ISSN: 2581-5989
PubMed - National Library of Medicine - ID: 101738774

International Journal of Dental Science and Innovative Research (IJDSIR)

IJDSIR : Dental Publication Service

Available Online at: www.ijdsir.com

Volume – 2, Issue – 5, September - October - 2019, Page No. : 295 - 303

Oral Manifestations of Endocrine System

Dr. Anuridhi Choudhary, MDS, Oral Medicine and Radiology

Dr. Kirti Raina, MDS, Public Health Dentistry

Dr. Meenakshi Thakur, MDS, Paediatric and Preventive Dentistry

Corresponding Author: Dr. Anuridhi Choudhary, MDS, Oral Medicine and Radiology

Type of Publication: Review Article

Conflicts of Interest: Nil

Abstract

In current modern medicine, a multitude of diseases have an impact on oral health care services. The endocrine system is responsible for hormonal secretion and is closely related to the central nervous system, as it diversifies its functions through the hypothalamus and pituitary glands. It controls physiological processes and maintains homeostasis. The neuroendocrine system is responsible for adaptation to environmental changes. Therefore, in dentistry, it is important to be aware of the risks and difficulties that may arise during the dental management of patients with endocrine disorders, and that visits to the dental clinics often represent a stressful situation.

Keywords: endocrine disorders, oral manifestations, dental management

Introduction

The human endocrine system is an efficient system that intimately controls cellular metabolism and maintains homeostasis. The endocrine system is responsible for hormonal secretion and is closely related to the central nervous system, as it diversifies its functions through the hypothalamus and pituitary. It controls physiological processes and maintains homeostasis. It includes pituitary Gland, hypothalamus, thyroid gland, thymus gland, heart, stomach,, pancreas, intestines, adrenal gland, ovaries and testes.[1]

Pituitary Glands Disorders

Hyperpituitarism

According to **Gaurav A et al in 2011**,[2] an increase in the number of granules in the acidophilic cells or an adenoma of the anterior lobe of the pituitary is associated with the condition known as gigantism or acromegaly.

Gigantism is the childhood version of growth hormone excess and is characterized by the general symmetrical overgrowth of the body parts.

Acromegaly is characterized by an acquired progressive somatic disfigurement, mainly involving the face and extremities, but also many other organs, that are associated with systemic manifestations. (**Sarment DP et al in 1998, Chanson P et al in 2008**).[3]

Oral Manifestations

Gigantism: It produces oral structures that are largely compared to the norm. Prognathic mandible, frontal bossing, dental malocclusion and interdental spacing are the main features. Intraoral radiograph may show hypercementosis of the roots (**Gaurav A et al in 2011**).[2]

Acromegaly: Craniofacial changes are characteristic of this disease and may involve facial skin, extraoral and intraoral soft and hard tissues (**Ezzat S et al in 1994**).[5] The most characteristic eatres are protruded glabella and increased anterior face height. Mandibular prognathism and jaw thickening is due to deposition of periosteal bone

in response to the excess growth hormone (**Chanson P et al in 2008**).[3] The lips become thick and negroid. Other intraoral changes are spacing in the teeth. Malocclusion, aperthognathia, macroglossia, hypertrophy of palatal tissues which may cause or accentuate sleep apnea buccal tipping of the teeth due to enlarged tongue (**Cohen RB et al in 1993** and **Sugata T et al in 1998**).[6,7] Dental radiograph may demonstrate large pulp chambers (taurodontism) and excessive deposition of cementum on the roots[2] and the cortical plate is radiodense and the condyles appear large in diameter.[8]

Hypopituitarism

Hypopituitarism is defined as the total or partial loss of anterior and posterior pituitary gland function that is caused by pituitary or hypothalamic disorders.[9] According to **Gaurav A et al in 2011**,[2] hypopituitarism is caused by compression or atrophy of anterior pituitary cells or a reduced capacity of the tissues to respond to growth hormone resulting in the condition known as pituitary dwarfism.[2]

Pituitary dwarfism: develops when the eosinophilic cells of the anterior pituitary gland fail to produce and secrete GH. The most common cause of hypopituitarism in children is a craniopharyngioma. The most striking feature of pituitary dwarfism is short stature of the affected patient and the low growth velocity for age.[2]

Oral Manifestations

The maxilla and mandible of affected patients are smaller than the normal and the face appears smaller with the permanent teeth showing a delayed pattern of eruption (**Kosowicz J et al in 1977**,**Bigeard L et al in 1991**).[10,11] The dental arches are smaller than the normal. Other findings such as agenesis of the upper central incisor and solitary maxillary central incisor have been observed.[12,13]

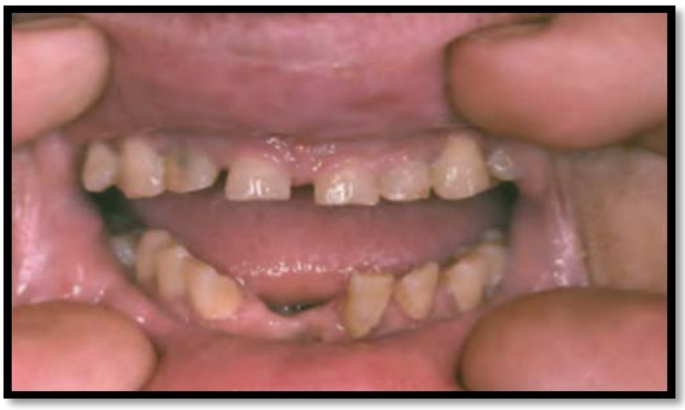

Figure 1: Dental characteristics of acromegaly

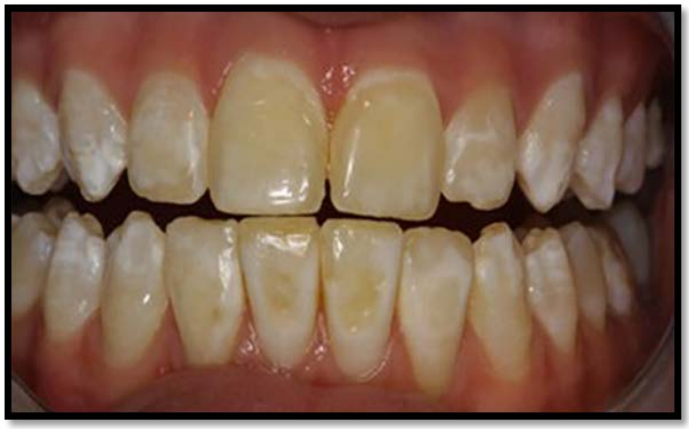

Figure 2: Amelogenesis Imperfect in patient suffering from Hypopituitarism

Thyroid Disorders

Hyperthyroidism

Hyperthyroidism or thyrotoxicosis is defined by a decrease in thyroid hormone production and thyroid gland function[1] which is caused by ectopic thyroid tissue, toxic thyroid adenoma, toxic multinodular goiter, subacute thyroiditis, factitious thyrotoxicosis and Graves' disease and diffuse toxic goiter, being the most common cause of hyperthyroidism (**Woeber KA, 2000**).[14]

Hypothyroidism

Hypothyroidism is defined by a deficiency of the thyroid hormone. It can be acquired or by congenital defects. When it is present in infancy, it is manifested as cretinism and if it occurs in adults it is known as myxedema (**Pinto A, 2002**).[15]

Oral Manifestations Of Patients With Thyroid Gland Disorders	
Hyperthyroidism	Hypothyroidism
1. Accelerated dental eruption in children 2. Maxillary or mandibular osteoporosis 3. Enlargement of extraglandular thyroid tissue (mainly in the lateral posterior tongue). 4. Increased susceptibility to caries 5. Periodontal disease 6. Burning mouth syndrome 7. Development of connective-tissue diseases like Sjögren's syndrome or systemic lupus erythematosus	1. Delayed eruption 2. Enamel hypoplasia in both dentitions, (being less intense in the permanent dentition) 3. Anterior open bite 4. Macroglossia 5. Micrognathia 6. Thick lips 7. Dysgeusia 8. Mouth breathing

Table 1: Oral manifestations of patients with Thyroid gland disorders

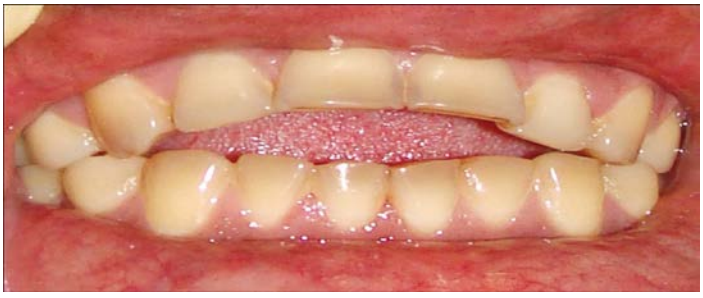

Figure 3: Anterior open bite in hypothyroidism

Parathyroid Disorders

Hyperparathyroidism

Hyperparathyroidism is a systemic disease that causes hypercalcemia and affects bone remodeling which is characterized by hypersecretion of parathyroid hormone.[16] According to **Triantafillidou K in 2006**,[17] one of the main clinical manifestations of hyperparathyroidism is bone disease. Brown tumor is a giant-cell granuloma produced in and replacing bone, occurring in osteitis fibrosa cystica and due to hyperparathyroidism (**Huang BK et al in 2010**).[18] Brown tumor presents itself as a friable red-brown mass. The characteristic brown coloration results from hemosiderin deposition into the osteolytic cysts.[1]

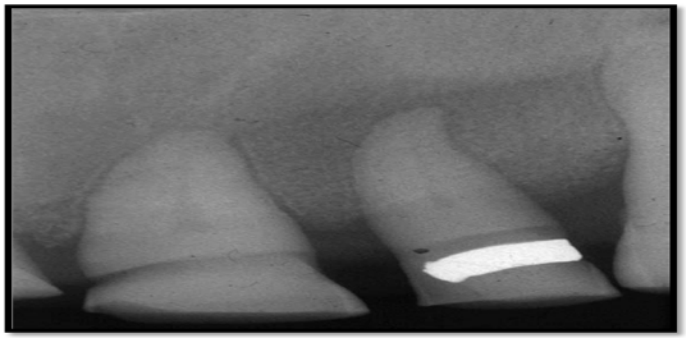

Figure 4: Demineralized maxillary bone with ground-glass appearance and loss of lamina dura.

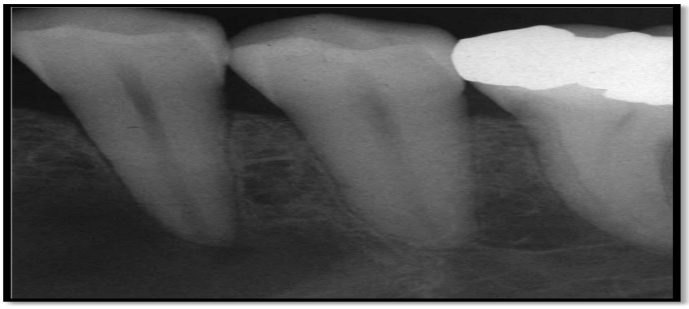

Figure 5: Osteitis fibrosa cystica of mandibular bone, which can resemble other types of nonendocrine bone pathology

Hypoparathyroidism

According to **Yamazaki H et al in 2003,**[18] Hypoparathyroidism is a metabolic disorder characterized by hypocalcemia and hypophosphatemia due to a deficiency or absence of parathyroid hormone secretion.

According to **Clark BL et al in 2016**,[19] Anterior neck surgery is the most common cause of acquired hypoparathyroidism and is responsible for about 75% of cases. The next most common acquired cause in adults is thought to be autoimmune disease, affecting either the parathyroid glands alone or multiple other endocrine glands. Remaining cases of acquired hypoparathyroidism are secondary due to a variety of rare infiltrative disorders in which the parathyroid glands are affected by metastatic disease or iron or copper overload or by ionizing radiation exposure (**Shoback DM et al in 2016**).[18]

Hypoparathyroidism can cause hypocalcemia with consequent paresthesia, tetany and seizures. Disorders of ectodermal tissues are also common in these patients. These disorders include alopecia, scaling of the skin, deformities of the nails and dental abnormalities. The main treatments available for these patients is vitamin D or its analogues, calcium salts and drugs that increase renal tubular resorption of calcium, to obtain adequate, but low, normal serum calcium levels.[18]

Oral Manifestations Of Patients With Parathyroid Gland Disorders	
Hyperparathyroidism	Hypoparathyroidism
1. Dental Abnormalities • Widened Pulp Chambers • Development Defects • Alterations In Dental Eruption • Weak Teeth • Maloclussions 2. Brown Tumor 3. Loss Of Bone Density 4. Soft Tissue Calcifications	1. Dental Abnormalities • Enamel Hypoplasia In Horizontal Lines • Poorly Calcified Dentin • Widened Pulp Chambers • Dental Pulp Calcifications • Shortened Roots • Hypodontia • Delay Or Cessation Of Dental Development 2. Mandibular Tori 3. Chronic Candidiasis 4. Paresthesia Of The Tongue Or Lips Alteration In Facial Muscles

Table 2: Oral manifestations of patients with parathyroid gland disorders

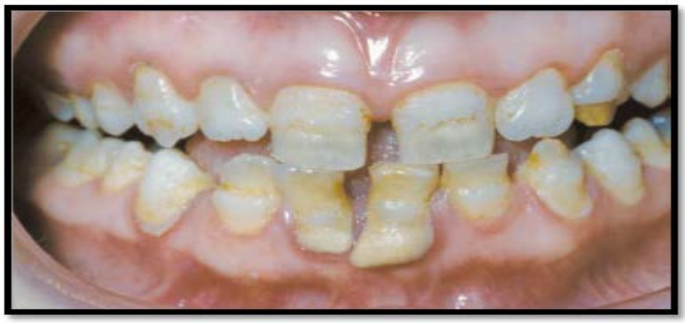

Figure 6: Congenital hypoparathyroidism showing mottled enamel from decreased serum calcium during tooth calcification.

Adrenal Gland Disorders

Hypoadrenocortism (addison disease)

In Addison's disease or primary adrenal insufficiency exists a deficiency in the secretion of glucocorticoid and mineralocorticoid hormones by the adrenal cortex (**Fabue LC et al in 2010**).[1] Cortisol deficiency clinically manifests as hypoglycemia, hypotension, asthenia, muscle weakness, anorexia, nausea, weight loss and diminished resistance to infections and stress. Characteristic melanic pigmentation may develop as a consequence of cessation of inhibition at hypophyseal level, with simultaneous increments of both ACTH and melanocyte stimulating hormone (MSH).[20] Addisonian crises or acute adrenococortical insufficiency is a rare but serious complication in patients with primary Addison's disease which is more likely to be attributable to secondary adrenal failure rather than to Addison's disease. It presents as a sudden failure of the adrenal cortex function resulting in clinical picture compromises shock with nausea, vomiting, abdominal pain and hypotension.[1]

Oral Manifestations

The primary orofacial feature of addison's disease is unusual skin pigmentation, most intensely over sunexposed areas. On the face, freckles and moles become more intense, as well as the appearance of a tan-like complexion, except that the increased pigmentation wills not disappear.[8]

The oral mucosa can in turn develop black-bluish plaques, mainly affecting buccal mucosa but it can also be seen on the gums, palate, tongue and lips (**Kauzman et al in 2004**[21]**, Lanza A et al in 2009**[22] and **Fabue LC et al in 2010**[1]).

Hyperadrenocorticism (cushing's syndrome)

Cushing's syndrome (CS) refers to manifestations induced by chronic exposure to excess glucocorticoids produced by the adrenal cortex (**Bertagna X et al in 2009**)[1] and

arises from iatrogenic causes (due to administration of exogenous glucocorticoids) and high production of ACTH. Hypertension, glucose intolerance, menstrual irregularity, osteoporosis and pathological fractures, delayed healing, increased risk of infection and neuropsychological disturbances including depression, emotional irritability, sleep disturbances and cognitive deficits are also observed.[23]

Purple striae and muscular atrophy are particularly positive stigmata in adults, whereas in child growth retardation are frequently present (**Bertagna X et al in 2009).**[24]

Oral Manifestations

The primary orofacial feature of Cushing's syndrome is a round, moon face due to muscle wasting and accumulation of fat (**Fabue LC et al in 2010**).[1] Surface capillaries in the face and other skin regions become fragile, rendering them readily susceptible to hematomas after mild trauma. Long-standing Cushing's syndrome produces delayed growth and development, including skeletal and dental structures (**Bertagna X et al in 2009**).[24] Oral signs and symptoms of immunosuppression can be seen, including oral candidiasis, recurrent herpes labialis and herpes zoster infections, gingival and periodontal diseases, and impaired wound healing.[8]

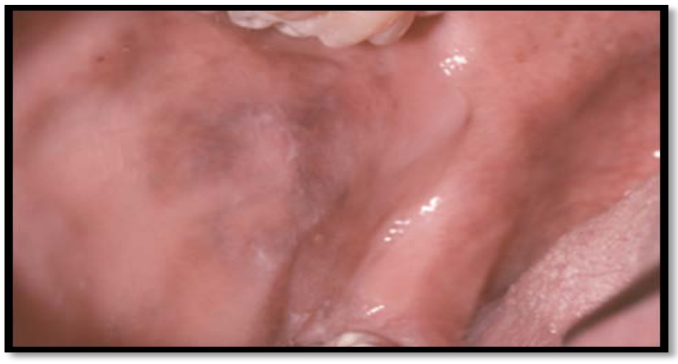

Figure 7: Diffuse, ill-defined melanin pigmentation of the buccal mucosa in a patient with Addison disease. This patient also exhibited bronzing of the skin.

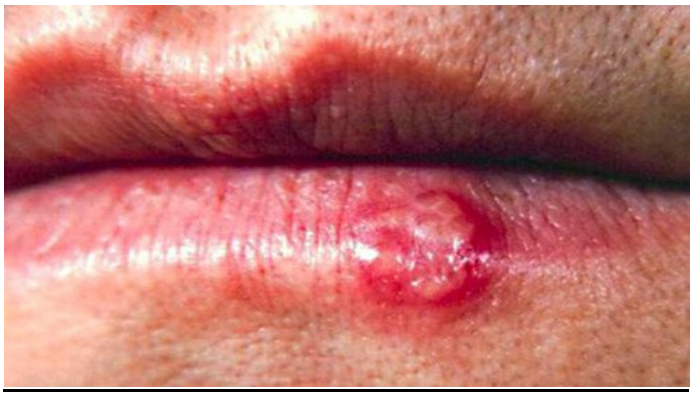

Figure 8: Recurrent Herpes Labialis seen in Cushing Syndrom

Pancreatic Disorders

Diabetes Mellitus

Diabetes mellitus is a chronic metabolic disorder characterized by a relative or absolute lack of insulin[25] Diabetes mellitus is increasing worldwide at an alarming rate with a global prevalence of 4% in 1995 and an expected rise to 5.4% by the year 2025, representing an estimated 300 million affected individuals (**King H et al in 1998**).[26] The complications of diabetes mellitus include cardiovascular disease, nephropathy, diabetic retinopathy, neuropathy and respiratory failure.[27]

Type 1 diabetes mellitus results primarily from destruction of the beta-cells in the islets of Langerhans of the pancreas whereas ***Type 2 diabetes mellitus*** is due to a range from insulin resistance with relative insulin deficiency to a predominantly secretory defect accompanied by insulin resistance. ***Gestational diabetes mellitus*** (GDM) is glucose intolerance that begins during pregnancy. The children of mothers with GDM are at greater risk of experiencing obesity and diabetes as young adults; there is a greater risk to the mother of developing type 2 diabetes in the futures. [28,29]

Oral Manifestations

Diabetes is a common disease with concomitant oral manifestations that impact dental care.[30] The oral complications include xerostomia, an increased

susceptibility to bacterial, viral, and fungal infections (oral candidiasis), increased risk for dental caries, poor wound healing, gingivitis, periodontal disease, peri-apical abscesses, taste impairment and burning mouth syndrome (**Rees TD in 2000** and **Vernillo AT in 2003**).[29]

According to **Akpan & Morgan in 2002,** the colonization and carriage of Candida in the oral cavity is found to be higher in diabetic subjects than in non-diabetics. **Sandberg et al in 2000**[31] found a significantly higher degree of xerostomia in type 2 diabetes mellitus. According to **Carda C in 2006,**[32] the oral manifestations of diabetes in the salivary glands include sialoadenosis or non-inflammatory, non-neoplastic enlargement of the parotid salivary glands, decreased salivary flow rates and changes in salivary composition.Bilateral enlargement of the parotid salivary glands has been reported to occur in 10–48% of diabetic patients, and may be more common in patients with poorly controlled diabetes (**Lalla RV et al in 2001** and **Manfredi M et al in 2004**). **Shrimali et al. in 2011** observed hyposalivation as the most common oral manifestation, seen in 68% of cases with controlled DM. According to **Gandara BK in 2011**,the mechanism by which salivary flow is affected in diabetic patients is thought to be the result of autonomic nerve dysfunction or microvascular changes that diminish the ability of the salivary glands to respond to neural or hormonal stimulation. **Souza Bastos A et al in 2011** and **Guggenheimer J et al in 2000**, disorders of the oral mucosa commonly occurring in diabetic patients include atrophy of the mucosa, candidiasis (thrush), and lichen planus or lichenoid mucositis.[33] According to **Guggenheimer J et al in 2000**,[34] median rhomboid glossitis was significantly more prevalent in diabetic patients than in nondiabetic patients and was associated with elevated levels of Candida pseudohyphae in oral smears and diabetic complications of nephropathy and retinopathy.

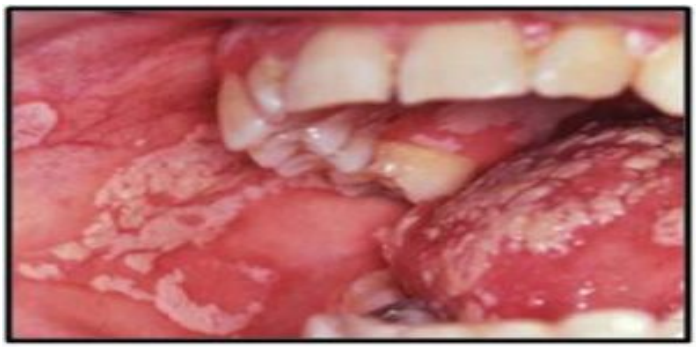

Figure 9: Oral cavity showing Candidiasis

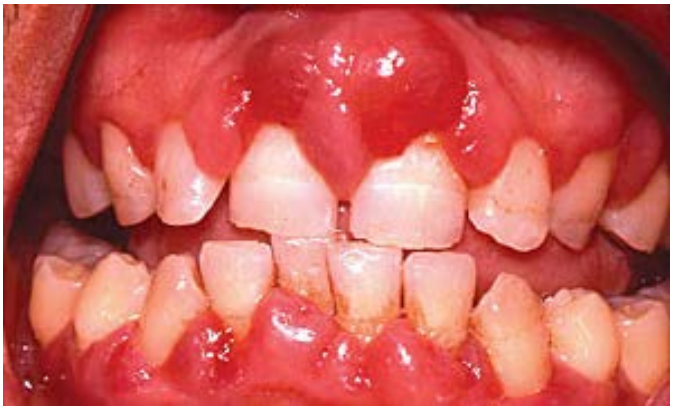

Figure 10: Gingivitis with diffuse gingival erythema, swelling, and blunted interdental papillae in a patient with diabetes mellitus

Endocrine Changes in Pregnancy

Thyroid Gland

There is an increase in the production of thyroxine-binding globulin (TBG) by the liver, resulting in increased levels of thyroxine (T4) and tri-iodothyronine (T3). Serum free T4 (fT4) and T3 (fT3) levels are slightly altered but are usually of no clinical significance. Levels of TSH increase again at the end of the first trimester, and the upper limit in pregnancy is raised to 5.5 μmol/l compared with the level of 4.0 μmol/l in the non-pregnant state.

Adrenal gland

Three types of steroids are produced by the adrenal glands: mineralocorticoids, glucocorticoids and sex steroids. The RAA system is stimulated due to reductions in vascular resistance and blood pressure, causing a three-

fold increase in aldosterone levels in the first trimester and a 10-fold increase in the third trimester. During pregnancy there is also an increase in serum levels of deoxycorticosterone, corticosteroid-binding globulin (CBG), adrenocorticotropic hormone (ACTH), cortisol and free cortisol. These changes cause a state of physiological hypercortisolism and may be clinically manifested by the striae, facial plethora, rising blood pressure or impaired glucose tolerance.

Pituitary gland

The pituitary gland enlarges in pregnancy and this is mainly due to proliferation of prolactin-producing cells in the anterior lobe. Serum prolactin levels increase in the first trimester and are 10 times higher at term which is most likely due to increasing serum oestradiol concentrations during pregnancy. Levels of follicle-stimulating hormone (FSH) and luteinising hormone (LH) are undetectable during pregnancy due to the negative feedback from elevated levels of oestrogen, progesterone and inhibin. Levels of antidiuretic hormone (ADH) remain unchanged but the decrease in sodium concentration in pregnancy causes a decrease in osmolality. There is therefore a resetting of osmoreceptors for ADH release and thirst.[35]

Oral Manifestations

The storm of hormones which is induced during pregnancy causes changes in the mother's body, and pregnancy gingivitis is observed.

The oral changes which are seen in pregnancy include gingivitis, gingival hyperplasia, pyogenic granuloma, and salivary changes. Increased facial pigmentation is also seen. Elevated levels of the circulating oestrogen, which cause an increased capillary permeability, predispose the pregnant women to gingivitis and gingival hyperplasia (**Soory M. in 2000**).[36] Pregnancy gingivitis usually affects the marginal and the interdental papilla and it is related to the preexisting gingivitis.

Pyogenic granulomas (pregnancy tumour) occur in about 1% to 5% of the pregnant women.The increased gonadotropins in the first trimester are associated with nausea and vomiting. The gastric acids which are present in the emesis erode the enamel on the inner surface of the teeth, most commonly the front teeth.[37]

The changes in the composition of the saliva include a decrease in the sodium concentration and pH, and an increase in the potassium, protein, and the oestrogen levels. (**Agueda A et al in 2008**).[38]

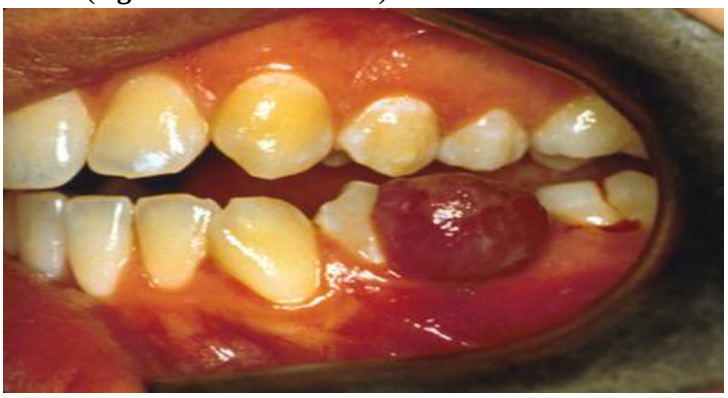

Figure 10: Pyogenic granuloma

Conclusion

The neuroendocrine system is responsible for adaptation to environmental changes. The need for oral health care professionals to understand basic principles of medicine and diagnosis has grown exponentially. Oral health is an integral part of total health; oral health care professionals must adapt to demographic changes and medical advances and shoulders the responsibility of being part of patient's overall health care team.

References

1. Carlos Fabue L, Jimenez Soriano Y, Sarrion Perez MG. Dental management of patients with endocrine disorders. J Clin Exp Dent. 2010;2(4):196-03.
2. Gaurav A, Shikhah A, Urvashi S, Nitul J. Oral Manifestations In Pituitary Disorders. International

Journal of Clinical Cases and Investigations 2011;2(6):13:17.

3. Philippe Chanson and Sylvie Salenave. Acromegaly. Orphanet J Rare Dis. 2008; 3:17.
4. Sarment DP, Weisgold AS: The importance of dentistry in the differential diagnosis of a medical disorder. Compend Contin Educ Dent. 1998;19(2):124-6.
5. Ezzat S, Forster MJ, Berchtold P, Redelmeier DA, Boerlin V, Harris AG. Acromegaly. Clinical and biochemical features in 500 patients. Medicine (Baltimore) 1994;73:233–40.
6. Cohen RB, Wilcox CW: A case of acromegaly identified after patient complaint of apertognathia. Oral Surg Oral Med Oral Pathol. 1993;75(5):583-6.
7. Sugata T, Myoken Y, Tanaka S: Acromegaly identified in a patient with a complaint of malocclusion.Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1998;85(1):44-6.
8. Bricker SL, Langlais RP, Miller CS. Oral Diagnosis, Oral Medicine, and Treatment Planning. 2nd edition. Philadelphia; Lea & Febiger. 1994.
9. Seong Yeon Kim. Diagnosis and Treatment of Hypopituitarism. Endocrinol Metab 2015;30:443-55.
10. Kosowicz J, Rzymski K. Abnormalities of tooth development in pituitary dwarfism. Oral Surg Oral Med Oral Pathol. 1977;44(6):853-63.
11. Bigeard L, Sommermater J. Dental delay and microdontia in children with somatotropin hormone deficiency. J Biol Buccale. 1991;19(4):291-6.
12. Breteche F, Delaire J, Ginguene Y. Agenesis of the superior central incisor. Its relation to pituitary nanism. Rev Stomatol Chir Maxillofac. 1984;85(1):72-4.
13. Lo FS, Lee YJ, Lin SP, Shen EY, Huang JK, Lee KS. Solitary maxillary central incisor and congenital nasal pyriform aperture stenosis. Eur J Pediatr. 1998;157(1):39-44.
14. Woeber KA. Update on the management of hyperthyroidism and hypothyroidism. Arch Fam Med. 2000;9:743-7.
15. Pinto A, Glick M. Management of patients with thyroid disease: oral health considerations. J Am Dent Assoc. 2002;133:849-58.
16. Padbury AD Jr, Tözüm TF, Taba M Jr, Ealba EL, West BT, Burney RE, et al. The impact of primary hyperparathyroidism on the oral cavity. J Clin Endocrinol Metab. 2006;91:3439-45.
17. Triantafillidou K, Zouloumis L, Karakinaris G, Kalimeras E, Iordanidis F. Brown tumors of the jaws associated with primary or secondary hyperparathyroidism. A clinical study and review of the literature. Am J Otolaryngol. 2006;27:281-6.
18. Huang BK, Chu YK. Multiple Brown Tumors Mimicking Bone Metastasis: A Case Report. Ann Nucl Med Sci 2010;23(4):227-33.
19. Clark CM, Lee DA. Prevention of complications of diabetes mellitus. N Engl J Med 1995;332:1210–7
20. Lorenzo-Calabria J, Grau D, Silvestre FJ, Hernandez-Mijares A. Management of patients with adrenocortical insufficiency in the dental clinic. Med Oral. 2003;8:207-14.
21. Kauzman, Pavone M, Blanas N, Bradley G. Pigmented lesions of the oral cavity. Review, differential diagnosis, and case presentation. J Can Dent Assoc 2004;70:682-3.
22. Lanza A, Heulfe I, Perillo L, DellErmo A, Cirillo N. Oral Pigmentation as a Sign of Addison's Disease: A Brief Reappraisal. The Open Dermatology Journal, 2009;3.
23. Arnaldi G, Angeli A, Atkinson AB, Bertagna X, Cavagnini F, Chrousos GP, et al. Diagnosis and

complications of Cushing's syndrome: a consensus statement. J Clin Endocrinol Metab. 2003;88:5593-602.

24. Bertagna X, Guignat L, Groussin L, Bertherat J.Cushing's disease. Best Pract Res Clin Endocrinol Metab. 2009;23:607-23.
25. Arrieta-Blanco JJ, Bartolome-Villar B, Jimenez-Martinez E, Saavedra-Vallejo P, Arrieta-Blanco FJ. Bucco-dental problems in patients with Diabetes Mellitus: Index of plaque and dental caries. Med Oral 2003;8(2):97-109.
26. King H, Aubert RE, Herman WH. Global burden of Diabetes, 1995-2025. Diabetes Care 1998;21(9):1414-31.
27. Boulbou MS., Gourgoulianis KI., Klisiaris VK, Tsikrikas TS, Stathakis NE, Molyyda PA.. Diabetes mellitus and lung function. Med Princ Pract 2003;12(2):87-91.
28. Meltzer S, Leiter L, Daneman D, Gerstein HC, Lau D, Ludwig S, et al., Clinical practice guidelines for the management of diabetes in Canada. Canadian Diabetes Association. CMAJ 1998;159(8):S1-29.
29. Abdulrahman K. Diabetes mellitus and its oral complications: a brief review. Pakistan Oral & Dent. Jr. 2006;26(1).
30. Bajaj S, Prasad S, Gupta A, Singh VB. Oral manifestations in type-2 diabetes and related complications. Indian J Endocr Metab 2012;16:777-9.
31. Sandberg GE, Sundberg HE, Fjellstrom CA, Wikblad KFl. Type 2 diabetes and oral health: a comparison between diabetic and non-diabetic subjects. Diabetes Res Clin Pract 2000;50(1):27-34.
32. Carda C, Mosquera-Lloreda N, Salom L, Gomez de Ferraris ME, Peydro Az. Structural and functional salivary disorders in type 2 diabetic patients. Med Oral Patol Oral Cir Bucal 2006;11:309–14.
33. Gandara BK, Morton TH. Non-Periodontal Oral Manifestations of Diabetes: A Framework for Medical Care Providers. Diabetes Spectrum 2011;24(4),199-205.
34. Guggenheimer J, Moore PA, Rossie K, Myers D, Mongelluzzo MB, Block HM et al. Insulin-dependent diabetes mellitus and oral soft tissue pathologies: II. Prevalence and characteristics of Candida and Candidal lesions. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2000;89(5):570-576.
35. Priya Soma-Pillay, Catherine Nelson-Piercy, Heli Tolppanen, Alexandre Mebazaa. physiological changes in pregnancy. Cardiovascular journal of africa 2016;27(2):89-94.
36. Soory M. Hormonal factors in periodontal disease. Dent Update. 2000; 27:380-83.
37. Yuan K, Wing LY, Lin MT. Pathogenetic roles of angiogenic factors in pyogenic granulomas in pregnancy are modulated by female sex hormones. J Periodontol. 2002;73:701-08.
38. Yuan K, Wing LY, Lin MT. Pathogenetic roles of angiogenic factors in pyogenic granulomas in pregnancy are modulated by female sex hormones. J Periodontol. 2002;73:701-08.