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Original Research

Is there Co-infection of Influenza and Covid-19 in Jos, North Central Nigeria?

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Abstract

Background: Influenza virus and severe acute respiratory syndrome virus-2 (SARS CoV-2) are known to cause respiratory disease in humans that may be fatal. They have caused epidemics and constitute significant public health challenges because of their ability to spread and cause severe disease. Co-infection with both viruses has been shown to increase the odds of fatality among affected patients. Our study aimed to investigate co-infection with influenza among patients with coronavirus disease-2019 (COVID-19) in Jos, Plateau State.

Methodology: We carried out a cross-sectional study using stored nasopharyngeal and oropharyngeal samples of patients diagnosed with COVID-19 using GeneXpert. The samples were collected at our institution and stored at −80 °C. The samples were analysed for influenza co-infection using real-time reverse transcriptase polymerase chain reaction.

Results: Two-hundred-and-forty-one (241) stored samples of patients diagnosed with COVID-19 were analysed. None of the samples tested positive for the influenza virus.

Conclusion: We found no case of influenza and SARS-CoV-2 co-infection among the patients studied. This suggests that the prevalence of influenza virus infection may be low in our setting and partly explains the relatively benign outcome of SARS-CoV-2 infections in our region.

Keywords: Co-infection; SARS-CoV-2; Influenza, Human; Nigeria; Epidemics.

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Quick Response Code:

Introduction

Coronavirus disease 2019 (COVID-19) is an acute respiratory infectious disease that was declared a global pandemic by the World Health Organization (WHO) on 11th March 2020 [1]. Influenza causes mild to severe disease and may lead to death; it has also caused pandemics in the past [2,3]. Dual infection with COVID-19 and influenza has been reported [4].

Since its inception, the COVID-19 pandemic has caused approximately 6.5 million deaths globally, with more than 621 million positive cases as of October 2022, imposing more burden on global health and economics [5]. A systematic review and meta-analysis indicated that 40.5 persons (95% CI = 24.3–67.4) per 100,000 population are hospitalised for influenza globally [6].

Globally, influenza was positive in 19% (614,907) of the 3,311,831 respiratory samples collected during inpatient and outpatient surveillance between early November 2019 and the end of December 2020 [7].

The prevalence of these infections varies across regions and countries of the world. Nigeria recorded 265,651 cases and 3,155 deaths due to COVID-19, of which 10,326 cases and 75 deaths were from Plateau State as of 9th October 2022 [8]. Surveillance data showed that the prevalence of influenza among patients with a severe acute respiratory infection (SARI) and influenza-like illness (ILI) was 7.6%, with approximately 5% and 8% of those with SARI and ILI, respectively, testing positive for influenza in Nigeria [9].

Co-infection with influenza and SARS CoV-2 is associated with more severe disease and increased odds of death [10, 11]. Therefore, the prevalence of co-infection with influenza and SARS CoV-2 may partly explain the frequency of severe disease or death. Data on influenza and COVID-19 co-infection is limited in our setting. Therefore, this retrospective study aimed to establish if co-infection with influenza and SARS CoV-2 was present among patients diagnosed with COVID-19 at our institution.

Materials and Methods

This retrospective study was carried out between 21st December 2021 and 31st May 2022 at a referral centre for COVID-19 testing and treatment in Nigeria. All patients with available nasopharyngeal and oropharyngeal swab samples who were positive for SARS-CoV-2between 1st June 2021 and 31st December 2021 were included in the study.

The minimum sample size was determined using the Kish and Leslie formula for cross-sectional studies [12]. Assuming a P of 50%, d of 5%, and Z of 1.96 (95% confidence level), the estimated sample size was 385. However, since the study population in our case (patients diagnosed with COVID-19 at the molecular biology laboratory of our institution during the study period) was 310, we further applied the formula for finite population adjustment in sample size determination [13]. The final sample size obtained was approximately 172.A total population sampling technique was employed where all SARS-CoV-2 positive oropharyngeal and nasopharyngeal swab samples still available at the time of data collection were included. Patients admitted for COVID-19 and those with symptoms of COVID-19 who were managed at home had their samples tested at the laboratory. Basic demographic data of participants that were available in the laboratory records were also collected.

Tests for COVID-19 and Influenza

The Xpert Xpress SARS-CoV-2 (Xpert) test (Cepheid, Sunnyvale, CA, USA) was used in diagnosing COVID-19[14]. In brief, 300 µL of the oropharyngeal and nasopharyngeal swab sample was transferred from the collection tube into the cartridge using a pipette. External controls of the same volume were also put in the cartridge. After powering on the machine, the cartridge was loaded into the machine, and the test was run.

The remaining samples were stored in a −80 °C freezer. The stored samples were subsequently assayed for influenza virus co-infection using the procedure described below.

The viral RNA extraction was performed at the BSL3 laboratory of the National Veterinary Research Institute, Vom. RNA was extracted using the QIAamp Viral RNA Mini kit (Qiagen, Chatsworth, California, USA) following the manufacturer's guidelines. Extracted RNA was kept at 4 ℃ for real-time RT-PCR. Real-time RT-PCR was done targeting the M gene of the influenza virus using Qiagen One-step RT-PCR kit reagents according to the manufacturer's guidelines. The 20 µl assay contained 10 µl of 2x Itaq reaction mix, one µl (10 µm) of primer M+25 (AGATGAGTCTTCTAACCGAGGTCG), one µl (10 µm) of primer M-124 (TGCAAAAACATCTTCAAGTCTCTG), 0.5 µl of M+64 probe (10 µm) FAM (TCAGGCCCCCTCAAAGCCGA), 0.25 µl of iScript Reverse Transcriptase, 5.25 µl of RNAse free water, and two µl of RNA using the following cycling programs 50 °C for 20 min, 95 °C for 5 min, followed by 40 cycles of 94 °C for 45 s and 54 °C for 45 s. The samples were run alongside negative and positive controls.

Statistical analysis

Data was extracted and cleaned using Microsoft Excel. Demographic data of the participants were summarised as frequencies (percentages) for qualitative data and means ± standard deviations for quantitative data.

Ethical consideration

Ethical approval was obtained from the National Health Research Ethics Committee of Nigeria (NHREC) (Approval Number: NHREC/01/01/2007-20/12/2020). The study was conducted according to the principles of the Helsinki Declaration of 1975, as revised in 2000.

Results

Of the 310 patients diagnosed with COVID-19 during the study period, 241 positive nasopharyngeal and oropharyngeal samples were available and were analysed for influenza virus co-infection. One-hundred and twenty (51.7%) of the patients were males, and 112 (48.3%) were females. The mean age of the patients was 41.5 ± 19.7 years. The age distribution of patients is shown in Figure 1. Fifty-eight (58) percent of the patients resided in Jos North Local Government area (LGA), 41.1% in Jos South LGA, and 0.5% in Mangu LGA of Plateau State, North Central Nigeria. None of the samples were positive for influenza virus infection; the prevalence of influenza SARS-COV 2 co-infection was 0%.

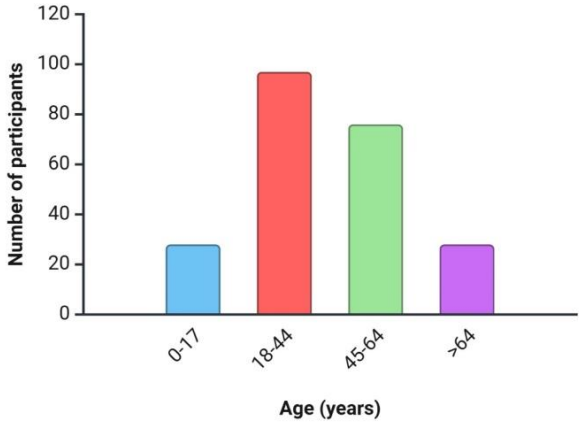

Figure 1: Age distribution of study participants

Discussion

This study sought to determine the frequency of co-infection of influenza and SARS-CoV-2 in the early phase of the COVID-19 pandemic in Nigeria. Coronaviruses and influenza are important pathogens of interest; the World Health Organization has listed them among the top 7 priority pathogens considered for research and development due to their epidemic and pandemic potentials [15].

Our study did not find any influenza and SARS-CoV-2 co-infection. In a similar study in another African country (Burkina Faso), one case of co-infection was identified out of 324 samples [16]. This suggests the rarity of this co-infection, especially in Africa. However, a systematic review of North American and Asian populations revealed a prevalence of 0.8% of influenza-SARS COV 2 co-infection [17]. Similarly, a recent study also showed regional variations in the prevalence of co-infection with influenza among patients with confirmed COVID-19, with the prevalence in Asia and America being 4.5% and 0.4%, respectively [17]. The prevalence of influenza is low in sub-Saharan Africa, ranging between 6 and 10% in Nigeria, Tanzania, Angola, Central Republic of Africa, Burkina Faso, Niger, and Ghana[18,19, 20,21, 22, 23, 24, 25]. This may explain why the prevalence of co-infection is low in our environment. Moreover, ultraviolet radiation and sunlight exposure are believed to reduce the risk of influenza virus infection [26, 27]. This may contribute to the lower prevalence of influenza in tropical regions, including Nigeria.

Furthermore, considering that influenza and COVID-19 are all respiratory viruses, preventive measures instituted during the COVID-19 pandemic may have contributed to preventing influenza infection, accounting for the results of our study. Although SARS-CoV-2 and influenza viruses are transmitted similarly, SARS-CoV-2 may be more contagious than influenza viruses [28]. Therefore, implementing preventive measures for COVID-19 may have disproportionately decreased influenza virus transmission. Moreover, a global decrease in seasonal influenza cases has been observed after the onset of the COVID-19 pandemic [29]. Our study suggests that co-infection with influenza in patients with COVID-19 may be rare in Plateau State, Nigeria.

In this study, males and females were equally represented. This is like a previous study of influenza infection among patients with *influenza-like* illness (ILI) and severe acute respiratory infections (*SARI*) [9]. The mean age of our study participants was 41.5 ± 19.7. However, a recent study showed a higher incidence of co-infection in children than in adults, although the difference was not significant [30]. In the context of COVID-19, patients with co-morbidities and older persons are at greater risk of severe disease; hence, most of the patients in our study belonged to this category. The incidence of influenza is higher among children (those below 18 years) and adults between50 and 64 years [2].

Our study has some limitations. The sample size was small. This limits the generalizability of our findings. However, we determined that the sample size was adequate for determining the co-infection prevalence among positive cases in Jos during this period. Furthermore, we could not analyse the clinical presentation of the patients who tested positive for COVID-19. This was because the study was a laboratory-based study using stored samples, and clinical data was not routinely collected at the laboratory. However, we demonstrated that co-infection with influenza in patients with COVID-19 is rare in Plateau State, Nigeria.

Surveillance and research on epidemic-prone diseases are invaluable public health measures to contain outbreaks. Equally important are studies that determine co-infections of pandemic-prone pathogens. This would help track and prevent handling dual epidemics or reducing the severity of one epidemic by another with similar modes of transmission and clinical profiles. Our study found zero prevalence of influenza-COVID-19 infection. It is necessary to put measures in place to track this co-infection.

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