Dental Caries and Salivary Immunoglobulin A in Down Syndrome

Mohammed Najmuddin^{1, 2*}, Darshan Devang³, Oyedunni Sola Arulogun⁴

¹Texila American University, Central University of Nicaragua

²Department of Maxillofacial Diagnostic Sciences, College of Dentistry Jazan University, Jazan. KSA

³Dental Biomaterials Research Chair, Dental Health Department, College of Applied Medical Sciences, King Saud University, Riyadh, Saudi Arabia ⁴Director Centre for entrepreneurship and innovation, university of Ibadan, Ibadan Nigeria

Abstract

Down syndrome (DS) is defined as trisomy chromosome 21, which is observed to be the most prevalent autosomal genetic anomaly. Salivary immunoglobulin A (sIgA) plays an important role in defence mechanism against the microbial pathogens that can invade the surface of mucosa. In children with DS, raised sIgA levels cause an increase in immune mechanism against dental caries. The evidence about the salivary IgA levels in children suffering from Down syndrome is contradictory and limited in the literature. Thus, there is a terrible requirement to conduct more longitudinal prospective studies on saliva of DS patients taking large sample sizes to assess the molecular interactions. The present review is aimed to evaluate the association of Dental caries and salivary immunoglobulin A in Down syndrome individuals. The sources were searched from a database of PubMed from 2004 to 2023 (last 19 years). The inclusion criteria included key words of microdontia, delayed eruption, dental anomalies, retained teeth, anodontia, fissured lip and tongue, macroglossia, hypodontia in Down syndrome. The 22 articles that met the selection criteria (most of them were review article and some observational studies) were included to this review, of which some of the studies have been conducted to assess the role of sIgA in relation to dental caries and observed that increased sIgA levels decrease the rate of incidence of dental caries. The present review revealed that patients suffering with Down syndrome are at an increased risk of dental caries because of impaired motor activities, malocclusion and affected quality of life.

Keywords: Dental Caries, Down Syndrome, Salivary Immunoglobulin A, Saliva.

Introduction

Down syndrome (DS) is known as the most prevalent autosomal genetic anomaly affecting children of mothers who are aged more than 35 years [1]. It results from trisomy affecting chromosome 21, resulting in various developmental and physical characteristic features [2]. The prevalence rate of DS is found to be approximately 1 in 800-1200 live births worldwide [2]. It has been advocated that carriers of Down syndrome are normally recognized at the time of their birth. They have particular physical characteristics, show retarded growth and delay in development [3, 4].

The present review is aimed to evaluate the association of Dental caries and salivary immunoglobulin A in Down syndrome individuals.

Materials and Methods

The sources were searched from a database of PubMed from 2004 to 2023 (last 19 years).

The inclusion criteria included key words of microdontia, delayed eruption, dental anomalies, retained teeth, anodontia, fissured lip and tongue, macroglossia, hypodontia in Down syndrome. The primary focus of the search was reviewing articles, case reports and observational studies explaining the common dental anomalies affecting Down syndrome individuals.

Results

The 22 articles that met the selection criteria (most of them were review article and some observational studies) were included to this review, of which some of the studies have been conducted to assess the role of sIgA in relation to dental caries and observed that increased sIgA levels decrease the rate of incidence of dental caries.

General Symptoms

Children affected with Down syndrome present with various signs and symptoms. They may have skin and skeletal disorders; mental retardation: hearing anomalies: congenital heart disease; retarded physical growth; dysfunction of temporomandibular joint; retarded maxillary growth; flat facial appearance; malocclusion; macroglossia; delayed eruption of tooth; dental agenesis; dental ailments like periodontal diseases; deformed ears; slanting eyes; cardiovascular and neural disorders; and reduced muscular tone [2].

Oral Symptoms

Patients with Down syndrome show deformities affecting the middle third of the face. It is characterised by a high arched palate; palatal atresia; V-shaped palatal shape, causing a severe impact on the stomatognathic system. It has been stated that around 90% of DS patients have hypoplastic maxillary sinus. The facial bones of Down syndrome patients are found to be smaller in size than normal individuals. Dysplasia affecting the craniofacial region leads to proclined mandibular incisors and anterior open bite. Patients also present with xerostomia, periodontal diseases and chronic respiratory infections leading to mouth breathing. Dental anomalies like fusion, enamel hypocalcification, decreased root length and twinning are also observed, causing mechanical problems [5].

A defective immunological system in patients suffering with Down syndrome leads to invasive periodontitis. This type of periodontal disease causes difficulty in eliminating microbes present in the biofilm. The presence of microbes in biofilm and immunosuppression in DS leads to dental caries. Increased micro-organism colonisation leads to demineralization of teeth causing cavitation [6].

Dental Caries and Down Syndrome

Because of different health issues, patients suffering from Down syndrome take lot of medicines with high sugar content, thus leading to raised incidence of dental caries. Besides exposure, unfavourable sugar behaviour and hypotonicity of muscles affect the maintenance of good oral hygiene, thus raising the prevalence of dental caries [7,8]. Down syndrome patients show raised levels of bacterial pathogens. In some studies, it has been observed that the rate of dental caries prevalence is less than healthy individuals. This can be associated with some protective factors like presence of macroglossia, diastema, shallow pits and fissures, dental agenesis, alkaline saliva, and delayed eruption, which causes decreased incidence of dental caries [9]. Other factors like altered salivary composition and rate of salivary flow can affect the incidence of dental caries [10].

Saliva and Down Syndrome

Saliva maintains the dynamics of oral health and helps in defence action due to presence of proteins and peptides. It also prevents incidence of dental caries by maintaining the neutral pH (mean pH: 6.7). Saliva helps in diagnosing various diseases of oral cavity like oral lichen planus, dental caries, systemic diseases, periodontal diseases, and oral cancer.¹¹ In oral cavity, the extracellular and intracellular pathways of secretion of saliva make it an appropriate medium for diagnosing various diseases [11].

Saliva hosts various antimicrobial agents like enzymes and different antibodies such as salivary immunoglobulin A (sIgA). sIgA is reported to be one of the major immunoglobulins, which plays an important role in defense mechanism against microbial pathogens that can invade the surface of mucosa. It also helps in increasing the immunity of oral environment by preventing the colonization of bacteria and adhesion of microbes. Various researchers have conducted studies assessing role of sIgA in relation to dental caries and observed that increased sIgA levels decrease the rate of incidence of dental caries [12, 13, 14].

Discussion

It has been postulated that incidence of dental caries is reduced and even prevented by presence of Immunoglobulin A in the saliva. Thus, in patients with reduced levels of salivary IgA the incidence of dental caries is increased, revealing a high caries index. Microorganisms lead to dissociation of the carbohydrates present in food and produce acidic environment, causing dental caries. Glucosyltransferase is observed to be the major enzyme that helps in progression of dental caries. This enzyme is found to be prevented by action of SIgA, thus we can consider that the progress of dental caries is prevented by salivary SIgA. The rate of caries prevalence in the oral cavity determines the release of SIgA. The amount that determines the production of SIgA is definite to mutans [13].

The levels of salivary IgA show an increase with age. Adults show higher sIgA levels than children. The evidence about the salivary IgA levels in paediatric patients suffering from Down syndrome is contradictory and limited in the literature. In children with DS, raised sIgA levels cause an increase in immune mechanism against dental caries. Various studies have been conducted to evaluate the association between sIgA levels and presence of dental caries in patients having down syndrome [14].

Various authors found that in saliva, presence of IgA antibodies helps to inactivate the enzymes and toxins by creating a neutralizing environment. They cause hindrance in the bacterial adherence, thus inhibiting the accretion of streptococcus on the surfaces of tooth, which is required to initiate the process of caries [15]. Increased rate of flow of saliva in patients with DS causes decreased incidence of dental caries as compared to healthy individuals. Other factors that influence the morphological traits of teeth and eruptive patterns in patients with DS can also affect incidence of dental caries. Delayed tooth eruption, and shallow pits and fissures reduce the rate of dental caries [16].

Research Studies

Various studies have been conducted that are based on the hypothesis of action of sIgA in hindering the bacterial adherence on the surface of tooth, and causing neutralization of the extracellular enzymes, thus preventing dental caries. In a study by Lee et al. [12] a decreased prevalence of dental caries was seen in children having Down syndrome. They stated that this is because of increased concentrations of salivary S. mutans specific IgA that causes immune protection against caries.

Areias et al. [16] conducted a study on patients with DS, revealing low *S. mutans* counts and increased *Streptococcus mutans* specific sIgA levels. They stated that decreased count of Streptococci mutans in saliva is one of the major contributing factors to decrease the rate of dental caries in children with Down syndrome, in spite of the presence of hyposalivation. They also observed that normally sIgA levels play an important role in protecting the mucosal structures of the oral cavity against the invasion of microorganisms. In this way, sIgA also helps to reduce the incidence of dental caries as well as periodontal diseases.

An inverse correlation was observed between levels of s-IgA with OHI-S and DMFS scores. They found that as levels of s-IgA increased, the rate of prevalence of dental caries decreased significantly [17]. They also stated that down syndrome patients cannot maintain oral hygiene status properly as compared to the normal subjects. Similarly, found that DS patients revealed a significantly lower rate of prevalence of dental caries, corresponding to the raised levels of salivary sIgA. The findings of this study support the hypothesis revealing that raised salivary sIgA levels increase the protection against dental caries [18].

A contrasting study by Hashizume LN et al. [19] revealed that rate of carries prevalence was same in children with or without DS. They found that age was the only dependent factor which was associated with dental caries affecting permanent teeth. Rosdiana R et al. [20] stated that delayed tooth eruption, spacing between the teeth, increased pH, microdontia, and raised levels of sodium, calcium, and bicarbonate causes reduced caries incidence in children with Down syndrome. They also found that caries decreases with increased levels of salivary sIgA.

The children suffering with Down's syndrome showed raised levels of salivary IgA and G. They showed a better capability of buffering, leading to decrease in incidence of dental caries. The decreased incidence of dental caries in children suffering with Down syndrome is linked to alkaline pH and low viscosity of saliva, decreased St. mutans count and raised levels of salivary immunoglobulin A [22].

Preventing Dental Caries in DS

Children with DS show lack of cooperation, with of behaviour impulsiveness and stubbornness, thus requiring the need of behaviour management techniques like positive reinforcement, desensitization, tellshow-do, pharmacological management by conscious sedation and general anesthesia [8]. It is required to prevent dental caries by maintaining adequate oral hygiene and fluoride applications. Patients are advised to brush their teeth twice daily with fluoridated toothpaste and a soft, age-appropriately sized toothbrush. It is required to implement oral hygiene habits by teaching and executing. The preventive role of fluoride in the process of dental caries is via cariostatic mechanisms. Fluoride interferes in the process of enamel demineralization by controlling the metabolism of bacteria, thus inhibiting acid production, leading to remineralization [1]. It is also required to alter eating habits, increasing the consumption of fruits and vegetables, and decreasing the intake of carbohydrates.

Conclusion

The present review revealed that patients suffering with Down syndrome are at an increased risk of dental caries because of impaired motor activities, malocclusion and affected quality of life. The reasons behind decreased levels of dental caries are still not well understood, but it has been stated by various studies that presence of increased sIgA levels causes a decrease in incidence of dental

References

[1] Martins, M., Mascarenhas, P., Evangelista, J. G., Barahona, I., Tavares, V., The Incidence of Dental Caries in Children with Down Syndrome: A Systematic Review and Meta-Analysis, *Dent J.* 2022;10(11):205.

[2] Hamid, H., Adanir, N., Asiri, F. Y. I., Abid, K., Zafar, M. S., Khurshid, Z., Salivary IgA as a useful biomarker for dental caries in down's syndrome patients: a systematic review and meta-analysis, *Eur J Dent.*, 2020, 14(4), 665-71.

[3] Human Genomics in Global Health. Genes and human diseases Available at: https://www.who.int/genomics/public/geneticdise ases/en/index1.html. Accessed October 12, 2023

[4] Descamps, I., Fernandez, C., Van Cleynenbreugel, D., Van Hoecke, Y., Marks, L., Dental care in children with down syndrome: A questionnaire for belgian dentists, *Med Oral Patol.Oral Cirugía Bucal*, 2019, 24(3), e385-e391.

[5] Araújo, D. L., Brito, M. V. D. S., Felipe, L. C.
S., Pacientes com síndrome de Down na odontologia: Revisão de literature, *Facit Bus Technol J.*, 2022, 36(2), 145.

[6] Meyer, F., Enax, J., Early childhood caries: epidemiology, aetiology, and prevention, *Int J Dent.*, 2018, 2018, 1415873.

[7] Pereira, C. M., Santos, N. S., Carlos, L. A., Neto, O. A. T., Andrade, L. A., Avaliação de doença periodontal e cárie em pacientes com síndrome Down: Incidência, características e conduta preventive, *Espec Med Saúde*, 2022, 22(7), 136-46. caries. We advise conducting various longitudinal prospective studies and clinical trials for evaluating the role of sIgA before considering it as a useful biomarker for causing dental caries in DS patients.

Conflict of Interest

None

Acknowledgements

None

[8] Silva, M. C. P. M. D., Lyra, M. C. A., Almeida, H. C. R., Alencar Filho, A. V., Heimer, M. V., Rosenblatt, A., Caries experience in children and adolescents with Down Syndrome: A systematic review and meta-analysis, *Arch Oral Biol.* 2020, 115, 104715.

[9] Deps, T. D., Angelo, G. L., Martins, C. C., Paiva, S. M., Pordeus, I. A., Borges-Oliveira, A. C., Association between Dental Caries and Down Syndrome: A Systematic Review and Meta-Analysis, *PLoS ONE*, 2015, 10, e0127484.

[10] Hashizume, L. N., Schwertner, C., Moreira, M. J. S., Coitinho, A. S., Faccini, L. S., Salivary secretory IgA concentration and dental caries in children with Down syndrome, *Spec Care Dentist.*, 2017, 37(03), 115-19.

[11] Shazam, H., Shaikh, F., Hussain, Z., Majeed, M. M., Khan, S., Khurshid, Z., Evaluation of osteocalcin levels in saliva of periodontitis patients and their correlation with the disease severity: a cross-sectional study. *Eur J Dent.*, 2020, 14(03), 352-9.

[12] Lee, S. R., Kwon, H. K., Song, K. B., Choi, Y. H., Dental caries and salivary immunoglobulin A in Down syndrome children, *J Paediatr Child Health.*, 2004, 40(9-10), 530-533.

[13] Pandey, S., Goel, M., Nagpal, R., Kar, A., Rapsang, E., Matani, P., Evaluation of Total Salivary Secretory Immunoglobulin A and Mutansspecific SIgA among Children having Dissimilar Caries Status, *J Contemp Dent Pract*, 2018, 19(6), 651-5. [14] Alzughaibi, O. S., Filimban, L. A., Arafa, A. A., Assessment of Salivary -amylase, pH and flowrate effects on dental caries experience of down'sαImmunoglobulin A, syndrome children in Makkah, Saudi Arabia, *Int J Health Sci Res.*, 2017, 7(3), 143-9.

[15] Nogueira, R. D., Alves, A. C., Napimoga, M. H., Smith, D. J., Mattos-Graner, R. O., Characterization of salivary immunoglobulin A responses in children heavily exposed to the oral bacterium Streptococcus mutans: influence of specific antigen recognition in infection, *Infect Immun.*, 2005, 73(09), 5675-84.

[16] Areias, C., Sampaio-Maia, B., Pereira, M. deL et al., Reduced salivary flow and colonization by mutans streptococci in children with Down syndrome, *Clinics (São Paulo)* 2012, 67(09), 1007-11.

[17] Ranadheer, E., Reddy N. Venugopal, Rao V Arun Prasad, Kumar Krishna. The relationship of salivary immunoglobulin-A with dental caries and oral hygiene status in Down's syndrome children. *Annals and Essences of Dentistry*, 2010, 2(2), 10-7. [18] Cogulu, D., Sabah, E., Kutukculer, N., Ozkinay, F., Evaluation of the relationship between caries indices and salivary secretory IgA, salivary pH, buffering capacity and flow rate in children with Down's syndrome, *Arch Oral Biol.*, 2006, 51(1), 23-8.

[19] Hashizume, L. N., Moreira, M. J. S., Hilgert, J.
B., Dental caries in children with Down syndrome and associated factors, *RGO*, *Rev Gaúch Odontol.*, 2021, 69, e20210044, http://dx.doi.org/10.1590/1981-

863720200004420200072.

[20] Rosdiana, R., Rizal, M. F., The relation between salivary sIgA level and caries incidence in Down syndrome children, *Dent J* 2012, 45(2), 79-83

[21] Radhi, N. J., El-Samarrai, S. K., Alkhafaji, J. T., Dental caries in relation to salivary parameters and immunoglobulins among Down's syndrome children in comparison to normal children, *J Bagh Coll Dentistry* 2009, 21(4), 118-24.

[22] Abou El-Yazeed, M., Taha, S., El shehaby, F., Salem, G., Relationship between salivary composition and dental caries among a group of Egyptian down syndrome children, *Aus J Basic Applied Sci*, 2009, 3(2), 720-30.