Original Research Article

Lessons Learnt from the Management of Severe COVID-19 Disease in a 93-year-old with Chronic Co-Morbidities at a resource-constrained Centre in Nigeria – A Retrospective Single Case Study

Abstract

Introduction: Severe COVID-19 infection is associated with significant mortality in the elderly. This iseven more so, when the elderly patient with the disease also has multiple chronic co-morbidities, and is resident in a resource-constrained area.

Aims/Objectives: To outline management strategies employed, and important lessons learnt from the successful management of a case of severe COVID-19 disease in a 93-year-old with chronic co-morbidities in a resource-limited setting.

Methods: We utilized a simple COVID-19 severity categorization algorithm on presentation, to assign the index patient to the appropriate COVID-19 disease severity class and subsequently employed patient's serial, weekly clinical and laboratory parameters to guide a multi-specialty management protocol.

Results: A 93-year-old man was referred to a tertiary hospital in Enugu during the second wave of the COVID-19 pandemic, with a 5-day-history ofhigh grade fever, severe fatigue, and altered sensorium. He had been living with diabetes for 48years; recently had worsening glycemic control, and was yet to pass urine in the previous 12hours.He was also being managed conservatively for prostate carcinoma.Examination revealed signs of severe pneumonia and he was drowsy, dehydrated, and had asterixis. A diagnosis of acute kidney injury from septicemia, following community acquired pneumonia and possibly urinary tract infection was made, with COVID-19 infection as a differential.Samples were collected for laboratory investigations while he was recommended for intensive care unit admission for further care. Para-enteral broad

spectrum antibiotics, intravenous fluid therapy, intranasal oxygen therapy, basal-bolus-insulin-regimen, and anti-coagulation prophylaxis were instituted. Following laboratory investigation results which included a positive COVID-19 test (clinically categorized as severe disease), severe systemic inflammation, evidence of uro-tractinfection, intravascular thrombosis and severe renal impairment, the Nephrology, Infectious disease, Urology teams were invited to co-manage the patient alongside the Endocrinologists. After 27days of collaborative care, patient was discharged with resolution of his symptoms and signs.

Conclusion: Multi-specialty collaborative care improves patients' outcome even in the face of severe COVID-19 with associated co-morbidities in elderly patients. Severity stratification ensures life-saving timely care for severe COVID-19 disease.

Keywords: Lessons learnt; COVID-19; Severe COVID-19; Nigeria.

1.0 Introduction

The severe acute respiratory syndrome coronavirus disease 2, - SARS-CoV-2 now called COVID-19 disease, which causes (in addition to other systemic symptoms) a severe acute respiratory syndrome, was declared a pandemic by the World Health Organization (WHO) in March 2020, barely four months after it was first reported [1].The SARS-Cov-2 is an enveloped single-stranded, positive-sense RNA virus of the *Coronaviridae* family and genus *Betacoronavirus*, with four main structural proteins (surface/spike glycoprotein, membrane glycoprotein, envelope protein and nucleocapsid phosphoprotein) and accessory proteins, as well as 16 non-structural proteins [2]. The binding of the virus to a host cell as well as viral entry into the host cell is mediated by the S-protein [3].

The two sub-units of the S-protein have different functions. The S1 sub-unit contains the viral receptor-binding domain that specifically binds to the peptidase domain of the angiotensin-converting enzyme 2 (ACE 2) while the S2 sub-unit fuses the viral particle to the host cell membrane, releasing its RNA into the host cell and initiating viral replication[3].The median incubation period of the virus was estimated to be 5.1 days, with 97.5% of those infected

developing symptoms within 11.5 days [4]. Common symptoms include – fever, cough, difficulty in breathing, sorethroat, malaise, headache, nausea, vomiting, diarrhea, loss of taste or smell. Individuals with severe disease may present with respiratory failure with severely reduced oxygen saturation, septic shock, thrombotic events and/or multi-organ dysfunction/failure[5], [6].The gold standard for diagnosis of COVID-19 disease is a positive real-time polymerase chain reaction (RT-PCR) [7].

The first case of COVID-19 disease in Nigeria was confirmed in February 2020, and as at November 13 2021, the total number of confirmed cases in Nigeria was 213,127, while the total number of COVID-19-related deaths stood at 2,960[8].

Over time, several factors have been noted to be associated with increased disease severity and heightened morbidity and mortality. For instance, older age (the elderly) and presence of chronic co-morbidities have been consistently found to increase mortality in patients with COVID-19 disease [9-11]. In a resource-limited setting, the clinical outcome/prognosis for such patients is almost always presumed to be quite diredue to the widely-held belief that lack of modern equipment and technologies in these areas, automatically translated to poor clinical outcomes.

Meanwhile studies have shown that early risk categorization of patients leads to better clinical outcomes in the presence of COVID-19 disease and as such, this should be done for every patient presenting to a healthcare facility, with the disease[12,13].

2.0 **Materials and Methods**

2.1 Study setting

Study was conducted at the isolation facility of the UNTH Enugu, a temporary, 20-bedded purpose-built complex (holding area plus main ward), erected and furnished with equipment by the hospital management in the space of one month; just a few weeks after the first case of COVID-19 was confirmed in Nigeria.

2.2 Inclusion criteria

Age ≥ 65 years;COVID-19 sero-positivity using RT-PCR test; COVID-19 disease severity classification on presentation, categorized as severe disease; presence of chronic co-morbidities.

2.3 Exclusion criteria

Patients that do not meet the inclusion criteria.

2.4 Data collection

Clinical and laboratory data were obtained retrospectively. Clinical data was culled from index patient's case file; while theCOVID-19 disease severity classification, as published by Son K. et. al.[12],was adopted for the severity categorization of the index case due to its high specificity, simplicity and ease of application, even in resource-limited settings. Laboratory data was extracted from index case's certified laboratory result forms and additional data was obtained from the virology reference laboratory of the UNTH Enugu.

2.4.1Laboratory data

Laboratory confirmation of COVID-19 disease on presentation, was based on a positive COVID-19-specificreal-time polymerase chain reaction (RT-PCR) test of nasal swab [7]and subsequently, patient's COVID-19 tests were obtained weekly, from serial samples collected from patient. Other laboratory investigations, which were recommended to be collected at least weekly from the patient, included blood film microscopy for presence of malaria parasites, full blood count, markers of acute inflammation, serum electrolytes, serum creatinine and urea, liver enzymes and coagulation studies. Plasma glucose levels were obtained as necessary, sometimes this was done multiple times during a 24-hour period.

3.0 Statistical analysis

Clinical and laboratory data were summarized using simple descriptive analysis, and results were presented in tables and prose as appropriate.

4.0 RESULTS

4.1 Case description

A 93-year-old man was referred to a tertiary hospital in Enugu during the second wave of the COVID-19 pandemic, with a 5-day-history of high grade fever, severe fatigue, and altered sensorium. He had been living with diabetes for 48years; recently had worsening glycemic control, with a random blood glucose of 275g/dl while on insulin therapy, and he was yet to pass any urine in the previous 12hours. He was also being managed conservatively for prostate carcinoma with bladder outlet obstruction prior to this time. Examination revealed signs of severe pneumonia: Respiratory rate - 32breaths/min, pulse - 114beats/min, oxygen saturation - 93%, blood pressure: 90/30mm/Hg. He was drowsy, dehydrated, and had asterixis. A diagnosis of acute kidney injury from septicemia, following community acquired pneumonia and possibly urinary tract infection was made, with COVID-19 infection as a differential. Blood samples were collected immediately for laboratory investigations and few hours later, his sample returned positive for COVID-19 disease using the RT-PCR test and subsequent disease categorization placed him under severe disease. He was promptly recommended for intensive care unit admission for continuing care. Para-enteral broad spectrum antibiotics, intravenous fluid therapy, intranasal oxygen therapy, basal-bolus-insulin-regimen, and anti-coagulation prophylaxis were instituted. Other laboratory investigation resultsconfirmed severe systemic inflammation, evidence of urinary tract infection, intravascular thrombosis and severe renal impairment. A combined team of specialists including the Nephrology, Infectious disease, Urology and later, Plastic Surgery (for pre-sacral pressure ulcers) teams were invited to co-manage the patient, alongside the Endocrinologists. After 27days of collaborative care, patient was discharged home (with scheduled home visits), with a negative RT-PCR COVID-19 test, in addition to resolution of his symptoms and signs.

4.2 COVID-19 Disease Severity Categorization

The clinical COVID-19 disease severity categorization promptly utilized for the index case on presentation is as shown in table 1, while table 2 shows the patient's clinical parameters on presentation and severity score.

Table 1. COVID-19 Severity Classification

CRITERIA		SCORE*		
	0	**1**	**2**	**3**
PULSE(beats/min)	51-100	41-50 OR 101-110	<40 OR 111-130	≥ 131
SYSTOLIC BP (mmHg)	101-199	81-100	71-80 OR ≥ 200	≤ 70
Resp. rate (breaths/min)	9-14	15-20	≤ 8 OR 21-29	≥ 30
Body Temp (^{0}C)	36.1-37.4 Normal	35.1-36.0 OR ≥ 37.5	≤ 35.0	Not applicable
Level of Consciousness	Normal	Voice reaction	Pain reaction	Non-reaction

*Score of 0-4 (mild); 5-6 (moderate); ≥ 7 (severe); need for renal replacement treatment or extracorporeal oxygenation (very severe/critical) [12].

Table 2. COVID-19 Severity score for patient on presentation.

CRITERIA	SCORE			
	0	**1**	**2**	**3**
PULSE(beats/min)	X	**108**	X	X
SYSTOLIC BP (mmHg)	X	**90**	X	X
Resp. rate (breaths/min)	X	X	X	**30**
Body Temp (^{0}C)	X	**38.4**	X	X
Level of Consciousness	X	X	**Pain reaction**	X
Total Score	**8 = Severe COVID-19 disease.**			

4.3 Patient's weekly clinical parameters

Patient's weekly clinical parameters are summarized in table 3 below.

Table 3. Patient's weekly clinical parameters

VARIABLE	TIME				
	Presentation	**Week 1**	**Week 2**	**Week 3**	**Week 4**
Temp.^{0}C (Highest/Lowest)	38.4	38.6/35.8	38.1/37	36.6/34.2	36.8/35.2
Pulse rate (mean)	108	101	104	96	92
Resp. rate (mean)	30	26	28	20	22
Oxygen saturation (mean SPO_2)	92*	95.5*	97*	98 (RA)	98 (RA)
Mean Systolic BP (mmHg)	90	140	154	126	114
Mean Diastolic BP (mmHg)	30	75	83	67	65
Glaxo Coma Score (lowest Vs highest)	9/15	10/15 Vs 14/15	9/15 Vs 13/15	14/15 Vs 15/15	15/15
Fatigue	+++	++	++++	+	-
Lung crepitations	+++	+++	++	+	-
Naso-gastric tube feeding	present	present	present	nil	nil
Mean Urine output/24hrs(mls)	< 50mls	<500	2650	2900	2780
Asterixis	present	present	nil	nil	nil

*Intra-nasal oxygen in-situ. RA – Room air, at sea level.

4.4 Patient's weekly laboratory parameters

A detailed summary of patient's weekly laboratory parameters is as shown in table 4.

Table 4. Patient's Weekly Laboratory Parameters

VARIABLE	TIME				
	Presentation	**Week 1**	**Week 2**	**Week 3**	**Week 4**
COVID-19 test.	Positive	Positive	Positive	-	Negative
Highest RBG (mean) mg/dl	275	475 (188.3)	349 (254.8)	357 (264)	250 (171)
Total WBC (x 10^9/L)	20.4	-	-	3.5	-
Neutrophils (%)	92	-	-	57	-
Monocytes	2.5	-	-	20.5	-
Lymphocytes	4.5	-	-	14.5	-
Platelets	191	-	-	228	-
Hb	8.7	-	-	11.1	-
MCV(fL)	68.6	-		80.0	-
ESR(mm/1st hr)	135	130	-	73	-
D-dimer (ng/ml)	-	1160.63	-	-	-
Na^+	134	143	142	146	141
HCO_3^-	19	15	14	20	22
Urea	12.6	17.6	15.2	8	6.8
Creatinine	250	301	174.1	145	128
Mean eGFR(ml/min/1.73m^2)	25.5	20.6	38.7	47.8	55.1
Blood culture	-	Nil bacterial growth	X	Nil Bacterial growth	X
Catheter tip M/C/S	-	-	Candida Spp.	Nil growth	X

LFT	-	Elevated transaminases	-	-	-

RBS – Random blood glucose; WBC – White blood cells; Hb – Haemoglobin; MCV – Mean corpuscular volume; ESR – Erythrocyte sedimentation rate; eGFR – Estimated glomerular filtration rate; M/C/S – Microscopy, culture and sensitivity; LFT – Liver function test.

5.0 Discussion

The COVID-19 disease, which clinical presentation ranges from asymptomatic to critical illness,and which symptoms and radiological imaging can mimic several other acute respiratory diseases like community-acquired severe pneumonia [14], and melioidosis [15],results in significant mortality in the elderly, and this is even more so, with the presence of multiple chronic co-morbidities. The index patient, quite advanced in age, with a history of type 2 diabetes spanning more than four decades, and being managed conservatively for prostate malignancy, represents the typical elderly patient with multiple co-morbidities, presenting with severe COVID-19 disease and presumed potential high mortality from the disease.

However, utilizing a simple but effective COVID-19 disease severity classification, as published by Son et. al.[12], enabled prompt categorization of index patient as severe COVID-19 disease, hence, ensuring that appropriate measures were taken quickly enough to ensure optimal clinical outcomes.This COVID-19 clinical severity scoring tool, employs the measurement of five clinical variables, to which scores ranging from 0 to 3 are assigned incrementally to each, as severity of disease increases. Subsequently, the individual scores are added together to arrive at the final severity score for the patient (Table 1). On presentation, the index case had a pulse rate of 108 beats/min (score 1); systolic blood pressure of 90mmHg (score 1); respiratory rate of 30 breaths/min (score 3); body temperature of 38.4^{O}C (score 1); and consciousness level represented by pain reaction (score 2), giving him a total score of 8. In addition, patient did not require renal replacement therapy and did not need extracorporeal oxygenation hence, he was categorized as having severe COVID-19 disease (table 2).

The period spanning the end of the first week, to the first half of the second week witnessed a deteriorationin patient's clinical state as evidenced by a drop in the GCS, from a high of 14/15 attained a few days, post-admission in the first week, to 9/15 by the beginning of the second

week. In addition to worsening respiratory distress with a peak respiratory rate of 30breaths/min and a peak pulse rate of 121beats/min, there was also the presence of profound fatigue, during this same period. Likewise, the period also recorded a deterioration in glycemic control even as insulin dosages were increased. The above clinical scenario may suggestthe onset of an immune-mediated, life-threatening, massive cytokine release into the circulation (an exaggeration of a normal and expected cytokine release during inflammation), which may result in multiple end-organ damage, a phenomenon known as the *"cytokine storm"* [16,17]. Remarkably, though not expectedly, patient's blood glucose control proved difficult, as increasingly higher doses of insulin had to be administered in other to achieve adequate control. Patient had to be switchedfrom a bi-phasic insulin regimen, using pre-mixed insulin, to a basal-bolus insulin intensification regimen [18], using the once-daily long-acting insulin glargine (Lantus),together with multiple dosages of the insulin analogue - glulisine (Apidra), a zinc-free rapid-acting injectable insulin analogue with a faster onset of action than the human insulin [19]. Several studies have suggested multiple complex mechanisms through which COVID-19 disease causes dysregulation of glycemic control, ranging from a direct destructive effect of the SARS-CoV-2 on pancreatic islet beta cells through the ACE2 protein;the liberal use of glucocorticoids for the containment of the envisaged cytokine storm; to an eventual beta cell apoptosis, leading to a blunted pancreatic insulin release[17], [20,21].

5.1 Triumphs

Some notable achievements include the fact that this very elderly patient with multiple chronic co-morbidities, presenting with severe COVID-19 disease, to a limited resourced facility, was successfully managed and discharged home. The above feat could be achieved, largely due to the prompt intervention of the Nephrologists who battled to ensure that patient's renal function was essentially restored before discharge.

5.2 Difficulties encountered

An important challenge encountered in the course of management of the index patient was the fact that patient's relatives had to pay out-of-pocket in other to access needed care for the patient. This inefficient method of healthcare financing resulted in severe gaps in patient

management and care, as some critical laboratory investigations required to guide patient treatment, could not be done, on account of financial constraints.

5.3Lessons learnt

A good number of important lessons were learnt, which could be applied in the future to improve clinical outcomes for patients with COVID-19 disease -

Early severity stratification, using simple and easy-to-apply clinical tools, ensures life-saving timely care for individuals presenting to the hospital with severe or even critical COVID-19 disease.Furthermore, multi-specialty collaborative care can make all the difference in a resource-constrained setting and has the potential to improve patients' clinical outcome and shorten hospital stay, even in the face of severe COVID-19 diseasein the elderly, with associated multiple chronic co-morbidities.

It is noteworthy that with severe COVID-19 disease, a period ofsudden deterioration of patient's clinical state, few days after diagnosis and commencement of treatment, may be an important pointer to a massive cytokine release syndrome, referred to as the cytokine storm. This life-threatening event, which may be managed successfully using glucocorticoids like dexamethasone and other support treatment modalities, should be looked out for, and treatment intensification commenced promptly.

Additionally, proactive leadership in health systems, results in better health outcome indices, as exemplified by the initiative taken by the hospital management. They quickly erected (and furnished with diagnostic equipment) a temporary isolation complex, at the early stages of the pandemic, instead of waiting for same to be provided by the federal government, which was already grappling with several pandemic-related challenges.

Finally, out of pocket payment for health care services is a highly cumbersome and in-efficient health care financing strategy, as it is usually not sustainable and hence, can impair access to needed health care services. This is evident in the index patient's case (Table 4), as several requested critical laboratory investigations could not be carried out as a result of financial constraints.

Conclusion: In a background of limited resources, multi-specialty collaborative care improves patients' outcome even in the face of severe COVID-19 disease with associated chronic co-morbidities in the elderly patient. Additionally, early severity stratification on presentation, ensures life-saving timely care for severe COVID-19 disease.

Consent – Obtained from index case's next of kin.

Ethical approval – Was obtained retrospectively after patient discharge, from the hospital management COVID-19 disease taskforce.

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