ASSOCIATION OF IL-1B GENE POLYMORPHISM WITH PERIODONTITIS IN INDIAN POPULATION: A SYSTEMATIC REVIEW

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ABSTRACT

Multiple factors play a pivotal role in causing periodontal tissue destruction, influenced by individual genetic pattern, ethnicity, complex host immune responses, environmental factors, systemic causes etc. Interleukin 1β (IL-1β) is one of the primary cytokine which is regulated by interleukin gene cluster located at chromosome 2, further influencing the cytokine release and thereby controlling periodontal destruction. There are several researches being undertaken in India where positive correlation between various gene polymorphisms and periodontitis has been established. Therefore present systematic review attempts to find an association between IL-1β and periodontitis in Indians. A review in literature was performed in several databases and studies published between 2010 to July 2021 were incorporated. No publication bias was found in allelic evaluation. This systematic review includes 1469 participants with 10 case/control/cross-sectional Indian studies and one review, but no substantial evidence is found to establish strong association between IL1β and periodontitis in Indian population.

Key words: Chronic Periodontitis, Aggressive periodontitis, Periodontitis, Indian, IL-1β Gene polymorphisms and SNPs

I. INTRODUCTION:

Current classification system marked the new era in Periodontology, which was introduced in year 2017 by American Academy of Periodontology and European federation of Periodontology in World Workshop on the classification of periodontal and peri-implant Diseases and conditions 2017.¹ This paradigm shift from 1999 to 2017 classification showed that apart from microbial plaque which is mandatory for destruction of periodontal tissues, systemic and environmental conditions do play a crucial role.² The progression of periodontal disease depends on individual genetic pattern, further varying among races. In a Survey by World Health Organization, prevalence of chronic periodontitis (CP) in North Indian population is 35.4% in between the age group of 35–44 years and further modified by tobacco usage, and diabetic status are well-established risk factors.³ Genetic pattern plays a key role in regulating and influencing the disease progression. There is substantial evidence in literature that periodontitis can be associated with genes linked for regulating IL-1β, Interleukin1α (IL-1α), Vitamin D Receptor, FcγR, COX-2, Taq1, IL-6, TLRs, TNF-α, MMPs, CD14 etc. IL-1β polymorphisms at +3954,-511 and -31, studied across the globe and in Indian population.

The several studies done by Researchers in a quest to find link between gene polymorphisms and periodontitis. Among them most widely studied polymorphism is Interleukin 1β. Interleukin-1β coded by gene cluster that can influence three inflammatory mediators IL-1β, IL1α and IL1RA (receptor antagonist).

IL-1β is has a positive correlation with tissue destruction under the influence of plaque pathogenic bacteria and their products. It also regulates host immune response by having influence on defense cells (macrophage, monocytes etc) ⁴

The present systematic review focuses on the question Is there a prevalence of IL-1 β gene polymorphisms in Indian periodontitis patients.

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II. MATERIAL AND METHOD:

Scope
The present systematic review focuses on providing a comprehensive summary of the evidence of IL-1β gene polymorphisms associated with Periodontitis in Indian population. Study designs which are case controls and cross-sectional having a mean age of 41.5 years (18-65 years), periodontitis of both types (chronic or aggressive/both) as per American academy classification of 1999 classification and European world workshop 2017 classification, were included in systematic review. The exclusion criteria was patients suffering from systemic diseases, smokers, pregnant and lactating females, history of bleeding disorders or any kinds of syndromes, antibiotics past 3 months, other than Indian study and articles published only in English language.

Search and screening
The electronic search strategy included the search of electronic databases from 2010 to July 2021 using MESH terms *Periodontitis/ Chronic periodontitis, aggressive periodontitis, Indian, IL-1β Gene polymorphisms,* and *SNPs.* Strategy was set as a priori according to each database (Cochrane Library, Ovid, MEDLINE, EMBASE). The electronic search framework was developed based on IL-1β gene polymorphisms, Indian and periodontitis search terms, tested to confirm its suitability to the focus of the systematic review.

Data acquisition
Data was abstracted from full-text articles directly into electronically generated evidence table templates. On included study data abstraction was done independently and cross checked to validate accuracy of the data abstraction

Data synthesis
This was done using descriptive method and all included studies and review were summarized and further checked for study variations in study characteristics (populations, outcomes, design, quality and results).

<table>
<thead>
<tr>
<th>Author and Year</th>
<th>Polymorphisms/Subject type</th>
<th>N/Geographical area</th>
<th>Classification</th>
<th>Association</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prakash et al 2010⁵</td>
<td>IL-1β +3954/CP/Healthy</td>
<td>50/25 South India</td>
<td>AAP 1999</td>
<td>CC/TT +</td>
</tr>
<tr>
<td>Shete et al 2010⁶</td>
<td>IL1β +3953,-511/CP/GAP/Healthy</td>
<td>198/ South India</td>
<td>AAP 1999</td>
<td>+3954 -511</td>
</tr>
<tr>
<td>Gayathri R et al 2011⁷</td>
<td>IL-1A +4845 and IL-1B +3954/CP/Healthy</td>
<td>51/52 South India</td>
<td>AAP 1999</td>
<td>-</td>
</tr>
<tr>
<td>Archana et al 2012 ⁸</td>
<td>IL1α +4845 IL1β +3954/mild CP/moderate CP/severe CP/healthy</td>
<td>15/15/15/15 South India</td>
<td>AAP 1999</td>
<td>+ advanced cases</td>
</tr>
<tr>
<td>Masamatti S et al 2012⁹</td>
<td>IL-1β +3954/CP/GAP/Healthy</td>
<td>30/30/30 South India</td>
<td>AAP 1999</td>
<td>+ CP</td>
</tr>
<tr>
<td>Amrisetty et al 2014¹⁰</td>
<td>IL1β/CP/healthy</td>
<td>29/31 North India</td>
<td>AAP 1999</td>
<td>-511 +395 -31</td>
</tr>
<tr>
<td>Daing et al 2015¹¹</td>
<td>Interleukin (IL)-1β + 3954 (rs1143634, C &gt; T)/CP/Healthy</td>
<td>28/47 North India</td>
<td>AAP 1999</td>
<td>-</td>
</tr>
<tr>
<td>Lavu et al 2015¹²</td>
<td>IL-1β ( - 511, + 3954), IL1A ( - 889, + 4845)/CP/healthy</td>
<td>200/200 South India</td>
<td>AAP 1999</td>
<td>+</td>
</tr>
<tr>
<td>Lavu et al 2015¹²</td>
<td>IL-1β +3954C/T</td>
<td>41/40 AAP</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>
### Results


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**Table: Summary of Studies**

<table>
<thead>
<tr>
<th>Year</th>
<th>Study</th>
<th>Region</th>
<th>Number of Subjects</th>
<th>Summary</th>
<th>Total Studies Reviewed</th>
<th>Association</th>
</tr>
</thead>
<tbody>
<tr>
<td>2017</td>
<td>Satija et al</td>
<td>South India</td>
<td>1999</td>
<td>Review related to all polymorphisms in Indians</td>
<td>24</td>
<td>+</td>
</tr>
<tr>
<td>2019</td>
<td>Majumder et al</td>
<td>East India</td>
<td>157/200</td>
<td>IL1α -889C/T, IL1β -31C/T, IL1B -511A/G, IL1B+3954C/T, IL2 -330 T/G, IL4 -33C/T, IL6 -597 G/A, IL8 -251A/T, IL10 -819C/T, IL10 -592A/C, IL13 -1111C/T</td>
<td>6</td>
<td>+</td>
</tr>
</tbody>
</table>

N: Number of subjects

CP: Chronic periodontitis

GAP: Generalized aggressive periodontitis

Association

- Non association

**Figure 1:** Flow diagram for identification, screening, eligibility and analysis of studies included in systematic review.

Records screened through database 35

Records after elimination 32

Duplicates removed 3

Papers screened 29

Papers Excluded =18
Based on Inclusion criteria n= 3
Other polymorphisms n= 15

Full text articles 11

10 Indian study and one Indian review included in systematic review n=11

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found that evidence exists between Interleukin 1 β +3954C/T and -511 A/G with chronic periodontitis in south Indian population.

### III. DISCUSSION:

Indian studies done on 763 CP patients and 706 healthy controls in various parts of India (predominantly southern part) have shown association between the IL-1β and CP.

Interleukin 1 β is widely studied gene marker across the globe. The first study done, showing increased risk of CP associated with the variations in IL-1 cluster was supported by Kornman et al 1997.

Numerous systematic reviews based on association between IL-1 β and CP exist, which are based on the geographical areas including Caucasians, Asians and mixed population. Deng et al 2013 in his meta-analysis in Asian and Caucasians have shown strong association of IL-1β and Chronic periodontitis. Ma et al 2015 meta analysis have also investigated the association of CP with IL-1 β polymorphism.

Meta-analysis by da Silva et al, 2017 showed T allele in rs1800587 IL-1β polymorphism escalates the risk to periodontitis.

Huang W et al 2017 IL-1β rs1143627 polymorphism is not related to periodontitis susceptibility in the overall population based on the current evidence, but further studies are required in more large scale sample size with risk factor adjusted.

Hong et al 2018 in Caucasians, Asians and Brazilian population lacks evidence of association of IL1 β polymorphisms in Korean population and statistically less evidence to prove it association in Caucasians.

Heidieri et al 2019 showed that evidence exists that SNPs in the IL-1α, IL-1β, IL1RN, IL-6, IL-10, TNF-α, TGF-β1, IFN-γ and VDR may be associated with CP susceptibility.

In the present systematic review there are total 11 studies considered from which majority of studies have shown the association of periodontitis with IL-1β polymorphism mostly at location +3954, and -511. However, considering the limitations in the Indian study firstly, the small sample size, secondly Haplotypic evaluation can provide more authenticity to the study, thirdly among Indians presence of geographical diversity, environmental conditions and various genetic factors further influencing the gene expression needs to be considered. Fourthly the subject selection criteria is different in most of the studies, therefore there is less evidence present to show strong association between IL-1β and periodontitis among Indians. Moreover most of the studies in India are being done in Southern part of India therefore considering all the above limitations, the statement cannot be generalized for entire nation since contrasting studies have also been reported, showing negative correlation of IL1β and Periodontitis. Therefore it can be concluded that there is association of IL1 β in South Indians, but still more studies on larger sample with multicenter trials covering bigger geographical locations across the country needs to be attempted to provide substantial evidence for the same.

It is recommended, that further research is needed to validate the biologic basis for genetic susceptibility testing, to evaluate the ability of IL-1 genotypes to predict disease initiation and to evaluate the effectiveness of IL-1 genotyping in making diagnostic or treatment intervention strategies

### REFERENCES:


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