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Deficient serum vitamin D level is not a risk factor for periodontitis. A cross-sectional clinical study

N. M. YUSSIF[1-2], K. SELIM[2]

[1]MSc-NILES, Cairo University, Cairo, Giza, Egypt
[2]PhD-Periodontology department, faculty of Dentistry, Cairo University, Giza, Egypt

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ABSTRACT

Aim Periodontal diseases are characterized by the presence of bleeding, inflammation, sensitivity, discomfort, mobility and tooth loss. Plenty of studies supported the assumption that vitamin D deficiency might be a risk factor for periodontal diseases. Our hypothesis aimed to investigate if there is a true association between serum vitamin D level and the presence of periodontal disease.

Materials and methods Using a cross-sectional study design, a total of 200 participants, 100 periodontitis and 100 non-periodontitis patients, were recruited during the routine examination and enrolled to 2 comparative groups.

Results Serum vitamin D levels of periodontitis patients (11.607±7.58 ng/ml) compared to non-periodontitis patients (11.756±5.608 ng/ml) presented non statistically significant differences (p-value = 0.878). Most of the population (97%) in both groups represented significantly lower serum vitamin D levels. Serum vitamin D levels showed inverse correlation with gender (r= - 0.39) as well as age (r= - 0.09), linear correlation with systemic conditions (r= 0.04) and no correlation with periodontal conditions (r= 0.00).

Conclusion The serum vitamin D deficiency is not a risk factor for periodontitis and their relationship is spurious.

INTRODUCTION

During the last decades, scientists and researchers reported conflicting results regarding the relationship between systemic health problems and periodontal conditions (1, 2). Such an understanding has recently become acceptable for diseases as infections (3), cardiovascular diseases (4), diabetes mellitus (5), kidney disorders (6), thyroid diseases (7), musculoskeletal problems (8) as well as nutritional deficiency.

The role of vitamins begins to attract attention of researchers and clinicians. Several studies hypothesized that reduced serum levels of vitamin D may be intimately correlated with persistent periodontal diseases (9-12). Vitamin D is one of the most significant lipid soluble vitamins (3-8). Green plants and fungi are the main source for D2, but sun rays, animal and dietary products are the fundamental sources of D3 (13). It was found that Vit D has an essential role in regulating cellular growth, producing pro-inflammatory cytokines and preserving skeletal integrity (13-15). Furthermore, it can also regulate cellular differentiation, ion homeostasis, ion reabsorption and cellular immune response (13-16). Malnutrition, malabsorption diseases and lack of sun exposure are the primary risk factors for vitamin D deficiency (17). Although the long term studying of the relationship between vitamin D level and periodontal diseases, the results remain diverse.

The purpose of the present study was to determine if vitamin D deficiency is significantly associated with deteriorated periodontal status. Here are 3 questions that need to find answers:

- Shall periodontally healthy individuals have a normal vitamin D level?
- Shall periodontally compromised patients have a low vitamin D level?
- Is there a true relationship between serum vitamin D levels and the incidence of periodontal diseases?

MATERIALS AND METHODS

Study design

The current study was designed as a cross-sectional study to analyzer the distribution of serum vitamin D deficiency among both periodontally affected and periodontally

healthy patients. The study was based on the STROBE (Strengthening the Reporting of Observational studies in Epidemiology) guidelines checklist as recommended for cross sectional studies. Each subject signed an informed written consent form.

Setting and participants

The current study was carried out by recruitment of patients undergoing routine periodontal examination. The recruited sample admitted at the Diagnosis, Oral medicine and Periodontology department, Faculty of Dentistry, Cairo University (Egypt). All admitted patients, who scheduled for routine periodontal examination (by NY) and approved to enrol in the current experiment, between February 2019 and May 2019 were considered eligible.

Patients with active periodontal diseases, including chronic and aggressive periodontitis, were allocated to the test group as diseased patients (100 patients) while non-periodontitis patients were allocated to the control group as periodontally healthy patients (100 patients). Furthermore, all patients were asked to fill a medical history questionnaire (in accordance with the Declaration of Helsinki), in which they were asked to specify details concerning chronic systemic disorders. Smokers as well as pregnant females were excluded. After reaching the needed sample size (200 participants), blood samples were collected. Periodontal charting, blood tests, and a structured self-administered medical history questionnaires completed by each participant, were collected (by NY), extracted and analysed (by KS).

Variables and data sources

Data about serum vitamin D level, systemic diseases, periodontal condition, and demographic data including age, gender, and marital status were collected. The vitamin D deficiency was considered as a risk factor while age, gender as well as systemic diseases (impaired glycated hemoglobin, autoimmune disease, cardiovascular diseases and gastro-intestinal tract problems) was considered as modifiers. The periodontal condition was considered as a disease.

All blood samples were drawn in the morning from the antecubital vein (a large vessel for the insertion of peripheral intravenous catheters). The serum vitamin D was classified and defined as normal (30-100 ng/mL), mild (20-30 ng/mL), moderate (10-20 ng/mL), and severe (<10 ng/mL) respectively (18). Liquid chromatography mass spectrometry was used to analyse the serum 25- hydroxy vitamin D (25 (OH) 2D) level in blood. The manufacturer's instructions were followed during analysis.

Finally, for each subject, full mouth periodontal examination was conducted using William's periodontal probe. Probing depth (PD), clinical attachment level (CAL) and gingival bleeding measures were used to assess the periodontal condition. Patients were considered with active periodontal disease in the presence of the full mouth plaque score >20%, full mouth bleeding score > 20% as well as interproximal attachment loss of ≥ 3mm in ≥ 2 non-adjacent teeth.

Sample size calculation

The sample size of the current study was calculated according to Abreu et al. (2016) (19), Where n' = sample size with finite population correction, N = population size, Z = Z statistic for a level of confidence which is conventional (Z value is 1.96), p = expected prevalence and d = precision (5%, d = 0.05). We planned the study of independent cases and controls with 1 control(s) per case. Based upon Abreu et al. (2016) (19), the sample size calculation estimated that 100 patients per group would be necessary to demonstrate an effect size of 0.5 and 95% power. The failure rate among controls was considered of a value equals 0.5. If the true failure rate for experimental subjects is 0.85, we needed to study 50 cases and 50 controls to be able to reject the null hypothesis that the failure rates for experimental and control subjects are equal with probability (power) 0.8. The Type I error probability associated with null hypothesis is 0.05.

Statistical analysis

Statistical analysis was performed using Minitab version 17.1.0 for Microsoft 2013. Continuous variables are presented as the mean ± standard deviation. Dichotomous variables are expressed as percentages. Categorical data of two or more groups were compared using Pearson correlation test. The continuous variables normally distributed between the two groups were tested using t-test. Data normality was examined using Anderson-Darling Normality test and outlier presence was examined using Grubb's test. $P < 0.05$ was considered statistically significant.

RESULTS

Descriptive data of the subjects are presented in Table 1. Of 248 eligible participants, 48 were excluded because 10 patients cancelled after accepting, 15 patients had to travel and the others were not willing to blood sampling. A total of 200 participants was included. Using Grubbs' test for outlier testing, no outlier at the 5% level of significance was detected in the examined parameters. The minimal value of serum vitamin D was 3 ng/ml while the maximum value was 34.5 ng/ml with a mean value of 31.5 ng/ml.

Vitamin D level and gender

One hundred and fifty-eight (79%) were females while forty-two (21%) were males. The distribution of male:female showed a statistically significant difference in favor of females ($p < 0.005$). The Pearson coefficient between gender and vitamin D levels represented inverse correlation ($r = -0.39$). There was statistically significant difference of the mean serum vitamin D level for females over males in both groups (p value ≤ 0.001).

Vitamin D Deficiency	Under 30 ng/ml			Normal level (30-100 ng/ml)	Over 100 ng/ml	Total
	Mild	Moderate	Severe			
Number of patients	23 (11.5%)	89(44.5%)	83 (41.5%)	5 (2.5%)	0	200
Male: female ratio	8:6	21:56	4: 90	2:4	0	
Impaired glycatedhaemoglobin	0	0	6 (3%)	0	0	6
Autoimmune diseases	2 (1%)	10 (5%)	20 (10%)	2 (1%)	0	34
Cardiovascular disorders (CVD)	3 (1.5%)	8 (4%)	3 (1.5%)	0	0	14
Gastro-intestinal disorders (GIT)	All patients suffered from gastro-intestinal disorders					200
Systemically free	18 (9%)	68 (34%)	74 (37%)	14 (7%)	0	174
Periodontitis	9 (4.5%)	45 (22.5%)	41 (20.5%)	5 (2.5%)	0 (0%)	100
Non-Periodontitis	14 (7%)	44 (22%)	42 (21%)	0 (0%)	0 (0%)	100

TABLE 1 The study's outcomes

Vitamin D level and age

The participants' age was categorized into 6 ranges; ≤10, 11-20, 21-30, 31-40, 41-50 and 51-60 years. The overall mean age of patients was 30.32 ± 12.473 (p value < 0.005) with 4 and 60 years represented the minimal and maximal values, respectively. The range between 21-30 years represented the largest category (39%) while the age ≤10 years represented the smallest category (4 patients, 4%). The Pearson coefficient between age and vitamin D levels represented inverse correlation (r=-0.09). No statistically significant differences between them was found (p value=0.38).

Vitamin D level and marital status

Of 200 participants, 126 (63%) were single and only 74 (37%) were married. Age and marital status did not alter this association.

Vitamin D level and systemic problems

All participants were non-smokers. Out of 200 patients, 194 (97%) suffered from vitamin D deficiency, 200 (100%) reported gastro-intestinal problems (GIT disorders included; diarrhoea, constipation, peptic ulcer, duodenal ulcer or esophageal regurgitation), 34 (17%) reported auto-immune diseases (Thalassemia, cyclic neutropenia, rheumatoid arthritis, systemic lupus, etc.), 14 (7%) reported cardiovascular diseases and 6 (3%) suffered from diabetes mellitus. The Pearson coefficient between systemic condition and vitamin D levels represented positive linear correlation (r=0.04). No statistically significant differences between them was found (p value=0.69).

Vitamin D level and periodontal condition

Regarding the test group, patients were classified according to disease severity into; stage III and IV. Among periodontitis patients, only 3 patients reported mild levels, 14 patients reported moderate deficiency and 18 patients reported severe deficiency. The highest (34.5) and lowest (3) records of serum vitamin D level were reported in 2 patients with stage III periodontitis. Among the non-periodontitis patients, 4 patients reported mild deficiency, 28 patients reported moderate deficiency and 30 patients reported severe deficiency. The Pearson coefficient between periodontal status and vitamin D levels represented that there is no association between the 2 variables (r=0.00). No statistically significant differences were reported between vitamin D deficiency and the stage of periodontitis (p value >0.7). No statistically significant differences between them (p value=0.89) was recorded. The mean serum vitamin D concentration was nearly equal in periodontitis (11.61 ± 7.58 ng/ml) versus non-periodontitis patients (11.76 ± 5.61 ng/ml) with no statistically significant differences between both groups (p-value=0.88).

DISCUSSION

In the current cross-sectional study, we did not report a significant association between serum vitamin D level and the risk of periodontitis. By analysing the potential risk factors, it was found that gender, age as well as periodontal condition did not reveal an alteration of such association. Furthermore, periodontal condition showed no correlation with the serum level of vitamin D. On the other hand, our results revealed a positive effect of the systemic condition.

Between 2004 and 2015 (20-23), several observational studies were conducted to test the association between vitamin D deficiency and periodontitis. The latter studies reported higher risk for periodontitis development with vitamin D deficiency. Our findings contradict the results of the studies conducted by Abreu et al. (2016) (19), Eshghi et al. (2016) (20), Isola et al. (2020) (24) and Machado et al. (2020) (25) that demonstrated that low levels of serum vitamin D was associated with periodontitis as an important risk factor. They recommended measurement of vitamin D level in periodontitis patients during phase I therapy. In 2017, Yoon et al. (26) reported vitamin D deficiency as one of the main factors to be considered for prevention against periodontitis in the Korean population.

Finally, in 2018 (27) and 2019 (28), Anbarcioglu et al. examined the relationship between vitamin D deficiency and aggressive periodontitis and proposed that it may be a potential risk factor for aggressive periodontitis.
Our results were supported by the findings of 2 previous studies supported and conducted by the National health and nutrition examination survey (NHANS III) in which authors did not find any significant association between serum vitamin D deficiency and chronic periodontitis (29, 30). Liu et al. (2009) (31) who reported that aggressive periodontitis affecting Chinese patients was significantly associated with high levels of serum vitamin D levels than controls, respectively. Furthermore, Millen et al. (2013) (32) reported normal levels of vitamin D could not protect against periodontal tissue destruction.
Several studies speculated several factors as a reason for such a scientific debate, including seasonal fluctuation of vitamin D (31), ethnic differences (33), nutritional problems (34) and chronic systemic problems (35). Liu et al. (2009) (31) recommended blood sampling from January to May to avoid vitamin D fluctuations. Due to racial bases (36), it was found that vitamin D deficiency is a common problem in Chinese (31) as well as Egyptian populations, as presented in the current study.
In the current study, as young females represented the majority of the examined population, we recommend that long-term menstrual cycles (37) as well as pregnancy periods (38) could be the cause behind the deficiency. Moreover, malabsorption syndrome affects a huge range of the Egyptian population, as supported by Parva et al. (2018) (39), and 100% of the examined sample suffered from gastrointestinal problems.

CONCLUSION

Based on our study results, we concluded the following.
- Both groups (97%) presented vitamin D deficiency.
- An independent association between serum vitamin D level and periodontal diseases.
- The Vitamin D deficiency could not be considered as a risk factor for periodontal disease.
- Evaluation of vitamin D levels before surgical interventions related to bone as implant therapy or augmentation procedures is highly recommended.
- Future studies with long-term prospective study design and larger sample size of patients from the same population is highly recommended.

Competing interests
None.

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Authors' contributions
The manuscript has been read and approved by all authors, who have contributed to prepare each step of the manuscript; experiment, writing and analysis.

Protocol registration
The study's protocol included the research question, key design features, and analysis plan which was prepared before the study.

Study limitations
Larger sample size was needed. The systemic condition of participants needed to be analyzed in depth.

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