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Research Article

Total Serum Immunoglobulin M in Asymptomatic COVID-19 Seropositive People

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Abstract

Background: Coronavirus has continued to ravage the world with several countries either currently experiencing a second wave of the pandemic or instituting more stringent control measures to forestall further spread. Laboratory testing plays a major role in diagnosing the disease, but the standard diagnostic test is very expensive. Several countries have reduced testing thereby jeopardizing the initial gains of case detection. There is now a need for cheaper and more readily available preliminary testing options to determine who really requires the standard testing especially in low- and middle-income countries.

Method: Serum samples from the pool of asymptomatic participants for COVID-19 testing were obtained. They were divided into two groups which included those who tested positive and those who tested negative. Levels of serum Immunoglobulin M was measured in those samples using ELISA techniques and the values were compared between the two groups to determine if there was a difference.

Result: A total of 83 samples were evaluated for this study. 44 of them were obtained from the COVID-19 positive pool while the remaining 39 were from the COVID-19 negative pool. There was no statistical difference in the age group, gender and occupation between the two groups. The mean (± SD) of serum Immunoglobulin M was 4.11 (± 3.70) **µg/ml** from the COVID-19 positive pool and 4.53 (± 3.49) µg/ml from the COVID-19 negative pool; there was no statistical difference between the two groups.

Conclusion: This study found no difference in the values of serum Immunoglobulin M between COVID-19 positive sample pool and COVID-19 negative sample pool. This calls for a continued search for other alternative cheaper testing platforms for COVID-19 especially in low- and middle-income countries.

Keywords: *COVID-19; IgM; Seropositive; Asymptomatic*

Introduction

Corona virus disease (COVID-19) is a high-risk infectious disease caused by the most recently discovered coronavirus, SARS-COV-2. The continued spread of coronavirus COVID-19 has prompted widespread concern around the world, and the World Health Organisation (WHO), on 11th March 2020, declared it a pandemic. As of 11 October 2020, over 37 million COVID-19 cases and 1 million deaths have been reported globally [1]. The Nigeria Center for Disease Control (NCDC) statistics as of 7th October 2020, showed a total of 61,307 cases

and 1,123 deaths in Nigeria [2]. These mortalities have been reported in large numbers among health care workers (HCW) since they are a high-risk population to acquire SARS-CoV-2 infection from patients or other fellow HCWs. A good number of these HCWs may not have the opportunity of testing using the standard RT-PCR because non manifestation of symptoms may be presumed as absence of the disease, but this is not always the case.

There are various modalities of screening and diagnosis of COVID-19 with their attendant strengths and limitations. Currently, the viral nucleic acid real-time polymerase chain reaction (RT-PCR) test based on patient nasopharyngeal and throat swabs is the standard method for clinical diagnosis of COVID-19, however, this method is not readily available in most third world countries due to high cost [3]. More so, collecting lower respiratory specimens poses the risk of exposure to SARS-CoV-2 for personnel collecting specimens because of the close-contact with potential COVID-19 patients and irritation of respiratory airways during sampling [4]. Also, a high false negative rate has been reported due to the challenges of obtaining good-quality throat swab samples in different stages of infection [5,6].

Studies on severe acute respiratory syndrome (SARS) and Middle East Respiratory Syndrome (MERS) showed that virus-specific antibodies were detectable in 80 - 100% of patients at 2 weeks after symptoms onset [7-11]. Most recently, serological tests for virus-specific IgM and IgG antibodies against SARS-CoV-2 have been developed, and similar serological responses were observed in a COVID-19 patient [12,13]. Thus, it may be rewarding to screen for COVID-19 using this simple and cheaper serological test which although, invasive, poses less risk of transmission [14]. Screening approach to COVID-19 is developing; many of the available options are expensive; cheap and readily available serological testing could help reduce exposure risk during repeated sampling and save valuable RT–PCR tests [15]. Total serum IgM which is the marker of acute infection may provide useful information regarding who to test for COVID-19 especially in resource poor and low-income countries. This study is designed to compare total serum IgM between asymptomatic people who tested positive and those who tested negative to COVID-19.

Methods

This was a cross sectional study conducted at the University College Hospital, Ibadan, Nigeria. Serum samples were selected from a pool for COVID-19 testing for asymptomatic participants. Some samples were randomly selected from the COVID-19 positive pool while others were selected from the COVID-19 negative pool. Demographic and Clinical information of participants whose samples were selected were obtained from their questionnaires. Those with history of recent febrile illnesses, hospital admission and any form of inflammatory diseases were excluded from this study. Ethical approval was granted by UI/UCH Health Research Ethics Committee. Total serum IgM was measured using Enzyme Linked Immunosorbent Assay (ELISA) method according to manufacturer's instruction (Melsin Medical Company Limited Changchun China).

Statistical analysis

Clinical and demographic variables were reported as frequency and percentages. Values of total serum IgM was reported as mean and standard deviation; data from COVID-19 positive pool was compared with those from the COVID-19 negative pool. A p-value of < 0.05 was taken as statistically significant. Analysis was done using statistical package for social sciences (SPSS) version 26.0 (IBM Inc., USA).

Results

Samples from 83 participants were selected for this study. Participants included 43 (51.9%) doctors, 18 (21.7%) nurses, 12 (14.5%) health assistants, 6 (7.2%) laboratory scientists and technologist and 4 (4.8%) non-medical members of staff. They emanated from different departments within the hospital including chemical pathology (12; 14.5%), microbiology (5; 6.0%), hematology (6; 7.2%), private

suites (8; 9.6%), emergency (20; 24.1%), surgery (11; 13.3%), medicine (15; 18.1%) and gynecology (6; 7.2%). More than half of the participants (53%) were from the 31 - 40 years age group, and there were 41 (49.4%) male participants in the study. Other details regarding demographic and clinical characteristics are reported in table 1.

Variables	Total (N = 83)	Positive (n = 44)	Negative (n = 39)	P-values
Age range (years)				
21 - 30	21 (25.3)	9 (20.5)	12 (30.8)	0.28
31 - 40	44 (53.0)	25 (56.8)	19 (48.7)	0.46
41 - 50	14 (16.9)	9 (20.5)	5 (12.8)	0.35
51 - 60	4 (4.8)	1 (2.3)	3 (7.7)	0.25
Gender				
Male	41 (49.4)	26 (59.1)	15 (38.5)	0.79
Female	42 (50.6)	18 (40.9)	24 (61.5)	
Occupation				
Non-medical	4 (4.8)	4 (9.1)	0 (0.0)	N/A
Doctor	43 (51.9)	22 (50.0)	21 (53.8)	0.73
Nurse	18 (21.7)	10 (22.7)	8 (20.5)	0.81
Health assistant	12 (14.5)	6 (13.6)	6 (15.4)	0.82
Laboratory Sci/Tech	6 (7.2)	2 (4.5)	4 (10.3)	0.41
Department				
Chemical pathology	12 (14.5)	6 (13.6)	6 (15.4)	0.82
Surgery	11 (13.3)	2 (4.5)	9 (23.1)	0.02
Medicine	15 (18.1)	8 (18.2)	7 (17.9)	0.98
Emergency	20 (24.1)	18 (40.9)	2 (5.1)	< 0.001
Private Suite	8 (9.6)	2 (4.5)	6 (15.4)	0.09
O & G*	6 (7.2)	6 (13.6)	0 (0)	N/A
Hematology	6 (7.2)	0 (0)	6 (15.4)	N/A
Microbiology	5 (6)	2 (4.5)	3 (7.7)	0.55
IgM Mean ± SD (µg/ml)	4.30 ± 3.58	4.11 ± 3.70	4.53 ± 3.49	0.60

Table 1: *Comparison of demographic characteristics and serum IgM values of study participants who tested positive and those who tested negative to COVID-19. Data are reported in number (%) and mean ± SD.*

**O & G: Obstetrics and Gynecology; SD = Standard Deviation.*

There were 44 samples selected from the COVID-19 positive pool and 39 from the COVID-19 negative pool. There were no statistical differences in the age groups, gender and occupation distribution between the two groups. However, the departments of surgery ($p = 0.02$) and the emergency ($p < 0.001$) had more participants in the COVID-19 positive pool. The mean (± SD) serum IgM of samples from the COVID-19 positive pool was 4.11 (± 3.70) while those from the COVID-19 negative pool was 4.53 (± 3.49); the difference was not statistically significant ($p = 0.6$).

Discussion

COVID-19 is still rife across different continents of the world. Despite being declared a pandemic about nine months ago, the disease continues to ravage the world with many countries still declaring high daily incidence figures [16,17]. The challenges in low and middle income countries include the high cost of procuring the standard diagnostic test; while most of those countries have reported a decline in the number of tests, several others have modified their indications for admission, frequency of test while on admission and laboratory criteria for discharge [18]. All these considerations were essentially to cut cost and maximise the use of the limited test materials available. There arose the need for cheaper alternatives, especially in developing countries, to prioritise the scarce test materials, by evaluating other markers in body fluids to identify who may qualify for the standard test [19,20]. In this study we evaluated total serum IgM as a potential candidate, it however did not prove to make any difference between participants who tested positive and those who tested negative to COVID-19.

Immunoglobulins generally begin to rise following exposures to infective agents. IgM is widely referred to as the antibody of acute immune response that rises first, and peak within two weeks before it starts to decline, paving way for IgG which persists longer in circulation [21]. Several studies have shown that COVID-19 specific IgM follows this pattern and has mostly been used in serological studies to determine seroprevalence [15,22]. It is expected that this elevation will reflect in the total serum IgM. Total serum IgM can easily be measured using serological assays including lateral flow assays and labelled immunoassays which are readily available. This was proposed to be a cheaper means of stratifying people who are suspected to be infected with COVID-19, a preliminary test to determine which of them will require the standard polymerase chain reaction diagnostic test, especially in resource poor settings. However, the findings in this study showed that there is no difference in the values of IgM between people who tested positive and those who tested negative to COVID-19.

Given the exorbitant cost of procuring COVID-19 test for its citizens, several governments have raised the bar and established criteria that make it difficult for citizens to access test [23]. Most of those excluded citizens pose the risk of disease progression and transmitting the disease to other unsuspecting citizens even if they were asymptomatic. It is imperative to find alternative means of screening citizens with cheaper tests which may reduce the cost of testing and also ensure that those who actually require the molecular test were not denied [19]. This calls for a more concerted effort at making test available. Industries and humanitarian organisations are also on encouraged to invest in the provision of test kits in order to flatten the curve of COVID-19 and safe the world from the ongoing pandemic.

Limitation of the Study

There are several limitations to this study. The sample size may not have been powered enough to detect the possible difference between the two groups, larger studies may likely show otherwise. The evaluation of IgM in this study reflected the acute stage, the other possibility is the evaluation of IgG, a marker of the chronic infection which may also show a difference between the two groups.

Conclusion

This study showed no difference in the total serum IgM between participants who tested positive and those who tested negative for COVID-19. This calls for provision of alternative cheaper and more readily available testing platforms for COVID-19 especially in resource poor settings.

Conflict of Interest

Authors have none to declare.

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