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Author
Shankarapillai, Rajesh, Nair, Manju Ananthakrishnan, George, Roy, Walsh, Laurence J.

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Periodontal and Gingival Parameters in Young Adults with Acute Myeloid Leukaemia in Kerala, South India

Rajesh Shankarapillai\textsuperscript{a}/Manju Ananthakrishnan Nair\textsuperscript{a}/Roy George\textsuperscript{b}/Laurence J. Walsh\textsuperscript{c}

**Purpose:** Patients presenting with leukaemic blast crisis with acute myeloid leukaemia (AML) may have gingival enlargements that interfere with oral hygiene. Few large cohort studies of gingival lesions have been carried out on AML patients. The aim of the present study was to assess gingival and periodontal pathology at the time of presentation, prior to chemotherapy, in a cohort of adult patients presenting at a cancer hospital in Kerala, a region located in southern India.

**Materials and Methods:** A total of 73 young adult patients (mean age 20.6 ± 2.3) who were diagnosed with AML were examined. These patients did not suffer from any other systemic disorder. The oral hygiene status, gingival overgrowth (GO) and periodontal status were assessed using traditional clinical indices.

**Results:** Around three-quarters of the patients had either fair or poor oral hygiene. A statistically significant association between dental plaque levels and both GO and periodontal index \((P < 0.001)\) was observed.

**Conclusions:** Poor oral hygiene is a risk factor for leukaemic GO and for destructive periodontal disease. Both conditions add to the microbial burden these patients are exposed to. In patients showing high levels of oral hygiene, the GO tends to be mild and does not seem to be problematic, especially with respect to mechanical tooth cleaning.

**Key words:** acute leukaemia, dental calculus, dental plaque, gingival overgrowth, oral hygiene

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Oncology patients can present significant challenges with regard to patient management from a dental practitioner’s perspective. It is essential that patients suffering from any form of cancer be carefully screened for dental diseases and conditions that may impair the patient’s oral hygiene or that could lead to acute problems, such as bleeding and infection, during the period of receiving care as an inpatient or outpatient (Walsh, 2010).

Leukaemias occur in several forms, with typical clinical presentations being acute lymphocytic leukaemia in children, acute myeloid leukaemia (AML) in teenagers and young adults, chronic myeloid leukaemia in adults and chronic lymphocytic leukaemia in patients aged above 40 years and in the elderly.

AML, also known as myelogenous or myeloblastic leukaemia, is a common malignancy that is found to occur among teenagers and young adults and accounts for approximately 80% of all cases of acute leukaemia reported in adults (Ghosh et al, 2003;...
Pui, 2006). In this condition, cells of monocyte lineage overgrow in the bone marrow spaces, triggering secondary problems such as neutropenia and thrombocytopenia. The malignant cells also accumulate at the sites of tissue injury where they can aggravate the existing inflammatory pathology (Walsh, 1997, 2010).

The incidence rates for AML are known to vary across the globe, with the lowest rates being reported in India and Kuwait (Neglia and Robison, 1988; Hoffman, 2005). In India, as many as 0.8 million new cases of cancer are being diagnosed every year, of which 9.5% (76,000) are attributed to haemopoietic malignancies (Indian Council of Medical Research, 2001). In the southern Indian state of Kerala, AML accounts for 19.6% of all cases of leukaemia (Varghese et al, 1984).

Patients presenting with AML are immunologically and haematologically compromised at the time of diagnosis, with secondary neutropenia or pancytopenia due to marrow infiltration by leukaemic blasts. More than one-third of patients have reported significant or life-threatening infections at presentation, most of which are bacterial in origin (Weatherall et al, 1996). The oral cavity is a major source of sepsis in these patients, because inflamed gingival tissues serve as a major portal of entry for bacteria and bacterial products such as endotoxins that elevate the serum levels of inflammatory cytokines and pyrogenic mediators such as interleukins 1 and 6 (Beck and Offenbacher, 2005; Offenbacher et al, 2007).

The management of oral and general health of AML patients is guided by pre-existing gingival and periodontal pathology. Such AML patients may show gingival infiltration by leukaemic blasts, which results in an overgrowth with a soft boggy consistency, spontaneous gingival bleeding and gingival erythema (Gallipoli and Leach, 2007). Leukaemic gingival enlargements occur in AML because gingival tissue supports continuous trafficking of myeloid cells and contains specialised post-capillary venules for egress of these cells from the circulation into the tissues at the sites of gingivitis or periodontitis (Wynne et al, 1988).

Isolated case reports of gingival overgrowth (GO) in AML patients suggest a causal association with a lack of local oral hygiene measures (Barrett, 1984, 1986; Genc et al, 1998) and with AML subtypes M4 and M5 (Felix and Lukens, 1986; Hou et al, 1997; McKenna, 2000). These problems aggravate the difficulty in helping such patients maintain an adequate standard of mouth care during chemotherapy, and they also increase the likelihood of both spontaneous bleeding and the burden of infection.

The present study was carried out to examine the associations between gingival and periodontal inflammation and oral hygiene status in a cohort of young adults with AML. While there are several single-case reports on gingival pathology in AML patients in the literature, there are no systematic studies on the patterns of gingival and periodontal conditions using large numbers of young adult patients.

**MATERIALS AND METHODS**

**Subjects**

The authors carried out the present study at the Regional Cancer Centre, Thiruvananthapuram, Kerala, India. The study was approved by the local medical ethics committee and was conducted in accordance with the Helsinki Declaration. Young adult patients who were presented to the Medical Oncology Outpatient Clinic of the Cancer Centre with AML were randomly selected and were invited to participate in the present study. The study cohort was recruited over a 14-month period. From among a total cohort of 110 selected patients, 35 patients were excluded, as the cohort consisted of patients who were smokers, were pregnant, suffered from systemic disorders other than AML at the time of evaluation or were consuming recreational substances or medications (other than analgesics). Two more patients dropped out after providing informed consent, prior to having their dental examination. The final study cohort was thus comprised of 73 young adult patients, each of whom gave written informed consent for a comprehensive dental examination that was immediately conducted prior to their commencing anti-neoplastic chemotherapy. The final cohort was comprised of 40 males and 33 females, with a mean age of 20.6 years (± 2.3 SD) and an age range of 18 to 27 years.

**Procedure**

All of the dental clinical assessments were performed by a single examiner using well-established clinical indices. Scores for dental plaque and calculus were allocated using the Oral Hygiene Index...
(OHI) (Greene and Vermillion, 1964). This score has a maximum range of 0 to 6. Four surfaces per tooth were recorded. Based on their mean OHI scores, the patients were then categorised into three groups as good (0 to 0.99), fair (1 to 1.99) or poor (2 to 6) according to their oral hygiene status (Oredugba and Akindayomi, 2008).

The extent of GO from leukaemic infiltration was scored using a published modification of the gingival hyperplasia index of Angelopoulos and Goaz (Pernu et al, 1992), as follows: 0 = no GO; 1 = mild overgrowth (thickening of the marginal gingiva and/or lobular granulation of the gingival pocket, together with overgrowth covering the gingival third of the crown, or less); 2 = moderate GO (covering two-thirds of the crown); and 3 = severe GO (covering two-thirds of the crown or the whole attached gingival tissues being affected).

The Russell Periodontal Index (PI) (Russell, 1956) was used for the global assessment of periodontal status and inflammatory changes in the supporting tissues of the teeth. The Russell PI was used because recordings that were made using this index were less invasive than the other periodontal indices. This was a prime consideration because the subjects were both immunologically and haematologically compromised at the time of the examination. A PI score of 0 indicates no overt inflammation in the supporting tissues or loss of function owing to destruction of supporting tissues. A PI score of 1 corresponds to mild gingivitis (overt inflammation in the free gingiva, but not circumscribing the tooth), whereas a PI score of 2 indicates gingivitis circumscribing a tooth. A PI score of 4 can be assigned only if dental radiographs are available. A PI score of 6 indicates gingivitis with a pocket formation. A PI score of 8 indicates advanced destruction of supporting tissues with loss of masticatory function, although this was not observed in any of the patients in the present study. There are no scores of 3, 5 or 7 in the Russell PI.

Scoring of the periodontal status involved careful visual assessment and periodontal probing, the latter being carried out at four sites per tooth with a sterile blunt-ended periodontal probe with William’s markings. The purpose of the probing was to identify whether the site met the criterion for a PI score of 6 (a probing depth of 4 mm or greater). Probing was performed without causing any discomfort to the patients. Attachment levels were not measured to reduce the possibility of severe bleeding or discomfort, and no dental radiographs were taken.

Analysis

Once the patients had been grouped as described above into three categories based on their oral hygiene status, the data for GO and the Russell PI were then analysed according to oral hygiene status. As the indices employ discontinuous scales, differences between groups were analysed using a non-parametric analysis of variance (Kruskal–Wallis test) with Dunn’s post hoc multiple comparison tests. Associations among oral hygiene, GO and periodontal destruction were assessed by linear regression using the least squares method.

To determine whether oral hygiene scores of AML subjects were comparable to those in the Kerala community who were not affected by AML, a separate group of 100 patients of similar age were also examined. These age-matched community-based healthy controls in Kerala were in the age range of 18 to 22 years and were comprised of equal numbers of males and females. The oral hygiene scores were determined using the same methods as for the AML cohort, but periodontal probing was not performed. The details of the control group are not shown.

RESULTS

Of the 73 young adult patients, a relatively even distribution into the three oral hygiene categories good 26.0%, fair 38.4% and poor 35.6% was observed. This corresponded to group means of 0.37, 1.57 and 2.65 for oral hygiene scores in the three respective categories (Table 1). When the average oral hygiene status of AML patients and healthy controls was compared, the mean oral hygiene score for all 73 AML patients (1.64 ± 0.37 SD) was not significantly different from that of the healthy cohort of 100 age-matched community-based healthy controls (1.59 ± 1.01 SD).

Patients with poor oral hygiene showed significantly more GO than those with fair (P < 0.05) or good oral hygiene (P < 0.001) (Fig 1A). The Russell PI scores of AML patients in the poor oral hygiene group were also significantly higher than those with fair (P < 0.01) or good oral hygiene (P < 0.001) (Fig 1B).

A linear correlation between OHI and GO scores (R = 0.62), between the Russell PI and GO scores (R = 0.75), and between OHI and PI (R = 0.74) (Fig 2A to C) was observed. In all three cases, the association between the X and Y variables
was statistically significant ($P < 0.001$ for each). A formal post hoc power analysis of the final AML cohort of 73 patients showed that for a threshold of $P < 0.05$, the observed R-squared values for all three effects (OHI versus GO, PI versus GO and OHI versus PI) gave a statistical power of 0.999.

**DISCUSSION**

To the authors’ knowledge, this is the first study of AML carried out in a substantial cohort of young adult patients to examine the oral hygiene status and inflammatory changes in the gingival and periodontal tissues as well as leukaemic gingival enlargement. While case reports have suggested that poor oral hygiene may be associated with more severe leukaemic infiltration, until the present study was undertaken this aspect had not been examined in a patient cohort of substantial size. The authors’ results indicate that poor oral hygiene and high levels of dental plaque and calculus are strongly associated with both leukaemic GO and loss of periodontal support for the teeth, reinforcing the concept that both are inherently driven by inflammation. Dental plaque is known to be the primary aetiological factor in both gingivitis and periodontal destruction, inflammatory conditions in which the traffic of leukocytes into tissues is greatly enhanced.

A range of factors that have been known to cause gingival enlargement include medications (calcium channel blockers, cyclosporine and anticonvulsants), genetic factors (such as those in hereditary gingival fibromatosis) and chronic inflammation,

**Table 1. Clinical parameters**

<table>
<thead>
<tr>
<th></th>
<th>Good oral hygiene (N = 19)</th>
<th>Fair oral hygiene (N = 28)</th>
<th>Poor oral hygiene (N = 26)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OHI</td>
<td>GO</td>
<td>PI</td>
</tr>
<tr>
<td>Mean</td>
<td>0.37</td>
<td>0.23***</td>
<td>0.36***</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>0.3</td>
<td>0.21</td>
<td>0.34</td>
</tr>
<tr>
<td>Minimum</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Maximum</td>
<td>0.79</td>
<td>0.57</td>
<td>0.86</td>
</tr>
<tr>
<td>Median</td>
<td>0.43</td>
<td>0.29</td>
<td>0.29</td>
</tr>
</tbody>
</table>

Data show descriptive statistics for the three patient subgroups. OHI = Oral Hygiene Index (maximum range 0 to 6); GO = gingival overgrowth (maximum range 0 to 3), and Russell Periodontal Index (PI, maximum range 0 to 8). Significant differences for the poor oral hygiene group are indicated as follows: *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$. Results for the oral hygiene status of the healthy controls are not shown.
in addition to leukaemic infiltration such as that observed among patients of the present study. These have different consistencies and rates of development, which allow them to be differentiated. A rapidly developing, soft and spontaneously bleeding gingival enlargement is highly suggestive of AML, and patients with this clinical presentation should be referred for a complete differential blood count to explore this possibility. In its early phases however, leukaemic infiltration may not be easily differentiated from oedema that occurs in healthy subjects suffering from dental plaque-induced gingivitis (Wu et al, 2002).

The patients in the present study were drawn from the region of Kerala, a southern Indian state that has a high socioeconomic status and enjoys one of the highest literacy rates in India (91%) (Kutty, 2000). This explains why some 25% of the AML patients and the community-based healthy controls had high standards of oral hygiene and no gingival inflammation. The combination of excellent oral hygiene and no gingival inflammation in the AML patients was strongly associated with less severe leukaemic infiltration.

Reinforcing high standards of oral health care in AML patients provides direct benefits because low levels of dental plaque reduce the severity of inflammation in the tissues, thus reducing the cleaning problems that are caused by enlarged gingival tissues. Improved oral hygiene can also reduce the levels of Gram-negative anaerobic dental plaque bacteria that numerically dominate in mature dental plaque. These bacteria can not only trigger local inflammatory processes, but also enter the bloodstream through periodontal pockets and cause systemic effects such as fever. The burden of infection from dental plaque bacteria is a contributing factor to persisting low-grade fever, malaise and fatigue experienced by patients with leukaemia (Walsh, 2010).

A further point of clinical relevance is that spontaneous and severe gingival bleeding is more likely from inflamed gingival tissues, particularly in leukaemic patients who have secondary thrombocytopenia owing to the infiltration of bone marrow. Bleeding of this type discourages patients from performing effective oral hygiene procedures. The results of the present study reinforce the importance of oral hygiene early in the pathway of diagnosis and management. It is already known that high standards of oral hygiene help reduce some of the complications experienced by the AML patients when they undergo chemotherapy (Carl and Schaff, 1974; Jones, 1975; Dreizen et al, 1983; Simonson, 1988; Wahlin, 1989; Krolls and Caskey, 1990; Peterson et al, 1990; Pompei et al, 1993; Orbak and Orbak, 1997).

Fig 2  Linear correlation analyses between the three clinical parameters recorded in the present study. Individual data points are shown for each patient (N = 73), together with the line of best fit. The linear correlation coefficients for the regression plots in panels A to C are 0.62, 0.75, and 0.74, respectively.
CONCLUSIONS
The present study shows that AML patients with poor oral hygiene have a greater risk for leukaemic GO, gingivitis and destructive periodontal disease.

CONFlict OF INTEREST
There was no conflict of interest.

ACKNOWLEDGEMENTS
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REFERENCES