
Nebras Mohamad

ABSTRACT

Purpose: This study aimed to investigate the role of oral health in determining the severity of COVID-19 infection among recovered COVID-19 Syrian patients.

Clinical Significance: The severity of COVID-19 infection varies among individuals, and the general health status of individuals plays a crucial role in determining the severity of symptoms. The association between oral health and COVID-19 severity has not been widely explored. Understanding the impact of oral health on COVID-19 severity can help in developing strategies to prevent severe and aggressive COVID-19 infection.

Material and Methods: A cross-sectional trial based on a questionnaire survey was conducted among 319 recovered COVID-19 Syrian patients. The questionnaire was divided into two main sections: oral health evaluation and COVID-19 severity assessment. Participants were classified into three groups based on their responses for oral health and COVID-19 severity.

Results: Our observations revealed a significant difference between overall health and the severity of COVID-19 infection. Participants with worse general health had higher COVID-19 severity index scores. Patients with chronic conditions also had a considerably higher prevalence of COVID-19 severity index. Furthermore, our findings suggest that individuals with poor overall health and chronic diseases exhibited the worst oral health. However, there was no relationship between oral health status and the recovery period of COVID-19 infection. The association between oral health status and COVID-19 severity index revealed a positive correlation, although it was not statistically significant.

Conclusions: Our study provides evidence that the oral cavity and its components may contribute to an elevated risk of COVID-19 infection, as the association between COVID-19 severity and oral health status revealed a positive correlation, although it was not statistically significant. Further research with larger sample sizes and more reliable study designs will be required to confirm our findings. In the light of our findings, we recommend following simple oral health measures such as tooth brushing, regular dental check-ups, and periodontal screening to prevent severe and aggressive COVID-19 infection.

Keywords: COVID-19, cross-sectional study, oral health, recovery period, severity.

I. INTRODUCTION

Coronavirus disease (COVID-19) is a highly contagious viral infection caused by the SARS-CoV-2 virus, which was first reported in Wuhan, China in December 2019 [1]. The virus quickly spread worldwide, and in March 2020, the World Health Organization declared a pandemic due to its severe public health implications [2]. The disease is primarily transmitted through respiratory droplets or fomites, but there is evidence to suggest that airborne and oro-fecal transmission may also be possible [1].

The severity of COVID-19 can range from mild respiratory tract infection to severe pneumonia, acute respiratory distress syndrome (ARDS), multiple organ failure, and death [1]. Fever, cough, and dyspnea are the most common symptoms, and older people, those with multiple chronic diseases, and obese individuals are at a higher risk of developing severe symptoms and complications [1], [2].

Given the close proximity of the oral cavity to the respiratory tract, it has been suggested that oral health status may influence the onset, progression, and pathology of respiratory infectious diseases, including COVID-19 [3]. The oral microbiota, which contains hundreds to thousands of different species, is an important component of the human microbiota and plays a critical role in maintaining oral and
systemic health [3]. Saliva, which is full of immune materials, is an important component of the host's defense against infection in the mouth and contributes to innate immunity [3]. Previous research has linked poor oral hygiene to the worsening of several diseases, including gum disease, which can lead to dysbiosis - a shift in the oral microbiota from a peaceful to an aggressive state [4]. When bacteria become aggravated, they can enter the bloodstream and spread throughout the body, leading to inflammation and contributing to a variety of chronic conditions over time [4]. Moreover, recent studies have shown that patients with severe COVID-19 symptoms have higher levels of a specific inflammatory marker called CRP compared to those with mild or moderate symptoms [5]. The level of CRP has been associated with the severity of COVID-19 on CT performance and longer hospital stays, suggesting that CRP testing could be useful as an early indicator of severe illness [5].

Given the potential role of oral health in the development and severity of COVID-19, this study aimed to investigate the impact of oral health and oral care on SARS-CoV-2 infection. Specifically, this study sought to determine whether the health of the oral cavity and its structures contributes to an increased or decreased risk of COVID-19, whether there is a link between the severity of COVID-19 infection and the oral health status of the sample, and whether oral health status affects the recovery period of COVID-19 infection.

II. MATERIALS AND METHODS

In this study, 319 Syrian patients who had recovered from COVID-19 were included, and the sample size was determined based on the population of recovered COVID-19 patients in Syria at the time of the study. The study design involved the use of a questionnaire survey that included demographic data such as age, gender, smoking status, level of education, and overall health condition. The questionnaire was divided into two main sections, one for assessing oral health by a group of dentists and the other for assessing COVID-19 severity by a group of physicians. The questionnaire was distributed via social media as a Google Form. The questionnaire design for the oral health section was based on previous studies conducted by [7]-[9], and included 17 questions with each answer assigned a specific number of points. The overall score ranged from 1-35, with a higher score indicating better oral health. Participants were categorized into three oral health groups based on their responses, including poor, fair, and good oral health, with a threshold of 1-14, 15-23, and 24-35, respectively. For the COVID-19 severity section, the questionnaire design was based on a study by [10] and data retrieved from [11] and [12]. This section included 18 questions, with each answer assigned a specific number of points. Patients were divided into three groups based on their symptoms, including asymptomatic/mild, moderate, and severe cases, with thresholds of 0-15, 16-26, and 27-46, respectively. All hospitalized patients who needed to be admitted to the intensive care unit were deemed severe cases. The overall score ranged from 0-46, with a higher score indicating severe COVID-19 infection.

III. RESULTS

A. Scoring and Grading of COVID-19 Severity and Oral Health Indices

Table 1 shows the scoring and grading of the COVID-19 severity index and oral health index. The severity index ranged between 1-46, with an average of 16.85 and a standard deviation of 8.53. Of the total sample, 47% were asymptomatic or had mild symptoms, 39.8% had moderate symptoms, and 13.2% had severe symptoms. The oral health index ranged between 3-28, with an average of 28 and a standard deviation of 4.34. Only 5.3% of the sample had good oral health, while 62.4% had fair oral health, and 32% had poor oral health.

<table>
<thead>
<tr>
<th>COVID-19 Severity Index</th>
<th>Count</th>
<th>Mean</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic/ mild</td>
<td>150</td>
<td>47.0%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>127</td>
<td>39.8%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>42</td>
<td>13.2%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Oral Health Index</th>
<th>Count</th>
<th>Mean</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor</td>
<td>103</td>
<td>32.3%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fair</td>
<td>199</td>
<td>62.4%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>17</td>
<td>5.3%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

B. Correlation Between the Demographic Variables and COVID-19 Severity and Oral Health Indices

Correlation between the demographic variables and COVID-19 severity index and oral health index were analyzed using Mann-Whitney U test (for variables of two groups) and Kruskal-Wallis test (for variables of over 2 groups). Table II shows the results of the statistical tests performed. Table II displays the significant difference between the general health and COVID-19 severity index (p=0.017), where participants with lower general health had a higher score of COVID-19 severity index. Moreover, participants with chronic diseases had a significantly higher rate of COVID-19 severity index (p=0.015). However, other variables did not show a significant difference with COVID-19 severity index (P-value>0.05).
Regarding the relation with oral health index, general health and having chronic diseases had a significant difference with oral health index (p=0.010, p=0.048, respectively). The results showed that the worst oral health was observed among patients with poor general health and those who had chronic diseases. However, other variables did not represent a significant difference with the oral health index (P-value>0.05).

C. Correlation Between the COVID-19 Severity Index and Oral Health Index

Correlation between COVID-19 severity index and oral health index was analyzed using Spearman's correlation test. Table III shows the results of the statistical test performed. The results of Spearman's correlation test revealed a positive correlation between COVID-19 severity index and oral health index, however, the correlation was not significant (P=0.530). Therefore, there was no evidence of a significant relationship between COVID-19 severity index and oral health index in the study population.

D. Correlation Between Oral Health and Time to Patient’s Full Recovery

To investigate the correlation between oral health index and time to full recovery from COVID-19, Kruskal-Wallis test was conducted. Table IV presents the results of the statistical test performed. The Kruskal-Wallis test did not reveal any significant difference between time to full recovery from COVID-19 and oral health index (P=0.489).

Therefore, there was no evidence of a significant relationship between the two variables in the study population.

![Fig. 2. Correlation between the COVID-19 severity and oral health indices.](image-url)
TABLE IV: CORRELATION BETWEEN ORAL HEALTH AND TIME TO FULLY RECOVERY

<table>
<thead>
<tr>
<th>Oral health status</th>
<th>N</th>
<th>Mean Rank (2)</th>
<th>Mean Rank (1)</th>
<th>P-value</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>less than 2 weeks</td>
<td>128</td>
<td>16.70</td>
<td>165.36</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 weeks</td>
<td>93</td>
<td>16.65</td>
<td>165.24</td>
<td>0.489</td>
<td>No significant difference</td>
</tr>
<tr>
<td>3-6 weeks more than 6 weeks</td>
<td>68</td>
<td>15.85</td>
<td>149.03</td>
<td></td>
<td></td>
</tr>
<tr>
<td>total</td>
<td>319</td>
<td>15.73</td>
<td>145.75</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

IV. DISCUSSION

The aim of this study was to collect and examine data to test the influence of oral health and dental hygiene on SARS-CoV-2 infection, as well as to examine the contribution of oral cavity health and its structures to increased or decreased risk of COVID-19 infection, and to determine whether or not there is an association between the severity of COVID-19 infection and the oral health status of the sample, and to examine whether or not oral health status has an influence on the recovery phase of COVID-19 infection. Our results show that there is a significant difference (p=0.017) between general health status and COVID-19 severity index, and participants with worse general health status had higher COVID-19 severity index scores. In addition, patients with chronic diseases, who accounted for 16.9% of the sample, had significantly higher prevalence of COVID-19 severity index (p=0.015). This implies that patients with poor general health or chronic diseases have a higher rate of Covid severity. This result agrees well with a previous study by [13], as their results suggest that patients with severe medical conditions such as heart disease, diabetes, chronic lung disease, or chronic kidney disease are more likely to develop severe disease as a result of COVID-19 infection. At the same time, poor oral health increases the likelihood of developing the same medical disorders. In addition, our results showed that general health status and the presence of chronic diseases had significant differences with the oral health index (0.010, 0.048), and the results suggest that individuals with poor general health status and chronic diseases have poorer oral health. This result is consistent with a previous study by [14], as their results suggest that individuals with severe periodontal disease are more likely to develop chronic disease than those without periodontal disease, as poor oral hygiene is considered one of the risk factors for periodontal disease. [15]. The ability of SARS-CoV-2 to enter cells determines its infection rate, and evidence suggests that the transmembrane protein angiotensin-converting enzyme (ACE2) is the main receptor and entry point of this virus into cells. In addition to the heart, lungs, kidneys, and intestines, which have been shown to express (ACE2), recent studies have shown that epithelial cells in various mucous membranes of the oral cavity, particularly the tongue mucosa, also express (ACE2) [16]. COVID-19 mortality and severity are higher in SARS-CoV2 infected patients with chronic diseases such as COPD and pneumonia. Periodontopathic bacteria are involved in the development of COVID-19. Aspiration of periodontopathic bacteria in COVID-19 patients may exacerbate the disease by increasing inflammatory cytokine production, (ACE2) expression, and the cleavage of the S protein of SARS-CoV-2. Good oral health management is therefore critical for patients with mild COVID-19 disease, as it can help prevent exacerbation of COVID-19 disease. Periodontitis and periodontopathic bacteria are associated with various diseases such as diabetes and cardiovascular disease. Consequently, periodontopathic bacteria can significantly affect the severity of COVID-19 [17].

According to [18], there is evidence that poor dental health may be a significant risk factor for lower respiratory tract infections, especially in at-risk groups. Our results showed that the association between the severity of COVID-19 infection and oral health status was positive, although not statistically significant. This indicates that oral health status could potentially influence the severity of COVID-19 infection, supporting the notion that the oral cavity and its structures may contribute to increased COVID-19 risk. However, given the small sample size and study design, as well as the limited correlation, further research is needed to investigate this association. These findings are consistent with [16] research showing that SARS-CoV-2 oral viral load was associated with the severity of COVID-19 infection, so a reduction in oral viral load may be associated with a reduction in disease severity. According to [7], a similar conclusion was drawn as their results showed that oral health status could influence the severity of COVID-19 disease, but again, further research is needed to investigate the correlation. A similar pattern of results was found in a case-control study by [3], which found an association between periodontitis and the severity of COVID-19 infection, and according to their results, there is a strong association between these two conditions, and this association was considered bidirectional. A similar conclusion to ours was also reached by [19], as their results indicated that periodontitis was associated with an increased prevalence of severe COVID-19 symptoms, showing that poor oral and periodontal health is associated with an increased risk of severe critical COVID-19 symptoms, admission to the intensive care unit, and a higher mortality rate. Good oral health is considered a way to prevent respiratory infections in patients, especially those over 70 years of age. More than 700 pathogens, including bacteria, viruses and fungi, can colonize the oral cavity. There are numerous microbiological habitats in the oral cavity; however, the most important bacterial inhabitants are: S. Mutans, P. Gingivalis, P. Intermedia, and F. Nucleatum. Numerous mechanisms have been proposed to describe the possible role of oral bacteria in the etiology of respiratory infections, the first mechanism is the inhalation of pathogens from the mouth into the lungs. The second mechanism is that enzymes associated with periodontal disease alter mucosal surfaces, allowing respiratory pathogens to adhere and colonize. The third hypothesis is that these same periodontal enzymes could degrade the salivary pellicles of bacteria, preventing the removal of mucosal surfaces, and finally, periodontal-associated cytokines could alter the epithelium of the airways, promoting infection by respiratory pathogens. Bacteria in the oral flora are aspirated into the respiratory tract and contribute to the development or progression of diseases.
such as pneumonia or sepsis [20]. Regarding recovery time, based on accessible preliminary data from the WHO China Joint Mission Report [21], which is based on 55,924 laboratory-reported cases, the following time from onset of symptoms to full recovery was determined. Mild cases took two weeks to recover, while severe or critical cases took between three and six weeks to fully recover, with the time from onset of symptoms to patient death ranging from two to eight weeks [11].

In our current study, 40.1% of the sample felt completely free of symptoms in less than two weeks, and 29.2% were fully recovered within two weeks, while 21.3% took between three and six weeks to recover, and a small percentage of the sample 9.4% took more than six weeks to recover. In this context, we investigated the association between oral health status and recovery duration. According to our results, there was no association between oral health status and recovery duration as our results showed no significant difference between the two variables (P-value = 0.489), which is not consistent with the results reported by [7] as the results indicated that individuals with poor oral health had significantly longer recovery duration (six weeks), while patients with good oral health recovered faster, confirming that further research is needed in this area. Since the oral cavity is considered one of the first connectors between the exterior and the interior of the body, there is a high possibility that this route of viral colonization and infection is critical for COVID-19 initiation [16]. Lack of oral hygiene increases the bulk and complexity of dental plaque structure, which may promote interspecies interactions between native plaque bacteria and identified respiratory pathogens like P. aeruginosa and enteric bacilli. As a result of these interactions, respiratory infections may colonize the dental plaque. As a consequence, dental plaque may act as a reservoir for respiratory pathogen colonization, which can then be released into saliva. Saliva containing such organisms can affect the lower respiratory tract's most remote parts, resulting in pulmonary infections [18].

Furthermore, dental plaque may provide sustenance for bacteria in the respiratory system, especially in people who have poor oral hygiene. Periodontal disease can alter the environment, allowing for mucosal colonization and respiratory infection [22]. It is critical to emphasize that when a soluble antigen enters the bloodstream, it may bind to a specific circulating antibody to form an immunocomplex. As the bacterial count colonizing teeth was demonstrated to be increased twofold to tenfold in people with poor oral health status, delivering more bacteria into the bloodstream and resulting in bacteremia, these macromolecular complexes cause a variety of chronic and acute inflammatory responses [7]. Saliva is considered a source of SARS-CoV-2 infection, droplet infection via saliva should be given special attention. Nonetheless, an increase in saliva secretion and SIgA concentration in saliva is thought to reduce SARS-CoV-2 infection. Chewing is associated with an increase in saliva secretion [3]. The COVID-19 virus supposedly gathers at the nasal, oral, and pharyngeal mucosa during the first 10 days after virus transmission, when the patient is typically asymptomatic but contagious, and only later spreads. It has also been observed that the amount of ACE2 receptors in the salivary glands is higher than the amount of receptors found in the lungs, implying that the salivary glands may act as a reservoir for SARS-CoV-2 in asymptomatic people [16].

Evidence suggests that alterations in oral microbial populations can impact the microenvironment by increasing infections and overstimulating the immune system. Pathobiont and SARS-CoV-2 virus co-infection, in combination with known risk factors and comorbidities, may contribute to an increased inflammatory response and cytokine storm. Thus, researchers believe a link exists between the lung microbiome and intensive care hospitalization. It is noted that in individuals with COVID-19, periodontal disease may make a contribution to the provocation of a systemic inflammatory response by the spreading of bacterial products and is considered as a source of inflammatory cytokines, which will lead to exacerbation of the COVID-19 infection [23].

In our study, 15.0% of our sample had mobile teeth, which is considered an important indicator of periodontal disease [24]. In addition to red or swollen gums, painful chewing, and gingival receding, 11.3% of the sample reported bleeding while brushing, 12.2% reported frequent tooth sensitivity, and 6.9% reported halitosis (bad mouth smell). All of these symptoms are considered periodontal disease symptoms, along with red or swollen gums, painful chewing, and gingival receding [25]. As a result, understanding the role of COVID-19 in periodontal disease is critical. The SARS-CoV-2 virus can quickly infiltrate periodontal tissue from bleeding periodontal ulcers. Bacteremia and endotoxemia can be caused by periodontopathic bacteria and endotoxins entering blood vessels, exacerbating the severity of COVID-19 in infected individuals. Periodontopathic bacteria can stimulate the expression of ACE2 via respiratory epithelial cells, confirming their involvement in the aggravation of COVID-19. In terms of poor oral hygiene contributing to an increase in COVID-19 severity, managing periodontal disease and maintaining proper oral health are crucially important for overall health [17].

Patient age, male sex, specific races and ethnicities, type A blood type, obesity, chronic obstructive pulmonary disease (COPD), diabetes, cardiovascular disease, Down syndrome, chronic kidney illness, physical disability, or learning difficulty are all risk factors for severe COVID-19 infection. Tobacco use is also a known risk factor for periodontitis [26]. Several hypotheses could explain the significant relationship between periodontitis and COVID-19 severity [27]. According to [17], [28] periodontopathic bacteria may increase SARS-CoV-2 pathogenicity by cleaving its S glycoproteins and that the oral cavity, particularly periodontal pockets, may serve as a viral reservoir according to [16], [29], [30].

Reference [17] proposed that aspiration of periodontopathic bacteria could worsen COVID-19 severity by increasing the production of angiotensin-converting enzyme 2, a SARS-CoV-2 receptor, and inflammatory cytokines in the lower respiratory tract. Reference [27], [31], state that life-threatening COVID-19 effects were significantly associated with higher D-dimer, WBC, and CRP concentration levels, as well as lower lymphocyte levels. Moreover, patients who were admitted to the intensive care unit, as well as those requiring ventilators, had elevated CRP

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and D-dimer levels in their blood. Both studies discovered elevated inflammatory markers in COVID-19 individuals who perished. Furthermore, their COVID-19 cases with periodontitis had significantly higher WBC and CRP serum levels compared to those without it, implying a possible link between the two variables. One limitation about the findings of the oral health status was that we were not able to perform a dental examinations, the results were based on a self-administered oral health questionnaire, another limitation is that and there was no clinical or laboratory tests performed to determine the severity of COVID-19 infection as we relied also on a self-administered questionnaire. Another limitation was that not all patients presented a positive PCR test during the data collection because of the financial aspect of the test in the country of the sample’s residence, which could lead to some bias in the sample as some of participants might have mistaken the COVID-19 infection with other infections with similar symptoms. Another important concern was the limited and relatively small size of the study sample alongside confounding factors, this may have resulted in inaccurate risk estimates. Larger sample size studies are needed to confirm the results of this observational study. In the future, it would be beneficial to conduct interventional studies to determine the effect of controlling harmful and complicated oral conditions on the risk of severe COVID-19 infection. For future studies, dental examination is required to determine the oral health status, laboratory tests and clinical investigation of COVID-19 patients are also necessary to assess the severity of the COVID-19 infection.

V. CONCLUSION

Within the limitations of our research, we found that the general health of patients has a significant impact on the severity of their COVID-19 infection. Patients with chronic conditions tend to have more severe COVID-19 symptoms. Additionally, we discovered that poor oral health is linked to poor general health and chronic diseases in our sample group. Our main discovery was that the status of oral health may potentially influence the severity of COVID-19 infection, suggesting that the oral cavity and its structures could have an overall effect on the disease. We also investigated the connection between the recovery period and oral health status but found no significant correlation. However, our small sample size and study design do not provide conclusive evidence of a connection between these variables, and further research with larger sample sizes and more reliable study designs is needed to explore this topic.

CONFLICT OF INTEREST

Authors declare that they do not have any conflict of interest.

REFERENCES


N. Mohamad
17-07-1997
DMD, University of Damascus, Syria, 2020