Increased mortality in patients suspected of having Covid-19: Findings at a treatment center in Delta State

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Abstract

Background: At the beginning of the COVID-19 pandemic there was great anxiety amongst healthcare workers because of the high infectivity and significant mortality associated with the disease. Also, patients were anxious about accessing medical facilities for fear of being labeled as suspected cases of COVID-19 infection. Therefore, we decided to determine the outcome of hospital admission among COVID-19 suspected cases.

Methods: This was a retrospective descriptive study of patients suspected of having COVID-19 as defined by the Nigeria Center for Disease Control, who were admitted to Delta State University Teaching Hospital, Oghara. The medical history, clinical examination, and test results of these patients were documented in their case notes and charts. Relevant data were extracted from these case notes and charts into a Microsoft Excel spreadsheet.

Results: During the study period 68 patients were admitted to the Treatment Center; 22 (32.3%) of them tested positive for SAR-CoV-2, while the other 46 (67.7%) tested negative. The patients who were SARS-CoV-2 negative had a statistically significant higher case fatality 20/46 (43.5%) than those that were SARS-CoV-2 positive 3/22 (13.6%) ($p = 0.012$). However, there was no statistically significant difference between the two groups in age, presence of co-morbidities, the severity of symptoms, intubation, dialysis, and the need for supplemental oxygen ($p > 0.05$). The time from admission to death for the negative cases was significantly shorter, compared to the positive cases. They died within an average of a day on admission compared to those that tested positive (5-6days); p-value = 0.009.

Conclusion: This study shows that among patients suspected of having COVID-19, those who tested negative for SAR-CoV-2 had higher mortality than those who tested positive. Future studies should explore if this increased mortality is related to the initial fear and misconceptions about the disease amongst the population in general and health care workers in particular.

Keywords: Mortality, suspected cases, COVID-19 cases

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Introduction

The coronavirus disease (COVID-19) that was first reported in Wuhan, China in December 2019 was declared a pandemic by the World Health Organisation on the 11th of March, 2020.[1] The first case in Nigeria was reported in Lagos on 26 February 2020 in an Italian returnee, and since then cases have been reported in all the states of the federation.[2]

The disease is caused by the newly discovered virus named Severe Acute Respiratory Syndrome Corona-virus-2 (SARS-CoV-2). SARS-CoV-2 is a novel beta coronavirus of the family of Coronaviruses which are enveloped positive-sense single-stranded RNA viruses sized 80–220nm in diameter. The envelope bears crown-like, 20nm spikes that resemble the corona of the sun under electron microscopy, hence given its name coronavirus.[3] The virus is transmitted to a large extent directly by respiratory droplets from an infected person to a susceptible host, particularly in asymptomatic carriers, or indirectly, through hands or fomites contaminated with the virus. The ease of direct transmission of the infection from person to person necessitated the setting up of isolation centers in almost all countries of the world. The purpose is to isolate the cases for the entire period of infectivity and to provide prompt and effective treatment.[4-5-]

After the declaration of the pandemic, Nigeria instituted lockdown measures on 29 March 2020 to restrict movement thereby limiting the spread of the virus. Only health care workers and other essential workers were allowed movement. To avoid being infected, there was an increasing demand for Personal Protective Equipment (PPEs) by health care workers which led to shortages around the world.[6] There were agitations amongst workers in the health care sector about personal safety, availability of health insurance, and the adopted treatment modalities for patients suspected or confirmed to have the novel virus.[7,8] News of patients being abandoned in emergency rooms and left uncared for due to lack of PPEs and the lack of treatment guidelines/protocol ruled the airwaves.[8]

On the part of patients, accessing medical facilities when afflicted with acute illnesses and/or chronic medical conditions became a huge challenge. Even critically ill persons avoided hospitals for fear of being

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labelled COVID-19 suspects.[9] Hospitals scaled down the number of staff and services rendered to reduce the infection rates among health workers who were fatally succumbing to the disease in their numbers in Europe.[10] Due to this lack of access to comprehensive health care, it is likely that mortality rates from COVID-19 and other ailments may have risen.[11,12]

Patients suspected of having COVID-19 as defined by the Nigeria Centre for Disease Control (NCDC), were admitted into our treatment center.[13] A suspected case of COVID-19 within this frame of reference was any patient presenting with fever and/or cough and/or difficulty in breathing/shortness of breath. Or any person either symptomatic or asymptomatic who had close contact with a suspected case or confirmed case of COVID-19 dead or alive or had a visit to a health care facility where COVID-19 cases had been reported or had a history of travel to a country with confirmed and ongoing community transmission of SARS CoV-2.[13] All the patients had nasopharyngeal and oropharyngeal samples collected for PCR-based SARS CoV-2, and the results were issued in 24 to 48 hours.

Considering the overlap between the COVID-19 symptoms and other health conditions, only a small fraction of patients may turn out SARS-CoV-2 positive. Differentials for the above symptoms are broad and include many cardiovascular and respiratory tract diseases: causes of infective pneumonia, other causes of pneumonia, chronic obstructive airway disease, pulmonary oedema, acute bronchitis, congestive heart failure, pulmonary embolism, pulmonary hypertension, pulmonary fibrosis, and hyperactive airway disease.[14,15] Acute life-threatening illnesses like sepsis, malaria in children, and hyperglycaemic emergencies may also present this way.[16,17] Nevertheless, a high index of suspicion had to be maintained even when there was no contact history as patients may not even be aware of contact or patients may deliberately withhold vital information including a travel history from medical personnel.[18] Therefore, this study aimed to evaluate suspected cases of COVID-19 at a treatment center, and compared the outcome of those who tested positive to those who tested negative for SAR-CoV-2, and perhaps a difference may be detected. The outcome measures gathered by this study may provide information on patients well-being following COVID-19 pandemic.

Materials and Methods

The study was conducted in Delta State University Teaching Hospital (DELSUTH), Oghara Isolation/ treatment center, and the study population consisted of patients suspected of having COVID-19 infection who were first seen at the Accident and Emergency Department of the Hospital and those referred from other health facilities with a positive result of SARS-COV-2 infection. Patients were admitted based on having symptoms of COVID-19 infection using the NCDC criteria or having a positive test to SARS-COV-2 with or without clinical symptoms.[13,16] The patients studied were those admitted into the Isolation/Treatment Centre from the 23rd of March 2020 when the Centre was established until the 7th of June 2020 when the Centre became dedicated to only confirmed positive cases of COVID-19. All suspected cases had nasopharyngeal and oropharyngeal samples taken for real-time reverse transcriptase-PCR for SARS-CoV-2 and further categorised into positive and negative cases.

At the time of the study all COVID-19 positive patients, including those that were asymptomatic were nursed in Isolation/Treatment Centers.

Study Design

The study was a retrospective descriptive study.

Data Collection

Relevant data were manually extracted into excel sheets from patient case notes, nursing charts, and anaesthetist charts. The age, sex, presenting symptoms, severity, comorbidity, the result of real-time reverse transcriptase-PCR for SARS-CoV-2, need for intubation, need for dialysis, and supplemental oxygen needs in those who survived and those who died were extracted. The baseline pulse rate, respiratory rate, temperature, oxygen delivery dose, SpO_2, time from admission to death, and fatality of those who tested positive were compared to those who tested negative for COVID-19 infection. A suspected case of COVID-19 was a person with fever and/or cough and or/difficulty in breathing, or shortness of breath. Or any person either symptomatic or asymptomatic who had close contact with a suspected case or confirmed case of COVID-19 dead or alive or exposure to a healthcare facility where COVID-19 cases had been reported or a history of travel to any country with confirmed and ongoing community transmission of SARS CoV-2.[13,16] A confirmed case was any patient with positive SARS-COV-2 laboratory report with or without clinical symptoms.[13,16]

The severity of COVID-19 was categorized into asymptomatic, mild, moderate, severe, and critical cases based on the NIH COVID-19 Treatment Guideline and National Interim Guidelines for Clinical Management of COVID-19 version 3.6.[13] Asymptomatic or presymptomatic cases were those with no symptoms but positive for RT-PCR SARS-COV-2 test (nucleic acid amplification test). Mild cases were patients who presented with any of these symptoms fever, cough, malaise, headache, sore throat, loss of smell and taste without difficulty in breathing or shortness of breath.

Moderate cases were those with fever, more severe cough, breathlessness on moderate exertion, no breathlessness at rest but oxygen saturation is (SpO_2) ≥ 94% on room air at sea level. Severe cases were those who had respiratory rate >30cycles/minute, SpO_2 less than 94% in room air at sea level.[13,19] Critical cases are those with the presence of Acute Respiratory Distress Syndrome (ARDS) and/or Sepsis/Septic Shock and/or multiple organ failure.[19]

Acute Respiratory Distress Syndrome in this study was defined as the development of rapid onset respiratory distress with the partial pressure of arterial oxygen (PaO_2) in mmHg to fraction of inspired oxygen (FiO_2) ratio (P/F ratio) of less than 200mmHg.[19] Sepsis was defined as life-threatening organ dysfunction caused by dysregulated host response to infection. Organ dysfunction was defined as an increased of two or more in the Sequential Organ Failure Assessment (SOFA) scoring system. In this study Organ dsyfunction was measured using the qSOFA in our resource limited environment. One point each for respiratory rate ≥ 22cycles/minute; systolic blood pressure ≥ 100mmHg and altered mental status.[20] Septic shock was defined as persistent hypotension requiring vasopressors to maintain mean arterial blood pressure ≥65 mmHg; and serum lactate > 2mmol/L (>18mg/dl) in a patient with sepsis.[20,21] Comorbidity examined in this study includes aged 65 years, hypertension, Cardiovascular disease, COPD, asthma, diabetes, cancers, CKD¸ HIV/AIDS, on chemotherapy, sickle cell disease, being pregnant.[18] Patients that needed oxygen supplementation were those with SpO_2 > 94% with/or respiratory rate > 22cycles/minute, with/or Glasgow Coma Scale < 13. Patients that needed intubation were those with SpO_2 < 88% with/or respiratory rate > 35cycles/minute, with/or Glasgow Coma Scale < 9. The outcome variables measured in this research are survival and death; being positive and negative to COVID-19 infection.

Statistical Analysis

Data was collated and analysed in a Microsoft Excel 2016 sheet. Frequency tables and bar charts were used to present results. Chi-square test and Yates correction were used to determine if there were statistical significant differences in need for supplemental oxygen, need for dialysis, need for intubation, co-morbidities and clinical features between patients that tested positive and those that tested negative. T-test was used to determine if there were statistical significant differences in the time from admission to death, pulse rate, respiratory rate, SpO2 between patients that tested positive and those that tested negative. P-value was set at 0.05.

Ethical Approval

Ethical approval was obtained from the DELSUTH Research Ethics Committee.

Results

During the study period 68 patients were admitted to the Treatment Center; 22 (32.3%) of them tested positive for SAR-CoV-2, while the other 46 (67.7%) tested negative. There was no statistically significant difference between those that were SARS-COV-2 negative and SARS-COV-2 positive for age, comorbidity, presence of dyspnoea, presences of sore throat, severity of illness, baseline vital signs, need for supplementary oxygen, and need for intubation. However, there was statistically significant difference between the two groups for gender, presence of fever, presence of cough, mortality, and time from admission to death. The proportion of males with positive COVID-19 test was 17 (77.3%) compared to females with positive COVID-19 test 5(22.7%), p-value = 0.03. The mortality rate in the negative COVID-19 group, 20 (43.5%) while the mortality rate in the positive COVID-19 group, 3 (13.6%), p-value = 0.012. The time from admission to death in the negative COVID-19 group was 1.33 days and in the positive COVID-19 group was 5.33days, p-value= 0.09

Discussion

The overall mortality rate of 33.8% in patients suspected of having COVID-19 was quite high, but what was even more surprising was that those who tested negative had significantly higher mortality than those that tested positive for COVID-19; even though there was no difference in the age, presence of co-morbidities, the severity of COVID-19 symptoms at presentation, or need for oxygen therapy. This may suggest that age, the presence of co-morbidities, and the presence of severe COVID-19 symptoms were not responsible for the increased mortality in patients who tested negative, unlike the situation in confirmed COVID-19 patients.[18]

Considering the overlap between the symptoms used in the triage and other severe health conditions, a high index of suspicion had to still be maintained even when there was no contact history as patients may not even be aware of contact or as it has been documented that patients may deliberately withhold vital information from health personnel.[13,19]

The high mortality rate may also be explained by the fact that these patients presented with acute life-threatening illnesses like community-acquired pneumonia, hyperglycemic emergencies, decompensated CCF, eclampsia, sepsis, haemorrhagic stroke as their symptoms fit into the case definition for COVID-19 and had to be referred to the DELSUTH treatment center. Additionally, chronic terminal illnesses such as advanced breast cancer with metastasis to the brain,

Table 1: Characteristics of Cases Admitted at the Centre from 27 March - 07 June 2020

Variables	Negative n= 46 (%)	Positive n=22 (%)	p-value/test statistics
Age (in years)			
Child (<18)	1(2.1)	0 (0.0)	
Young Adulthood (18-45)	24 (52.2)	6 (27.3)	X2 = 4.578
Middle Adulthood (46-59)	12 (26.1)	9 (40.9)	p-value = 0.205
Elderly (60 and above)	9 (19.6)	7(31.8)	
Sex			
Male	23 (50.0)	17 (77.3)	X2 = 4.5701
Female	23 (50.0)	5 (22.7)	p-value = 0.03
Time from admission to death	1.33 days	5.33 days	t(66) = -3.0594, p-value = 0.009
Fever			
Yes	15 (32.6)	18 (81.8)	X2 =14.428
No	31(67.4)	04 (18.2)	P-value =0.0001
Cough			
Yes	15 (32.6)	17 (77.3)	X2 = 11.917
No	31 (67.4)	05 (22.7)	P-value =0.001
Dyspnoea			
Yes	18 (39.1)	13 (59.1)	X2 = 2.39
No	28 (60.9)	09 (40.9)	P-value = 0.122
Sore Throat			
Yes	03 (6.5)	03 (13.6)	X2 = 0.936
No	43 (93.5)	19 (86.4)	P-value = 0.333
Hypertension			
Present	19 (41.3)	13 (59.1)	X2 = 1.8898
Absent	27 (58.7)	9 (40.9)	p-value = 0.17
Diabetes Mellitus			
Present	14(30.4)	8(36.4)	X2 = 0.239
Absent	32(69.6)	14(63.6)	p-value = 0.62
Chronic Liver Diseases			
Present	2(4.3)	1(4.5)	X2 = 0.0014
Absent	44(96.7)	21(95.5)	p-value = 0.97
Cancers			
Present	3(6.5)	0(0.0)	Fisher's Exact Test = 0.546
Absent	43(93.5)	22(100.0)	p-value = 0.303
Severity			
Asymptomatic	3 (13.0)	1(4.6)	
Mild	12 (19.6)	3 (13.6)	
Moderate	10(21.7)	4 (18.2)	
Severe	21(45.7)	11(59.0)	X2 = 7.569
Critical	0 (0.0)	3 (4.6)	p-value = 0.109
Supplementary Oxygen			
Given	23(50.0)	13(28.3)	X2 = 0.4937
Not given	23 (50.0)	9(71.9)	p-value = 0.48
Needed intubation			
Yes	3 (6.5)	3 (13.6)	X2 = 0.9364
No	43 (93.5)	19 (86.4)	p-value= 0.33
Baseline vital signs (mean+SD)			
Pulse rate	98.59+21.42	95.79+17.02	t(66) = 0.5565, p-value =0.58
Temperature	37.12+1.31	37.38+2.03	t(66) = 0.65346, p-value = 0.52
Respiratory rate	31.85+9.94	29.2+11.15	t(66) = 0.91, p-value = 0.18474
SpO2	94.9+5.42	94.37+7.44	t(66) = 0.275, p-value = 0.7844

*some patients had multiple co-morbidities

decompensated chronic liver disease, and clinical Acquired Immunodeficiency Syndrome (AIDS) were the documented causes of death in the COVID-19 negative patients.[20,21,22] Indeed, among those patients who tested negative, three-quarters of them had acute life-threatening/terminal illness which may explain the higher mortality rate.

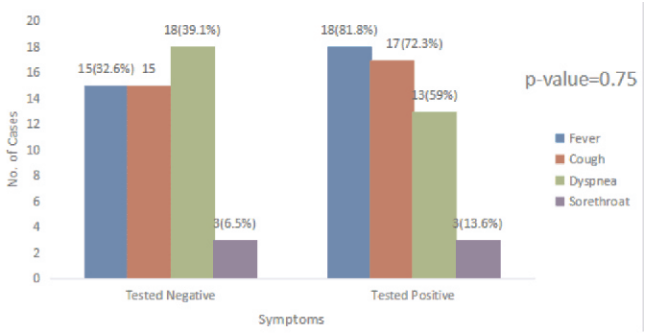

Figure 1: Comparison Clinical Symptoms and Test Result of patients

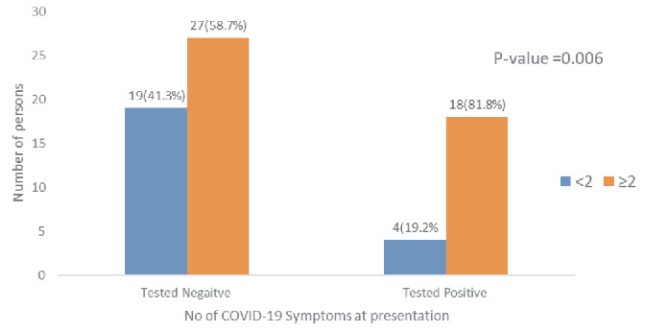

Figure 2: Proportion of Patients that had 2 or more COVID-19 symptoms

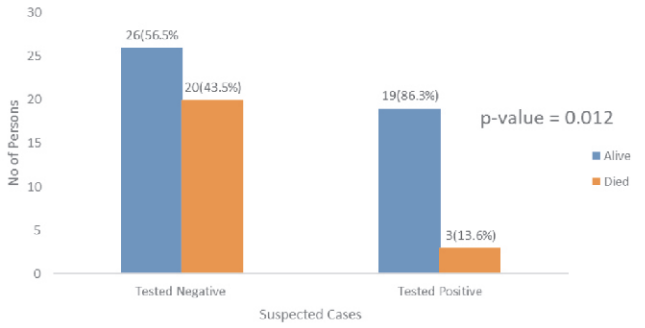

Figure 3: Relationship between Test Result and Mortality

At the beginning of the pandemic, there was significant fear amongst the population in general and health care workers in particular. Caregivers were scared of coming into contact with suspected cases of COVID-19. They provided care from a distance, they insisted on COVID-19 test results before treating patients, and sometimes practically watched patients die. Lack of adequate personal protective equipment (PPE) and misconceptions about the appropriate use of PPE may have also contributed to the fear.[7] This fear factor may have contributed to the higher mortality in patients that tested negative. Indeed, a significant proportion of them (41%) died before their result became available.

There is currently no clear indication of how long SARS-CoV-2 may survive in humans after death.[22] However, SARS-CoV-2 has been detected up to four months after death.[23] Therefore it is unlikely that those patients that tested negative for the virus posthumously truly had the infection. Nevertheless, the one person that had a post-mortem has findings that were suggestive of COVID-19[24] even though she tested negative posthumously.

The nationwide lockdown and the initial disruption of services in the hospital at the beginning of the pandemic may also have contributed to the high mortality.

As of 1st of July, 2020 the worldwide statistics showed that Yemen had the highest COVID-19 mortality rate at 26.94% and Singapore had the least at 0.06%, and Nigeria had a case fatality rate of 2.3%.[25] As of 08 January 2023 Delta State had a COVID-19 case fatality rate of 1.9%.[26] Our in-hospital COVID-19 mortality rate of 13.6% was relatively high. As a tertiary referral/teaching hospital, all the severe cases with significant co-morbidities were referred to us and hence our mortality rate is expected to be higher than the State average.

Conclusion

This study has shown that among patients suspected of having COVID-19, those who tested negative for SAR-CoV-2 had higher mortality than those who tested positive. Future studies should explore if this increased mortality is related to the initial fear and misconceptions about the disease amongst the population in general and health care workers in particular.

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