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Anti-SARS-Cov-2 IgG Antibody Response in COVID- 19 Ischemic Heart Disease Patients

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Abstract **Original Research Article**

Background: Coronavirus disease-2019 (COVID-19), a contagious disease caused by severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), has reached pandemic status, overwhelmed health care systems, strangled the global economy, and led to a devastating loss of life. The presence of cardiovascular comorbidities in COVID-19 patients acts as risk factor for disease severity and is associated with higher rates of cardiac injury, cardiac attack, intensive care unit admission and high mortality. Without pre-existing cardiovascular comorbidities, COVID-19 itself can cause serious heart damage. Serum Anti-SARS-CoV-2 IgG estimation is an important tool for monitoring of COVID-19 patients. ***Objectives:*** To assess post COVID-19 Anti-SARS-CoV-2 IgG antibody response in Ischemic heart disease patients. ***Method:*** This cross-sectional analytical study was conducted in the Department of Biochemistry, Dhaka Medical College, Dhaka during the period of January 2021 to December 2021. For this study, a total number of 70 diagnosed COVID-19 patients with or without IHD, were selected according to inclusion and exclusion criteria from Cardiology Department (OPD and Indoor) and Post COVID-19 Follow-up Clinic of Dhaka Medical College Hospital, Dhaka. Among 70 subjects, 35 were post COVID-19 with IHD patients (Cases in group-A) and 35 were post COVID-19 without IHD patients (Comparison group in Group-B). By using safety measures, informed written consent was taken from each patient and venous blood sample was collected for estimation of serum Anti-SARS-CoV-2 IgG level. The results were compared statistically between two groups and the significance was defined as $p \leq 0.05$. ***Results:*** Mean ± SD years of age of the subjects in group-A and Group-B were 57.62 ± 11.32 years and 54.14 ± 11.29 years respectively. Majority of patients were in >60 year's age group followed by 51-60 years. The serum Anti-SARS-CoV-2 IgG level was significantly higher in group-A than Group-B (Median [IQR]: 10786.5 [1756.4-19346.9] Vs 2221.6 [747.9-8554.5]AU/ml, p-value: 0.041). In both groups, the Anti-SARS-CoV-2 IgG level was higher in presence of comorbidity, significantly higher in male, positively correlated with age and negatively correlated with the duration between RT-PCR positive and IgG test. ***Conclusion:*** Serum Anti-SARS-CoV-2 IgG level was significantly higher in post COVID-19 with IHD patients compared to post COVID-19 without IHD patients. In both groups, the Anti-SARS-CoV-2 IgG level was higher in presence of comorbidity, significantly higher in male, positively correlated with age and negatively correlated with the duration between RT-PCR positive and IgG test.

Keywords: Coronavirus-2 (SARS-Cov-2), Serum Anti-SARS-Cov-2 Igg, Ischemic Heart Disease (IHD).

INTRODUCTION

Coronavirus disease 2019 (COVID-19), the highly contagious infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has had a catastrophic effect on the world's demographics resulting in more than 2.9 million deaths worldwide, emerging as the most consequential global health crisis since the era of the influenza pandemic of 1918. After the first cases of this predominantly respiratory viral illness were first reported in Wuhan, Hubei Province, China, in late December 2019, SARS-CoV-2 rapidly disseminated across the world in a short span of time, compelling the World Health Organization (WHO) to declare it as a global pandemic on March 11, 2020 [1].

Owing to a population of over 160 million, inadequate healthcare system, and poor personal hygiene among the general population, Bangladesh is considered one of the high-risk countries for coronavirus spread. The first official case of COVID-19 was reported on 8 March 2020, and the epidemic still appears to be in a growing phase. On 18 March, 2022 as of a total 1,950,357 confirmed cases and death 29,112 have been reported in Bangladesh [2].

Coronaviruses belong to the family *Coronaviridae*. They can be classified into four genera: *Alphacoronavirus, Betacoronavirus, Gammacoronavirus,* and *Deltacoronavirus* [3]. Among them, alpha-and beta coronaviruses infect mammals [4]. Coronaviruses are large, enveloped, positive-stranded RNA viruses. They have the largest genome among all RNA viruses, typically ranging from 27 to 32 kb. The genome is packed inside a helical capsid formed by the nucleocapsid protein (N) and further surrounded by an envelope. Associated with the viral envelope are at least three structural proteins: The membrane protein (M) and the envelope protein (E) are involved in virus assembly, whereas the spike protein (S) mediates virus entry into host cells by Angiotensinogen Converting Enzyme 2 (ACE2) receptors [5].

The S protein of SARS-CoV-2 maintains a high binding affinity to human ACE2. This high binding affinity is likely to be related to the high transmissibility of SARS-CoV-2 and the severity of COVID-19 [6]. Like other corona viruses, the primary mechanism of transmission of SARS-CoV-2 is via infected respiratory droplets, with viral infection occurring by direct or indirect contact with nasal, conjunctival, or oral mucosa, when respiratory particles are inhaled or deposited on these mucous membranes [7].

ACE2 receptors are present in various organs including heart, lungs, kidney etc. When corona virus binds with this ACE2 receptor, the genetic materials of the virus enters the cell and the cell is harnessed to produce viral proteins, thus the virus multiplies and the cell dies which resulted in the production or release of specific inflammatory mediators by the type 2 alveolar cells.

The mediators stimulate the existing immune cells ‘macrophages’ and secrete chemical substances called cytokines. Three types of cytokines are produced namely; Interleukin 1 (IL1), Interleukin 6 (IL6) and Tumor necrosis factor (TNF- α) which reaches the blood stream and causing symptoms associated with COVID 19 [8]. ACE2 plays an essential role in the neurohumoral regulation of the cardiovascular system. The binding of SARS-CoV-2 to ACE2 causes acute myocardial and lung injury through the alternation in ACE2 signaling pathways [9].

ACE2 protects the heart against activation of the renin-angiotensin-aldosterone system (RAAS) because it converts angiotensin II to angiotensin (1-7). Angiotensin II is a vasoconstrictor, proinflammatory mediator, and damages capillary endothelium, while angiotensin (1-7) is a vasodilator. However, the virus entry causes down-regulation of ACE2 and increases angiotensin II levels, leading to increased heart damage [10]. There is association between COVID-19 and cardiovascular disease. COVID-19 patients with or without pre-existing heart disease may suffer a heart attack, heart failure, myocarditis, even death [11]. Patients with CVD are at higher risk of cytokine storms [12].

The cytokine storm is a complex network of severe molecular events, including a clinical phenotype of systemic inflammation, multi-organ failure, hyper-ferritinemia. It is generated by the activation of an innumerable amount of white blood cells, including B cells, T cells, NK cells, macrophages, dendritic cells, neutrophils, monocytes, and resident tissue cells, which release high amounts of proinflammatory cytokines [13]. IgM and IgG appears in blood around 6-10 days after infection. IgM comes first but disappears earlier than IgG. IgG antibody rises and goes to peak after 2nd week and persists for long days [14]. The median day of seroconversion on day 13 for IgG after symptom onset [15].

Premkumar e*t al.,* (2020) [16] examined 77 samples at different time points from 63 patients with COVID-19 and compared immune responses to the RBD of the spike protein of SARS-CoV-2 by ELISA to 71 control patients. They found that 9 days after the onset of symptoms, 98% of patients had a positive IgG response with a specificity of 100%. The median day of seroconversion on day 10 for IgM and day 12 for IgG after symptom onset [17]. IgG antibodies persist for at least several months in most persons, but the precise duration of time that antibodies persist after infection is unknown. Persons with more severe disease appear to develop a more robust antibody response with IgM, IgG, and IgA, all achieving higher titers and exhibiting longer persistence.

The observed persistence of antibodies can vary by assay and some studies have found that approximately 5%-10% do not develop detectable IgG antibodies following infection [18]. Serology tests are used to measure the level of antibody. Rapid serology tests, typically lateral flow assays (LFAs), are qualitative serology tests and provide a positive/negative readout. Quantitative serology tests are enzyme-linked immunosorbent assays (ELISAs) and chemiluminescent immunoassays (ChLIAs) and provide more information than qualitative serology tests [19].

The prevalence of COVID-19 in IHD patients is 17% [14]. The assessment of post COVID-19 Anti-

SARS-COV-2 IgG antibody response in IHD patients might be helpful in reduction of mortality from COVID-19 in this pandemic situation. But no data regarding this is available. Due to time and budget shortage the study has confined to tertiary level hospital. But the results obtained from this study might be helpful to find out difference of antibody response among the patients of COVID-19 with IHD and COVID-19 without IHD.

OBJECTIVES

General Objective:

To assess the post COVID-19 Anti-SARS-CoV-2 IgG antibody response in patients with ischemic heart disease

Specific Objective:

- To measure serum Anti-SARS-CoV-2 IgG antibody in post COVID-19 patients with and without ischemic heart disease.
- To compare serum Anti-SARS-CoV-2 IgG response between post COVID-19 with IHD and post COVID–19 without IHD patients.

METHODOLOGY

This was a cross-sectional analytical study conducted in the Department of Biochemistry, Dhaka Medical College, Dhaka, Bangladesh from January 2021 to December 2021. In total 70 diagnosed COVID-19 patients with or without IHD, were enrolled in this study as the study population. A convenient purposive sampling technic was used in sample selection. Among the total study population, 35 were post-COVID-19 with IHD (Cases in group-A) and 35 were post-COVID-19 without IHD (Control in Group-B). The study was approved by the ethical committee of the mentioned hospital. Properly written consent was taken from all the participants before data collection. As per the inclusion criteria of this study, only RT-PCR-confirmed adult patients with or without IHD who performed an anti-SARS-CoV-2 IgG test within 3 to 12 weeks of COVID-19 detection, were included. On the other hand, according to the exclusion criteria of this study, patients who received vaccination against SARS-COV-2, cases with acute infection or recent fever, malignancy cases and pregnant women were excluded. All the demographic and clinical information of the participants was recorded. All data were processed, analyzed and disseminated by using MS Excel and SPSS version 23.0 program as the necessity. In statistical analysis, a P value <0.05 was considered as the indicator of significance.

Ethical Clearance

Ethical permission was taken from Ethical Review Committee of Dhaka Medical College.

Inclusion Criteria for Cases:

- Adult patients (18 years and above) of both gender.
- Diagnosed case of IHD patients.
- Diagnosed case of post COVID-19 patients by RT-PCR test.
- Serum Anti-SARS-CoV-2 IgG test was done within 3 to 12 weeks of COVID-19 detection by RT-PCR test.

Inclusion Criteria for Comparison Group:

- Age, gender and duration (Between RT-PCR positive and IgG test) matched post COVID-19 patients without history of IHD.

Exclusion Criteria:

- Subjects who received vaccination against SARS-COV-2.
- Acute infection or recent fever.
- Malignancy
- Pregnancy

Study Procedure:

Collection and Preservation of Blood Samples:

With all aseptic precautions and by using personal protective equipment like gown, gloves, goggles, N95 mask, face shield, shoe cover, informed written consent was taken from each study subject, and 5 ml of venous blood sample was collected in a disposable plastic syringe and immediately transferred to a dry clean test tube which was allowed to clot at room temperature. The sample (clear serum) was separated after centrifuging at 3000 rpm for 10 minutes into a sterile Eppendorf tube and the separated serum was stored at -20^0C at Microbiology laboratory of DMC up to the date of analysis. The laboratory procedure was performed in the department of Biochemistry & Molecular Biology, BSMMU, Dhaka.

Laboratory Procedure:

Estimation of serum Anti-SARS-CoV-2 IgG by Chemiluminescent microparticle immunoassay (CMIA) (Abbott Diagnostics, USA)

Performed in the Department of Biochemistry & Molecular Biology, Bangabandhu Sheikh Mujib Medical University, Dhaka.

Serum Anti-SARS-Cov-2 Igg:

Anti- SARS-CoV-2 IgG II Quant assay is a chemiluminescent microparticle immunoassay (CMIA) used for the qualitative and quantitative determination of IgG antibodies to SARS-CoV-2 in human serum on the Alinity i system.

RESULTS

Table 1: Distribution of the study subjects according to age (N=70)

Age (In years)	Group-A (n=35)	Group-A (n=35)	p-value
18 - 30 yrs.	2(5.7)	1(2.8)	
31 - 40 yrs.	1(2.8)	3(8.6)	
41 -50 yrs.	5(14.4)	7(20.0)	0.684[b]
51 - 60 yrs.	11(31.4)	12(34.3)	
>60 yrs.	16(45.7)	12(34.3)	
Mean ± SD	57.62 ± 11.32	54.14 ± 11.29	0.202[a]
Range	25 - 70	27 - 72	

[a]Unpaired student's t-test & [b]Chi-square test was done to measure the level of significance

Table 1showed age distribution of the study subjects. Mean ± SD of age were 57.62 ± 11.32 years and 54.14 ± 11.29 years in group-A and Group-B respectively. Majority of patients were in >60 years followed by 51-60 year's age group. There was no significant age difference between group-A and Group-B.

Table 2: Distribution of the study subjects according to gender. (N=70)

Gender	Group-A (n=35)	Group-B (n=35)	p-value
Male	19(54.3)	15(42.9)	0.339
Female	16(45.7)	20(57.1)	

Chi-Square test was done to measure the level of significance

Table 2 showed gender distribution of the study subjects. Male (54.3%) was predominant in group-A and female (57.1%) was predominant in Group-B without any significant difference between two groups.

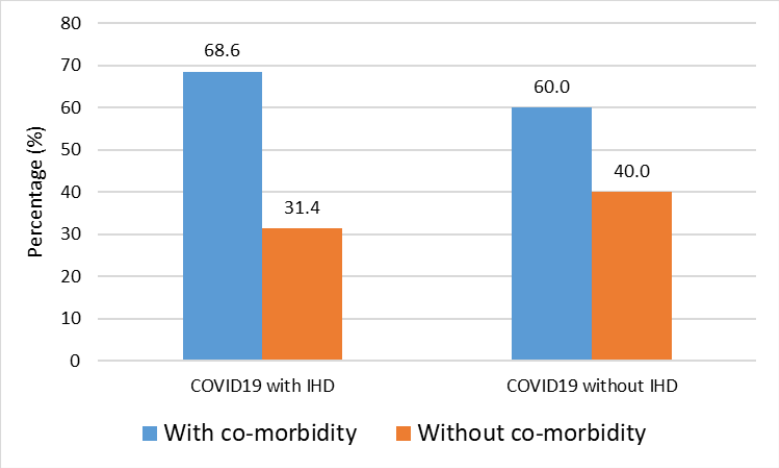

Figure 1: Bar diagram showing co-morbidity in COVID 19 patients with and without IHD

Figure 1 shows presence of comorbidity was 68.6% and 60.0% in group-A and Group-B respectively.

Table 3: Co-morbidities of the study subjects. (N=70)

Co-morbidities	Group-A (n=35)	Group-A (n=35)	p-value
Hypertension	16(45.7)	9(25.7)	0.081 [a]
Diabetes mellitus	0(0.0)	3(8.6)	0.239[b]
Chronic kidney disease	0(0.0)	1(2.9)	1.000[b]
Hypertension with DM	6(17.1)	7(20.0)	0.759[a]
Hypertension with CKD	2(5.7)	1(2.9)	1.000[b]
Total	24(68.6)	21(60.0)	0.454[a]

[a]Chi-Square test and [b]Fisher's Exact test were done to measure the level of significance

Table 3 showed comorbidities of the study subjects. Hypertension was the commonest comorbidity in both groups. There was no significant difference between two groups in terms of comorbidities.

Table 4: Duration between RT-PCR positive and IgG test of the study subjects. (N=70)

	Group-A (n=35) (Mean ± SD) Min-Max	Group-B (n=35) (Mean ± SD) Min-Max	p-value
Duration between RT-PCR positive and IgG test(In days)	44.4 ± 18.85 (21 - 90)	47.77 ± 17.32 (21 - 87)	0.489

Unpaired student's t-test was done to measure the level of significance

Table 4 showed the duration between RT-PCR positive and IgG test of the study subjects. There was no significant difference between two groups in term of duration between RT-PCR positive and IgG test.

Table 5: Blood pressure and BMI of the study subjects. (N=70)

	Group-A (n=35) Mean ± SD (Min-Max)	Group-B (n=35) Mean ± SD (Min-Max)	p-value
Systolic BP (mmHg)	129.57 ± 14.62 (100 - 160)	129.97 ± 14.38 (100 - 160)	0.908
Diastolic BP (mmHg)	81.71 ± 5.28 (70 - 90)	82.57 ± 5.47 (70 - 95)	0.507
BMI (kg/m^2)	25.17 ± 3.44 (17.32 - 38.16)	25.07 ± 1.99 (21.13 - 29.72)	0.876

Unpaired student's t-test was done to measure the level of significance

Table 5 showed mean ± SD of systolic blood pressure, diastolic blood pressure and BMI of the study subjects. There were no significant difference of systolic and diastolic blood pressure and BMI between group-A and Group-B.

Table 6: Anti-SARS-CoV-2 IgG level of the study subjects. (N=70)

Anti-SARS-CoV-2 IgG level (AU/ml)	Group-A (n=35)	Group-B (n=35)	p-value
Median	10786.5	2221.6	0.041
IQR	1756.4–19346.9	747.9–8554.5	

Mann-Whitney U test was done to measure the level of significance

Table 6 showed Anti-SARS-CoV-2 IgG levels of the study subjects. Median value of Anti-SARS-CoV-2 IgG level was significantly higher in group-A (Post COVID-19 with IHD) in comparison to Group-B (Post COVID-19 without IHD).

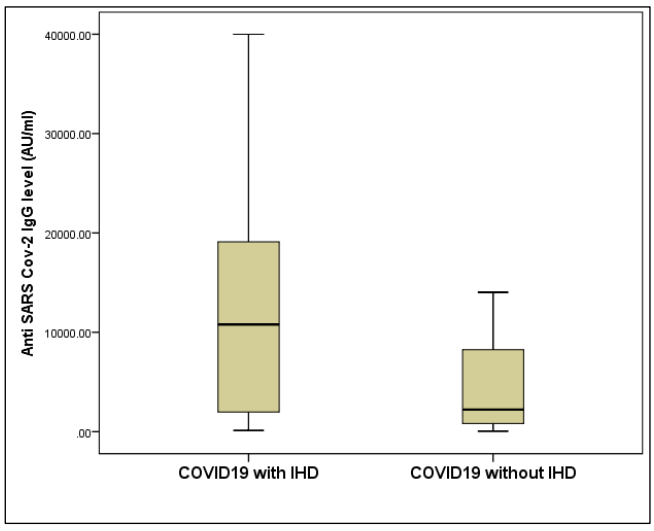

Figure II: Box plot showing Anti-SARS-CoV-2 IgG level in COVID-19 with IHD and COVID-19 without IHD patients.

Figure 2 showed median value, upper and lower quartile, maximum and minimum value of Anti-SARS-CoV-2 IgG level of both groups. For group-A, median value of Anti-SARS-CoV-2 IgG was 10786.5 AU/ml with IQR (1756.4-19346.9 AU/ml), maximum value (31998.60 AU/ml) and minimum value (122.20 AU/ml). For Group-B, median value was 2221.6 AU/ml with IQR (747.9-8554.5 AU/ml), maximum value (39155.00 AU/ml) and minimum value (47.90 AU/ml).

Table 7: Distribution of the study subjects by Anti-SARS-CoV-2 IgG status. (N=70)

IgG status	Group-A (n=35)	Group-B (n=35)	p-value
Positive (≥50 AU/ml)	35(100.0)	34(97.1)	1.000
Negative (<50 AU/ml)	0(0.0)	1(2.9)	

Fisher's Exact test was done to measure the level of significance

Table 7 showed the Anti-SARS-CoV-2 IgG status of the study subjects. No significant difference of Anti-SARS-CoV-2 IgG status was present between two groups.

Table 8: Anti-SARS-CoV-2 IgG level of the study subjects according to gender. (N=70)

Group		IgG level (AU/ml) in male	IgG level (AU/ml) in female	p-value
Group-A	Median	14034.90	2085.80	0.017
	IQR	2202.9-22154.3	1299.7-18307.6	
Group-B	Median	3585.25	2232.35	0.882
	IQR	495.6-14024.0	931.0-7749.1	

Mann-Whitney U test was done to measure the level of significance

Table 8 showed the Anti-SARS-CoV-2 IgG level of the study subjects according to gender. The Anti-SARS-CoV-2 IgG level was significantly higher in male than female in Group-A. But in Group-B, no statistically significant difference was found between male and female.

Table 9: Anti-SARS-CoV-2 IgG level of the study subjects with and without co-morbidity. (N=70)

Group		IgG level (AU/ml) With comorbidity	IgG level (AU/ml) without comorbidity	p-value
Group-A	Median	8192.0	7304.7	0.793
	IQR	2470.3-17013.5	1257.6-26179.2	
Group-B	Median	3113	1080.6	0.089
	IQR	1213.3-16897.3	386.1-6187.0	

Mann-Whitney U test was done to measure the level of significance

Table 9 showed the Anti-SARS-CoV-2 IgG level of the study subjects with and without co-morbidity. The Anti-SARS-CoV-2 IgG was higher in presence of co-morbidity than absence of it in both groups. But the difference of antibody level was not statistically significant.

Table 10: Correlation of Anti-SARS-CoV-2 IgG level with age, duration between RT-PCR positive and IgG test and BMI of the study subjects. (N=70)

	COVID-19 with IHD (Group-A)		COVID-19 without IHD (Group-B)	
	r-value	p-value	r-value	p-value
Age	0.388	0.021	0.350	0.039
Duration between RT-PCR positive and IgG test	-0.602	<0.001	-0.563	<0.001
BMI	0.040	0.819	0.212	0.222

Spearman's rank correlation coefficient test was done to see the level of significance

Table 10 showed correlation of Anti-SARS-CoV-2 IgG level with age, duration between RT-PCR positive and IgG test and BMI of the study subjects. In both groups, there was significant positive correlation between age and Anti-SARS-CoV-2 IgG and significant negative correlation of Anti-SARS-CoV-2 IgG with duration between RT-PCR positive and IgG test.

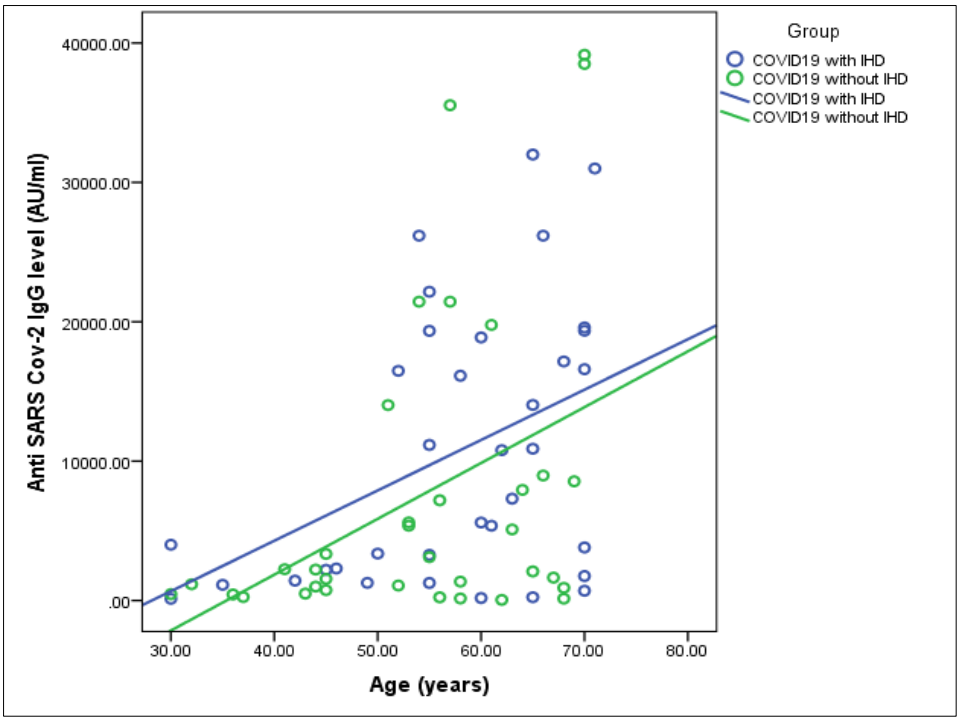

Figure III: Scatter diagram showed correlation between age and Anti-SARS-CoV-2 IgG level in post COVID-19 with IHD and post COVID-19 without IHD patients.

Figure III showed a significant positive correlation between age and Anti-SARS-CoV-2 IgG level in two groups.

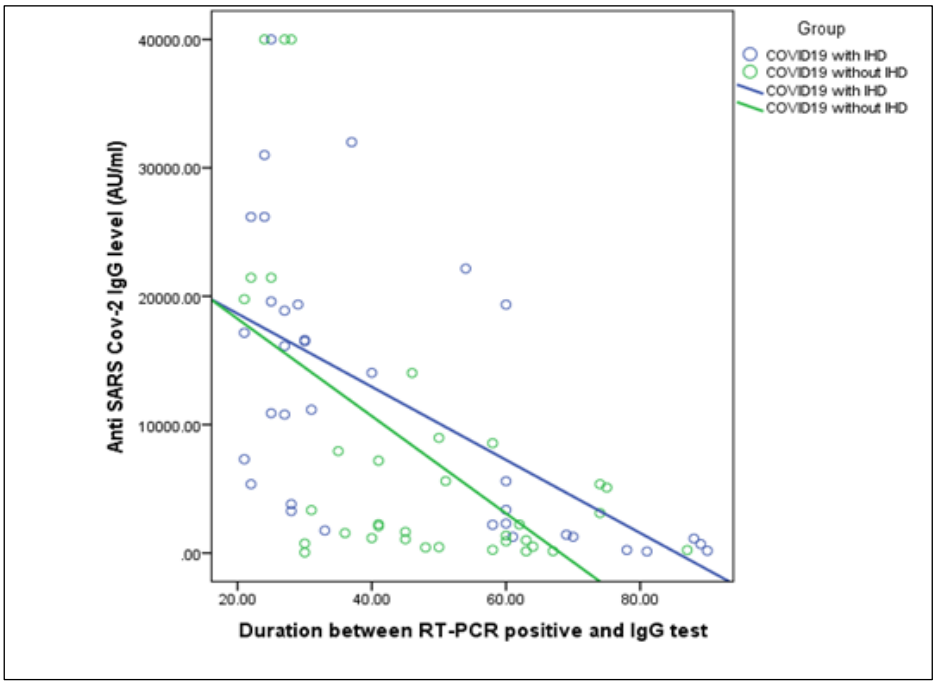

Figure 4: Scatter diagram showed correlation of duration between RT-PCR positive IgG test with Anti-SARS-CoV-2 IgG level in post COVID-19 with IHD and post COVID-19 without IHD patients.

Figure 4 showed a significant negative correlation of duration between RT-PCR positive and IgG test with Anti-SARS-CoV-2 IgG level in two groups.

DISCUSSION

This cross sectional analytical study was carried out with the aim to assess the post COVID-19 Anti-SARS-CoV-2 IgG antibody response in IHD patients. For this purpose, a total of 70 patients were selected on

the basis of inclusion and exclusion criteria from the cardiology department (OPD and Indoor) and 'Post COVID-19 follow up clinic' of Dhaka Medical College hospital, Dhaka. Among them 35 patients were post COVID-19 with IHD and considered as Group-A (Cases), rest 35 patients were post COVID-19 without IHD and considered as Group-B (For comparison). In this study, Both the COVID-19 and IHD patients were previously diagnosed. COVID-19 was confirmed by RT-PCR test. Previous history of MI, ECG changes (ST elevation, T-wave inversion), previously rise of Troponin-I, history of use of anti-ischemic medications were taken into consideration for diagnosis of Ischemic Heart Disease. In present study, the mean age of group-A and Group-B were 57.62±11.32 years and 54.14±11.29 years respectively. Xiang *et al.,* (2021) [20] found in his study the median age of 60(46.5-67.0) years which was almost similar to this study. Guo *et al.,* (2021) [21] found the mean age 48.6±15.5 years in his study which was a little bit different from this study. This may be due to different in sample size. In current study, there were male 19(54.3%) and female 16(45.7%) in group-A and male 15(42.9%) and female 20(57.1%) in Group-B and there was no significant gender difference in between two groups. Xiao *et al.,* (2021) [22] found in his study that there were 28(50%) male and 28(50%) female and Guo *et al.,* (2021) [21] found 57.4% male in his study. Both findings were almost similar to this study. In this study, both group-A and Group-B had one or more co-existing medical comorbidities. Underlying comorbidities were found including hypertension, diabetes mellitus, CKD. Hypertension 68.6% and 48.6% in group A and group B respectively, Diabetes mellitus 17.1% and 28.6% and CKD 5.7% and 5.8% in group-A Group-B respectively. There was no significant difference of comorbidities between two groups of the study subjects (p=0.454). A total of 24 participants (68.6%) in group-A and 21 participants (60.0%) in Group-B had at least one above mentioned comorbidity. Callender *et al.,* (2020) [23] found in his study Hypertension (16%), cardiovascular disease (12.11%), and diabetes (7.87%) were the most prevalent pre-existing co-morbidities among hospitalized COVID patients. Guo *et al.,* (2021) [21] found in his study a total of 19 participants (35.2%) had at least one underlying comorbidity, such as hypertension, diabetes, coronary heart disease or chronic liver disease. Akter *et al.,* (2020) [24] found about 84% of asymptomatic cases had no co-morbid diseases, while 52% of the severe cases had more than one co-morbid disease. The majority of the severe cases reported diabetes (60%) followed by hypertension (36%), and asthma (32%). All the above studies are similar to this study. This study showed the mean duration between RT-PCR positive and IgG test was 44.4±18.85 days and 47.77±17.32 days in group-A and Group-B respectively. No significant difference of duration was found in between two groups. And in my study duration of doing IgG test was from 21days to 90 days after RT-PCR positive. Guo *et al.,* (2021) [21] performed a study where the mean interval from onset of the disease to antibody testing was 247.5±11.2 days. The present study showed that the mean systolic BP was 129.57±14.62 mmHg and 129.9±14.38 mmHg in group-A and Group-B respectively, diastolic BP was 81.71±5.28 mmHg and 82.57±5.47 mmHg in group-A and Group-B respectively. There was no significant difference of systolic and diastolic BP in between two groups. In current study, the mean BMI was 25.17±3.44 kg/m and 25.07±1.99 kg/m in group-A and Group-B respectively and there was no significant difference in between group-A and Group-B. In this study, Anti SARS Cov-2 IgG status was found 100% and 97.1% positive in group-A and Group-B respectively. Guo *et al.,* (2021) found in his study among a total of 52 participants where 96% tested positive for SARS-CoV-2 IgG which was almost similar with this study. In this study, Anti-SARS-CoV-2 IgG level was found (Median [IQR]:10786.5 [1756.4-19346.9] and 2221.6 [747.9–8554.5]AU/ml) in group-A and Group-B respectively. The antibody level was higher in group-A (COVID-19 with IHD patients) than Group-B (COVID-19 without IHD patients). This difference was statistically significant. Kutsuna *et al.,* (2021) [25] found that male sex, diabetes mellitus and high C-reactive protein levels during the disease course were associated with elevated IgG antibodies. In their study, DM was a risk factor of COVID-19 severity and severity of disease is associated with high rise of antibody titre. IHD was a risk factor for COVID-19 severity in this study. Callender *et al.,* (2020) [23] in their study regarding the impact of comorbidity on COVID-19, found that the individuals who were asymptomatic or mild symptomatic were without any comorbidity or healthy individuals. And symptomatic or the individuals of critical cases were with one or more comorbidity. Long *et al.,* (2020b) [26] studied serological responses in 37 patients with asymptomatic infection with SARS-CoV-2 and compared those with 37 symptomatic comparators matched by sex, age, and comorbidities. The asymptomatic group showed an IgG seropositivity rate of 84% 3- comparators. Shirin *et al.,* (2020) [27] found in their study, serological responses in asymptomatic individuals that were significantly lower than in individuals with even mild symptoms of infection and patients with moderate or severe disease had significantly higher IgG responses than mild or asymptomatic infection. Guo *et al.,* (2021) [21] showed that IgG levels were significantly higher in participants with severe disease than in those with non-severe disease (median [IQR]: 15.76 [9.50-35.76] vs 6.87 [2.90-13.12]; p= 0.001). These all findings were similar with this study. In the present study, there was statistically significant difference (P value =<0.05) in between male and female in terms of Anti-SARS-CoV-2 IgG level in Group-A. The median value of IgG was found 14034.90 AU/ml (with IQR: 2202.9-22154.3) in male patients and 2085.80 AU/ml (with IQR: 1299.7-18307.6) in female patients in Group-A. In Group-B, The IgG level was found 3585.25 AU/ml (with IQR: 495.6-14024.0) in male patients and 2232.35 AU/ml (with IQR: 931.0-7749.1) in female patients. In both group, IgG level was

higher in male patients than female patients. Similar statistically significant findings were present in the study of Kutsuna *et al.,* (2021) [25]. In this study, the median serum Anti-SARS-CoV-2 IgG level was found higher with co-morbidity than without comorbidity in both groups. Median value of IgG was found 8192.0 AU/ml (with IQR: 2470.3-17013.5 AU/ml) in presence of comorbidity and 7304.7 AU/ml (with IQR: 1257.6-26179.2 AU/ml) in absence of comorbidity in Group-A. In Group-B, median value of IgG was found 3113.0 AU/ml (with IQR: 1213.3-16897.3 AU/ml) in presence of comorbidity and 1080.6AU/ml (with IQR: 386.1-6187.0 AU/ml) in absence of comorbidity. In both group, Anti-SARS-CoV-2 IgG level was higher in presence of comorbidity but much higher in group-A than Group-B. This may be because of presence of pre-existing comorbidity that is Ischemic heart disease may raise the antibody level with other comorbidities. Almost similar findings were found in the study of Kutsuna *et al.,* (2021) [25]. He found that male sex, Diabetes mellitus and high CRP levels were associated with elevated Anti-SARS-CoV-2 IgG level. And DM was one of the important co-morbidity associated with COVID-19 in their study. IHD was another preexisting comorbidity in this study. For this reason, antibody level was higher in group-A (COVID19 with IHD patients). In this study, Spearman's rank correlation coefficient test was done and there was significant weakly positive correlation of Anti-SARS-CoV-2 IgG level with age (r= 0.388; P=0.021 and r = 0.350; P= 0.039) in group-A and Group-B respectively. Yang *et al.,* (2021) [28] studied about association of age with SARS-CoV-2 antibody. In their study they found that the IgG level in the adult population exhibited a weakly positive correlation with age (r = 0.24; P< 0.001) which was similar with this present study. Significant negative correlation was found of Anti-SARS-CoV-2 IgG with duration between RT-PCR positive and IgG test (r = -0.602; P < 0.001in group-A and r = -0.563; P<0.001in Group-B). Xiao *et al.,* (2021) [22] found the overall IgG titers gradually decreased over time, particularly in the first 6 months after discharge.

CONCLUSION

In conclusion, the level of Anti-SARS-CoV-2 IgG antibody is significantly higher in post COVID-19 with IHD patients compared to post COVID-19 without IHD patients. Also the Anti-SARS-CoV-2 IgG level is significantly higher in male than female, positively correlated with age and negatively correlated with the duration between RT-PCR positive and IgG test.

Limitation of the Study:

This was a single-centered study with small-sized samples. Moreover, the study was conducted over a very short period. So, the findings of this study may not reflect the exact scenario of the whole country.

RECOMMENDATIONS

Large scale population based, multicentre study should be conducted to get the real scenario in COVID-19 with Ischemic Heart Disease patients of Bangladesh. A longitudinal prospective study is needed to know the real scenario about duration of persistence of antibody level in COVID-19 with IHD patients and for their better management.

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