

# Impact of Tumor Necrosis Factor Alfa on Dental Caries Development in Children with Severe SNC Disorders

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## Abstract

The aim of the present study was to perform a comparative evaluation of TNF- $\alpha$ level in saliva and blood serum at children with severe disorders of the central nervous system (CNS) and conventionally healthy children in order to highlight the role of TNF- $\alpha$ in the initiation and development of dental caries. To assess the degree of the dental caries (DC) development were clinically examined 1272 children aged between 1 and 18 years. The study included 636 children with severe CNS disorders, which constituted the research group (L1) and 636 conditionally healthy children formed the control group (L0). The concentration of TNF- $\alpha$  in the oral fluid (OF) and blood serum was estimated in 212 children randomly selected from both groups. In children with severe CNS diseases TNF-a concentration in saliva is 5.53 times higher, and in blood serum it is 10.19 times higher compared to healthy children. In children with severe CNS diseases there was revealed a strong inverse relationship between TNF- $\alpha$  concentration in saliva and blood serum and the chances of avoiding new caries development, as opposed to the inverse average relationship estimated in healthy children. Excess TNF- $\alpha$  production, both locally and systemically influenced increased caries risk and dental caries morbidity in children with severe CNS diseases, which is necessary to consider when planning individualized prevention measures.

Keywords: children dental caries, severe disorders, central nervous system,



#### References

1. Nagasawa, Y., et al.: Title IgA nephropathy and oral bacterial species related to dental caries and periodontitis. Int. J. Mol. Sci. **2**(23), 725 (2022). <u>https://doi.org/10.3390/ijms23020725</u>

2. Nero, N.R.,Diniz,D.R.: Immunological aspects related to diseases incident in dental practice: literature review. Revista Científica Multidisciplinar Núcleo do Conhecimento **10**(15), 48–57 (2020). https://doi.org/10.32749/nucleodoconhecimento.com.br/dentistry/diseases

3. Babu, A.L., et al.: Immunology of dental caries. Biomed. Pharmacol. J. **2**(9), 823–826 (2016). https://doi.org/10.13005/bpj/1009

4. Yang, Y., et al.: Comparison of immunological andmicrobiological characteristics in children and the elderly with or without dental caries. Eur. J. Oral Sci. **2**(123), 80–87 (2015). https://doi.org/10.1111/eos.12172

5. Galler, K.M., et al.: Inflammatory response mechanisms of the dentine-pulp complex and the periapical tissues. Int. J. Mol. Sci. **3**(22), 1480 (2021). <u>https://doi.org/10.3390/ijms22031480</u>

6. Heigetyan, A., et al.: The immunologic indicators in patients with caries of contact surfaces of lateral teeth. Klin. Lab. Diagn. **8**(60), 52–54 (2015)

7. Rinderknecht, C., et al.: Associations between salivary cytokines and oral health, age, and sex in healthy children. Sci. Rep. **1**(12), 15991 (2022). <u>https://doi.org/10.1038/s41598-022-20475-2</u>

8. Gornowicz, A., et al.: Pro-inflammatory cytokines in saliva of adolescents with dental caries disease. Ann. Agric. Environ. Med. **219**, 711–716 (2012)

9. Tazawa, K., et al.: Revisiting the role of IL-1 signaling in the development of apical periodontitis. Front. Dent. Med. **3**, 985558 (2022). <u>https://doi.org/10.3389/fdmed.2022.985558</u>

10. Feng, Y., et al.: Role of Interleukin-17A in the Pathomechanisms of Periodontitis and related systemic chronic inflammatory diseases. Front. Immunol. **13**, 862415 (2022). https://doi.org/10.3389/fimmu.2022.862415

11. Cogulu, D., et al.: Associations of interleukin (IL)-1 $\beta$ , IL-1 receptor antagonist, and IL-10 with dental caries. J. Oral Sci. **1**(57), 31–36 (2015)

12. Horst, O.V., et al.: TGF-beta1 Inhibits TLR-mediated odontoblast responses to oral bacteria. J. Dent. Res. **88**, 333–338 (2009). <u>https://doi.org/10.1177/0022034509334846</u>



13. Medara, N., et al.: A review of T helper 17 cell-related cytokines in serum and saliva in periodontitis. Cytokine **138**, 155340 (2021). <u>https://doi.org/10.1016/j.cyto.2020.155340</u>

 Gómez-García, A.P., et al.: Overexpression of proinflammatory cytokines in dental pulp tissue and distinct bacterial microbiota in carious teeth of Mexican Individuals. Front. Cell Infect. Microbiol. 12, 958722 (2022). <u>https://doi.org/10.3389/fcimb.2022.958722</u>

15. Paqué, P.N., et al.: Salivary biomarkers for dental caries detection and personalized monitoring. J. Pers. Med. **3**(11), 235 (2021). <u>https://doi.org/10.3390/jpm11030235</u>

16. Antunes, L.A., et al.: Genetic polymorphisms in TNF-α as a potential biomarker for oral healthrelated quality of life in children. Braz. Oral Res. **2**(36), e059 (2022). <u>https://doi.org/10.1590/1807-</u> <u>3107bor-2022.vol36.0059</u>

17. Kitaura, H., et al.: Osteocyte-related cytokines regulate osteoclast formation and bone resorption. Int. J. Mol. Sci. **14**(21), 5169 (2020). <u>https://doi.org/10.3390/ijms21145169</u>

18. De Paepe, B., et al.: The tumor necrosis factor superfamily of cytokines in the inflammatory myopathies: potential targets for therapy. Clin. Dev. Immunol. Article ID 369462 (2012)

19. Kaczy'nski, T., et al.: Salivary interleukin 6, interleukin 8, interleukin 17A, and tumour necrosis factor  $\alpha$  levels in patients with periodontitis and rheumatoid arthritis. Cent. Eur. J. Immunol. **3**(44), 269–276 (2019). <u>https://doi.org/10.5114/ceji.2019.89601</u>

20. Kitaura, H., et al.: Role of the interaction of tumor necrosis factor- $\alpha$  and tumor necrosis factor receptors 1 and 2 in bone-related cells. Int. J. Mol. Sci. **3**(23), 1481 (2022). https://doi.org/10.3390/ijms23031481

21. You, K., Gu, H., Yuan, Z., Xu, X.: Tumor necrosis factor alpha signaling and organogenesis. Front Cell Dev. Biol. **9**(30), 727075 (2021). <u>https://doi.org/10.3389/fcell.2021.727075</u>

22. Tani-Ishii, N., et al.: Autocrine regulation of osteoclast formation and bone resorption by IL-1 alpha and TNF alpha. J. Dent. Res. **10**(78), 1617–1623 (1999)

23. Kurtis, B., et al.: Gingival crevicular fluid levels of monocyte chemoattractant protein-1 and tumor necrosis factor- $\alpha$  in patients with chronic and aggressive periodontitis. J. Periodontol. **11**(76), 1849–1855 (2005)

24. Leous, P., Tikhonova, S.: Caries risk assessment in young people based on the Cariogram. OHDMBSC **1**(5), 7–11 (2006)



25. Bratthall, D., Hänsel Petersson, G.: Cariogram - multifactorial risk assessment model for multifactorial disease. Commun. Dent. Oral Epidemiol. **4**(33), 256–264 (2005). https://doi.org/10.1111/j.1600-0528.2005.00233.x

26. Martusevich, A.K., Kamakin, N.F.: Crystallography of biological fluid as a method for evaluating its physicochemical characteristics. Bull. Exp. Biol. Med. **3**(143), 385–388 (2007). https://doi.org/10.1007/s10517-007-0118-7

27. Spinei, A., et al.: The study of oral liquid microcrystallization in children with gastroesophageal reflux disease. Clujul Med. **4**(84), 269–276 (2014). <u>https://doi.org/10.15386/cjmed-387</u>

28. Spinei, A.: Impact of cytokine profile on dental caries morbidity in children with severe diseases of the central nervous system. Romanian J. Dent. Med. **3**(19), 166–190 (2016)

29. Spinei, A., et al.: Particularities of the chemical composition of dental enamel in children with neuromotor disabilities and gastro-esophageal reflux disease. Human Vet. Med. Int. J. Bioflux Soc. **4**(6), 214–221 (2014)

30. Spinei, A.: Salivary cytokines in disabled children with dental caries. Oral Health Dent. Manag.
4(15)(Suppl), 70 (2016). <u>https://doi.org/10.4172/2247-2452.C1.034</u>

31. Spinei,A., et al.: Relationship between dental caries and phosphocalcicmetabolism in children with severe central nervous system diseases caused by perinatal hypoxia. J. Stomatol. Med. **1**(61), 67–83 (2022). https://doi.org/10.53530/1857-1328.22.61.09

32. Lin, Y., Wen, L.: Inflammatory response following diffuse axonal injury. Int. J. Med. Sci. **10**, 515–521 (2013). [PMC free article] [PubMed]

33. Wang,W.Y., et al.:Role of pro-inflammatory cytokines released frommicroglia in Alzheimer's disease. Ann. Transl.Med. **3**(10), 136 (2015). <u>https://doi.org/10.3978/j.issn.2305-5839.2015.03.49</u>

34. Meyer-Arndt, L.,et al.: Inflammatory cytokines associated with multiple sclerosis directly induce alterations of neuronal cytoarchitecture in human neurons. J. Neuroimmune Pharmacol. (2023). https://doi.org/10.1007/s11481-023-10059-w

35. Borsini, A., et al.: Pro- and anti-inflammatory properties of interleukin in vitro: relevance for major depression and human hippocampal neurogenesis. Int. J. Neuropsychopharmacol. **11**(23), 738–750 (2020). https://doi.org/10.1093/ijnp/pyaa055



36. De Jongh, R.F., et al.: The role of interleukin-6 in nociception and pain. Anesth. Analg. **4**(96), 1096–1103 (2003)

37. Tanaka, M., Toldi, J., Vécsei, L.: Exploring the etiological links behind neurodegenerative diseases: inflammatory cytokines and bioactive kynurenines. Int. J. Mol. Sci. **7**(21), 2431 (2020). <u>https://doi.org/10.3390/ijms21072431</u>

38. Ahmad, M.A., et al.: Neuroinflammation: a potential risk for dementia. Int. J.Mol. Sci. **2**(23), 616 (2022). <u>https://doi.org/10.3390/ijms23020616</u>

39. Prso, I.B., et al.: Tumor necrosis factor-alpha and interleukin 6 in human periapical lesions. Mediat. Inflamm. 38210 (2007). https://doi.org/10.1155/2007/38210

40. Silva, T.A., et al.: Differential expression of chemokines and chemokine receptors in inflammatory periapical diseases. Oral Microbiol. Immunol. **5**(20), 310–316 (2005)

41. Luo, G., et al.: TNF-α and RANKL promote osteoclastogenesis by upregulating RANK via the NFκB pathway. Mol.Med. Rep. **5**(17), 6605–6611 (2018). <u>https://doi.org/10.3892/mmr.2018.8698</u>

42. Noguchi, T., et al.: TNF-α stimulates the expression of RANK during orthodontic tooth movement. Arch. Oral Biol. **117**, 104796 (2020). <u>https://doi.org/10.1016/j.archoralbio.2020.104796</u>

**43.** Kokkas, A.B., et al.: Irreversible but not reversible pulpitis is associated with up-regulation of tumour necrosis factor-alpha gene expression in human pulp. Int. Endod. J. **40**, 198–203 (2007). https://doi.org/10.1111/j.1365-2591.2007.01215.x