



RESEARCH ARTICLE



Clinical Outcome Of Corona Virus Disease-19 Patients In An Infectious Disease Center, Olodo, Ibadan, Oyo State, Nigeria

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Abstract

Introduction: Corona Virus Disease (COVID-19) is a severe respiratory infection caused by the newly emerged Severe Acute Respiratory Syndrome-Corona Virus-2 (SARS-CoV-2). Globally, mortality from this disease is high and infection sequelae can result in long-term illness. COVID-19 is a new disease and the best way to manage patients remains uncertain, particularly in resource-limited settings. An evaluation of the clinical outcome of COVID-19 cases managed at the Infectious Disease Center (IDC), Olodo in Ibadan, Oyo State, Nigeria over a period of eighteen weeks was carried out. This center (IDC), Olodo was designated by the Oyo State COVID-19 Task Force to manage mild to severe cases of COVID-19 in Oyo state.

Materials and Methods: A treatment protocol designed by the Case Management Team of the Oyo State COVID-19 Task Force was adopted. The protocol included classifying patients based on clinical signs and symptoms and qPCR Cycle Threshold (CT) values, treating with a cocktail that included chloroquine or hydroxychloroquine, zinc, vitamins C and D and or antibiotic(s) as indicated. Physiotherapy and nutritional support for these patients were also considered as priority.

Results: During the period of study, 3,119 individuals tested for SARS-CoV-2 infection in Oyo State received a positive result and 310 (9.9%) were admitted to the IDC, Olodo, Ibadan. The average duration of admission was 10.22 ± 3.48 days, with 22(7.1%) patients requiring respiratory support by way of supplemental oxygen using re-breather bags and Continuous Positive Airway Pressure (CPAP) was used on one patient. No mortality was recorded among the 310 patients managed according to the protocol at the IDC, Olodo, Ibadan during the study period.

Conclusion: This clinical outcome suggests that the management protocol used in our center is effective and thus deserves evaluation for use in resource poor settings.

Keywords: COVID-19 pandemic, Management protocol, Oyo State.

1 | INTRODUCTION

The Severe Acute Respiratory Syndrome-Corona Virus-2 (SARS-CoV-2) responsible for the coronavirus disease 19 (COVID-19)

pandemic is a new virus of the Coronaviridae family in the Nidovirales order. This group of virus, including the Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) and the Middle East Respiratory Syndrome (MERS) Coronavirus, has been shown to cause acute lung injury (ALI) and Acute Respiratory Distress Syndrome (ARDS) resulting in respiratory failure and death in some patients. The signs and symptoms of SARS-CoV-2 viral infection may be similar to those of influenza and seasonal allergies and in the tropical setting may mimic common ailments including malaria (Yang et al., 2020 and Shereen et al., 2020).

Human to human transmission of coronavirus occurs via droplets or aerosol and the virus uses spike proteins to attach to the angiotensin-converting enzyme 2 (ACE-2) on the surface of normal cells. Conformational change in the spike protein facilitates viral envelope fusion with the cell membrane. Once within the cell, the virus initiates replication, ultimately producing more viruses that infect other cells (Shereen et al., 2020). SARS-CoV-2 viral infection activates antiviral immune responses that are often accompanied by marked and uncontrolled pro-inflammatory cytokines overdrive also referred to as cytokine storm (Yang et al., 2020).

Severe SARS-CoV-2 infection has been found to cause lymphopenia which can arise because of ACE-2 receptor expression on lymphocytes permitting viral entry and consequent lymphocyte cell death. SARS-CoV-2 infection is also accompanied by increase serum lactic acidemia, a condition that is also known to inhibit lymphocyte proliferation. Subsequently, there is associated lymphocyte, granulocyte and monocyte dysfunction, and a high neutrophil-to-lymphocyte ratio, in severe SARS-CoV-2 infection (Yang et al., 2020). Severe and critically ill- COVID-19 cases exhibits severe pneumonia and metabolic disorders developing into acute respiratory distress syndrome, multiple organ dysfunctions, septic shock and death (Huang et al.,

2020). Some studies suggested that the immunopathogenesis after SARS-CoV-2 infection has been linked to the development of the disease into severe cases (Qin et al., 2020).

No known specific and effective drugs or vaccines have been developed to manage or prevent COVID-19 (Wu et al., 2020) thus many drugs have been evaluated in its management and further search continues. National Institute of Health (NIH) and Food and Drug Administration (FDA) recommended, remdesivir and convalescent blood products as promising potentials for COVID-19 treatment apart from the uses of chloroquine, hydroxychloroquine, favipiravir, ivermectin, and colchicines (Hossen et al., 2020). Usage of another antihelminthic drug (apart from ivermectin) was also proposed (Onifade and Arinola, 2020). Tocilizumab was deemed as adjunctive therapy for patients with cytokine release syndrome while baricitinib and ruxolitinib were reported to have additive immunosuppressive effect (Hossen et al., 2020). Santos et al (2020) reported that therapeutics for COVID-19 includes camostatmesylate, remdesivir, favipiravir, tocilizumab, baricitinib, convalescent plasma, and humanized monoclonal antibodies.

Oyo State, in the South Western region of Nigeria, has a population of about seven million people. The index case of coronavirus infection in the state was reported in Ibadan, the state capital on 21st March 2020 and the patient was temporarily isolated and managed at the Agbami Chest Clinic in Jericho, Ibadan, Nigeria. Three other patients who tested positive for the viral infection were subsequently transferred to the Infectious Disease Center (IDC) at Olodo, Ibadan on 27th April 2020 when this designated center was commissioned. This fully furnished center was established by the Oyo State Government to provide clinical care for residents of the state who test positive for SARS-CoV-2 virus and were symptomatic enough to warrant institutional care as well as some asymptomatic

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patients whose home environments were not conducive for the approved self isolation policy of the Nigerian Center for Disease Control (NCDC). Oyo State has two NCDC-approved laboratories that conduct qPCR testing and release results of testing within 48 hours as mandated by the Oyo State Task Force on COVID-19. At the time of reporting these clinical outcomes, Oyo State, Nigeria had conducted 15,733 tests of which 3,119 were positive for the virus with 1,952 recoveries and 37 deaths. None of the deaths was recorded at the IDC, Olodo and this may be a pointer to the relative effectiveness of management protocol being practiced in this center and this may be worth reviewing particularly in other resource-limited settings.

Methodology

Over a period of 18 weeks, three hundred and ten (310) consecutive COVID-19 patients were managed as in-patients at the Infectious Disease Center, Olodo in Ibadan. On admission, their SARS-CoV-2 qPCR Cycle Threshold (CT) values were documented based on assays for the N-gene and ORFlab genes, baseline laboratory investigations were carried out including electrolytes and urea, liver function test and blood film (thick and thin films) for malaria parasite. Co-morbidities were also documented and patients with severe respiratory difficulties as defined by oxygen saturation (SpO₂) of less than 90% were managed in the 10-bed Intensive Care Unit (ICU). For all other patients, disease severity classification was a determinant of CT values, clinical signs and symptoms, rather than symptoms alone. As the clinical conditions of the ICU patients improved, and the CT values increased, these patients were weaned from the ICU to a High Dependency Unit (HDU) and finally the general male and female wards, from where patients were discharged. During the study period, the protocol for discharge as laid by the NCDC was that the patients should have two negative qPCR results. This has since changed in line with best global practices and international consensus. A unilateral flow was maintained for patients and another

parallel flow was established for the staff as part of the Infection Prevention and Control protocols. Whilst on admission, patients were commenced on a cocktail of medications; oral chloroquine or hydroxychloroquine for three days; oral zinc for three weeks; azithromycin for three days; Vitamin C for three weeks and Vitamin D was added to the protocol in patients with respiratory symptoms along with those whose oxygen saturation falls below 95% in room air. Chest physiotherapy was commenced and antibiotics listed in the antibiogram for community pneumonia in Nigeria was administered via the intravenous route for a minimum of 48 hours (and later changed to oral medications) if patients had clinical features of chest infection.

Subcutaneous enoxaparin (Clexane) 40 mg daily or twice daily and dexamethasone with doses ranging from 6mg daily to 10mg depending on the weight of the patient were added to the regime of medications in patients with lung infiltration on plain radiograph or on computerized tomography of the chest. All the patients were well hydrated and served high protein diet except when contraindicated. In addition, the physiotherapist carried out breathing exercises, conducted physical workout and aerobic exercises for patients twice weekly whilst indoor games were provided as the needs arose. Twenty two patients requiring supplemental oxygen were managed with re-breather bags and CPAP mask but no patient required mechanical ventilation although the center currently has two mechanical ventilators and three CPAP machines.

Medical staff at the center had pre-exposure prophylaxis comprising oral chloroquine for three days or hydroxychloroquine for three days; zinc tablet for three weeks; azithromycin three days and vitamin C tablet for three weeks. The medical staffs were also required to work on a one-week-on and one-week-off shift duty and were accommodated in designated hotels without contact with their families during the time that they were on duty and two weeks after completing their shifts.

Results

A total of three hundred and ten (310) patients with a median age of 36 years with ages ranging from 2 years to 95 years were managed at the center over an eighteen-week period. More than half of the patients (53.9%) were aged 21 to 40 years with 1% of the cases aged >80 years. There were more males (66.1%) among the patients than females (33.9%) (Table 1). The dosage of vitamin D (1000 iu), vitamin C (1000 iu), Zn (20mg), azithromycin, hydroxychloroquine or chloroquine as given to COVID-19 patients and medical staff at the center is presented in Table 2. In Table 3, 60.5% of the patients had symptoms especially among the 21-40years age group (50.3%). Only 35 (17.9%) patients presented with only one symptom whilst 20.5% had three symptoms. The five commonest symptoms in

descending order were; fever (18.4%), headache (18.1%), anosmia (10.9%), agenuia (10.1%) and cough (9.1%) in Table 4. One hundred and three (103) patients had co-morbidities as follows: only hypertension in 69(53.9%), only peptic ulcer disease in 23(18.0%) whilst 11(8.6%) had only diabetes mellitus. Combinations of at least two of these conditions were present in 25 out of 103 patients (Table 5). The mean length of stay at the isolation center was 10.22 ± 3.48 days whilst the mean CT value on admission was 30.42 ± 5.49. There was a significant negative association between the length of stay and the CT value on admission (Table 6). In addition, patients with co-morbidities stayed on admission longer even if they were admitted with lower CT values (Table 7).

Table 1: Socio-Demographic presentation of COVID-19 patients at IDC, Olodo, Ibadan, Nigeria.

Socio-Demographics	Frequency	Percentage
Age Group (Mean = 36.00, Range (2 – 95 years)		
1 - 20 years	25	8.1
21 - 40 years	167	53.9
41 - 60 years	82	26.5
61 - 80 years	33	10.6
≥ 81years	3	1.0
Gender		
Males	205	66.1
Females	105	33.9

Table 2: Medication Used Among COVID-19 patients and Pre-Exposure Prophylaxis for Un-Infected Medical Staff at IDC, Ibadan, Nigeria.

Medications	Groups	
	COVID-19 Patients	Uninfected Medical Staff
Vitamin D (1,000 iu)	1,000 iu twice daily for 3 weeks	1,000 iu daily for 3 weeks
Vitamin C (1,000 mg)	1,000 mg twice daily for 3 weeks	1,000 mg daily for 3 weeks
Zn (20mg)	100 mg daily for 3 weeks	20 mg daily for 3 weeks
Azithromycin	500 mg daily for 3 days	500 mg daily for 3 days
Hydroxychloroquine	400 mg on day 1 and 200 mg daily for 3 more days	400 mg on day 1 and 200 mg daily for 3 more days
Chloroquine (As an alternative to Hydroxychloroquine)	500 mg on day 1 and 250 mg daily for 3 more days	500 mg on day 1 and 250 mg daily for 3 more days

Table: 3 Relationship between Symptoms and Age of COVID-19 Patients at the IDC, Olodo, Ibadan, Nigeria.

	Symptom		χ^2	p-value
	No	Yes		
All patients irrespective of age group	90 (78.3)	118 (60.5)		
Age Group			12.915	0.012*
1 - 20 years	15 (13.0)	10 (5.1)		
21 - 40 years	69 (60.0)	98 (50.3)		
31 - 60 years	21 (18.3)	61 (31.3)		
61 - 80 years	9 (7.8)	24 (12.3)		
≥ 81 years	1 (0.9)	2 (1.0)		

Table 4: Percentages of Symptoms Number and Types Among COVID-19 Patients at the IDC, Olodo, Ibadan, Nigeria

Number of Symptom	Percentages	Types of Symptoms	Percentages
1	17.9	Fever	18.4%
2	14.9	Headache	18.1%
3	20.5	Anosmia	10.9%
4	19.5	Agenusia	10.1%
5	16.4	Cough	9.1%
6	7.2		
7	3.1		
11	0.5		

Table 5: Frequencies and Percentages of Co-morbidity Types Among COVID-19 Patients at the IDC, Olodo, Ibadan, Nigeria.

Co-morbidity types	Frequency	Percentages
Hypertension	69	53.9%
Peptic Ulcer Disease	23	18.0%
Diabetes mellitus	11	8.6%
Total	103	

Table 6: Correlation of Length of stay and CT Value Among COVID-19 Patients in IDC, Olodo, Ibadan, Nigeria.

			Mean
Length of admission	2.00 days	3.00-21.00 days	10.22 ± 3.48
C _T value on admission	11.58	44.33	30.42 ± 5.49
Test of Association			
$r = -0.213$, $p - value = 0.001*$			

Table 6: Correlation of Length of stay and CT Value Among COVID-19 Patients in IDC, Olodo, Ibadan, Nigeria.

	Co-Morbidity	Mean \pm SD	Mean Difference	T	p-value
Length of admission	Yes	10.83 \pm 3.89	0.926	2.212	0.028*
	No	9.91 \pm 3.21			
C _T value on admission	Yes	29.09 \pm 5.92	-1.930	-2.516	0.013*
	No	31.02 \pm 5.19			

Discussion

Inflammation, renal dysfunction, respiratory burst, immune dysregulation and accumulation of immune complexes are common in Nigerian COVID-19 patients (Arinola, 2021; Arinola et al., 2021a-d; Arinola et al., 2020; Akinwumi et al., 2021; Arinola et al., 2022). The present study shows that COVID-19 patients in IDC, Olodo were mostly males, mainly between the 21-40years age range, spent between 2-21days on admission with few co-morbid conditions. Also, there was no mortality recorded during the eighteen week period spanning 27th April 2020 and 24th August 2020. These corroborates our earlier reports (Arinola et al., 2020) which emphasised the impact of age, occupation and gender on incidence or case fatality of COVID-19 and that low mortality of COVID-19 patients in the IDC may be related to effective management, non-fatal nature of SAR-COV-2 among IDC patients or mild to severe form of COVID-19 disease when admitted (Arinola et al., 2020).

The treatment options for COVID-19 are largely supportive as there is no universally agreed protocol of care. Therapeutics targeting the spike protein attachment to human cells and replication of SARS-CoV-2 has generated a lot of interest and this is the mechanism of action of remdesivir either used singly or in combination with chloroquine. Monoclonal antibodies targeting the spike protein receptor binding domain (RBD) are undergoing trials as well as other therapeutics (Yang et al., 2020 and Shereen et al., 2020). It is important to note that, with the exception of the repurposed drugs, most of these experimental therapies will be out of reach of Nigerian patients even when they receive approval. Therefore, careful evaluation of repurposed drugs, including chloroquine or hydroxychloroquine and vitamins and zinc

supplementation used at the Oyo State IDC is important. Unfortunately, few clinical trials are currently underway in Nigeria and most facilities are yet to share observational data such as we present in this report. The repurposing of chloroquine and hydroxychloroquine for treatment of SARS-CoV-2 infection was premised on the anti-inflammatory properties of these antimalarial which may be beneficial to the patients if there is underlying malaria parasitaemia and also to reduce pre-empted occurrence of inflammatory cytokine storm which is associated with SARS-Cov-2 infection (Yang et al., 2020).

Various reports in the early phase of the pandemic showed that a number of existing drugs could inhibit SARS-CoV-2 replication in vitro, including chloroquine and hydroxychloroquine (two established anti-malarial drugs which share similar chemical structures and mechanisms of action), as well as azithromycin and ivermectin spawned interest in repurposing these drugs at various treatment centers including the IDC, Olodo, Ibadan. Whilst initial clinical trial data has not revealed a role for these compounds in preventing or treating COVID-19, other trials remain in progress and very few trials are being conducted in Africa where the pandemic's trajectory is markedly different. These medications were not used in the context of a trial and the positive outcomes in this high-risk disease, encouraged their continued use during the 18-week period. The fact that the patients tolerated these medications without a risk of bacterial and malarial super-infection needs further evaluation. Meo et al (2020) proposed that chloroquine and hydroxychloroquine are beneficial in the management of COVID-19 and highlighted specific mechanisms of action, viz: inhibition of

the receptor binding by the virus, inhibition of membrane fusion by the virus and immune modulation leading to a decrease in cytokine release.

The use of Vitamin D in the management of COVID-19 patients hinged on the autocrine function and has been supported by a single center, retrospective cohort study which found that persons who are deficient in Vitamin D at the time of testing were more likely to test positive for COVID-19 (Onifade and Arinola, 2020). A recent study concluded that vitamin D intoxication is common among Nigerian patients with COVID-19 and the vitamin D intoxication is associated with low plasma hsCRP level. There is the need for public enlightenment on the dangers inherent in vitamin D supplement abuse in Nigerians (Onifade et al., 2022).

Immuno-modulatory function of Vitamin C depends on its requirement for collagen biosynthesis, maintenance of epithelial integrity, chemotaxis and phagocytosis (Arinola and Edem, 2020; Sureda et al., 2013). Vitamin C has a highly effective antioxidant capacity, thus protecting important biomolecules from damage by oxidants generated during normal cell metabolism (Alvarado et al., 2006). Zinc affect the number and function of immune cells (macrophages, neutrophils, dendritic cells, mast cells, T cells and B cells) (Haase and Rink, 2007). Zinc also play essential roles in the signaling and inflammatory output of monocytes and macrophages, including activation of mitogen-activated protein kinase and NF- κ B (Haase and Rink, 2007), reduction of lysosomes integrity (Siebenlist et al., 1994), activation of NLRP3 inflammasome (Brieger et al., 2013), induction of IL-1 β secretion by macrophages (Summersgill et al., 2014), reduction of IL-6 and TNF- α in human monocytes (Mayer et al., 2014).

Activation of the immune system results in increased generation of reactive oxygen species which is neutralized by Zn (Arinola and Edem, 2020b). Immunomodulatory and anti-inflammatory functions of vitamin D, vitamin C and Zn makes them appropriately supportive in the management of COVID-19 patients.

In a resource poor settings lacking access to novel therapies and local pharmaceutical industries engaged in drug discovery, exhaustive evaluation of well-tolerated repurposed drugs is probably justified. This is particularly true in the case of chloroquine, hydroxychloroquine and azithromycin for which clinical trial data suggesting a lack of effectiveness in very dissimilar settings and modes of use contrasts with our experience of notably good outcomes and other lines of evidence pointing to the contrary (Yang et al., 2020; Chowdhury et al., 2020; Boulware et al., 2020). As many trials that could be informative are still in progress, the case management team of the Oyo State COVID-19 Task Force maintained its consensus for continued use of these two anti-malarial medications for persons with the coronavirus infection along with other medications aimed at improving the immune systems of the patients, pending further review. While there is lack of clinical trial or comparator data, the use of a cocktail of chloroquine or hydroxychloroquine, Zinc, vitamin C and vitamin D along with azithromycin, clexane, dexamethasone and the appropriate antibiotic choice made in line with the antibiotic ladder for community pneumonia when required has been associated with full recovery of all patients without any mortality over an eighteen-week period (Joshua et al., 2019; Meltzer et al., 2020). The consensus is therefore that strong evidence will be required to justify altering this affordable cocktail of medication during the pandemic in a resource poor setting while effective and acceptable COVID-19 vaccine is sourced by the government of Nigeria.

Conclusion

A treatment protocol based on prevailing scientific knowledge designed by the Case Management Team of the Oyo State COVID-19 Task Force was adopted in the management of patients with mild and severe diseases at the first Oyo State Infectious Disease Center at Olodo, Ibadan from April, 2020.

The outcome of care over the initial 18 weeks is impressively strong. In a resource poor setting, this protocol of supportive care may be considered along with the other preventive measures until such time when accessible therapies backed by strong evidence are available for treating COVID-19 patients. With the availability of vaccines in the developed countries, it is hoped that sub-Saharan Africa will soon benefit from this scheme.

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Conflict of Interest: None

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