Advances in Bioresearch
Adv. Biores., Vol 12 (5B) September 2021: 342-346

Print ISSN 0976-4585; Online ISSN 2277-1573
Journal's URL:http://www.soeagra.com/abr.html
CODEN: ABRDC3
DOI: 10.15515/abr.0976-4585.12.5B.342346

Advances in Bioresearch

REVIEW ARTICLE

Oral Manifestations of Metabolic Disorders

Diksha Mohapatra[1], Neeta Mohanty[2], Sayantanee Chaudhury[1] and Jagannath Patra[3]
[1]Post-graduate student, [2]Professor & Head, [3]Research Associate,
Department of Oral Pathology and Microbiology, Institute of Dental Sciences, Siksha 'O' Anusandhan(Deemed to be University), Bhubaneswar-751003, Odisha, India,
Corresponding Author: dr.neetamohanty@gmail.com

ABSTRACT
The human being is a complex biological unit in this evolved environment. Metabolism is defined as a total of all tissue activities in terms of physiochemical changes associated with availability, consumption as well as the dispatch of various nutrients like proteins, carbohydrates, lipids, vitamins, minerals as well as water and influence the endocrine system involved in the various processes. Alteration in any form of these normal metabolic processes leads to disturbances of metabolism, manifested as metabolic disorders in the human body.
Keywords: *Metabolic disorders, Amyloidosis, Porphyria, Mucopolysaccharidosis, Lipoid proteinosis, Langerhans Cell Disease*

Received 04.06.2021 Revised 22.06.2021 Accepted 19.08.2021

How to cite this article:
D Mohapatra, N Mohanty, S Chaudhury and J Patra. Oral Manifestations of Metabolic Disorders. Adv. Biores. Vol 12 [5B] September 2021. 342-346

INTRODUCTION

A nutrient is a substance that is required by a living being to keep it a lives well as to help it to grow. Nutrients not only provide nourishment to a body but also help in maintaining the growth and development of a body as well as sustain life. Carbohydrates, proteins, fats, vitamins, minerals as well as water are thevarious components of nutrition. While carbohydrates and fats provide energy, protein helps in growth, vitamins and minerals maintain the physiological activities and water transports food along with playing a crucial role in regulating the body temperature. When the body is unable to absorb or get from the food the necessary amount of nutrients then the nutritional deficiency is seen. But, when an adequate amount of nutrients is supplied to the body, but the body is unable to metabolize the nutrients, then metabolic disorders are seen.

The oral cavity shows a considerable change in its normal physiological structure as well as a wide range of variations due to metabolic disorders. These variations are mostly harmless and are usually seen as a secondary effect to some systemic diseases. The chances of occurrence are quite rare so their diagnosis also becomes difficult [1]. This reviews article highlights the oral manifestations of various metabolic disorders like Amyloidosis, Porphyria, Mucopolysaccharidosis including Hurler Syndrome (gargoylism), Hunter Syndrome, Morquio Syndrome, Maroteaux-Lamy Syndrome and Sly Syndrome, Lipoid proteinosis, Eosinophilic granuloma, Hand Schuller Christian disease, Leterrier Siwe disease, Niemann-Pick disease, Gaucher's disease, Acrodermatitis Enteropathica, Hypophosphatasia and Avitaminosis.

DISORDERS OF PROTEIN METABOLISM

Amyloidosis

Deposition of an insoluble fibrillar protein extracellularly in different tissues of the body is a predominant feature of amyloidosis. While many organs are involved, the most commonly affected are kidneys, heart, gastrointestinal tract, liver and spleen. In the oral cavity, the tongue is the most routinely reported location of amyloid deposition leading to macroglossia. As a result, there is difficulty in chewing food as well as in speech. Other sites of deposition of fibrillar proteins are mucosa of the buccal region, palatal

region, gingiva and floor of the mouth [2]. At some instances xerostomia can also be evident due to salivary gland involvement.

Porphyria

Porphyria is a term that has been generally used to connote one of the hereditary errors of porphyrin metabolism, characterized by the overproduction of uroporphyrin and related substances. They are a group of disorders related to definite enzymes in the heme biosynthetic pathway that are either hereditary or acquired. An affected individual presents with long eyelashes, bushy eyebrows and facial hairs. Intraorallybullae formation and erosions may be seen. In congenital erythropoietic porphyria oral mucosa appears pale as well as deciduous dentition of the individual appears reddish-brown. The cervical region of teeth is more intensely discoloured as compared to the occlusal region. Extensive periodontal diseases and high caries incidence as well as yellowish-orange discolouration of oral mucosa is evident [3].

DISORDERS OF CARBOHYDRATE METABOLISM

Mucopolysaccharidosis

Mucopolysaccharidosis is referred to a group of conditions that are mostly inherited by an individual giving rise to either defective or absence of activity of lysosomal hydrolase-1-iduronidase.

Mucopolysaccharidosis I or Hurler Syndrome (Gargoylism)

Mucopolysaccharidosis type I (Hurler Syndrome) is caused due to chromosomal abnormality that has been mapped to 4p16. Accumulation of mucopolysaccharides is seen in the fibroblasts giving them a clear or gargoyle cells like appearance, which is also termed as gargoylism. Oral and dental findings include gingival hyperplasia, macroglossia, high arched palate, shortening of rami of the mandible with an abnormality of the condyles, hypoplastic peg-shaped teeth with spacing, retarded eruption and presence ofdentigerous cysts [4, 5].

Mucopolysaccharidosis II or Hunter Syndrome

Hunter syndrome is caused due to insufficiency inactivity of iduronate-2-sulfatase and is marked by dermatan sulfate and heparan sulfate build-up in the tissues. Mucopolysaccharidosis II is identified by ivory white papules which are characterized as distinctive skin lesions about 2-10mm in diameter. Coarsening of facial features is seen which includes nose with flared nostrils, prominence of supraorbital ridges, jaw enlargement and protruding enlarged tongue [6].

Mucopolysaccharidosis IV or Morquio Syndrome

Morquio syndrome has been distinguished into two types; type A brought about by insufficiency of N-acetyl galactosamine and type B due t oinadequate beta-galactosidase. As a result, there is TMJ damage, mineralization disturbances of the enamel as well as small teeth with severe attrition and pointed cusps are seen [7].

Mucopolysaccharidosis V or Maroteaux-Lamy Syndrome

Mucopolysaccharidosis V occurs due to a lack of arylsulfatase B as a result of which there is an accumulation of dermatan sulfate within the lysosomes. Even during rest, the mouth of the patient remains open with an enlarged tongue protruding outside. The teeth are short and stubby, poorly formed, poorly calcified and hypoplastic with abnormal and malformed peg shape. Anterior open bite is present with radiolucent areas resembling dentigerous cysts [8].

Mucopolysaccharidosis VII or Sly Syndrome

Sly Syndrome is caused due to insufficiency of the enzyme beta-glucuronidase, leading to accumulation of heparan and dermatan sulfate in the tissues. Clinically severe lethal hydrops fetalis is seen along with hepatosplenomegaly, dysostosis multiplex, stunted growth, kyphosis and scoliosis. Epicanthus, Mongoloid eyelids, shortening of the nose along with anteversion of nostrils, taurodontism, hyperplastic dental follicles and macroglossia are some of the craniofacial deformities that are seen in Sly syndrome [9].

Lipoid Proteinosis

Lipoid proteinosis is also known as hyalinosis cutis et mucosae which is a rare autosomal recessive disorder caused by mutation mapped to a locus on chromosome 1q21 in a glycoprotein present in various tissues. Babies exhibiting this disorder are unable to cry and produce hoarseness of voice in early childhood. Thickening of oral mucosa is a predominant feature along with macroglossia and "wood hard" tongue. The lips appear enlarged and nodular along with traces of gingival hyperplasia [10].

DISORDERS OF LIPID METABOLISM

Eosinophilic Granuloma

Eosinophilic granuloma is the most common appearance of Langerhans Cell Disease(LCD) also known as chronic localized histiocytosis X characterized by benign, solitary lesion of bone. It can affect any bone in

the body but is most commonly noticed in the skull, mandible, ribs and long bones. Occasionally gross periodontal destruction can also be witnessed leading to exposure of roots of teeth. Radiographically rounded areas with indistinct margins are seen around the tooth giving it a "floating in air" appearance to the teeth [11, 12].

Hand Schuller Christian Syndrome

Hand Schuller Christian Syndrome is also known as chronic disseminated histiocytosis X, xanthomatosis or multifocal eosinophilic granuloma. It consists of a special clinical trial of diabetes insipidus, lytic bone lesions and exophthalmos. It is a chronic form of eosinophilic granuloma characterized by a disseminated form of skeletal and soft tissue lesion. Halitosis is commonly encountered along with inflammation and purulent discharge from the gingiva. Spontaneous exfoliation of teeth is also noticed with added extensive loss of alveolar bone. Loss of taste sensation along with mucosal ulceration in the oral cavity is also evident. They scoped out the shape of the bone is recognized radiographically since bone destruction starts below the alveolar process maintaining the superior aspect of bone at the mesial and distal margins [12, 13].

Leterrier Siwe Disease

Leterrier Siwe disease or acute disseminated Langerhans cell disease is an acute fulminating disease almost found in infancy. It is an aggressive form of histiocytosis and affects infants or young children presenting as splenomegaly, hepatomegaly and lymphadenopathy. Oral mucosal ulceration associated with gingival inflammation and haemorrhageis detected added with extensive loss of maxilla and mandible and spontaneous exfoliation of teeth. The" Floating in air" appearance of teeth is sometimes revealed in the radiograph along with teeth displacement [12].

Niemann-Pick Disease

The Niemann-Pick disease is also known as sphingomyelin lipidosis where the affected individual lacks enzymes responsible for processing specific lipids. As a result, there is an accumulation of lipids within various types of tissues which give it an appearance of cells attempting to store the lipids for which sphingomyelin lipidosis is also considered as a storage disease. Niemann-Pick disease does not have any effects in the oral cavity so no considerable prominent oral repercussions of this disease have been recorded.

Gaucher Disease

Gaucher disease is a rare autosomal recessive disorder genetically determined by improper functioning of the catabolic enzyme beta-glucocerebrosidase, resulting in the assemblage of glucocerebroside in the mononuclear phagocyte system, lymph nodes, bone marrow and Kupffer cells [14]. In Gaucher disease the oral mucosa appears yellow presenting as petechiae. Due to generalized osteopenia, there is loss of trabecular structure effacement of lamina dura leading to the displacement of the mandibular canal as well as the appearance of pseudo cystic radiolucent lesions along with apical root resorption of teeth [15].

DISORDERS OF MINERAL METABOLISM

Acrodermatitis Enteropathica

Disturbances in the metabolism of mineral Zinc is a rare inherited autosomal recessive character presenting its characteristic features during infancy and childhood. The primary signs are the appearance of skin lesions, hair loss and diarrhoea [16]. In the craniofacial region buccal mucosa is the most commonly affected region followed by palate and gingiva. A large number of affected children present with candidiasis, stomatitis and glossitis along with the presence of papilloma, red and white spots, erosions, ulcers and desquamation in the buccal mucosa and tongue borders.

Hypophosphatasia

Hypophosphatasia is a genetically acquired recessive autosomal disease characterized by a deficiency of serum alkaline phosphatase. It has a somewhat resemblance to rickets. Dental anomalies are noticed in all subtypes of hypophosphatasia and are mostly referred to as odontohypophosphatasia [17]. Low level of serum alkaline phosphatase activity elevates urinary secretion of phosphoryl ethanolamine resulting in the formation of defective bone matrix. Due to this reason, there is premature loss of teeth along with root resorption resulting from improper development of alveolar bone supporting the teeth, lack of cementum and poorly attached periodontal fibres. The teeth may be hypoplastic with the size of the pulp chamber and root canal appearing larger than normal with instances of gingival inflammation. There is the generalized reduction of bone density in the jaw bone, alveolar bone loss with thinning of cortical and lamina dura [18].

Avitaminosis

Vitamins act as catalysts for all the metabolic reactions in the body using proteins, carbohydrates and lipids for energy production, growth and development. Vitamin A is a member of the retinoid family

which is present in food like milk, cheese, butter, cod liver oil, yellow, orange and green leafy vegetables as well as yellow fruits like mango and papaya. Vitamin A plays a pivotal role in the visual cycle and also reduces the risk of epithelial cancers [19]. Deficiency of vitamin A leads to inadequate cell differentiation proceeding to impaired healing and tissue regeneration. So, there is increased desquamation of oral mucosa with the added risk of candidiasis. Keratosis of labial mucosa, gingival hypertrophy, leukoplakia, decreased taste sensation, decrease salivation, disturbances in enamel development, irregular tubular dentin formation and increased caries risk are also some of the oral manifestations of vitamin A deficiency. Deficiency of Vitamin D is manifested as rickets and osteomalacia and in the oral cavity, the deficiency is manifested by the involvement of alveolar bone with poorly defined lamina dura and hypoplastic alveolar ridge, enamel hypoplasia, dental caries susceptibility, pulp calcification, recurrent aphthous ulcers and dental and gingival abscess [20, 21]. Vitamin E which is found in abundance in vegetables and seed oils including soya bean acts as an antioxidant and is required for maintaining membrane structure and integrity of cells as well as for the synthesis of haemoglobin. No oral manifestations are apparent but severe neurological deficiency like gross ataxia can be found. Vitamin K acts as a cofactor for blood clotting factor production. Due to deficiency of Vitamin K, there is an increased risk of bleeding during dental procedures and more chances of occurrence of candidiasis [22].

Vitamin C or Ascorbic acid is s simple sugar and is present in abundance in fresh fruits and vegetables, especially sour ones. It acts as a powerful reducing agent and helps in maintaining redox potential within cells. It also helps in the prevention of atherosclerosis and cancers. Deficiency of ascorbic acid is mainly manifested in the oral cavity as scurvy characterized by swollen and bleeding gums, periodontal destruction, sore and burning mouth with increased risk of candidiasis [23].

Thiamin (Vitamin B1) deficiency in the oral cavity is marked by tongue enlargement with the flabby, red and edematous appearance of enlarged fungiform papillae and 'old rose' colour appearance of the gingiva [24]. Riboflavin (Vitamin B2) deficiency causes glossitis, angular cheilosis, atrophy of filiform papilla, enlargement of the fungiform papilla and magenta colour appearance of tongue in the oral cavity [25]. Deficiency of Niacin (Vitamin B3) is marked by mucositis, stomatitis, angular cheilosis, glossitis and ulceration over tongue and gingiva. Vitamin H or Biotin is needed by the body for metabolizing carbohydrates, fats and amino acids. Lack of biotin can cause anorexia, anaemia as well as glossitis. Angular cheilosis, soreness as well as burning sensation in the mouth with glossitis and glossodynia are some of the signs of Vitamin B6 deficiency [26]. Meat, fish, eggs and milk are a good source of Vitamin B12. Lack of supply or disrupted metabolism of vitamin B12 in the human body can cause angular cheilosis, stomatitis, diffuse erythematous mucositis and recurrent oral ulcers in the mouth with increased chances of oral candidiasis, halitosis, glossodynia and delayed wound healing with bone loss [27]. Vitamin B9 is also known as folate or folic acid, deficiency of which causes megaloblastic anaemia and pancytopenia. Orally deficiency of folic acid is manifested as mucositis, stomatitis, glossitis, burning sensation of the mouth, increased risk of candidiasis and aphthous ulcer along with ulcerative gingivitis with tip and border of tongue appearing red and swollen [28].

CONCLUSION

Metabolic disorders can occur either due to poor nutritional intake like starvation or due to malabsorption of specific nutrients. Maximum of the cases of metabolic disorders are mostly inherited genetically. For management of certain disorders treatment options are present while for some finding out a proper treatment modality is still under research and relay mostly on supportive therapies.

FUNDING: None

CONFLICTS OF INTERESTS: Nil

ACKNOWLEDGEMENTS: None

REFERENCES

1. Pinna R, Cocco F, Campus G, Conti G, Milia E, Sardella A, et al. (2019). Genetic and developmental disorders of the oral mucosa: Epidemiology; molecular mechanisms; diagnostic criteria; management. Periodontol 2000.80(1):12–27.
2. Deng J, Chen Q, Ji P, Zeng X, Jin X. (2109). Oral amyloidosis: A strategy to differentiate systemic amyloidosis involving the oral cavity and localized amyloidosis. Oral Diseases. 25(3):670–5.
3. Kooijman MMD, Brand HS. Oral aspects of porphyria. Int Dent J. 2005 Apr;55(2):61–6.
4. Gardner DG. The oral manifestations of Hurler's syndrome. (1971). Oral Surgery, Oral Medicine, Oral Pathology, and Oral Radiology;32(1):46–57.

5. Guven G, Cehreli ZC, Altun C, Sençimen M, Ide S, Bayari SH, et al. (2008). Mucopolysaccharidosis type I (Hurler syndrome): oral and radiographic findings and ultrastructural/chemical features of enamel and dentin. Oral Surgery, Oral Medicine, Oral Pathology, and Oral Radiology.105(1):72–8.
6. Torres R de O, Pintor AVB, Guedes FR, Freitas-Fernandes LB, Barth AL, Horovitz DDG, et al (2018). Oral and craniofacial manifestations in a Hunter syndrome patient with hematopoietic stem cell transplantation: A case report. Special Care in Dentistry.38(1):51–4.
7. Levin LS, Jorgenson RJ, Salinas CF. (1975). Oral findings in the Morquio syndrome (mucopolysaccharidosis IV). Oral Surgery, Oral Medicine, Oral Pathology, and Oral Radiology. 39(3):390–5.
8. Alpöz AR, Coker M, Celen E, Ersin NK, Gökçen D, van Diggelenc OP, et al. (2006). The oral manifestations of Maroteaux-Lamy syndrome (mucopolysaccharidosis VI): a case report. Oral Surgery, Oral Medicine, Oral Pathology, and Oral Radiology. 101(5):632–7.
9. Kantaputra PN, Smith LJ, Casal ML, Kuptanon C, Chang Y-C, Nampoothiri S, et al . (2019). Oral manifestations in patients and dogs with mucopolysaccharidosis Type VII. American Journal of Medical Genetics.179(3):486–93.
10. Lee KC, Peters SM, Ko YCK, Kunkle TC, Perrino MA, Yoon AJ, et al. (2018). Oral manifestations of lipoid proteinosis in a 10-year-old female: A case report and literature update. Oral Surgery, Oral Medicine, Oral Pathology, and Oral Radiology.126(4):e228–32.
11. Hansen JV. Eosinophilic granuloma in the oral cavity (1962). Acta Oto-Laryngologica. 55:111–5.
12. Madrigal-Martínez-Pereda C, Guerrero-Rodríguez V, Guisado-Moya B, Meniz-García C. (2009). Langerhans cell histiocytosis: literature review and descriptive analysis of oral manifestations. Med Oral Patol Oral Cirugia Bucal.14(5):E222-228.
13. Pinkus H, Copps LA.(1949). Reticulogranuloma; report of a case of eosinophilic granuloma of bone associated with nonlipid reticulosis of skin and oral mucosa under the clinical picture of Hand-Schüller-Christian disease. The American Journal of Diseases in Children.77(4):503–19.
14. Bender IB, Bender AL.(1996). Dental observations in Gaucher's disease: review of the literature and two case reports with 13- and 60-year follow-ups. Oral Surgery, Oral Medicine, Oral Pathology, and Oral Radiology.82(6):650–9.
15. Sousa LLA, Rocha MMF, Mendes RF, Pradox RR.(2014). Oral health of a child being treated for subtype I Gaucher's disease. Special Care in Dentistry.34(2):100–4.
16. Lehnert T, Küry S, Bürk G, Hoepffner W, Schuster V. Acrodermatitis enteropathica (AE) is caused by mutations in the zinc transporter gene SLC39A4 (2006). Klinische Padiatre.218(4):221–3.
17. Bloch-Zupan A, Vaysse F. Hypophosphatasia: oral cavity and dental disorders (2017). Archives De Pediatre.24(5S2):5S80-85S84.
18. Chapple IL. (1993). Hypophosphatasia: dental aspects and mode of inheritance. Journal of Clinical Periodontology.20(9):615–22.
19. Stich HF, Mathew B, Sankaranarayanan R, Nair MK (1991). Remission of precancerous lesions in the oral cavity of tobacco chewers and maintenance of the protective effect of beta-carotene or vitamin A. Americal Journal of Clinical Nutrition. 53(1 Suppl):298S-304S.
20. Seminario AL, Velan E. (2016). Vitamin D and Dental Caries in Primary Dentition. J Dent Child Chic Ill. 15;83(3):114–9.
21. Ślebioda Z, Szponar E, Dorocka-Bobkowska B. (2016). Vitamin D and Its Relevance in the Etiopathogenesis of Oral Cavity Diseases. Archivum Immunologiae et Therapiae Experimentalis (Warsz).64(5):385–97.
22. Ockerman A, Vanhaverbeke M, Miclotte I, Belmans A, Vanassche T, Politis C, et al.(2019). Tranexamic acid to reduce bleeding after dental extraction in patients treated with non-vitamin K oral anticoagulants: design and rationale of the EXTRACT-NOAC trial. British Journal of Oral and Maxillofacial Surgery.57(10):1107–12.
23. Chakraborthy A, Ramani P, Sherlin HJ, Premkumar P, Natesan A. (2014). Antioxidant and pro-oxidant activity of Vitamin C in oral environment. Indian Journal Dental Research. 25(4):499–504.
24. Nolan A, McIntosh WB, Allam BF, Lamey PJ. (1991). Recurrent aphthous ulceration: vitamin B1, B2 and B6 status and response to replacement therapy. Journal of Oral Pathology & Medicine.20(8):389–91.
25. Morr Verenzuela CS, Davis MDP, Bruce AJ, Torgerson RR. (2017). Burning mouth syndrome: results of screening tests for vitamin and mineral deficiencies, thyroid hormone, and glucose levels-experience at Mayo Clinic over a decade. International Journal of Dermatology.56(9):952–6.
26. Dieb W, Boucher Y. (2017). Burning Mouth Syndome and Vitamin B6. Pain Med Malden Mass.18(8):1593–4.
27. Reamy BV, Derby R, Bunt CW. (2010). Common tongue conditions in primary care. American Journal Family Physicians. 81(5):627–34.
28. Chang JY-F, Wang Y-P, Wu Y-C, Cheng S-J, Chen H-M, Sun A. (2015). Hematinic deficiencies and anemia statuses in oral mucosal disease patients with folic acid deficiency. J Formos Med Assoc Taiwan Yi Zhi.114(9):806–12.