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Research Article

Impact of Fabry Disease on Salivary Gland Function and Oral Health: Implications for Multidisciplinary Care

Sajjad Salam[1], Taru Gupta[2], Amit Kumar[3], Shilpa LS[4], Farheen Chunara[5], Anukriti Kumari[6] and Ritik Kashwani[7]*

[1]*Dental and Maxillofacial Services, Bahrain Defense Forces - Military Hospital, Bahrain*

[2]*Senior Lecturer, Department of Pediatric and Preventive Dentistry, Uttaranchal Dental and Medical Research Institute, Dehradun, India*

[3]*Orthodontist, Muskan Dental Care, Deoghar, Jharkhand, India*

[4]*Senior Lecturer, Department of Periodontology, KVG Dental College and Hospital, Sullia, Karnataka, India*

[5]*Biostatistician, Medical College of Wisconsin, 8701 W Watertown Plank Rd, Milwaukee, Wisconsin, USA.*

[6]*Private Practitioner, School of Dental Sciences, Sharda University, Greater Noida, India*

[7]*Private Practitioner, School of Dental Sciences, Sharda University, Greater Noida, India*

***Corresponding Author:** Ritik Kashwani, BDS, Private Practitioner, School of Dental Sciences, Sharda University, Greater Noida, India.

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Abstract

Fabry disease is an X-linked lysosomal storage illness caused by mutations in the GLA gene that result in reduced activity of the α-galactosidase A enzyme globotriaosylceramide (Gb3) gradually accumulates as a result of this shortage in a number of tissues, notably salivary glands and tissues of the mouth. Studies show that there is a considerable impact on salivary gland function, which in turn leads to changed salivary flow rates and composition, which in turn causes xerostomia (dry mouth). The mouth cavity's inherent defence mechanisms, which include reduced saliva production, impact mucosal hydration, pH buffering, and antibacterial qualities. As a result, cavities, periodontal disorders, and infections of the mouth are frequently more common in patients with Fabry disease. In addition, the build-up of Gb3 in vascular endothelial cells causes microangiopathy, which makes oral tissue more susceptible. This study emphasises the requirement for interdisciplinary methods for better dental treatment administration in affected patients by highlighting the molecular basis of Fabry disease in connection to the salivary gland malfunction and its wider consequences on oral health.

Keywords: Alpha Galactosidase; Fabry Disease; Hypertrophy; Proteinuria

Introduction

Fabry disease is a rare X-linked metabolic condition caused by a lack of the lysosomal enzyme α-galactosidase. This catabolic enzyme deficiency leads to the ongoing buildup of glycosphingolipids containing α-galactosyl, which appears in multiple organs [1]. A broad range of clinical symptoms are brought on by the increasing accumulation of Gb3 within cellular lysosomes, which impacts multiple systems of organs, such as the neurological, cardiovascular, and renal systems [2]. But because Fabry disease affects oral health and the general quality of life of those who have it, there is increasing interest in how the glands that produce saliva and oral cavity are involved [3].

Through producing and releasing saliva, the salivary glands contribute significantly to the maintenance of oral homeostasis by aiding in digestion, lubrication, antibacterial defence, and pH buffering. A person's susceptibility to a condition known as (dry mouth) can be increased by impaired the salivary gland functioning, as shown in Fabry disease [4]. This can result in hyposalivation, or decreased salivary flow, and changes in the content of saliva. Patients are more vulnerable to oral health issues such as cavities, gum disease, and oral infections of the mucous membrane as a result of these alterations to saliva's protective properties [5]. Moreover, microangiopathy and neuropathic pain in the oral region may be

exacerbated by the vascular and neural problems typical of Fabry disease, thus increasing the burden of the illness.

Developing focused treatment and management options for Fabry disease requires an understanding of the fundamental mechanisms affecting the salivary gland functioning and dental health. By examining the pathophysiological mechanisms that connect Fabry disease to problems with salivary function and oral health, this study hopes to improve the oral care of those who suffer from this systemic ailment and offer insights into future treatment therapies.

Methodology

Literature on the effect of Fabry disease on the salivary gland was done narratively and synthesized in order to establish the literature on this basis. To achieve the desired purpose, the relevant peer-reviewed articles, clinical studies, and review papers have been retrieved systematically as well. The databases, including PubMed, Scopus, and Google Scholar, were searched, limiting the articles to those published up to October 2024. The keywords for searches included: "Fabry disease", "salivary gland function", "oral health", "xerostomia", and "multidisciplinary care".

Articles included for review were those studies and reviews directly examining the association of Fabry disease to oral or salivary health and published in the English language and dealt with clinical, physiological, or management aspects relevant to Fabry disease and its oral health implications. Case reports with minimal data, those not relevant to Fabry disease, and articles not in the English language that could not be accessed via translation were excluded.

Articles identified through database searching were screened by title and abstract for relevance. The full texts of any potentially eligible studies were further assessed for inclusion. Relevant data extracted from selected studies included study design, patient demographics, outcomes related to salivary gland function and oral health, and recommendations for care management.

The data were then thematically organised to find how Fabry disease affects the salivary secretion, xerostomia, oral mucosal health, along with the requirement of multifaceted treatment in these patients. Results are synthesised so the clinical implication of the disorder can be highlighted among the dental as well as the medical practitioner and thus aids in aiding better management of oral health in the patient.

Review

Certain studies highlight the importance of craniofacial and oral anomalies in male Fabry's disease patients, underscoring the necessity of thorough stomatologic examinations [6]. A significant frequency of mucocutaneous symptoms, such as telangiectasias and angiokeratomas, as well as prominent dental anomalies, such as maxillary prognathism, dental agenesis, and enamel discolouration, were found by clinical examination and imaging [7]. Furthermore, malocclusion and maxillary sinus cysts/pseudocysts were commonly seen. These results highlight how critical it is to identify and treat Fabry's disease issues related to the mouth and cranium as soon as possible.

Fabry disease is a X-linked lysosomal storage disorder that is caused by deficiency or absence of alpha-galactosidase A(α-GAL A) activity as a result of genetic mutation in the GLA gene (Xq21.3-q22) leading to lysosomal accumulation of glycosphingolipids, predominantly cerebroside trihexoside. As a result, patients have a markedly increased risk of developing ischaemic stroke, small-fibre peripheral neuropathy, cardiac dysfunction and chronic kidney disease [8]. The prevalence of Fabry disease has been estimated to be 1 per 40,000 people. Hypertension occurs with increased frequency in patients with Fabry disease because of progressive renal impairment. The diagnosis and treatment of Fabry disease can be challenging. The signs and symptoms of Fabry disease may be non-specific, and if manifestations in different organs are considered in isolation, the unifying diagnosis may be missed [8].

The X-linked lysosomal storage illness Fabry disease causes globotriaosylceramide (Gb3) to gradually accumulate in glandular cells, which has a substantial effect on salivary gland function. The main pathophysiological mechanism is the insufficient production of the enzyme known as α-galactosidase A, which causes Gb3 to be intracellularly deposited in the salivary glands' acinar, endothelial, and epithelial cells [9]. The glands experience structural and functional deficits as a result of this glycosphingolipid buildup, which interferes with regular cellular functions. Patients suffering from Fabry disease often have hyposalivation, which is a marked decrease in salivary flow [figure 1]. This decrease is ascribed to glandular tissue fibrosis and acinar cell atrophy. The composition of saliva is also altered, with lower amounts of vital substances including electrolytes, antimicrobial proteins (like lysozyme and lactoferrin), and enzymes (like amylase), in addition to a decrease in salivary flow. The natural functions of saliva to moisten the oral

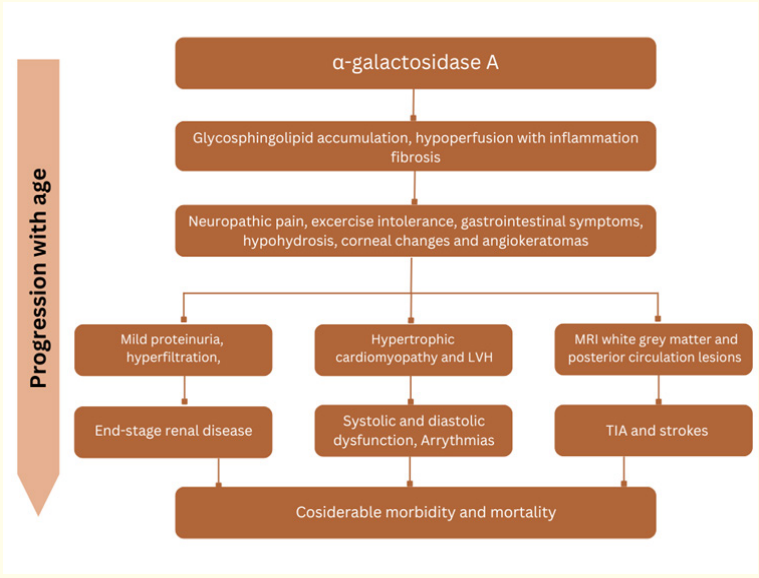

Figure 1: Pathophysiology of fabry disease.

cavity, buffer acids, and protect against microbial infections are compromised by these alterations [10]. Moreover, Gb3 buildup in the salivary glands' endothelial cells causes microvascular dysfunction, which lowers perfusion and worsens glandular function. These changes altogether cause xerostomia, or dry mouth, which raises the risk of periodontal disease, dental caries, and oral infections. Furthermore, autonomic neuropathy may be exacerbated by Fabry disease, which would further lessen the parasympathetic stimulus needed for salivary production. This complex dysfunction emphasises how seriously Fabry disease affects salivary gland functioning and the implications this has for dental health [11].

As globotriaosylceramide (Gb3) builds up in salivary glands and oral tissues, Fabry disease has a substantial effect on oral wellness via both direct and indirect processes. The most notable side effect is xerostomia, or dry mouth, which is brought about by hyposalivation as a result of Gb3 deposition in the salivary glands' acinar and endothelial cells. This results in decreased salivary flow, undermining saliva's vital roles in maintaining oral pH balance, offering antibacterial protection, and aiding in enamel remineralization [12]. Because of a lasting prevalence of cariogenic microbes and their incapacity of neutralising acidity in the oral cavity, people with Fabry disease are at heightened risk for dental caries. Furthermore, the oral cavity's defence against pathogenic germs is weakened by the decrease in saliva antimicrobial substances like lactoferrin and lysozyme, which predisposes people to periodontal ailments including gingivitis and periodontitis [13]. Additionally contributing to microvascular dysfunction, the build-up of Gb3 in vascular endothelial cells additionally lowers tissue perfusion and hinders wound healing in the oral mucosa. In addition to the autonomic neuropathy often noticed in Fabry disease, this vascular involvement can result in chronic neuropathic pain, which can exacerbate disorders like burning mouth syndrome [14]. The lack of moisture and deteriorated condition of the oral cavity might worsen oral mucosal infections, recurrent aphthous ulcers, and Candida infections in patients. When combined, these variables cause serious problems for the oral health of people with Fabry disease, which negatively affects their general level of life and calls for early intervention and specialist dental care to address the complex side effects [15].

Discussion

This clinical and public health paper affirms that coordinated dentist-patient relationships are essential for Fabry disease oral health consequences management. In order to synthesise care, it is important that dentists, physicians and other professionals work closely together. Proper dental examination that should be done routinely would involve effective examination of the teeth for any problems and diseases that may affect the health of the mouth. Hyposalivia may also be managed through dental counselling, for instance, provision of fluorides and saliva substitutes [16].

However, in certain instances, dental care may be accompanied by pharmacological mediational of pain and inflammation due to

Impact of Fabry Disease on Salivary Gland Function	Impact of Fabry Disease on Oral Health
Hyposalivation	Xerostomia
Altered Saliva Composition (Decreased levels of electrolytes, antimicrobial proteins e.g., lysozyme, lactoferrin, and digestive enzymes e.g., amylase)	Increased Dental Caries
Microvascular Dysfunction	Periodontal Disease (Gingivitis/Periodontitis)
Autonomic Neuropathy	Oral Infections(oral candidiasis)
Structural Changes in Glandular Tissue (glandular fibrosis and cellular vacuolization)	Oral Mucosal Lesions(Recurrent aphthous ulcers and angular cheilitis)
	Altered Taste Sensation (Dysgeusia)
	Oral Neuropathic Pain(burning mouth syndrome and chronic facial pain)
	Delayed Wound Healing
	Craniofacial Changes

Table 1: Oral Manifestation of fabry disease.

the disorders in salivary glands. Currently the treatment for Fabry disease is enzyme replacement therapy and it may have a positive impact on salivary gland function by decreasing the levels of Gb3. Nevertheless, more investigation is required in order to assess a clear influence of ERT on the oral degradation in Fabry disease patients [17].

Oropharyngeal manifestation of Fabry disease includes alterations in salivary glands and consequently oral health status. These conditions include; hyposalivation, altered composition in saliva, and inflammation can lead to different oral health complications. These oral health complications should be managed through non-pharmacological and pharmacological treatments like an effective dental check-up and appropriate medicines that can help in enhancing the standard of life of people having Fabry disease [17].

Conclusion

Oral health and salivary gland function are significantly impacted by Fabry disease, which is caused by globotriaosylceramide (Gb3) buildup and insufficient activity of α-galactosidase A. Because of glandular atrophy, dysfunction of the microvascular system, and autonomic neuropathy, which affect salivary secretion, xerostomia and hyposalivat ion occur, changing the composition of saliva and diminishing its antibacterial, lubricating, and protecting properties. Oral health is severely compromised by these alterations, which increase the incidence of dental cavities, periodontal disorders, and oral infections. Further, the extensive vascular and neurological consequences of Fabry disease lead to prolonged healing of wounds, oral neuropathic discomfort, and mucosal lesions, thereby raising the oral disease burden. Enhancing the standard of life for Fabry patients requires early detection and treatment of these oral symptoms, underscoring the necessity of interdisciplinary care incorporating dental and medical viewpoints. For those who are affected, early diagnosis and focused interventions can help minimise the effects of Fabry disease on their oral cavity and support the maintenance of their best possible oral health.

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