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Detection Of Anti SARS-COV 2 Specific - IgG and - IgM Antibodies in Covid-19 Patients Using Rapid Screening Immunochromatographic Cassettes

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Abstract

Background: SARS-COV 2 is a novel and rapidly spreading virus without specific drug treatment, thus the need to understand the dynamic of host antibody responses for possible plasma therapy.

Aim: To determine the prevalence of anti-SARS-COV 2 specific -IgG and -IgM antibodies in COVID-19 Nigerian patients.

Methodology: The antibodies against SARS-COV 2 (anti-CovIgG and -CovIgM antibodies) were detected by cassette system lateral flow immunoassay in the plasma of control and COVID-19 patients (newly diagnosed and at discharge).

Results: Thirty-two (57.1%) of COVID-19 patients were positive for anti-CovIgG antibody and only one (5.4%) COVID-19 patient was positive for anti-CovIgM antibody. Twenty (71.4%) COVID-19 patients at discharge were positive for anti-CovIgG antibody and 12 (42.9%) newly diagnosed COVID-19 patients were positive for anti-CovIgG antibody. The difference in the frequency of anti-CovIgG antibody in newly diagnosed COVID-19 patients compared with anti-CovIgG antibody in COVID-19 at discharge was significant ($p<0.05$). Two (7.1%) COVID-19 patients at discharge were positive for anti-CovIgM antibody and only one (3.6%) newly diagnosed COVID-19 patient was positive for anti-CovIgM antibody. Two (7.1%) COVID-19 patients were positive for combination of anti-CovIgG and anti-CovIgM antibodies at discharge.

Conclusion: Cassette system lateral flow immunoassay has limited use for screening anti-SARS 2 -IgG and -IgM antibodies in COVID-19 patients and that these antibodies are more prevalent in COVID-19 patients at discharge than those newly diagnosed, thus not all plasma from COVID-19 patients should be consider for plasma therapy.

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Introduction

Previous studies provided insights into the pathogenesis and diagnosis of COVID-19 [1-4]. However, rapid spreading of virulent SARS-CoV 2 and existence of asymptomatic COVID-19 patients pose urgent need for both quick diagnostic interventions to manage containment measures and the outcome of the disease. COVID-19 diagnosis based on the molecular detection of the viral RNA using RT-PCR requires certified laboratories, expensive equipment, and often gives false negative results due to low viral load in the nasal and pharyngeal swabs [5,6]. Therefore, a huge number of symptomatic subjects might not be detected, causing the spread of the virus [7]. Therefore, rapid and sensitive methods to screen the population are urgently needed. Thus, serological tests might complement RT-PCR molecular test, as several reports showed the presence of an antibody response in absence of detectable viral load [6,7]. In addition, differences in the profile of the antibody response across patients might reveal important aspects of the pathogenesis of COVID-19, explaining the great differences observed in the general population [5]. Indeed, the correlation disease severity with clinic characteristics is poorly understood [5,6].

In patients with SARS-CoV infection, B cell in concomitantly with T follicular helper cell responses starts from 1 week after symptom onset [8] against the nucleocapsid (N) protein. Within 4–8 days after symptom onset, antibody responses to S protein were reported [8, 9]. Neutralizing antibody responses to S protein begins by week 2, and most patients develop neutralizing antibodies by week 3 [10]. However, a subset of patients may not develop long-lasting antibodies to SARS-COV 2 [11] but it remains unknown whether these patients are susceptible to reinfection [12]. A study showed that convalescent serum samples have been applied with apparently good clinical results in COVID-19 management [13] as previously used in the treatment of SARS [14,15].

The humoral immune response is critical for the clearance of cytopathic viruses and is a major part of the memory response that prevents reinfection. SARS-COV 2 elicits robust B-lymphocyte response as evidenced by the rapid and near-universal detection of virus-specific IgM, IgG and IgA, and neutralizing IgG antibodies (nAbs) in the days following infection [13-15]. The kinetics of the antibody response to SARS-COV 2 was well described [16]. Virus-specific IgM and IgG are detectable in serum between 7 and 14 days after the onset of symptoms [17]. Viral RNA is inversely correlated with neutralizing antibody titers. Higher titers have been observed in critically ill patients, but it is unknown whether antibody responses contribute to pulmonary pathology [18].

Above literatures showed that the characterization of the antibody response of COVID-19 patients will elucidate the mechanism of protection and will guide through the development of specific SARS-CoV 2 recombinant antibodies as prophylactic and therapeutic option to manage the disease. Moreover, it would be interesting to understand whether the progression of COVID-19 might be related to the level and type of antibody response. The present study screened for the presence of anti SARS-COV 2 specific -IgG and -IgM antibodies in RT-PCR confirmed Nigerian COVID-19 patients and un-infected control.

Materials and methods

Confirmed cases of COVID-19 (n=56) were recruited from an Infectious Diseases Isolation Center, Ibadan, Nigeria. The control (n=20) was recruited from staff and students of University of Ibadan. Blood samples collected from both patients and control were processed for the collection of plasma by spinning in centrifuge at 1500 x g for 20minutes. In the plasma of control and COVID-19 patients (newly diagnosed and at discharge), the presence of anti-SARS-COV 2 specific -IgG and -IgM antibodies were detected using cassette-based immunoassay method. Cassette-based systems rely on a coloured line that is visible within 20 minutes. Cassette systems use the principle of lateral flow immunoassay or immunochromatography. The cassette has a shallow well into which one drop (approximately 10µl) plasma was placed along with one drop of buffer. The plasma and buffer were absorbed into a porous test strip which was impregnated with recombinant viral antigens doped with an indicator. Antibodies from the plasma bound to antigens in the test strip and were wicked laterally along the length of the test strip. In the indicator regions of the test kit, anti-human antibodies which were immobilized in the test strip bound to the antigen-antibody complex leading to a visible change in colour along a narrow band of the wicking substrate. Coloured lines were indicated at the point of appropriate COVID immunoglobulin. All valid tests contained a “control” indicator line. Data were represented as frequencies and percentages. Proportions were compared using Chi-square analysis. $P \leq 0.05$ was taken as significant.

Results

All cassettes used for the investigation gave valid results. In Table 1, no control subject was positive for either anti-CovIgG or anti-CovIgM antibody while 32 (57.1%) COVID-19 patients were positive for anti-CovIgG antibody and one (5.4%) COVID-19 patient was positive for anti-CovIgM antibody. Two (3.6%) COVID-19 patients were positive for combination of both anti-CovIgG and anti-CovIgM antibodies. The difference in the prevalence of anti-CovIgG antibody in COVID-19 patients compared with the control was significant ($p<0.05$). In Table 2, twenty (71.4%) COVID-19 patients on discharge were positive for anti-CovIgG antibody and 12 (42.9%) newly diagnosed COVID-19 patients were positive for anti-CovIgG antibody. The difference in the frequency of anti-CovIgG antibody in newly diagnosed COVID-19 patients compared with anti-CovIgG antibody in COVID-19 at discharge was significant ($p<0.05$). Also in table 2, two (7.1%) COVID-19 patients at discharge were positive for anti-CovIgM antibody and one (3.6%) newly diagnosed COVID-19 patient was positive for anti-CovIgM antibody. The difference in the frequency of anti-CovIgM antibody in newly diagnosed COVID-19 patients compared with anti-CovIgM antibody in COVID-19 patients at discharge was not significant. Two (7.1%) COVID patients at discharge were positive for the combination of both anti-CovIgG and anti-CovIgM.

Table 1: The frequency (percentage) of anti-CovIgG and -CovIgM antibodies in COVID-19 patients compared with control.

Variable	All COVID-19 patients (n=56)	Control (n=20)	χ^2	P
Only anti-CovIgG antibody				
Positive	32 (57.1%)	0 (0.0%)	11.092	0.001*
Negative	24 (42.9%)	20 (100.0%)		
Only anti-CovIgM antibody				
Positive	1 (5.4%)	0 (0.0%)	0.561	0.454
Negative	55 (94.6%)	20 (100.0%)		
Both anti-CovIgG/IgM antibodies				
Both positive	2 (3.6%)	0 (0.0%)	11.786	0.003*
Both negative	23 (41.1%)	20 (100.0%)		

Table 2: The frequency (percentage) of anti-CovIgG and -CovIgM antibodies in newly diagnosed COVID-19 patients compared with COVID-19 patients at discharge.

Variable	Newly Diagnosed COVID-19 (n=28)	COVID-19 at discharge (n=28)	χ^2	P
Only anti-CovIgG antibody				
Positive	12 (42.9%)	20 (71.4%)	4.667	0.031*
Negative	16 (57.1%)	8 (28.6%)		
Only anti-CovIgM antibody				
Positive	1 (3.6%)	2 (7.1%)	0.352	0.553
Negative	27 (96.4%)	26 (92.9%)		
Both anti-CovIgG/IgM antibodies				
Both positive	0 (0.0%)	2 (7.1%)	4.937	0.085
Both negative	28 (100.0%)	26 (92.9%)		

Table 3: Gender distribution of anti-CovIgG and anti-CovIgM antibodies in newly diagnosed COVID-19 patients and discharge.

Variable		Newly Diagnosed COVID-19	P	COVID-19 at discharge	P
Only anti-CovIgG antibody					
Positive	Male	5 (55.6%)	0.665	8 (50.0%)	1.000
	Female	4 (44.4%)		8 (50.0%)	
Negative	Male	6 (46.2%)		3 (50.0%)	
	Female	7 (53.8%)		3 (50.0%)	
Only anti-CovIgM antibody					
Positive	Male	1 (100.0%)	0.306	2 (100.0%)	0.138
	Female	0 (0.0%)		0 (0.0%)	
Negative	Male	10 (47.6%)		9 (45.0%)	
	Female	11 (52.4%)		11 (55.0%)	

Discussion

Evidences of antibody responses to SARS-COV 2 infection were reported [7-10, 17,18] and that people who recovered from the infection have antibodies to the virus [13-15]. SARS-COV 2 antibodies were tested at population level or in specific groups (health workers, close contacts of known cases or within households) because COVID-19 antibodies are critical for understanding the extent of risk factors associated with SARS-COV 2 infection [19]. The present study provided data on the percentage of people with detectable anti-SARS-COV 2 -IgG and - IgM antibodies. This is relevant to population at risk, plasma therapy and herd immunity.

Generally, immunoglobulin M (IgM) is majorly produced during primary immune response to protect against new infection while IgG is the most abundant type of antibody produced in the later stages of an infection to protect till recovery [20]. The present study is the first to show the existence of anti-CovIgG and -CovIgM antibodies in symptomatic newly diagnosed COVID-19 Nigerian patients and in COVID-19 patients at discharge. Our results corroborate previous studies from other regions of the world which reported that symptomatic COVID-19 patients develop anti-SARS-COV 2 antibodies, but how long these antibodies lasted remained unknown [7,13-15]. COVID-19 free Nigerians considered for this study had no detectable anti-CovIgG and anti-IgM antibodies in their plasma using rapid screening immunochromatographic cassettes.

Plasma anti-CovIgG antibody was detected in 57.1% of COVID-19 patients while plasma anti-CovIgM antibody was detected in only one (3.6%) COVID-19 patients. Lower prevalence of anti-CovIgM antibody compared with anti-CovIgG antibody might be due to half-life of the immunoglobulin class, production rate of the immunoglobulin class coupled with time of screening relative to when SARS-COV 2 infection was contacted. Generally, IgM is detected at approximately 5 to 7 days after the initial onset of symptoms which rises to 21 days while IgG production continues to rise for 28 to 35 days after symptom onset till clinical recovery [21]. IgG typically has a long half-life and remains detectable for months or even years after the resolution of infection [20].

Presence of anti-Cov antibodies has immunological implications. IgM was reported to promote early inflammation through activation of the Complement pathway [20]. Based on this, anti-CovIgM antibody may lead to severe form of COVID-19 through Antibody-Mediated Immune Enhancement (ADE). During ADE, the non-neutralizing antibodies bind to virus particles, initiate upregulation of pro-inflammatory cytokines and downregulate anti-inflammatory cytokines [22]. Neutralizing IgG antibodies provides protective immunity by binding receptor-binding domain (RBD) of the viral spike protein to prevent virus from attaching onto ACE 2 receptor for SARS-COV 2. It was however reported that concentration of each antibody class is crucial in its function as either protective or pathogenic which is important to vaccine design and immunization delivery [23,24].

Detection of anti-CovIgG antibody in COVID-19 patients implied some degree of functional protective immunity to the virus and this group of patients might not spread SARS-COV 2. The COVID-19 patient with detectable anti-CovIgM antibody indicated recent SARS-COV 2 infection, thus likely to spread SARS-COV 2 to others. Moreover, having both anti-CovIgG and -IgM antibodies might be an indication of active antibody production to an ongoing SARS-COV 2 infection. However, the absence of detectable anti-CovIgG/IgM antibodies might be due to lack or low levels of these antibodies but not necessarily mean absence of active infection.

We found no gender differences in the prevalences of anti-CoV antibodies among the COVID-19 patients considered for this study. This finding deserves further investigation because previous studies found that men were more infected by COVID-19 than women, and male subjects with underlying conditions, including diabetes, hypertension, and cardiovascular diseases developed a severe form of the affection, with increased mortality rate [25-28]. Many factors such as hormone-specific reaction and activity of X-linked genes, which modulate the innate and adaptive immune response to virus infection were suggested [25,28].

The result of the present study has implications for vaccine and serological surveys, though not all COVID-19 patients produced anti-CoV antibodies detectable by cassette system lateral flow immunoassay. Certain hospitals have initiated the use of convalescent plasma as a source of therapeutic polyclonal antibodies for treatment of COVID-19, and early data suggest a positive impact on respiratory viral load and mortality [29-32]. However, the selection of therapeutic antibody candidates should be carefully considered to prevent potential unwanted side effects.

Conclusion

In conclusion, cassette system lateral flow immunoassay did not detect anti-SARS 2 Cov-IgG and -IgM antibodies in all COVID-19 patients and that these antibodies are more prevalent in COVID-19 patients at discharge, thus not all plasma from COVID-19 patients should be consider for plasma therapy.

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