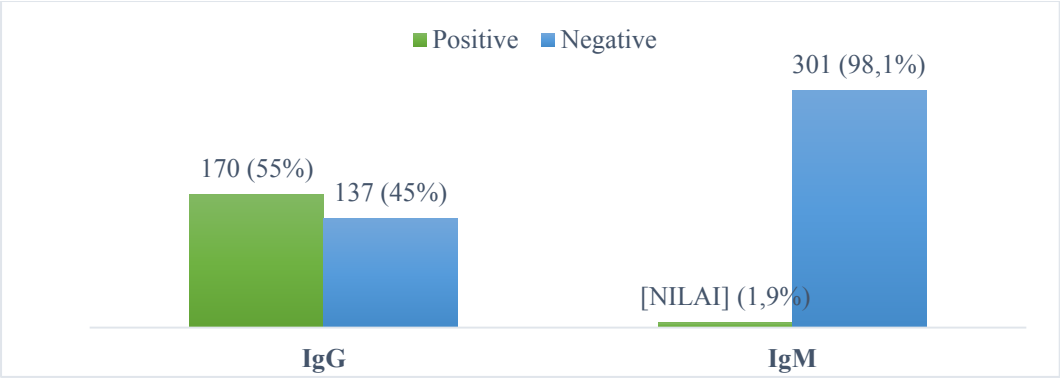

Figure 4. Serological Profiles of the COVID-19 Antibody in the PWHA Population Sera

There was 61.3% seroconversion of the SARS CoV-2 IgG antibody following COVID-19 first-dose vaccination, of which the association was statistically significant (*p-value* <0.05).

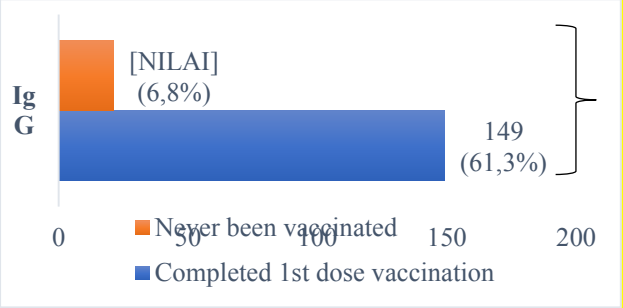

Figure 5. Seroconversion of the SARS CoV-2 IgG Antibody Following the First-Dose Vaccination in the PWHA Population
p-value < 0.05

DISCUSSION

To date, no epidemiological data regarding COVID-19 coinfection and vaccination are available in PWHA population in Indonesia. A study from Wuhan, China conducted by Jiao Huang et al revealed that during the early period of pandemic, there were 35 out of 6001 PWHA experienced COVID-19 coinfecttion, with a cumulative incidence of 0.58% [2] In New York, 3 months after the pandemic has started, Braunstein et al recorded 2410 PWHA with COVID-19 coinfection, or approximately 1.06% of all COVID-19 cases [7]. In this study, the median age of the PWHA was 37 (35 – 38) years, whereas in the other studies the mean age was much older: 52 - 53 years [2,8]. The PWHA were dominated by male patients, both in this study and the other studies [2,7]. Aligned with the predominant male patients, the key population in our study was male have sex with male. The other studies echoed similar finding [2,7]. Most of the study did not include HIV stadium and opportunistic infection, particularly TB [2,3,7,8]. This might be due to low endemicity of the TB coinfection in the other countries [9]. In our study, the PWHA had CD4 > 200 cells/uL and viral load >1000 copies/mL; somewhat similar to another study [10]. Majority of the patients in this study continued their ARV treatment on daily basis. Huang et al discovered that the PWHA who discontinued their ARV during pandemic had the highest COVID-19 incidence (2.2%) compared to those who continued ARV (0.52%) and who did not receive ARV (0.63%) [2]. Sigel et al conducted a study in New York where they found no differences in adverse outcomes associated with HIV infection in COVID-19 coinfected hospitalised patients[11]. Our study, however, did not compare the PWHA in inpatient setting.

There were 13.6% (48 people) of PWHA in our study with COVID-19 coinfection history. Another study with large-scale PWHA cohort demonstrated the cumulative incidence of 0.58% and 1.06% of all COVID-19 cases[7]. First-dose COVID-19 vaccination has been administered within 78.6% (246 people) PWHA in our study, whereas there were 59.5% (188 people) PWHA who received second-dose vaccination. This did not prove the hesitancy to get vaccination amongst PWHA in Indonesia. The latest COVID-19 vaccination from the Indonesian Society of Internal

Medicine stated that HIV patients who are at stable health condition and undergo routine treatment are eligible for COVID-19 vaccination, without mentioning the minimum CD4 level[5]. Another study conducted by Bert et al in Italy demonstrated that about 86.2% of patients in their cross-sectional study were vaccinated for COVID-19, while 7.6% do not want to be vaccinated[12]. In another study done by Zheng et al, there was 8.7% of PWHA who received COVID-19 vaccination in mainland China[13]. There were participants who did not intend to do vaccination, with concern regarding side effects and disclosure of HIV status stayed at the top two reasons[13]. Another study in Latin America, completed by Ortiz-Martinez et al, showed that about 87.1% (460 PWHA) were willing to be vaccinated and only 10.6% of the participants who demonstrated hesitancy toward COVID-19 vaccination[14].

There was 61.3% seroconversion of the SARS CoV-2 IgG antibody following COVID-19 first-dose vaccination, of which the association was statistically significant (*p-value* <0.05). In a systematic review of COVID-19 vaccination, the pooled seroconversion rates among the first and second doses were 67.51% and 96.65%, respectively[15]. They found that the seroconversion rate was similar to the healthy controls following the first-dose and the second-dose vaccination[15]. In our study, however, we have not compared the serocomversion rate with the healthy controls. If time permits, for future study it might be more beneficial if we compared the PWHA with healthy controls. We also did not include yet the comorbidities of the PWHA, where the other study found that comorbidites such as obesity, hypertension, and cardiovascular disease were associated with more severe COVID-19 disease[16]. Future study concerning the immunological status post COVID-19 vaccination, as well as the boosters, may give us further information about efficacy and effectiveness of the vaccines in the PWHA population.

CONCLUSION

This was the first epidemiological study regarding COVID-19 coinfection and vaccination in the PWHA population in Indonesia. Vaccination was significantly associated with seroconversion towards IgG SARS CoV-2 antibody in the PWHA population. COVID-19 vaccination is recommended for the PWHA population.

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