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# Interleukin - 1 Polymorphisms And Chronic Periodontitis In A Rural Kenyan Population

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***Abstract:*** *Susceptibility to Chronic periodontitis (CP) has been associated with genetic polymorphisms in the proinflammatory cytokine, interleukin-1 (IL-1A and IL-1B) isoforms but little is known about their role in rural Africans. Therefore, the aim of this study was to resolve the association between genetic polymorphisms in IL-1A and IL-1B isoforms and chronic periodontitis in the Taita people of Kenya.*

***Methods:*** *This was a case-control study. After informed consent, a clinical examination was then conducted which included assessment of dental plaque, gingival inflammation, pocket depths and gingival recession. Buccal swab samples were then obtained. Deoxyribonucleic acid (DNA) was isolated from the swabs using QIAamp DNA purification protocol followed by polymerase chain reaction (PCR) amplification using specific primers to IL-1A (rs 1800587(-889) & rs17561(+4845)) and IL-1B (rs 16944 (-511) & rs 11443624(+3954)). The amplicons were digested using Nco1, Fnu4H1, Ava1 and Taq1 respectively. Restriction fragment length polymorphisms (RFLP) were recorded. Association analyses of the RFLP and clinical data were carried out.*

***Results****: No deviation from the Hardy Weinberg equilibrium was observed. Carriage of allele2 at IL-1B +3954 (i.e. combination of '2-2' or'1-2' at locus +3954) was associated with CP in the Taita participants (OR = 1.94, 95%CI=1.01-3.70, p=0.045). There were no confounders or effect modifiers in the Taita participants and no association with severity of CP was observed in this population. None of the composite genotypes were associated with CP in the Taita participants. Haplotype 3 (i.e. allele1 at all the four loci) was significantly associated with CP amongst the Taita (OR=2.4, 95%CI=1.1-5.14, p=0.022).*

***Conclusion****: The significant association of allele2 at IL-1B +3954 with CP in the Taita participants confirmed the importance of this genotype in disease pathogenesis.*

***Keywords:*** *chronic periodontitis, IL-1polymorphisms, Rural Kenya, Taita*

## I. Literature Review

Periodontal diseases are conditions associated with dental plaque formation [1]. These diseases and conditions affect the tissues of the periodontium, leading to the destruction of the connective tissue attachment of the teeth. The connective tissue attachment includes the gingiva, the periodontal ligament, the root cementum and the alveolar bone [2]. Periodontal diseases are broadly categorized into eight groups [3]. Gingivitis is the first group and is described as inflammation confined to the gingival tissues. Chronic periodontitis on the other hand is the second group and occurs when there is destruction of the periodontal ligament and the alveolar bone leading to the apical migration of the junctional epithelium.

The primary etiological factor in the initiation of chronic periodontitis is plaque with host susceptibility being reported as an important modifying factor in the progression of the disease [4]. Many patients with periodontitis do not have the classical risk factors, whereas others with comparable risk factors do not show the same level of periodontal destruction or progression [4]. This seems to indicate that other additional risk factors and etiological factors may explain the differences seen [5]. Recently, several gene polymorphisms have been investigated as possible contributors to the increased host susceptibility. Studies on genetic susceptibility come from twins, [5,6,7] linkage studies, segregation analysis in families with aggressive forms of periodontitis [8, 9] and association studies [10]. A strong association has been observed between the severity of periodontitis and a specific genotype of the interleukin-1 (IL-1) gene cluster [11].

IL-1 polymorphisms have only recently become of interest in the Kenyan population. Data on IL-1 polymorphisms in native African populations are limited. One study was carried out amongst the Xhosa in South Africa and reported a prevalence of IL-1A (+4845) allele 2 at 46.9 % in cases and 22 % in controls and

IL-1B (+3954) at 15.8 % in cases and 14.3 % in controls [12]. This study showed that IL-1 composite polymorphism was not associated with severity of periodontitis in this South African population [12]. The other known study on Africans was carried out on the Swahilis an urban population in Kenya where IlL-1A (-889) was associated with chronic periodontitis [13].

It is in this regard that a rural community was identified for this study. The Taita are Bantus and occupy the southeastern part of Kenya, known as the Taita Hills.

## II. Material And Methods

The study was carried out in Taita Taveta County which is one of the forty seven counties in Kenya. The Taita population consists of approximately 250,000 people according to the 2009 census. The Taita are a Bantu speaking group of rural people who are mainly subsistence farmers. They occupy the southeastern part of Kenya in the Taita Hills and do not generally marry outside their community.

This was a case-control study design. This study was done at the same time as a recently published study on Swahilis therefore the material and methods is similar except that this is a rural population whereas the Swahili are an urban group [13]. The design allowed for selection of cases and controls without randomization as long as the inclusion criteria were adhered to [14]. The test was, whether the marker genotypes distributed differently between the cases and controls. The selection of participants involved matching by age and gender of the cases with unaffected controls. Cases comprised individuals with chronic periodontitis selected on the basis of having clinical loss of attachment of $\geq$ 3mm on several teeth but a minimum of at least 2 non-adjacent teeth with proximal attachment loss of $\geq$ 3mm [15,16] and controls were individuals with a clinically healthy gingiva that did not bleed on probing and had no probing depth of >3mm. Controls were individuals who would have been designated study cases if they had developed the disease. Study participants were adults of ages 35-44 years since this is the age at which cumulative effects of Chronic Periodontitis will present according to the World Health Organization Basic Methods Criteria. These participants were selected from subjects who presented themselves to the various recreational centers and health centers and met the inclusion criteria. Controls were recruited from the same area and were used to characterize the distribution of the genotype.

Included persons had to have most of their teeth but a minimum of 18 teeth including 2 molars and 2 premolars in the same arch. This allowed representation of all tooth types including molars and premolars so as to capture the presentation of chronic periodontitis in single rooted teeth as well as multi-rooted teeth because progression of chronic periodontitis may differ in the different tooth types [17]. Only those who consented to participate in the study were recruited. Those excluded were persons with a history of periodontal treatment, six months prior to the study since this would have interfered with disease definition by the inclusion of cases with a reduced but healthy periodontium as control subjects. Those on any medication, smokers or with any systemic illness were also excluded.

The required minimum sample size for case control studies was calculated using a formula developed by Kirkwood and Sterne (2003) [18]. The exposure rate reported in the study by Kornman et al 1997 [9] was used since there were no known Kenyan African studies on genetic polymorphism and chronic periodontitis at the time of the study. The specifications yielded a sample size of 88. Anticipating a 10% loss due to inadequate DNA collection, the sample size (per group) was 88/0.9 = 98. A minimum appropriate sample ensured proper utilization of resources since sample size is often determined by logistic and financial considerations [16].

A modified WHO questionnaire on oral health seeking behavior, oral health practices and sugar consumption was used (WHO, 1997). A Kiswahili version was used for participants who did not understand English. A clinical examination form was used to record data on recession on the following six sites, mesio-buccal, buccal, disto-buccal, mesio-lingual, lingual and disto-lingual areas. Probing depth measurements were also carried out on the same six sites per tooth. Bleeding on probing, calculus and plaque were recorded as present or absent. DNA collection was carried out using the isohelix buccal swabs (Boca Scientific, Isohelix, Kent, England) as per the manufacturer's instructions.

Labeled swabs were used to collect buccal cells from the cheeks of the participants from which DNA samples were obtained. DNA was purified from cells adhering on the swabs using QlAmp DNA Minikit spin protocol (Qiagen, Turnberry Lane, Valencia, CA) following the manufacturer's instructions. Centrifugation steps were carried out at room temperature (15-25$^0$C). Purity and concentration of isolated DNA was determined using NanoDrop 2000c spectrophotometer (Thermo Scientific, Waltham, Mass., USA). Genomic DNA from cases and controls were analyzed for polymorphisms within the IL-1A gene loci -889 [19] and +4845 [20] and the IL-1B gene loci -511 [21], and +3954 [22]. PCR reaction conditions were as previously described [23, 24]. Briefly, a reaction mix excluding Taq polymerase was prepared with template DNA added prior to heating at 95°C for 15 min. Taq polymerase (Invitrogen Corporation, Grand Island NY, USA) was added and PCR initiated. $MgCl_2$ and primer concentrations were varied in each type of reaction for the different loci ([rs1800587] -889, [rs17561] +4845, [rs16944] -511 and [rs1143634] +3954). Restriction fragment length polymorphism (RFLP) assays of PCR-amplified gene fragments were carried out as previously described [23]

before subjecting the digests to polyacrylamide gel electrophoresis followed by staining with ethidium bromide (0.2pg/ml) and visualized under ultraviolet light. Descriptive and bivariate analyses were done. Associations between exposure variables and chronic periodontitis were done using Pearson Chi-squared and risk assessed by odds ratio (OR) with 95% confidence interval. Multivariate analysis was carried out using the Binary Logistic Regression to test for significance of being a case in the presence of factors that were found to be significant at the bivariate stage. Hardy – Weinberg equilibrium for the four loci (-511, +3954, -889, +4845) was tested for genotype frequency by chi square test, with 1 degree of freedom. The three recognized haplotypes [25] were tested for association with chronic periodontitis. Haplotype 1: Allele 2 at IL-1A +4845 and allele 2 at IL-1B+3954, Haplotype 2: Allele 2 at IL-1B-511, Haplotype 3: Allele1 at the IL-1A and allele 1 at IL- 1B markers.

## III. Results

Of the 502 persons screened, only 198 were entered into the study according to the inclusion criteria. Of the 198 Taita participants examined, 99 were cases and 99 age and sex matched healthy controls where there was no bleeding on probing. The age range for the participants was 35-44 years with a mean of 37.88 (SD 3.29). There were 64(32%) males and 134(67.7%) females OR = 0.97, 95% CI = 0.523-1.799 p=0.923. Most of the Taitas were unemployed and subsistence farmers. 117 (59%) of the participants had all the teeth present. Of the 81 (41%) participants with missing teeth, majority 56(69%) had only one or two teeth missing. After the field study it was later realized that eight smokers were inadvertently included in the recruits. They were removed and excluded from subsequent analysis, leaving 94 cases and 94 controls.

There was more plaque on the tooth surfaces of those with chronic periodontitis (cases) than in the control participants, OR = 21, with 95% CI = 7.8-56.4, p<0.001 as shown in figure 1. The mean number of tooth surfaces having plaque per individual in cases was 25(SD3.6) and for controls 14(SD 9.9).

The mean number of gingival sites per individual found to be bleeding was 17(SD 10.2). 28 gingival sites were examined per individual. When all 28 gingival sites per individual, in cases, were examined for bleeding, it was found that cumulatively, 6% of individuals had all gingival sites bleeding on probing. 30% had 27 gingival sites with bleeding out of a possible 28 gingival sites examined per individual, figure 2. In the 94 control participants, only 6(0.2%) gingival sites out of a total of 2,584 sites examined were found to bleed on probing in the controls amongst the Taita participants.

The median value (50%) showed that 13 tooth surfaces had calculus in cases. The controls had less calculus with 22% of individuals, having calculus. Therefore there was more calculus on the tooth surfaces amongst those with chronic periodontitis OR = 33.9, 95%CI = 13.3-86.3, p<0.001.

On probing the periodontal pockets, it was found that cases had probing depths of more than 3mm but none of the controls had pockets of more than 3mm (normal probing depths range from 0-3mm). The mean periodontal pocket depth was 1.58(SD1.01). 564 sites (3.8%) had pockets of ≥4mm.

The mean number of sites with ≥4mm CAL were 20 (SD 21.1), ≥5mm were 11 (SD17.9) and those with CAL of ≥6mm were 6(SD 11.2). The mean total CAL was 2.34(SD 1.09).

Amongst the Taita participants, the distribution of disease according to the CDC/AAP definitions (Page and Eke 2007) revealed a high prevalence of severe chronic periodontitis with 10(10.6%) of the Taita participants having the mild form of the disease; 43(45.7%) had the moderate form and 41(43.6%) had the severe form of chronic periodontitis.

Interleukin-1B polymorphism was tested at loci -511 and +3954, whereas interleukin-1A was tested at -889 and +4845. The genotype frequency was tested for allele 1 and 2 at the four loci tested. Thus the presence of homozygous allele1 (1-1), presence of heterozygous allele 1and 2 (1-2) and the presence of homozygous allele2 (2-2) were tested.

Table 1 shows the various frequency distributions of the four genotypes in cases and controls amongst Taita participants. A higher frequency of heterozygous IL-1B (-511) was found in cases 47(63.5%) than in controls 37 (57.8%), p=0.112. Allele1 of the IL-1B -511 polymorphism was carried by 57 (38.5%) cases and 49(38.3%) controls, p=0.968. Of these, only 5 (6.8%) cases and 6(9.4%) controls were homozygous, p=0.784.

On the other hand, allele2 of IL-1B polymorphism at -511 was carried by 91(61.5%) and 79(61.7%) cases and controls respectively, with homozygous distribution of allele2 at 22(29.7%) and 21(32.8%) in cases and controls, with a p value of 0.801.

The homozygous distribution of allele1 at locus +3954 was 34(54%) and 34(70.8%) in cases and controls respectively, p=0.914. Homozygous allele2 was 8(12.7%) and 3(6.3 %) in cases and controls respectively, p=0.112. The heterozygous distribution of allele 1 and 2 (1-2) was 21(33.3%) in cases and 11(22.9%) in controls with a p- value of 0.045, which was significant.

The carriage rate for allele1 polymorphism at position +3954 was 89(70.6%) in cases and 79(82.3%) in controls, OR=0.52 95%CI=0.27-0.99, p=0.045. Allele2 was carried by 37(29.4%) and 17(17.7%) in cases and controls respectively, OR=1.936 95%CI=1.009-3.698, p=0.045 (Table 1).

Homozygous frequency for allele1 of -889 was 36(41.4%) and 28(34.1%) for cases and controls, p=0.183. Heterozygous frequency was 34(39.1%) and 36(43.9%) for cases and controls, p=0.849. Homozygous distribution for allele2 was also not significant, with 17(19.5%) and 18(22%) for cases and controls respectively, p=0.906.

The carriage rate of allele1 and allele2 were 106(60.9%) and 92(56.1%) for allele1 and 68(39.1%) and 72(43.9%) for allele2 in cases and controls, p=0.368 (Table 1).

The frequency of the homozygous allele1 for +4845 was found to be statistically significantly distributed between cases, 1(1.4%) and controls, 8(11.6%) although the numbers are low, p=0.018. Heterozygous for +4845 was 58(78.4%) and 50(72.5%) for cases and controls respectively, p=0.181. Homozygous for allele2 was 15(20.3%) and 11(15.9%) for cases and controls respectively, p=0.367.

The carriage rate for allele1 polymorphism at position +4845 was 60(40.8%) and 66(47.8%) in cases and controls respectively. Whereas the carriers of allele2 polymorphism at +4845 in cases and controls, were 88(59.5%) and 72(52.2%) respectively, p=0.215.

When Hardy Weinberg Principle was tested, $\chi^2$ distribution with 1df (3.84) showed that equilibrium exists for IL-1A loci -889 ($\chi^2$ = 3.84, p<0.05) and +4845 ($\chi^2$ = 40.5, p<0.05) and IL-1B at locus -511 ($\chi^2$ = 11.42, p<0.05) and +3954 ($\chi^2$ = 6.48, p<0.05) in the Taita participants.

The positive genotype which is allele2 +889 and allele2 +3954 was carried by 29(46.8%) of cases and 23(51.1%) controls, p=0.287.The difference between cases and controls was not significant.

When the association between alleles and the severity of chronic periodontitis was tested (table 2), carriage rate of allele1 polymorphism at position IL-B locus -511, was 4 (33.3%) for mild CP, 29 (41.4%) for moderate CP and 24 (38.7%) for severe CP. For total allele2 at the same position was 8 (66.7%) for mild CP, 41 (58.6%) for moderate CP and 38 (61.3%) for severe CP, p=0.854.

For IL-1B at locus +3954 the results showed that for allele1, the number of Taita participants having this allele were 8 (66.7%) in those with the mild form of CP, 42 (70.0%) in those with the moderate form and 39 (72.2%) in those with the severe form of CP. Allele2 on the other hand was, 4 (33.3%) for mild CP, 18 (30.0%) for moderate and 15 (27.8%) for severe CP, p=0.919.

The results for IL-1A at locus -889 according to severity of CP were, for allele1, the number of Taita participants having this allele were, 11 (61.1%) in those with mild CP, 51 (63.8%) in those with moderate CP and 44 (57.9%) in those with severe CP. Whereas, allele2 at the same locus (-889), 7 (38.9%) individuals had mild CP, 29 (36.3%) moderate CP and 32 (42.1%) severe CP. There were no significant differences in the frequency of allele1 and 2 and severity of CP at IL-1A locus -889, p=0.755.

IL-1A at locus +4845, the frequency distribution of allele1 was 7 (38.9%) in the mild form of CP, 29 (41.4%) in the moderate form and 24 (40.0%) in the severe form of CP. Whereas, for allele2, at the same locus (+4845), 11 (61.1%) of the Taita participants had mild CP, 41 (58.6%) had moderate CP and 36 (60.0%) had severe CP. There were no significant differences in severity of CP and allele 1 and 2 at locus +4845, p=0.975 (table 2).

There are three recognized haplotype [25] and these are:-

- Haplotype 1: Allele2 at IL-1A +4845 and IL-1B+3954
- Haplotype 2: IL-1B-511 allele2
- Haplotype 3: Allele1 at the IL-1A and IL-1B markers

The first and second haplotype were not associated with chronic periodontitis in this ethnic group. The third haplotype is presented in table 3 where having allele1 in all four genotypes was significantly associated with chronic periodontitis in the Taita participants OR= 2.4, 95%CI = 1.12-5.14, p=0.022.

Multivariate analysis were done to investigate the association between plaque levels and the significant genotypes. Table 4 shows that plaque level continued to be significantly associated with CP, OR=18.97, 95%CI=7.01 – 51.31, p<0.001. However, genotype +4845 (1-1) and +3954 (1-2) were no longer associated with CP in this multivariate model as shown.

## IV. Discussion

Interleukin-1 gene variations have been shown to influence the risk of disease progression in many chronic illnesses like rheumatoid arthritis, inflammatory bowel disease, cardiovascular disease, osteoporosis and periodontitis [26]. They do not cause the disease but influence the development and progression of the disease by amplifying the body's response to disease challenge [27]. Interleukin-1 genetic variations have been reported to influence the transcription of IL-1 and thus the susceptibility and outcome of disease [26]. Interleukin-1B, the SNP variant -511 is at the promoter region and +3954 at the fifth exon site with both the polymorphisms caused by C to T transitions [22, 28]. These polymorphisms are associated with higher levels of IL-1β cytokines produced by the peripheral blood mononuclear cells. Thus there is a higher concentration of IL-1β cytokine in plasma and GCF [11, 29, 30]. The increase in IL-1β cytokine may lead to increase in inflammation since this is a pro-inflammatory cytokine.

In the present study, the association between interleukin-1 and chronic periodontitis amongst Taita participants was seen in heterozygous (C/T) IL-1B at position [rs1143634] +3954, p=0.045 and allele2 (T) at position +3954. Heterozygotes Interleukin-1 B +3954 C/T carriers were found to be at an increase risk of having chronic periodontitis amongst the Taita participants, (p=0.045). This is similar to a case control study done on Chilean subjects where heterozygotes of the IL-1B+3954 C/T were significantly higher in cases than in controls and were associated with periodontitis ( p= 0.001) [31]. Other studies on Caucasians also found a significant association between IL-1B+3954 C/T and periodontitis as reviewed by [32].

The association of IL-1B with CP amongst the Taita participants may be explained by the reported finding in other studies [11, 29], in that this polymorphism leads to higher production levels of cytokine IL-1 β in plasma and GCF which in turn leads to amplification of the inflammatory response. A high level of inflammatory response was observed amongst the Taita participants where 61.8% of sites per individual were found to bleed on probing and 88% had at least one site with BOP. Interleukin-1 β cytokine is produced by activated monocytes, macrophages and epithelial cells [25,32]. Pociot et al 1992[28], showed a 2-4 fold increase in production of cytokine IL-1β levels in response to bacterial challenge in heterozygous subjects. More recently, Ferriera et al 2008[33] showed an association between IL-1B+3954T/T (allele2), Porphyromonas gingivalis, Treponema denticola and Tannerella forsythia and an increase in cytokine IL-1β levels in the diseased periodontal tissues. Interleukin-1B [rs1143634] SNP +3954 at exon 5 results in coding synonymous where there is no change in the amino acid produced which is phenylalanine. However the increase production in cytokine IL-1β may be due to the effect this allele [rs1143634] may have in the splicing mechanism (http://www.ncbi.nlm.nih.gov/projects/SNP/snp_ref.cgi?rs=17561 [34]. This allele may enhance the splicing process and thus make the production of cytokine IL-1β easier. The Taita participants had a positive association between allele2 at +3954 and CP and a high inflammatory response of the gingival tissues. A higher inflammatory response leads to more destruction of the periodontal tissues thus more disease. Inflammation has also been shown to have a synergistic effect on plaque formation [33]. The presence of more plaque in the Taita cases corroborates the fact that there is more plaque in the presence of more inflammation.

The positive composite genotype (allele2 of IL-1A -889 and allele2 of IL-1B +3954) distribution in cases and control amongst the Taita participants was basically equally distributed. The composite genotype +3954 and +4845 was not associated with CP in the Taita participants. This finding is similar to a study done on Xhosas in South Africa where they also did not find an association between the composite genotype and CP [12]. It is also similar to a study on Swahilis in Kenya [13].The explanation for these findings could be that the composite genotype does not have an effect on CP in Africans.

Homozygous allele1 at IL-1A position +4845 (G) was significantly different in cases (1.4%) and controls (11.6%) p=0.018 amongst the Taita participants. This suggested that in this study, IL-1A [rs17561] +4845G/G (homozygous allele1) was protective. It could be that the presence of allele1 (G/G) confers protection. However, the numbers were very small. A larger sample is required to explore this association.

There was no relationship between all the four allele (-511, +3954, -889, +4845) distributions and severity of disease amongst the Taita participants. This finding appears to be unique to the Taita, an African group that has not intermixed much with people from non Bantu origin. This lack of association could also be attributed to the age of the participants. The age range was relatively evenly distributed between 35-44 years. Severity of chronic periodontitis increases with age especially in the absence of treatment. An older age group may reveal a different picture.

Further analysis revealed that in the Taita participants, plaque remained associated with chronic periodontitis at bivariate and multivariate levels. This suggests that the more important risk factor of chronic periodontitis is plaque. Chronic periodontitis may actually be a disease of multiple genes and IL-1 is just one of the several gene polymorphisms involved in the genetic risk factors. Plaque initiates the disease process and in those with the positive genotype in this case IL-1B +3954, there is a hyper sensitive reaction to the pathogenic bacteria that may be present. This will eventually lead to CP.

This study has shown that in the rural African population of Bantu origin, the polymorphism that produced significant p-values in this study was IL-1B+3954 amongst the Taita. Additionally haplotype 3, where the wild type allele at loci -511, +3954, -889 and +4845, was associated with CP. Finally, plaque control as a well tested mode of prevention of CP has been proven in this study.

## V. Conclusions

A significant association (p=0.045) was found between IL-1B +3954 and chronic periodontitis amongst Taita participants. There was a 2 fold increase risk of developing CP in those with any allele2 (1-2 and 2-2) at IL-1B+3954.

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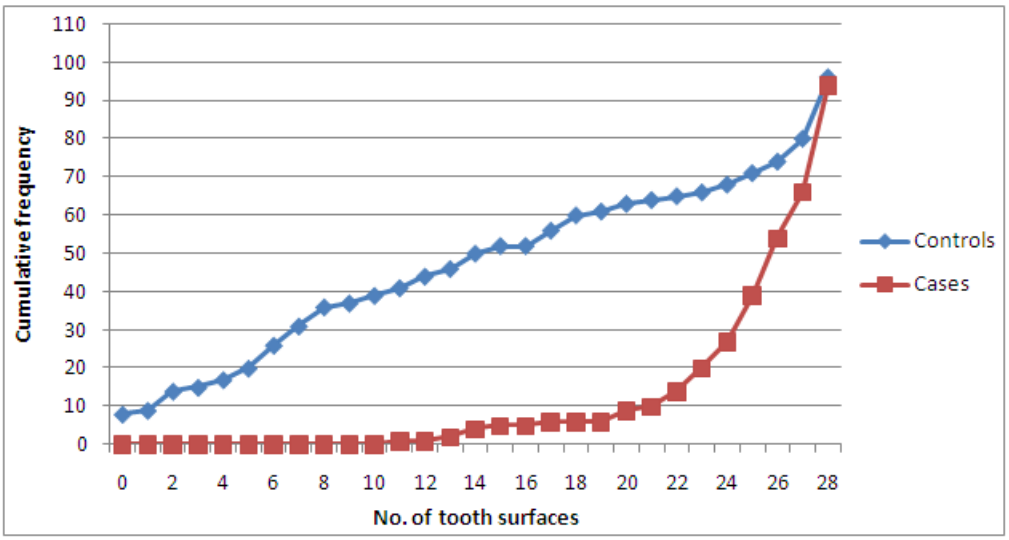


**Figure 1: Cumulative frequency distribution of plaque on the tooth surfaces amongst the Taita participants, cases and controls.**

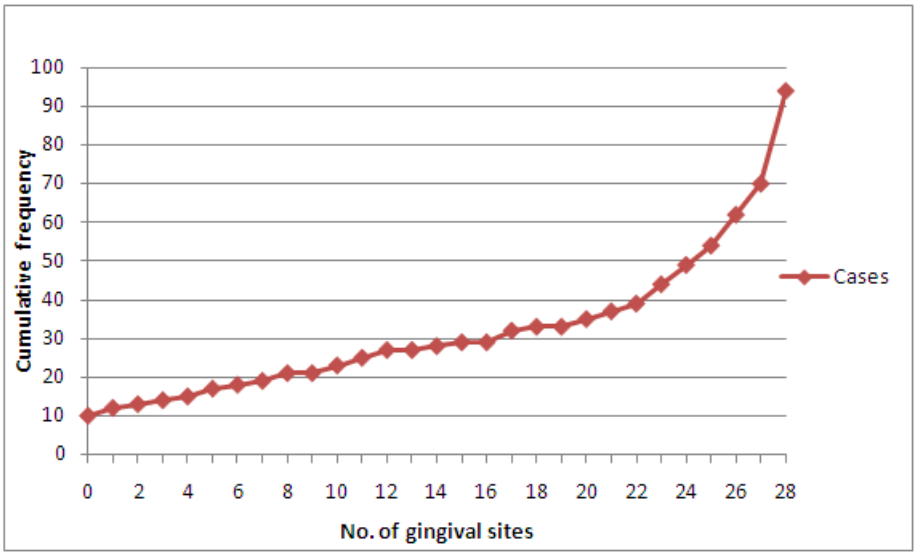


**Figure 2: Cumulative frequency distribution of the number of teeth with bleeding on probing of the gingival tissues amongst the Taita participants**

**Table 1: Distribution of IL-1B and IL-1A genotype and allele frequencies amongst the Taita participants**

| | | Cases (n=94) | | Controls (n=96) | | | | 95% CI for OR | |
|---|---|---|---|---|---|---|---|---|---|
| **Genotype** | | **n** | **%** | **n** | **%** | **P-Value** | **OR** | **Lower** | **Upper** |
| IL-1B-511 | 1—1 | 5 | 6.8 | 6 | 9.4 | 0.784 | | | |
| | 1—2 | 47 | 63.5 | 37 | 57.8 | 0.112 | | | |
| | 2—2 | 22 | 29.7 | 21 | 32.8 | 0.801 | | | |
| Allele | 1 | 57 | 38.5 | 49 | 38.3 | 0.968 | 1.01 | 0.62 | 1.64 |
| | 2 | 91 | 61.5 | 79 | 61.7 | | | | |
| IL-1B+3954 | 1—1 | 34 | 54 | 34 | 70.8 | 0.914 | | | |
| | 1—2 | 21 | 33.3 | 11 | 22.9 | 0.045* | | | |
| | 2—2 | 8 | 12.7 | 3 | 6.3 | 0.112 | | | |
| Allele | 1 | 89 | 70.6 | 79 | 82.3 | | | | |
| | 2 | 37 | 29.4 | 17 | 17.7 | 0.045* | 1.94 | 1.01 | 3.70 |
| IL-1A-889 | 1—1 | 36 | 41.4 | 28 | 34.1 | 0.183 | | | |
| | 1—2 | 34 | 39.1 | 36 | 43.9 | 0.849 | | | |
| | 2—2 | 17 | 19.5 | 18 | 22 | 0.906 | | | |
| Allele | 1 | 106 | 60.9 | 92 | 56.1 | 0.368 | 1.22 | 0.79 | 1.88 |
| | 2 | 68 | 39.1 | 72 | 43.9 | | | | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| IL-1A+4845 | 1—1 | 1 | 1.4 | 8 | 11.6 | 0.018* | | | |
| | 1—2 | 58 | 78.4 | 50 | 72.5 | 0.181 | | | |
| | 2—2 | 15 | 20.3 | 11 | 15.9 | 0.367 | | | |
| Allele | 1 | 60 | 40.5 | 66 | 47.8 | 0.215 | 0.74 | 0.46 | 1.19 |
| | 2 | 88 | 59.5 | 72 | 52.2 | | | | |

Significance at *p<0.05, OR = odds ratio, CI = confidence interval

**Table 2: Distribution of IL-1B and IL-1A genotype and allele frequencies with mild, moderate and severe periodontitis amongst the Taita participants**

| | | Mild CP (n=10(10.6%)) | | Moderate CP (n=43(45.7%)) | | Severe CP (n=41(43.6%)) | | |
|---|---|---|---|---|---|---|---|---|
| **Genotype** | | **n** | **%** | **n** | **%** | **n** | **%** | **P-Value** |
| IL-1B -511 | 1—1 | 0 | 0.0 | 3 | 8.6 | 2 | 6.5 | 0.666 |
| | 1—2 | 4 | 50.0 | 23 | 65.7 | 20 | 64.5 | 0.728 |
| | 2—2 | 4 | 50.0 | 9 | 25.7 | 9 | 29.0 | 0.421 |
| Allele | 1 | 4 | 33.3 | 29 | 41.4 | 24 | 38.7 | 0.854 |
| | 2 | 8 | 66.7 | 41 | 58.6 | 38 | 61.3 | |
| IL-1B+3954 | 1—1 | 3 | 50.0 | 17 | 56.7 | 14 | 51.9 | 0.799 |
| | 1—2 | 2 | 33.3 | 8 | 26.7 | 11 | 40.7 | 0.653 |
| | 2—2 | 1 | 16.7 | 5 | 16.7 | 2 | 7.4 | 0.533 |
| Allele | 1 | 8 | 66.7 | 42 | 70.0 | 39 | 72.2 | 0.919 |
| | 2 | 4 | 33.3 | 18 | 30.0 | 15 | 27.8 | |
| IL-1A-889 | 1--1 | 3 | 33.3 | 18 | 45.0 | 15 | 39.5 | 0.751 |
| | 1--2 | 5 | 55.6 | 15 | 37.5 | 14 | 36.8 | 0.628 |
| | 2--2 | 1 | 11.1 | 7 | 17.5 | 9 | 23.7 | 0.622 |
| Allele | 1 | 11 | 61.1 | 51 | 63.8 | 44 | 57.9 | 0.755 |
| | 2 | 7 | 38.9 | 29 | 36.3 | 32 | 42.1 | |
| IL-1A +4845 | 1--1 | 0 | 0.0 | 1 | 2.9 | 0 | 0.0 | 0.549 |
| | 1--2 | 7 | 77.8 | 27 | 77.1 | 24 | 80.0 | 0.784 |
| | 2--2 | 2 | 22.2 | 7 | 20.0 | 6 | 20.0 | 0.915 |
| Allele | 1 | 7 | 38.9 | 29 | 41.4 | 24 | 40.0 | 0.975 |
| | 2 | 11 | 61.1 | 41 | 58.6 | 36 | 60.0 | |
| Significance at*P<0.05 | | | | | | | | |

**Table 3: Association between chronic periodontitis and Haplotype 3: Allele1 at the IL-1A (-511 and +3954) and IL-1B (-889 and +4845) amongst the Taita participants**

| | | | **Taita participants** | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | **Control** | | **Case** | | | | **95% C.I for OR** | |
| | | **N** | **%** | **N** | **%** | **P-Value** | **OR** | **Lower** | **Upper** |
| | | | | | | | | | |
| Allele1 in All | Absent | 84 | 87.5 | 70 | 74.5 | | | | |
| | Present | 12 | 12.5 | 24 | 25.5 | 0.022* | 2.4 | 1.12 | 5.143 |
| | | | | | | | | | |
| Allele2 in All | Absent | 92 | 95.8 | 91 | 96.8 | | | | |
| | Present | 4 | 4.2 | 3 | 3.2 | 1 | 0.8 | 0.165 | 3.483 |

**Table 4: Multivariate analysis of Taita participants' plaque levels and significant genotype data**

| | | | | | | **95% C.I. for OR** | |
|---|---|---|---|---|---|---|---|
| | | **B** | **S.E.** | **P-value** | **OR** | **Lower** | **Upper** |
| **Plaque** | <=15 | **Reference** | | | 1 | | |
| | >15 | 2.943 | 0.508 | <0.001* | 18.971 | 7.014 | 51.309 |
| **Genotype4845 1-1** | Absent | **Reference** | | | 1 | | |
| | Present | -1.108 | 1.209 | 0.359 | 0.330 | 0.031 | 3.530 |
| **Genotype3954 1-2** | Absent | **Reference** | | | 1 | | |
| | Present | 0.630 | 0.476 | 0.186 | 1.878 | 0.738 | 4.777 |