

Evaluation of Vitamin D-level in patients with rhinoscleroma

Ali Mahrous¹; Wael Fawzy Ismaeil²; Mohamed Hussein Abdelazim² and Mohamad Ayed Rashawn³

**Original
Article**

¹Otorhinolaryngology Department, Faculty of Medicine, Al-Azhar University

²Otorhinolaryngology Department, Faculty of Medicine New Damietta, Al-Azhar University

³Clinical Pathology Department, Faculty of Medicine, Mansoura University(c)

ABSTRACT

Background: Rhinoscleroma represents a challenging health problem especially in Egypt, in which it is an endemic condition. Vitamin D3 deficiency may play a role in the pathogenesis of the disease.

Aim of the work: To compare vitamin D3 level in subjects with rhinoscleroma versus control.

Patients and methods: The study was conducted at Ear, Nose and Throat (ENT) departments, AL-Azhar University Hospitals, (Al-Hussein, Bab Alsheria, and Damietta, Egypt) The participants were divided into two groups: Group A comprised 20 patients with confirmed diagnosis of rhinoscleroma through punch biopsies with the assistance of nasal endoscopy and Group B which comprised 20 participants of healthy volunteers. All participants were subjected to thorough history taking and clinical examination. 40 participants were incorporated in the study. Then, serum vitamin D3 levels were determined for all participants.

Results: 85 % of group A were vitamin D3 deficient (vitamin D3 < 20.0ng/dl), 15% were insufficient (vitamin D3 20-29ng/dl) and none was sufficient (vitamin D3 ≥30ng/dl), while in control group vitamin D3 was deficient in 1 subject (5.0%), insufficient in 35% and sufficient in 60.0%. There was no significant relation between site or side of rhinoscleroma and vitamin D3 level.

Conclusion: Vitamin D3 levels were significantly reduced in patients with rhinoscleroma (group A) as opposed to group B and this reduction may have a role in pathogenesis of rhinoscleroma and vitamin D3 supplementations may affect the course of the disease

Key Words: Endemic, granuloma, rhinoscleroma, upper airway, vitamin D.

Received: 05 August 2018, **Accepted:** 23 October 2018

Corresponding Author: Mohamed Hussein Abdelazim, Lecturer of Otorhinolaryngology Department Faculty of Medicine New Damietta Al-Azhar University; Egypt, **Tel.:** +20 1006095530, **E-mail:** mohammedabdelazeem35@yahoo.com

ISSN: 2090-0740, November 2018, Vol.19, No. 3

INTRODUCTION

Vitamin D3-deficiency is a global health problem^[1-3]. The traditional role of vitamin D3 is mainly in the endocrine system, concerned with calcium and phosphate homeostasis^[4]. There are many studies which revealed that, deficiency of vitamin D3 is linked to conditions other than skeletal disorders such as infectious diseases, type-1 and type-2 diabetes mellitus, many types of cancer, autoimmune diseases, neurocognitive dysfunction, mental illness, ocular conditions, cardiovascular diseases, and allergic disorders, e.g., bronchial asthma, as well as infertility and adverse outcome of pregnancy and birth^[5-14]. Wang et al.^[15] concluded that, the lack of vitamin D3 was significantly associated with chronic rhinosinusitis (CRS) with nasal polyposis and showed an association with the polyp size. They proposed that, plasma vitamin D3 values could be assessed in the routine Laboratory workup of patients who

had CRS and could be used to help in determination of disease severity. Moreover, the available data proposed that, vitamin D3 supplementation may denote a unique and safe approach to prevent respiratory tract infections (RTIs). In addition, daily or weekly dose regimens appear to be more effective than pulse therapy^[16-17].

Rhinoscleroma (RS) is a chronic granulomatous disease affecting the upper respiratory tract. It is an endemic condition in Egypt as well in other countries including Chili, India and Indonesia^[18-20]. Clinically, RS is a disease of gradual onset and slowly progressive indolent course. It affects mainly the nasal cavity in 95 to 100% of patients with or without involvement of the naso-pharynx, nasal sinuses, pharynx, larynx, trachea or bronchi^[18-20].

Based on ubiquitous impact of various body systems, we thought that, vitamin D3 could be linked to development

and could be used as supportive treatment of rhinoscleroma. Thus, we conducted this study to estimate vitamin D3 levels in patients with histopathologically proven RS comparing them with control healthy volunteers.

PATIENTS AND METHODS

This is a prospective control study which was conducted at Ear, Nose and Throat (ENT) departments, AL-Azhar University Hospitals, (Al-Hussein, Bab Alsheria, and Damietta, Egypt). Approval to perform this work was obtained from the institutional Research Ethical Committee and written informed consent was obtained from all participants. All patients were subjected to thorough history taking and clinical examination. All patients in group A underwent nasal punch biopsies at Ear, Nose and Throat (ENT) department for diagnostic purposes of chronic nasal symptoms between January 2016 and April 2017 using nasal endoscopy.

2.1. The inclusion criteria of group A: the patient was included if he/she had a suspicious clinical manifestation of rhinoscleroma such as unexplained chronic nasal symptoms including nasal obstruction, nasal crustation of specific odour or repeated epistaxis. Then, on histopathological examination of the punch biopsy, it was proven to have rhinoscleroma (Figure 1). The existence of malignant neoplastic or benign lesions was the sole exclusion criterion. The age ranged from 18 to 56 of group A. Another 20 healthy subjects (control group) (6 males and 14 females; age ranged from 16 to 55 years, the mean age was 36.70 ± 11.97 years) were included in the trial for the purpose of comparison. All participants were subjected to routine blood tests complete blood count (CBC); serum glutamic-pyruvic transaminase (SGPT); serum glutamic-oxaloacetic transaminase serum glutamic-oxaloacetic transaminase (SGOT); Creatinine; Random blood sugar level); none of the them was diabetic or having kidney disease.

2.2. Measurement of systemic vitamin D (25VD3) levels: Serum samples were separated by centrifugation and frozen immediately at -20°C . Plasma 25 OH Vitamin D3 values were determined by a VIDAS 25 OH Vitamin D evaluation kits (Biomerieux, Marcy l'Etoile, France) on mini VIDAS automated immunoassay platform. It is a quantitative test using Enzyme Linked Fluorescent Assay (ELFA) technology. The vitamin D3 values of the studied subjects were categorized as deficient (<20 ng/ml), insufficient (20–29 ng/ml), sufficient (30–100 ng/ml) and potential toxicity (>100 ng/ml).

2.3. Quality control of laboratory methods: The reliability of the study results was guaranteed by applying quality control measures throughout the whole procedure

of the laboratory work. All materials, equipments and procedures were adequately controlled.

2.4. Statistical analysis of data: the collected data were coded, organized and tabulated using statistical package for social science (SPSS) version 19 (IBM®SPSS®, Inc., Chicago, USA). Numerical variables were presented as mean \pm (SD: standard deviation), while categorical variables were presented as relative frequency and percent distribution. Comparison between groups was done by independent samples student (t) test, while Chi square test or Mann-Whitney test were used for comparison between categorical variables. P value < 0.05 was considered significant.

RESULTS

In the present study, there was no significant difference between study and control groups as regard to sex or age of studied subjects (table 1).

However, there was statistically significant decrease of vitamin D3 levels in study when compared to control group (14.17 ± 5.10 vs 33.28 ± 9.66 ng/ml respectively). 85.0% of the study group were deficient (vitamin D3 < 20.0 ng/dl), 15% were insufficient (vitamin D3 20–29 ng/dl) and none was sufficient (vitamin D3 ≥ 30 ng/dl), while in control group 1 subject (5.0%) had deficient levels, 35.0% had insufficient levels and 60.0% had sufficient levels (table 2, figure 2). Also, there was no significant relation between site or side of rhinoscleroma and vitamin D3 level (table 3).

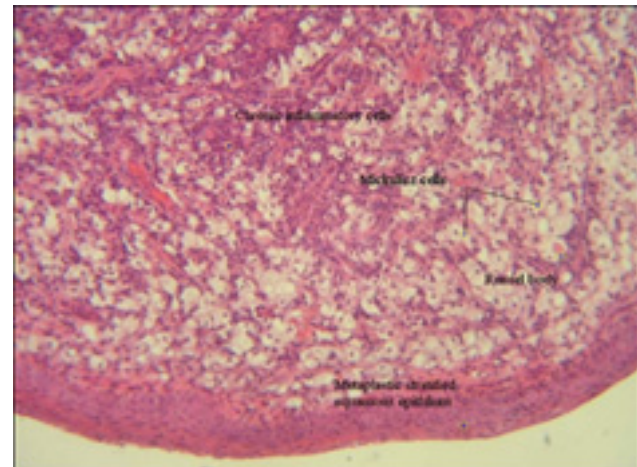


Fig. 1: The epithelium: metaplastic squamous epithelium.

The sub-epithelium contains:

* A background of chronic inflammatory cells: plasma cells, macrophages and lymphocytes).

* Mickulicz cells: groups of vacuolated macrophages engulfing the bacteria and undergo hydropic degeneration.

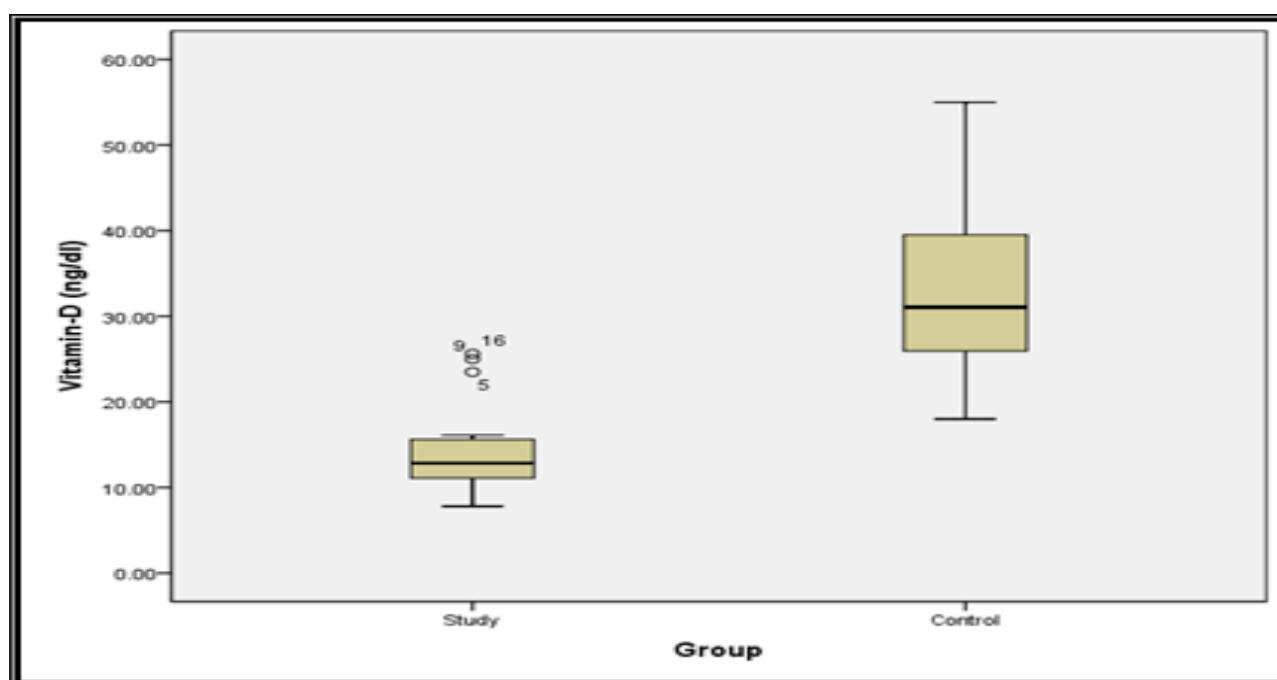


Fig. 2: Boxplot presentation showing vitamin-D levels in studied groups

Table (1): Sex, age distribution in studied populations

		Study	Control	Test	p
Sex (n,%)	Male	8 (40.0%)	6(30.0%)	0.44	0.50(ns)
	Female	12 (60.0%)	14(70.0%)		
Age (mean±SD)		35.80±12.09; 15-52	36.70±11.97; 16-55	0.23	0.81(ns)

Table (2): Comparison between study and control groups as regard to vitamin D₃

		Study	Control	Test	p
Vitamin D ₃ (ng/dl)		14.17±5.10; 7.80-25.60	33.28±9.66; 18-55	7.81	<0.001*
Vitamin-D ₃ Status	Deficient	34(85.0%)	1(5.0%)	27.82	<0.001*
	Insufficient	6(15.0%)	7(35.0%)		
	Sufficient	0(0.0%)	12(60.0%)		

Table (3): Relation between vitamin D3 and clinical characteristics of rhinoscleroma

		Mean	SD	F	p
Site	Nasal	13.34	4.12	1.04	0.37 (ns)
	Nasopharynx	16.98	7.41		
	nasopharyngotracheal	11.90	.		
Site	Bilateral	14.22	5.07	1.38	0.27(ns)
	Right	16.82	5.86		
	Left	10.46	2.65		

* Russel bodies: scattered red homogenous oval bodies with pyknotic eccentric nuclei due to hyaline degeneration of plasma cells.

DISCUSSION

Vitamin D3 was found to play significant roles outside the skeletal system, especially in infection, allergy, and autoimmunity. Thus, we searched for the levels of vitamin D3 in patients with rhinoscleroma and interestingly we found significant decrease of vitamin D3 levels in patients when compared to controls or when compared to reference value. Thus, vitamin D3 deficiency may be associated with the development or the clinical course of rhinoscleroma. The possible mechanisms are not studied as yet. However, it may be through the effects on the immune system as it is well known that, the Vitamin D3 regulates the activity of various immune cells, including monocytes, dendritic cells, T and B lymphocytes and immune functions of epithelial cells^[21]. Additionally, vitamin D3 increases the conversion of immature monocytes to mature macrophages and lead to an increase in other macrophage functions. Thus, Vitamin D3 deficiency can lead to inflammation^[22]. This entity was confirmed by the abundance of inflammatory cells (plasma cells, eosinophils and lymphocytes)^[23-24].

Observational studies indicate that vitamin D3 deficiency is a predisposing factor for infections and may contribute to increased risk of lower and upper respiratory tract infections^[25-27]. In their review, Vanherwegen et al.^[28] reported that, inflammation is a common factor in many chronic disorders, and concern has been raised about the impact of vitamin D3 deficiency on several inflammatory immune processes. There is a clear link between infections, inflammation, and autoimmunity. Furthermore, epidemiologic studies indicate a strong correlation between vitamin D deficiency and the increased incidence of autoimmune and chronic inflammatory diseases. These findings, together with the in vitro and in vivo immunomodulatory effects of 1,25(OH)2D3, form the basis to suggest that using vitamin D3 supplementation might provide protection against these immune diseases. Furthermore, there is an evidence to support an association of decreased 25(OH) D3 with chronic rhinosinusitis in adults^[15,29], also in a study by Badr El-Din et al^[30] they found that Serum level of VD3 in patients with chronic rhinosinusitis with nasal polyposis and Allergic fungal rhinosinusitis is significantly lower than that of patients with Chronic rhinosinusitis without nasal polyposis and control subjects. Which may share pathogenic mechanisms with rhinoscleroma.

We would like to admit that despite the limited number of participants in our study, it still has proved that vitamin D3 may have a significant role to play in relation to rhinoscleroma.

CONCLUSION

Our study showed that the levels of vitamin D3 were significantly lower in patients with rhinoscleroma. Therefore, we recommend that vitamin D3 supplementations may affect the course of the disease.

CONFLICT OF INTEREST

There are no conflict of Interest.

REFERENCES

1. Peters BS, dos Santos LC, Fisberg M, Wood RJ, Martini LA. Prevalence of vitamin D insufficiency in Brazilian adolescents. *Ann Nutr Metab* 2009;54(1):15-21.
2. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Controversy in clinical endocrinology: guidelines for preventing and treating vitamin D deficiency and insufficiency revisited. *J Clin Endocrinol Metab* 2012; 97:1153–8.
3. Batieha A, Khader Y, Jaddou H, Hyassat D, Batieha Z, Khateeb M, Belbisi A, Ajlouni K. Vitamin D status in Jordan: dress style and gender discrepancies. *Ann Nutr Metab* 2011;58(1):10-8.
4. Holick MF. Vitamin D deficiency. *N Engl J Med* 2007; 357:266–281.
5. Rejnmark L. Effects of vitamin D on muscle function and performance: a review of evidence from randomized controlled trials. *Ther Adv Chronic Dis* 2011; 2(1): 25–37.
6. Frieri M, and Valluri A. Vitamin D deficiency as a risk factor for allergic disorders and immune mechanisms. *Allergy Asthma Proc* 2011; 32:438–444.
7. Bischoff-Ferrari HA, Dawson-Hughes B, Staehelin HB, Orav JE, Stuck AE, Theiler R, et al. Fall prevention with supplemental and active forms of vitamin D: a meta-analysis of randomised controlled trials. *BMJ* 2009;339: b3692.
8. Lang PO, Samaras N, Samaras D, Aspinall R. How important is vitamin D in preventing infections? *Osteoporos Int* 2013; 24(5):1537-53.
9. Watkins RR, Yamshchikov AV, Lemonovich TL, Salata RA. The role of vitamin D deficiency in sepsis and potential therapeutic implications. *J Infect* Nov 2011; 63(5):321–6.
10. Souberbielle J-C, Body J-J, Laappe JM, Plebani M, Shoenfeld Y, Wang TJ, et al. Vitamin D and musculoskeletal health, cardiovascular disease, autoimmunity and cancer: recommendations for clinical practice. *Autoimmun Rev* 2010; 9:709–15.

11. Muscogiuri G, Sorice GP, Ajjan R, Mezza T, Pilz S, Prioretta A, et al. Can vitamin D deficiency cause diabetes and cardiovascular diseases? Present evidence and future perspectives. *Nutr Metab Cardiovasc Dis* 2012; 22(2):81–7.
12. Avenella A, MacLennan GS, Jenkinson DJ, McPherson GC, McDonald AM, Pant PR, et al. RECORD Trial Group: long-term follow-up for mortality and cancer in a randomized placebo-controlled trial of vitamin D(3) and/or calcium (RECORD trial). *J Clin Endocrinol Metab* 2012; 97:614–22
13. Bjelakovic G, Gluud LL, Nikolova D, Whitfield K, Wetterslev J, Simonetti RG, et al. Vitamin D supplementation for prevention of mortality in adults. *Cochrane Database Syst Rev* 2011(7):CD007470
14. Rejnmark L, Avenell A, Masud T, Anderson F, Meyer HE, Sanders KM, et al. Vitamin D with calcium reduces mortality: patient level pooled analysis of 70,528 patients from eight major vitamin D trials. *J Clin Endocrinol Metab* 2012; 97(8): 2670–81.
15. Wang L-F, Lee C-H, Chien C-Y, Chen JY, Chiang F-U, Tai C-F. Serum 25-hydroxyvitamin D levels are lower in chronic rhinosinusitis with nasal polyposis and are correlated with disease severity in Taiwanese patients. *Am J Rhinol Allergy* 2013; 27, e162–e165.
16. Martineau AR, Jolliffe DA, Hooper RL, Greenberg L, et al. Vitamin D supplementation to prevent acute respiratory tract infections: Systematic review and meta-analysis of individual participant data. *BMJ* 2017; 356: i6583.
17. Bergman P, Lindh ÅU, Björkhem-Bergman L, Lindh JD. Vitamin D and respiratory tract infections: A systematic review and meta-analysis of randomized controlled trials. *PLoS ONE* 2013; 8: e65835.
18. Hazem A. Gaafar, Alaa H. Gaafar, Yasser A. Nour. Rhinoscleroma: An updated experience through the last 10 years. *Acta Oto-Laryngologica* 2011; 131: 440-6.
19. Chan TV, Spiegel JH. Klebsiella rhinoscleromatis of the membranous nasal septum. *J Laryngol Otol* 2007; 121: 998-1002.
20. Hart CA, Rao SK. Rhinoscleroma. *J Med Microbiol* 2000; 49: 395-6.
21. Hewison M. Vitamin D, and innate and adaptive immunity. *Vitam Horm* 2011; 86:23–62.
22. Canning MO, Grotenhuis K, de Wit H, Ruwhof C, Drexhage HA. 1-alpha,25 dihydroxyvitamin D3 [1,25(OH)(2)D(3)] hampers the maturation of fully active immature dendritic cells from monocytes. *Eur J Endocrinol* 2001; 145:351–7.
23. Abalkhail A, Satti MB, Uthman MA, Al Hilli F, Darwish A, Satir A. Rhinoscleroma: a clinico-pathological study from the Gulf region. *Singapore Med J* 2007; 48: 148-51.
24. Pattankar VL, Roohi S, Reddy BN. Clinicopathological study of Rhinoscleroma with Mast cell profile. *Int J Sci Res Pub* 2013; 3: 1-5.
25. Larkin A, Lassetter J. Vitamin D deficiency and acute lower respiratory infections in children younger than 5 y: identification and treatment. *J Pediatr Health Care* 2014; 28: 572–82.
26. Ahmed P, Babaniyi B, Yusuf KK, et al. Vitamin D status and hospitalization for childhood acute lower respiratory tract infections in Nigeria. *Pediatr Int Child Health* 2015; 35:151–6.
27. Roth DE, Shah R, Black RE, Baqui AH. Vitamin D status and acute lower respiratory infection in early childhood in Sylhet, Bangladesh. *Acta Paediatr* 2010; 99: 389–93.
28. Vanherwegen AS, Gysemans C, Mathieu C. Regulation of Immune Function by Vitamin D and Its Use in Diseases of Immunity. *Endocrinol Metab Clin N Am* 2017; 46: 1061–1094
29. Schlosser RJ, Soler ZM, Schmedes GW, Storck K, Mulligan JK. Impact of vitamin D deficiency upon clinical presentation in nasal polyposis. *Int Forum Allergy Rhinol* 2014; 4:196–69.
30. Badr El-Din M, Mohammed ST, Tarek A, Azza O, Neema L. Evaluation of vitamin D levels in allergic fungal sinusitis, chronic rhinosinusitis, and chronic rhinosinusitis with polyposis. *Int Forum Allergy Rhinol* 2016; 6:185-190