

Original article

Antibodies production in gender groups for surviving COVID-19

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ARTICLE INFO

Article history:

Received 27 November 2020

Received in revised form 28 December 2020

Accepted 29 December 2020

Keywords:

COVID-19

Survival

Pandemic

Anti SAR-COV-2 IgG antibodies

ABSTRACT

Aim: A pilot study was executed in the months of June-July 2020 in Qazi Hussain Ahmed Medical Complex Nowshera with aim to determine the gender protective role in term of production of neutralizing anti SARS-COV-2 antibodies. **Methods:** A total of 39 coronavirus disease 2019 (COVID-19) patients who recovered from COVID-19 were selected. Their antibodies cut off values were measured by electro-chemiluminescence immunoassay using Roche Cobas E411 Chemistry Analyzer for which commercial kits of Roche diagnostics were used as per the instructions of the manufacturer. **Results:** A statistically significant difference in mean post infection antibodies level was observed with higher cut off values in patient who had symptoms at time of being reported positive by polymerase chain reaction (PCR) as compared to patient who were asymptomatic (p -value:0.04). Using Kaplan Meir it was predicted that in female gender, the probability of survival is 100% at cut off antibodies levels of 50, While a vertical drop up to less than 40% of probability of survival was predicted in male gender even at higher antibodies levels of >100, that supports the prediction of production of higher levels of antibodies in female gender in early infections. **Conclusion:** The female gender produces higher titer of antibodies in early infections to confer immunity in COVID-19.

Introduction

According to the World Health Organization, the viral diseases continue to emerge and are representing serious health issues in time and future. The outbreak in 2019 was totally different with presentation of pneumonia of unknown cause, later on, the Chinese Centre for Disease Control and Prevention and local CDC attributed it to a novel virus belonging to corona family and was termed as 2019-nCoV. That was first reported from the city of Wuhan in China [1,2]. The demographic variables like gender and age play an important role in prognosis and outcome of coronavirus disease 2019 (COVID-19). This deadly disease has killed more Italian males as compared to females in extreme of age because of their weak immunity status. The same

observations were reported in China with more causality in male gender and at extreme age [1,3]. Male and female genders have the same prevalence, but the severity of the disease was markedly higher in male gender with worst outcomes [4]. Pakistan is not an exception for COVID-19, and we published on the impact of demographic variable in COVID-19. We observed that the infection rate was 1.25 times more in males than females without significant p value (OR=1.25). The case fatality rate was 5.41% in our population. The infection was more common in younger age and mortality was more in older age irrespective of gender ($p=0.014$) [5].

Many factors could contribute for gender differences including low viral load in females

DOI: 10.21608/MID.2020.52705.1094

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because of less exposure as compared to the male gender in our religious society. Some of the scientists are of the opinion that the number of deaths reported are caused by the gender behavior (lifestyle) i.e. smoking, drinking and working abroad are more among men as compared to women [6]. The IgG antibodies production in mild, moderate and severe COVID-19 in female gender tends to rise promptly as compared to males which may account for different outcome of COVID-19 [7]. Present pilot study was conducted to assess the role of COVID-19 antibodies expression in gender groups to predict the gender protection and surviving in the current pandemic in a hospital-based pilot study.

Material and Methods

To quantify the role of antibodies production in gender groups in corona infection we did a cross sectional study covering 39 patients who were tested positive in Qazi Hussain Ahmed Medical Complex Nowshera, Pakistan in the month of July 2020.

Ethical approval was taken from Ethical Review Board of Nowshera Medical College Nowshera.

The criteria for selection of the candidates was that only those patients who were reportedly negative on PCR for 2019-nCoV done 3 week ago, were included for their antibodies status. All those candidates who came for antibodies test without being reported with infection with confirmed PCR test for virus detection were excluded. Similarly, patient with duration less than three week of being reported negative for corona virus were also excluded from the study.

The technique was to collect 3ml of the blood in gel tube under aseptic conditions. Antibodies levels were measured by electrochemiluminescence immunoassay using Roche Cobas E411 Chemistry Analyzer for which commercial kits of Roche diagnostics were used as per the instructions of the manufacturer

Data was entered in SPSS 25 version. Independent t test was used to determine the difference of neutralizing antibodies in positive patient with or without symptoms at time of infection. Kaplan Meir test was used to predict the probability of survival in age and gender groups based on the antibodies levels.

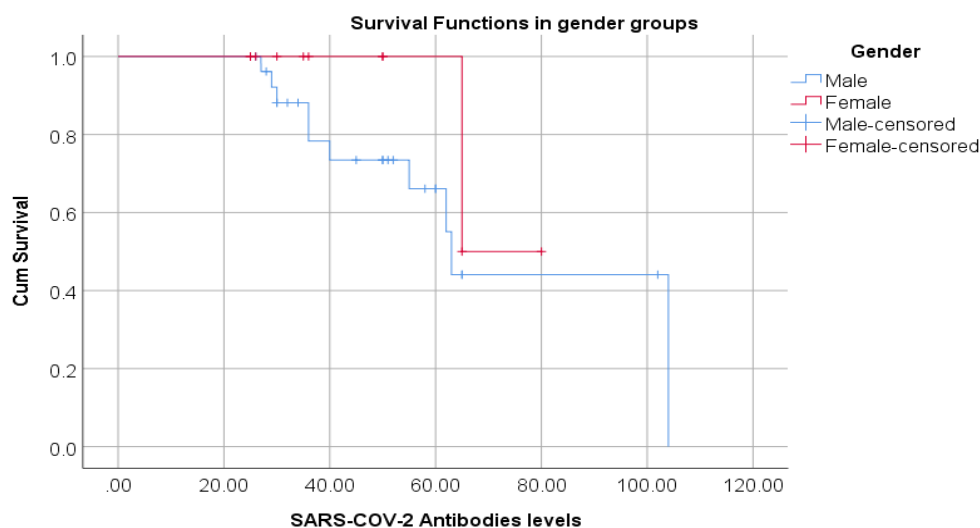
Results

Difference in mean post infection antibodies level irrespective of gender was statistically significant with higher cut off values in patient who had symptoms at time of being reported positive by PCR as compared to patient who were asymptomatic (*p-value:0.04*) (Table 1).

We tried to predict the survival in gender group based on the post infection antibodies cut off values and we observed using Kaplan Meir that female gender the probability of survival is predicted at 100% in infection with post infection antibodies with cut off values of 50, which shows that female gender produces higher titer of antibodies in early infection, while a vertical drop up to less than 40% probability of survival was predicted in severe infection with post infection cut off antibodies levels of >100. This confers female gender being more protective with higher capacity of survival even in severe cases of COVID-19 (Figure 1).

Table 1. Clinical presentation at time of infection and its association with post infection antibodies levels.

| Clinical presentation | Number | Mean \pm SD of anti SARS-COV-2 Antibodies | <i>p-value</i> (Independent t test) |
|--|------------|---|-------------------------------------|
| Clinically asymptomatic at time of diagnosis with COVID-19 | 22(56.41%) | 22 \pm 2.4 | 0.04 |
| Clinically symptomatic or hospitalized COVID-19 patients | 17(43.58%) | 47 \pm 7.3 | |
| Total | 39 | | |

Figure 1. Survival in gender groups based on production of SARS-COV-2 antibodies

Discussion

The clinical presentation and immune response of symptom free individual infected with corona virus have not been well reported in the literature. **Long et al.** study from China reported that patients infected with COVID-19 without having any obvious symptoms had significantly lower virus specific IgG antibodies (median S/CO, 3.4; IQR, 1.6–10.7) as compared to the symptomatic group (median S/CO, 20.5; IQR, 5.8–38.2) [7] that strongly matches our findings that the rate of post infection antibodies irrespective of gender was statistically significantly higher in patient who had symptoms at time of being reported positive by PCR as compared to asymptomatic patients. However, they reported their data with median probably due to scattered distribution [7].

From the above assumption in **table (1)**, we came to know that a higher level of antibodies was statistically significantly supportive of the prediction that the patient might have had symptoms/hospitalization at time of diagnosis being victim of COVID-19. The levels of antibodies and duration of immunity after infection provides shield immunity to the patients and is a measure of better outcome [8].

Studies do support these findings and from China **Zhang et al.** have reported 2.4 times higher mortality in males as compared to females, while the susceptibility for infection was almost equal in both the genders [9]. Many assumptions are floating that why female gender is more protective in viral disease specially COVID-19, some suggest a high plasma concentration of retonavir and high cholesterols high density lipoproties have been

reported in females that confer immunity in COVID-19 [10]. Other quoted high levels of sex hormones and expression of angiotensin converting enzyme-2 (ACE-2) in men along with lifestyle such as smoking and drinking among men as compared to women [6].

Hence by observing the outcome of COVID-19 in men demands for attention to move forward for treatment based on gender basis, future studies to address sex differences in morbidity and mortality due to Covid-19, as the virus behaves differently in both genders [11]. **Conti et al.** reported the genetic basis in the support of female gender being more protective that X Chromosome influences the immune system by acting on many proteins like TLR8, CD40L and CXCR3 which are expressed in female gender that influence response to this deadly viral infection [12].

The limitations of this study were the low sample size and secondly that we could not be able to check the antibodies levels of all the cases who were positive as they could not attend the follow up visit.

Conclusion

We concluded that female gender is more protective and offers more resistance to the 2019n CoV infection as compared to the male gender with worst outcome in the form of case fatality. Therefore, in way forward we recommend that there is a need to better understand the impact of gender in COVID-19 and to tailor the treatment according to the gender perspective and stress that therapeutic trials must include gender sensitive analysis.

Funding: None declared

Competing interests: None.

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