VOLUME 39, NUMBER 2
February 2022

ISSN 0189 - 160X

# WAJM

## WEST AFRICAN JOURNAL OF MEDICINE

ORIGINALITY AND EXCELLENCE IN MEDICINE AND SURGERY

**OFFICIAL PUBLICATION OF**
THE WEST AFRICAN COLLEGE OF PHYSICIANS *AND*
WEST AFRICAN COLLEGE OF SURGEONS

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ORIGINAL ARTICLE

# Comparison of the Ivermectin and Lopinavir/Ritonavir Treatment Outcomes among COVID-19 Mild to Moderate Cases in Kaduna State

## *Comparaison des Résultats du Traitement par l'Ivermectine et le Lopinavir/Ritonavirparmi les cas Légers à Modérés de COVID-19 dans l'État de Kaduna*

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**ABSTRACT**

**BACKGROUND:** Ivermectin has been a popular anti-parasitic drug since the late 1970s. The promising result of in-vitro studies on the antiviral activity of the drug has led clinicians in many countries to use this drug to treat COVID-19 patients. This study determined and compared the mean number of days at clinical recovery for mild to moderate cases of COVID -19 treated with Lopinavir/Ritonavir (Alluvia) and Ivermectin at the Kaduna State Infectious Disease Control Centres.

**METHODS:** This was a comparative cross-sectional study conducted among 300 mild to moderate COVID- 19 cases enrolled for the study. The outcome variables were the time required for the resolution of symptoms from the onset and at commencement of the treatment regimens. Data were collected from patient folders using a questionnaire. Data were analysed with the IBM SPSS Version 25.0 and STATA/SE 13. Statistical significance was set at $p<0.05$.

**RESULTS:** The mean recovery time (MRT) from symptom onset was significantly lower for Covid-19 patients treated with ivermectin (7.15±4.18 days) compared to lopinavir/ritonavir (9.7±5.3 days), 95%CI=7.37–9.62. Multivariate logistic regression showed that there was no significant relationship between the patients age (AOR=0.36, 95%CI=0.09–1.49), sex (AOR=0.34,95%CI=0.54–5.93), educational status (AOR=1.04, 95%CI=0.3–3.57), marital status (AOR=0.55,95%CI=0.14–2.11) place of treatment (AOR=1.66, 95%CI=0.54–5.11) and MRT. There was also no significant relationship between patients' comorbid chronic illness (AOR=0.83, 95%CI=0.27–2.61) and MRT.

**CONCLUSION:** The mean recovery time for COVID-19 patients managed with ivermectin was slightly lower than for the lopinavir/ritonavir regimen.

**RECOMMENDATION:** Clinical trials to further prove the efficacy of Ivermectin as a supportive therapy in clinical management of mild to moderate cases of COVID-19 in this setting should be carried out. **WAJM 2022; 39(2): 140–146.**

**Keywords:** Ivermectin, Alluvia, Treatment, MRT, Clinical trial, COVID-19.

**RÉSUMÉ**

**CONTEXTE:** L'ivermectine a été un médicament antiparasitaire populaire depuis la fin des années 1970. Le résultat prometteur d'études in vitro sur l'activité antivirale du médicament a conduit les cliniciens de nombreux pays à utiliser ce médicament pour traiter les patients atteints de COVID-19. Cette étude a déterminé et comparé le nombre moyen de jours de récupération clinique pour les jours légers à cas modérés de COVID-19 traités par Lopinavir/Ritonavir (Alluvions) et ivermectine à la maladie infectieuse de l'État de Kaduna Centres de contrôle.

**MÉTHODES:** Il s'agissait d'une étude comparative transversale menée auprès de 300 cas légers à modérés de COVID-19 inscrits pour l'étude. Les variables de résultat étaient le temps requis pour la résolution des symptômes dès le début et au début de la schémas thérapeutiques. Les données ont été recueillies à partir des dossiers des patients à l'aide d'un questionnaire. Les données ont été analysées avec version 25.0 du IBM SPSS et STATA/SE 13. La signification statistique a été fixée à $p<0.05$.

**RÉSULTATS:** Le temps moyen de récupération (TRM) à partir de l'apparition des symptômes était significativement plus faible chez les patients Covid-19 traités par l'ivermectine(7.15±4.18 jours) par rapport au lopinavir/ritonavir (9.7±5.3 jours), IC à 95 % = 7.37 à 9.62. La régression logistique multivariée a montré qu'iln'avait pas de relation significative entre l'âge des patients (AOR = 0.36, IC à 95 % = 0.09 à 1.49), sexe (AOR = 0.34, 95 % IC = 0.54 à 5.93), education statut (AOR =1.04, IC à 95 % = 0.3–3.57), état matrimonial(AOR = 0.55, 95% IC = 0.14–2.11) lieu de traitement (AOR = 1.66, IC à 95 % = 0.54 à 5.11) et TRM. Il n'y avait pas non plus de relation entre la maladie chronique comorbide des patients (AOR = 0.83, IC à 95 % = 0.27 à 2.61) et TRM.

**CONCLUSION:** Le temps de récupération moyen pour les patients atteints de COVID-19 gérés avec de l'ivermectine était légèrement inférieur à celui du lopinavir/régime de ritonavir.

**RECOMMANDATION:** Essais cliniques pour prouver l'efficacité de l'ivermectine comme traitement de soutien dans la prise en charge clinique des cas lègers à modérés de COVID-19 dans ce contexte devraient être effectués. **WAJM 2022; 39(2): 140–146.**

**Mot-clés:** Ivermectine, Alluvie, Traitement, MRT, Essai clinique, COVID-19.

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## INTRODUCTION

There is a global quest for a regimen that can be administered for the prevention and control of COVID-19, a disease of public health emergency of international concern which has devastated the global community since the first reported case in Wuhan, China in December 2019.[1] Different supportive regimens have been used in different countries for the management of the SARS-Cov-2 patients. Chloroquine,[3] hydroxychloroquine,[3] Lopinavir/ Ritonavir,[4] Nafamostat and Camostat,[5] famotidine,[6] interferon,[7] convalescent plasma[8] monoclonal or polyclonal antibodies[9] and other therapies including multivitamins and antimicrobial agents[10] have been used for the treatment of SARS-Cov-2 by clinicians in different part of the world. Most of these therapies are in different stages of clinical trials.[11]

Recently there was increased interest in exploiting the antiviral activities of ivermectin [12] for the treatment of the SARS-Cov-2. The drug had previously been used in the tropics as an antiparasitic for the treatment of Onchocerciasis.[13] The clinical efficacy of ivermectin against specific flaviviruses such as the Dengue, Japanese encephalitis, and tick-borne encephalitis and the chikungunya virus has been established.[14,15]

A previous study from Florida revealed that patients on admission for the SARS-Cov-2 infection who received ivermectin had a statistically significant lower mortality rate compared to those treated with the usual care of the multivitamin regimen.[16] Caly, *et al* also demonstrated in a clinical trial that vero cells infected with SARS-CoV-2 when treated with ivermectin resulted in a 5,000-fold reduction in viral RNA after 48 hours,[17] though exact mechanism for this observation is not yet known. Another study in Bangladesh involving 100 Covid-19 patients treated with a combination of ivermectin and doxycycline showed adequate viral clearance in mild and moderately ill patients.[18]

Another recently published randomised controlled trial also in Bangladesh found that a combination of ivermectin and doxycycline showed no significant adverse events and had an improved tolerance compared to a combination of hydroxychloroquine and azithromycin.[19]

The promising result of the in-vitro studies mentioned above has led clinicians in many countries to use ivermectin to treat COVID-19 patients. Babalola et al in Nigeria also revealed the clinical benefit of ivermectin in the management of mild to moderate cases of COVID-19 in Nigeria.[20]

Although these various observational data suggest beneficial effects of ivermectin in the treatment of COVID-19 cases, there has been no study in Kaduna State, or indeed in Northern Nigeria, to confirm the efficacy and usefulness of the drug for the COVID-19 patients in our setting.

There have also been various publications on the use of lopinavir/ ritonavir for the management of the COVID-19 patients. While some studies would not recommend its use,[4,21] others including studies from Nigeria have proven the usefulness and efficacy the lopinavir/ ritonavir therapy.[21,22] The drug is known for the management of HIV patients as a 2nd line therapeutic agent. [23] The drug is being repurposed in many centres in Nigeria for the management of the COVID-19 patients.

During this survey, mild to moderate Covid 19 cases were managed with the lopinavir/ritonavir (400/100mg 12hrly) or ivermectin regimen (12mg once daily) given for 5 days while on admission at the isolation centres. Some of the patients were also admitted at home, if they met with the criteria for home management as specified by the Nigeria Centre for Disease Control.[22]

This study determined and compared the mean number of days from the onset of symptom and at the commencement of therapy to clinical recovery for the patients treated with either

lopinavir/ritonavir (Alluvia) or ivermectin regimen during the study period in Kaduna State, Nigeria.

## SUBJECTS, MATERIALS AND METHODS

This was a was comparative cross-sectional study that involved a retrospective review of the clinical records of confirmed COVID-19 patients managed on lopinavir/ ritonavir and ivermectin regimens from 30th March 2020 to 27th February 2021.

### Background of the Study Area

The study was conducted at the Infectious Disease Control Centre (IDCC) in Kaduna, the capital of Kaduna State, in North Western Nigeria. The IDCC runs two isolation centres in Kaduna city as at the time of this survey; the Kakuri IDCC and the Hamdala Alternative Isolation. Other isolation centres in the state were located in Kafanchan and Zaria. The state had a total of 218 beds in the five Isolation centres and has managed more than 10,000 COVID 19 cases. Kaduna State responds to the COVID-19 pandemic via nine pillars set up by the state Emergency Operation Centre. These pillars include Epidemiology and surveillance, Laboratory services, Point of Entry (POE), Infection Prevention and Control, case management, Risk communication, Logistics and supplies, Coordination and Research.

**The Study Population** comprised of all mild to moderate cases of COVID- 19 under the care of the case management team and aged ≥18years. Severe-to critical cases of COVID-19, pregnant patients, lactating mothers and those with known history of hypersensitivity to ivermectin/ lopinavir/Zinc sulphate were excluded from the study. The mild to moderate cases were defined based on the WHO COVID-19 disease classification standard.[21]

**Mild cases** were identified as patients without evidence of viral pneumonia or hypoxia with the SpO2 >93% on room air.

**Moderate cases** were defined as symptomatic patients with non-severe signs of pneumonia (fever ±cough ± dyspnea) and also presenting with normal SpO2 ≥ 90% at room air. [21]

**The sample size** was calculated using the formula:

$$n = \frac{(Z_{1-\alpha/2} + Z_{1-\beta})^2 \times 2(p_1q_1 + p_2q_2)^{24}}{(p_1 - p_2)^2}$$

Z1-α/2= 1.96 when α=0.05 for two-sided test

Z1-β=1.282 when β= 0.1 (90% power)

$p_1$= Proportion of Covid 19 confirmed cases treated with Lopinavir/ Ritonavir regimen and was discharged within 28 days from a previous study was 69%.[25]

$p_1$ =69%

$p_2$= Proportion of patients on Ivermectin who had positive RT PCR on day 10 from previous study 10%[26]

The sample size(n) was calculated as = 133 patients per group.

For an anticipated nonresponse or attrition of 10%, the adjusted sample size =n/1–0.1 = 133/0.9= 133/0.9 = 147 H" 150 patients (minimum sample size).

We identified a cohort of patients who were treated with lopinavir /ritonavir for mild moderate cases between March and August 2020 and found 176 such patients. Relevant information was collected from the patients' hospital records using a proforma. Some inconsistent and incomplete data were discarded. We used the records of 150 patients with complete data for this survey. For the ivermectin group, the patients were recruited consecutively as they were placed on treatment and information collected from their hospital records using a proforma until the sample size was attained. The recruitment of the ivermectin group was from September 2020 till February 2021.

Data analysis was done with the Stata software version12 SE. The t-test for comparison of 2 independent means with unequal variance was used to compare the mean time at clinical recovery for ivermectin and Lopinavir-ritonavir regimen. Level of statistical significance was set at $p<0.05$.

**Ethical Permission** was obtained from the Kaduna State Ministry of Health Research Ethic Committee (HREC). Participation in the study was voluntary. Informed written consent was also obtained from the patients.

## RESULTS

A total of 300 mild to moderate cases were enrolled for the study. One hundred and fifty patients managed on ivermectin were compared with a cohort of 150 patients previously managed on the lopinavir/ritonavir regimen. There was statistically significant difference in mean age of the patients on ivermectin, 39.53±1.18 years (95% CI=37.1–41.89) compared to those on lopinavir/ritonavir, 40.53±1.11 years (95% CI= 38.2–42.7).

There were 67 males (44.7%) and 83 females (55.3%) on ivermectin while 100 (66.7%) males and 50 (33.3%) females were on lopinavir/ritonavir, and this was statistically significant ($\chi^2$ = 14.67, p=0.001). There was also a statistical difference between the respondents' ethnicity ($\chi^2$ = 8.81, p=0.003) occupation ($\chi^2$=46.48, p=0.001,) educational status ($\chi^2$=4.59, p=0.03) and the type of regimen administered (Table 1).

For ivermectin, 96 (64%) of patients on the regimen were mild while 54(36%) were moderate cases compared to 108 (72%) mild and 42(28%) moderate cases on the lopinavir/ ritonavir regimen. No significant relationship between regimen administered and type of cases. ($\chi^2$= 0.22, p= 0.14). Majority of the mild cases were on home care management while most of the patients on the lopinavir /ritonavir regimen were moderate cases. More patients with chronic illness (24.7%) took the Lopinavir/ritonavir regimen than ivermectin (10.7%). There was a significant difference between home care management ($\chi^2$= 241.5, p= 0.001), history of chronic illness ($\chi^2$= 10.10, p= 0.001) and type of regimen administered. Most of the patients with cough were treated with lopinavir/ritonavir 25(59.5%) compared with ivermectin 14(26.4%) and the difference was statistically significant ($\chi^2$=10.61, p=0.001). Patients with myalgia were treated more with ivermectin than Lopinavir/ritonavir while patients who presented with headache were managed more with the lopinavir regimen and these

**Table 1: Socio-demographics Characteristics of the Patients**

| Variables | Ivermectin (n=150)n (%) | Lopinavir/Ritonavir (n=150)n (%) | Test statistics | p values |
|---|---|---|---|---|
| Mean age ± (SE) | 39.53± 1.18 (95% CI = 37.1–41.89) | 40.53± 1.11 (95% CI = 38.2–42.7) | T-test = –5.61, | <0.001 |
| **Sex** | | | | |
| Male | 67 (44.7) | 100 (66.7) | 14.71 | 0.001 |
| Female | 83 (55.3) | 50(33.3) | | |
| **Ethnicity** | | | | |
| Hausa | 80 (53.0) | 105 (70.0) | 8.81 | 0.003 |
| Others | 70 (47.0) | 45 (30.0) | | |
| **Occupation** | | | | |
| Civil servants | 91(60.7) | 40 (26.7) | 46.48 | 0.001 |
| Health Care workers | 3 (2.0) | 21 (14.0) | | |
| Self employed | 31(20.7) | 31(20.6) | | |
| Unemployed | 25 (16.6) | 58 (38.7) | | |
| **Education** | | | | |
| No formal | 4(2.7) | 9(6.0) | 5.59 | 0.133 |
| Primary | 6(4.0) | 7(4.7) | | |
| Secondary | 21(14) | 32(21.3) | | |
| Tertiary | 119(79.3) | 102(68) | | |

**Others – Yoruba, Igbo, Bajju, Gbagyi, Atyap, Koro, Adara*

were statistically significant ($p<0.05$) (Table 2).

No patient on the ivermectin regimen complained of any side effect post medications; however, 24 (16%) of the patients on the lopinavir/ ritonavir regimen had side effects of epigastric pain 8(5.3%), insomnia 5(3.4%), nausea and vomiting 5 (3.4%), bodily pain 2(1.3%), diarrhea 2(1.3%) and lethargy 2 (1.3%) (Figure 1).

The mean difference in days from symptom onset to clinical recovery between COVID-19 patients treated with ivermectin was (7.15±4.18 days) compared to lopinavir/ritonavir (9.7±5.3 days) was –2.56±1.1. This difference was statistically significant (p value= 0.02) (Table 3).

However, from commencement of therapy to the day of clinical recovery, the mean difference (ttest=0.39, 95% CI= –1.4–2.07) for the two regimens was not statistically significant (Table 4). Multivariate logistic regression further showed that the odds for clinical recovery on day five was significantly lower for patients treated with lopinavir who were unemployed AOR=0.02, (95% CI=0.01–0.86) compared to other occupation groups. No difference was observed with the occupation and clinical recovery for patients on ivermectin regimen. ($p>0.05$). Age, sex, educational status, marital status, place of treatment and history of chronic illness did not predict clinical recovery for both regimens (Table 5).

**Table 2: Clinical Characteristics of the Covid-19 Patients involved in the Survey**

| Characteristics | Ivermectin (n=150)n (%) | Lopinavir/r (n=150)n (%) | Chi | p |
|---|---|---|---|---|
| **Type of cases** | | | | |
| Mild | 96 (64.0) | 108 (72) | 2.21 | 0.14 |
| Moderate | 54 (36.0) | 42(28) | | |
| **Place of Admission** | | | | |
| Home | 149(99.3) | 15 (10.0) | 241.52 | 0.001* |
| Facility | 01 (0.7) | 135(90.0) | | |
| **History of chronic illness** | | | | |
| Yes | 16 (10.7) | 37 (24.7) | 10.10 | 0.001* |
| No | 134(89.3) | 113(75.3) | | |
| **Symptom Fever** | **n = 54** | **n = 42** | | |
| Yes | 26(48.1) | 25(59.5) | 1.23 | 0.27 |
| No | 28(51.9) | 17(40.5) | | |
| **Cough** | | | | |
| Yes | 14 (25.9) | 25 (59.5) | 11.05 | 0.001 |
| No | 40 (74.1) | 17(40.5) | | |
| **Myalgia** | | | | |
| Yes | 19 (35.2) | 4(9.5) | 8.54 | 0.003 |
| No | 35 (64.8) | 38 (90.5) | | |
| **Anosmia** | | | | |
| Yes | 6 (11.1) | 8(19.0) | 1.20 | 0.27 |
| No | 48 (88.9) | 34 (81.0) | | |
| **Dyspnea** | | | | |
| Yes | 5 (9.3) | 7 (16.7) | 1.19 | 0.28 |
| No | 49 (90.7) | 35 (83.3) | | |
| **Headache** | | | | |
| Yes | 1 (1.9) | 7(16.7) | 6.79 | 0.01 |
| No | 53 (98.1) | 35 (83.3) | | |
| **Sore throat** | | | | |
| Yes | 6 (11.1) | 2(4.8) | 1.24 | 0.46 |
| No | 48 (88.9) | 40 (95.2) | | |
| **Rhinorrhea** | | | | |
| Yes | 1 (1.9) | 3 (7.1) | 1.65 | 0.20 |
| No | 53 (98.1) | 39(92.9) | | |

## DISCUSSION

This survey showed that the majority of the COVID-19 patients managed at the IDCC Kaduna were mild cases. Previous studies had shown that most of the COVID-19 cases in Nigeria were mild- moderate in presentation.[27,28] This category of patients was managed by the Kaduna State Case Management team either at the facility (after baseline clinical assessment) or at patients' homes if the clinicians were satisfied that the clients met the eligibility criteria for the home care management.[29]

The drug regimen used for the patients was either the lopinavir/ritonavir (Alluvia$^{R}$) or ivermectin regimen. The Alluvia is commonly used in Nigeria as an antiretroviral drug for the management of the HIV/AIDS patients.[30] It is however repurposed by most infectious disease control centres in Nigeria for the treatment of COVID-19 patients with reports of good clinical outcomes.[27,28]

There was increased demand for the use of ivermectin for COVID-19 cases in the country following the report of clinical trials that demonstrated the safety and efficacy of the therapy for the COVID-19 patients. Our findings in this study also showed that overall, the numbers of days to clinical recovery measured from the symptom onset for patients on ivermectin was shorter than those on Alluvia regimen (Table 3). This result corroborates earlier findings by Babalola *et al* that the number of days to clinical recovery was significantly shorter with the ivermectin regimen compared to lopinavir/ ritonavir regimen used in the management of the SARS-Cov-2 mild to moderate cases.[20] An American study[31] had also proven the efficacy of ivermectin for the treatment of early-onset mild COVID-19 disease in adult patients[31]. Another randomized clinical trial conducted by Roy et al in India also showed that a significant proportion of mild to moderate cases of COVID-19 patients were discharged alive on the sixth day of admission when given the ivermectin regimen[32] This study also showed that for some specific symptoms like fever, cough, sore throat and rhinorrhea, the patients recovered relatively quicker with the Alluvia regimen compared to the ivermectin regimen

(Table 4.) Previous studies have also demonstrated the efficacy of the lopinavir/ ritonavir regimen in clinical recovery of the COVID-19 patients.[33,20]

The added advantage of the ivermectin regimen in this study, however, was the fact that none of the patients reported any adverse effect with the use of the therapy, while 10% of the patients on the Alluvia regimen complained of diarrhea, lethargy or epigastric pain after taking the drug.

This study also showed that the clinical recovery was significantly lower for the unemployed patients in the lopinavir/ritonavir treatment group. The delay in clinical recovery of these patients could be related to poor socioeconomic status of this group.[35] Previous studies had demonstrated that old age and chronic illness comorbidity were predictors of severe COVID-19 due to weakened immune function in the elderly population[36,37] but these factors might not necessarily predict the treatment outcome for mild to moderate cases as seen in this study. This implies that, if confirmed cases can get access to clinical management earlier before disease progression to the severe or critical COVID-19, the clinical outcome will not be dictated by the age, comorbidity or any other factors related to weakened immunity. Therefore, there is a need for the state and federal health authorities in charge of the prevention and control of the Covid 19 pandemic to engage with the populace on the need to seek medical attention early for the suspected or confirmed cases before disease progression to severe or critical cases.[38]

The lack of random assignment is the limitation of this study. We also do not know the clinical outcome for patients who took no therapy (placebo) in this setting. We used secondary data and therefore could not analyse the data of some patients with incomplete or missing data. The report on ivermectin was based on the oral report from the patients and this might be liable to information bias.

In Conclusion, the study showed that both lopinavir/ritonavir and

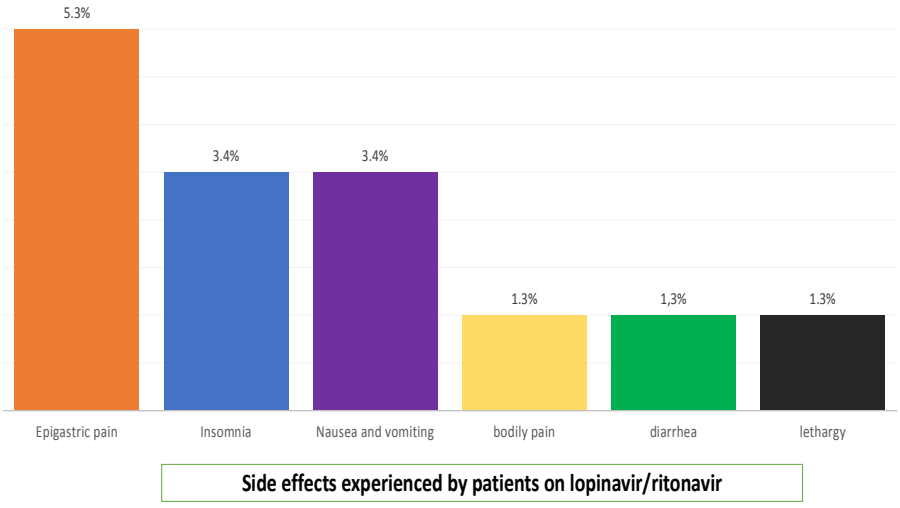


**Fig. 1:**

**Table 3: Comparisons of the Mean Number of Days Required for Clinical Recovery from Symptom Onset**

| Clinical Conditions | Ivermectin MRT (days) | Lopinavir/r MRT (days) | Diff of 2 means | t-test(df) | 95% CI diff of 2 means | | p |
|---|---|---|---|---|---|---|---|
| | | | | | Lower | Upper | |
| All symptoms | 7.15±4.18 | 9.7±5.27 | –2.56+1.11 | –2.31 (73) | 7.37 | 9.62 | 0.02* |
| Fever | 6.8±0.91 | 7.24±0.74 | –4.16+1.17 | –0.35 (40) | –2.78 | 1.94 | 0.72 |
| Cough | 9.4+2.23 | 10.13±1.08 | –7.01-2.31 | –3.04 (30) | –5.43 | 4.03 | 0.76 |
| Myalgia | 7.25+1.21 | 6.85±0.86 | 0.75±2.16 | 0.34 (14) | –3.94 | 5.44 | 0.73 |
| Headache | 3.5±0.50 | 7.17±1.40 | –3.67±2.5 | –1.42 (6) | –9.95 | 2.62 | 0.20 |
| Sore throat | 7.0±2.20 | 17.0±3.0 | –10.00±4.32 | –2.31(6) | –20.57 | 0.57 | 0.03*[a] |
| Rhinorrhea | 8.0±4.0 | 4.5±0.5 | 3.50+4.03 | 0.87(2) | –13.85 | 20.85 | 0.47 |

[a] *One tail t-test ($H_o$ <0) *significant*

**Table 4: Comparisons of Mean Number of Days Required for Clinical Recovery from Commencement Therapy**

| Clinical Conditions | Ivermectin MRT (days) | Lopinavir/r MRT (days) | Difference of two means | t-test (df) | 95% CI of diff of means | | p |
|---|---|---|---|---|---|---|---|
| Complete recovery | 5.29±4.08 | 4.95±3.47 | 0.34±0.87 | 0.39 | –1.4 | 2.07 | 0.75 |
| Fever | 7.76±4.95 | 6.95±3.69 | 0.83±1.61 | 0.52(27) | –2.46 | 4.13 | 0.611 |
| Cough | 7.6±1.23 | 4.8±0.92 | 2.75±1.65 | 1.65(32) | –0.63 | 6.08 | 0.108 |
| Myalgia | 3.5±0.47 | 5.5±0.95 | –2.05±0.98 | –2.05(14) | –4.09 | 0.09 | 0.059 |
| Headache | 4.5±0.50 | 7.0±1.48 | –2.0±2.72 | –0.91(6) | –9.15 | 4.15 | 0.393 |
| Sore throat | 8.0±2.9 | 3.5±1.5 | 4.5±5.35 | 0.83(6) | –8.61 | 17.61 | 0.433 |
| Rhinorrhea | 4.5±0.48 | 4.0±1.0 | 0.5±1.12 | 0.44(2) | –4.31 | 5.31 | 0.695 |

**Table 5: Multivariate Regression for Predictors of Clinical Recovery on Day Five of Drug Therapy among the Clients**

| Variables | Ivermectin Adjusted OR (95%CI) | p | Lopinavir/ ritonavir Adjusted OR (95%CI) | p |
|---|---|---|---|---|
| **Age** | | | | |
| <40* | 1 | | 1 | |
| ≥40 | 0.93(0.05–17.22) | 0.97 | 0.05(0.02–1.12) | 0.06 |
| **Sex** | | | | |
| *Male | 1 | | 1 | |
| Female | 2.50(0.26–24.32) | 0.43 | 2.22 (0.27–17.91) | 0.45 |
| **Ethnicity** | | | | |
| Hausa | 1 | | 1 | |
| Others | 0.79 (0.09–7.02) | 0.83 | 0.41(0.07–2.34) | 0.32 |
| **Occupation** | | | | |
| *Civil servants | 1 | | 1 | – |
| Health care workers | 1 | | 0.12(0.07–2.08) | 0.14 |
| Self employed | 0.65(0.05–8.33) | 0.74 | 1.06 (0.14–8.20) | 0.96 |
| Unemployment | 1.97(0.09–45.34) | 0.67 | 0.02(0.01–0.86) | 0.04 |
| **Education** | | | | |
| *Primary | 1 | | – | – |
| Secondary | 3.3 (0.04–246.68) | 0.58 | 1 | – |
| Tertiary | 2.0(0.05–78.95) | 0.71 | 2.66(0.38–18.51) | 0.32 |
| None | 1 | | 15.92 (0.19–1337.5) | 0.22 |
| **Marital Status** | | | | |
| *Married | 0.95 | 0.97 | 1 | |
| Not currently married | 1 | | 0.28(0.04-2.20) | 0.23 |
| **Place of Treatment** | | | | |
| *Home | 1 | – | 1 | |
| Facility | 1 | | 20.49 (0.78–536.86) | 0.07 |
| **History of Chronic Illness** | | | | |
| Yes | 1 | | 1 | |
| *No | 0.10(0.01–167.41) | 0.07 | 1.28 (0.17–9.63) | 0.81 |

ivermectin regimens could be useful as supportive therapy for COVID -19 mild to moderate cases. The mean symptom recovery time for COVID-19 patients managed with ivermectin was slightly shorter compared with the Lopinavir/ ritonavir regimen. The ivermectin regimen presented with no side effects while some patients on the lopinavir/ ritonavir have mild to moderate side effects. We do not recommend self-medications with this regimen.

## ACKNOWLEDGMENTS

The authors wish to appreciate the the Kaduna state Ministry of Health for the funding support for this research. We also want to acknowledge the World Health Organization, Kaduna office for the logistic support for the Kaduna State Covid 19 Home- based care management team during this survey. We appreciate all frontline health care workers in the state for their commitment to duty and for keeping the records used for this study.

## Conflict of Interest

Nil.

## REFERENCE

1. Sohrabi C, Alsafi Z, O'Neill N. World Health Organization declares global emergency: a review of the 2019 novel coronavirus (COVID-19). *Int J Surg.* 2020; **76:** 71– https://doi.org/10.1016/j.ijsu.2020.02.034.
2. Lu H, Stratton CW, Tang Y-W. Outbreak of pneumonia of unknown etiology in Wuhan, China: the mystery and the miracle. *J Med Virol.* 2020; **92:** 401–402. https://doi.org/10.1002/jmv.25678.
3. Mitjà O, Corbacho-Monné M, Ubals M, Tebe C, Peñafiel J, Tobias A, *et al.* Hydroxychloroquine for early treatment of adults with mild Covid-19: a randomized-controlled trial. *Clinical Infectious Diseases.* 2020 Jul 16.
4. Dalerba P, Levin B, Thompson JL. A Trial of Lopinavir-Ritonavir in Covid-19. *The New England Journal of Medicine.* 2020; **382**.
5. Hoffmann M, Schroeder S, Kleine-Weber H, Müller MA, Drosten C, Pöhlmann S. Nafamostat mesylate blocks activation of SARS-CoV-2: new treatment option for COVID-19. Antimicrobial agents and chemotherapy. 2020 Apr 20.
6. Malone RW, Tisdall P, Fremont-Smith P, Liu Y, Huang XP, White KM, Miorin L, Moreno E, Alon A, Delaforge E, Hennecker CD. COVID-19: famotidine, histamine, mast cells, and mechanisms. *Frontiers in Pharmacology.* 2021: 12.
7. Zhou Q, Chen V, Shannon CP, Wei XS, Xiang X, Wang X, Wang ZH, Tebbutt SJ, Kollmann TR, Fish EN. Interferon-α2b Treatment for COVID-19. *Frontiers in Immunology.* 2020; **11:** 1061.
8. Chen L, Xiong J, Bao L, Shi Y. Convalescent plasma as a potential therapy for COVID-19. *The Lancet Infectious Diseases.* 2020; **20:** 398–400.
9. Marovich M, Mascola JR, Cohen MS. Monoclonal antibodies for prevention and treatment of COVID-19. *JAMA.* 2020; **324:** 131–132.
10. Echeverría-Esnal D, Martin-Ontiyuelo C, Navarrete-Rouco ME, De-Antonio Cuscó M, Ferrández O, Horcajada JP, Grau S. Azithromycin in the treatment of COVID-19: a review. *Expert review of Anti-infective Therapy.* 2021; **19:** 147–163.
11. Shi J, Xiao Y, Zhang Y, Geng D, Cong D, Shi KX, Knapp RJ. Challenges of drug development during the COVID 19 pandemic: Key considerations for clinical trial designs. *British Journal of Clinical Pharmacology.* 2021; **87:** 2170–2185.
12. Rizzo E. Ivermectin, antiviral properties and COVID-19: a possible new mechanism of action. *Naunyn-Schmiedeberg's Archives of Pharmacology.* 2020; **393:** 1153–1156.
13. Campbell WC, Fisher MH, Stapley EO, Albers-Schonberg G, Jacob TA. Ivermectin: a potent new antiparasitic agent. *Science.* 1983; **221:** 823–828.

14. Mastrangelo E, Pezzullo M, De Burghgraeve T, Kaptein S, Pastorino B, Dallmeier K, *et al.* Ivermectin is a potent inhibitor of flavivirus replication specifically targeting NS3 helicase activity: new prospects for an old drug. *J Antimicrob Chemother.* 2012; **67:** 1884–1894. 11
15. Varghese FS, Kaukinen P, Gläsker S, Bespalov M, Hanski L, Wennerberg K, *et al.* Discovery of berberine, abamectin and ivermectin as antivirals against chikungunya and other alphaviruses. *Antiviral Res.* 2016; **126:** 117–124.
16. Rajter JC, Sherman MS, Fatteh N, Vogel F, Sacks J, Rajter JJ. ICON (Ivermectin in COvid Nineteen) Study: use of ivermectin is associated with lower mortality in hospitalized patients with COVID-19. Available at SSRN 3631261. 2020 Jun 16.
17. Caly L, Druce JD, Catton MG, Jans DA, Wagstaff KM. The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 *in vitro*. *Antiviral Res.* 2020; **178:** 104787.
18. Alom M, Murshed R, Bhiuyan E, Saber S, Alam R, Robin R. A Case Series of 100 COVID-19 Positive Patients Treated with Combination of Ivermectin and Doxycycline. *J Bangladesh Coll Phys Surg.* 2020; **38:** 10–15.
19. Rahman M, Iqbal S, Islam M, Niaz M, Hussain T, Siddiquee T. Comparison of Viral Clearance IMC J Med Sci. 2020; 14: 002 7/8 between Ivermectin with Doxycycline and Hydroxychloroquine with Azithromycin in COVID-19 Patients. *J Bangladesh Coll Phys Surg.* 2020: **38.**
20. Babalola OE, Bode CO, Ajayi AA, Alakaloko FM, Akase IE, Otrofanowei E, Salu OB, Adeyemo WL, Ademuyiwa AO, Omilabu SA. Ivermectin shows clinical benefits in mild to moderate Covid19 disease: A randomised controlled double blind dose response study in Lagos. medRxiv. 2021 Jan 1
21. Gandhi RT, Lynch JB, Del Rio C. Mild or moderate Covid-19. *New England Journal of Medicine.* 2020; **383:** 1757–1766.
22. Nigeria Centre for Diseases Control. Patient hand book for home-based care in Nigeria.covid19.ncdc.gov.ng/media/files/COVID-19PatientsBookforHomebasedCare.pdf. pg 1-32. Accessed 12 Dec 2021.
23. Rawizza HE, Chaplin B, Meloni ST, Darin KM, Olaitan O, Scarsi KK, *et al.* Accumulation of protease mutations among patients failing second-line antiretroviral therapy and response to salvage therapy in Nigeria. *PLoS One.* 2013; **8:** e73582.
24. Araoye MO. Research Methodology with Statistics for Health and Social Science, Ilorin:Nathadex Limited; 2007. p. 119–122.
25. Horby PW, Mafham M, Bell JL, Linsell L, Staplin N, Emberson J, *et al.* Lopinavir-ritonavir in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. *The Lancet.* 2020; **396:** 1345–1352.
26. Podder CS, Chowdhury N, Sina MI, Haque WM. Outcome of ivermectin treated mild to moderate COVID-19 cases: a single-centre, open-label, randomised controlled study. *IMC Journal of Medical Science.* 2020; **14:** 1–8.
27. Bowale A, Abayomi A, Idris J, Omilabu S, Abdus-Salam I, Adebayo B, *et al.* Clinical presentation, case management and outcomes for the first 32 COVID-19 patients in Nigeria. *The Pan African Medical Journal.* 2020: 35(2).
28. Ibrahim OR, Suleiman BM, Sanda A, Oloyede T, Bello SO, Bello UI, Yahaya S, Dawud A, Bashir SS. COVID-19 in children: a case series from Nigeria. *The Pan African Medical Journal.* 2020: 35(53).
29. Ilesanmi OS, Afolabi A. A scope review on home-based care practices for COVID-19: What Nigeria can learn from other countries. *Ibom Med J.* 2021; **14:** 1–9.
30. Chukwuemeka A, Adeyemi O, Dolapo A, Chima M. Evaluation of the frequency of use of herbal drugs with concomitant administration of highly active antiretroviral therapy and its effect on medication adherence in two health care facilities in south western Nigeria. *Journal of AIDS and HIV Research.* 2017; **9:** 8–16.
31. Kory P, Meduri GU, Varon J, Iglesias J, Marik PE. Review of the Emerging Evidence Demonstrating the Efficacy of Ivermectin in the Prophylaxis and Treatment of COVID-19. *American Journal of Therapeutics.* 2021; **28:** e299.
32. Roy R, Pattadar C, Raj R, Agarwal N, Biswas B, Majhi PK, *et al.* Ivermectin as a potential treatment for mild to moderate COVID-19–a double blind randomized placebo-controlled trial. MedRxiv. 2021 Jan 1.
33. Osborne V, Davies M, Lane S, Evans A, Denyer J, Dhanda S, *et al.* Lopinavir-ritonavir in the treatment of COVID-19: a dynamic systematic benefit-risk assessment. *Drug Safety.* 2020; **43:** 809–821.
34. Osikomaiya B, Erinoso O, Wright KO, Odusola AO, Thomas B, Adeyemi O, *et al*. 'Long COVID': persistent COVID-19 symptoms in survivors managed in Lagos State, Nigeria. *BMC Infectious Diseases.* 2021; **21:** 1–7.
35. Gao YD, Ding M, Dong X, Zhang JJ, Kursat Azkur A, Azkur D, *et al.* Risk factors for severe and critically ill COVID 19 patients: a review. *Allergy.* 2021; **76:** 428–455.
36. Li S, Jiang L, Li X, Lin F, Wang Y, Li B, *et al*. Clinical and pathological investigation of patients with severe COVID-19. *JCI insight.* 2020: 5(12).
37. Li L, Sun W, Han M, Ying Y, Wang Q. A Study on the Predictors of Disease Severity of COVID-19. Medical Science Monitor: International Medical Journal of Experimental and Clinical Research. 2020; **26:** e927167–1.