The Correlation between Oral Health Status with the Recovery Period, C - reactive protein Values and Severity of Covid-19 Recovered Patients of Raichur - A Cross-Sectional Study

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Abstract:-

➢ **Introduction**

COVID-19 manifests a wide range of symptoms, from fever and dry cough to severe pneumonia progressing to adult respiratory distress syndrome. C-reactive protein (CRP) is known as a marker of hyperinflation. Patients with high levels of CRP have worse prognoses with COVID-19. Recent studies have shown the association between oral health status and systemic diseases and the impact of good oral care on risk reduction of viral respiratory diseases.

➢ **Objectives of the Study**

To find the impact of oral hygiene condition on the severity, duration of hospitalization and CRP values of post-Covid-19 recovered patients of Raichur.

➢ **Methodology**

The study design was a cross-sectional, questionnaire survey. Convenient sampling was used.105 patients were included from Navodaya Medical College and Hospital (NMCH) from April 2021 to August 2021. An open-ended, pretested questionnaire was used which was divided into two sections. First section for oral health evaluation and second section for COVID-19 severity. This was done via telephonic interviews. The HRCT chest report and C - reactive protein reports were collected from medical records department of NMCH included patients above 18 years old, both genders with positive RT- PCR report. Excluded patients with medical complications and who failed to complete the questionnaire or refuses to provide consent.

➢ **Result**

Inverse co-relation between the oral health status and the Covid-19 severity, duration of hospital stays and the CRP values were found using the ANOVA and Pearson correlation coefficient and was found statistically significant.

➢ **Conclusion**

This study found patients with poor oral health status had longer duration of hospital stay, increased Covid-19 severity and the CRP values.

Keywords:-Covid-19, Oral Health, C - reactive protein, Covid Severity, Oral Hygiene

I. INTRODUCTION

The outbreak of the Coronavirus Disease 2019 (COVID-19) was first seen in Wuhan city from where the disease has spread around the world.[1] The virus responsible for the disease is Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2).[2] On 11 march 2020 World Health Organization declared Covid-19 as a global pandemic. Globally, as of 28 December 2021, there have been 280,119,931 confirmed cases, including 5,403,662 deaths, reported to WHO.[3] In India as of 28 December 2021 there is a total of 3.48cr positive cases including 4.8lakhs death cases are reported.[3] In Raichur district of Karnataka state of India total cases reported till now are 23,499 including deaths of 126 Covid-19 infected patients.[3] The novel Coronavirus belongs to a family of single-stranded RNA viruses known as *Coronaviridae* and are zoonotic or transmitted from animals to humans.[4]This family includes Severe acute respiratory syndrome coronavirus (SARS-CoV), first discovered in 2002, and the Middle East respiratory syndrome coronavirus (MERS-CoV), found in 2012.[5] The symptoms of Covid-19 range from fever, dry cough, myalgia, loss of taste and smell sensation to acute respiratory distress syndrome or acute

pneumonia. The chest X-ray and the HRCT chest reveal the presence of the typical ground-glass opacities.[6,7] Other case may be deteriorated to aggressive counteracting of the immune system, referred to as 'cytokine storm syndrome', in which the levels of released cytokines – tumor necrosis factor (TNF), interleukin-6 (IL-6), and interleukin-1β (IL-1β) – which are injurious to host cells. This may expose patients to an increased hazard of vascular permeability which may cause damage to many organs, such as the kidneys and heart which causes death as reported in many cases.[8] WHO and Centers for disease control and prevention (CDC) and Indian Council Of Medical Research (ICMR) have stated that certain risk factors for Covid-19 infection mainly include aging, diabetes, hypertension, cardiovascular diseases, and immunodeficiency conditions.[9] Along with the radiological findings the C-reactive protein (CRP) values of the patients are also determined as in the studies it has been found that the patients with the higher levels of the CRP values had a worse prognosis of the Covid-19 infection.[10] Studies indicate that the rise in the CRP values are mainly seen because of the acute inflammatory pathogenesis of the Covid-19.[11] The relation between the oral cavity and the covid-19 can be established from studies were done by Neuman et al and Jin Y et al.[12,13] These studies stated that SARS-CoV-2 enters the body of the host and invades the host cells via the ACE2 membrane receptor; which leads to the cleavage of the S protein from the virion leading to the release of the nucleocapsid into the cytoplasm.[12,13,14] Studies by Xu H et al and Haga et al stated that ACE2 expression is found high in the oral cavity.[15,16] Therefore, the alveolar tissues, oropharyngeal mucosal cells, and the other oral tissues are considered to be potential risk sites for the SARS-CoV2 virus.[15,17] Studies have shown that there exists an association between oral health status and systemic diseases mainly viral acute respiratory diseases.[18,19] Since the oral cavity is a huge reservoir of respiratory pathogens containing about 700 bacterial species and prophytes. The oral cavity is a risk site for the Covid-19 infection and also a reservoir of microbes therefore the maintenance of the balance of the oral hygiene to control the bacterial and viral load in the oropharyngeal cavity becomes a crucial part. A study done by Kamel A et al[20] on the impact of the oral health status on the covid-19 severity has shown that there is an inverse correlation between the oral health status with the recovery period and CRP values and also concluded that poor oral health has a potential impact on the severity of the covid-19 infection. The main aim of the study was to find the impact of oral hygiene conditions on the severity, duration of hospitalization, and CRP values of post-Covid-19 recovered patients of Raichur.

II. MATERIALS AND METHODS

Cross-sectional study based on a questionnaire survey was designed for the study. The sample was determined from the targeted population which comprised of the post-Covid-19 recovered patients that were hospitalized at Navodaya Medical College Hospital, Raichur (NMCH) center from April 2021 to August 2021. A total of 434 Covid positive patients were hospitalized in these three months. After applying the inclusion and exclusion criteria and excluding the deaths and patients not willing to or patients that we were unable to contact,105 patients were included in the study. A convenient sampling technique was used for determining the sample size. The inclusion criteria included patients above 18 years of age and with a confirmed positive RT-PCR Covid-19 test report that were hospitalized at NMCH. The patients were excluded if they had medical conditions like pregnancy, cardiovascular diseases, chronic kidney or lung diseases, and other immuno-compromised disorders like post-radiotherapy or patients on long-term immune-suppressant medications. Patients that were unable or unwilling to participate in the study were also excluded.The treatment records of the patients were procured from the Medical Records Department of NMCH with the permission of the Medical Superintendent of the hospital. Along with medical history and their contact number with the residential address of the patient, the computed tomography (HRCT) chest score and the C - reactive protein (CRP) values during the first week of hospitalization and duration of hospitalization were also recorded for each patient. Two questionnaires were designed, Questionnaire I, comprising of questions for evaluating the Oral Health and Hygiene status of the patient, and Questionnaire II comprising of questions regarding the severity of the Covid-19 infection. The questionnaire was prepared by the questionnaire used by Kamel A et al[20] in their study and was pretested. These questionnaires were provided to the patients and the answers were recorded by telephonic interviews in their language. A double-blinding technique was applied. Ethical clearance was taken from the Institutional Ethical Committee of Navodaya Dental College and Hospital, Raichur. Oral Health interpretation was done according to the scoring system of the questionnaire. The questionnaire comprised 11 questions and each answer was given a score. The total score ranged from 0-33 with a higher score denoting better oral health and hygiene status. The patients were categorized according to the scoring from their answers into three categories as 0-11 (poor), 12-23(fair), 24-33(good). The covid severity interpretation was done according to the HRCT chest score containing a total of 25 points and they were classified into three categories comprising of mild, moderate, and severe with the scores ranging from 0-7, 8-17, 18-25 respectively.The CRP values and duration of hospitalization were obtained and were correlated with the oral health status and the Covid-19 severity interpretation.

III. STATISTICAL ANALYSIS

Descriptive and inferential statistical analyses were carried out in the present study. Results on continuous measurements were presented on Mean ± SD and results on categorical measurement were presented in number (%). Level of significance was fixed at p=0.05 and any value less than or equal to 0.05 was considered to be statistically significant. Chi square analysis was used to find the significance of study parameters on categorical scale. Student t tests (two tailed, unpaired) was used to find the significance of study parameters on continuous scale between two groups. Analysis of variance (ANOVA) was used to find the significance of study parameters between the groups (Inter group analysis). Further post hoc analysis was carried out if

the values of ANOVA test were significant. Based on the results of normality test (Kolmogorov smirnov& Shapiro wilk test), it was concluded that part of the data is not following the normal distribution, hence non parametric test was used. Mann Whitney U test was used to find the significance of study parameters on continuous scale between two groups. Kruskal Wallis test was used to find the significance of study parameters between three or more groups. Pearson'.

Correlation coefficient was computed to measure correlation between oral health status and different variables. The Statistical software IBM SPSS statistics 20.0 (IBM Corporation, Armonk, NY, USA) was used for the analyses of the data and Microsoft word and Excel were used to generate graphs, tables etc.

IV. RESULTS

➢ *Demographic Characteristics of the Study Participants*
In this study it was found that incidence of the covid-19 infection among the participants with mean age of 47.66 ± 13.787 was more prevalent among males (61.9%) than that of the females 38.1% (Table1, figure 1and 2).

Table 1 Demographic Characteristics of the
Study Participants (N=105)

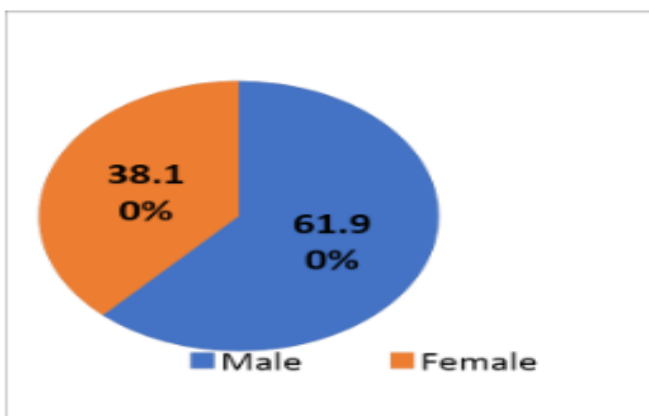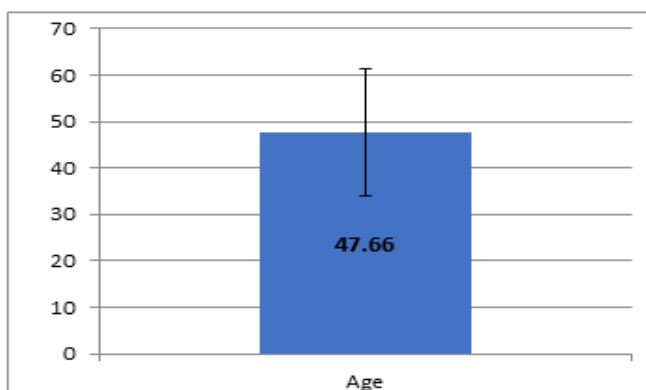| Variables	Sub-Groups	N	%
Gender	Male	65	61.9
	Female	40	38.1
Age (Mean ± SD)		47.66 ± 13.787	

Fig 1 Gender

Fig 2 Age (Mean ± SD)

Among the patients 27.6% had mild (n=29), 56.2% moderate (n=59), 16.2% severe (n=17) Covid-19 severity and the oral health status was found to be 27.6% good (n=29), fair 39% (n=41) and poor 35% (n=35). The mean duration of hospital stay was found to be 7.49 ± 4.744 and the mean CT score was found to be 11.51 ± 5.378 and the mean CRP value was found to be 53.31 ± 50.08.(Table 2, Figure 3,4,5,6,7)

Table 2 Descriptive Statistics (N=105)

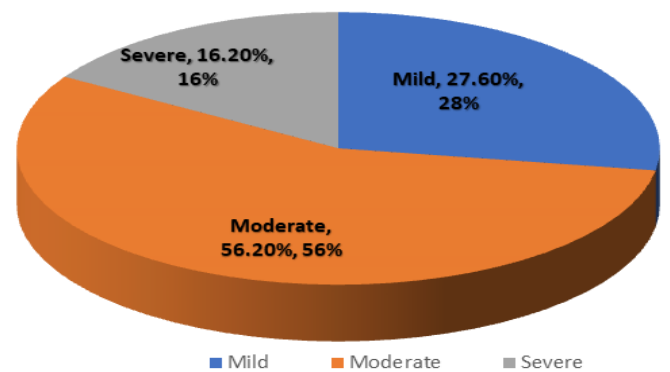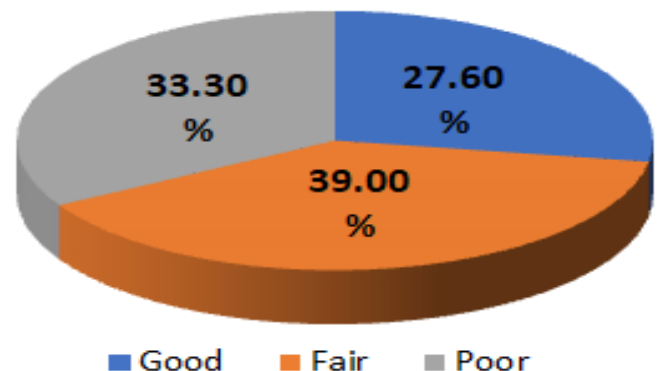| Variables	Sub-Groups	N	%
CovidSeverity	Mild	29	27.6
	Moderate	59	56.2
	Severe	17	16.2
Oral Health Status	Good	29	27.6
	Fair	41	39.0
	Poor	35	33.3
Duration of Hospital stay (Mean ± SD)		7.49 ± 4.744	
CT Score (Mean ± SD)		11.51 ± 5.378	
CRP values (Mean ± SD)		53.31 ± 50.08	

Fig 3 CovidSeverity

Fig 4 Oral Health Status
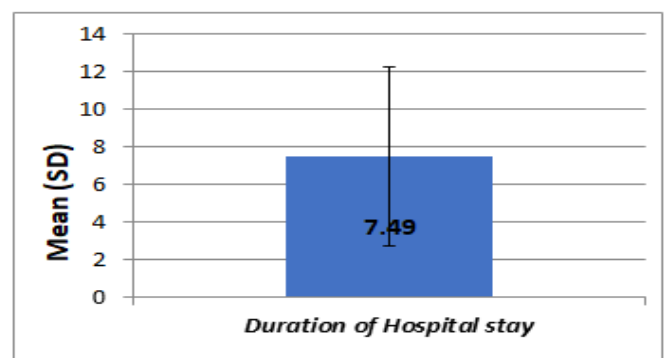

Fig 5 Duration of Hospital Stay (Mean ± SD)
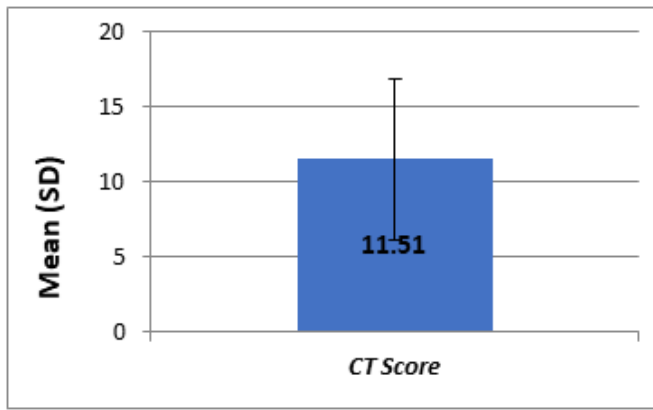
Fig 6 CT Score (Mean ± SD)
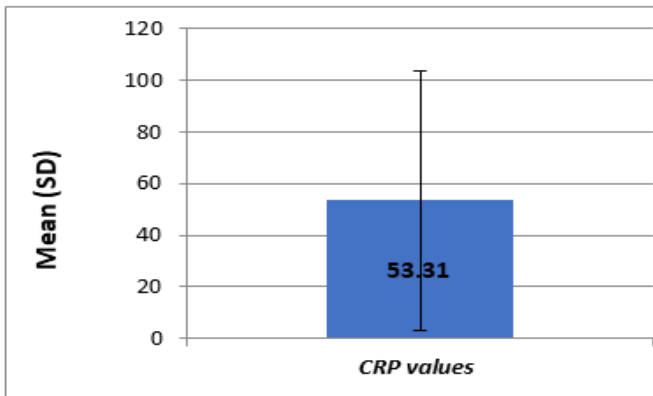
Fig 7 CRP Values

➢ *Comparison of Duration of Hospital Stay Among Oral Health Status:*

The average days of hospitalization were 7.49±4.744 days. Patients with poor oral hygiene had longer duration of hospitalization in comparison to the patients with fair and good oral hygiene. Patients with good oral hygiene had a mean duration of hospitalization 5.242±2.340 days and patients with fair and poor oral hygiene had 6.85±3.575 days, 10.09±6.128 days respectively (F value 10.484, $p < 0.001$). (Table 3, Figure 8)**.**

Table 3 Comparison of Duration of Hospital Stay in Terms of {Mean (SD)} Among Oral Health Status using ANOVA Test

Oral Health Status	N	Mean	Std. Deviation	F Value	P value
Good	29	5.24	2.340	10.484	<0.001**
Fair	41	6.85	3.575		
Poor	35	10.09	6.128		
Total	105	7.49	4.744		

($p < 0.05$ - Significant*, $p < 0.001$ - Highly significant**)

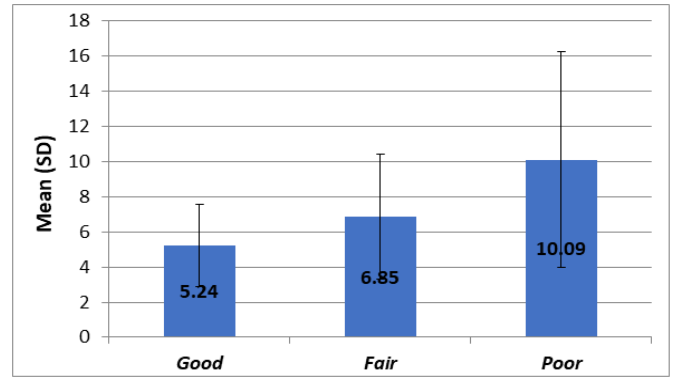|	Good	Fair	Poor
Good	-	0.284	<0.001**
Fair	0.284	-	
Poor	<0.001**	0.005*	-

(Tukey'sPost Hoc Analysis)

Fig 8 Comparison of duration of hospital stay in terms of {Mean (SD)} among oral health status using ANOVA test Comparison of CT score among oral health status

The average CT score was 11.51±5.378. Patients with poor oral hygiene had higher CT score in comparison to the patients with fair and good oral hygiene. Patients with good oral hygiene had a mean CT score 7.52±4.882 and patients with fair and poor oral hygiene had 11.20±3.537, 15.20±5.138 respectively (F value 23.285, $p < 0.001$). (Table 4, Figure 9)

Table 4Comparison of CT Score in Terms of {Mean (SD)} Among Oral Health Status Using ANOVA Test

Oral Health Status	N	Mean	Std. Deviation	F Value	P Value
Good	29	7.52	4.882	23.285	<0.001**
Fair	41	11.20	3.537		
Poor	35	15.20	5.138		
Total	105	11.51	5.378		

($p < 0.05$ - Significant*, $p < 0.001$ - Highly Significant**)

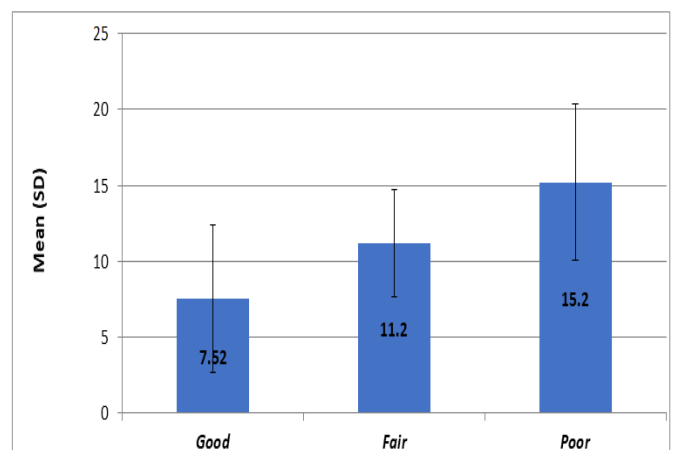|	Good	Fair	Poor
Good	-	0.003*	<0.001**
Fair	0.003*	-	<0.001**
Poor	<0.001**	<0.001**	-

(Tukey'sPost Hoc Analysis)

Fig 9 Comparison of CT Score in Terms of {Mean (SD)} Among Oral Health Status Using ANOVA Test

➤ *Comparison of CRP Values Among Oral Health Status:*

The average CRP value 53.3125±50.088. Patients with poor oral hygiene had higher CRP value in comparison to the patients with fair and good oral hygiene. Patients with good oral hygiene had a mean CRP value 12.939±12.939 and patients with fair and poor oral hygiene had 42.962±27.668, 98.88±54.216 respectively (F value 56.573,$p < 0.001$). (Table 5, Figure 10)

Table 5Comparison of CRP Values in Terms of {Mean (SD)} Among Oral Health Status Using Kruskal Wallis Test

Oral Health Status	N	Mean	Std. Deviation	Chi Square Value	P Value
Good	29	12.9393	12.93998	56.573	<0.001**
Fair	41	42.9624	27.66816		
Poor	35	98.8889	54.21655		
Total	105	53.3125	50.08828		

($p< 0.05$ - Significant*, $p < 0.001$ - Highly significant**)

	Good	Fair	Poor
Good	-	<0.001**	<0.001**
Fair	<0.001**	-	<0.001**
Poor	<0.001**	<0.001**	-

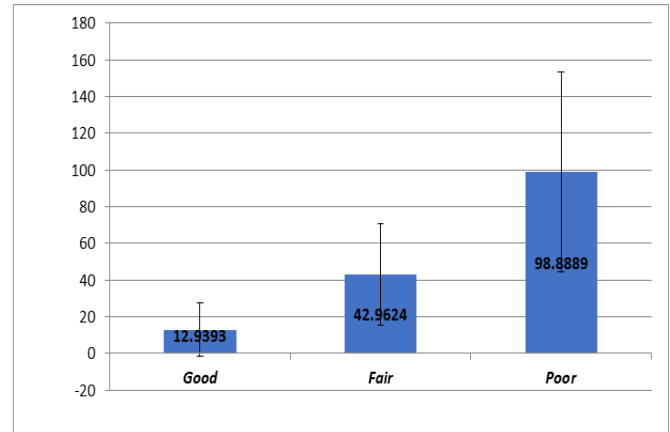(Individual Comparison Using Mann Whitney U Test)

Fig 10 Comparison of CRP Values in Terms of {Mean (SD)} Among Oral Health Status Using Kruskal Wallis Test

Table 6: Comparison of Covid Severity among People with Different Oral Health Status Using Chi Square Test

			Covid Severity			Total
			Mild	Moderate	Severe	
ORAL STATUS	Good	Count	17	12	0	29
		% within ORAL STATUS	58.6%	41.4%	0.0%	100.0%
	Fair	Count	9	30	2	41
		% within ORAL STATUS	22.0%	73.2%	4.9%	100.0%
	Poor	Count	3	17	15	35
		% within ORAL STATUS	8.6%	48.6%	42.9%	100.0%
Total		Count	29	59	17	105
		% within ORAL STATUS	27.6%	56.2%	16.2%	100.0%
Chi-square value: 42.072 P value: <0.001**						

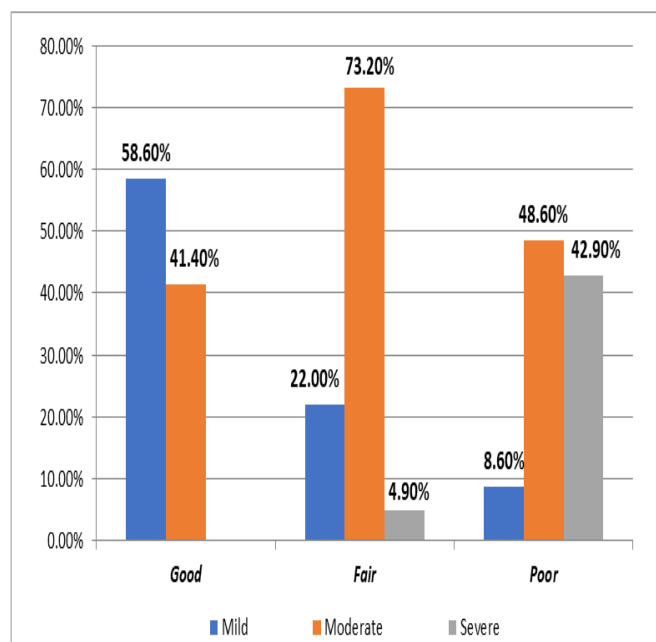($p< 0.05$ - Significant*, $p < 0.001$ - Highly Significant**)

Fig 10 Comparison of Covid Severity among People with Different Oral Health Status Using Chi Square Test

➤ *Correlation between Duration of Hospital Stay, Covid Severity, CRP Values and Oral Health Status:*

Inverse co-relation between the oral health status and the Covid-19 severity(r=0.404), duration of hospital stays(r=0.560) and the CRP values(r=0.679) were found.

Table 7 Correlation between Duration of Hospital Stay, Covid Severity, CRP Values and Oral Health Status Using Pearson's Correlation Coefficient

Variables	Oral health status	
	R (correlation coefficient)	P value
Duration of Hospital Stay	-0.404	<0.001**
Covid Severity	-0.560	<0.001**
CRP Values	-0.679	<0.001**

($p< 0.05$ - Significant*, $p < 0.001$ - Highly significant**)

V. DISCUSSION

The main aim of the study was to investigate the effect of oral health and hygiene on the covid-19 severity in the post-recovered patients, which was done using a detailed questionnaire and the medical and the blood investigation reports procured from the Medical Records Department of NMCH. The analysis of the questionnaire was done by the faculties of the Public Health Dentistry department, Navodaya Dental College, and hospital Raichur. The blinding technique was used to reduce the bias. Patient with acute and chronic medical conditions were excluded along with the participants that were not interested or were unavailable for the study due to improper communication details, provided by them to the hospital. Assessment of the oral health and the Covid-19 severity was done using the questionnaire. The oral health and Covid-19 severity assessment questionnaire were prepared according to the Kamel A et al[20]. The Covid-19 severity was also measured using the HRCT score of the patient as advised by the World Health Organization, Indian Council of Medical Research, CDC, NHS, National Institute for Health and Care Excellence (NICE).[21, 22, 23] Due to the inability to examine the patients clinically because Covid-19 restrictions were imposed, telephonic interviews were done. In some recent trials, it has shown good results in assessing patients using phone calls, video calls, or hospital forms. Therefore using the questionnaire look may be beneficial.[24,25,26] In this study, it was found that the covid-19 severity was significantly more severe among the patients with poor oral health status rather than the patients having good oral health ($p<0.001$) which shows high statistical significance. Therefore the result of this study comes in agreement with some of the previous studies by Scannapieco F A and Imsand M et al which showed the role of oral health in secondary respiratory infections.[27,28] This was also in agreement with the result of Kamel A et al in their research.[20] Bacterial colonization increases twofold to ten folds among the patients with poor oral health status and thus it increases the bacterial count in the blood flow, which leads to Bacteremia.[29] According to reports on the entry of the soluble antigens into the bloodstream and on interacting with a specific circulating antibody it produces an immune complex that causes a chronic and acute inflammatory reaction in the body.[30] However, it is found that in cases of periodontitis the concentration of certain cytokines that are pro-inflammatory for eg. Gamma interferon, PGE2, interleukin, and TNF increases in the tissues, which fight with micro-organisms but on the hyperactivity of the immunologic responses, may result in tissue damage. Therefore, the platelet function, blood coagulation can be affected by the entry of such cytokines into the blood from the periodontium which can be referred to as the reservoir of these macro-molecular complexes.[30] Studies have shown that the CRP levels are higher in cases of severe Covid-19 patients rather than the mild and moderate cases.[31] It is also found that the CRP levels were higher in the patients who have died rather than the patients who have recovered. This rise in the CRP levels can be due to the overproduction of the cytokines in the patients with poor oral health due to increased bacterial colonization.[32,33] The oral cavity with high viral and bacterial load worsens many systemic diseases which shows a strong relationship between the oral cavity and the body. the increased risk of the inter-bacterial exchange between the lungs and mouth in poor oral hygiene patients aggravates the chances of respiratory infection and even post-infection complications.[27,34] The presence of the periodontopathic bacteria and detection of increased concentrations of the Provotella, Fusobacterium, and Staphylococcus in the metagenome of patients with severe covid-19 infection was verified by khan A A et al.[35] more than 50% of deaths caused due to the Covid-19 infection has resulted due to the bacterial super-infection.[36, 37] The explanation of the involvement of the oral bacterial in the pathogenesis of certain respiratory infections can be done by the following possible mechanisms. Firstly aspiration of the oral pathogens into the lungs, secondly in certain conditions, pulmonary pathogens not only gets refuge but also get promoted to grow in dental plaque[38] Thirdly adherence of the respiratory pathogens to respiratory pathogens to the airway due to the enzymes released due to periodontal diseases.[20] Finally the continuous release of the cytokines in the periodontal diseases may cause the change in the pulmonary epithelium which makes them prone to get infected by the pulmonary pathogens.[39]

Studies have shown the relation between the severity of Covid-19 and the viral load.[40,41] Active replication of SARS CoV-2 in the throat, particularly during the first five days was shown in the studies by Wolfel et al (2020) which was proved by the presence of the viral RNA in the specimens.[42] Since transcription of the viral mRNA was confirmed in infected cells rather than being packed into virions, which suggests the existence of the virus, it can be assured that throat infections at an early stage of the infection can be initiated by the microorganisms in case of the poor oral health and hygiene and therefore maintaining proper oral hygiene and oral antiseptics and solutions may help in reducing the replication of the virus and thus even help in reducing the rate of transmission of the disease and also the severity of the disease.[43,44] Yoon et al (2020) proved that the use of chlorhexidine has reduced the viral load in saliva for a short period.[45] In this study, we have found among the participants 42.9% who had severe Covid-19 infection had poor oral health, whereas 58.6% of the patients who suffered from the mild infection had good oral health. Moreover, the average days of hospitalization and found to be 15±5.138 ($p<0.001$) and 10.09± 6.128 which is much higher than that for the patients with good oral with a mean CT score of 7.52±882 and mean duration of hospitalization 5.24±2.340. This holds even for the CRP values. The normal blood CRP <10mg/l, it has proved that in the case of the Covid-19 infection, the level of blood CRP valued increases as the severity of the Covid-19 infection.[46, 47, 48,49,50,51] In this study, we have found that mean CRP values for patients with poor oral health were 98.89±54.217 whereas the mean CRP values of the patients with good oral health status were 12.93±14.63 ($p<0.001$). This supports the hypothesis that poor oral health has an impact on the severity of the Covid-19 infection as poorer oral health, increases in the CRP values which indicate higher the severity of the Covid-19 infection. At the end of the discussion, we can say that there is enough evidence that there exists a correlation between oral health status and Covid-19 infection. More such questionnaire

studies should be performed to establish and prove this hypothesis and also to find a way to curve the transmission of the covid-19 pandemic.

VI. CONCLUSION

Though certain limitations are present in the study that we were not able to perform a clinical examination of the patient and also secondly the limited sample size, we concluded that the result showed that there is a significant impact of the oral health status on the severity of Covid-19 infection and CRP values of the patients. Hence as dental professionals it's our duty, to make the public aware of the fact to movie step forward in our fight towards the pandemic covid-19

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