Influence of sex hormone levels on gingival enlargement in adolescent patients undergoing fixed orthodontic therapy: A pilot study

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Abstract

Background: Sex hormones may be a modifying factor in the periodontal disease pathogenesis. **Aim:** The association between gingival enlargement and sex hormone levels in adolescent patients undergoing fixed orthodontic therapy needs to be determined. **Settings and Design:** This study was conducted in the Department of Periodontology in association with the Department of Orthodontics, Yenepoya Dental College, Yenepoya University, Mangaluru. **Materials and Methods:** A pilot study was conducted on 21 adolescent patients between the age group of 13–19 years, who had undergone fixed orthodontic therapy for at least 3 months. Apicocoronally, the gingival enlargement was assessed by the index described by Miller and Damm. Miranda and Brunet index was used to assess gingival overgrowth in the buccal–lingual direction in the interdental papilla. Furthermore, the patients were assigned to two groups - Group 1-GE and Group 2-non-GE. Sex hormones assessed were estradiol and progesterone in females and testosterone in males in both groups. **Results:** 57.1% of the study population had enlargement of the gingiva. The mean plaque score was 0.59 and 0.56, respectively, in both groups. A statistically significant relationship was found between estradiol and testosterone levels with gingival enlargement. However, a significant relationship was not obtained for progesterone levels with the gingival enlargement. **Conclusion:** Direct correlation between estradiol, testosterone, and gingival enlargement was seen.

Keywords: Adolescents, fixed orthodontic therapy, gingival enlargement, sex hormones

Introduction

Periodontic-orthodontic interconnection has been subjected to a lot of investigation till today but still is a controversial issue. Malocclusion can affect the health of periodontal tissues, and orthodontic therapy aims to improve the health and prolong the life of dentition.[1] The association of malocclusion with inadequate oral hygiene, temporomandibular joint disease, periodontal disease, mouth breathing, speech problems is well established.[2] The progression of these complications can be corrected by orthodontic treatment; enabling adequate alignment of the teeth and achieving harmonious occlusal relationships.[3] Orthodontic treatment can contribute to improved oral hygiene by correcting the dental problems and reducing occlusal trauma. For these reasons, orthodontic treatment can contribute to an improved periodontal status.[4]

The placement of fixed appliances can alter the oral hygiene accessibility and may complicate the periodontal health although it can correct various skeletal and dental problems. The mechanical irritation from the orthodontic appliance can cause local inflammatory responses in the gingiva. The orthodontic appliances in proximity to the gingival sulcus and subsequent plaque accumulation which results, further complicate the efficiency of salutary orthodontic care.[5] Formation of gingival pockets, occurrence of gingival recession can result from orthodontic treatment. The gingival enlargement associated with orthodontic treatment may cause pseudopocketing with no attachment loss. A shift to more anaerobic flora occurs when pseudopockets are present. An increased frequency of anaerobic bacterial species such as *Porphyromonas gingivalis*, *Prevotella* intermedia, *Bacteroides* forsythus, *Actinobacillus actinomycetemcomitans*, *Fusobacterium nucleatum*, and *Treponema denticola*. is found in the dental plaque of patients who undergo orthodontic therapy.[6]

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Access this article online	
Quick Response Code:	Website: www.contempclindent.org
	DOI: 10.4103/0976-237X.194099

How to cite this article: Hosadurga R, Nabeel Althaf MS, Hegde S, Rajesh KS, Arun Kumar MS. Influence of sex hormone levels on gingival enlargement in adolescent patients undergoing fixed orthodontic therapy: A pilot study. Contemp Clin Dent 2016;7:506-11.

It is established that without a susceptible host, the periodontal pathogens cannot be considered as a sole disease causing factor. Hence, the influence of host systemic factors on the prevalence, progression, and severity of the disease must be understood at this time.[7]

Furthermore, the influence of sex hormones in the pathogenesis of periodontal disease was studied. Estrogen and progesterone were shown to have an influential role in the periodontal disease pathogenesis. Both these hormones can significantly affect different organ systems. The new periodontal disease classification which includes puberty, menstrual cycle pregnancy-associated gingivitis establishes this association.[8]

Gingivitis peak prevalence was observed at 12 years, 10 months in females and 13 years, 7 months in males.[9] The sex hormones level increases during puberty which will remain constant for the entire reproductive period. Sex hormone level can cause an increased inflammatory response of the gingiva to the dental plaque during puberty. Increased plaque accumulation, calculus formation, bleeding, and gingival overgrowth (GO) can occur during orthodontic treatment.[10] Therefore, the aim of this study was to determine the correlation between the sex hormonal levels and gingival enlargement in adolescent patients undergoing active fixed orthodontic treatment with the following objectives.

- To assess the gingival enlargement in adolescents undergoing fixed orthodontic treatment
- To determine the serum estradiol, progesterone, and testosterone levels in adolescents undergoing fixed orthodontic treatment
- To determine the correlation between the hormonal levels and gingival enlargement in adolescents undergoing fixed orthodontic treatment.

Materials and Methods

A pilot study was conducted on 21 adolescent patients (7 males and 14 females) who had undergone orthodontic treatment for at least 3 months from the Department of Orthodontics, Yenepoya Dental College, Yenepoya University, Mangaluru, Karnataka. The Institutional Ethical Clearance was obtained (YUBC 55/20/2/2015) before the study. Participation was voluntary, and all the participants were asked to sign written consent after informing the objective of the study.

Adolescent patients between the age group of 13–19 years, who had undergone fixed orthodontic therapy for minimum 3 months were included in the study. Pregnant or lactating patients, patients under medication, presence of disease, and conditions that could interfere with a clinical examination that are likely to cause gingival enlargement were excluded from the study. Random selection of patients was done by the coin-toss method.

All the patients were observed under adequate natural light, mouth mirror, and University of North Carolina 15 periodontal probe in a dental chair. Apicocoronally, the gingival enlargement was measured by the index described by Angelopoulos and Goaz (1972) and later modified by Miller and Damm (1992) (GO index [GOi]). The gingival tissue height was measured from the cementoenamel junction to the free gingival margin [Figure 1]. The scores obtained for this index are as follows: Grade 0-normal gingiva. Grade 1-gingiva covered the cervical third or less of the anatomic crown and/or <2 mm increase in the size of gingiva. Grade 2-gingiva extended into the middle third of anatomic crown and/or 2–4 mm increase in size. Grade 3-gingiva covered more than two-thirds of the tooth crown and/or >4 mm increase in the size of the gingiva.

Miranda and Brunet index (MBi) (2001) was used to assess GO in the buccal–lingual direction in the interdental papilla which was the modification of the index described by Seymour *et al*. (1985). The increased papilla height was measured from the enamel surface, at the interdental contact area, to the outer papillary layer [Figure 2]. Two scores were obtained for the buccal papilla and lingual/palatal papilla. Grade 0 - thickness of papilla <1 mm. Grade 1 - thickness of papilla between 1 and 2 mm. Grade 2 - thickness of papilla >2 mm. Based on this, the patients were assigned to two groups - Group 1 - gingival enlargement and Group 2 - No gingival enlargement.

A mean score was calculated in the anterior, buccal, lingual/palatal surfaces for both the indices. The scores other than zero in one/both the indices suggested the occurrence of gingival enlargement. Other measures included the probing depth, clinical attachment loss, papillary bleeding index (Muhlemann HR) 1975, and Plaque index (PI) (Silness and Loe) 1964.

Sex hormonal levels were assessed, mainly for estradiol and progesterone in females and testosterone in males. Venous blood was collected in 10 ml tubes by disposable syringes, and centrifugation of the samples was done at 2000 rpm for 5 min to separate the serum. Aspiration of serum was done in a pipette and is transferred to a plastic-covered test tube and stored at −20°C in a deep freezer for hormone testing. The hormone assay was performed by chemiluminescent immunoassay technique in the Bayer immuno 1 system.

Statistical analysis

Data were collected, and statistical analysis was done using SPSS version 22 (IBM Corp., Chicago, illinois, USA). The descriptive statistics such as mean (standard deviation) is used to report continuous variables. Frequency (percentage) is used to report categorical variables. $P < 0.05$ was considered to be statistically significant. Mann–Whitney test was used to compare the median score across two groups for PI and bleeding index.

Results

Twenty-one patients, 14 female and 7 male orthodontic patients between the age group of 16–19 years (mean age 18.3 ± 0.9 years) participated in this study. The demographic characteristics of the involved patients are given in Tables 1 and 2. The clinical examination of their oral health status showed that 12 patients had gingival enlargement, i.e., the frequency of distribution of gingival enlargement was found to be 57.1%. The detailed distribution of patients is given in Table 3. 75% of patients in gingival enlargement group had probing depth >3 mm with no clinical loss of attachment, whereas only one patient in nongingival enlargement group had probing depth >3 mm [Table 4]. There is a statistically significant association between the advancement of pocket formation in gingival enlargement and nonenlargement groups ($P = 0.001$). The clinical loss of attachment was not evident in all the 21 patients examined. The presence of pocket with no clinical attachment loss suggests the formation of pseudopockets in gingival enlargement groups during orthodontic treatment which may subside after the completion of the treatment. The mean plaque score in both groups was 0.59 and 0.56, respectively, which did not show any statistically significant difference between the groups ($P = 0.624$) [Table 5]. It appears that the plaque has no direct correlation with the gingival enlargement.

The mean bleeding score for gingival enlargement and nonenlargement groups was found to be 2.08 and 1.77, respectively, which showed statistically significant difference between the groups ($P = 0.001$) [Table 6]. The higher bleeding score in gingival enlargement group may be attributed to increased vascularity and change in oral flora.

Overall, GOi overgrowth scores were higher than MBi scores, and the presence of gingival enlargement was more pronounced in the incisors area [Table 7]. 37.8% patients had gingival enlargement according to vertical GOi, whereas only 17.5% patients had gingival enlargement according to MBi [Table 7].

There was statistically significant relationship between estradiol levels (Pearson correlation $r = 0.857$, $P < 0.001$)

Table 1: Sex distribution

Male/female ratio	Frequency (%)
Valid	
Female	14 (66.7)
Male	7 (33.3)
Total	21 (100.0)

Table 2: Age distribution

	Descriptive statistics				
	Number of patients	Minimum	Maximum	Mean	SD
Age	21	16.0	19.0	18.3	0.9024

Mean age group was 18.3±0.9. SD: Standard deviation

Table 3: Frequency of distribution of gingival enlargement

Gingival enlargement	Frequency (%)
Value	
Absent	9 (42.9)
Present	12 (57.1)
Total	21 (100.0)

57.1% had gingival enlargement

Table 4: Probing depth

Probing depth	Non-GE Group (%)	GE Group (%)
<3 mm	8 (89)	3 (25)
>3 mm	1 (11)	9 (75)

P=0.001, statistically significant, 75% of patients in gingival enlargement group had probing depth >3 mm

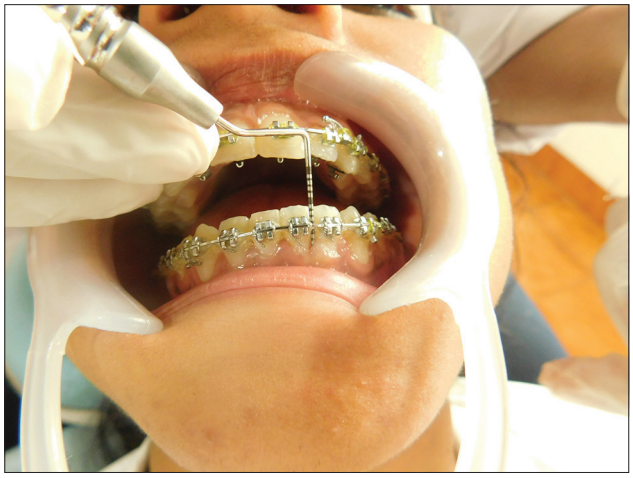

Figure 1: Apicocoronally, the gingival enlargement was assessed by the index described by Miller and Damm

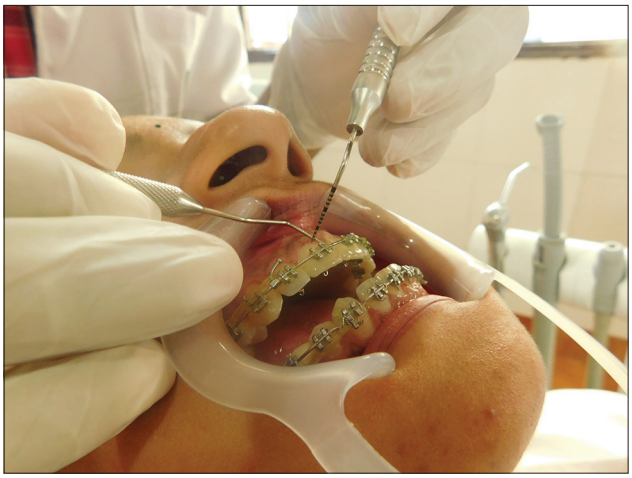

Figure 2: Miranda and Brunet index was used to assess gingival overgrowth in the buccal–lingual direction in the interdental papilla

and testosterone levels ($r = 0.970$, $P < 0.001$) with gingival enlargement. However, the progesterone levels ($r = 0.364$, $P > 0.05$) did not show any statistically significant relationship with gingival enlargement [Table 8].

Discussion

The area between the brackets and gingival margin tends to have greater plaque accumulation due to difficulty in cleaning the teeth associated with the placement of an orthodontic appliance.[11] The increased levels of the steroid sex hormones, testosterone in males and estradiol in females, are responsible for changes in physical appearance and behavior during puberty, which is a complex process.[12] Higher levels of dental plaque accumulation, gingivitis, and enlargement are seen in adolescents. Adolescents tend to have an increased gingival inflammatory response to the dental plaque with the influence of sex hormones.[13]

Gingivitis can occur within 1–2 months after appliance placement even after maintaining good oral hygiene. Different from these studies, Liu *et al*.[14] suggested that increased dental plaque formation and gingival inflammation increases the PI and gingival Index in a short time after orthodontic treatment started.

Table 5: Plaque index

Plaque score	Non-GE Group	GE Group
Mean	0.59	0.56
Median	0.62	0.62

Mann-Whitney test was used to compare the median score across two groups. *P*=0.624, nonsignificant, no significant results were obtained between the groups

Table 6: Bleeding index

Bleeding score	Non-GE Group	GE Group
Mean	1.77	2.08
Median	2	2

P=0.001, significant, significant results were obtained for gingival enlargement group

Puberty gingivitis is marked with the onset of profuse inflammation involving the marginal gingiva and extension to the adjacent attached gingiva, especially in the interdental papillae which increases the gingival bleeding.[15] Children in puberty and pubertal period tend to have increased prevalence of gingivitis.[16] The present study was carried out to assess the gingival enlargement in adolescents independent of plaque factors.

Gingival enlargement is often associated with multiple factors and can exhibit pleomorphic properties. The growth of gingiva occurs toward the incisal edge of the clinical crown and also buccolingually. Buccal surface of the gingiva is more commonly affected. The enlargement of the gingiva appears as a localized nodular growth of the interdental papilla (horizontal growth) in the initial stages and extends to the crown of the teeth (vertical growth). The overall increase in a severe case covers a large portion of the crown of the teeth.[17]

In our study, the frequency of distribution of gingival enlargement was found to be 57.1%. 75% of patients in gingival enlargement group had probing depth >3 mm with no clinical loss of attachment. These findings are in accordance with findings by Gomes *et al*.[18] and Sadowsky and BeGole[19] who proposed that periodontal supporting structures are not permanently damaged during orthodontic treatment, the changes are being transient.

Alterations in the molecular composition of the gingiva are noted by Csiszar *et al*.[20] There is a significant difference in the molecular composition of the marginal gingiva and interdental papilla, suggesting that interdental papilla has cells which are in an activated state and immanently display a specific phenotype resembling wound healing. Thus, the interdental papilla compared to other parts of gingiva has increased susceptibility toward nodullary enlargement in the initial stages of GO.

The mean plaque score in both groups was 0.59 and 0.56, respectively. There was no significant difference between the

Table 7: Global distribution of scores for both indices

Index	5-4	4-3	3-2	2-1	1-1	1-2	2-3	3-4	4–5	Total
GOi score										
GOi=0	34 (80.9)	27 (64.2)	24 (57.1)	23 (54.7)	22 (52.3)	24 (57.1)	26 (61.9)	30 (71.4)	25 (59.5)	235 (62.2)
GOi=1	7 (16.6)	12 (28.5)	16 (38)	15 (35.7)	16 (38)	15 (35.7)	13 (30.9)	11 (26.1)	15 (35.7)	120 (31.7)
GOi=2, 3	1 (2.3)	3 (7.1)	2 (4.7)	4 (9.5)	4 (9.5)	3 (7.1)	3 (7.1)	1 (2.3)	2 (4.7)	23 (6.1)
MBi score										
MBi=0	42 (100)	34 (80.9)	29 (69)	31 (71.8)	32 (76.1)	32 (76.1)	39 (92.8)	41 (97.6)	32 (76.1)	312 (82.5)
MBi=1	0	8 (19)	9 (21.4)	11 (26.1)	9 (21.4)	9 (21.4)	3 (7.1)	0	10 (23.9)	59 (15.6)
MBi=2	0	0	4 (9.5)	0	1 (2.3)	1 (2.3)	0	1 (2.3)	0	7 (1.9)

Prevalence of gingival enlargement was 37.8% according to the GOi and 17.5% according to the MBi. The global distribution of scores for both the indices showed an increased prevalence of gingival enlargement in the incisor region. GOi: Gingival overgrowth index; MBi: Miranda and Brunet index

Table 8: Correlation between the hormonal levels and gingival enlargement

Hormones	Pearson's (*r*)	*P*
Testosterone	0.970	0.00000035
Estrogen	0.857	0.0
Progesterone	0.364	0.052

Statistically significant results were obtained for testosterone and estrogen levels with gingival enlargement ($P<0.001$). No statistically significant relationship between progesterone levels and gingival enlargement ($P>0.05$)

groups. It appears that the plaque has no direct correlation with the gingival enlargement. Low mean plaque score may be attributed to continuous oral hygiene. These findings are in accordance with Davies *et al*.[21] who observed lower plaque and gingivitis levels in children who underwent orthodontic treatment than children who did not receive treatment. The regular appointment with the orthodontist enables them to maintain good oral hygiene.

A significant relationship between gingival bleeding and gingival enlargement was obtained which is in agreement with the findings by Alexander[22] The increased bleeding tendency may be attributed to increased vascularity due to hormonal influence and change in microbial flora. However, contradicting reports found positive increase in plaque and gingivitis. Sallum *et al*.[23] reported a significant reduction in plaque levels, probing depth, and bleeding on probing after the termination of fixed appliance therapy.

We have noticed that 37.8% of patients had gingival enlargement according to GOi and 17.5% according to the MBi. Both the indices showed an increased occurrence of gingival enlargement in the incisor region. The study by Miranda *et al*.[17] used both GOi and MBi to determine the prevalence of drug-induced gingival enlargement. They reported two main advantages for MBi than GOi: (i) The horizontal GO can be measured and (ii) it discriminates overgrowth of gingiva in the vertical and horizontal direction. In their opinion, the GOi and the MBi assist in the screening and diagnosis of patients with GO. Both the maxillary and mandibular anterior teeth showed increased incidence and severity of drug-induced gingival hyperplasia.[24]

Statistically significant relationship was noted between hormonal levels and gingival enlargement. These findings are in accordance with findings by Mariotti[8] Researchers have shown that sex hormone level variation may cause alteration of the periodontium. However, we did not notice a significant relationship between progesterone levels and gingival enlargement which is not in agreement with other studies.[25]

Gingivitis peak prevalence was observed at 12 years, 10 months in females and 13 years, 7 months in males. Estrogen and progesterone can be substituted for Vitamin K by prevotella intermedia which could partly explain the increased gingivitis during adolescence.[16] Furthermore, increased plaque accumulation can be seen. Increased bleeding is associated *Capnocytophaga* sp., and also *Actinomycetes* sp. and *Eikenella corrodens*.[16]

Various biological actions exhibited by estrogen and progesterone can affect different organ systems including the oral cavity.[26] Squamous epithelial cells cytodifferentiation, synthesis, and maintenance of fibrous collagen can be influenced by estrogen.[27] Osteoblast-like cells exhibit estrogen receptors which could explain the direct action on bone.[28] Furthermore, the periosteal fibroblasts, scattered fibroblasts of the lamina propria, and periodontal ligament (PDL) fibroblasts exhibit these receptors suggesting a direct action of estrogen on periodontal tissues.[28] Periodontal tissues also exhibits specific receptors for testosterone. Interestingly, the inflamed or overgrown gingiva showed increased number of these receptors. Under the influence of testosterone, the PDL cells showed increased matrix synthesis.

In contrast to our studies, Liu *et al*.[29] showed that gingivitis during puberty was closely related to plaque build-up rather than to hormones. Hormone-related gingivitis can be managed by various oral hygiene measures which remove the local predisposing factors. In a longitudinal study, no changes in oral microbiota were observed during puberty and no correlation between black pigmented species and plasma estradiol levels.[30] Our findings do support the statement that improvement in gingival health during active fixed orthodontic therapy results from regular brushing and flossing and increased awareness among orthodontic patients.[31]

Conclusion

Based on the findings of this study, it is evident that 57.1% patients had gingival enlargement during orthodontic therapy. Increased occurrence of gingival enlargement was seen in incisor region. Direct correlation between estradiol, testosterone, and gingival enlargement was seen. However, further longitudinal study with a larger sample size is required to validate the findings of this study. Detailed menstrual history has to be taken, and progesterone level in the follicular phase and luteal phase needs to be assessed in the future study.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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