



# Vitamin D Deficiency and Clinically Detected Scoliosis among Male Adolescents at High-Altitude Area in Southwestern Saudi Arabia

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## Abstract

**BACKGROUND AND OBJECTIVES:** Reports suggest that Vitamin D deficiency (VDD) is common and is a general health challenge worldwide and at high altitude in particular.

**AIM:** The objectives were to explore Vitamin D status, to examine the association of VDD and clinically detected scoliosis, and to find a cutoff point of Vitamin D level predicting clinical scoliosis in Abha City (high-altitude area).

**METHODS:** A nested case-control design was conducted among a screened population of 417 male adolescents from intermediate and secondary schools in Abha City, Southwest Saudi Arabia. From the surveyed adolescents, 62 cases with clinically detected scoliosis and 205 age-matched controls without scoliosis were selected. For both groups, serum level of 25-hydroxyvitamin D was assessed by standardized technique.

**RESULTS:** More than two-thirds (68.5%) of male adolescents suffered from VDD (<25 nmol/L). The risk of clinical scoliosis was significantly higher among adolescents with VDD compared to those without deficiency (grade adjusted odds ratio = 6.88, 95% CI: 2.63–17.99). Receiver operating characteristic curve analysis showed acceptable discriminative ability of serum Vitamin D (area under the curve = 0.702) to predict scoliosis at a threshold value of  $\leq 20.2$  nmol/L.

**CONCLUSIONS:** Overall levels of Vitamin D in the study adolescents suggest a high prevalence of VDD at high-altitude area in Southwest Saudi Arabia. There is evidence for a positive association between VDD and clinically detected scoliosis. A threshold cutoff value of 20.2 nmol/L has been identified to predict clinically detected scoliosis. The role of possible preventive effect of Vitamin D supplementation should be considered by school health authorities.

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## Introduction

Vitamin D is formed in the skin, under the effect of ultraviolet B radiation. Vitamin D deficiency (VDD) is currently documented as prevalent in several areas of the globe including North America, Europe, and the Middle East [1]. A recent study in a Gulf country, Kuwait, reported a high prevalence of VDD among adolescents in spite of the excess sunlight, which may reveal strong sun avoidance behavior [2]. Similarly, a study in Saudi Arabia, in three different regions (central, western, and eastern regions), showed a prevalence of 49.5% of VDD among school students [3].

The prevalence rates of schoolchildren scoliosis vary widely worldwide. A systematic review of 20 studies performed between 1977 and 2011 found a prevalence rate of scoliosis among schoolchildren ranging from 1% to 14.8% [4]. A recent study in Iran published in 2018 found a prevalence of clinical scoliosis of 10.4% among schoolchildren [5]. A local

study in Abha City found a higher prevalence rate of 19.1% among adolescents [6].

Studies suggest an association between VDD and musculoskeletal problems such as adolescent scoliosis [7]. A study in India documented the significant association between VDD and musculoskeletal problems [8]. In Hong Kong, researchers found also that VDD has a significant role in the development of scoliosis [9].

Taking into consideration that the most common reason for VDD being inadequate sunlight exposure, it is not astonishing that countries at high altitude have high occurrence of VDD [10]. Aseer region (population 2,211,000) is situated in the southwest of Saudi Arabia extended over an area of more than 80,000 km<sup>2</sup>. The city of Abha is the capital of Aseer and is located at an altitude of 2270 m (7500 feet) [11].

The aims of the current work were to explore Vitamin D status, to examine the association of VDD and clinically detected scoliosis, and to find a cutoff

point of Vitamin D level predicting clinical scoliosis among adolescents in Abha City.

## Materials and Methods

### Study setting

The study was conducted among male students from intermediate and secondary schools in Abha City.

### Design

A nested case–control design in a 1:3 ratio was performed on a sample of male adolescents in Abha City. Screening for scoliosis was performed. Out of 417 surveyed adolescents, we identified 90 positive adolescents. More details of this cross-sectional study were published before [6]. Of the identified positive cases, 62 persons approved to provide a blood sample. They were matched by age in a 1:3 ratio individually. Of the 327 adolescents free from scoliosis, 205 were selected as controls and gave blood samples.

### Clinical screening for scoliosis

Screening of students was clinically accomplished in an isolated place to keep the privacy and self-respect of the students [6]. The Adam's forward bending test joined with the measurement of angle of trunk inclination (ATI) by scoliometer (Orthopedic Systems Inc., Union City, California, USA) was executed, while permitting the upper limbs to suspend freely with the palms opposed in a comfortable way [12]. Adolescents with an ATI measurement of  $\geq 5$  degrees were considered positive for clinical scoliosis screening [13].

The study proposal was approved by the Ethical Committee of King Khalid University. Parental approval on paper was taken. Pupils absent during the survey were not included. All required official approvals were taken.

### Vitamin D assessment

Serum level of 25-hydroxyvitamin D [25(OH)D] was assessed using enzyme-linked immunosorbent assay technique. Levels  $< 25$  nmol/L were considered as VDD [14].

### Data analysis

Data were explored using SPSS. Frequency, arithmetic mean, mode, median, standard deviation, and skewness were used to present the data. Chi-square,

Mann–Whitney U, and one-sample Kolmogorov–Smirnov were used as tests of significance at 5% level.

A receiver operating characteristic (ROC) curve was created to predict the role of Vitamin D in identifying adolescents with clinical scoliosis. It showed the performing of the cutoff points in terms of sensitivity versus 1-specificity. The area under the curve (AUC) is an estimate of the accurateness of cutoff point. The AUC estimate lies between 0.5 and 1. Values  $< 0.6$  indicate a weak classifier and 1 indicates an outstanding classifier.

To examine Vitamin D association with clinical scoliosis, crude odds ratio and concomitant 95% confidence intervals were computed. Multivariable binary logistic regression analysis was calculated to assess the adjusted odds ratio and the concomitant 95% confidence intervals.

## Results

The current research paper included 267 male adolescents. Out of them, 62 were clinically positive for scoliosis and the rest (205) were not. The sample included 73 students from intermediate level (aged 13–16 years) and 194 from secondary level (aged 17+ years).

### Vitamin D levels

The overall Vitamin D level among the study sample of male adolescents ranged from 9 to 74.0 nmol/L with an average of  $25.27 \pm 12.06$  nmol/L, a mode of 17.4 nmol/L, and a median of 21.6 nmol/L. Figure 1 and results of one-sample Kolmogorov–Smirnov test ( $KS = 0.218$ ,  $p = 0.001$ ) showed that the distribution of Vitamin D was not normally distributed. The distribution has a mean value more than the mode and skewness value of 1.759 (standard error 0.149), indicating positive skewness to the right. Overall results showed that more than two-thirds (68.5%, 183) of male adolescents were diagnosed having VDD ( $< 25$  nmol/L).

### Vitamin D levels by clinically detected scoliosis

Vitamin D level among adolescents free from scoliosis varied from 9 nmol/L to 74.0 nmol/L with a median of 22.6 nmol/L and an average of  $27.01 \pm 13.03$  nmol/L. On the other hand, Vitamin D levels among adolescents with clinical scoliosis were lower, ranging from 10.10 to 31.60 nmol/L with a median of 18.65 nmol/L and an average of  $19.25 \pm 4.28$  nmol/L. The difference was statistically significant (Mann–Whitney U,  $Z = 4.825$ ,  $p = 0.001$ ). Figure 2 presents the 95% confidence intervals of Vitamin D level averages among adolescents

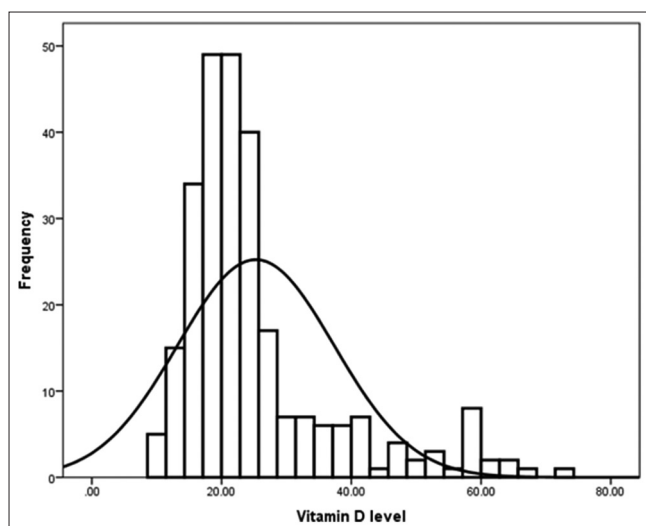


Figure 1: Distribution of Vitamin D values (nmol/L) among the study sample of male adolescents at Abha City

with (Mean = 19.25 nmol/L, 95% CI: 18.17–20.34 nmol/L) and without clinical scoliosis (Mean = 27.09 nmol/L, 95% CI: 25.31–28.89 nmol/L). The lack of overlap denotes significant differences between both groups.

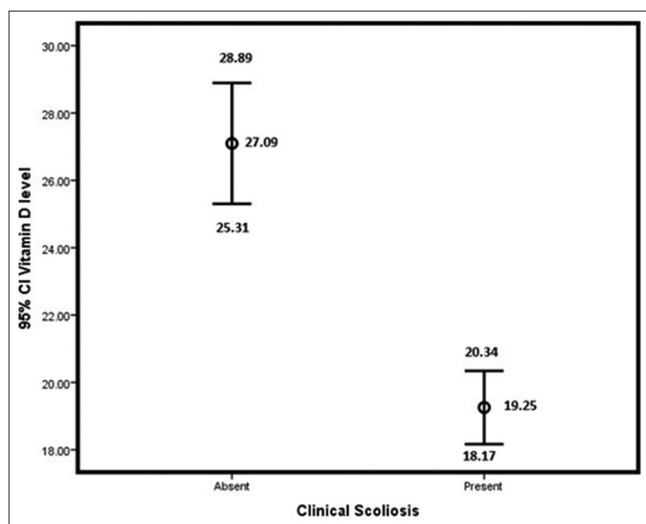


Figure 2: Error bars showing 95% confidence intervals (95% CI) of Vitamin D averages among adolescents with and without clinical scoliosis at Abha City

VDD (<25 nmol/L) among cases with clinical scoliosis amounted to 91.9% (57) compared to 61.5% (126) among adolescent free from clinical scoliosis. The risk of clinical scoliosis was significantly higher among adolescents with VDD compared to those without deficiency (cOR = 7.15, 95% CI: 2.74–18.60). In a multivariable logistic regression adjusting for grade, the adjusted odds ratio amounted to 6.88 (95% CI: 2.63–17.99).

### Prediction of clinical scoliosis by Vitamin D level

Table 1 and Figure 3 show ROC curve analysis of the prediction ability of Vitamin D level for clinical

Table 1: Result of receiver operating characteristic for Vitamin D level in nmol/L to predict clinical scoliosis at Abha City

Clinical condition	AUC (95% CI)	Optimal cutoff point of Vitamin D nmol/L	Sensitivity % (95% CI)	Specificity % (95% CI)
Clinical scoliosis	0.702 (0.643–0.756)	≤20.2	62.9 (49.7–74.8)	66.8 (59.9–73.2)

AUC: Area under the curve, 95% CI: 95% confidence interval.

scoliosis. The ability of Vitamin D, expressed as a continuous variable, to predict clinical scoliosis was good (AUC = 0.702, 95% CI: 0.643–0.756). The ROC curve identified the optimal cutoff point of Vitamin D to be ≤20.2 nmol/L. The corresponding sensitivity was 62.9% (95% CI: 49.7–74.8) and the specificity was 66.8% (95% CI: 59.9–73.2).

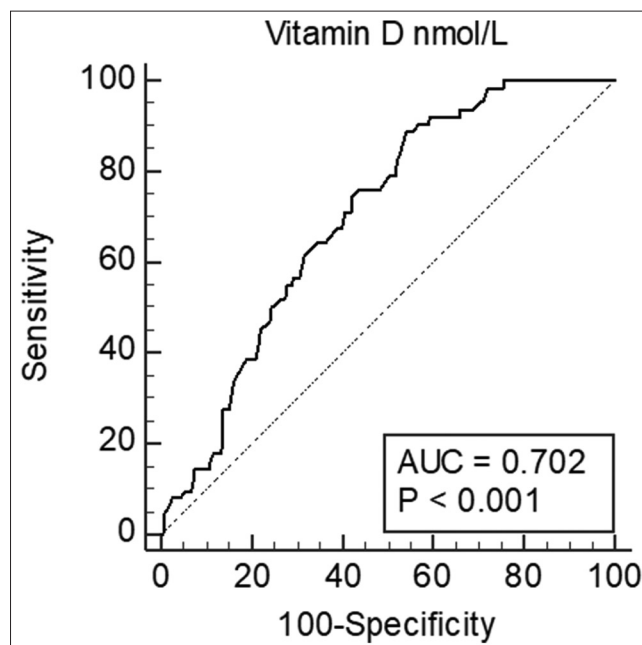


Figure 3: Receiver operating characteristic curve analysis of Vitamin D level in nmol/L to predict clinical scoliosis among study sample of school adolescents at Abha City

## Discussion

Vitamin D performs a chief physiological function in keeping extracellular calcium ion levels in the body. Extracellular calcium is essential for the performance of many processes and activities. Vitamin D affects calcium levels by managing the absorption of calcium from the intestine and through its impacts on parathyroid hormone production [15]. Vitamin D is obtained both through dietary means (10–20%) and by the production through the skin under the effect of sunlight (80–90%) [15]. Values <25 nmol/L were considered as VDD [14]. The current work showed that the average value of the serum Vitamin D was 25.27 nmol/L and more than two-thirds (68.5%) of the study sample of male adolescents suffered from VDD (<25 nmol/L). Studies from the globe indicate that hypovitaminosis D is prevalent and is regarded as a

general health issue [15], [16], [17]. There are consistent data suggestive of highest prevalence of VDD in Asia, the Middle East, and Africa [18].

A recent study in Jeddah in Saudi Arabia (sea level sunny city) on 303 adolescents aged 13–19 years revealed a prevalence of VDD of 34.4% and the mean concentration of 25(OH)D of 32.6 nmol/L [19]. This Vitamin D status was much better than that reported in the current study. This difference could partly be explained by the difference in altitude and sun exposure between the two study areas.

Latitude and relevant lifestyle factors could be of significant importance to Vitamin D condition in racial clusters with dark skin (e.g., African, Middle Eastern, and South Asian), who are at present at higher chance of VDD due to melanin density, dress mode, sun protection behavior, and genetics [10]. Altitude is another issue that influences skin synthesis of Vitamin D. At high altitudes, cloudy weather may interfere with ultraviolet B radiation. Published articles on altitude and Vitamin D synthesis are inadequate. However, it is recognized that altitude minimizes the duration of Vitamin D production [20]. A high occurrence of VDD (81%) was observed among children living in two districts situated at high altitude of Himachal Pradesh, India [21]. The subjects with VDD amounted to 83.8% in another high-altitude area in India [22]. A study among Argentinean children showed that 46.5% living at high altitude suffered from VDD [23]. Abha City lies at an altitude of 2270 m [11]. Being at high altitude, it is expected to find low Vitamin D, especially during winter period, where there is no sunlight of suitable wavelength for production of cutaneous pre-Vitamin D. Cloudy weather may also reduce Vitamin D level by minimizing sunlight exposure. This condition may augment the situation of VDD among adolescents in Abha City.

Adolescent scoliosis is a disease of public health significance both globally and in Saudi Arabia. It is a multifactorial disease with uncertain primary etiology and pathogenesis [24]. The potential role of Vitamin-D in the developing adolescent scoliosis is recently being considered [25], [26]. The results of the present study provide adequate evidence of a positive relation between VDD (<25 nmol/L) and clinically detected scoliosis in adolescents. This finding is similar to results obtained by previously conducted studies which demonstrated that the level Vitamin D was significantly lower in patients with scoliosis than in healthy age- and sex-matched controls [25], [26], [27]. The mechanisms of Vitamin D in the pathogenesis of scoliosis are still uncertain. A recent review study assumed that VDD increases the risk of scoliosis development by its influence on the regulation of fibrosis, postural control, and bone mineral density [9]. Another explanation for the role of Vitamin D in the development of scoliosis was made by another review study which postulated that Vitamin D levels at high-altitude areas are decreased

and delays the onset of puberty which, in turn, increases the vulnerability of vertebral column and increases the prevalence of scoliosis [28]. This could explain the observed higher prevalence of scoliosis among male adolescents in Abha City [6] which located at high altitude [11]. Identifying the role of Vitamin D in the development of scoliosis could suggest the preventive role of Vitamin D supplementation. Furthermore, Vitamin D supplementation could improve bone health and minimize spine curvature in scoliotic patients [29].

In the present study, a trial has been done to identify a clear threshold cutoff of Vitamin D level to predict clinically detected scoliosis. The results of ROC curve analysis showed acceptable discriminative ability of Vitamin D to predict scoliosis at a threshold value of  $\leq 20.2$  nmol/L. No similar analysis has been undertaken previously. Hence, comparison with other studies is difficult. However, these results provide further evidence that preventing VDD (keeping Vitamin D level above 20 nmol/L) could help in minimizing the burden of scoliosis, especially at high-altitude areas.

The present study documented for the 1<sup>st</sup> time the high prevalence of VDD in high-altitude areas in Saudi Arabia. Furthermore, the present study revealed the positive association of VDD and clinical scoliosis. Similar findings were reported in different regions in Turkey [25], Poland [26], and Brazil [27].

## Conclusions

The finding of overall levels of Vitamin D in the study adolescents suggests a high prevalence of VDD in a high-altitude area in Southwest Saudi Arabia. There is adequate evidence for a positive association between VDD and clinically detected scoliosis. It is possibly that Vitamin D plays a role in the etiology and pathogenesis of adolescent scoliosis at high-altitude areas. A threshold cutoff value of 20.2 nmol/L has been identified to predict clinically detected scoliosis. A larger population-based study involved both males and females and different levels of altitudes are warranted. Furthermore, prospective studies are recommended to provide a higher level of evidence regarding the relationship of Vitamin D with scoliosis among adolescents. The role of possible preventive and therapeutic effect of Vitamin D supplementation should be thoroughly considered by school health authorities.

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