Relationship of the antibody level between male and female SARS-CoV-2 infected patients in Dhaka city

*I Chowdhury[1], FA Mishu[2], SMT Haque[3], PK Chanda[4], FH Mollah[5]

ABSTRACT

Background: The Coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) created an emergency situation experienced by the world.

Objective: To compare the antibody status after SARS-CoV-2 infection in male and female patients.

Methods: This cross-sectional study was conducted in the Department of Biochemistry and Molecular Biology, BIRDEM General Hospital, from July, 2020 to June, 2021. A total of 154 patients (age 18 – 70 years) infected by SARS-CoV-2 were enrolled for this study. Among them, 78 were male and 76 were female. The study subjects were non-vaccinated. For this study, serum IgG level was measured by the automated analyser. For statistical analysis, the Mann Whitney U test was done.

Results: the age distribution of male and female patients. The age group of 50-59 years comprised most of the male patients in comparison to the female study group. Patients with hypertension, diabetes mellitus were more prone to SARS-CoV-2 infection in both groups. Here male patients had more positive history of comorbidities than female patients. Mann-Whitney U test was done to analyze the data which revealed presence of significantly higher IgG in female patients. Here, $p < 0.02$ which was fairly statistically significant.

Conclusion: The antibody level of female patients was significantly higher than that of male patients after SARS-CoV-2 infection.

Key words: SARS-CoV-2, Antibody, Comparison

Introduction

The Coronavirus disease 2019 (COVID-19) is a pandemic situation experienced by the world. It is caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) which is an enveloped single stranded RNA virus of Coronaviridae family and Orthocoronaviridae sub family.[1] It has four structural proteins: spike (S), envelope (E), membrane (M) and nucleocapsid (N) proteins. The spike protein facilitates viral entry into host cells by binding to a host receptor through the RBD in the S1 subunit.

Afterwards, viral and host membranes fuse through the S2 subunit.[2] Body immune system responses to a pathogen with both innate and adaptive immunity. One aspect of the adaptive immunity is humoral response that features the production of antibodies recognizing specific antigens.[3] S1 and S2 subunits of the viral spike protein act as antigen. After immunological reaction anti-S1, anti-S2 IgG are produced within the body.[4] People in Central Europe were much more affected than people in East Asia in

[1]*Dr. Indira Chowdhury, Lecturer, Department of Biochemistry, Sheikh Hasina Medical College, Jamalpur

[2]Dr. Farzana Akonjee Mishu, Associate Professor, Department of Biochemistry and Molecular Biology, BIRDEM General Hospital

[3]Dr. Syed Mohammad Tanjilul Haque, Associate Professor, Department of Forensic Medicine & Toxicology, Anwer Khan Modern Medical College

[4]Dr. Papon Kumar Chanda, Medical Officer, Modhupur Upazilla Health Complex, Modhupur

[5]Dr. Forhadul Hoque Mollah, Professor, Department of Biochemistry and Molecular Biology, (BSMMU)

*Corresponding Author

comparison to the numbers of cases and deaths due to SARS-CoV-2.5 The idea about serological findings after 30 days in non-severe disease remain limited and conflicting. Several follow-up studies of hospitalized patients in Sweden had reported about the development of IgG in majority of patients.[6] An experimental study in Italy noticed non-hospitalized subjects developed lower antibody titer compared to patients in Intensive Care Units (ICU). The highest levels of IgG antibody was associated with severe disease. The persistence period of IgG antibodies in circulation was not well defined but within a month after being COVID-19 negative, antibody titer was half then before.[7] A case control study investigated that the concentration of IgG was lowest in early disease stages but raised at 15 days of post illness. Moreover the IgG concentration reached peak during 21-25 days after illness as 16.5 μg/mL, and stayed at a comparatively high concentration 11.4 μg/mL until 31-41 days in hospital admitted patients.[8] A single center study in Iran reported majority of cases were in the age group of 50 to 60 years of old. The male-to-female ratio was 1.93:1. Male gender, older age, history of comorbidities like hypertension, diabetes mellitus were the important risk factors. Male patients within age group 50 to 60 year and with comorbidities are in vulnerable condition in case of SARS-CoV-2 infection.[9] SARS-CoV-2 infected male patients aged 50 years or more were associated with 15.4-folds significantly increased risk of mortality.[10] A Retrospective observational study in India reported that patients with T2DMwere more likely to be negative for anti-SARS-CoV-2 antibodies than those without DM. Impaired sero conversion could theoretically increase the risk of re infections in patients with DM.[11] The noticed expanded seriousness and mortality of COVID-19 pneumonia with hyperglycaemia was not the aftereffect of a hindered humoral reaction against SARS-CoV-2. Produced IgG was related with a noteworthy defensive impact with diabetes.[12] Increasing age, male gender, hypertension, diabetes, and cardiovascular diseases adversely affect viral clearance.13 Another study reported that COVID-19 positive hypertensive patients deteriorated more

rapidly than non-hypertensive group.[14] However there are limited idea about the duration of persistence of antibody after infection, IgG level in patients with co-morbidities like hypertension, diabetes etc and is there any re-infection within the interval. So far literature review reveals scarce of relevant co-relational study in Bangladesh. We need to know about the quantitative antibody status of male and female patients after SARS-CoV-2 infection .

The study of antibody level after SARS-CoV-2 infection may give idea about any difference of immunological protection between male and female patients.

Methods

This cross-sectional study was conducted at Department of Biochemistry and Molecular Biology, BIRDEM General Hospital, Shahbag, Dhaka from July, 2020 to June, 2021. A total of 154 study subjects, who had confirmed COVID-19 and recovered (78 male patients were taken as group I and another 76 female patients were taken as group II). In this study, 84 patients were treated in hospital and 70 patients were treated at home. Inclusion criteria for both group I and II were RT-PCR positive for SARS-CoV-2 within last 3 to 6 months, age 18 to 70 years. Vaccinated patients against SARS-CoV-2 virus, pregnancy, lactation, chronic liver and renal disease, history of heart failure, any malignancy, any immunosuppressive disorders and radiation therapy were the exclusion criteria for both groups. Institutional Review Board (IRB) of BIRDEM Academy, Shahbag, Dhaka approved the research protocol. A structured questionnaire and data sheet were prepared for this research including all the variables of interest. Blood sample was collected by maintaining all aseptic precautions. The serum was separated from individual sample and stored at -56ºC. Estimation of serum IgG was performed at the Department of Biochemistry and Molecular Biology, BSMMU and assessed by Chemiluminescent Microparticle Immunoassay (CMIA) using Abbott Allinity i Autoanalyzer (USA).

Collected data were entered, checked and edited (to remove the outliers) with the help of the Statistical

Package for Social Sciences (SPSS) software, version 26 and analysed. The data were expressed as frequency and percentage, mean ± SD for normally distributed data or median (inter-quartile range) for data not normally distributed. The Mann-Whitney U test was done to compare IgG status between male and female SARS-CoV-2 infected patients. p value ≤ 0.05 was considered statistically significant.

Results

A total of 154 study subjects, who were infected 3 to 6 months ago, were enrolled for this study. The mean ± SD age of male patients was 45.98±13.05 and female patients was 46.36±13.22 years. It was observed that males needed hospital support in comparison to the females (Table-I).

Table I: Grouping of the SARS-CoV-2 infected study subjects on the basis of Home and hospital treatment (n=154)

	Male	Female
Hospital treated	64(82.10%)	20(26.30%)
Home treated	14(17.90%)	56(73.70%)
Total	78	76

Table-II showed age, gender and habitats of the study subjects. Many of the SARS-CoV-2 infected patients were distributed in the age group 50-59. In this study, except 18 study subjects, all were from suburban area.

Table-II: Demographic characteristics of the study population (n=154)

Variables	No. of patients (n)	Percentage (%)
Age group (years)		
20-29	26	16.90
30-39	25	16.20
40-49	29	18.80
50-59	50	32.50
60-70	24	15.60
Gender		
Male	78	50.60
Female	76	49.40
Habitat		
Urban	136	87.7
Suburban	18	11.7

Results are expressed as frequency (n) and percentage (%)

Table-III showed the age distribution of male and female patients. The age group of 50-59 years comprised most of the male patients in comparison to the female study group.

Table-III: Age distribution of the study population (n=154)

Age group (years)	Male (n=78)	Female (n=76)
20-29	12 (15.40%)	16 (21.10%)
30-39	13 (16.70%)	19 (25.00%)
40-49	17 (21.80%)	15 (19.70%)
50-59	28 (35.90%)[*]	09 (11.80%)
60-70	08 (10.30%)	17 (22.80%)
Total	78 (100.0%)	76 (100.0%)

Table-IV showed distribution of comorbidity among the study population. Patients with hypertension, diabetes mellitus were more prone to SARS-CoV-2 infection in both groups. Here male patients had more positive history of comorbidities than female patients.

Table-IV: Distribution of the respondents by comorbidity (n=154)

Specific of comorbidity of the patients	Male (n=78)	Female (n=76)
HTN, DM	18(23.10%)	15(19.70%)
DM	31(39.7%)	14(18.40%)
HTN	18(23.1%)	21(27.60%)
None	11(14.10%)	26(34.20%)
Total	78(100.0%)	76(100.0%)

Mann-Whitney U test was done to analyze the data which revealed presence of significantly higher IgG in female patients. Here, p <0.02 which was fairly statistically significant (Table-V).

Table V: Distribution of the respondents according to IgG (AU/ml) status (n=154)

	Male (n=78)	Female (n=76)	p-value
Median with range of IgG (AU/ml)	720.90 (314.0-2620.50)	1858.00 (484.20-5046.60)	<0.02[*]

Data were expressed as median (Inter Quartile Range, IQR).

Discussion

This cross-sectional study reported that male patients needed hospital support after SARS-CoV-2 infection. There was difference between the number of home and hospital treated patients regarding gender. Gomez et al. observed that rate of hospital admission after SARS-CoV-2 infectio was higher in male patients.[15] This finding was also in aggrement with a recent study in Italy done by Vahidy et al. The study reported 17% males needed hospital support and as compared to females were 14.6%.[16]

In this current study, the participants within age group 50-59 years were more infected. This result was consistent with Nikpouraghdam et al. a recent study in Iran. The study reported that the majority COVID-19 infected patients were in the age group of 50 to 60 years old.[17]

It was observed that most of the male patients had previous history of comorbidity. On the other hand female patients showed less history of comorbidity. A retrospective cohort study in Peru mentioned that 65.31% were male in the study. More frequency of diabetes mellitus (21.95%) and hypertension (21.68%) were recorded among the patients.[18] A systemic review and meta analysis reported that male patients, age more then 50 years, or had history of comorbidities were significantly associated with increased risk of mortality after SARS-CoV-2 infection.[19]

This cross-sectional study identified a discrepancy in SARS-CoV-2 IgG status in male and female patients. The amount of antibody produced by female patients reported fairly significant difference than that of male patients. In a study Zeng et al. observed that female patients had high concentration of serum SARS-CoV-2 IgG antibody in comparison to male patients. It was also reported that in early phase of infection the generation of IgG was stronger in female patients.[20]

Conclusion

The antibody level of female patients was significantly higher than that of male patients after SARS-CoV-2 infection.

Conflicts of interest: None.

References

1. Jothimani D, Venugopal R, Abedin MF, Kaliamoorthy I, Rela M. COVID-19 and the liver. Journal of Hepatology. 2020; 73(5): 1231-40.

2. Shirin T, Bhuiyan TR, Charles RC, Amin S, Bhuiyan I, Kawser Z, et al. Antibody responses after COVID-19 infection in patients who are mildly symptomatic or asymptomatic in Bangladesh. International Journal of Infectious Diseases 2020; 101(12): 220-5.

3. Long QX, Tang XJ, Shi QL, Li Q, Deng HJ, Yuan J, Hu JL, Xu W, Zhang Y, Lv FJ, Su K. Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections. Nature medicine. 2020; 26(8): 1200-4.

4. Zeng, F., Hon, C.C., Yip, C.W., Law, K.M., Yeung, Y.S. and Chan, K.H. (2006) Quantitative comparison of the efficiency of antibodies against S1 and S2 subunit of SARS coronavirus spike protein in virus neutralization and blocking of receptor binding: implications for the functional roles of S2 subunit. FEBS letters. 580(24), 5612-5620.

5. Yamamoto N, Bauer G. Apparent difference in fatalities between Central Europe and East Asia due to SARS-COV-2 and COVID-19: Four hypotheses for possible explanation. Medical hypotheses. 2020; 144: 110160.

6. Marklund E, Leach S, Axelsson H, Nyström K, Norder H, Bemark M, Angeletti D, Lundgren A, Nilsson S, Andersson LM, Yilmaz A. Serum-IgG responses to SARS-CoV-2 after mild and severe COVID-19 infection and analysis of IgG non-responders. PLOS ONE. 2020 Oct 21; 15(10): e0241104.

7. Bruni M, Cecatiello V, Diaz-Basabe A, Lattanzi G, Mileti E, Monzani S, Pirovano L, Rizzelli F, Visintin C, Bonizzi G, Giani M. Persistence of anti-SARS-CoV-2 antibodies in non-hospitalized COVID-19 convalescent health care workers. Journal of Clinical Medicine. 2020; 9(10): 3188.

8. Ma H, Zeng W, He H, Zhao D, Yang Y, Jiang D, et al. COVID-19 diagnosis and study of serum SARS-CoV-2 specific IgA, IgM and IgG by chemiluminescence immunoanalysis. MedRxiv 2020; 8(5): 1-9.

9. Nikpouraghdam M, Farahani AJ, Alishiri G, Heydari S, Ebrahimnia M, Samadinia H, Sepandi M, Jafari NJ, Izadi M, Qazvini A, Dorostkar R. Epidemiological characteristics of coronavirus disease 2019 (COVID-19) patients in IRAN: A single center study. Journal of Clinical Virology. 2020; 127: 104378.

10. Biswas M, Rahaman S, Biswas TK, Haque Z, Ibrahim B. Association of sex, age, and comorbidities with mortality in COVID-19 patients: a systematic review and meta-analysis. Intervirology. 2021; 64(1): 36-47.

11. Pal R, Sachdeva N, Mukherjee S, Suri V, Zohmangaihi D, Ram S, Puri GD, Bhalla A, Soni SL, Pandey N, Bhansali A. Impaired anti-SARS-CoV-2 antibody response in non-severe COVID-19 patients with diabetes mellitus: a preliminary report. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2021; 15(1): 193-6.

12. Lampasona V, Secchi M, Scavini M, Bazzigaluppi E, Brigatti C, Marzinotto I, Davalli A, Caretto A, Laurenzi A, Martinenghi S, Molinari C. Antibody response to multiple antigens of SARS-CoV-2 in patients with diabetes: an observational cohort study. Diabetologia. 2020; 63(12): 2548-58.

13. Chen X, Hu W, Ling J, Mo P, Zhang Y, Jiang Q, Ma Z, Cao Q, Deng L, Song S, Zheng R. Hypertension and diabetes delay the viral clearance in COVID-19 patients. MedRxiv. 2020; 65: 1-9.

14. Emami A, Javanmardi F, Akbari A, Kojuri J, Bakhtiari H, Rezaei T, Keshavarzi A, Falahati F. Survival rate in hypertensive patients with COVID-19. Clinical and Experimental Hypertension. 2021; 43(1): 77-80.

15. Gomez JM, Du-Fay-de-Lavallaz JM, Fugar S, Sarau A, Simmons JA, Clark B, et al. Sex Differences in COVID-19 Hospitalisation and Mortality. Journal of Women's Health 2021; 30(5): 646-53.

16. Vahidy FS, Pan AP, Ahnstedt H, Munshi Y, Choi HA, Tiruneh Y, et al. Sex differences in susceptibility, severity, and outcomes of coronavirus disease 2019: Cross-sectional analysis from a diverse US metropolitan area. PLOS ONE 2021; 16(1): e0245556.

17. Nikpouraghdam M, Farahani AJ, Alishiri G, Heydari S, Ebrahimnia M, Samadinia H, Sepandi M, Jafari NJ, Izadi M, Qazvini A, Dorostkar R. Epidemiological characteristics of coronavirus disease 2019 (COVID-19) patients in IRAN: A single center study. Journal of Clinical Virology. 2020; 127: 104378.

18. Mejía F, Medina C, Cornejo E, Morello E, Vásquez S, Alave J, et al. Oxygen saturation as a predictor of mortality in hospitalized adult patients with COVID-19 in a public hospital in Lima, Peru. PLOS ONE 2020; 15(12): e0244171.

19. Biswas M, Rahaman S, Biswas TK, Haque Z, Ibrahim B. Association of sex, age, and comorbidities with mortality in COVID-19 patients: A Systematic Review and Meta-analysis. Intervirology. 2021; 64(1): 36-47.

20. Zeng F, Dai C, Cai P, Wang J, Xu L, Li J, Hu G, Wang Z, Zheng F, Wang L. A comparison study of SARS-CoV-2 IgG antibody between male and female COVID-19 patients: a possible reason underlying different outcome between sex. Journal of Medical Virology. 2020; 92(10): 2050-4.