AFRICAN JOURNAL OF MEDICINE and medical sciences

VOLUME 32 NUMBER 4 DECEMBER 2003

EDITOR
B. O. OSOTIMEHIN

ASSISTANT EDITOR
A. O. UWAIFO

ISSN 1116—4077

Afr J Med med Sci (2003) 32, 329-334

Juvenile periodontitis – a review of literature

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Summary
Juvenile Periodontitis (JP), a condition that was previously regarded as a rare disease has of recent come into the fore as a model for the study of inflammatory periodontal disease. It has also been found to be considerably more common in occurrence than previously thought. This article reviews the literature on the epidemiology, aetiology, pathogenesis, clinical features, histopathological and immunological findings, differential diagnosis, treatment and prognosis of JP. The objective of this article is to give the clinician the current opinions of researchers in all aspects of the disease as compared to previous age long views. It is observed that there are contradictory reports on the epidemiology, etiology and treatment of the disease and hence the need for further studies in these areas.

Keywords: *Juvenile, periodontitis and literature*

Rèsumè
La pèriodentite juvenile est une condition qui ètait avant regarde comme un cas de maladie rare, a rècemment emergée comme un modèle pour etudier l'inflammation de la maladie pèriodontale. Il est aussi bien connu d'etre plus commun en prevalence que avant cru. Cette article revoit la littèrature sur l'èpidemiologie, l'ètiologie' les manifestations cliniques, des donnèes histopathologiques et immunologiques, le diagnosie differentielle, le traitement et prognostie de la pèriodontite juvènile. Ceci afin de proposer aux mèdecins d'options currente des recherches dans tous les aspects de cette maladie et comparer a d'autres revues littèraires. Il a ètè observè des rapports contradictories sur l'èpidemiologie, l'ètiologie et le traitemnt de la maladie et ainsi le besion de faire d'autres ètudes dans cet environement

Historical perspective

In 1920, Gottlieb [1] described a non-inflammatory periodontal condition which he called "*diffuse atrophy of the alveolar bone*". In a later work [2], he noted that the inflammatory reaction observed was a secondary development; the chief characteristics of the disease being atrophy of the alveolar bone and widening of the periodontal membrane. With further research, Gottlieb [3] attributed this condition to the inhibition of continuous cementum formation which he considered was essential for maintenance of periodontal ligament fibres and then termed it *deep cementopathia*. In 1938, Wanneumacher [4] described the incisor-molar location of the disease which he called *parodontosis marginalis progressia*. Thoma and Goldman [5] used the term *parodontosis* to describe the disease in 1940.

In 1942, Orban and Weinman [6] named the condition *periodontosis* while reporting their findings from the study of two human skulls which had been diagnosed as having diffuse atrophy. Miller [7] discussed the systemic aspects, the young age of onset (18-25 years), and the predominance of females seen with what he called *"Precocious advanced alveolar atrophy"*. He noted that the pattern of bone loss was diffuse in older patients, but localized to the first molar and incisor regions in young individuals.

The 1949 committee on Nomenclature of the American Academy of Periodontology [8] defined periodontosis as "a general term" to include a degenerative non-inflammatory destruction of the periodontium originating in one or more of the periodontal structures, characterized by migration and loosening of the teeth in the presence or absence of secondary epithelial proliferation and pocket formation or secondary gingival disease.

In 1952, Glickman [9] believed that the conditions described in these studies did not represent a different type of periodontal disease, but rather extreme variants of destructive process common to all periodontal diseases.

The world workshop on periodontics [10] in 1966 concluded that "evidence to support the conventional concept of periodontosis is unsubstantiated and that the term periodontosis is ambiguous and should be eliminated from periodontal nomenclature. The committee did recognize that a clinical entity different from adult periodontitis may occur in adolescents and young adults. However, Butler [11] in 1969 introduced the term juvenile periodontitis in this disease condition.

Baer [12] in 1971 enumerated seven features which he felt justified the classification of periodontosis as a clinical entity distinct from adult periodontitis thus:

(i) Onset of disease during the circumpubertal period,
(ii) The three to one female to male ratio,
(iii) The familial tendency for the disease,
(iv) The lack of relationship between local etiologic factors and presence of deep periodontal pockets,
(v) The distinct roentgenographic pattern of alveolar bone loss,
(vi) The rapid rate of progression and
(vii) The lack of effect of the disease on the primary dentition.

Juvenile Periodontitis is now currently considered as a well-defined inflammatory condition of the periodontium with clinical symptoms distinctly different from those seen in adult forms of periodontal disease [13,14].

Two forms of the disease have been identified [15]

a Localized juvenile periodontitis (LJP) and
b Generalized juvenile periodontitis (GJP)

LJP is characterized by bone loss around the incisor, first molars and the mesial surface of the second molar teeth, not more than fourteen teeth. A more generalized pattern of periodontal destruction involving teeth other than or in addition to incisors and first molars is recognized as GJP [15].

Review of literature

Epidemiology of JP

Prevalence of the disease has been reported to be between 0.1% and 3.7% depending on the stringency of the diagnostic criteria, the race, age of the population screened and the extent of the disease [16-19]. The prevalence of JP in Nigeria was reported to be between 0.75% to 1.56% [13,17,20].

Report on the sex predilection varies, while some reported a female predilection [11,13,20], some reported no sex predilection [21]. Hormand and Frandsen [22] reported that the

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higher rate in women decreases with increasing age indicating that the decrease may occur at an earlier age in women than men and the ratio approaching equality in later years of age.

Actiology of JP

The concepts on the etiology of juvenile periodontitis (JP) include bacterial infection, defects in the host defence system and heredity. Saglie *et al* [23] Asikanem [24], Astenbonski *et al* [25], Aritzi and Moses *et al* [26], Michalowicz *et al* [27], Yuan *et al* [28] and Nonnenmacher *et al* [29] identified the following tissue invading organisms in juvenile periodontitis:- *Actinobacillus actinomycetemcomitans (Aa), Capnocytophaga sputigena, porphyromonas gingivalis,* Mycoplasma and Spirochaetes and human herpes viruses. Actinobacillus actinomycetemcomitan (Aa) has been implicated in the etiology of JP as a result of the following findings reported by Asikanem [24]:-

a. The prevalence and humoral immune response of this organism are elevated in these patients.

b *Actinobacillus actinomycetemcomitans (Aa)* can be identified by electron microscopy, immunofluorescence and culture within the gingival connective tissues from LJP lesions.

c. The organism is quite virulent, producing a leukotoxin collagenase, phosphatase and bone resorbing factors as well as other factors important in evasion of host defence and destruction of periodontal tissue.

d. There is a positive correlation between the elimination of this organism from the subgingival flora and the successful clinical treatment of LJP.

However, Dubrez *et al* [30], reported a high prevalence and high levels of *prevotella intermedia*, but a low level of *Actinobacillus actinomycetemcomitans (Aa)* which differs from other previous studies which showed *Actinobacillus actinomycetemcomitans (Aa)* predominante.

Arai *et al* [31] and Nishimura *et al* [32] reported defect in host defensive functions in cases of juvenile periodontitis. Immunologic studies [33,34] have revealed that JP patients often exhibit markedly elevated titres of serum, salivary and gingival crevicular immunoglobin G, immunoglobin A and Immunoglobin M (IgG, IgA, and IgM) antibodies directed against *Actinobacillus actinomycetemcomitans (Aa)* antigens in general and specifically against the 37 kDA (37 kilo dalton) outer membrane protein of *Actinobacillus actinomycetemcomitans (Aa)* pathogen.

The exact mode of inheritance remains unclear as *Actinobacillus actinomycetemcomitans (Aa)* in JP patients may be derived from the mother, other family members or exogenous sources [35]. Autosomal recessive and X-linked inheritance patterns have been suggested and one large pedigree has demonstrated autosomal dominant inheritance [36]. Studies [37,38] on the relationship of ABO blood group to adult chronic periodontitis have been documented and Arowojolu *et al* [39] found JP patients to exhibit either blood group B/AB rhesus positive and haemoglobin type A.

Pathogenesis

Current concepts on the pathogenesis of JP support the hypothesis that specific microbial groups are present during active periods of the disease [23-30]. *Actinobacillus actinomycetemcomitans* was reported to possess a large number of virulence factors with a wide range of activities which enable it to colonise the oral cavity, invade periodontal tissues, evade host defence, initiate connective tissue destruction and interfere with tissue repair [38,39]. It also stimulates the release of interleukins (IL-1, IL-6, IL-8) and tumour necrosis factors (TNF) by peripheral blood monocytes that could contribute to the bone loss associated with JP [38].

The process by which the organism *Actinobacillus actinomycetemcomitans (Aa)* evades host defences as reported by Wilson and Henerson [41] include:-

- Inhibiting polymorphenuclear leukocyte (PMN) chemo taxis.
- Killing PMNs and monocytes by leukotoxins.
- Producing immuno-suppressive factors.
- Secreting proteases capable of clearing IgG and
- Producing co-binding proteins.

Actinobacillus actinomycetemcomitans (Aa) have also been reported to overcome host defences by inhibition of PMN chemotaxis, production of Fc-binding proteins [42], killing of lymphocytes [41], inhibition of lymphocyte proliferation [41], inhibition of antibody production [41] and degradation of antibodies [41-43].

Tani *et al* [44] reported that *Actinobacillus actinomycetemcomitans(Aa)* contain a 37 kilodalton (37-kDA) protein which is a major immune complex with monoclonal antibodies against rhamnose-fucose polysacharide inducing the release of inflammatory cytokines which are associated with alveolar bone loss. Dongari-Bagtzolou *et al* [45], Yamaguchi *et al* [46] and Kurita-Ochiai and Ochiai [47] reported the release of cytokines which are directly or indirectly involved in connective tissue and bone catabolism following interaction of human gingival fibroblast (HGF) and *Actinobacillus actinomycetemcomitans (Aa)*. Such cytokines are interleukin IL -1 alpha, II -1 beta, IL-2, IL-4, IL – 5, IL-6, IL-8, , tumor necrosis factor (TNF), and gamma interferon. Although osteoblasts complete bone formation, the capsular-like poly-saccharide antigen (CPA) from *Actinobacillus actinomycetemcomitans (Aa)* was shown by Yamamoto *et al* [48] to contain a potent antiproliferative polysaccharide whose activity is associated with apoptotic cell death in mouse osteoblastic cell.

A genetic basis for this disease has been recently supported by its association with specific human leukocyte antigens (HLA) [32]. The association of HLA phenotypes, especially class II antigens with early-onset periodontitis as reported by Kaslick [49] and Reinholdt *et al* [50] is particularly interesting since these suggested a role for genes in the major histocompatibility complex (MHC) which influences immune responsiveness. These are the most widely reported genetic predisposition while the relationship of periodontal disease to neutrophil phagocytosis and bactericidal activity require further investigation.

Clinical features

Juvenile periodontitis is rarely diagnosed in its incipiency where there are few signs and symptoms [14,17). Early diagnosis is sometimes made fortuitously on examination of routine X-rays. Severe distinctive features of this disease justifies its classification as a discrete clinical entity separate from adult periodontitis. These features include lack of clinical inflammation in the presence of deep periodontal pockets with mobility, pathologic tooth migration, deranged occlusion, periodontal abscess formation, disto-labial migration of the incisors with diastemata formation, loss of teeth with tendency to full edentulousness and small amount of plaque that is not commensurate to the clinical condition of the teeth [19,25,36,51,52]. The X-ray shows a cupped-out vertical defect in the alveolar bone which is symmetrically distributed [17,21] (Figure 1). Sjoden *et al* [53] reported that juvenile periodontitis may have its onset already in the primary dentition in some individuals while Odell and Hughes [54] reported possible association of JP with supernumerary teeth

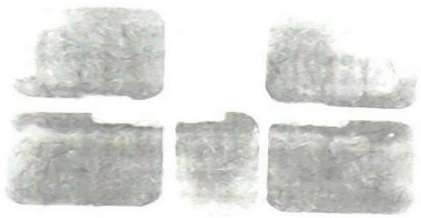

Fig. 1: Photograph of a periapical radiography of a Juvenile Periodontitis patient showing the characteristic arc-like pattern of bone resorption around the teeth.

Histopathological and immunological findings

Studies of localized juvenile periodontitis (LJP) were the first to demonstrate the importance of neutrophils in periodontal disease [34,46,48,50]. Associated with the high numbers of *Actinobacillus actinomycetemcomitans (Aa)*, there are elevated antibody levels to this organism in the serum, crevicular fluid and the saliva from LJP patients [45]. Sixty to ninety percent of patients were reported to have serum IgG antibodies and to a lesser extent IgM, IgA and TgE [46] Ebersole *et al* [55] reported that generalized juvenile periodontitis (GJP) patients exhibited high IgG antibody titres to *Bacteroides gingivalis*.

Differential diagnosis

Cases of severe, rapid periodontal destruction and premature tooth loss in children and teenagers associated with a variety of disease of other systems form the differential diagnosis of JP. These include: Acquired Immune Deficiency Syndromes (AIDS) [56], rapidly progressive periodontitis [57,15] necrotizing ulcerative periodontitis [58], lazy leucocyte syndrome [59]; Ehlers Danlos Syndrome [60]; Down's syndrome [61]; Papillon-lefevre syndrome [62]; prepubertal periodontitis [56]; Maffucci's syndrome [63]; hypophosphatasia [64] and agralucocytosis associated with methemazole therapy for hyperthyrodism [65].

Treatment

The aim of periodontal treatment is to arrest progressive destruction of periodontal tissues and to restore them to a healthy state which the patient can maintain. The efficacy of various treatments to eradicate the defects of JP as well as prevent colonisation by *Actinobacillus actinomycetemcomitans (Aa)* has been studied and reported with occasional contradictory results [26,66-71]. The reasons for contradictory results according to Machtei *et al* [68] may be due to differences in patient selection and/or response to treatment. Dosumu *et al* [72] used the split mouth therapy technique in their study to take care of the differences in patient selection and/or response to treatment and concluded that the efficacy of any treatment modality depend on the stage of the disease process.

Prognosis

Some studies on the prognosis of JP suggests that the 5year prognosis can be quite good [73-76]. The prognosis depend on whether the disease is localized or generalized, the age of the patient and the degree of destruction present at the time of examination. Generalized periodontitis usually associated with some systemic diseases have worse prognosis than localized juvenile periodontitis [59,76]. However, Alger et al [73] Mattout et al [77] and Sewon [78] reported that the periodontal lesions in patients with JP healed more rapidly than similar lesions in other patients. Barnett & Baker [75] found that JP sometimes, undergo spontaneous remission. The rapid healing observed in JP could have been due to the treatment method, the young age of the patient, the type and form of the bony defect [77,78].

Concluding remarks

In the past decades since the identification of the disease entity juvenile periodontitis, there has been an explosion of clinical studies on various aspects of this disease outside this country.

In reviewing this literature, it is challenging to reconcile the results of studies with such a diverse variety of study design. This article gives a concise report of all clinical aspects of juvenile periodontitis from the time that it was identified as a clinical entity in 1920 by Gottlieb [1] to the current opinion of the disease [72]. Based on these studies, the following conclusions can be made:-

- JP is now currently considered as a well defined inflammatory condition of the periodontium with clinical features distinctly different from those seen in adult forms of periodontal disease [13,14].
- Prevalence reports of the disease depend on the strin gency of the diagnostic criteria, the race and the population screened and extent of the disease [15-19].
- Reports on the sex predilection varies [11,13,20-22].
- Concepts on the aetiology of the disease include bacterial infection, defects in the host defence system and heredity [23-36].
- While several studies [23-29] reported *Actinobacillus actinomycetemcomitans (Aa)* as the main aetiologic invading micro-organism, Dubrez *et al* [30] found a high prevalence of prevotella intermedia but low level of *Actinobacillus actinomycetemcomitans (Aa)* in their study.
- Pathogenesis of JP reveals the stimulation of the release of interleukins (IL-1 alpha, IL-1 beta, IL-2, IL-4, IL-5, IL-6, IL-8) [39,40,44-46] tumour necrosis factor (TNF) [46], antibody degradation [40-41], production of Fc-binding protein [41] and its association with specific human leucocyte antibogens (HLA) [32].
- The clinical features of JP are those of chronic periodontitis including its inception at prepuberty and the amount of destruction not been commensurate with the amount of local irritants observed [14,17]. Its association with primary and supernumerary teeth have also been reported [52,53].
- The X-ray shows a cupped-out vertical defect in the alveolar bone which is symmetrically distributed [16,21]. Histopahological and immunological findings of JP from SEM and TEM show gross distortions in pocket walls, increased beaded appearance of micro ridges and sepa ration between pocket epithelial cells [54]. JP patients were also reported to exhibit high IgG antibodies and to a lesser extent IgM, IgA and IgE [45,55].
- Reports from the treatment of JP lesions are contradic tory [26,67-72].-
- Some of the differential diagnosis of the disease were noted [56-66].

The prognosis of JP have been reported to be quite good [74-79] while Barnett and Barker [76] reported that the disease sometimes undergo spontaneous remission. These studies were done outside this country and hence the need for similar studies in our environment since racial influence has been identified. This will enable clinicians to further improve the success rate of the peri odontal treatment they provide for JP patients.

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