Getting Negative for COVID-19: Role of Ethnicity and Demographic Factors
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ABSTRACT

Objectives: To explore the relationship between ethnicity and demographic factors with the time taken by patients to get negative on PCR for COVID-19.

Study Design: Prospective Comparative Study.

Place and Duration of Study: Combined Military Hospital, Malir Pakistan, from Mar to May 2020.

Methodology: All patients who tested positive for COVID-19 with less than one week of exposure time and were admitted to the COVID-19 ward of Combined Military Hospital, Malir without any complications were included in the study. They were tested after every seven days with PCR. Time taken to get two consecutive negative tests were noted for each patient.

Results: Out of 84 patients included in the study, 12 (14.3%) tested negative on the 7th day, 34 (40.4%) on the 14th day and 38 (45.3%) tested negative after 14 days. 12 (20.2%) were Sindhi, 13 (15.5%) were Muhajir, 19 (22.6%) were Punjabi, 25 (29.7%) were Pathan, and 10 (11.9%) were Kashmiris. Chi-square revealed that ethnicity and advancing age have a statistically significant relationship (p-value<0.05) with the time taken by patients to get negative on PCR for COVID-19.

Conclusion: Ethnicity emerged as a significant factor in getting negative for COVID-19. Punjabis and Kashmiris required a shorter period to get negative than Sindhis and Pathans. Older age emerged as a factor requiring a longer period to get negative.

Keywords: COVID-19, Ethnicity, PCR-negative.


INTRODUCTION

Pandemics are not new to humankind; they have been hitting the human population regularly in one form or another every few years.1 COVID-19 started in China in the last quarter of 2019 and spread to almost all corners of the world in the first few months of this year.2 Number of new cases, patients requiring ICU admissions and the number of deaths have still been rising in most parts of the affected areas. In this crisis, when everybody has been emphasizing preventive measures, screening, early recognition and provision of necessary equipment,3 less emphasis has been laid on the association of various factors with early resolution of symptoms and getting negative on PCR for patients without serious complications.4

COVID-19 has been a new happening to humankind and has changed the mechanics of the whole world in the past few months; therefore, researchers have started looking at various aspects of this viral illness. A recent CDC MMWR report included race and ethnicity data from 580 patients hospitalized with lab-confirmed COVID-19 and found that 45% of individuals for whom race or ethnicity data was available were white, compared to 55% of individuals in the surrounding community. However, 33% of hospitalized patients were black compared to 18% in the community, and 8% were Hispanic, compared to 14% in the community. These data suggest an over-representation of blacks among hospitalized patients.5 The UK’s Intensive Care National Audit and Research Centre reported on May 1, 2020, that 2300 (34%) of 6770 critically ill COVID-19 patients were from ethnic/ racial minority groups.6 A very recent study published by Yancy et al. concluded that in Chicago, nearly 52% of deaths from COVID-19 were among African Americans. However, they represent only about 30% of the city's population.7 Khunti et al. published a paper in April 2020 highlighting the fact that clear evidence to confirm or rule out an association between ethnicity and outcome in COVID-19 is important not only for the UK but also for other regions such as South Asia and Africa, where the pandemic is at an earlier stage.8,9

Different responses to systemic illness in different ethnicities have already been reported in Pakistan, a multi-ethnicity country.10 Limited work has been done...
all around to explore the influence of ethnicity on the course of COVID-19 infection. We took the challenge to take up one part of this phenomenon. We assessed the relationship between ethnicity and other factors with the time taken by patients to get negative on PCR for COVID-19 among the patients admitted in the COVID-19 ward of Combined Military Hospital, Malir with the vision that it will prove to help identify those factors which could reduce the burden on health care facilities and quarantine centres.

**METHODOLOGY**

This prospective comparative study was planned and conducted at Combined Military Hospital, Malir between March and May 2020. The sample size was calculated using the WHO sample size calculation by using the population prevalence proportion of ethnic disparity in response to COVID-19 as 2.2%.[11] Non-probability consecutive sampling was used to gather the sample. Patients (18 to 60 years of age) tested positive (routine PCR in a tertiary care teaching laboratory under a consultant virologist),[12] with confirmed exposure of less than a week with COVID-19,[13] and admitted to the COVID-19 ward of our hospital without any complications were included in the study.

**Inclusion Criteria:** All such patients, either asymptomatic or with mild symptoms like fever, sore throat and body aches, were included in the study.

**Exclusion Criteria:** Patients with exposure to COVID-19 for more than a week or unclear exposure time or those who developed complications and needed oxygen or shifted to the intensive care unit were excluded from the study. In addition, pregnant females, patients on any steroid or cytotoxic therapy, or those over 60 years of age were excluded from the study.

Ethical approval was taken from the Ethical Committee of the hospital (via letter no 08/2020/Trg/Adm). Patients who tested positive for COVID-19 admitted to the COVID-19 ward of our hospital, meeting the inclusion criteria, were included in the study after written informed consent. They were tested on days 7, 14 and 21 after the first positive test. Those who became negative on two tests 24 hours apart were discharged and not tested further. Socio-demographic proforma comprising basic details including ethnicity was filled by the patients at the time of enrollment in the study. Other variables in the study included age, gender, ethnicity, medical comorbidities and smoking status. Common ethnic groups in Pakistan include Punjabi, Sindhi, Balochi, Pathan, Kashmiri and Muhajirs. Common comorbidities included DM, HTN, IHD or any diseases not mentioned in the exclusion criteria.

Statistical Package for Social Sciences (SPSS) version 24.0 was used for the data analysis. Frequency and percentage were calculated for the qualitative variables, whereas mean and standard deviation were calculated for the quantitative ones. Chi-square test was used to look for the relationship between age, gender, ethnicity, medical comorbidities and smoking status of the individuals with the time taken to get negative PCR results for COVID-19. The p-value less than or equal to 0.05 was considered significant.

**RESULTS**

After applying inclusion and exclusion criteria, 84 patients were included in the final analysis. 61(72.6%) were males, while 23(27.4%) were females. The sociodemographic characteristics of the study population were summarized in Table-I.

<table>
<thead>
<tr>
<th>Ethnic Distribution</th>
<th>n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Punjabi</td>
<td>19(22.6)</td>
</tr>
<tr>
<td>Sindhi</td>
<td>17(20.2)</td>
</tr>
<tr>
<td>Pathan</td>
<td>25(29.7)</td>
</tr>
<tr>
<td>Muhajir</td>
<td>13(15.5)</td>
</tr>
<tr>
<td>Kashmiri</td>
<td>10(11.9)</td>
</tr>
</tbody>
</table>

The mean age of the patients was 36.75±6.33 years. Out of 84 patients included in the study, 12(14.3%) tested negative on the 7th day, 34(40.4%) on the 14th day and 38(45.3%) tested negative after 14 days. In addition, 17(20.2%) were Sindhi, 13(15.5%) were Muhajir, 19(22.6%) were Punjabi, 25(29.7%) were Pathan, and 10(11.9%) were Kashmiris. Chi-square revealed that ethnicity and advancing age have a statistically significant association (p-value<0.05) with the time taken by patients to get negative on PCR for COVID-19. In contrast, smoking status and gender (p-value>0.05) had no such association (Table-II).

**DISCUSSION**
Viral illnesses have been living with humankind for ages. Endemic diseases are usually dealt with well because clinicians and researchers have enough time and resources to cater for them holistically and find all possible management plans. Unfortunately, pandemics do not give health care professionals and scientists enough time to intervene at primary and secondary levels. In the case of COVID-19; since its start in China a few months ago, there has been a debate regarding the difference in virulence of the virus and disease course in various populations.\textsuperscript{14,15} Ours is a country comprising of various climate regions and ethnicities under one umbrella so we may expect different course and outcome even within our population. Due to limited data in this regard, we planned this study to explore the relationship between ethnicity and other factors with the time patients take to get negative on PCR for COVID-19.

Table-II: Outcome of Various Variables Studied in the Analysis (n=84)

<table>
<thead>
<tr>
<th>Factors Studied</th>
<th>7 days (n=12)</th>
<th>7-14 days (n=34)</th>
<th>&gt;14 days (n=38)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-40 years</td>
<td>04 (33.3)</td>
<td>26 (76.5)</td>
<td>22 (57.9)</td>
<td>0.023</td>
</tr>
<tr>
<td>&gt;40 years</td>
<td>08 (66.7)</td>
<td>08 (23.5)</td>
<td>16 (42.1)</td>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Punjabi</td>
<td>01 (8.3)</td>
<td>13 (38.2)</td>
<td>05 (13.1)</td>
<td></td>
</tr>
<tr>
<td>Sindhi</td>
<td>02 (16.7)</td>
<td>02 (5.8)</td>
<td>13 (34.2)</td>
<td></td>
</tr>
<tr>
<td>Pathan</td>
<td>02 (16.7)</td>
<td>11 (32.4)</td>
<td>12 (31.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Muhajir</td>
<td>06 (50%)</td>
<td>06 (17.6)</td>
<td>01 (2.6)</td>
<td></td>
</tr>
<tr>
<td>Kashmiri</td>
<td>01 (8.3%)</td>
<td>02 (5.8)</td>
<td>07 (18.4%)</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>08 (66.7%)</td>
<td>27 (79.4%)</td>
<td>26 (68.4%)</td>
<td>0.504</td>
</tr>
<tr>
<td>Female</td>
<td>04 (33.3%)</td>
<td>07 (20.6%)</td>
<td>12 (31.6%)</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>10 (83.3%)</td>
<td>30 (88.2%)</td>
<td>33 (86.8%)</td>
<td>0.914</td>
</tr>
<tr>
<td>Yes</td>
<td>02 (16.7%)</td>
<td>04 (11.8%)</td>
<td>05 (13.2%)</td>
<td></td>
</tr>
</tbody>
</table>

Bhala \textit{et al.} in their recent review, concluded that ethnical/racial disparities in the health outcomes of people with COVID-19 need to be studied alongside age, sex, gender, socioeconomic status, and comorbidities in disaggregated public health data. A provisional analysis by the UK Office for National Statistics suggests that the risk of COVID-19-related death among some ethnic groups is higher than that among those of White ethnicity in the UK. After adjustment for age, Black men are 4-2 times more likely to have a COVID-19-related death, and Black women are 4-3 times more likely than White ethnicity men and women in the UK.\textsuperscript{16} Our country has no black/white discrimination. However, differences usually exist based on provinces and ethnicities. There could be differences in biological response among different ethnicities, or the difference in health care facilities or attitude of local healthcare professionals may be responsible for the findings in our study.

Pareek \textit{et al.} pointed out various reasons for ethnic differences and responses to COVID-19. For several reasons, they highlighted that minority communities might be at increased risk of acquisition, disease severity, and poor outcomes in COVID-19. First, specific ethnic groups, such as south Asians, have higher rates of comorbidities, such as diabetes, hypertension, and cardiovascular diseases, which have been associated with severe disease and mortality in COVID-19. Second, ethnicity could interplay with the virus spread through cultural, behavioural, and societal differences, including lower socioeconomic status, health-seeking behaviour, and intergenerational cohabitation.\textsuperscript{17} Such as ethnic differences exist in our part of the world. Third, Pathans and Sindhis were found more at risk of getting negative results late than other communities due to the many reasons pointed out by Pareek \textit{et al.} Pan \textit{et al.} did a literature review and concluded that of 690 articles identified from medical journals, 12 reported ethnicity; three reported no association between ethnicity and mortality. Of 209 preprints, 34 reported ethnicity-13 found Black, Asian and Minority Ethnic (BAME) individuals had an increased risk of infection with SARS-CoV-2 and 12 reported worse clinical outcomes, including ITU admission and mortality, in BAME patients compared to White patients. Of 12 grey literature reports, seven with original data reported poorer clinical outcomes in BAME groups compared to White groups.\textsuperscript{18} Our results strengthened their findings. Whatever reasons may be ethnic differences exist among the patients regarding their response to this novel infection.

Voinsky \textit{et al.} in May 2020 published a paper with a conclusion that male and female patients aged >30 years had significantly longer recovery periods compared with younger patients (FD=0.95, p<0.0001 and FD=0.97 days, p=0.038, for men and women, respectively).\textsuperscript{19} These differences, while statistically significant, may seem small. Nevertheless, they suggest that younger individuals, in addition, to being less likely to have severe COVID-19 symptoms requiring intensive care unit hospitalization, are also recovering on average faster from SARS-CoV-2 infection.\textsuperscript{19} Our findings were similar in this regard. In addition, patients more than 40 years of age recovered late and became PCR
negative significantly late as compared to patients with age less than 40 years.

LIMITATIONS OF STUDY

COVID-19 is a novel infection, we may need some time and could only come up with definitive and generalizable findings for our population.

CONCLUSION

Ethnicity emerged as a significant factor in the time taken by patients to get negative PCR for COVID-19. Punjabis and Kashmiris were quickest to have a negative PCR, while Sindhis and Pathans had delayed negative results. Patients older than 40 years also became negative late compared to patients younger than 40 years of age.

Conflict of Interest: None.

Author’s Contribution

Following authors have made substantial contributions to the manuscript as under:

MHA & UBZ: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

MSS: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

HBZ & MY: Critical review, drafting the manuscript, approval of the final version to be published.

MI & NZ: Study design, data analysis, critical review, drafting the manuscript, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES