**Table 3: Case-control differences in oral hygiene and number of teeth.**

| Oral hygiene | Study groups | | | | P-value |
|---|---|---|---|---|---|
| | Patients group (N=50) | | Control group (N=35) | | |
| | N | % | N | % | 0.024* |
| | Oral hygiene | | | | |
| Good | 30 | 60 | 29 | 83 | |
| Poor | 20 | 40 | 6 | 17 | |

**Table 4: Distribution of oral hygiene according to severity of COVID19.**

| | | Severity of COVID-19 | | | |
|---|---|---|---|---|---|
| Oral Hygiene | | Severe | Moderate | Mild | P-value |
| Good | N | 0 | 12 | 18 | 0.000** |
| | % | - | 40% | 60% | |
| Poor | N | 10 | 4 | 6 | |
| | % | 50% | 20% | 30% | |

As shown in Table 5 there is significant decrease (P<0.01) in median serum level of cathelicidin in patients group (11.72 ng/ml) as compared to that in healthy control group (12.67 ng/ml). While, there is no significant difference (P>0.05) in serum level of cathelicidin among three groups of patients according to severity of disease, However, the median level for severe, moderate and mild cases were (15.7 ng/ml, 12.12 ng/ml and 16.56 ng/ml) respectively, as observed in (Table 6). Likewise this work the current study failed to show statistically significant differences in median serum cathelicidin levels between patients group with good oral hygiene (25.52 pg/ml and 25.31 ng/ml) and patients group with bad oral hygiene (25.84 pg/ml and 28.4 ng/ml), as observed in (Tables 7).

**Table 5: Case control difference in serum levels of cathelicidin (ng/ml).**

| Antimicrobial Peptides | Study groups | | P-value |
|---|---|---|---|
| | Covid-19 patients (N=50) | Healthy control (N=35) | |
| | Serum Cathelicidin | | 0.013* |
| Min | 3.28 | 9.79 | |
| Max | 26.38 | 25.72 | |
| Median | 11.72 | 12.67 | |
| Mean Rank | 37.45 | 50.93 | |

**Table 6: Comparison the levels of Serum Cathelicidin (ng/ml) in patients group according to Severity disease.**

| Serum Cathelicidin | Patients group | | | |
|---|---|---|---|---|
| | Severe (N=10) | Moderate (N=16) | Mild (N=24) | P-value |
| Min | 9.37 | 3.28 | 5.77 | 0.433NS |
| Max | 23.32 | 23.49 | 26.38 | |
| Median | 12.195 | 10.875 | 11.44 | |
| Mean Rank | 15.7 | 12.12 | 16.56 | |

**Table 7: Comparison the levels of serum Cathelicidin (ng/ml) in patients group according to oral hygiene.**

| Serum Cathelicidin | Good (N=30) | Poor (N=20) |
|---|---|---|
| Min | 3.28 | 8.03 |
| Max | 26.38 | 23.32 |
| Median | 11.235 | 12.13 |
| Mean Rank | 25.31 | 28.4 |
| P-value | 0.477NS | |

## DISCUSSION

Cathelicidin LL-37 is a small cationic peptide that plays major role in antimicrobial defenses, which kills a wide-range of infective agents by disrupting their membranes, involving viruses [18]. The present results showed that the serum cathelicidins level was significantly decreased in COVID-19 subjects as compared to controls and the level was non-significantly decrease as the severity of disease increase. Evidence has reported that cathelicidin can be deemed as a potent sign for response of immune system in bacterial or viral infections [19]. Low level of serum cathelicidin in this study may be due to a disruption of the immune system in COVID-19 patients, or could be attributed to vitamin D deficiency that leads to reduced cathelicidin production. This is in agreement with Crane-Godreau et al., (2020) who reported, it is possible that vitamin D deficiency may lead to reduced LL-37 levels and a weakened antimicrobial response to SARS-CoV-2 [20]. Dixon et al. revealed that the active 1, 25-dihydroxy metabolite stimulates transcription of the cathelicidin gene, and there is a positive correlation between circulating bioactive vitamin D and hCAP18/ LL-37 levels in healthy subjects [21]. Similarly, White et al., (2010) illustrated that 1,25D is a direct promoter of antimicrobial peptides genes expression, in particular cathelicidin [22]. Vitamin D and LL-37 play important roles in lung immunity and response to respiratory diseases [23]. Vitamin D stimulates the production of antiviral molecules such as cathelicidins and defensins, which reduces the rate of viral replication, decrease the pro-inflammatory cytokine concentration, and increase of anti-inflammatory molecules production [24]. In similar way, previous study conducted on asthmatic patients reported that a low level of cathelicidin may lead to contagious complications in healthy children and children with asthmatic [25].

This study also showed that the level of cathelicidin decrease as covid-19 disease progress with no significant differences. There were no available studies on this correlation in covid-19 to compare with it. Anyhow, [26] observed relationship among LL-37, vitamin D and severity of COVID-19. Analysis of Surface Plasmon resonance showed that LL-37 links to SARS-CoV-2 (S) protein and prevents linking to ACE2 receptor, and probably the virus enters into cell. This study supports the protective utilize of vitamin D to encourage LL-37 which keep from SARS-CoV-2 infection, and administration of vitamin D as a therapy for the COVID-19 patients treatment. Furthermore, their results give proof that the direct utilize of LL-37 by inhalation and systemic application may decrease the severity of disease.

Additionally, the current study failed to show significant differences in the levels of cathelidicin in COVID-19 patients with good oral health compared to those patients with poor oral health. A possible explanation for no significant difference could be due to that AMP levels were not correlated with oral health status and the presence of oral bacteria. However; Shin and Choi reported that oral bacteria in dental plaque as Treponema denticola inhibits expression pathway and secretion of AMP by inhibition secretion of TNF-alpha and TLR-2 [27]. One limitation of the current study is to study only one type of AMP, as other types also has antiviral role. In conclusion low Level of cathelicidin in patients with COVID-19 may give additional evidence that immune response is impaired in SARS-CoV-2 infection.

## CONFLICTS OF INTEREST

The authors have disclosed no potential conflicts of interest.

## ACKNOWLEDGEMENTS

Thanks to all participants in the present study.

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