



hospital/medical city from November 2020 to January 2021. All patients were diagnosed with SARS-CoV-2 infection, according to the World Health Organization criteria [12]. Real-Time Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) assay was used to identify SARS-CoV-2 infection. The clinical classification of patients was categorized by disease severity into mild, moderate and severe, according to sign and symptoms by clinical management guidelines outlined in the diagnosis and treatment protocol for COVID-19. Inclusion criteria; the patients enrolled in this study and considered eligible must have met the following criteria; COVID-19 infection signs and symptoms (fever, generalized malaise, cough and difficulty breathing) as well as COVID-19 RT-PCR. This study excluded children and pregnant women, patients with chronic viral infections and systemic disorders, allergic rhinitis and chronic sinusitis, and patients who were unable to give informed consent.

**Controls group:** consisted of 35 individuals (16 males and 19 females), their ages and sexes were matched to patients their ages ranged between (18-73) years.

Oral hygiene status was determined by the simplified oral hygiene index "Oral Hygiene Index=Debris Index +Calculus Index" [13].

**Sample collection:** Four millilitre of venous blood was collected from all participants. Blood was transferred to sterile plain tube, and serum was separated by

centrifugation at 3000 rpm for 10 minutes, then divided into small aliquots and kept at -20°C until used for analysis.

**Interleukin-6:** Serum IL-6 was estimated by ELISA and done according to the instructions on the kit's booklet.

**Statistical analysis:** The data was non-parametric and described by median, as evidenced by histograms and the Smemirnov-Kolmogorove test, and non-parametric tests of significance were recommended. Statistical significance was defined as a P value of less than 0.05.

## RESULTS

The present study found that there is significant elevation ( $P < 0.024$ ) in the median serum level of IL-6 among patients with COVID-19 (42.68 pg/ml) as compared to healthy controls (36.71 pg/ml), (Table 1). As well, results in Table 2 showed a significant difference ( $p < 0.05$ ) in median serum level of IL-6 among three groups of patients, the median level of severe cases was (84 pg/ml), for moderate (41 pg/ml) and mild cases was (44 pg/ml). On the other hand, there is a significant difference ( $p < 0.05$ ) between severe group and each of moderate and mild groups, while there is no significant difference between moderate and mild group.

**Table 1: Comparison of sickled RBC in anti-sickling analysis of two methods with pre-treatment (n=49).**

| Serum IL-6 | Study groups      |                 | P-value |
|------------|-------------------|-----------------|---------|
|            | COVID-19 patients | Healthy control |         |
|            | N=50              | N=35            |         |
| Min        | 13.57             | 22.53           |         |
| Max        | 561.25            | 545.06          | 0.024*  |
| Median     | 42.68             | 36.71           |         |
| Mean Rank  | 48.05             | 36.87           |         |

\*:Significant, No: Number

**Table 2: Serum levels of IL-6 (pg/ml) in patients group according to disease severity.**

| Serum IL-6 | Patients group                  |          |       | P-value  |
|------------|---------------------------------|----------|-------|----------|
|            | Severe                          | Moderate | Mild  |          |
|            | N=10                            | N=29     | N=11  |          |
| Min        | 44                              | 13       | 26    |          |
| Max        | 233                             | 561      | 121   |          |
| Median     | 84                              | 41       | 44    | 0.019*   |
| Mean Rank  | 28.05                           | 17.22    | 19.82 |          |
|            | Severe group vs. moderate group |          |       | 0.010*   |
|            | Severe group vs. mild group     |          |       | 0.016*   |
|            | Moderate group vs. mild group   |          |       | 0.833 NS |

NS: Non-Significant,

Concerning oral hygiene, the level of serum IL-6 is significantly increased ( $p < 0.05$ ) in patients with poor

oral hygiene was (77 pg/ml) than those patients with good oral hygiene (41 pg/ml), as demonstrated in Table 3.

**Table 3: Serum levels of IL-6 (pg/ml) in patients group according to oral hygiene.**

| Serum IL-6 | Good   | Poor  |
|------------|--------|-------|
|            | N=18   | N=32  |
| Min        | 26     | 26    |
| Max        | 161    | 356   |
| Median     | 41     | 77    |
| Mean Rank  | 19.72  | 29.42 |
| P-value    | 0.026* |       |

### DISCUSSION

Not surprisingly, research into SARS-CoV-2 infection is currently the major priority for science communities worldwide. So this encouraged us to study the role of IL-6 in COVID-19 patients with different stages of disease. Although this was the main aim of the present study but nevertheless the impact of oral health status in COVID-19 patients compared to healthy controls was also investigated.

The present results found that the levels of IL-6 are significantly higher in COVID-19 patients than those in healthy control. As well, there is significant increase in level of IL-6 among patients with severe cases than that in moderate and mild cases. The present observations were in line with previous findings reported that the level of IL-6 was increase in patients with SARS-CoV-2 infection [14-16]. Showed that the highest level of IL-6 was found in newly diagnosed COVID-19 patients comparing with healthy control [17]. In addition, Cazzolla reported a significant directly proportional correlation between IL-6 levels and the presence of self-reported olfactory dysfunction [18]. However, the elevated cytokine levels may also be responsible for the lethal complications of COVID-19, patients with COVID-19, SARS or MERS presented distinct cytokine profiles. Patients with COVID-19 presented elevated T helper 2 cytokines (IL-4) in addition to T helper 1 cytokines compared to those in patients with SARS or MERS [19].

Moreover, a study of 452 patients infected with SARS-CoV-2 reported that the elevation of IL-6 levels was more marked with more severe symptoms [20]. As well Sabaka revealed that patients with severe COVID-19 had a high mean level of IL-6 compared to patients in mild disease, this was in agreement with the results of the current study. Serum IL-6 concentrations were associated with a greater likelihood of progression to critical illness status, indicating the need for more active interventions to prevent further deterioration to a life-threatening condition [21]. On the other hand, pointed out to that elevated IL [23]. Mechanistically, IL-6 is essential for the generation of T helper 17 (Th17) cells in the dendritic

cell-T cell interaction [24]. The excessive IL-6 may explain the overly activated Th17 cells observed in COVID-19 patients [25]. Animal studies of SARS-CoV have demonstrated that inhibiting nuclear factor kappa-B (NF- $\kappa$ B), a key transcription factor of IL-6, or infecting animals with SARS-CoV lacking the CoV E protein, a strong stimulus to NF- $\kappa$ B signalling, increased animal survival, with reduced IL-6 levels [26].

The present study also indicated that the serum IL-6 level was significantly higher in patients with COVID-19 poor oral hygiene than in patients with good oral health this could explain in part due to that pro-inflammatory cytokines levels were correlated with oral health status and the presence of oral microorganisms. Unfortunately, no previous studies with such comparison were found. In this context, periodontitis has been linked to increased levels of pro-inflammatory cytokines, including IL-6, which is a recognized mediator in the periodontal destruction process [27]. The ability of nonsurgical periodontal treatment to lower cytokine levels has been highlighted in the dental literature [28,29]. Thus, lower IL-6 levels and inflammation resulting from periodontal treatment can potentially protect COVID-19 patients against life threatening respiratory complications. In fact, previous studies have linked periodontitis to respiratory conditions, with increased risk for complications and higher mortality rate in hospitalized patients [30]. The impact of a connection between periodontal treatment, IL-6 levels, respiratory conditions and COVID-19 can be powerful considering the high prevalence of periodontal disease in adults, the high transmission rate of SARS-CoV-2, the limited access to periodontal treatment during the pandemic and the shortage of health care resources related to hospitalized COVID-19 patients who require mechanical ventilation [31].

### CONCLUSION

In conclusion elevated IL-6 levels are associated with worse infection with SARS-CoV-2 and are an important predictor for COVID-19 patients in severe stage.

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**COMPETING INTERESTS**

The authors declare that they have no competing interests.

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