INVESTIGATION OF HIV AND COVID-19 CO-INFECTION AMONG TUBERCULOSIS-POSITIVE PATIENTS ATTENDING DIRECTLY OBSERVED TREATMENT CLINICS IN KANO, NIGERIA

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ABSTRACT

Background: Tuberculosis, Human immunodeficiency virus and COVID-19 are infectious diseases that have impacted negatively on global health systems, economies and societies, leading to millions of infections and deaths worldwide.

Aim: This study aimed to assess the HIV and COVID-19 co-infection and the associated possible risk factors among Tuberculosis patients attending some selected Directly Observed Treatment clinics in Kano, Nigeria.

Methods: A descriptive cross-sectional study was conducted on 384 patients. Clinical and sociodemographic data were collected and subjects were screened for HIV seropositivity and COVID-19 by RT-PCR. Data were analyzed to identify independent predictors of dependent variables. Dependent variable selection was based on prior knowledge that the participants were individuals with tuberculosis. A *p*-value for a two-tailed test less than 0.05 was considered statistically significant.

Results: No statistical association between HIV and COVID-19 was seen among the subjects, as 12 COVID-19 samples tested positive, giving a prevalence of 3.1% and coincidentally 12 HIV samples tested positive, giving a similar prevalence. The *p*-value of 0.64 implies that no significant association between HIV infection and COVID-19 was found among the subjects. In addition, the study found no significant association between HIV infection and/or COVID-19 and, average monthly income, and household population. The good knowledge of COVID-19 preventive measures justified the participant's low level of exposure to COVID-19, which is largely due to the massive awareness created on COVID-19 preventive measures.

Conclusion: The study suggested that tuberculosis-positive patients, especially those with HIV infection, should continue to receive effective antiretroviral therapy and adhere to preventive measures to reduce their risk of COVID-19. Healthcare providers should also consider the possibility of COVID-19 in tuberculosis-positive patients presenting with respiratory symptoms and take appropriate measures to diagnose and treat the infection promptly.

Keywords: COVID-19, Tuberculosis, HIV, Coinfection**.**

INTRODUCTION

Notwithstanding the widespread implementation of a commonly adopted strategy to combat tuberculosis, the disease continues to pose a significant public health issue, particularly in developing nations (Okonko *et al.*, 2021). In 2020, approximately 9.2 million individuals contracted Tuberculosis, resulting in 1.4 million deaths (Vaughan, 2020).

Similarly, the global Human immunodeficiency virus (HIV) epidemic remains a substantial challenge, with an estimated 37.3 million people living with the virus in 2020, leading to 1.4 million fatalities (Sarari & Oyeyi, 2011). The prevalence of co-infection between tuberculosis and HIV varies considerably: the occurrence of HIV among Tuberculosis patients ranged from 3.4% to 69.8%, while the occurrence of tuberculosis among HIV-positive individuals ranged from 1.8% to 61.9% (Ssentongo *et al.,* 2021). The African region accounted for 73% of the estimated cases of incident tuberculosis in HIV-positive individuals (Vaughan, 2020). Although numerous countries have made significant progress in addressing the co-occurrence of tuberculosis and HIV, they have not achieved the global targets for HIV testing among tuberculosis patients or the provision of antiretroviral therapy for those who are HIV positive (Iversen *et al.,* 2020). HIV significantly elevates the risk of developing active tuberculosis and increases the mortality associated with tuberculosis (Kanwugu & Adadi, 2021). Tuberculosis affects around 2 billion people globally, with 11 million new cases and 1.5 million deaths reported each year (Sah *et al.,* 2021). It is the leading cause of death from infectious diseases and particularly impacts individuals with HIV/acquired immunodeficiency syndrome (AIDS) (Mar *et al.,* 2021). India has the highest number of reported tuberculosis cases (Natarajan *et al.,* 2020). The interaction between tuberculosis and HIV is poorly understood, as HIV weakens the immune system and increases vulnerability to various infections (Vaughan, 2020). The coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2 virus), has caused a global pandemic with significant loss of life (Byrd *et al.,* 2020). COVID-19 has surpassed previous coronavirus outbreaks in terms of infection rates and fatalities (Kanwugu & Adadi, 2021). The impact of COVID-19 on individuals with HIV/AIDS is unclear, with conflicting evidence regarding increased risk and the role of antiretroviral therapy (Guo *et al.,* 2020). Limited research exists on co-infections between HIV and SARS-CoV-2 and the associated outcomes (Vaughan, 2020). The extent of the intersection between HIV and COVID-19 globally and the combined impact of demographic, social, economic, behavioural and clinical factors on these infectious diseases are not well known (Chinen & Shearer, 2002). The vulnerability and risk of death from SARS-CoV-2 among people living with HIV/AIDS remains largely unidentified (Gesesew *et al.,* 2021). There is growing concern that the immunosuppressive nature of HIV may increase susceptibility to SARS-CoV-2 and severe COVID-19, but this proposition has not been validated (Riou *et al.,* 2021).

This study aimed to assess the HIV and COVID-19 co-infection and the associated possible risk factors among Tuberculosis patients attending some selected Directly Observed Treatment clinics in Kano, Nigeria.

MATERIALS AND METHODS

Study Design and Population

A health institution-based cross-sectional study was conducted between December 2022 to March 2023. Samples were collected from Tuberculosis-positive patients following sample size estimation using a prevalence of 50%, error margin of 5% and 95% CI from 384 participants attending Aminu Kano Teaching Hospital, Infectious Diseases Hospital, and Muhammad Abdullahi Wase Teaching Hospital, all in Kano Metropolis, Nigeria.

Data collection

Using a structured, pre-tested questionnaire, patients were interviewed by trained laboratory Technicians on basic Sociodemographic characteristics and their symptoms.

Sample collection and storage

Samples were collected from consented individuals and consent to publish findings was also obtained. For HIV testing, four milliliters (4mL) of venous blood were collected aseptically from each participant using a disposable syringe and transferred into a labelled EDTA container and mixed gently to avoid hemolysis and formation of clots, then stored at a temperature between 2-8^{o} c until it is ready for the assay (Monica, 2006).

For COVID-19 testing, personal protective equipment (PPE) was worn following standard operating procedures. Wide-mouth plastic sample containers were labelled with patient details and the patient investigation form was completed accordingly. Patients were educated on the difference between sputum and saliva and provided water to rinse their mouths. They were instructed to sit comfortably, take a deep breath and cough to produce a sputum sample in a sterile, labelled container (WHO, 2020).

HIV Test

The HIV testing was done using The Abbott Determine™ HIV-1/2 (Abbott Diagnostics, Scarborough, Inc., ME, USA) as a screening test, HIV1/2 STAT-PAK ASSAY (CHEMBIO Diagnostic Systems, Inc., Medford, NY, USA) as a confirmatory test, and Uni-Gold TM (Trinity Biotech, Jamestown, NY, USA) as a tie-breaker according to the national algorithm. This was done after counselling, those patients with HIV infection were referred to HIV care and treatment clinics after post-test counselling (MoH Ethiopia, 2007).

COVID-19 Test

The COVID-19 sample (sputum) viral RNA extraction was performed using QIAamp VIRAL RNA MINI KIT (Qiagen, Inc. Hilden, Germany), and the amplification of the extracted nucleic acid extracted was performed using GeneFinder COVID-19 Plus Real*Amp* Kit (OSANG Healthcare Co., Ltd) following the manufacturer's protocol (GeneFinder, 2020).

Ethics

Ethical approval was obtained from the Kano State Ministry of Health (NHREC/17/03/2018), and the research and ethics committee of Aminu Kano Teaching Hospital.

Data analysis

Data were entered into Microsoft Excel 365 and exported into SPSS for Windows version 20 for further analysis. Univariable analysis followed by multivariable analysis (logistic regression) was done to identify independent predictors of dependent variables. Variable selection was based on prior knowledge that the participants were individuals with tuberculosis. The outcome variables were HIV infection and COVID-19. A *p*-value for a two-tailed test less than 0.05 was considered statistically significant.

RESULTS

Of the 384 participants enrolled in this study, 12(3.1 %) were found to be positive for HIV infection while 372(96.9%) were found to be negative for HIV infection. Coincidentally, the same proportion was found for COVID-19, giving a *P*-value of 0.64 and indicating that there was no coinfection of COVID-19 and HIV among the study subjects (Table 1.0). Among the participants with a household population of 1-5, 151(39.3%) were negative while 3(0.8%) were positive for COVID-19. Among the participants with a household population of 5-10, 215(56.0%) were negative while 7(1.8%) were positive for COVID-19. Enrolled subjects with a household population of >10, 6(1.6%) were negative while 2(0.5%) were positive for COVID-19. A *p*-value of 0.77 implies that no significant association exists between the participant's household population and the level of COVID-19 exposure (Table 2). Of the 384 participants enrolled in this study, 37(9.6 %) had poor knowledge, 162(42.2 %) had fair knowledge and 176(45.9 %) had good knowledge of COVID-19 preventive measures and were negative for COVID-19.

On the other hand, out of the 12 participants who tested positive for COVID-19, 9(2.3%) had poor knowledge and 3(0.7%) had fair knowledge of COVID-19 preventive measures. A *p*-value of 0.02 found implies a significant association between participants' knowledge of COVID-19 preventive measures and exposure to COVID-19 (Table 3). Of the 384 participants enrolled in this study, 217(56.5 %) earned a relatively low income, while 20(5.2 %) earned a higher income and were found to be negative for COVID-19. Furthermore, 219(57.0%) with a low income and 19(4.9 %) with a high income were found to be negative for HIV infection. A *p*-value of 0.69 and 0.90 were found for these groups implying no significant association between the participants' average monthly income and exposure to HIV infection and COVID-19 respectively (Table 4). Concerning initial source of awareness about COVID-19 preventive measures 354(92.3%) learned from the media, 12(3.1 %) from school, 14(3.6 %) from hospital, 3(0.8%) from mosque while 1(0.3 %) from others sources (Table 5).

Table 1: Distribution of Participant's HIV and COVID-19 exposure status

Status	**HIV**	**COVID-19**	**Co-infection**	***p-value***
Positive	12(3.1%)	12(3.1%)	-	0.64
Negative	372(96.9%)	372(96.9%)	-	
Total	**384(100%)**	**384(100%)**		

$P \leq 0.05$ is significant

Table 2: Distribution of Household population and COVID-19 exposure

	Status	**1-5 people**	**5-10 people**	**>10 people**	***p-value***
COVID-19	Negative	151(30.3%)	215(56.0%)	6(1.6%)	0.77
	Positive	3(0.8%)	7(1.8%)	2(0.5%)	
Total		**154(40.1%)**	**222(57.8%)**	**8(2.1%)**	

$P \leq 0.05$ is significant

Table 3: Distribution of Participants' knowledge of COVID-19 preventive measures and exposure

	Status	**Poor**	**Fair**	**Good**	***p-value***
COVID-19	Negative	37(9.6%)	158(41.2%)	176(45.9%)	0.02
	Positive	9(2.3%)	3(0.7%)	0(0.0%)	
		46(12.0%)	162(42.2%)	176(45.8%)	
Total		**46(12.0%)**	**162(42.2%)**	**176(45.8%)**	

$P \leq 0.05$ is significant

Table 4: Participants' average monthly income and exposure to COVID-19/HIV infection

	Status	**Low income**	**Middle income**	**High income**	***p-value***
COVID-19	Negative	217(56.5%)	135(35.1%)	20(5.2%)	0.69
	Positive	9(2.3%)	3(0.8%)	0(0.0%)	
Total		226(58.9%)	138(35.9%)	20(5.2%)	
HIV	Negative	219(57.0%)	134(34.9%)	19(4.9%)	0.90
	Positive	7(1.8%)	4(1.0%)	1(0.3%)	
Total		**226(58.9%)**	**138(35.9%)**	**20(5.2%)**	

$P \leq 0.05$ is significant

Table 5: Participants' initial source of information on COVID-19 preventive measures

Source of information	Frequency(N)	Percentage (%)
Media	354	92.3
School	12	3.1
Hospital	14	3.6
Mosque	3	0.8
Others	1	0.3
Total	**384**	**100.0**

DISCUSSION

The co-infection of HIV and COVID-19 infections can cause severe health outcomes for individuals with tuberculosis. In the present study, we analyzed blood and sputum samples of tuberculosis-positive patients to identify whether it is associated with HIV and COVID-19 co-infection. The results of this study (0/384) showed no significant association between HIV and COVID-19 infections among the subjects (p=0.64). These findings are consistent with a study by Kanwugu and Adadi, (2021), who reported a lack of significant association between HIV and COVID-19 infection, where only 0.98% coinfection (378/38345) was found among the study population. A possible explanation for this finding could be the differences in the pathophysiology of HIV and COVID-19. HIV primarily affects the CD4+ T-cells of the immune system, leading to immunodeficiency, while COVID-19 primarily affects the respiratory system and can cause acute respiratory distress syndrome (ARDS). Despite tuberculosis being a respiratory system disease, it has a different pathophysiology from that of COVID-19 (Riou *et al.*, 2021).

Another possible explanation is that the HIV Positive patients in this study have been receiving highly active antiretroviral therapy (HAART) for their HIV infection, which could have played a role in reducing their risk of contracting COVID-19 or its development. Additionally, the use of preventive measures such as wearing masks, social distancing and frequent hand washing might play a significant role in reducing the risk of COVID-19 in our study population.

This study has shown the indispensable role played by the media in the spread of awareness about COVID-19 and its preventive measures as 92% of the study population became aware of COVID-19 from the media. Massive media outreach and sensitization may be one of the possible reasons why the participants' level of exposure to COVID-19 was low (3.1%). The lack of association between the participant's income (socioeconomic status) and exposure to COVID-19 further reiterates COVID-19 is probably not a disease associated with low socioeconomic status, unlike tuberculosis which has been tagged as such as previously reported (Riou *et al.*, 2021).

In addition, this study showed that there was no significant association found between the participants' household population and COVID-19, where majority (222/384) of the participants are from a household of 5-10 people (p=0.77). These findings are surprising, as previous research conducted in the People's Republic of China by Guo *et al.* (2020) suggested that overpopulation, lack of social distancing, and other factors related to household population can increase the risk of contracting COVID-19. One possible explanation for the lack of association between household population and COVID-19 in this study is that other factors may be more significant in determining the risk of exposure (since our study shows the participants have a good knowledge of COVID-19 preventive measures).

For example, individual behaviors, such as wearing masks, practising good hand hygiene, and adhering to social distancing guidelines, may have a more significant impact on the risk of contracting COVID-19 than the household population. A study by Ssentongo *et al*. (2021), revealed that access to healthcare and other resources, such as transportation, may also play a role in the likelihood of exposure to COVID-19. Another possible explanation is that the study did not capture all of the relevant variables that could impact the association between household population and exposure to COVID-19. For example, the study did not account for the type of housing (apartment vs. house), the number of rooms in the household or the number of people sharing a bedroom. These variables could have an impact on the risk of exposure to COVID-19.

CONCLUSION

This study found no coinfection between HIV and COVID-19 infections among tuberculosis-positive patients. This suggests that HIV-positive tuberculosis patients are not at a higher risk of contracting COVID-19 compared to HIV-negative tuberculosis patients. Additionally, there was no significant association between HIV and COVID-19, and average monthly income, household population and knowledge of COVID-19 preventive measures. One limitation was that the study had a relatively small sample size and was conducted in a specific setting. However, the inability of the study to analyze the immune status of participants as well as the relatively small sample size were the major limitations of the study. Hence, further studies that might address these limitations are needed to ad more light to these findings and determine the potential effects of other factors on HIV and COVID-19 co-infections among tuberculosis-positive patient.

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Conflict of interest

The authors have no conflict of interest.

Contributions of Authors

Joshua J.D. and Aliyu I.A. conceptualized the work, Danjuma J.J., Kabir I.M. and Aliyu I.A. presented the methods, carried out the experiment, analysed the data, Danjuma J.J. wrote the manuscript, Kabir I.M. reviewed the final manuscript, and Aliyu I.A. supervised the work. All Authors approved the manuscript as submitted.

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