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# Laboratory Based Preliminary Study on Anti-SARS-CoV-2 Antibody Response among State Sector Healthcare Workers in a Single District in Sri Lanka

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**Research Article**

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## Abstract

**Background:** Severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) is responsible for the current COVID-19 pandemic. Healthcare workers are one of the risk groups due to their strategic role in patient management. Presence of anti-SARS-CoV-2antibodies in serum following seroconversion could be determined through antibody ELISA assay.

**Objectives:** This study was to analyze the laboratory identified viral markers of Anti SARS-CoV-2 antibody in blood samples of health care workers to demonstrate the seroconversion to SARS-CoV-2 virus following exposures, natural infection or vaccination and to describe the sociodemographic, and clinical parameters among them.

**Study design:** This laboratory based retrospective study was conducted at the National Virus Reference Laboratory (NVRL), at the Medical Research Institute (MRI). The study retrospectively analyzed 235 blood samples received to the NVRL, for testing of anti-SARS-CoV-2 antibody among health care workers in a one month period. All samples requested for anti-SARS-CoV-2 antibody were tested with SARS-CoV-2 spike protein specific IgG antibody, and with SARS-CoV-2 Total Ab ELISA. The socio-demographic data were gathered through the request forms were also analyzed.

**Results:** Total 235blood samples were tested for anti-SARS-CoV-2 antibody and 234(99.6%) were confirmed to have spike protein specific IgG antibody while 2% were confirmed to have Nucleo-capsid protein targeting antibodies of the positives, 100% were vaccinated with two doses of vaccine and 1% had positive PCR.

**Conclusion:** The current study encounters a significantly high prevalence of vaccine induces SARS-CoV-2 antibody carriers among the healthcare workers in the study community.

**Keywords:** SARS-CoV-2 Infection; Health Care Workers; COVID-19 vaccination; Anti-SARS-CoV-2 antibody response; Enzyme Link Immunosorbent Assay (ELISA)

**Abbreviations:** ELISA: Enzyme Link Immunosorbent Assay; MRI: Medical Research Institute; NVRL: National Virus Reference Laboratory; SPSS: Statistical Package for Social Sciences; MOH: Medical Officer of Health.

## Introduction

The severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) is responsible for the current COVID-19

global pandemic due to its high transmissibility around the world. This led to infecting millions of individuals with an unprecedented impact in the health care systems worldwide. Healthcare workers are one of the risk groups due to their strategic role in patient management presently, thus need to be well protected and to prevent healthcare related outbreaks. Here, we present the results of the SARS-CoV-2 seroconversion results among a group of healthcare workers serving at the state sector in Sri Lanka.

Infection with SARS-CoV-2 initiates a humoral immune response that produces antibodies against specific viral antigens such as the nucleocapsid (N) protein and the spike (S) protein. Specific anti-S protein antibodies are produced targeting the spike's S1 protein subunit and receptor binding domains (RBD) [1-3]. Serologic tests can detect the presence of these antibodies in serum within one to two weeks following acute infection [1-3]. Thus, it can identify persons with seroconversion to SARS-CoV-2 infection and thereby help health experts better understand the epidemiology of SARS-CoV-2 and populations at higher risk of infection.

## Objective

The current study was formulated to analyze the laboratory identified viral markers of Anti SARS-CoV-2 antibody in blood samples of health care workers received to the Medical Research Institute (MRI) during a one month period, with the intent of demonstrating the seroconversion to SARS-CoV-2 virus following exposures, natural infection or vaccination. Further, this study also aims to describe the sociodemographic, and clinical parameters among them.

## Study Design

This laboratory based retrospective study was conducted at the National Virus Reference Laboratory (NVRL), at the Medical Research Institute (MRI), Sri Lanka which is the central facility for the viral diagnosis in the country. The study retrospectively analyzes 235 blood samples received to the NVRL, MRI, for testing of anti-SARS-CoV-2 antibody among health care workers in a month period. All blood samples which requested anti-SARS-CoV-2 antibody testing were tested and assessed, irrespective of suspected COVID-19 infection and the brief history on the request forms.

A highly specific and sensitive, FDA-EU recommended assay was employed to measure SARS-CoV-2 spike protein specific IgG antibody, paired with SARS-CoV-2 Total Ab Enzyme Link Immunosorbent Assay (ELISA) to demonstrate the SARS-CoV-2 Total Ab positive proportion, which is also recommended by the FDA-EU. Firstly, all received blood samples were tested at the NVRL with the Euroimmun Anti-SARS-CoV-2 Virus Indirect IgG antibody ELISA kit (EuroimmunLuebeck, Germany) [4] and then Bio-Rad Platelia anti- SARS-CoV-2 Total Ab ELISA kit (Bio-Rad Laboratories, Inc France) [5] which targeted the spike protein S1and Nucleo-capsid protein respectively. The test runs were validated, and results were analyzed according to the manufacturer's instructions. The anti- SARS-CoV-2 IgG and / or Total Ab detected samples were considered as serological evidence of positive anti-SARS-CoV-2 antibody cases. Blood samples which gave negative results from both testing were considered as negative for anti-SARS-CoV-2 antibody.

However, clinical and vaccination histories received in the test request forms along with the samples were carefully reviewed to identify and differentiate natural infection with positive PCR test results, significant exposures according to the National guideline [6] and vaccinated Health Care Workers among the study group. The socio-demographic data such as age, geography, and different health care categories were also gathered and scrutinized with the ELISA test results. Statistical analysis was done using descriptive statistics by the Statistical Package for Social Sciences (SPSS), version 28.

## Results

During the 4-week study period, 235 blood samples received were tested for anti-SARS-CoV-2 antibody among health care workers. All the samples were tested for SARS-CoV-2 spike protein specific IgG antibody, and with SARS-CoV-2 Total Ab (IgM/IgA/IgG) ELISA assay to demonstrate the SARS-CoV-2 Total Ab positive proportion targeting Nucleo-capsid protein. In the study population 234(99.6%) were confirmed to have SARS-CoV-2 spike protein specific IgG antibody by positive SARS-CoV-2 spike protein specific IgG antibody ELISA while 2% were confirmed to have SARS-CoV-2 Total Ab (IgM/IgA/IgG) by SARS-CoV-2 Total Ab ELISA assay (Table 1).

| Parameter | Frequency (Percentage) |
|---|---|
| **SARS-CoV-2 spike protein specific IgG antibody (n = 235)** | |
| Negative (Ratio < 1.1) | 1 (0.4%) |
| Positive with low ratio (Ratio 1.2 -4) | 48 (15.8%) |
| Positive (Ratio 4.1- 9.9) | 176 (57.9%) |
| Positive with high ratio (Ratio >10) | 10 (3.3%) |
| **Anti -SARS-CoV-2 Total Ab(IgM/IgA/IgG) (n=235)** | |
| Positive | 4 (1.7%) |
| Negative | 231 (98.3%) |

**Table 1:** Laboratory parameters of SARS-CoV-2 infection among the study group.

| Variable | Frequency (percentage) |
|---|---|
| **Age range, Mean, Mode (n=234)** | 26-66 years (44.26, 46) |
| < 30 years | 19 (8.1%) |
| 31-40 years | 61 (26.1%) |
| 41-50 years | 92 (39.3%) |
| 51-60 years | 52 (22.6%) |
| >61 years | 9 (3.8%) |
| **Gender (n=234)** | |
| Female | 135 (57.7%) |
| Male | 99 (42.3%) |
| **Distribution based on occupation (n=234)** | |
| Medical Officers | 48 (20.5%) |
| Nursing Officers | 26 (11.1%) |
| Public Health Inspectors | 33 (14.1%) |
| Public Health Midwives | 27 (11.5%) |
| Health Care Assistants | 24 (10.3%) |
| Development Officers | 20 (8.5%) |
| Drivers | 12 (5.1%) |
| Entomologists | 6 (2.6%) |
| Field Officers | 5 (2.1%) |
| Field Assistants | 10 (4.3%) |
| Management Service Officers | 9 (3.8%) |
| Schools Dental Therapists | 4 (1.7%) |
| Other | 8 (3.4%) |
| Unknown | 2 (0.9%) |
| **Geographical distribution of Medical Officer of Health areas (n=234)** | |
| MOH Areas-1,4,5,6,8,9,13 & 15 | 13 (5.6%) in each |
| MOH Area-2 | 14 (6%) |
| MOH Area-3 | 11 (4.7%) |
| MOH Area-7 | 20 (8.5%) |
| MOH Area-10 &14 | 10 (4.3%) in each |
| MOH Area-11& 16 | 30 (12.8%) in each |
| MOH Area-12 | 5 (2.1%) |

**Table 2:** Socio-demographic and epidemiological details of positive cases.

In the study population the age range of positive patients was 26-66 years, with majority being females (57.7%). The samples tested were mainly from a single district of the Western Province of the country and those samples were distributed among 16 Medical Officer of Health (MOH) areas in the district. Although the study samples belonged to different health care categories based on the occupation, the highest numbers of samples were from Medical Officers (20%) and Public Health Inspectors (14%) in the district (Table 2).

Retrospective analysis of the positives revealed that 100% of the study population was vaccinated with two doses of Oxford Astra Zeneca vaccine. Moreover, it was evident 1% of them had reports of confirmed positive Real time Polymerase Chain Reaction (rt-PCR) results while 6% had significant exposures according to the National guideline [6] (Table 3).

| Parameter | Frequency (Percentage) |
|---|---|
| COVID-19 infection confirmed by PCR | 2 (0.85%) |
| Exposure to confirmed COVID-19 patients | 15 (6.38%) |
| Fully vaccinated | 235 (100%) |

**Table 3:** Clinical parameters and vaccination.

Following administration of the first dose of vaccine fever as a side effect was observed in 128(54%) while 81(34%) gave no complains, whereas 198 (84%) were silent and did not show up any side effects following the administration of the second dose of the vaccine (Table 4).

| Symptom | Frequency (Percentage) |
|---|---|
| After first dose (n=235) | |
| Fever | 128 (54.46%) |
| Body aches | 33 (14.04%) |
| Headache | 27 (11.49%) |
| Myalgia | 15 (6.38%) |
| Arthralgia | 8 (3.40%) |
| Other (Vomiting, diarrhoea, nausea, vaccine site pain, loss of appetite, sore throat) | 17 (7.23%) |
| None | 81 (34.47%) |
| No response | 14 (5.96%) |
| **After second dose (n=235)** | |
| Fever | 8 (3.40%) |
| Headache | 5 (2.13%) |
| Body pains | 4 (1.70%) |
| Other (pain at injection site, lethargy, allergy, diarrhoea, giddiness, insomnia, arthralgia, myalgia) | 7 (2.98%) |
| None | 198 (84.26%) |
| No response | 15 (6.38%) |

**Table 4:** Side effects following vaccination.

## Discussion

Sri Lanka reported the first case of COVID-19 on 27th January 2020 and thereafter several clusters were experienced in different intensity which was controlled satisfactorily. While continuing the outbreak control activities the second wave emerged and disseminated a little faster than the first wave. By this time global vaccination programme was initiated and Sri Lanka too initiated priority category-based vaccination in February 2021, with the target of prevention of community transmission, mortality and morbidity [7]. A number of studies have already been published globally regarding the antibody response to COVID-19 infection [2,3,8-10].

The current study analyzed the laboratory determined anti SARS-CoV-2 antibody in blood against different viral markers of the SARS-CoV-2 virus. We also directly observed the antibody responses of those vaccinated with two doses of vaccine and naturally infected individuals. Participants counted to this study were vaccinated 100% with the Oxford Astra Zeneca COVID-19 vaccine with an interval of above 12 weeks between two doses according to the WHO recommendations [11,12]. Accordingly, assays were used to test the samples and collective interpretation was done to identify the vaccine induced immune response and naturally infected cases. The total IgG assay with the detection of Nucleo-capsid protein helps to determine the presence of antibodies due to natural infection and inactivated SARS-CoV-2 vaccine whereas the assay with spike protein helps to determine the presence of post-infection and antibodies induced by vaccines with spike protein [8,13].

Out of the vaccines, 234 individuals were identified as positive with this assay indicating seroconversion to vaccine. Detection of SARS-CoV-2 antibody in blood against spike protein specific IgG antibody ELISA assay is a widely used method to demonstrate vaccine induce antibody in individuals who have received S1 protein vaccine [3,14,15].

In the enlist study population only a single health care worker did not show up any antibody response in spite of vaccination with two doses accordingly in contrast to the rest of the study individuals. The history given along with the sample of the antibody negative health care worker highlighted that the individual has had chronic kidney disease and has undergone kidney transplantation three years back. Further, it was found that the individual is on triple immunosuppressive therapy since then. Hence, it was divulged seroconversion or development of detectable antibodies is poor if the individual is on immunosuppressive therapy. The fact was explained and observed in some other studies as well [16-18].

However, only 2% of the study population was positive with SARS-CoV-2 Total Ab (IgM/IgA/IgG) ELISA assay targeting Nucleo-capsid protein, in contrast to the spike protein specific IgG antibody ELISA assay. Since this assay targeted Nucleo-capsid protein induced antibodies and 100% of this study population was vaccinated with Oxford AstraZeneca vaccine, it could differentiate the natural infection from Oxford AstraZeneca vaccine induces immunity [9]. Thus, laboratory findings uphold the history of 2% individuals who expressed natural infection with confirmed positive rt-PCR test results.

Timing of collection of the sample is crucial to reveal the immune response and all the blood samples were collected between 4-6 weeks of the second dose of the vaccine. It was evident that the optical densities (OD value) of the Spike protein specific IgG antibody ELISA assay were significantly higher in some participants' samples. Thus, participants positive Ratio was categorized disregarding the previous SARS-CoV-2 infection. It marked out the individuals with a history of positive PCR or significant exposures demonstrated the higher IgG positive ratio indicating that those individuals have had past immunologic experience through SARS-CoV-2 natural infection than non-infected members. Similarly, a few studies have shown higher IgG Antibody titers in previously infected individuals [10,19].

Moreover, two vaccine doses achieved SARS-CoV-2 spike protein specific IgG antibody responses across all ages in the analyzed samples. However, immune response did not show any significant difference among different age groups even though the age range of the participants was 26-66 years [15,20,21]. Although the duration of vaccination with the second dose and the sample collection was almost uniform in the participants, it was noted that low ratio and average ratio antibody responses among the study group negate to outline the waning off of individual antibodies [22].

In addition, this study also highlighted side effects following vaccination were very minimal other than fever in some participants [21,23]. Furthermore, retrospective analysis of the patient samples disclosed study samples were distributed among sixteen MOH areas representing a single district in the Western Province. This led to confirm that a range of vaccinated health care categories in the district possess immune response to the vaccine, which is a favorable sign [24,25], since the health care workers being one of the front-line risk groups in this SARS-CoV-2 battle.

In conclusion, the current study encountered a significantly high prevalence of vaccine induced SARS-CoV-2 antibody carriers irrespective the age, among the healthcare workers in the study community.

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