



The Average of Serum 25(OH)D in Children with Chronic Tonsillitis

Melati Sudiro*^{ORCID}, Arif Dermawan^{ORCID}, Alfira Ulfa^{ORCID}

Department of Otorhinolaryngology-Head and Neck Surgery, Faculty of Medicine, Universitas Padjadjaran, Dr. Hasan Sadikin General Hospital, Bandung, Indonesia

Abstract

Edited by: Ksenija Bogoeva-Kostovska
Citation: Sudiro M, Dermawan A, Ulfa A. The Average of Serum 25(OH)D in Children with Chronic Tonsillitis. Open Access Maced J Med Sci. 2023 May 26; 11(B):571-575. https://doi.org/10.3889/oamjms.2023.11618
Keywords: Chronic tonsillitis; Vitamin D level; Serum 25(OH)D
***Correspondence:** Melati Sudiro, Department of Otorhinolaryngology-Head and Neck Surgery, Faculty of Medicine, Universitas Padjadjaran, Dr. Hasan Sadikin General Hospital, Bandung, Indonesia. Phone: +628112212745, E-mail: melati.sudiro@unpad.ac.id
Received: 24-Mar-2023
Revised: 04-Apr-2023
Accepted: 16-May-2023
Copyright: © 2023 Melati Sudiro, Arif Dermawan, Alfira Ulfa
Funding: This research did not receive any financial support.
Competing Interests: The authors have declared that no competing interests exist.
Open Access: This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (CC BY-NC 4.0)

BACKGROUND: Chronic tonsillitis is an inflammation of the tonsils that persists for more than three months, and vitamin D deficiency is frequently associated with an increased incidence of acute respiratory tract infections. These result in the risk of progression to chronic tonsillitis in approximately 16% of cases.

AIM: This study aims to determine serum 25(OH)D levels in children with chronic tonsillitis at Dr. Hasan Sadikin Bandung General Hospital.

METHODS: This descriptive and cross-sectional study was conducted in patients with chronic tonsillitis aged 3–15 years from August 26, 2021, to April 26, 2022. The exclusion criteria include children who consumed Vitamin D for the past month, are in ongoing treatment for chronic tonsillitis, and have comorbidities that affect Vitamin D serum. Characteristics were taken from anamnesis, while Vitamin D serum was analyzed using the ELISA method, then data were presented in numbers and percentages.

RESULTS: The average serum level of 25(OH)D was 16.43 ± 3.5 ng/mL. All 44 subjects suffered from a lack of Vitamin D, categorized as deficiency, insufficiency, and severe deficiency, at 72.7%, 22.7%, and 4.6%, respectively. The majority of the cases were boys compared to girls, with 70.5% and 29.5%, respectively.

CONCLUSION: All children with chronic tonsillitis were found to have 25(OH)D serum below the normal level, with an average of 16.43 ± 3.5 ng/mL, especially in boys aged 3–10 years.

Introduction

The Tonsils are a set of lymphoid organs, that play an important role in the immune system, which is known as Waldeyer's ring and consists of the two Palatine tonsils, Adenoid tonsils, and the Lingual tonsils. Waldeyer's ring protects the digestive and respiratory tract against pathogens. In children, the palatine tonsils are the most active when an antigen enters the body [1].

Chronic tonsillitis is an inflammation of the lymphoid organs, mostly palatine tonsils, that persists due to acute or subclinical infection lasting for more than 3 months and characterized by crypts widening and hypertrophic or atrophic tonsils. Furthermore, its diagnosis is made when there is a history of chronic tonsillitis 3–4 times a year with no improvement after administering adequate antibiotics [1], [2].

Chronic tonsillitis is rarely seen in children <2 years old due to the less active immune system of the tonsils [1]. According to Bakar *et al.*, the highest distribution of chronic tonsillitis occurs at the age of 1–10 years, accounting for 36% [2]. However, Haidara *et al.* reported that the peak incidence of chronic tonsillitis occurred at the age of 5–14 years at 50% [3].

Another study reported that more than half, accounting for 55.97%, of 2176 chronic tonsillitis patients were in the age range of 0–15 years [4].

The incidence of chronic tonsillitis in children varies among countries. According to Haidara *et al.*, there are 40 million cases annually in the United States, 9 million in France, and 4 million in Spain [3]. Riskesdas 2018 reported that the prevalence of upper respiratory tract infections, including tonsillitis was 9.3% [5]. In addition, approximately 145 cases of children were reported at the Laryngo-pharyng division Otorhinolaryngology-Head and Neck Surgery (ORL-HNS) clinic in Dr. Hasan Sadikin Hospital (RSHS) from 2015 to 2020.

The mechanism of chronic tonsillitis is unclear, but tonsils are known to prevent infections. The immune system, environmental factors, and pathogens are also known to play an important role in the occurrence of chronic tonsillitis. Another factor currently associated with chronic tonsillitis is Vitamin D deficiency, which participates in immune system regulation, both innate and adaptive immune response [6], [7]. According to Yildiz *et al.*, Vitamin D deficiency was found in 4.7% of children with chronic tonsillopharyngitis [8]. Bergman *et al.* reported that oral Vitamin D supplementation can reduce the severity and prevent respiratory tract infections in 47 cases in the 18–75 year age group,

accounting for 23% [9]. However, Rao *et al.* stated a different opinion that there was no significant relationship between children patients with chronic tonsillitis and Vitamin D levels [7]. Indonesia is located on the equator, where the sun shines throughout the year. However, Indonesia's population has low serum vitamin D levels [10], [11], [12]. According to Fiannisa, countries crossed by the equator, such as Indonesia and Malaysia, do not prove sufficient levels of Vitamin D in the body [11].

Based on the study above, Vitamin D deficiency still has to be considered in children with chronic tonsillitis in Indonesia. Therefore, this study aims to determine serum 25(OH)D levels in children with chronic tonsillitis at Dr. Hasan Sadikin Bandung General Hospital.

Methods

This descriptive and cross-sectional study was conducted in Dr. Hasan Sadikin Bandung General Hospital from August 26 2021, to April 26 2022, using a consecutive sampling method. The participants include children aged 3–15 years with chronic tonsillitis. Subjects with a history of Vitamin D supplements consumption in the past 1 month, treated chronic tonsillitis, and diseases that interfere with Vitamin D levels, such as autoimmune, chronic disease, atopic, and malignancy, were excluded to minimize bias. Data were collected after obtaining informed consent from parents. Furthermore, general characteristics such as age and gender were collected from medical records. Chronic tonsillitis was diagnosed based on history taking and physical examination during a visit.

Laboratory examinations were carried out by taking 3 cc of blood, placed and stored in sterile tubes to be sent to the laboratory. The sample yielded was analyzed by the ELISA method and measured by examining the color reaction on the well microplate. The intensity of the color is inversely proportional to the concentration of 25(OH)D in the sample. Furthermore, serum 25(OH)D was classified as very severe deficiency (<5 ng/mL), severe deficiency (5–<11 ng/mL), deficiency (11–<20 ng/mL), insufficiency (20–<30 ng/mL), and normal (20–30 ng/mL) serum level [12]. The results are presented descriptively by calculating the mean, standard deviation, median, and range. Data were then processed using Microsoft Excel and presented as tables.

Results

During the study period, there were 46 children with chronic tonsillitis. However, two patients were excluded due to a history of atopic and chronic disease that could affect serum Vitamin D levels.

Table 1: General characteristics (n = 44)

Characteristics	n = 44
Gender	
Male	31
Female	13
Age (years old)	
3–10	35
11–15	9
Mean ± SD	6.95 ± 4.15
Range	3–15

SD: Standard deviation.

Tables 1 and 2 show the characteristics of gender, age, nutritional status, and Vitamin D level status of patients with chronic tonsillitis. The majority of patients were boys at 70.5% and aged 3–10 years accounting for 79.5%, with an average age of 6.95 years. The result shows that the average serum 25(OH)D was 16.43 ng/mL, classified as Vitamin D deficiency. Furthermore, no participants were reported with normal or very severe Vitamin D deficiency.

Table 2: Total serum 25(OH) D

Characteristics	n = 44, n (%)
Serum 25(OH) D (ng/mL)	
Mean ± SD	16.43 ± 3.54
Range	10.30–24.37
Vitamin D status	
Insufficiency	10 (22.7)
Deficiency	32 (72.7)
Severe deficiency	2 (4.6)

SD: Standard deviation.

A total of 80.7% of boys and 53.8% of girls suffered from Vitamin D deficiency, as shown in Table 3. In all age groups, Vitamin D deficiency was the most common in the 3–10 year age group, accounting for 87.5%. Table 4 shows the descriptive statistics of serum 25(OH)D. Vitamin D levels were measured with serum samples using the ELISA method and classified according to the Holick classification. From the descriptive table, gender and average age Vitamin D levels are not significant/ homogenes.

Table 3: Age and gender distribution based on Vitamin D serum level

Characteristics	Vitamin D status		
	Insufficiency (n = 10), n (%)	Deficiency (n = 32), n (%)	Severe deficiency (n = 2), n (%)
Gender			
Male	5 (16.1)	25 (80.7)	1 (3.2)
Female	5 (38.5)	7 (53.8)	1 (7.7)
Age (years old)			
3–10	6 (11.4)	28 (87.5)	1 (14.3)
11–15	4 (44.4)	4 (44.4)	1 (11.1)

Discussion

This study found that chronic tonsillitis was most common in boys in 70.5% of the cases. This

Table 4: Descriptive statistics of Vitamin D serum

Characteristics	Vitamin D status		
	Insufficiency (n = 10)	Deficiency (n = 32)	Severe deficiency (n = 2)
Serum 25(OH) D (ng/mL)			
Mean ± SD	21.19 ± 1.61	15.31 ± 2.40	10.50 ± 0.28
Median	20.88	15.10	Minimum: 10.3 Maximum: 10.7
Range ¹²	20–30	11–19	5–10

¹²Vitamin D levels were measured with serum samples using the ELISA method and classified according to the Holick classification, *From the descriptive table, gender and average age Vitamin D levels are not significant/ homogenes. SD: Standard deviation.

is similar to a study conducted by Rao *et al.* and as well as Rahayu *et al.*, reporting that chronic tonsillitis was more common in boys, with a percentage of 55% and 67.6%, respectively [7], [13]. The high case of chronic tonsillitis in boys is due to a different lifestyle, such as high consumption of oily food, poor oral hygiene, and unhygienic habits, as reported by Shalihah *et al.* [14].

According to Onal *et al.*, chronic tonsillitis is a condition caused by hyper immunity, characterized by the presence of chronic inflammatory cells on histopathological examination [15]. Malapane *et al.* reported that only a small proportion occurs in boys because of a weaker adaptive immune system. Androgens in boys have anti-inflammatory properties that inhibit the secretion of IL-2 and IL-4 cytokines and increase IL-10 production. This study also states that IL-2 is the first group of cytokines shown to have an important role in T-cell development. Conversely, estrogen in girls was reported with pro-inflammatory properties, resulting in increased activity of humoral and cellular immune cells by stimulating the secretion of cytokines such as IL-2, IL-4, IL-6, TNF- α , and TNF- β [16].

The result of this study showed that chronic tonsillitis was most common in the age group of 3–10 years at 79.5%, with a peak age of 4 years, accounting for 25%. Furthermore, a total of 87.5% of subjects in the age group 3–10 years had Vitamin D deficiency, while 44.4% experienced insufficiency and Vitamin D deficiency in 11–15 years. According to Buname *et al.*, chronic tonsillitis can occur in various age groups due to different causes [17].

Mahfuz reported similar results that out of 2176 chronic tonsillitis patients, more than half, accounting for 55.97%, were aged 0–15 years [4]. Another study in Jambi reported that the peak incidence of chronic tonsillitis occurred at the age of 5–14 years, with a percentage of 50% [18].

The development of the immune system is one of the factors causing chronic tonsillitis in children. The most active immune system can influence the decreasing prevalence of chronic tonsillitis at age 3–10 years. Furthermore, the function of the tonsils in the formation of antibodies increased at the age of 5 years, then decreased and increased again at the age of 10 years. It then declines again at the age of 15 years due to involution during puberty. This results in a decrease in antibody production, thereby reducing the inflammatory response [1].

Microbes cause an increase in lymphocyte proliferation, which is also correlated with an increase in apoptosis to limit cellular hyperplasia. However, Onal *et al.* reported that apoptosis depends on age, and its process at <6 years is still not perfect, such that tonsillar hypertrophy is often found [15].

Laboratory examinations in this study showed that 72.7% of children with chronic tonsillitis had Vitamin

D deficiency. According to Mahfuz *et al.*, there is a 50% increased risk of respiratory tract infection in children. This includes tonsillitis with Vitamin D levels <70 nmol/L and a 70% increase in levels below 50 nmol/L [4]. Meanwhile, Safak *et al.* reported that VEGF was higher in children with serum Vitamin D <20 ng/mL. The expression of VEGF increases vascular permeability and angiogenesis as a sign of the adaptive inflammatory response [19]. Another study in Auckland reported that 16% of children undergoing tonsillectomy were Vitamin D deficient, and 80% had <75 nmol/L [20].

Vitamin D plays an important role in the adaptive immune system of children, especially in changing the pro-inflammatory state to be tolerogenic. It binds to the VDR in the nucleus of B lymphocytes and T cells. Furthermore, it plays a role in inhibiting the process of differentiation, proliferation, and reducing immunoglobulin production. Calcitriol also directly inhibits memory T and plasma cell formation, thereby reducing the activities of B cells. It is believed that the regulation of T and B cell activation and proliferation affects tonsil size [21].

Vitamin D deficiency in children is thought to be influenced by many factors, such as less exposure to sunlight, living in the mountains, darker skin color, obesity, and comorbidities. In this study, Vitamin D deficiency was more common in boys than girls. However, severe insufficiency and deficiency are more common in girls. A study in 2013 stated that most of the male population recently spends more time indoors, thereby reducing their exposure to sunlight [22].

The duration taken to form Vitamin D is related to the amount of melanin in the skin, expressed by darker skin color. Melanin in darker skin competes with 7-dehydrocholesterol to absorb UVB photons, resulting in the production of Vitamin D. Most Indonesians have darker skin, thus they require more sunlight exposure for optimal Vitamin D production [22].

Sunlight-exposed body surface area also affects the production of Vitamin D. Mohamed *et al.* reported an impaired conversion of 7-dehydrocholesterol to pre-Vitamin D due to reduced sunlight irradiation on covered skin [23].

Most of the subjects are an alpha generation born from 2010 to 2025. McCrindle reports that the alpha generation is the first to grow with a portable digital device culture. This study shows that children aged 8–12 years spend about 4 h 44 min playing with gadgets, and this increases at the age of 13–18 years to 7 h 22 min/day. Furthermore, a sedentary lifestyle is currently found in many children that correlates with sunlight exposure. Screen time is associated with a sedentary lifestyle, decreased physical activity, and less sunlight exposure, all of which contribute to the lack of children with normal serum Vitamin D in this study [24]. The results also show that children aged 3–10 years had more vitamin D deficiency, accounting for 87.5%

compared to 11–15, with a percentage of 44.4%. Higher mean Vitamin D levels were found in children aged 11–15 years, which is 17.58 ng/mL versus 16.13 ng/mL. The insufficiency and deficiency groups were balanced at ages 11–15 years, accounting for 44.4%. In addition, the average age in this study was 6.95 years, with the youngest and the oldest being 3.66 and 15.44 years, respectively.

Taylor *et al.* stated that in developed countries, Vitamin D deficiency is more common in adolescents and adults because they spend a lot of time indoors and receive less exposure to sunlight. However, it is more common in younger children in developing countries due to the lack of fortified milk and juice as a source of Vitamin D. This result is consistent with this study that the levels of Vitamin D deficiency are more common in younger children aged 3–10 years [25].

Conclusion

All children with chronic tonsillitis in Dr. Hasan Sadikin Bandung General Hospital have 25(OH) D serum, below the normal level, with an average of 16.43 ± 3.5 ng/mL, especially in boys aged 3–10 years.

Patient Consent Form

All participants were informed about the subject of the study.

Ethics Approval and Consent

This study has received ethical approval from the Health Research Ethics Committee of the Hasan Sadikin Hospital (LB.02.01/X.6.5/225/2021).

Author's Contribution

MS, AD, and AU conceived and designed the study, conducted research, provided research materials, collected and organized data, analyzed and interpreted data, wrote initial and final draft of article, and provided logistic support. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

Acknowledgment

The authors are grateful to Dr. Drs. Hadyana Sukandar, MSc, as the manuscript statistical consultant.

References

1. Fakh IM, Novialdi N, Elmatris E. Characteristics of chronic tonsillitis children in the ENT-KL department of RSUP Dr. M. Djamil Padang 2013. *J Health Andalas*. 2016;5(2):436-42.
2. Bakar MA, McKimm J, Haque SZ, Majumder MA, Haque M. Chronic tonsillitis, and biofilms: A brief overview of treatment modalities. *J Inflamm Res*. 2018;11:329-37. <https://doi.org/10.2147/JIR.S162486>
PMid:30233227
3. Haidara AW, Sidibé Y, Samaké D, Coulibaly A, Touré MK, Coulibaly BB, *et al.* Tonsillitis and their complications: Epidemiological, clinical and therapeutic profiles. *Int J Otolaryngol Head Neck Surg*. 2019;8(3):98-105. <https://doi.org/10.4236/ijohns.2019.83011>
4. Mahfuz MS, Kabir MA. Sociodemographic characteristics of the patients of tonsillitis attended in OPD of a district level hospital. *Bangladesh J Otorhinolaryngol*. 2020;23(2):180-6. <https://doi.org/10.3329/bjo.v23i2.45165>
5. Ministry of Health Research and Development Agency. Results of Basic Health Research. 2018;57,58.
6. Mirza AA, Alharbi AA, Marzouki H, Al-Khatib T, Zawawi F. The association between Vitamin D deficiency and recurrent tonsillitis: A systematic review and meta-analysis. *Otolaryngol Head Neck Surg*. 2020;163(5):883-91. <https://doi.org/10.1177/0194599820935442>
PMid:32689892
7. Rao MS, Karade D. A clinical study of serum Vitamin D levels in chronic tonsillitis among the paediatric age group. *Bengal J Otolaryngol Head Neck Surg*. 2020;28(1):23-9. <https://doi.org/10.47210/bjohns.2020.v28i1.21>
8. Yildiz I, Unuvar E, Zeybek U, Toptas B, Cacina C, Toprak S, *et al.* The role of Vitamin D in children with recurrent tonsillopharyngitis. *Ital J Pediatr*. 2012;38(1):25. <https://doi.org/10.1186/1824-7288-38-25>
PMid:22682426
9. Bergman P, Norlin AC, Hansen S, Rekha, RS Agerberth B, Björkhem-Bergman L, *et al.* Vitamin D3 supplementation in patients with frequent respiratory tract infections: A randomised and double-blind intervention study. *BMJ Open*. 2012;2(6):e001663. <https://doi.org/10.1136/bmjopen-2012-001663>
PMid:23242238
10. Aryani L, Riyandry M. Vitamin D as a potential therapy for children malnutrition. *J Nurse Researcher Prof*. 2019;1(1):61-70. <https://doi.org/10.37287/jppp.v1i1.24>
11. Fiannisa R. Vitamin D as prevention of degenerative diseases to malignancy. *medulla*. 2019;9(3):385-92.
12. Sudiro M, Lestari BW, Madiapoera T, Setiabudiawan B, Boesoirie TS. Vitamin D deficiency is correlated with the severity of allergic rhinitis. *Open Access Lib J*. 2017;4(8):1-9. <https://doi.org/10.4236/oalib.1103813>
13. Rahayu RD, Arief T, Anggraeni S. Characteristics of tonsillitis patients in children aged 5-12 years at RSPBA Bandar Lampung in 2020. *Arteries J Health Sciences*. 2021;2(1):30-5. <https://doi.org/10.4236/oalib.1103813>

- org/10.37148/arteri.v2i1.143
14. Shalihah AO, Irawati L. Relationship between gender, tonsil size and management in chronic tonsillitis patients in ORL-HNS Clinic dr M. Djamil General Hospital Padang 2013. *J Health Andalas*. 2013;4(3):786-94. <https://doi.org/10.25077/jka.v4i3.365>
 15. Önal M, Yılmaz T, Bilgiç E, Müftüoğlu SF, Kuşçu O, Günaydin RÖ. Apoptosis in chronic tonsillitis and tonsillar hypertrophy. *Int J Pediatr Otorhinolaryngol*. 2015;79(2):191-5. <https://doi.org/10.1016/j.ijporl.2014.12.005>
PMid:25555639
 16. Malapane E, Solomon EM, Pellow J. Efficacy of a homeopathic complex on acute viral tonsillitis. *J Altern Complement Med*. 2014;20(11):868-73. <https://doi.org/10.1089/acm.2014.0189>
PMid:25238506
 17. Buname G, Kiwale GA, Mushi MF, Silago V, Rambau P, Mshana SE. Bacteria patterns on tonsillar surface and tonsillar core tissue among patients scheduled for tonsillectomy at Bugando medical centre, Mwanza, Tanzania. *Pathogens*. 2021;10(12):1560. <https://doi.org/10.3390/pathogens10121560>
PMid:34959515
 18. Sapitri V. Karakteristik Penderita Tonsilitis Kronis Yang Diindikasikan Tonsilektomi Di RSUD Raden Mattaher Jambi. *Fkik Unja*. Vol. 12. Indonesia: Universitas Jambi; 2013. p. 67-72.
 19. Safak AS, Bulut F, Cumbul A. Histopathological role of Vitamin D deficiency in recurrent/chronic tonsillitis pathogenesis: Vascular epithelial growth factor-mediated angiogenesis in tonsil. *Clin Exp Dent Res*. 2022;8(3):699-706. <https://doi.org/10.1002/cre2.539>
PMid:35213796
 20. Esposito S, Lelii M. Vitamin D and respiratory tract infections in childhood. *BMC Infect Dis*. 2015;15(1):487. <https://doi.org/10.1186/s12879-015-1196-1>
PMid:26521023
 21. Wang Y, Zhu J, DeLuca HF. Where is the Vitamin D receptor? *Arch Biochem Biophys*. 2012;523(1):123-33. <https://doi.org/10.1016/j.abb.2012.04.001>
PMid:22503810
 22. Nimitphong H, Holick MF. Vitamin D status and sun exposure in Southeast Asia. *Dermatoendocrinol*. 2013;5(1):34-7. <https://doi.org/10.4161/derm.24054>
PMid:24494040
 23. Mohamed SH, Alizadeh S, Tessema M, Samuel A, Petros A, Hussen A. Clothing type and Vitamin D status: A systematic review and meta-analysis. *Res Sq*. 2021;25:1-13. <https://doi.org/10.21203/rs.3.rs-376562/v1>
 24. McCrindle M, Fell A. *Generation Alpha*. Australia: McCrindle Research; 2020. p. 1-22.
 25. Taylor SN. Vitamin D in toddlers, preschool children, and adolescents. *Ann Nutr Metab*. 2020;76(suppl 2):30-41. <https://doi.org/10.1159/000505635>
PMid:33232959