

# Hypothyroidism as a risk factor of periodontitis and its relation with vitamin D deficiency: mini-review of literature and a case report

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## Summary

**Objective.** The purpose of this report is to investigate the role and efficiency of the intra-ligamentary injection of vitamin D and calcium in the treatment of chronic periodontitis associated with hypothyroidism.

**Design.** A 43-year-old female with suspected hypothyroidism who revealed severe chronic periodontitis with grade III mobility. Pre-operative periodontal and systemic control preceded the used intervention. After 3 months, intra-ligamentary injectable vitamin D with calcium was introduced.

**Results.** Clinical evaluation revealed great improvement of the injected sites. Marked reduction of mobility, pocket depth and bleeding were detected.

**Conclusions.** Injectable vitamin D is an adjunctive treatment modality that needs to be discovered in another way. It may provide further solutions for the periodontal regeneration problem. Clinical studies with large sample sizes and long term follow up are needed.

**KEY WORDS:** periodontitis; hypothyroidism; vitamin D; intraligamentary injection.

## Introduction

Periodontitis is an inflammatory disease that affects the periodontal supporting structures surrounding teeth. In the last

decades, various researches reported the role of the systemic condition in disturbing of the periodontal balance causing destruction of periodontal apparatus (1).

Thyroxine is an essential hormone for preserving the physiologic body functions. Thyroid function test and anti-thyroid antibodies should be analyzed for disease detection. The level of TSH is inversely proportional to the level of T3 and T4 (2-4).

In females, it plays an important role through direct and indirect mechanisms. Directly, thyroxine keeps the normal function of ovaries on the other hand it interacts with the female sex hormone binding proteins indirectly. Hyper-stimulation of ovaries and menstrual disturbance could be detected in the form of prolonged cycle and heavy blood flow. On the other hand, hypo-secretion causes, menstrual disturbance and infertility. The chronic autoimmune thyroid disorder is one of the main causes of thyroid gland hypo-function. Nearly 20-40% of the affected individuals are not easily discovered (2, 3).

Anemia, cardiomegaly, constipation, dry and brittle hair, tachycardia, seizures, myxedema and weight gain are the most common manifestations of hypothyroidism. During childhood, hypothyroidism is known as cretinism which manifested by thickening of oral and paraoral structures as lips, tongue and delayed teeth eruption. This enlargement is attributed to higher accumulation of mucopolysaccharides (5). While the long standing manifestation of hypothyroidism includes: enamel hypoplasia, delayed wound healing, inflammation of the periodontal tissues and alveolar bone loss. Higher rate of thyroid hypo-function was detected in adult females.

The mechanism of bone loss due to hypo-thyroidism depends on several factors. Higher serum and salivary levels of TNF- $\alpha$  and IL-6 were detected (6). On the other hand, higher number of osteoclasts was detected in relation to the alveolar bone affecting the quality and quantity of the tooth supported alveolar bone (7). Furthermore, lower bone density and higher subsitability to fracture was also reported (8).

Most of the recent studies support the incidence of vitamin D deficiency with autoimmune thyroiditis (3, 9). The vitamin D insufficiency is usually accompanied by higher TSH level. The low vitamin D level may be also due to malnutrition, lack of sun exposure, chronic corticosteroid therapy (10). The detected vitamin D deficiency accompanying thyroid gland insufficiency may be attributed to either; poor intestinal absorption as in celiac disease or improper activation process (11).

Vitamin D has a central role in controlling the different body functions. Recently, it is considered as a hormone rather than a vitamin which acts mainly on the nuclear receptors of thyroid cells. It has an important role in regulating the T-lymphocytes and antigen presenting cells function. It also stimulates the macrophages phagocytosis. Furthermore, it regulates the release of various types of the pro-inflammatory cytokines as IL-2, IL-4, IL-12. Nowadays, it is used in the treatment of psoriasis and controls the proliferation rate of cancer cells in leukemia, breast and colon cancer (3, 12).

In human beings and animals, vitamin D is found in the form

of ergocalciferol (vitamin D<sub>2</sub>). The main sources of vitamin D are sun rays and dietary intake (ex. eggs, meat, milk, fish oils) (11). Our body needs 15-30 minutes a day of sun exposure for adequate dose of vitamin D. Proper wavelength occurs in spring and summer that is suitable for buildup of vitamin D stores (11). The normal range of vitamin D ranges between 30-100 ng/ml. It is stored intracellularly in the form of calcidiol [25 (OH) D<sub>3</sub>]. About 99% of the circulating calcidiol is bounded to vitamin D binding proteins while 1% is free (3). Calcidiol [25 (OH) D<sub>3</sub>] is hydroxylated intracellularly into its active form i.e. calcitriol [1,25- (OH)<sub>2</sub>D<sub>3</sub>]. The active form (calcitriol) has shorter half life (4-6 h) than the inactive form (days to weeks). This procedure is controlled by the circulating calcium, phosphates and parathormone. The active form penetrates the nucleus which gives rise to retinoic acid complex. This complex interacts with vitamin D promoter regions. About 200-500 genes are responsible for the activation or suppression of vitamin D metabolism (3, 9).

Vitamin D receptors were detected in bone, kidney, intestine, muscles, brain, liver and immune system (T, B cells, macrophages, monocytes). Vitamin D has a potent role in regulating calcium-phosphorus metabolism (4).

Vitamin D is considered as an essential immunoregulator. It regulates and modulates the T and B-cell function and proliferation. It inhibits the cellular activation and promotes the tolerogenic properties of T-cells. It also promotes Th2 phenotype (IL-4,5 production) and inhibit the Th1 activity (interferon-gamma and IL-2) (11).

It inhibits the proliferation and differentiation of plasma cells. Intimate relationship was detected between the autoimmune thyroid deficiency and the vitamin D receptor gene polymorphism (4).

Nowadays, vitamin D deficiency was detected to be the causative factor of a wide range of systemic diseases other than bony disorders as autoimmune, inflammatory and oncological as rheumatoid arthritis, systemic lupus erythematosus, type I diabetes, and inflammatory bowel disease (3, 4, 14, 15). Below 20 ng/ml, the vitamin D is considered to be deficient. Furthermore, the level of vitamin D below 10 is considered as thyroid hypofunction (3).

In patients with low vitamin D, malabsorption of calcium occurs leading to rickets in children and osteomalacia in adults. The activation process of vitamin D that occurs in kidney cells is catalyzed by parathyroid hormone (PTH). The dark skinned individuals need over exposure to sunlight due to their skin absorb less vitamin D when exposed to sunlight (11).

Old people and children are the main category at risk for vitamin D deficiency. Significant association was detected between aging in females, thyroid deficiency and vitamin D deficiency. This could be due to the close relation between the vitamin D deficiency and the anti-thyroid antibody titer (11).

The treatment of vitamin D deficiency may be either tanning three times per week or supplements (400 international unit per day) which could be sufficient for mild cases. While in severe deficiency, 50,000 international units are needed once or twice per week. The calcium and vitamin D level should be monitored monthly to avoid hypercalcemia. Patients with kidney dysfunction should be examined for vitamin D deficiency (11, 13).

Many complications could occur during dental procedure. They are at higher susceptibility to infection. Furthermore, they are at higher risk to cardiovascular disorders; arterial fibrillation, arrhythmia. The patient should be under anticoag-

ulant therapy. Myxoedematous coma may also occur during the dental procedure (5).

### **Case report**

A 43-year-old female attended the periodontology department, faculty of oral and dental medicine, Cairo University. The patient chief complaint was the hypermobility of most of her teeth for 4 years ago. Diagnosis, medical and dental history and comprehensive periodontal examination were performed. The medical history was complex and extended for long period of time. The blood pressure showed to be higher than the normal levels several years ago. Furthermore, the extraoral examination revealed puffiness of the face and eyelids, weight gain, joints pain, limitation of movement, skin dryness, tachycardia, disturbed menstruation with hot flashes, skin rash and insomnia.

The patient was referred to endocrinologist in order to detect undiagnosed systemic disease. The patient underwent detailed hormonal and blood analysis. Severe thyroid deficiency was detected. The patient suffered from mild normocytic normochromic anemia with anisocytosis. Negative ANA level, Anti-CCP level; CRP was detected with elevated ESR. Marked serum and urine albuminuria (1155) was also reported. Marked elevation of TSH level was >100 revealed impaired thyroid functions. Marked serum and urine uric acid level was detected. Normal glycated haemoglobin was reported (6%) (Figure 1).

The patient complained from uncontrolled hypertension with normal echocardiography reflecting normal cardiac functions. The patient suffered finally from severe gaseous distension.

On intraoral examination, the patient suffered from generalized severe chronic periodontitis with moderately vertical to horizontal bone loss and widening of the periodontal membrane spaces surrounding all teeth. Deep pocket depth and clinical attachment loss ranged between 6-9 mm. It was found that the patient suffered from grade III mobility related to the lower right posterior teeth and grade II in relation to the remaining dentition. Moderate, horizontal generalized bone loss was radiographically detected with characteristic widening of the periodontal membrane space. The patient has extracted the mobile teeth in relation to the left mandibular side 4 years ago.

Informed consent was obtained prior to the commencement of therapy. Information given to the patient included the following:

The treatment plan based firstly on controlling the systemic condition with comprehensive periodontal treatment with supra and subgingival debridement parallel with each other till normal levels of the blood tests was achieved. Periodontal recall visits were performed in order to control the periodontal condition. Occlusal therapy was also performed trying to adjust the impaired occlusal relations mouth wash. Only chlorohexidine was the only dental product that prescribed by the periodontist. Re-evaluation of the blood levels (TSH, T<sub>3</sub>, T<sub>4</sub>, ALT) was performed after 3 months. The patient's response to treatment was perfect. The blood tests were nearly normal and positively reflected to mobility level. Mobility level has been improved from grade III to II.

The time was suitable for periodontal regeneration regarding the shallow vertical bony defects, as the surgical intervention was not recommended by her physician which directed us to try a new non-surgical treatment modality.

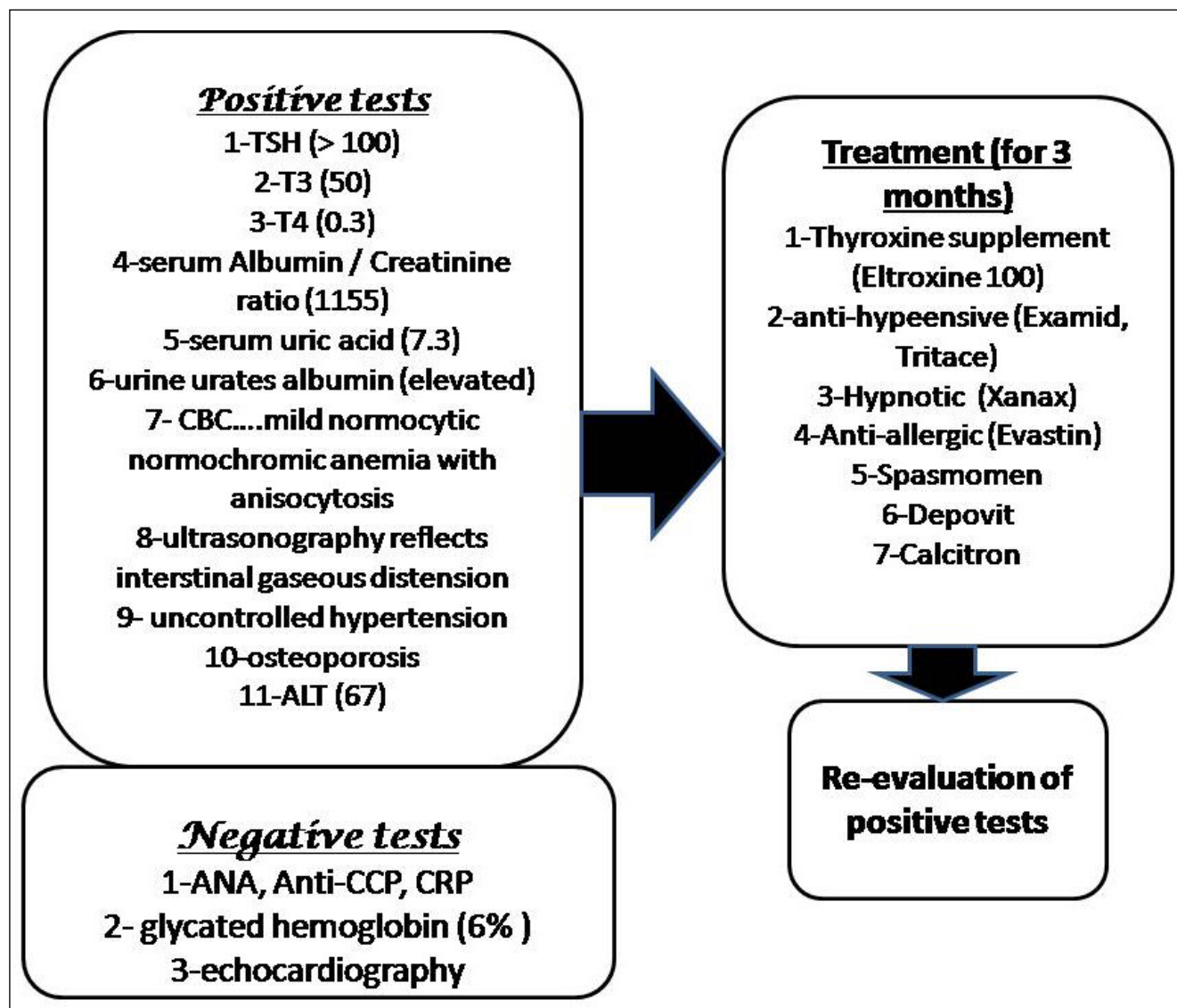


Figure 1 - Representation of the essential tests needed during the treatment of periodontitis with hypothyroidism.

Locally slow intra-ligamentary vitamin D and calcium injection (Cal-D, Memphis, Egypt) was performed according to Husain et al. (14). No pre-operative local anesthesia was recommended. Four visits of vitamin D injection with the recommended dose for each tooth (1.0 IU for each tooth interproximal surfaces) without dilution. Disposable insulin syringes with small gauge was used to lessen the proposed trauma. These injections were repeated once per week (for 1 month).

The clinical evaluation was performed by clinical photographs, clinical attachment loss scoring and standardized periapical radiographs prior and after 4 months of treatment. The follow-up period was 4 months. The patient underwent restricted diet regimen with control of the systemic (Figure 2).

## Discussion

Nowadays, thyroid hypofunction become a common disease

among adult females (15). Early diagnosis and protective investigations are recommended in order to avoid the side effects of thyroid deficiency (16).

In the current study, the physician discovered the hypothyroidism accidentally after the periodontist recommendation. Before treating the patient periodontally, the correct diagnosis and etiology for the thyroid disorder should be obtained.

The patient suffered pitting edema involving the whole body which is a rare condition. The increased mobility and widening of the periodontal membrane space were due to accumulation of fluids in the periodontal membrane space causing "periodontal edema". It may be due to the increased capillary permeability, decreased constrictor tone and increased serotonin (vasodilator) metabolism (17). The affected teeth moved in an apical direction because venous fluid and blood of the periodontal structures is pushed towards the venous lacunae and the cancellous bone.

The level of TSH exceeded 100 which explained by the over production of the stimulating hormone by the pituitary gland

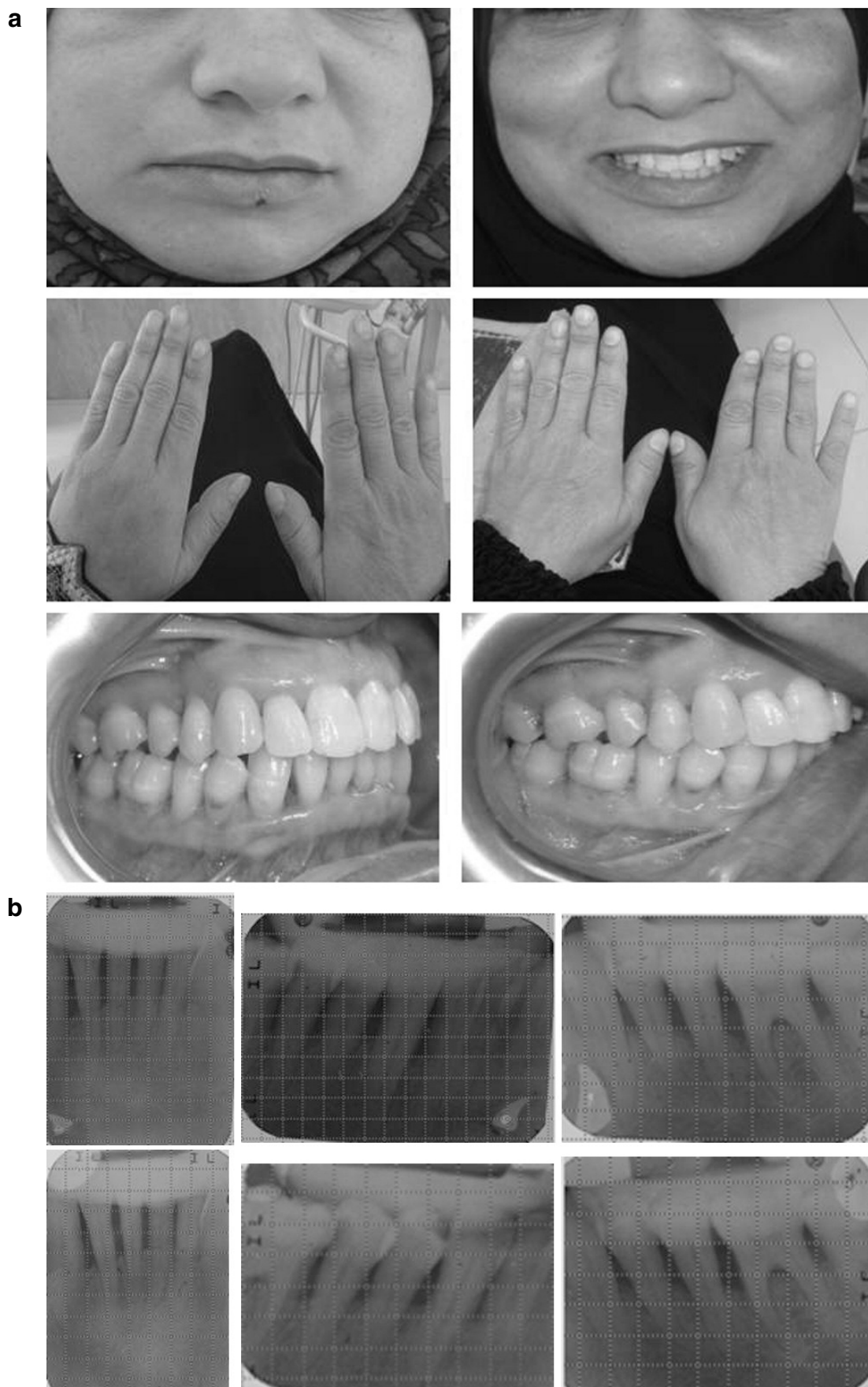


Figure 2 a, b - a) Pre and post-operative clinical; b) pre and post radiographic results.

and lack of hormones produced by the thyroid gland. It was nearly diagnosed as Hashimoto thyroiditis. It is a rare disease with 5% incidence. It is commonly detected in 45-65 year-old females. It is an autoimmune disease characterized by excessive stimulation of T-helper cells which stimulates the programmed cell death of thyroid cells causing hypothyroidism. Lifelong exogenous thyroxin supplementation is obligatory to the affected patients (18).

Controlling the systemic condition seemed to be the main problem. Complete resolution of the oral and extra-oral signs and symptoms were postulated after 3 months. The comprehensive periodontal follow-up aimed the re-establishment of a health-compatible microflora and resolve inflammation.

Surgical periodontal regeneration was not recommended at all even after controlling the systemic condition due to the uncontrolled wound healing mainly. The non-surgical vitamin D injection visits provide a non traumatic, short appointment therapy, no stress with no side effects. The procedure was not painful. No pre-operative local anesthesia was recommended to avoid the effect of the local anesthesia on the sensitive blood pressure.

The rationale behind using supplement containing vitamin D with calcium was attributed to the reported effect of both vitamin D and calcium on both the bone and soft tissue condition. On the other hand, higher regenerative power was obtained when maintaining the periosteum adapted over the alveolar bone. The trial didn't cause any harmful effect to the patient to administrate such products locally.

Such trial was reported several years ago in order to accelerate the process of bone remodeling during orthodontic treatment. On the clinical level, great improvement (no mobility) in the reported mobility which was the main chief complaint of the patient. No bleeding on probing was also detected indicating the absence of inflammation. Great reduction of the clinical attachment loss was reported due to pocket reduction. On the radiographic examination, improved bone density and accentuated lamina dura. The level of alveolar bone was elevated with average range of 1-1.5 mm. Normal width of the periodontal ligament space was also detected.

## Conclusion

Based on our experience and the data collected from the literature, periodontitis enhanced or associated with systemic diseases is an important topic that has to be considered and discussed in depth. In the current study, we tried to suggest a new point of research that requires further studies. The current study may provide a non-surgical modality regenerate the lost periodontal tissues. It is worthy to be investigated in depth rather than the researches concerning the new bone grafts and membranes. Such research will provide a

suitable solution to part of the periodontal problems especially for all patients with systemic diseases especially in developing countries.

## References

1. Igari K, Kudo T, Toyofuku T, Inoue Y, Iwai T. Association between periodontitis and the development of systemic diseases. *Oral Biology and Dentistry*. 2014;2053-5775.
2. Farasat T, Liaqat A, Mughal T. Assessment Of Thyroid Hormones Level In Premenopausal And Postmenopausal Females. *J App Pharm*. 2010;1(3):165-178.
3. Vondra K, Stárka L, Hampel R. Vitamin D and Thyroid Diseases. *Physiol Res*. 2015;64(2):S95-S100.
4. Wang J, Lv S, Chen G, Gao C, He J, Zhong H, Xu Y. Meta-Analysis of the Association between Vitamin D and Autoimmune Thyroid Disease. *Nutrients*. 2015;7:2485-2498.
5. Subramaniam P, Jagannathan N. Oral Manifestations of Hypothyroidism. *International Journal of Pharmaceutical and Clinical Research*. 2014;6(4):281-283.
6. Monea A, Elod N, Sitaru A, Stoica A, Monea M. Can Thyroid Dysfunction Induce Periodontal Disease? *European Scientific Journal*. 2014;10(15):1857-7431.
7. Feitosa D, Marques M, Casati M, Sallum E, Nociti I, de Toledo S. The influence of thyroid hormones on periodontitis-related bone loss and tooth-supporting alveolar bone: a histological study in rats. *J Periodont Res*. 2009;44:472-478.
8. Tuchendler D, Bolanowski M. The influence of thyroid dysfunction on bone metabolism. *Thyroid Research*. 2014;7(12).
9. Bizzaro G, Shoenfeld Y. Vitamin D and autoimmune thyroid diseases: facts and unresolved questions. *Immunol Res*. 2015;61:46-52.
10. Kim D. Low vitamin D status is associated with hypothyroid Hashimoto's thyroiditis. *Hormones*. 2016.
11. Shin D, Kim K, Kim D, Hwang S, Lee E. Low Serum Vitamin D Is Associated with Anti-Thyroid Peroxidase Antibody in Autoimmune Thyroiditis. *Yonsei Med J*. 2014;55(2):476-481.
12. Demille D, Piscitelli M, Ocker A, Vuong C, Hartner L, Lynch M. Vitamin D deficiency in the oncology setting. *J Community Support Oncol*. 2014;12:13-19.
13. Agmon-Levin N, Theodor E, Segal R, Schoenfeld Y. Vitamin D in systemic and organ-specific autoimmune diseases. *Clin Rev Allergy Immunol*. 2013;45:256-266.
14. Al-Hasani N, Al-Bustani A, Ghareeb M, Hussain S. Clinical Efficacy of Locally Injected Calcitriol In Orthodontic Tooth Movement. *Int J Pharm Pharm Sci*. 2011;3(5):139-143.
15. Brent G. Environmental Exposures and Autoimmune Thyroid Disease. *Thyroid*. 2010;20(7).
16. Garber J, Cobin R, Gharib H, Hennessey J, Klein I, Mechanick J, Pessah-Pollack R, Singer P, Woeber K. Clinical Practice Guidelines For Hypothyroidism In Adults: Cosponsored By The American Association Of Clinical Endocrinologists And The American Thyroid Association. *ATA/AACE guidelines for hypothyroidism in adults*. *Endoc Pract*. 2012;18(8).
17. Mahajan S, Machhan P, Sood B, Taneja S, Raina R, Thakur S. Pitting edema in hypothyroidism. *J Assoc physicians India*. 2003;51(885).
18. Pyzik A, Grywalska E, Matyjaszek-Matuszek B, Roliński J. Immune Disorders in Hashimoto's Thyroiditis: What Do We Know So Far? *Journal of Immunology Research*. 2015:8.