

**THE ASSOCIATION BETWEEN TUMOR NECROSIS  
FACTOR-ALPHA (TNF- $\alpha$ ) GENE POLYMORPHISM  
AND SUSCEPTIBILITY TO DIFFERENT FORMS OF  
PERIODONTAL DISEASE**

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# *List of Contents*

<b>Serial</b>	<b>Title</b>	<b>page</b>
<b>1</b>	<b>Introduction and Review of Literature</b>	<b>1</b>
<b>2</b>	<b>Aim of the Study</b>	<b>34</b>
<b>3</b>	<b>Subjects and Method</b>	<b>35</b>
<b>4</b>	<b>Results</b>	<b>53</b>
<b>5</b>	<b>Discussion</b>	<b>82</b>
<b>6</b>	<b>Summary</b>	<b>91</b>
<b>7</b>	<b>Conclusion</b>	<b>94</b>
<b>8</b>	<b>Recommendation</b>	<b>95</b>
<b>9</b>	<b>References</b>	<b>96</b>
<b>10</b>	<b>Arabic Summary</b>	<b>133</b>

# *List of Tables*

<b>Serial</b>	<b>Title</b>	<b>Page</b>
Table (1):	Disease-associated polymorphisms	20
Table (2):	Studied TNF- $\alpha$ gene polymorphisms	32
Table (3):	The means, SD values and results of ANOVA test for comparison between ages in the four groups.	56
Table (4):	The means, SD values and results of ANOVA test for comparison between ages in the four groups.	57
Table (5):	The means, SD values and results of ANOVA test for comparison between GI in the four groups	58
Table (6):	The means, SD values and results of ANOVA test for comparison between PI in the four groups	59
Table (7):	The frequencies, percentages and results of chi-square test for comparison between genotype distributions in the four groups	65
Table (8):	The frequencies, percentages and results of chi-square test for comparison between genotype distribution in gingivitis and control groups	66
Table (9):	The frequencies, percentages and results of chi-square test for comparison between genotype distribution in gingivitis and control groups	67
Table (10):	The frequencies, percentages and results of chi-square test for comparison between genotype distribution in aggressive periodontitis and control groups	68
Table (11):	The frequencies, percentages and results of chi-square test for comparison between genotype distribution in gingivitis and chronic periodontitis groups	69
Table (12):	The frequencies, percentages and results of chi-square	70

	test for comparison between genotype distribution in gingivitis and aggressive periodontitis groups	
Table (13):	The frequencies, percentages and results of chi-square test for comparison between genotype distribution in chronic periodontitis and aggressive periodontitis groups	71
Table (14):	The frequencies, percentages and results of chi-square test for comparison between allele distribution in gingivitis and control groups	76
Table (15):	The frequencies, percentages and results of chi-square test for comparison between allele distribution in chronic periodontitis and control groups	77
Table (16):	The frequencies, percentages and results of chi-square test for comparison between allele distribution in aggressive periodontitis and control groups	78
Table (17):	The frequencies, percentages and results of chi-square test for comparison between allele distribution in gingivitis and chronic periodontitis groups	79
Table (18):	The frequencies, percentages and results of chi-square test for comparison between allele distribution in gingivitis and aggressive periodontitis groups	80
Table (19):	The frequencies, percentages and results of chi-square test for comparison between allele distribution in chronic periodontitis and aggressive periodontitis groups	81

# *List of Figures*

<b>Serial</b>	<b>Title</b>	<b>Page</b>
Fig. (1):	Diagrammatic representation of the main regions of the MHC. Highlighted below is the 'TNF locus' together with some of the polymorphic sites that are known within the TNF locus. Those defined by RFLP are highlighted above the line whilst the microsatellites (TNF a, b, c, e) are delineated above. LT $\alpha$ is synonymous with TNF $\beta$	23
Fig. (2):	A case of 33 years old female patient with chronic periodontitis	39
Fig. (3):	Showing a case of 20 years old female with Aggressive Periodontitis	40
Fig. (4):	Periapical radiograph of aggressive periodontitis cases	41
Fig. (5):	Panoramic radiograph of aggressive periodontitis case	41
Fig. (6):	Periapical radiograph of a chronic periodontitis case	42
Fig. (7):	Kit used for DNA extraction	48
Fig. (8):	Cooling Centrifuge	49
Fig. (9):	Apparatus used for PCR	49
Fig. (10):	Microwave (For gel dissolution).	50
Fig. (11):	Apparatus for Electrophoresis	50
Fig. (12):	Ultraviolet Transilluminator	51
Fig. (13):	Representative agarose gel electrophoresis of 4 periodontitis patients. Homozygous AA, Heterozygous AG, Homozygous GG.	51
Fig. (14):	Representative agarose gel electrophoresis of 4 control subjects. Homozygous AA, Heterozygous AG	51
Fig. (15):	Representative agarose gel electrophoresis of 3 gingivitis subjects. Homozygous AA, Heterozygous AG and Homozygous GG	51
Fig. (16):	Bar Chart representing means of age in the four groups.	56
Fig. (17):	Bar Chart representing means of gender in the four groups.	57
Fig. (18):	Bar Chart representing means of GI in the four groups.	58
Fig. (19):	Bar Chart representing means of PI in the four groups.	59
Fig. (20):	Bar Chart representing the percentages for comparison between genotype distributions in the four groups.	65



<b>Fig. (21):</b>	<b>Bar Chart representing the percentages for comparison between genotype distribution in gingivitis and control groups</b>	<b>66</b>
<b>Fig. (22):</b>	<b>Bar Chart representing the percentages for comparison between genotype distribution in chronic priodontitis and control groups</b>	<b>67</b>
<b>Fig. (23):</b>	<b>Bar Chart representing the percentages for comparison between genotype distribution in aggressive priodontitis and control groups</b>	<b>68</b>
<b>Fig. (24):</b>	<b>Bar Chart representing the percentages for comparison between genotype distribution in chronic priodontitis and gingivitis groups</b>	<b>69</b>
<b>Fig. (25):</b>	<b>Bar Chart representing the percentages for comparison between genotype distribution in aggressive priodontitis and gingivitis groups</b>	<b>70</b>
<b>Fig. (26):</b>	<b>Bar Chart representing the percentages for comparison between genotype distribution in aggressive priodontitis and chronic periodontitis groups</b>	<b>71</b>
<b>Fig. (27):</b>	<b>Bar Chart representing the percentages for comparison between allele distribution for in gingivitis and control groups</b>	<b>76</b>
<b>Fig. (28):</b>	<b>Bar Chart representing the percentages for comparison between allele distribution for in chronic periodontitis and control groups</b>	<b>77</b>
<b>Fig. (29):</b>	<b>Bar Chart representing the percentages for comparison between allele distribution for in aggressive periodontitis and control groups</b>	<b>78</b>
<b>Fig. (30):</b>	<b>Bar Chart representing the percentages for comparison between allele distribution for in chronic periodontitis and gingivitis groups</b>	<b>79</b>
<b>Fig. (31):</b>	<b>Bar Chart representing the percentages for comparison between allele distribution for in aggressive periodontitis and gingivitis groups</b>	<b>80</b>
<b>Fig. (32):</b>	<b>Bar Chart representing the percentages for comparison between allele distribution for in aggressive periodontitis and chronic periodontitis groups</b>	<b>81</b>

## *list of Abbreviations*

<b>A :</b>	<b>Adenosine</b>
<b>A. a. :</b>	<b>Aggregatebacter actinomycetem comitans</b>
<b>ACE :</b>	<b>Angiotensin converting enzyme</b>
<b>AF :</b>	<b>Amniotic fluid</b>
<b>AIDS :</b>	<b>Acquired Immunodeficiency Syndrome</b>
<b>B-cells :</b>	<b>B-lymphocytes</b>
<b>BD :</b>	<b>Behcet's disease</b>
<b>C :</b>	<b>Cytosine</b>
<b>C2 :</b>	<b>Complement component 2 gene</b>
<b>C4 :</b>	<b>Complement component 4 gene</b>
<b>CAL :</b>	<b>Clinical attachment loss</b>
<b>CCL :</b>	<b>C-C Chemokine Ligand</b>
<b>CCR :</b>	<b>C-C Chemokine Receptor</b>
<b>CD14 :</b>	<b>Cluster of differentiation 14</b>
<b>CEJ :</b>	<b>Cemento-enamel junction</b>
<b>Ch6 :</b>	<b>Chromosome 6</b>
<b>CIs :</b>	<b>Confidence intervals</b>
<b>CTLA4 :</b>	<b>Cytotoxic T-lymphocyte antigen 4</b>
<b>DNA :</b>	<b>Deoxyribonucleic acid</b>
<b>EOP :</b>	<b>Early-onset periodontitis</b>
<b>FcγRIIB1 :</b>	<b>Fc-gamma receptor type II B1</b>
<b>G :</b>	<b>Guanine</b>
<b>G-EOP :</b>	<b>Generalized early-onset periodontitis</b>
<b>GCF :</b>	<b>Gingival crevicular fluid</b>
<b>GI :</b>	<b>Gingival index</b>
<b>GM-CSF :</b>	<b>Granulocyte monocyte -colony stimulating factor</b>
<b>HIV :</b>	<b>Human Immunodeficiency Virus</b>
<b>HLA :</b>	<b>Human Leukocyte Antigen</b>
<b>HSP :</b>	<b>Heat Shock Proteins gene</b>

<b>IBDs :</b>	<b>Inflammatory bowel diseases</b>
<b>IL:</b>	<b>Interleukin</b>
<b>IL-1RA :</b>	<b>IL-1 receptor antagonist</b>
<b>IL-5R<math>\alpha</math> :</b>	<b>IL-5 receptor alpha</b>
<b>IL-6R :</b>	<b>IL-6 receptor</b>
<b>IL-12 R :</b>	<b>IL-12 receptor</b>
<b>IDDM :</b>	<b>Insulin-dependent diabetes mellitus</b>
<b>IFN<math>\gamma</math> :</b>	<b>Interferon gamma</b>
<b>JRA :</b>	<b>Juvenile Rheumatoid Arthritis</b>
<b>LPS :</b>	<b>Lipopolysaccharides</b>
<b>LST.1 :</b>	<b>Leukocyte-specific transcript 1 protein</b>
<b>LT :</b>	<b>Lymphotoxin</b>
<b>MHC :</b>	<b>Major histocompatibility complex</b>
<b>MHC-I A :</b>	<b>MHC class I A antigen locus</b>
<b>MHC-I B :</b>	<b>MHC class I B antigen locus</b>
<b>MHC-I C :</b>	<b>MHC class I C locus</b>
<b>MHC-I G :</b>	<b>MHC class I G locus</b>
<b>MHC-II DP :</b>	<b>MHC class II DP locus</b>
<b>MHC-II DQ :</b>	<b>MHC class II DQ locus</b>
<b>MHC-II DR :</b>	<b>MHC class II DR locus</b>
<b>MMPs :</b>	<b>Matrix metalloproteinases</b>
<b>NIH GAD :</b>	<b>NIH Genetic Association Database</b>
<b>NK cells :</b>	<b>Natural killer cells</b>
<b>NOS 3 :</b>	<b>Nitric oxide synthase 3</b>
<b>Nramp :</b>	<b>Natural resistance-associated macrophage protein</b>
<b>OMIM :</b>	<b>Online Mendelian Inheritance of Men</b>
<b>OPG :</b>	<b>Osteoprotegrin</b>
<b>ORs :</b>	<b>Odds Ratios</b>
<b>P. gingivalis :</b>	<b>Porphyromonas gingivalis</b>
<b>PCR-RFLP :</b>	<b>Polymerase Chain Reaction-Restriction Fragment Length Polymorphism</b>

<b>PGE2 :</b>	<b>Prostaglandin E2</b>
<b>PI :</b>	<b>Plaque index</b>
<b>PTB :</b>	<b>Preterm birth</b>
<b>R-allele :</b>	<b>Rare allele</b>
<b>RA :</b>	<b>Rheumatoid arthritis</b>
<b>RAS :</b>	<b>Recurrent Aphthus Stomatitis</b>
<b>RFLP :</b>	<b>Restriction Fragment Length Polymorphism</b>
<b>SD :</b>	<b>Standard deviation</b>
<b>SLE :</b>	<b>Systemic Lupus Erythematosis</b>
<b>SNP :</b>	<b>Single nucleotide polymorphism</b>
<b>sPTB :</b>	<b>Spontaneous preterm birth</b>
<b>SS :</b>	<b>Sjogren's syndrome</b>
<b>STRs :</b>	<b>Simple tandem repeats</b>
<b>T :</b>	<b>Thymine</b>
<b>Taq :</b>	<b>Thermus aquaticus</b>
<b>T-cells :</b>	<b>T-lymphocytes</b>
<b>TB :</b>	<b>Tuberculosis</b>
<b>TBE :</b>	<b>Tris-borate EDTA</b>
<b>TGF <math>\beta</math> :</b>	<b>Transforming growth factor beta</b>
<b>TNF :</b>	<b>Tumor necrosis factor</b>
<b>TNFRs :</b>	<b>TNF receptors</b>
<b>TP 53 :</b>	<b>Tumor protein 53</b>
<b>Tpm1 :</b>	<b>T-cell phenotype modifier-1</b>
<b>VNTRs :</b>	<b>Variable number of tandem repeats</b>

## **Abstract**

This study was performed on 160 patients, divided into four groups, 40 normal healthy controls, 40 suffering from gingivitis, 40 suffering from chronic periodontitis and 40 suffering from aggressive periodontitis.

The results suggested that GG genotype is associated with chronic periodontitis in Egyptian patients and that harboring the G allele is associated with the development of aggressive periodontitis and chronic periodontitis.

**Key words:** TNF- $\alpha$ , Cytokines, Gene Polymorphism, Periodontitis

## **المستخلص**

GG

G

- :

## **INTRODUCTION AND REVIEW OF** **LITERATURE**

Periodontal diseases are chronic inflammatory conditions which result in loss of the tooth-supporting structures including osteoclastic resorption of alveolar bone in the jaw (*Page and Schroeder, 1982*).

Periodontal diseases comprise a variety of conditions affecting the health of the periodontium. Although the classification scheme defined at the 1989 World Workshop in Clinical Periodontics subdivided these diseases into a number of clinically defined subforms, subsequent attempts to categorize patients according to the defined criteria have demonstrated the considerable problem of overlap in the disease definitions (*Armitage, 1996*).

Later on, periodontal diseases were classified into gingivitis, chronic periodontitis, aggressive periodontitis, periodontitis as a manifestation of systemic disease, necrotizing periodontal diseases, periodontal abscess, periodontitis with endodontic lesions and finally, developed and acquired deformations and conditions (*ADA classification, 1999*).

Research dating back to the 1980s has shown that relatively few sites with gingivitis go on to develop periodontitis (*Listgarten et al., 1985; Haffajee et al., 1988; Okamoto et al., 1988; Lindhe et al., 1989; Machtei et al., 1999; Kornman, 2001*).

Clinical models of disease activity in periodontitis range from a continuous progression of disease during which loss of attachment

occurs at a slow rate over long periods of time to an episodic burst model in which loss of attachment occurs relatively rapidly during short periods of disease activity (*Socransky et al., 1984; Jeffcoat and Reddy, 1991; Reddy and Jeffcoat, 1993*).

Development of gingivitis requires the presence of plaque bacteria (*Löe et al., 1965; Theilade et al., 1966*), which are thought to induce pathological changes in the tissues by both direct and indirect means (*Page, 1986*).

The early vascular changes occur in the periodontium, with exudation and migration of phagocytic cells, including neutrophils and monocytes/macrophages, into the junctional epithelium and gingival sulcus, resulting in initial gingival inflammation. These changes are accompanied by increases in the size of the connective tissue infiltrated by leukocytes, loss of perivascular collagen fibres, and proliferation of junctional epithelium. During the early stage, the inflammatory infiltrate is mostly T-cells, whereas in the established lesions, B-cells become the most common inflammatory cells (*Page and Schroeder, 1976*).

The contribution of the acquired immune cells in the progression of periodontal disease has long been controversial, with its exact role in the protection versus destruction of the host's periodontium being unclear (*Klausen, 1991; Ebersole and Taubman, 1994; Zambon, 1996*).

Although direct evidence for specific mechanisms explaining the appearance and progression of gingivitis lesions is not available, the chronic inflammatory infiltrate characteristic of the early and