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Oral Manifestations of Metabolic Disorders - A Comprehensive Review

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ABSTRACT

Metabolic disorders encompass a wide range of conditions affecting various biochemical pathways within the human body. While these disorders primarily manifest systemic symptoms, they can also significantly impact oral health and oral cavity structures. This review aims to explore the diverse oral manifestations associated with metabolic disorders, including but not limited to diabetes mellitus, hyperparathyroidism, hypothyroidism, and various storage diseases. These oral manifestations may present as changes in the gingiva, teeth, salivary glands, mucosal tissues, and periodontal tissues. Additionally, metabolic disorders can influence the healing process following oral surgeries and affect dental treatment outcomes. Understanding these oral manifestations is crucial for dental practitioners to provide comprehensive care and collaborate effectively with medical professionals in managing patients with metabolic disorders. This review consolidates existing literature on the topic and underscores the importance in addressing the oral health needs of individuals with metabolic disorders.

KEYWORDS: Metabolic syndrome, Carbohydrate metabolism, porphyria, Amyloidosis, eosinophilic granuloma.

INTRODUCTION

Metabolic syndrome also known as metabolic syndrome X, insulin resistance syndrome, dysmetabolic syndrome, hypertriglyceridaemic waist, obesity syndrome, Reaven syndrome. It refers to the group of risk factors that increase the risk for ischaemic heart disease (IHD), Diabetes and stroke. It is diagnosed when atleast three of the IHD risk factors such as Hypertension (Blood pressure 130/85mmHg or higher), Hyperglycemia (Fasting blood glucose of 5.6mmol/L or higher), Dyslipidaemia (Triglycerides 150mg/dl or higher HDL < 50mg/dl for women and < 40mg/dl for men), Abdominal Obesity (Large waistline: women, 35in or more; men, 40in or more)[(1)].

ETIOLOGY:

The important underlying causes for developing metabolic syndrome includes lack of physical activity, obesity, genetics and older age. It is associated with diseases and signs such as increases uric acid levels, hepatic steatosis, hemochromatosis & acanthosis nigricans[(1)].

CLASSIFICATION OF METABOLIC DISORDERS

I. Inborn errors
II. Acquired errors - Amyloid Disease, Trimethylaminuria

INBORN ERRORS:

Numerous uncommon metabolic disorders stem from genetic enzyme deficiencies passed down through inheritance. The majority of these metabolic disorders emerge from recessive genetic traits, showing symptoms only when both parents carry the gene mutation. Specific metabolic disorders such as suxamethonium sensitivity, malignant hyperpyrexia, hyperlipoproteinemias, and porphyria pose significant challenges in managing patients requiring general anesthesia [1]. These include defects in carbohydrate, lipids, proteins, metal, enzyme and mineral metabolism[1,2].

GLYCOGEN STORAGE DISEASES (GSDs):

It is an inherited defect of degradative enzymes, which converts glycogen to glucose. So that increased accumulation of glycogen occurs resulting in hypoglycemia(1). There are 23 types of GSDs have been recognized based on the enzyme defect and organ affected(3). Clinical features include Hepatomegaly, muscle pain, weakness, respiratory muscle weakness and cardiac failure, Hypoglycemia. Oral manifestations involve Enlarged tongue, periodontal breakdown and masticatory muscle pain, Patients have a bleeding tendency which can be corrected pre-operatively by 24–48hours glucose infusion(1).

HURLER SYNDROME:

This is a genetic condition inherited in an autosomal recessive pattern, affecting the metabolism of mucopolysaccharides. It's identified by higher excretion levels and a buildup of chondroitin sulfate B and heparin sulfate within cells. Symptoms typically emerge within the first two years of life, worsen through childhood and adolescence, and sadly, lead to death before reaching puberty(2).

people with this condition often display characteristics such as an enlarged head, prominent forehead, broad nose with wide nostrils, widely spaced eyes, swollen eyelids with thick eyebrows, thick lips, enlarged tongue, mouth open, nasal congestion, and noisy breathing. They may also have a short neck, spine issues, and hand deformities known as "claw hand" due to flexion contractures. Oral manifestations consist of a shortened lower jaw, noticeable angles of the jawbone, and a broad space between these angles. Teeth are small and spaced apart, accompanied by overgrown gums. On radiographic examination, a distinct pattern emerges, revealing localized bone deterioration in the jaw, resembling an enlarged dental follicle filled with a significant amount of mucopolysaccharide material. Furthermore, a radiolucent area presents a resemblance to a dentigerous cyst(2).

EOSINOPHILIC GRANULOMA: This condition, known as non-lipid reticuloendotheliosis or unifocal eosinophilic granuloma, primarily affects young adults and children, with a higher incidence in the mandible and skull. Symptoms often include local pain, swelling, and tenderness. Additionally, individuals may experience general discomfort and fever alongside the bone granuloma. The lesion is characterized by its destructive nature, forming a well-defined, roughly round or oval shape. Soft tissue typically replaces the destroyed area. The tissue in the initial stage of the lesion appears soft and brown, without necrosis. As it progresses, the tissue becomes fibrous and takes on a greyish hue. Oral symptoms involve the loss of superficial alveolar bone, resembling juvenile periodontitis. Common signs include gingivitis, ulceration. Loosening and shedding of teeth typically follow the destruction of the alveolar bone(2). Radiographically, jaw lesions typically exhibit well-defined borders, seldom showing excessive bone formation and often appearing punched out. Osteolytic activity near the alveolar processes can create a floating teeth appearance. Biopsy results commonly reveal Langerhans cells and Birbeck granules, along with plasma cells,

lymphocytes, and multinucleated giant cells. Patients may also experience anemia, and less commonly, leukopenia and thrombocytopenia. While serum cholesterol levels remain normal, tissue cholesterol levels are elevated[2].

HYPERLIPOPROTEINAEMIA AND HYPOLIPOPROTEINAEMIAS:

Increased level of cholesterol in blood is also known as Hyperlipoproteinaemia; hyperlipidaemia; hypercholesterolaemia. Hypercholesterolemia predisposes to atherosclerosis. Based on the density and electrophoretic mobility, lipoproteins are classified as Chylomicron, very Low density lipoproteins (VLDL), low density lipoproteins (LDL) and high density lipoproteins (HDL). Clinically patients suffer from gout, cutaneous xanthomas and arthritis along with atherosclerosis and coronary heart disease. Decrease in lipoproteins in circulating blood results in hypolipoproteinemia which results in typical oral manifestations such as tangier's disease due to deficiency of HDL resulting in orange deposits in the tonsils, pulpal calcifications, odontomes[1].

THE PORPHYRIAS:

These are disorders due to rare inborn errors of enzymes involved in heme metabolism. This results in the accumulation of intermediate compounds known as porphyrins. Based on the site of enzyme defect, they are divided as Hepatic porphyrias and Erythropoietic porphyrias[1]. They are broadly classified as Acute and cutaneous porphyrias[4]. It manifests as major convulsions and neuropsychiatric disturbances, profuse sweating, pallor and pyrexia. Anaesthetics, analgesics, antimicrobials and anxiolytics are contraindicated in affected individuals. Congenital erythropoietic porphyria is characterized by red discoloration of the teeth due to fluoresce in the ultraviolet light[1].

HAEMOCHROMATOSIS:

It is a disorder characterized by excessive absorption of iron. It results in high serum ferritin levels and deposition of haemosiderin, in liver, abdominal lymph nodes, joints, skin, adrenals, pancreas, salivary glands, pituitary and heart leading to further damage[1].More common clinical features associated are skin pigmentation, spider angiomas of V of the neck, dilatation of the superficial veins of the bridge of the nose. Oral manifestations involve gingival and mucosal pigmentations, bone loss and disruption of lamina dura in the periapical radiographs[5].

DEFECTS IN DRUG METABOLIZING ENZYMES:

Drug responses between individuals vary greatly in case of pharmacodynamics and pharmacokinetics. Genetic variations in drug metabolism occurs due to variation in the activity of enzymes involved. Disorders in the enzymes involved are glucose 6 phosphatase dehydrogenase deficiency, malignant hyperthermia, methaemoglobinaemia[1].

GLUCOSE 6 PHOSPHATE DEHYDROGENASE DEFICIENCY:

Glucose 6 phosphate dehydrogenase(G6PD) occurs due to enzymatic disorder affecting Red blood cells[6]. It is an X-linked hereditary defect due to mutation in the G6PD gene typically males being affected[7]. According to WHO, G6PD deficiency has been classified into 5 classes, class 1 involves <1% or not detectable residual enzyme activity. It is the most severe congenital non spherocytic form of deficiency. These patients may present with symptoms of chronic hemolytic anaemia. Class 2 includes <10% of residual enzyme activity and affected individual present with symptoms of acute hemolytic anaemia. Class 3 involves 10-60% of residual enzyme activity associated with occasional symptoms of acute hemolytic anaemia. Class 4 (60-90%) suggestive of normal enzyme activity and patients are asymptomatic. Class 5 (>110%) suggestive

of increased activity with no specific symptoms in affected individuals[8].
The mechanism involved is that any exogenous trigger produces oxidative stress so that the G6PD deficient red cells breakdown easily. The most common clinical manifestations involved are neonatal jaundice and hemolytic anaemia [9]. Dental management involves avoiding the triggers such as oxidant drugs like sulphonamides and Dapsone. Local anaesthesia with prilocaine in high doses may induce methaemoglobinaemia, so it should be avoided[1].

MALIGNANT HYPERTHERMIA:
It is a rare, potentially fatal, inherited condition, characterized by a rapid rise in temperature (>42˚C) when the patient has a General Anesthesia or other drugs that trigger an attack[1]. In the dental chair, when these patients are exposed to excess stress may develop its signs and symptoms, which may become fatal[10]. Intravenous conscious sedation with local anesthesia may be safely administered to the MHS patient in the office setting for such procedures as the surgical removal of impacted third molars[10].

ETIOPATHOGENESIS [11,12]:
Triggering agents → Mutation RYR1 gene → increase cytoplasmic calcium level → increase cell metabolism & contracture of musculature → excess heat production.
CLINICAL FEATURES: Signs of malignant hyperthermia includes Increasing End-Tidal Carbon dioxide (ET CO_2), Trunk or total body rigidity, Masseter spasm or trismus, Tachycardia/tachypnoea, Mixed respiratory and metabolic acidosis, Increased temperature (may be late sign), Myoglobinuria[13]. Effective dental management can be done my minimizing anxiety, stress and pain by using Local anesthesia with adrenaline, In the event of hyperthermia, surgery must be stopped and the patient cooled. Oxygen and a bicarbonate intravenous infusion to counteract the metabolic acidosis should also be given. Dantrolene sodium or procainamide are effective in controlling the reaction. Dantrolene given pre-operatively and postoperatively for about 3 days may prevent Malignant hyperthermia[1].

AMYLOIDOSIS:
It is a group of rare diseases caused by deposition and build-up of proteins in tissues and organs throughout the body. It can be classified as systemic and localised or by the type of protein pre-cursor that forms the amyloid fibrils present[14]. Systemic amyloidosis affects tissues throughout the body and has high morbidity and mortality and localised amyloidosis affects a single site and rarely has serious consequences, but both the types affects the oral cavity[15,16,17]. Oral manifestations of amyloidosis includes Macroglossia due to amyloid deposition in the submucosal layer, gingival swellings, oral petechiae, bullae or, rarely, a sicca syndrome[1]. Yellow nodules are the predominant presentation on lateral border of tongue along with speech impairment and dysphagia[18].Speech impediment arises from vocal cord weakness caused by amyloid buildup in the upper portion of the larynx. Additionally, the tongue appears enlarged and speckled with small, garnet-colored protrusions, accompanied by nodes on the cheeks and lips. [2].

CONCLUSION
Metabolic disorders have impact on dental treatment in diverse ways. A thorough history and a high index of suspicion are essential for safe patient management. Knowledge of the dentists in assessing the relationship between metabolic disorders and oral manifestations highlights their vital role in recognizing systemic health implications during dental procedures.

Conflict Of Interest: Nil

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