ORAL MANIFESTATION ON SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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ABSTRACT

Background: Periodontitis worldwide reported increasing 57.3% between 20 years also reported 6th most prevalence disease around the world. Immune response abnormalities, hyperactivity of production of autoantibodies deposited in human tissue and organ could affect oral cavity condition.

Objectives: To find oral manifestation on SLE patients and correlate with SLE severity.

Methods: Subjects were 61 patients with SLE (age 17-51 years; diagnosed using SLICC) collected from Dr. Saiful Anwar General Hospital, Malang Indonesia. Oral Manifestation is measured by clinical examination and SLE severity measured using SLEDAI.

Result: A total 61 SLE subjects were included in this study. We found that 54 patients (88.53%) subjects with SLE had periodontitis, 7 subject had no periodontitis, 11 mild periodontitis, 43 severe periodontitis. There is correlation between oral condition and SLE severity. Periodontitis and SLEDAI score showed significant (p<0.0001) and strong positive correlation (r=0.948)

Discussion : Our study found high rates of gingivitis, periodontitis, bop, low plaque index, and low calculus index. SLE is chronic autoimmune disease develop autoantibodies and immune complexes, because of immune respon abnormalities. It could be forming autoantibodies cause DNA damage, lipid peroxidation, protein. This condition induce collagen breakdown, RANKL, osteoclast stimulation until alveolar bone resorption resulting poor oral condition and periodontitis.

Conclusion: Our study showed that oral condition were associated with SLE disease activity

Keywords: Oral Manifestation, Periodontitis; SLEDAI; SLE
1.0 INTRODUCTION

Periodontal disease commonly associated with infection of periodontal tissue. Periodontitis is an inflammatory condition characterized by alveolar bone loss and connective tissue breakdown around teeth, forming periodontal pockets. Clinical sign of periodontitis is bleeding on probing at initial stage, presence periodontal pockets result to connective tissue breakdown and alveolar bone loss vertically or horizontally. Tooth mobility sometimes found in terminal case. Dental x-ray needed to view loss of lamina dura, periodontal space widening and alveolar bone loss (Vivian et al, 2008).

Periodontitis worldwide reported approximately around 20% adult population, with 11.2% affected by severe periodontitis and increasing 57.3% between 20 years. Periodontitis also reported 6th most prevalence disease around the world, and lead to complicated problem (Tonetti et al, 2017). Periodontitis could resulting multiple tooth loss and edentulous, affect masticatory dysfunction, reducing nutrition, lowering life quality, self esteem and impact socio-economic condition. Moreover, periodontitis likely increasing systemic disease as cardiovascular disease, autoimmune, metabolic disease also increasing mortality incidence (Nazir et al, 2017).

Main causes of periodontitis is plaque induced bacteria. Periodontitis begins with plaque formation attached to the surface of the tooth. Dental plaque is a thin layer of multi-species biofilms containing bacterial colonization, bacterial products, and food scraps. Dental plaque usually in the subgingival area, is extending to apical direction. Bacteria could ruin periodontal tissue resulting inflammation of periodontal tissues and periodontal breakdown (Vernino et al, 2007). Nowdays, instead of infection, host immune response may also plays multiple roles on periodontal damaged, associated with autoimmune disease (Rutter-Locher et al, 2017).

Recently, studies reported an association between periodontitis with Systemic Lupus Erythematosus (SLE) disease, SLE as periodontitis risk factor also two way direction. SLE patients had higer periodontitis incidence reported 60-93% worldwide (Rhodus et al, 1990) and 70% on Japan (Kobayashi et al, 2003), higher than healthy patients with no systemic disease. Association between SLE and periodontitis rarely explained. The connection of SLE with periodontitis is assuming that in SLE patients had abnormalities immune response, had direct impact on periodontal tissue and resulting periodontitis.

Imune response abnormalities in SLE, hyperactivity of production of autoantibodies deposited in human tissue and organ could affect oral cavity condition. Higher SLE activity disease also resulting poor oral cavity condition, such as oral ulcer, oral hygiene, periodontal disease thus tooth loss (Caldecaro et al, 2017; Meyer et al, 2000). Furthermore, this article explaining oral cavity condition on SLE patients, especially periodontal tissue in Indonesia. Also finding association between periodontitis severity and SLE disease activity.
2.0 MATERIAL AND METHOD

The design of this study was an descriptive study with cross sectional approach. The research received an ethical approval from the UB Medical Ethics Committee from Faculty of Medical, Brawijaya University Malang, East Java. All patients included in this study were required to sign an informed consent.

The study was conducted on 61 SLE patients. Study held from September 2017 until June 2018 on Rheumatology Department Saiful Anwar Hospital Malang, Indonesia. In all SLE patients clinical examination of the oral cavity to assess the presence of periodontal abnormalities using periodontal index (PI), gingival index (GI), plaque index, and calculus index. Clinical examination and laboratory tests are conducted to assess the activity of the disease. Severity of SLE measured using SLE Disease Activity Index (SLEDAI). Inclusion criteria was female subjects with a confirmed diagnoses of SLE, willing to become the subject of study, could read and write and had full consciousness. Exclusion criteria were smoking, pregnancy, diabetes, and another systemic disease.

The collected data will be analyzed using of SPSS version 20 program. The difference LES patients with and without periodontitis was analyzed by Kolmogorov Smirnoff for normality test, Spearman/Pearson for correlation test and Mann Whitney for comparation test (Mukaka, 2012).

3.0 RESULTS

3.1 Oral Manifestation Findings of SLE Patients

A total 61 SLE subjects were included in this study. We found that 54 patients (88.53%) subjects with SLE had periodontitis. 7 subject had no periodontitis, 11 mild periodontitis, 43 severe periodontitis. Subject result was high average periodontal index 2.64 ± 1.20, moderate gingival index 1.95 ± 1.20, low plaque index 0.34 ± 0.44, low calculus index. The mean SLEDAI score was 17.70 ± 12.70. SLE

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean (± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Periodontal Index</td>
<td>2.66 ± 1.20</td>
</tr>
<tr>
<td>2. Gingival Index</td>
<td>1.95 ± 1.20</td>
</tr>
<tr>
<td>3. Plaque Index</td>
<td>0.34 ± 0.44</td>
</tr>
<tr>
<td>4. Calculus Index</td>
<td>0.35 ± 0.16</td>
</tr>
<tr>
<td>5. SLEDAI score</td>
<td>17.70 ± 12.70</td>
</tr>
</tbody>
</table>

3.2 Comparison Oral Manifestation based on SLE severity.

Oral manifestation examination was performed in SLE subjects, divided into low SLE severity and high SLE severity. Low SLE severity based on SLEDAI score 5 and below, high SLE severity SLEDAI score more than 5. Result were shown in table 2. There was a significant difference in two group on periodontitis and gingivitis findings.
Table 2. Comparisons of oral condition in SLE patients between low and high SLE severity

<table>
<thead>
<tr>
<th>Variables</th>
<th>Low SLE severity</th>
<th>High SLE severity</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Periodontal Index</td>
<td>1.47 ± 0.92</td>
<td>2.98 ± 1.07</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Gingival index</td>
<td>1.69 ± 0.85</td>
<td>1.79 ± 0.94</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Plaque Index</td>
<td>0.53 ± 0.80</td>
<td>0.53 ± 0.74</td>
<td>0.992</td>
</tr>
<tr>
<td>Calculus Index</td>
<td>0.35±0.16</td>
<td>0.64±0.56</td>
<td>0.065</td>
</tr>
</tbody>
</table>

3.3 Correlation between Periodontitis and SLE Disease Activity

The correlation between periodontitis (based on Periodontal Index) with SLE manifestation severity were assessed using Pearson correlation test and the results were shown in figure1. It can be seen that there was a significant and strong correlation between SLE Disease Activity with periodontitis.

![Figure 1. Correlation between oral condition and SLE severity.](image)

A) Periodontal index and SLEDAI score showed significant (p<0.0001) and strong positive correlation (r=0.824); B) Gingivitis and SLEDAI score showed significant (p<0.0001) and positive correlation (r=0.647);

4.0 DISCUSSION

Oral health condition is one important concern in human body. Oral diseases could affect other organ of the body or increase the severity systemic diseases. Focal infection states that
infection in the oral cavity is responsible for the initiation or prognosis of various inflammatory diseases in two ways. As we know, systemic disease could be risk factor to oral health. Recently, autoimmune disease, Systemic Lupus Erythematosus (SLE) had an association with oral condition such as xerostomia, oral ulcer, gingivitis and periodontitis.

SLE is chronic autoimmune disease develop autoantibodies and immune complexes, because of immune respon abnormalities. SLE patients associated with various clinical manifestations and tissue damage (Hajishenggalis, 2014). Tissue damage lead to organ failure, like nefritis, lung failure and periodontal. Recently SLE association with periodontitis started to be considered as oral health problem (Caldecaro et al, 2017).

Periodontitis is an inflammatory on periodontal tissue stimulates lymphosite abnormalities changing inflammatory cells into the extracellular. Resulting DNA damage, lipid peroxidation, protein, other important enzyme oxidation and stimulation in the release of proinflammatory cytokines by monocytes and macrophages. Inflammatory chronic induce collagen breakdown, RANKL, osteoclast stimulation until alveolar bone resorption (Pandruvada, 2016).

Result shows that there is significant different between mild SLE and severe SLE on oral cavity condition, patients with severe SLE has higher periodontitis, gingivitis and bop incidence. Periodontitis has strong positive correlation with SLE Disease Activity. It matches with previous studies in UK, patients with SLE more likely to have periodontitis 7.25 higher. On other hand, study found non significant findings that periodontitis is more prevalent in SLE patients. The lack of statistical significance may be due to small sample size, use of immunosuppressants, age, patient condition and systemic disease (Rutter-Locher et al, 2017).

Strong correlation between periodontitis, with SLE, prove that SLE is a periodontitis risk factor, playing role on periodontitis pathway. Moreover, SLE disease activity measured by SLEDAI could be predictor of periodontitis severity, strengthened by previous study. Periodontitis severity has association with SLE severity (Caldecaro et al, 2017).

There is SLE no correlation within plaque index and calculus index, suggest that it is not plaque induced periodontitis, most common form of periodontitis. Previous study prove no correlation within autoimmune disease, especially SLE and plaque. Plaque is accumulated food scrap and bacterial developing into calculus, main causes of periodontitis. No correlation showing it was not local condition but dysregulation immune result (Rhodus et al, 1990).

SLE patients was having loss of immune system tolerance. This condition causes immune cells that are hyperactive and produce autoantibodies. T cell abnormalities, B cells, plasma cells, dendritic cells, and regulatory T cells (Treg) occur. In SLE patients the occurrence of hyperactivity of dendritic cells and hypoactivity of T-cell reg. Hypoactivity of Treg cells causes directly killing itself and vulnerable to infection (Pandruvada, 2016).

As a result of hyperactivity of dendritic cells, it stimulates T cell hyperactivity resulting in a change in the balance of Th1, Th2 and Th17 cytokines. This imbalance changes from the cytokines secreted by Th1, Th2 and Th 17. When the response to an antigen mature, T cells or B cells that develop can form cross reactions reactivity to other autoantigens. T cells include
CD4 + T cells and CD8 + T cells experience abnormalities, cells will excrete cytokines. Th1 will stimulate an increase in IFNγ and IL-2 levels, while Th2 will reduce IL-10 levels. Whereas Th2 and Th17 also stimulate B lymphocyte cells to produce autoantibodies (Nazir et al, 2017; Pandruvada, 2016).

Specific autoantibodies in LES and the first ones appear are anti dsDNA. Anti-dsDNA autoantibodies bind to nucleosomes, laminin, type IV collagen, and heparan sulfate forms immune complexes and is deposited in various tissues, one of which is periodontal (Rutter-Locher, 2017). These autoantibodies will be directly deposited in tissues causing chronic inflammation, inflammation in periodontal tissues increases RANKL and stimulates osteoclasts. Deposition in other organs can increase LES manifestations in other organs and SLE Disease Activity (Pandruvada, 2016).

Furthermore, observing saliva and whole blood are needed in order to ascertain any causation factors, common etiology pathways between periodontitis and SLE. It lead to founding marker between periodontitis and SLE.

5.0 CONCLUSION AND SUGGESTION

There were association between oral manifestation especially periodontitis with SLE. Further studies are needed to finding pathway between SLE and periodontitis. Furthermore, comparison between SLE patients and healthy control is needed. Hopefully dentist and healthcare monitor of oral cavity SLE patients.

DECLARATION

The authors declare that we have no competing and conflict of interests.

AUTHORS CONTRIBUTION

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Author 2: Nurdiyana  
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REFERENCES


