

Original Research Article

TIME TO NEGATIVE TEST RESULT AMONG PATIENTS WITH A COVID19 **INFECTION**: A RETROSPECTIVE STUDY

Abstract

Background

Coronavirus disease 2019 (COVID-19) is a public health emergency, however, there is still limited data on the length of infectiveness of the disease especially in Nigeria.

Methods.

In this retrospective study, time to a negative result with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA was evaluated in a cohort of 490 patients who were tested in the Satellite Molecular Laboratory of the Rivers State University Teaching Hospital, Port Harcourt.

Results.

The mean age of the 490 patients was 39.8 ± 13.9 . There were 379 (77.3%) males and 111 (22.7%) females. The mean duration of SARS-CoV-2 RNA detection was approximately 15 ± 2 days. When comparing patients who were tested twice with those who were tested more than two times, a significant difference between mean time to a negative result and the number of tests done was identified ($t = P\text{-Value} = <0.001$)

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Conclusions.

Findings from this study suggests that the average time to transition from a positive to negative PCR test result was approximately 15 days, regardless of the gender. This can provide an estimated duration of hospital stay among COVID-19 patients and prevent or minimize re-infection in the healthcare facilities.

Keywords. SARS-COV-2; COVID-19; Polymerase Chain Reaction.

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Introduction

The coronavirus disease 2019 (COVID-19) pandemic's etiological agent is SARS-CoV-2, which has been a major source of concern for worldwide human health (1).

As of October 2021, there have been 250 million cases worldwide, with just 5.05 million deaths. Over 8 million cases and 149041 fatalities have been reported in

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Africa (2). There were 212,713 cases and 2906 deaths in Nigeria, with Rivers State accounting for 12751 (6%) of the total cases (3). The clinical and epidemiological characteristics of individuals with coronavirus disease 2019 (COVID-19) have been reported in several publications (4). During treatment, the pattern of SARS-CoV-2 RNA shedding has not been extensively defined. Only 25% of patients show negative oral swabs after 5 days of therapy, according to Zhang et al (6). Although, the actual test for infectivity would be the presence of viable cell cultures of which are rarely the case 10 days post-symptom-onset or after first

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positive test (7). According to a recent study, the median length of SARS-CoV-2 RNA was 17 (13–22) days from the commencement of illness to the end of therapy (5). Prolonged SARS-CoV-2 viral presence has been linked to the male sex, old age, concurrent hypertension, delayed admission to hospital after illness onset, and severe illness at admission when comparing patients with early (within 15 days) and late (15 days after illness onset) viral RNA clearance (5).

COVID-19 patients have a wide range of clinical symptoms that affect different body systems, including the respiratory and digestive systems. Mild self-limited disease to severe pneumonia, acute respiratory distress syndrome, septic shock, and systemic multiple organ failure syndromes are examples of these symptoms (8). COVID-19 patients are typically admitted to a hospital for routine therapy, and if their condition improves, they are discharged according to local health authorities' protocols and guidelines.

Although no official guidance is available in Nigeria for time to de-isolation, symptomatic individuals were usually discharged 14 days after a positive test, according to the Nigerian Centre for Disease Control, and a negative laboratory test is no longer required (9). However, local evidence supporting this is unavailable yet. The goal of our research is to describe the time it takes for a patient in Nigeria to have a negative COVID-19 result, which may help to

anticipate and manage self-isolation, hospital stay and treatment in our local setting.

Methods

Study Design and Participants

A total of 490 patient records with confirmed SARS-CoV-2 infection at the COVID-19 laboratory of the Rivers State University Teaching Hospital, Port-Harcourt were retrospectively reviewed within a 12-month period from May 2020 to August 2021. Patients were enrolled into the study if they met the inclusion criterion of a positive Covid-19 result. SARS-CoV-2 infection was confirmed in all patients by testing respiratory specimens with a real-time reverse transcription-polymerase chain reaction assay. Ethics approval was obtained from the Institutional Review Board of the Rivers State University Teaching Hospital. Microsoft Excel 2016 and the Statistical Package for Social Sciences (SPSS) version 23 were used to analyze the data. Sex comparisons were made for age of study patients and mean time to negative results were analysed for sex, age and number of COVID-19 RNA tests done. To summarize the characteristics of the participants, descriptive statistics were employed, and inferentially chi-square, T-Test, and ANOVA were used to determine statistical significance set at $p < 0.05$ for categorical and continuous variables as appropriate.

Results

A total of 490 patient files were eligible for the study. Tables 1 shows the distribution of the socio-demographic characteristics of the participants including age and sex. A major proportion of 379 (77.3%) of the patients were males. The overall mean age of study participants was 39.8 ± 13.9 years. A majority of the study patients 153(31.2%) were between 35-44 years and was closely followed by those between 18-34 years 103(21%). Table 2 shows a significant association between age and sex (P-Value = <0.001). No significant association was found between sex and mean time to negative result as displayed in table 3, and no significant association was identified between age and mean time to negative (Table 4). The mean time to transition from a positive test to a negative test was 14.8 days. The number of repeat tests done and time to a negative COVID – 19 result was significant between those who were tested two times versus those who were tested more than two times (P-Value = <0.001) as shown in table 5

Discussion

The majority of COVID-19 research has focused on describing the early clinical and epidemiological findings. There has been minimal research into the time to sero-negative conversion among SARS-CoV-2 RNA patients in Nigeria after a confirmed positive test result. Male patients with COVID-19 were shown to be more infected by the SARS-CoV-2 RNA and to have a longer disease duration than female patients. This finding could indicate that the COVID-19 sickness

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affects males more severely than females (5,10) From May 2020 to August 2021, the average time it took for a patient to get a negative result after testing positive was about 15 days, regardless of age or sex. This report appears to be comparable to one from a Chinese study. After the commencement of a clinical complaint, a patient's test result was negative after 17 days, according to the previous study (5).

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However, another study experienced a 24-day duration as the mean time to seronegative transition (11). The differences in this study can be attributable to age differences in the participants and the study designs. Findings from our research suggests that COVID-19 patients can be discharged 14 days after receiving a confirmation of a positive result as stated by the Nigerian Centre for Disease Control. As a result, this information adds to the current de-isolation strategies for individuals with COVID-19 disease (12) and can indicate the estimated length of hospital stay among patients admitted for the management of COVID-19, consequently limiting re-infection and catastrophic losses from healthcare expenses. Nonetheless, our study has a limitation as patients only performed a follow-up test at their own discretion or their doctor's recommendation. So, it is possible that they may have tested negative earlier as the United State Centre for Disease Control has currently recommended a shortened time of 5 days for isolation for prevention (13).

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Conclusion

In conclusion, management of COVID-19 patients, particularly male patients should be commenced soonest since they make up the bulk of admitted COVID-19 patients. Additionally, the average time to seroconversion from positive to negative can be considered for estimating hospital length of stay or time to resuming work activities and other social interactions.

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Financial support. None

Potential conflicts of interest. No reported conflicts of interest.

Table 1: Age and Sex Distribution

Variable	Frequency (n = 490)	Percent
Age Group of Patients (years)		
<18 (minors)	30	6.1
18 – 24 (young people)	44	9.0
25 – 34	90	18.4
35 – 44	153	31.2
45 – 54	103	21.0
>54	70	14.3
Mean Age: 39.8 ± 13.9		
Sex		
Male	379	77.3
Female	111	22.7

Table 2: Age by Sex Distribution

Variable	Sex		Chi-square	P-Value
Age Group of Patients (years)				
<18 (minors)	Male	Female		
	16 (4.2)	14 (12.6)		
18 – 24 (young people)	22 (5.8)	22 (19.8)		
25 – 34	66 (17.4)	24 (21.6)		
35 – 44	129 (34.0)	24 (21.6)	42.149	<0.001*
45 – 54	92 (24.3)	11 (9.9)		
>54	54 (14.2)	16 (14.4)		

Table 3: Time to Negative and Sex Relationship

t = Students' T-test

Variable	Sex		T-test	P - value
	Males	Females		
Mean Time to Negative (Log) ± SD	15.31 ± 2.24	13.06 ± 1.84	1.803	0.072

Table 4: Time to Negative and Age Relationship

Variable	Frequency	Mean Time to Negative (Log)	Test Statistics (ANOVA)	
			F	p-value
Age Group of Patients (years)				
<18 (minors)	24	13.24 ± 2.39		
18 – 24 (young people)	40	13.40 ± 2.20		
25 – 34	81	15.21 ± 1.95	0.531	0.753
35 – 44	138	15.21 ± 2.33		
45 – 54	88	15.67 ± 2.09		
>54	60	13.55 ± 2.05		

F = ANOVA

Table 5: Time to Negative and Number of Tests Relationship

*(statistically significant), t = students' T-test

Variable	Number of Tests Done		T-test	P - value
	Two	More than Two		
Mean Time to Negative (Log) ± SD	14.09 ± 2.16	23.93 ± 1.77	-5.186	<0.001*

Mean Time to Negative

The average number of days it took for patients to convert to negative was 14.760 ± 2.160 Days.

There was a statistically significant relationship between the number of tests done and the Time to Negative, having a p-value of <0.001, as shown by Student's T-test; where statistical significance is set at ≤ 0.05.

Reference

1. Mallah SI, Ghorab OK, Al-Salmi, S, Abdellatif OS, Tharmaratnam Iskandar MA, Atef J, Sefen N et al. COVID-19: breaking down a global health Crisis. *Ann Clin Microbiol Antimicrob.* 2021. 20:35
2. World Health Organization. Covid-19 Weekly Epidemiological Update. Edition 62, Published 19 October 2021
3. NCDC (2021). NCDC Coronavirus COVID-19 MicrositeCovid-19.ncdc.gov.ng/state
4. Xu XW, Wu XX, Jiang XG. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. *BMJ.* 2020. 368:m606.
5. Xu K, Chen Y, Yuan J, Yi P, Ding C, Wu W et al. Factors Associated with Prolonged Viral RNA Shedding in Patients with Coronavirus Disease 2019 (COVID-19). *Clinical Infectious Disease.* 2020.
6. Zhang W, Du RH, Li B (2020). Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. *Emerg Microbes Infect.* 9:386–9.
7. Basile K, McPhie K, Carter I, Alderson S, Rahman H, Donovan L et al. Cell-based Culture Informs Infectivity and Safe De-Isolation Assessments in Patients with Coronavirus Disease 2019 *Clinical Infectious Diseases*, Volume 73, Issue 9, 1 November 2021, Pages e2952–e2959, <https://doi.org/10.1093/cid/ciaa1579>)
8. Parasher A. COVID-19: Current understanding of its pathophysiology, clinical presentation, and treatment. *Postgrad Med J* 2020:postgradmedj-2020-138577.
9. Premium Times. COVID-19: Nigeria Disease Control Agency Says Negative Result No Longer Required to Discharge Patients by Nike Adebowale-June 5,2020

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10. Valerie C, Luna C, Alice N, Giovanna T, Ornella C, Elisa M et al. Persistent positivity and fluctuations of SARS-CoV-2 RNA in clinically-recovered COVID-19 patients. *Journal of Infection*. 2020. 81 .
 11. Gombar S, Chang M, Hogan CA, Zehndera J, Boyd J, Benjamin A et al. Persistent detection of SARS-CoV-2 RNA in patients and healthcare workers with COVID-19. *Journal of Clinical Virology*. 2020
 12. World Health Organization. Criteria for releasing COVID-19 patients from isolation. Available from: <https://www.who.int/news-room/commentaries/detail/criteria-for-releasing-covid-19-patients-from-isolation>. Accessed: 18/01/2020.
 13. Centre for Disease Control. CDC Updates and Shortens Recommended Isolation and Quarantine Period for General Population. 2021 <http://www.cdc.gov/media/releases/2021/s1227-isolation-quarantine-guidance.html>

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