

## Correlation between TGF- $\beta$ 1 with Immunoglobulin IgG in Patients with Periodontitis

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### ABSTRACT

Periodontitis is a microbially driven inflammatory conditions of the gingiva causing destruction of the ligaments and alveolar bone supporting the teeth resulting in oral malodor and tooth loss. The aim of the present research was to estimate the serum level of TGF- $\beta$ 1 in patients with periodontitis compared with healthy individual and to assess the relationship between the TGF- $\beta$ 1serum and the Immunoglobulin(IgG). A total of 60 patients were included in this research and 20 individuals was healthy group. Serum samples separated from the whole blood of patients and healthy. Level of TGF- $\beta$ 1 was determined by an enzyme linked immunosorbent assay. The results showed statistically significant elevation in level of TGF- $\beta$ 1 in patients than in healthy group and there was a significant correlation between the levels of TGF- $\beta$ 1 and immunoglobulin IgG in patients with periodontitis.

**Keywords:**immunoglobulin, IgG, periodontitis

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### INTRODUCTION

Periodontal disease is one of the most prevalent diseases worldwide and includes two major conditions, gingivitis and periodontitis. It is a microbially-driven inflammatory condition of the gingivae causing destruction of the ligament and alveolar bone supporting the teeth resulting in oral malodor and tooth loss with the resultant loss of quality of life<sup>1</sup>. Cytokines play a key role in a number of different physiologic processes, but if secreted inappropriately, they also induce pathology. In periodontal disease, the balance between pro- and anti-inflammation is directed towards proinflammatory activity<sup>2</sup>.

Transforming Growth Factor  $\beta$ 1 (TGF- $\beta$ 1) is one of the cytokines involved in the complex mechanism of periodontal disease<sup>3</sup>. The higher concentration of TGF- $\beta$ 1 has been detected from periodontal tissue and gingival pocket fluid of patients with chronic periodontitis<sup>4</sup>. It is a protein with anti-inflammatory properties and seems to have an important role in regulating the development and progression of periodontal diseases<sup>5,6</sup>. Vikram *et al*, suggested that TGF- $\beta$ 1 may play a role in the pathogenesis and diagnosis of periodontal disease and could be considered as a disease predictive biomarker. Mize *et al*, found that the gingival expression levels of TGF $\beta$ 1 mRNA in individuals with periodontitis are upregulated and correlated. In addition, Khalaf and coworkers, indicated that the ease of sampling and analyzing cytokine expression profiles, including TGF- $\beta$ 1, in saliva and gingival crevicular fluid (GCF) may serve to predict the progression of periodontitis and associated systemic inflammatory diseases.

IgG is the immunoglobulin class is found in highest concentration in blood, it plays the major role in antibody-mediated defense mechanisms<sup>10</sup>. Some studies revealed increased serum IgG, IgA and IgM in patients with periodontitis<sup>11</sup>, while others showed no significant differences in serum IgG levels between periodontitis patients and healthy individuals<sup>12</sup>.

### METHODS

Sixteen patients (male =39 and female=21) participated in this study, and twenty healthy individual (male=11, female=9) as control group. The specimens were collected between February to May 2017 from faculty of Dentistry at University of kufa with the assistance of dentists.

Five ml of venous blood were obtained from each individual and pushed slowly into disposable tubes and allowed to clot at room temperature for 30 minutes and then centrifuged at 2000  $\times$ g for approximately 15 minutes then the serum was obtained and stored at -20°C until analysis. The levels of TGF- $\beta$ 1 and IgG were measured by using commercially available enzyme linked immunosorbent assay (ELISA)kits and performed as recommended in leaflet with kit (Elabscience, USA). Statistical analysis was performed by using SPSS v.24 software program. It Application t- independent test for all variables that followed normality of the distribution, and non- parametric tests for variables that weren't followed normality of the distribution was including Kruskal-Wallis Test (Multiple Comparisons) and Mann-Whitney Test, in addition to Chi-square Test. Also, it was drawing histograms and figures of correlation test by Microsoft Excel 2013. Data were expressed as (mean  $\pm$

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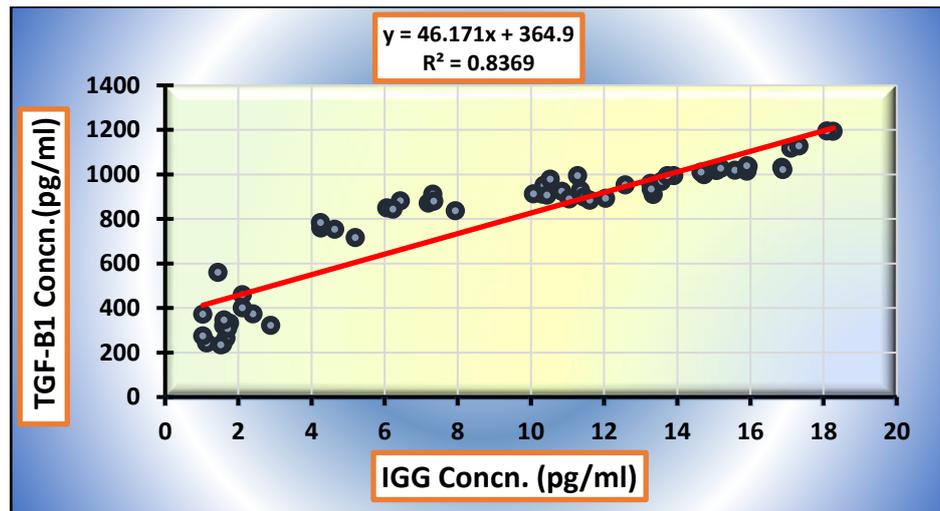


Figure 1: correlation between concentration of IgG with TGF-β1.

Table 1: Comparison of the level of serum TGF-β1 in patients with periodontitis and control group.

Type of cytokines	Concentration pg/ml	
	Mean ± Sd	
	patients	Control
TGF-β1 (pg/ml)	796.80 ± 285.87 *	133.26±31.55

\*Significant differences at  $p \leq 0.05$  between patients and control groups.

Table 2: Comparison the level of serum immunoglobulin IgG between patients and healthy group.

Type of immunoglobulin	Concentration	
	Mean ± Sd	
	Patients	Control
IgG (pg/ml)	9.35 ± 3.66 *	0.67 ± 0.28

Sd), statistically significant at  $p$ - value < 0.05.

## RESULTS AND DISCUSSION

The results in this research showed that a significant statistical difference between the levels of TGF-β1 in patients and healthy control. This result agreement with many studies such as<sup>13</sup> show that was a significant association between C/C genotype and generalized aggressive periodontitis, and it may be more prone to the risk of development aggressive periodontitis. TGF-β is highly preserved and over expressed cytokines and most cells express many of the TGF-β receptor family<sup>14</sup>. Morandini *et al*, show that the gingival fibroblast produced a significantly increased level of TGF-β compared with control. Various studies show that in periodontal and peri-implant tissues, cytokines such as TNF-α and TGF-β have main role in arrangement and magnification the inflammatory response<sup>16</sup>. Gurkan *et al*, found that aggressive and chronic periodontitis had significantly increased total amount GCF in TGF-β1 compared to healthy group.

Immunoglobulins IgG play important role in inflammatory disease such periodontitis as IgG are the essential circulating antibody in the blood and can passes

from blood in to tissue<sup>10</sup>. AL- Jebouri and AL-Hadeethi, showed that was higher significantly of IgG with sever periodontitis, and significant positive linear correlation between C3and C4, C4 with IgA. Other studies reported by Galaviz *et al*, that 57% of patients with periodontitis were positive IgG. Califano *et al* and Kobayashi *et al*, mentioned that the elevation in level of IgG consider a result of host response to bacterial colonization .Other research found that IgG have been considered important antibody in prevention periodontal damage in patients with aggressive and chronic periodontitis<sup>22</sup>. On the other hand study by<sup>23</sup> showed that levels of total IgG ,IgM and IgA were not different between patients and control ,but observed a higher levels of IgG1 and IgG2 in periodontitis . IgG might enhance phagocytosis and dispatch of oral microorganisms through stimulation of complement or opsonization<sup>24</sup>.

Several biological media such as serum, saliva, and gingival crevicular fluid are used to limitation biomarker in periodontal health and disease. A lone biomarker will not capable to portend periodontal disease activity and severity. Also, consolidation of biomarker is used to portend the disease activity<sup>25</sup>. Figure (1) shows that, a significant correlation between the levels of TGF-β1 in patients with periodontitis and immunoglobulin IgG ( $r=0.915^{**}$ ).

## CONCLUSION

There was a positive correlation between the level of TGF-β1 concentration and IgG concentration in the sera of patients with periodontitis.

## REFERENCES

1. Al-Harathi, L. S., Cullinan, M. P., Leichter, J. W., and Thomson, W. M. (2013). The impact of periodontitis on oral health-related quality of life: a review of the evidence from observational studies. *Aust. Dent. J.* 58, 274–277.
2. Graves, D. T. & Cochran, D. (2003) The contribution of interleukin-1 and tumor necrosis factor to

- periodontal tissue destruction. *J. Periodontology* 74, 391–401.
3. de Souza AP, Trevilatto PC, Scarel-Caminaga RM, et al. (2003) Analysis of the TGF-beta1 promoter polymorphism (C-509T) in patients with chronic periodontitis. *J. Clin Periodontol.*30(6):519-23.
  4. Holla LI, Fassmann A, Benes P, et al. (2002) polymorphisms in the transforming growth factor-beta 1 gene (TGF-beta 1) in adult periodontitis. *J. Clin Periodontol.* 29(4):336-41.
  5. Buduneli, N., Kutukculer, N., Aksu, G. & Atilla, G. (2001) Evaluation of transforming growth factor-b1 level in crevicular fluid of cyclosporine A-treated patients. *J. Periodontology.* 72, 526–531.
  6. Wright, H. J., Chapple, I. L. C. & Matthews, J.B. (2003) Levels of TGF-b1 in gingival crevicular fluid during 21-day experimental model gingivitis. *J. Oral Diseases.* 9, 88-94.
  7. Vikram, V., Ramakrishnan, T., Anilkumar, K. and Ambalavanan, N. (2015). Changes in Transforming Growth Factor -β1 in Gingival Crevicular Fluid of patients with Chronic periodontitis Following periodontal Flap Surgery. *J. Clin. Diagn. Res.* 9:13-6.
  8. Mize, T. W., Sundaraj, K. P., Leite, R. S. and Hunag, Y. (2015). Increased and correlated expression of connective tissue growth factor and transforming growth factor beta 1 in surgically removed periodontal tissues with chronic periodontitis. *Periodontal Res.* 50:315-9.
  9. Khalaf H, Lonn J, Bengtsson T. (2014) Cytokines and chemokines are differentially expressed in patients with periodontitis: possible role for TGF-beta1 as a marker for disease progression. *Cytokine.* 67:29–35.
  10. Kulshrestha R., Srinivasa T.S. and Biswas, J. (2013). Role of Immunoglobulin G and A in Periodontitis: A Review. *J. PURE. APPL. MICROBIO.* 7(1):673-676.
  11. Huerto, C.G., Toro, J.J. and LaSalma, G. (2016). Levels of IgM, IgG and IgA antibodies in gingival crevicular fluid of subjects with severe chronic periodontitis. *Afr. J. Infect. Dis. Res.* 3(1):084-089.
  12. Srinivasan P.C., Nsvk, D., Venkateshwarw S. (2012). Immunoglobulin Levels and Periodontal Disease - A Clinical Immunological Study. *J. Sci. Rep. India.* 1(4):254.
  13. Arab, H.R., Afshari, J.T., Radvar, M., Tagavi, A.M., Sargolzaee N., Mokhtari, M.R. and Farazi, F. (2012). Association between TGF-β1-509 Gene Polymorphism with Aggressive Periodontitis. *Int J. Gen. Eng.* 2(4):33-37.
  14. Chen W, Wahl SM. (2002). TGF-beta: receptors, signaling pathways and autoimmunity. In: Altman A, editor. *Signal transduction pathways in autoimmunity.* Basel: Karger. 62-91.
  15. Morandini, A.C.F., Sipert, C.R., Ramos Junior, E.S., Brozowski, D.T.H., Santos, C.F. (2011). Periodontal ligament and gingival fibroblast participate in the production of TGF-β, interleukin (IL)-8 and IL-10. *J. Braz Oral Res.* 25(2):157-62.
  16. Schierano, G., Bellone, G., Cassarino, E., Pagano, M., Preti, G. & Emanuelli, G. (2003). Transforming growth factor-beta and interleukin10 in oral implant sites in humans. *J. Dental Research.* 82, 428–432.
  17. Gurkan, A., Emingil G., Cinarcik S. and Berdeli, A. (2006). Gingival crevicular fluid transforming growth factor -β1 in several forms of periodontal disease. *J. Arch. Oral Biol.* 51:906-912.
  18. AL-Jebouri, M.M., AL-Hadeethi, H.M. (2015). Some immunological aspects of Iraqi patients with periodontal disease. *w.j.p.r.* 4(7):1869-1882.
  19. Galaviz LA, Bernal MP, Medina MA, Rodríguez SS, and Luna ML. (2010) Nuclear and cytoplasmic antibodies in severe periodontitis. *J. Immunology.* 184(48): 16.
  20. Califano JV, Chou D, Lewis JP, Rogers JD, Best AM, and Schenkein HA. (2004). Antibody reactive with *Porphyromonas gingivalis* hemagglutinin in chronic and generalized aggressive periodontitis. *J. Periodontol. Res.* 39: 263-268.
  21. Kobayashi T, Kaneko S, Tahara T, Hayakawa M, Abiko Y, and Yoshie H. (2006). Antibody responses to *Porphyromonas gingivalis* hemagglutinin A and outer membrane protein in chronic periodontitis. *J. Periodontol.* 77: 364-369.
  22. Quinn SM, Zhang JB, Gunsolley JC, Schenkein JG, Schenkein HA, and Tew JG. (1996). Influence of smoking and race on immunoglobulin G subclass concentrations in early-onset periodontitis patients. *Infect. Immun.* 64: 2500-2505.
  23. Graswinckel, J.E.M., van der Velden U., van Winkelhoff A.J., Hoek, F.J., Loos, B.G. (2004). Plasma antibody levels in periodontitis patients and controls. *J. Clin. periodontol.* 31:562-568.
  24. Streckfus CF, Bigler LR. (2002). Saliva as a diagnostic fluid. *J. Oral Dis.* 8(2):69-76.
  25. Pavankumar, A., Jagdishreddy, G and Raja Babu p. (2015). Biomarker in periodontal Disease. *J. Mol. Biomark Diagn.* 6(3):3-6.