Characteristics and Immunoglobulin G Seropositivity among Covid-19 Positive Healthcare Workers in a Tertiary Care Hospital in Oman

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Abstract

Objectives: The aim of this study was to analyze the characteristics of Covid-19 infected Health care workers (HCWs), and to measure their of immunoglobulin G (IgG) response.

Methods: This is a retrospective and prospective cohort study where details of Covid-19 infected HCWs were collected in a pre-designed database. A single serum sample was collected from participating HCWs to detect the presence of (IgG) in their sera. Data were analyzed using SPSS statistical package.

Results: Out of a total of 974 HCWs in Al-Nahdha Hospital, 103 (10.5%) were infected and tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by Real time reverse transcriptase polymerase chain reaction (RT-PCR). Nurses and doctors were the most affected groups. The source of infection was hospital in 50% of cases. Nurses were more than 4 times likely to have a hospital-acquired Covid-19 infection (OR: 4.63, 95% CI 1.711to12.523, p-value 0.002). HCWs working in Covid-19 areas were more likely to have hospital-acquired infection than community-acquired (p-value <0.005). All infected HCWs made a full recovery with only 4% requiring admission. Out of 74 tested HCWs for IgG, 60 (81%) were positive. IgG positivity rate was significantly higher among HCWs in Covid-19 areas (p-value 0.026) and among non-Omanis (p-value 0.008). Moreover, the median IgG level was significantly higher among non-Omanis (p-value 0.004).

Conclusions: This study has highlighted the group at higher risk of hospital acquired Covid-19 infection which was the nurses and those working in Covid-19 areas. It highlighted as well, the high seropositivity among this infected group. These findings support the national guidelines on priority group for vaccination among HCWs which are those working in Covid-19 areas with no previous laboratory confirmed Covid-19.

Introduction

On March 11, 2020, the World Health Organization (WHO) has declared the rapidly spreading outbreak due to the newly emerging severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as a global pandemic and the diseases caused by it as Corona Virus Disease 2019 (Covid-19).[1] Healthcare workers (HCWs) are at the front line of outbreak responses and as such are particularly at risk of being infected from either occupational exposure or due to infection from surrounding community. Furthermore, the infected workers can subsequently transmit the virus to other people either in healthcare settings or to their households and communities.[2]

Serological response to Covid-19 is still an area for further research as different studies have showed variable results in terms of factors associated with seropositivity, detectable antibodies, duration of positivity and protection against reinfection. Venugopal and Garcia-Basteiro et al., reported significant seropositivity with certain specific symptoms compared to other symptoms.[3,4] Further, differences in seropositivity to SARS-CoV-2 between different races and ethnic groups has also been reported by Feehan et al.[5] The duration of detectable antibodies in the sera of infected people is yet to be determined, although studies from the Middle East respiratory syndrome coronavirus have shown that antibodies remained detectable for up to one year post infection.[6]

In this study we present data of HCWs with positive Covid-19 infection from one of the main tertiary hospitals that provides care for Covid-19 patients in Oman. The aim was to identify the source of infection among HCWs (hospital or community acquired), categories of the infected HCWs, their common symptoms, degree of severity and their outcome. In addition, the Immunoglobulin G (IgG) response to Covid-19 infection for this population was also assessed and

presented to determine any significant factors that might affect the seropositivity to SARS-CoV-2 infection.

Methods

In this combined retrospective and prospective (Abmidirectional) cohort study, we collected data of all HCWs who tested positive for Covid-19 in Al-Nahdha Hospital (a tertiary care hospital in Oman) between April 2nd and July 24th, 2020. Data were collected timely through direct interview or telephonic communications , when a positive PCR test was released by the Laboratory to minimize recall bias. Additional information were obtained from hospital electronic database (Al-Shifa 3 Plus System, locally designed by the Ministry of Health, Oman). Data were transferred to Excel spreadsheet (Microsoft Corporation, Excel version 2013) for analysis.

A reverse transcriptase polymerase chain reaction (RT-PCR) test was used to identify positive HCWs with Covid-19 disease. The majority of them were tested using GeneXpert system (Cepheid, USA) while few were tested using Sansure Nucleic Acid Diagnostic Kit (Sansure Biotech, China). Collected variables included age, gender, nationality, presenting symptoms, working area in the hospital, adherence to infection prevention and control measures (yes, no) and possible source of infection (hospital vs. community), severity of illness (mild, moderate, severe) in addition to other variables shown in Table 1. Covid-19 infection among HCWs was considered as hospital-acquired if the infected person had contact with a confirmed Covid-19 case in the hospital setting with no contact in the community while a community-acquired infection was considered if the infected HCW was in contact with a confirmed Covid-19 case in the community setting. Unknown source was considered if there was no evidence to exposure neither in hospital or community. A serum sample was also collected from HCWs between August 10th to September

2nd, 2020, except for two staff whose samples were stored from July; nonetheless were processed with the rest of the samples to detect IgG serological response using ELISA (Architect i 1000 SR system, Abbott, USA). Samples that were not processed timely, were stored at (-20ºC) immediately until subsequent time of processing.

Table 1: Characteristics of Covid-19 infected HCW with numbers and percentages from total and the IgG response with P-value for the correlation of the IgG response with different variables where p-value of ≤0.05 is considered as significant

Variable	Number of HCWs (%)	IgG positive	IgG negative	Not tested	*P* value
Age groups					
20-29	20 (19%)	8 (40%)	4 (20%)	8 (40%)	0.098
30-39	44 (43%)	28(64%)	3 (6.8%)	13 (29.5%)	
40-49	28 (27%)	15(53.5%)	7 (25%)	6 (21%)	
50-59	9 (9%)	7(77.7%)	0	2 (22.2%)	
>60	2 (2%)	2(100%)	0	0	
Gender					
Male	41 (40%)	25 (61%)	4 (9.7%)	12 (29.3%)	0.262
Female	62 (60%)	35 (56%)	10 (16%)	17 (27.4%)	
Profession					
Doctors	18 (17%)	10 (55.5%)	2 (11%)	6 (33.3%)	0.67
Nurses	47 (45%)	27 (57.4%)	7 (14.8%)	13 (27.6%)	
Others	38 (37%)	23 (60.5%)	5 (13%)	10 (26.3%)	
Symptoms					
Fever	67 (65%)	40 (59.7%)	7 (10%)	20 (29.8%)	0.243
Cough	55 (53%)	32 (58%)	8 (14.5%)	15 (27%)	0.797
Sore throat	51 (49%)	30 (58.8%)	7 (13.7%)	14 (27.4%)	1
Bodyache	44 (42%)	22 (50%)	6 (13.6%)	16 (36.4%)	0.667 0.443
Headache	17 (16%)	8 (47%)	3 (17.6%)	6 (35.3%)	0.949 0.627
Anosmia	7 (6%)	4 (57%)	1 (14.3%)	2 (28.6%)	0.103 0.515
Ageusia	2 (2%)	1 (50%)	0	1 (50%)	0.489
Diarrhea	4 (4%)	2 (50%)	2 (50%)	0	
Vomiting	3 (3%)	2 (66.7%)	1 (33.3%)	0	
SOB*	4 (4%)	2 (50%)	0	2 (50%)	
Flu-like symptoms	15 (14%)				
Asymptomatic	1 (1%)	1 (100%)	0	0	
Outcome					-
Recovered	99 (96%)	57 (57.5%)	14 (14%)	28 (28%)	
Admitted	4 (4%)	3 (75%)	0	1 (25%)	
Daily contact with patients					
Yes	79 (76.6%)	44 (55.7%)	13 (16.5%)	22 (27.8%)	0.118
No	24 (23.3%)	16 (66.7%)	1 (4.2%)	7 (29.2%)	
Working in					

The SARS-CoV-2 IgG assay is a qualitative chemiluminescent microparticle immunoassay that detects IgG antibodies to nucleocapsid protein of SARS-CoV-2 in human serum and plasma using Abbott-Architect i system and reports an Index of signal to cut-off (S/C) where the cutoff point for a positive test is ≥1.40. According to the manufacture, the sensitivity of this test is 100% and the specificity is 99.6%.

Data were analyzed using SPSS statistical package (SPSS for Windows, Version 22.0. Chicago, SPSS Inc.). Categorical data including IgG positivity rate and comparison of proportions of positive IgG with age, sex, symptoms, time to serology testing (> or < 2months) and cycle threshold (Ct) levels (> or < 30) were compared using chi-square test. Measure of association between different symptoms was also assessed using chi-square test. Linear relationship and statistically significant differences between IgG level and different independent variables (age, Ct for N2 (Nucleocapsid) and E (Envelope) gene values) were determined by Pearson's correlation, two-tailed *t*-test and analysis of variance (ANOVA) respectively to obtain odds ratios (OR), 95% confidence intervals (95% CI) and p-values. Fisher's exact test was used to find association between symptoms, different age groups and between different professions and source of infection. A p-value of <0.05 was considered to be statistically significant.

A written informed consent was obtained from all HCWs studied prior to each sample collection. The study was approved by the Research Committee in the Directorate General of Health Services of Muscat Region in the Ministry of Health (Identification code: 23843 dated 30th August 2020).

Results

From a total of 974 HCWs in Al Nahdha hospital, 540 (55%) were tested for SARS-CoV-2. Of those, 103 (19%) tested positive by RT-PCR test, which constitutes 10.5% of the total healthcare workers in the hospital. The mean age of HCWs positive for Covid-19 was 38 years (range 25 to 64 years) with 60% being females (Table 1). Nurses were the main affected group (45%), followed by doctors (17%) with other categories of HCWs being is in smaller percentages. From the total infected HCWs, 79 (76.6%) were in daily contact with patients of which 53%, were working in Covid-19 areas.

The most common symptoms were fever (65 %,), followed by cough (53 %,), sore throat (49%) and body ache (42 %) (Table1). Loss of smell and taste were found in few cases. Fever was significantly more prevalent in HCWs who were aged 40 years and above (p-value 0.033).

Only 4% of HCWs required admission with one patient requiring admission to an intensive care unit. There was no mortality among this studied group. The possible source of infection of SARS-CoV-2 in 50% of cases of was exposure within the healthcare facility, 38% in community and in 12% the source of infection could not be determined. Working in Covid-19 areas was more likely to be associated with hospital-acquired than community-acquired infection (p-value <0.005). Nurses were more likely to have a hospital acquired Covid-19 infection than other categories (OR 4.63, 95% CI 1.7 to 12.5, p-value 0.002). The most common source of hospital-acquired infection was from a colleague eating together in groups or mixing in changing rooms (94%), while (6%) were from direct contact with patients. There was no significant difference for the source of infection between different age groups or between genders (p-value 0.28, 0.20, respectively).

The highest rate of infection was noted in the period, between 5th to 11th July 2020, (Figure 1). The main source in this week was the community (46%) and the rest either healthcare associated (29%) or unknown source (25%).

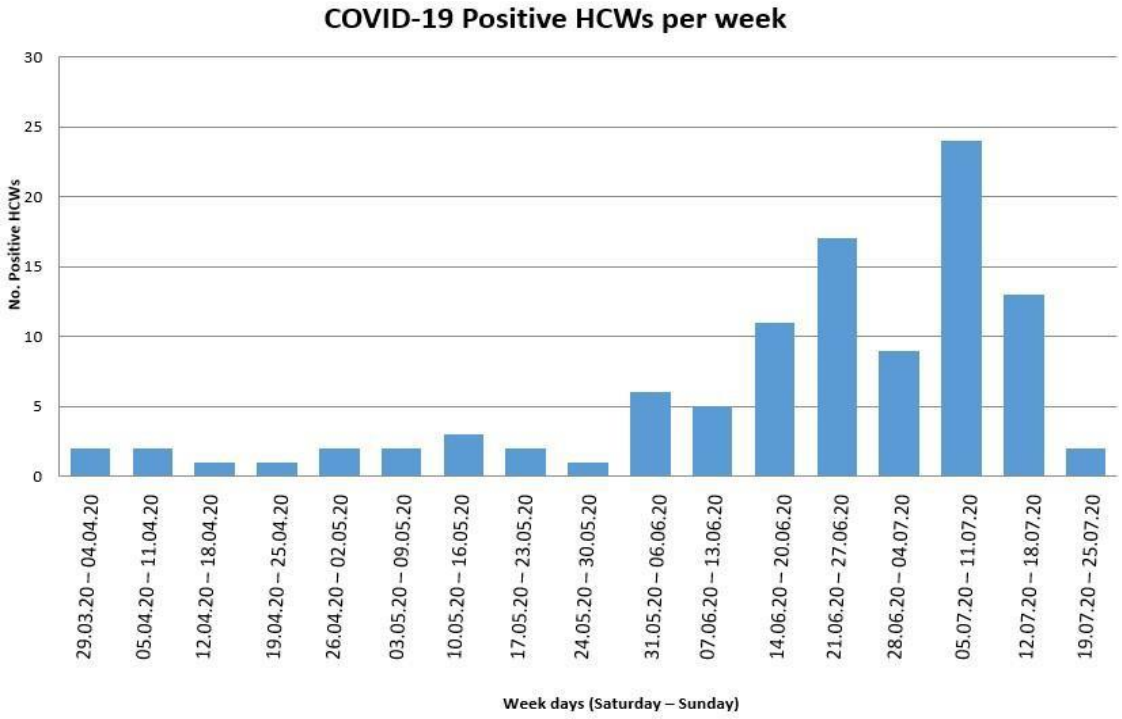


Figure 1: Distribution of Covid-19 positive HCW per week during the study period with the rate starting to creep upstarting from 31st of May and peaked in the week 5th to 11th July 2020.

From the total of 103 HCWs, 72%, n=74 were tested for SARS-CoV-2 IgG. From those, 81%, n=60, tested positive and 19%, n=14 tested negative. The elapsed time between positive PCR and serum sample collection ranged from 3 weeks to 20 weeks with 50% less than 8 weeks. Working in Covid-19 areas and being a non-Omani national was significantly associated with positive IgG test (p-value 0.026 and 0.008, respectively). Median IgG level (4.58 S/C) was significantly higher in non-Omani nationals (p-value 0.004) (Figure 2). There was no significant correlation between

seropositivity of IgG with gender (p-value 0.26), age (p-value 0.098, linear regression R2=0.025), time to testing (p-value 0.55), symptoms (p-value range from 0.1-1) and Ct. Value (p-value for Ct E 1.09 and for N2 0.09) (Figure 3). There was no statistical significance observed in those with daily contact with patients (p-value 0.118) or with source of infection (p-value 0.491).

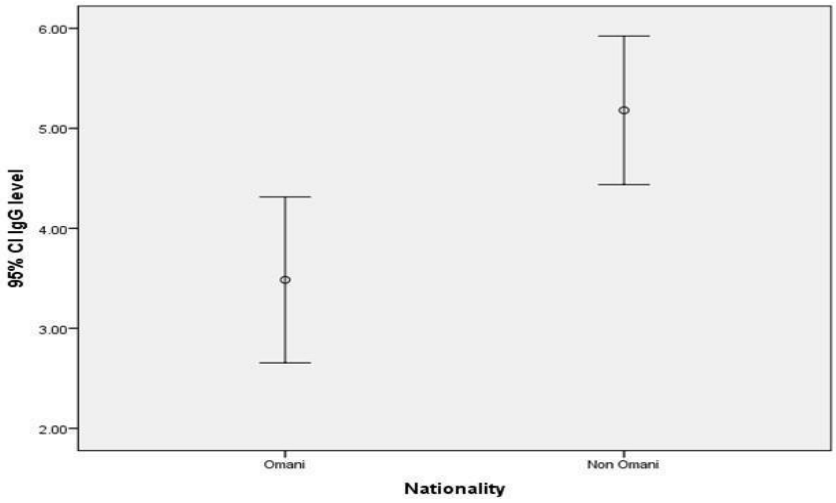
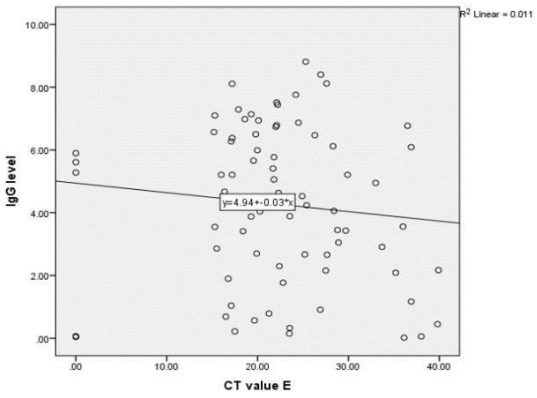


Figure 2: Effect of ethnicity on IgG level. The bar graph represents IgG level on Y axis versus nationality on X axis. The lines inside of the box indicates 95% confidence interval range for the mean value (circled) of each nationality. The mean IgG level increase in non-Omanis compared toOmanis ($p < 0.050$).



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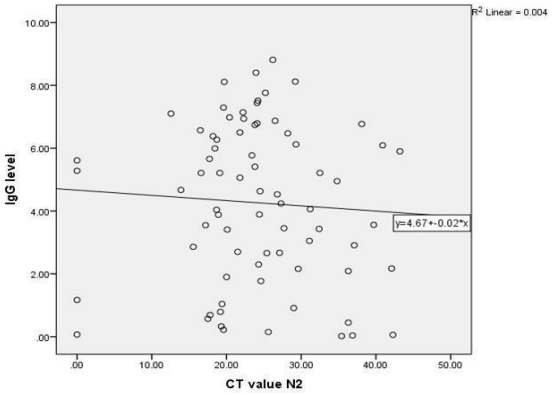

b

Figure 3 (a): shows correlation between IgG level and C_t value (E). Two-tailed *t* test and Pearson correlation was used to determine the significance. There is no significant relationship between IgG level and C_t value E , $r(69) = -0.160$, $p = 0.184$. **(b):** shows correlation between IgG level and C_t value (N2). Two-tailed *t* test and Pearson correlation was used to determine the significance. There is no significant relationship between IgG level and C_t value N2 , $r(70) = -0.116$, $p = 0.330$.

Discussion

To our knowledge, this is the first study from Oman that documents the serological response of HCWs to Covid-19 infection and their characteristics. HCWs are the frontline in the battle against Covid-19, therefore, it is important to know their serological response and to be aware of how they can be protected from re-infection with the repeated exposure as they are continuing their clinical duties.

The rate of infection among HCWs in our study was higher over a 4-month period (10.5%) than that reported in a study from a local hospital (4.3%)[7], and in two Dutch hospitals (1%)[8], but lower than rates reported from a large Spanish hospital (11.6%) over one month period.[4] Like many other studies, the rate of infection among female staff was higher than their male counterparts (60%), yet it was similar to what was reported by several other studies.[7-9] This was in sharp contrast to what was reported from the community, where the rate of infection was higher in males.[10] Nurses

in particular were at a higher risk of acquiring the Covid-19 infection from healthcare settings compared to other professions. This was similar to what was reported by Al Maskari (38%) and Garcia-Basteiro(48%).[4,7] This can be attributed to their closer and prolonged contact with Covid-19 infected patients compared to other professions.[2] In addition to this fact, the majority of the nurses in many healthcare settings are females, this also explains the higher rate of infection in this group.[11]

The reported symptoms among HCWs were similar to that reported in other hospitals[4,7,9] with fever, cough and other respiratory symptoms as the most common presentations. The majority (96%) of HCWs had mild illness with uneventful recovery. Although no mortality was noted among HCWs in this study, however other studies reported mortalities especially in older than 65 years of age or HCWs with comorbidities.[9]

In our study, 50% of infections among HCWs were attributed to exposure to individuals (a colleague or a patient) within healthcare setting. A similar rate was reported from the US (55%), while lower rates were documented from a local hospital in Oman (25%).[7,9] In spite of regular reinforcement of infection control measures (social distancing and universal masking), higher rates of hospital acquired Covid-19 infections were mainly due staff gathering with colleagues (94%) during break time in the beginning of the pandemic, as per the information provided by the participants. Other possible reasons could be shortages of PPE but PPE supplies were monitored weekly and supplies were adequately available. .. The other possibility would be contact with the patients while giving care, this was the case in 6% only , as the compliance with infection control

practices were strictly monitored by ward in-charges, in addition to daily rounds, frequent audits and training by infection prevention and control practitioners.

Working in COVID area was significantly associated with higher risk of acquiring infection from a healthcare setting than from a community. A similar finding was also reported by Al Maskeri et al.,[7] where healthcare associated infections were also significantly higher among staff members working in Covid-19 areas ($p < 0.001$). This could be due to prolonged and repeated exposure to Covid-19 infected individuals.

During this study, the peak number of cases were noted in the period from 5th to 11th July 2020 where most cases thought to have been contracted from community rather than hospital. The peak of Covid-19 infections in the general population where over 2000 cases were reported at about the same period of time and then subsequently gradually declined.[12]

In our study, we found 19% of tested HCWs had no detectable IgG antibodies in their sera. Similarly, a large study from a Spanish hospital found 15% seronegativity among RT-PCR confirmed infected HCWs.[4] Another study from the UK found that only 0.2 % of the previously PCR-positive HCWs were seronegative.[13] It could be possible that seronegative HCWs in our study had very low peak titers or had waning of their antibody levels that could not be detected by the analyzer despite the fact they were tested between 21 to 140 days of clinical presentation and positivity of RT-PCR. In addition, the nucleocapsid antibodies are less stable than antispike antibodies and this might had contributed to seronegativity in some cases. Subsequent longitudinal cohort serological studies by Lumley and colleagues from the UK found waning anti-nucleocapsid, but stable anti-spike antibodies.[13]

Although the antibody level was reported to peak at day (20-25) of symptoms by Garcia-Basteiro et al.[4] Furthermore, none of this cohort presented with re-infection (at least until the submission of this article), which could suggest that HCWs previously infected with Covid-19 might still have an element of protection, even in the absence of antibodies, possibly due to cell-mediated immunity.[14] The duration of this protection could not be determined from this study and eliciting that may require further follow-up with repeated serology testing

Immunological response varies between patients following either infection or vaccination, including the level of formed antibodies and their sustainability.[15,16] This interesting fact was evident in the statistically significant difference in the seropositivity rates to SARS-CoV-2 between Omani and Non-Omani HCWs, where we found non-Omanis had higher rates of seropositivity and median level of IgG antibodies. The etiology behind this difference is uncertain. A similar response to vaccine will be worth studying and to understand contributing factors. Further, there were no significant difference between the age groups and genders in seropositivity, which is in line with findings by others.[4] In contrast to the findings by Garcia-Basteiro[4], higher seropositivity was found in those working in Covid-19 areas in our study. . This might be explained by the repeated exposure to the virus.

Garcia-Basteiro have found a significant correlation of some symptoms with seropositivity including (in order): anosmia, ageusia, fever and fatigue[4]. Anosmia and ageusia were also found to have increased the odds of seroconversion compared to other symptoms in a study from New York City hospital.[3] In our cohort, only 7 HCWs had anosmia and two with ageusia and this might not have provided enough power to the study to show associated significance. However, out of the seven with anosmia, four were positive for IgG and one negative, while the other two didn't come for testing. For ageusia, one was positive and the other was not tested.

Our study has several limitations. First, it included only one Centre with a small number of subjects and a subgroup who were investigated for serological response. Nonetheless, it is the only study which provides an insight to serological testing to date in Oman. Secondly, serological testing was performed once only, while serial testing would have been optimal and could have provided a more comprehensive picture of the serological response to Covid-19. However, this data still provide a window of what initially occurs as serological response to a novel virus in a pandemic situation. A larger multicenter study with follow-up of serial antibody measurements would provide a better understanding of the immunological response among this important group to be able to set up policies and guidelines on quarantine and vaccination polices.

In conclusion, this study highlights that nurses and other HCWs in Covid-19 areas are at the highest risk of contracting hospital acquired infection. Which in turn emphasizes the importance of the adherence to infection control measures in order to prevent these infections. It also outlines high seropositivity among Covid-19 infected HCWs. These findings are in support of the national guidelines that priority for vaccination should be given to HCWs in Covid-19 areas with no previous laboratory confirmed infection.

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