Periodontal Health in Sickle Cell Disease - A Case Control Study

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Authors’ contributions

This work was carried out in collaboration among all authors. Author KSS designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. And managed the analyses of the study as well as managed the literature searches. Author read and approved the final manuscript.

ABSTRACT

Introduction: A hereditary autosomal recessive condition goes by the name of sickle cell disease. Hemoglobin S polymerization in red blood cells under hypoxic circumstances results in vascular blockage, which is the pathophysiology of sickle cell disease. For the sake of maintaining group homogeneity, participants in the healthy group were either related to or friends of those with sickle cell disease, whereas those in the sickle cell trait group were related to those with sickle cell illness.
Materials and Methods: A total of 150 participants were recruited for this research, 43 percent of them were female and 57 percent male. Patients in the control group were on average 30 years old, whereas those in the SCT group were 33 years old, and the average age of patients with SCD was 26. Those with sickle cell trait (SCT) and those with sickle cell disease (SCD) were divided into three categories. Patients were screened and diagnosed with chronic periodontitis using clinical criteria developed at the 1999 International World Workshop for Classification of Periodontal Diseases and Conditions.

Results: The SCD, ST, and healthy groups did not vary significantly in terms of clinical indicators such as gastrointestinal (GI), peritoneal (PPD), and caloric (CAL). SCT group PI-1.550.45, GI 1.540.43, PPD-2.170.72 was greater than the mean and standard deviation of the SCD and control groups, but the chi square test revealed it to be non-significantly different.

Conclusion: It is possible that patients with the Indian haplotype of SCD, albeit having milder symptoms of the illness, contributed to our conclusion that SCD, SCT patients had no significantly greater periodontal breakdown than healthy people. Although SCD's fundamental pathophysiology raises issues about our knowledge of periodontitis, additional study is needed.

Keywords: Sickle cell disease; periodontitis.

1. INTRODUCTION

Sickle cell disease (SCD) refers to a range of disorders in which the presence of HBS causes a pathological process (Sickle Cell Hemoglobin). It is an autosomal recessive condition that is passed down from generation to generation [1].

Sickle cell disease has six different genotypes, with the most common one being –

- "Homozygous sickle cell disease –SS"
- Sickled hemoglobin C disease-SC"

At position 6, the codon that dictates the amino acid chain has been changed from GAG to GTG in HbS. It is also possible that it is caused by a combination of HbS and one of the beta thalassemia 1 genes. Erythrocytes and sickle cell trait have a similar link; however, the latter requires a larger degree of hypoxia, since low oxygen tension causes sickle-shaped red blood cells [2-7]. There are two forms of the disease: one is caused by a homozygous mutation, and the other is caused by a heterozygous mutation.

Dr. James Henrick of Chicago discovered the first instance of sickle cell disease in a 1904–2007 dental student from Africa at the Chicago College of Dental Surgery in November of that year [8].

“In the Nilgiri Hills of South India, Catbush discovered sickle haemoglobin for the first time in 1957 [9]. Later, it was recorded from the tribal people of central India, I.e. Madhya Pradesh and Chhattisgarh, and its neighbouring territories in the states of Rajasthan, Gujarat, Maharashtra, Andhra Pradesh, and Orissa.” [10,11]. Sickle cell trait is most common in tribal populations, such as the Abujhmaria tribe of Bastar area (24%) and the Kondhs of Orissa (20%) [10,11].

SCA in Indians connected to the Arab-Indian haplotype is commonly said to have a moderate clinical presentation that passes unrecognised, perhaps for the rest of one's life [12-19]. High foetal haemoglobin levels have been linked to this, as well as thalassaemia in many of these individuals. Sickle cell disease is more common in India, although its severity may vary greatly from patient to patient because of the country’s large population of people with the condition [20].

Periodontitis is commonly referred to as a "ecologic illness," This indicates that there is dysbiosis and an increase in the number of pathogenic organisms when environmental and behavioural variables are present together with predisposing genetic and epigenetic factors. Damage to periodontal connective tissue is caused by a host's over-response to pathogenic threats [21-26]. Unresolved inflammation is a vicious cycle that damages teeth’s supporting tissues further.

There are many tiny vascular pathways in the periodontal tissues that support the teeth. Red blood cells in Sickle cell disease are reversible when exposed to increasing oxygen levels, but repeated sickling causes the cell walls of red blood cells to become stiff, resulting in irreversible sickle cell characteristics. [ISC] [27]. There was a maximum of 32 hospitalizations in a 24-year-old girl who had 80 units of blood transfusions in the sickle cell anaemic group in
our research. As these cells move through the microvasculature, they clog and restrict oxygen capacity, resulting in circulatory problems.

“These delicate, vascularized tissue compartments of supporting structure of tooth namely the periodontal ligament, gingival components, and especially junctional epithelium may be adversely affected by this feature of sickle cell disease. [28-31]” The periodontal ligament, for example, has a close proximity to the gingival plexus, which is the vascular plexus that connects the gingival epithelium directly to the tooth surface [32]. Since mitotic activity replaces the decaying cells on the tooth surface, the junctional epithelium is regarded to be a very metabolically active zone. As a result, damage to the dentogingival unit at this level might be caused by sickle cell disease’s decreased oxygen delivery to this important component.

According to viscoelastic theory, the capacity of the periodontal ligament to resist different stresses applied to the tooth surface may also be connected to its ability to endure stenosis and arterial back pressure and ballooning of arteries. This is an important area in which the illness may play a role [33]. The aberrant adhesion of HBS-containing red cells in sickle cell disease, on the other hand, is most likely mediated by the expression of CD36 marker by microvascular endothelium, while bigger vessel endothelial cells do not produce this marker. ischemia and infarction occur as a result of the diminished flexibility and aberrant endothelium adhesion of HBS-containing red blood cells [8].

Vaso occlusion in the microvasculature and decreased oxygen carrying capacity are two disease traits that might harm the periodontal ligament and junctional epithelium, according to theory [34-40].

There are various systemic consequences associated with sickle cell anaemia, particularly in places that have a low oxygen level, including microvascular blockage, which may lead to infarctions.

Red blood cells’ lifespans are reduced to between eight and twenty-five days in people with sickle cell anaemia, resulting to compensatory bone marrow activity [27]. The erythropoietic growth is steady, although there are occasional bouts of acute necrosis that are quite painful.

Protrusion of the front section of the maxillary bone and protrusion of the upper incisors may occur as a result of erythropoietic growth. Facial deformities and malocclusion may grow more pronounced as we get older, with the jaw protruding and the teeth in the lower arch angling anteriorly [41]. There may be a link between the disease’s above-mentioned symptoms and increased plaque buildup and other contributing variables such damage from occlusion, which may play a role in the onset and development of localised periodontitis [42-44].

The lamina dura is Even while compact bone insufficiency makes the normal more obvious, tooth pulp abnormalities have been recorded and periodontal infection may lead to severe crises [45,46].

“A painful crisis, mental nerve neuropathy, and molar peri apical inflammation may all lead to mandibular infarction.” At times of extreme pain, the nervous system may be affected by numbness or paralysis [20]. There have been reports of osteomyelitis of the mandible, which varies from other bone infections in terms of bacteriology [47]. Ischemia and/or avascularity may worsen osteonecrosis of the jaw bones that is already present. Tempromandibular joint osteonecrosis has been documented [48]. When a person has sickle cell anaemia, their bones lose density because to insufficient blood flow (avascularity). Periapical radiographs of patients with sickle cell anaemia should be extensively examined for signs of trabeculation [49]. It becomes larger in childhood owing to the presence of sickle red blood cells that clog the reticular gaps, and it shrinks to a little wrinkled remnant by adulthood due to an extreme buildup of blood clots and haemorrhage in the terminal arterioles [50].

Deficiencies in the immune system include those related to complement, immunoglobulin, leucocyte, and cell mediated immunity, as well as the early loss of splenic function that puts circulating antigen into intimate contact with the reticuloendothelial system [51-55]. Phagocytosis of encapsulated bacteria is hampered by opsonization defects. Additionally, the alternate route for complement fixation seems to be aberrant [56].

“Since gingivitis and chronic periodontitis have been identified as key activators of the alternative pathway,” periodontal tissues should be impacted by anomalies in this system. Antibodies specific to the pathogens that cause chronic periodontitis have been generated,
however activation of the complement system continues to occur through an alternate route [41].

Following up on what we discussed before, the occlusion of microvasculature and the presence of permanently sickled cells may have a negative impact on the gingival and periodontal compartments. There are several reasons of periodontitis, and people with sickle cell disease may be more prone to the condition, which is caused by a variety of factors. Because of the biological plausibility of the findings, this study is being conducted. To find out whether sickle cell disease patients had a higher rate of periodontitis than sickle cell trait patients and healthy controls, our study set out to examine this question.

2. MATERIALS AND METHODS

The study was scheduled to take place over the course of three months. Research was conducted on outpatients from the Sickle Cell Disease Institute at the Government Medical College in Raipur. Sickle cell disease patients were linked to both healthy and sickle cell trait persons in order to create a uniform sample size for the research. Since the Sickle Cell Institute Raipur serves as the state's tertiary referral institution, we saw sickle cell patients from all across Chhattisgarh. The haemoglobin variation in patients was determined using high-performance liquid chromatography. Each patient was given a thorough explanation of the study, and a written consent was signed. Sickle cell disease patients had extensive medical histories in addition to the number of hospitalizations and blood transfusions. 43 percent of the 150 participants were female, while the other 57 percent were men. There was a significant age difference between individuals in the SCT and SCD groups, which averaged 33 and 26 years of age, respectively.

The patients were divided into three groups:

1. Group 1- Healthy patients
2. Group 2-Sickle cell trait group=SCT
3. Group 3-Sickle cell disease group=SCD

“For the purpose of diagnosing patients with chronic periodontitis, doctors employed criteria established at the 1999 International World Workshop on Classification of Periodontal Diseases and Conditions.”

Clinical Indices

1. Missing teeth were documented in the patient’s medical history.
2. Both Silness J and Loe H [57] and Loe H [58] were assessed for their plaque and gingival indexes.
3. Each tooth's mesial and distal line angles, as well as its mid-facial and lingual facets, were tested for probing depth and probing attachment levels, except for the third molars.
4. Cemento enamel Junction (CEJ) No. [59] was used as a reference point for probing attachment levels.
5. When teeth were coated with calculus, they were unable to detect attachment levels or depths.
6. The UNC15 probe was gently moved around the tooth to quantify bleeding using a modified sulcular bleeding index [60].
7. The same examiner (JC) assessed three different groups of patients in the same dental chair under identical lighting conditions.
8. Throughout the investigation, UNC15 periodontal probes were utilised that had been thoroughly inspected for consistency in marks.

2.1 Observation

The GI, PI, PPD, CAL, and Mubi mean and standard deviation for each of the three groups...
are shown in the table. The chi square test was used to see whether there was a correlation between the mean GI of the three groups. Mean and SD values of GI, PI, and PPD in the sickle cell trait group are greater compared to other groups, although the p value of the chi square test is not statistically significant. There was a statistically significant difference in sulcular bleeding between the groups of healthy individuals and those with sickle cell trait (P=0.018) in contrast to those with sickle cell anemia (P=0.001).

Chart 1 A comparison of the mean values of GI, PI, PPD, and CAL across the healthy, SCD, and SCT groups reveals significant differences. Mean values of all parameters are greater in SCT than in the other two groups. Sickle cell trait patients had greater mean values than healthy subjects even when the p value is not significant.

Table 1. In this case, the Chi Square Test is performed and the results are shown

<table>
<thead>
<tr>
<th>INDICES</th>
<th>GROUPS</th>
<th>MEAN ± SD</th>
<th>CHI SQUARE VALUE</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>GI</td>
<td>Healthy</td>
<td>1.53 ± 0.43</td>
<td>84.80</td>
<td>0.28</td>
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<tr>
<td></td>
<td>Sickle Cell Trait</td>
<td>1.55 ± 0.42</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sickle Cell disease</td>
<td>1.40 ± 0.44</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PI</td>
<td>Healthy</td>
<td>1.53 ± 0.43</td>
<td>72.52</td>
<td>0.33</td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sickle Cell disease</td>
<td>1.38 ± 0.45</td>
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<td>PPD</td>
<td>Healthy</td>
<td>2.04 ± 0.68</td>
<td>100.21</td>
<td>0.26</td>
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<tr>
<td></td>
<td>Sickle Cell Trait</td>
<td>2.17 ± 0.72</td>
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<td></td>
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<td></td>
<td>Sickle Cell disease</td>
<td>1.91 ± 0.47</td>
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<td></td>
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<tr>
<td>CAL</td>
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<td>1.44±2.97</td>
<td>86.60</td>
<td>0.36</td>
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<td>Sickle Cell Trait</td>
<td>1.82±2.98</td>
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<td></td>
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<td></td>
<td>Sickle Cell disease</td>
<td>1.52±3.28</td>
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<td>MSBI</td>
<td>Healthy</td>
<td>1.68 ± 0.97</td>
<td>15.26</td>
<td>0.018</td>
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<td>Sickle Cell Trait</td>
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<td>Sickle Cell disease</td>
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<tr>
<td>HB</td>
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<td>11.24 ±2.10</td>
<td>25.68</td>
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<td>Sickle Cell Trait</td>
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<td></td>
<td>Sickle Cell disease</td>
<td>8.82 ±1.30</td>
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</table>
Chart 1. Showing comparison of mean value among the groups

Chart 2. Showing variations in HB total among groups

Chart 3. Showing Mean age of subjects among the three groups
A post hoc ANOVA test was used to examine intra-group variance in haemoglobin total levels among the three research groups. The mean difference between the healthy and SCD groups and the SCD and ST groups was statistically significant.

Variation was also examined using a post hoc Anova test in order to compare the three research groups. Between the healthy and SCD groups, there was a statistically significant difference in the mean difference.

### 3. RESULTS

SCD patients are expected to have poor oral hygiene owing to their low socioeconomic status and lack of formal education, however our research found that virtually all of the patients reported brushing their teeth at least once daily, with just 1% reporting using Datun as a method of cleaning their teeth. Both the ST and the control groups came up with similar outcomes. There were sickle-related crises reported by two percent of ST patients at some point in their lives. Hospitalizations due to sickle-related events were on average 8.1 times more frequent in the SCD group than the general population. There were an average of 9.7 units of blood transfusions per person in the SCD group. The SCD, ST, and healthy groups did not vary significantly in terms of clinical indicators such as gastrointestinal (GI), peritoneal (PPD), and caloric (CAL).

According to standard deviations, PPD- 2.170.72 was greater in the SCT group than the SCD and control group, but the chi square test revealed it to be insignificant [Table 1].

P=0.018 shows that healthy persons had substantially greater sulcular bleeding than those in the sickle cell group when comparing the mean and standard deviation for sulcular bleeding in the Msbi group to 1.680.97 and SCT to 1.380.96. There is a [Table 1].

Table 3 shows the importance of Msbi (p=0.001) and Hemoglobin levels (p=0.000) in the ANOVA test findings.

After doing a post hoc ANOVA, the data showed that Msbi was significantly greater in healthy individuals than in SCT and SCD (P=0.001 in comparison to SCT and SCD).

Hemoglobin levels healthy compared to SCT and SCD p=0.001 and SCT compared to SCD
p=0.01 were found to have similar outcomes (p=0.001). Tables 2 and 3 are included.

4. DISCUSSION

Sickle cell disease's systemic consequences have been widely explored and recorded. “There are limited articles on the periodontal aspects of sickle cell disease in the dental literature. Sickle cell disease has been linked to periodontal disease for the first time. Crawford JM 1988, Arowojolu 1999, Famili et al 2004, Guzeldemir et al 2011.”

There have been a large number of periodontal implications investigations conducted on patients from Africa or with ancestry from Africa. OHIS-S, PD, CAL, GI, PI & DMFT, OHIS-S, PD, CAL have all been included in studies conducted in India that primarily examined oral hygiene in SCD patients. “Studies by Singh J, Singh N, Kumar A, Kedia NB, Agarwal A. 2015, Rathod S, Brahmanakar R 2013, Bhat N et al. 2015 are among the studies cited above, among them.” It is likely that this study is the first of its kind in India to examine the relationship between sickle cell anaemia (SCA) and periodontitis, using a standardised probe to compare SCA patients with healthy controls in a group that is completely homogenous in terms of educational attainment, dietary habits, and socioeconomic status.

Crawford in 1987 [61] clinical and radiographic indicators of periodontal disease severity were used to compare individuals with sickle cell anemia (SS), hemoglobin SC disease (SC), or S Thalassemia to an appropriate control group. He came to the conclusion that even though this research failed to show a link between sickle cell illness and periodontal disease, it is feasible that periodontal disease provides a sufficient inflammatory stimulation in certain sickle cell disease participants to induce a crisis. Destructive periodontal disease does not seem clinically more severe in sickle cell individuals matched for age and overall oral care, according to Crawford.

Guzeldemir et al in 2011 [62] “It was shown that sickle cell disease patients and healthy people were both affected by periodontal disease, which was measured by the plaque index, gingival index, probe depth, bleeding on probe (BOP), alveolar bone level, mandibular cortex, and bone quality index (BQI). While P1, GI, and BOP in sickle cell disease patients were significantly higher than in normal individuals (P 0.0001), PD did not differ between groups.” They ascribed this to an unexplained variation in microbial response in persons with SCD. SCD and periodontal disease did not seem to be linked in this study. All three of our groups had signs of attachment loss; however, there was no statistically significant difference between those with sickle cell trait and those without it when comparing our findings with those from their study group.

Our results concur with Arowojolu 1999 [63] SCA group and healthy control group in their research on young Nigerians with sickle cell anaemia were examined for their depth of penetration. This study revealed that there was no evidence of periodontal disease or attachment loss in patients with Sickle Cell Disease who had PD values that were more than 5 millimetres on average and standard deviation (SD) of 2.680.44%. It is hard to compare their findings with those of ours since their study included African native children ranging in age from 11 to 19 years old. PPD mean and SD were 1.910.47 in the SCA group in our research. Compared to the healthy and SCA groups, the mean and standard deviation of PPD in the SCT group were 2.17 and 0.72, respectively.

Despite the findings of Famili et al. (2008), we are unable to compare our results to theirs, maybe due to the haplotype variation of hemoglobin or other variables. Jaideep et al in 2013 [64]. According to their research, beta thalassemic patients had a higher prevalence of dental caries and periodontal disease than individuals with sickle cell anemia, whereas the control group had a lower frequency.

When beta thalassemia and sickle cell anemia were examined, findings were shown to be very significant (P 0.001) only for decaying missing filled teeth. Plaque index (PI), decay-missing-filled teeth index (DMFT Index), and gingival index (GI) were the clinical indices employed in this investigation (GI). These indicators led them to draw the conclusion that periodontitis is more common.

“Although thalassemic patients were not included in our research, we included PPD, CAL, and Msbi into it and found no significant mean difference in our study groups, despite the fact that this study omitted thalassemic patients. Rathod and Brahmanakar released it in 2013 [65]. Although oral health is not a priority for sickle cell disease patients, they determined
that they should be urged to practise rigorous dental hygiene. In their research, they looked at the age group of 18 to 40, as well as the characteristics of probing depth, CAL, GI, modified PI, and DMFTS. Their research only included sickle cell anaemic individuals, thus no comparisons can be drawn. 53 percent of patients had average dental hygiene, 21 percent had poor oral hygiene, and just 2.5 percent had excellent oral hygiene. Probing depth, GI, modified PI, and CAL have also been documented. Analysis of findings of this research shows that the results of these parameters are much higher than those in our sickle cell group. 44.5 percent of patients had CAL 4-6mm and larger than 6mm, however in our research only 10 percent of SCA patients had CAL 4-6mm and 8 percent of SCT patients had CAL higher than 6mm, and in 18 percent of our SCT patients, CAL greater than 6mm was detected.”

Our findings contrast those of Bhat et al. 2015 [66], who reported that individuals with Sickle cell illness had poor oral hygiene due to their concern with repeated medical visits in the Dhamtari area of Chhattisgarh. For clinical purposes, they adopted a reduced version of the oral hygiene index. This is because our patients came from all the main districts of Chhattisgarh in our research. As a consequence, our findings on oral hygiene are not consistent with theirs, even though our mean and standard difference for PI and GI was larger.

Because sickle cell anaemic patients have a short life expectancy, recruiting a large number of participants is a major problem for our research. The Institute of Sickle Cell Disease supplied us with a respectable number of patients, but obtaining participants in the older age range — those over 45 — was not feasible for whatever reason.

Sickle cell illness has a negative impact on the life of a person suffering from a painful sickle crises, which may be precipitated by dental diseases such as periapical infection, periodontitis, or interventional therapeutic procedures such as extraction. The life expectancy of sickle cell sufferers is growing as a result of government efforts to raise awareness. As a result, the number of patients that dentists see on a daily basis is steadily growing.

It is possible to avoid intraoperative or postoperative problems by getting a thorough history from patients, learning about ethnic / caste groups that are more susceptible to the illness, and identifying clinical symptoms that are common to each group. There is a pressing need for a consistent strategy for treating sickle cell patients in light of rising urbanization and development since the prior situation of sickle cell patients living in a certain belt is no longer relevant. Understanding the oral and systemic aspects of sickle cell illness is essential. “An in-depth histological investigation of the gingival vasculature with an emphasis on the vascularity of the junctional epithelium as well as if the presence of irreversibly sickled cells leads to compromised periodontal apparatus functioning in response to various occlusal forces in people with sickle cell disease requires further investigation.”

The alternative route of complement fixation is critical in both gingivitis and periodontitis, despite the fact that other anaemic disorders also have a weakened immune system. The deficiencies in the alternative pathway of complement fixation activation are particularly essential. New paradigms in the study of periodontitis may emerge from research on sickle cell disease patients focusing on the junctional epithelium, periodontal ligament and immunological pathways.

5. CONCLUSION

People with SCD have an autosomal recessive genetic condition that is passed down from generation to generation. SCD is caused by hemoglobin S in red blood cells polymerizing under hypoxic circumstances, which blocks blood arteries. There were 150 participants in this research, with 43% of them being female and 57% being male. Patients in the control group were 30 years old, those in the SCT group were 33 years old, and those in the SCD group were 26 years old, on average. Sickle cell trait (SCT), sickle cell disease (SCD), and healthy individuals were categorized into three categories. The 1999 International World Workshop for Classification of Periodontal Diseases and Conditions developed clinical criteria for the screening and diagnosis of individuals with chronic periodontitis. SCT group, ST group, and healthy group did not vary significantly in terms of clinical indices such as GI, PPD, and CAL when compared to each other. SCT group PI-1.550.45, GI 1.540.43, PPD-
REFERENCES


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