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Serum Level of 25-Hydroxyvitamin D and Symptoms of Pica Among Adolescent School Children in Northern Sudan: A Cross-Sectional Study

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Abstract

Objectives. To assess levels of 25(OH)D among adolescents with symptoms of pica in northern Sudan. *Methods.* A cross-sectional study was conducted in North Sudan. Questionaries were used to collect adolescents' sociodemographics. The enzyme-linked immunosorbent assay was used to measure 25(OH)D level. *Results.* Of the 344 adolescents enrolled, 161 (46.8%) and 183 (53.2%) were male and female, respectively and 103 (29.9%) had symptoms of pica. The median (IQR) of 25(OH)D level was significantly lower in adolescents with symptoms of pica. Multiple linear regression analysis showed that while age (coefficient = 1.1, $P = .023$) was positively associated with 25(OH)D level, female sex (coefficient = −7.5, $P < .001$), and pica symptoms (coefficient = −3.5, $P = .032$) were negatively associated with 25(OH)D level. *Conclusion.* Adolescents with symptoms of pica had lower 25(OH)D levels. Adolescents with symptoms of pica have to be assessed for vitamin D status.

Keywords

adolescent, age, vitamin D, Pica, 25(OH)D, body mass index, female

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Introduction

Vitamin D is a fat-soluble vitamin that can be obtained from diet or can be synthesized in the body by ultraviolet-B radiation.[1,2] Besides its central role in the homeostasis of calcium and primary bone health, vitamin D has several functions in the immune system and cell proliferation.[1,2] Vitamin D deficiency is a worldwide health problem especially important in Africa.[3] It has been reported that there is a high prevalence of vitamin D deficiency among children and adolescents on a global scale.[4]

It has recently been shown that patients with impulsive behaviors, such as those that characterize eating disorders, have lower levels of 25-hydroxyvitamin D (25(OH)D).[5] Previously, Barron et al[6] reported that patients with eating disorders, specifically anorexia nervosa and bulimia nervosa, have lower levels of 25(OH)D. Likewise, Modan-Moses et al[7] reported a high prevalence of vitamin D deficiency in adolescents with eating disorders, and Nagata et al[8] reported that around half of adolescents (males and females) admitted to the hospital for malnutrition secondary to eating disorders had low 25(OH)D levels.[8] Moreover, in a recent meta-analysis of 15 studies and 927 participants, 25(OH)D was significantly lower in patients with anorexia nervosa compared with healthy controls.[9]

Pica is "the craving and purposive eating of non-food items," according to a new diagnostic entity in the American Psychiatric Association's fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) and the World Health Organization's 11th International Classification of Diseases.[10] Pica is a worldwide health problem among children and adolescents.[11-13] While the exact etiology of pica remains

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unknown, several factors such as nutritional deficiency, cultural factors, stress, low socioeconomic status, and child neglect are reported as risk factors for pica.[14] Pica, and specifically geophagia, can lead to anemia,[11] gastrointestinal dysfunction, and heavy metal poisoning.[15,16] Generally, avoidant/restrictive food intake disorders and less positive body image are associated with pica.[17] It has also been reported that pica is associated with iron and zinc deficiencies,[18] but to the best of our knowledge, there is no published data on pica and vitamin D status yet.

Taking these points together, we hypothesize that adolescents with pica symptoms have lower 25(OH)D levels than their non-pica counterparts. Investigating 25(OH)D in adolescents with pica symptoms is important because it could yield vital data for evidence-based intervention, and pica symptoms could be used as guidance about nutrient deficiency, especially in low-resource countries such as Sudan. Therefore, we aimed to assess 25(OH)D levels among male and female adolescents with symptoms of pica in northern Sudan.

Materials and Methods

Study Setting and Design

The methods have been previously described in detail.[19] In summary, a school-based cross-sectional study was conducted from July to September 2022 in the Nile region of northern Sudan. The Strengthening the Reporting of Observational Studies in Epidemiology standard checklists were followed.[20] The Director of School Education granted permission, and the guardian of each adolescent provided written and signed informed consent. Simple random selection (lottery method) was used to select 4 schools (Hajer Alteer, Athawra Kabota, Alkoumer, and Wadi Alshohda) out of 16 public primary and secondary schools in the Almatamah locality. Of the 4931 students at these 4 schools, 384 individuals were randomly (simple random technique) selected according to the total number of students in the specific school (proportional to size) so that schools with a larger number of students contributed more to the sample.

Inclusion and Exclusion Criteria

The recruits were generally healthy students without chronic illness, such as hypertension, diabetes mellitus, bone diseases, or thyroid disorder, who were not on any medications or supplements, including vitamin D and metformin. The consenting students were interviewed using a questionnaire (Supplemental File 1) to gage age, sex, parents' education, and mother's occupation, which was filled in by 1 of 4 trained medical officers under the supervision of the first author, who is a physician. The definition of pica symptoms, which we recently reported as the persistent desire to eat uncooked food or non-food substances for at least 1 month, was used in questions such as "*What type of uncooked or non-food substance do you desire or eat?" and "Have you eaten this substance during the last month?"*

*Using standard procedures, weight and height were taken twice from each student to calculate averages. Body mass index (*BMI) was computed using the World Health Organization's BMI *Z*-score reference (BMIZ).[21] Under aseptic conditions, 5 mL of blood was withdrawn by a qualified trained nurse (at a random time during the day between 7 00 AM and 2 00 PM) from the cubital vein into a plain tube that was well labeled. The blood was allowed to clot at room temperature and then centrifuged (Hettich Centrifuge UNIVERSAL 320, Föhrenstraße 12, D-78532 Tuttlingen/Germany) at 2500 rpm for 5 minutes and stored at −20°C until the 25(OH)D assay was performed. The enzyme-linked immunosorbent assay was conducted following the manufacturer's instructions (EUROIMMUN, Lubeck, Germany) with reference wavelengths between 620 and 650 nm in duplicate, and the mean of the 2 was the final result. The control measures 6 calibrator levels (standard solution) set to between 0 and 120 ng/mL and applied for each assay per the manufacturer's instructions.

Although there is a controversy on the classification of vitamin D sufficiency, insufficiency, and deficiency, in this study, we define vitamin D insufficiency as 20 to 30 ng/mL and deficiency as $<$20 ng/mL as per "The Endocrine Society[22] and Society for Adolescent Health and Medicine[23] guidelines."

Sample Size

According to a previous study, the sample size was initially calculated to be 384.[19] However, 344 adolescents provided enough data for assessing 25(OH)D levels following re-estimation, given the 30% prevalence of pica symptoms among this group. This was calculated using a single proportional formula of $n = Z^2pq/d^2$ where $q = (1-p)$, $Z1\text{-}\alpha = 95\%$ confidence interval (CI) = 1.96, and d = margin of error of 5% = 0.05.[24]

Statistics

Data were entered into IBM's Statistical Package for the Social Sciences® for Windows version 22.0 (SPSS Inc., New York, USA). The proportions were expressed as frequencies (%). Continuous data were evaluated for normality using the Shapiro–Wilk test and were non-normally

Table 1. Comparing Characteristics of the Adolescents With Symptoms of Pica and Adolescents Without Symptoms of Pica.

Variables		Adolescents with symptoms of pica (number = 103)	Adolescents with no symptoms of pica (number = 241)	*P*
	Median (interquartile range)			
Age, years		15.3 (14.1–16.6)	15.0 (13.9–16.0)	.241
Body mass *Z*-score		−0.38 (−1.3–0.49)	−0.75 (−1.7–0.32)	.104
25(OH)D level, ng/mL		17.8 (6.8–26.5)	21.2 (10.8–31.9)	.020
	Frequency (proportion)			
Sex	Male	29 (28.2)	132 (54.8)	
	Female	74 (71.8)	109 (45.2)	<.001
Mother education	≥Secondary level	61 (59.2)	153 (63.5)	
	<Secondary level	42 (40.8)	88 (36.5)	.468
Mother occupation	Housewife	92 (89.3)	244 (91.7)	
	Employed	11 (10.3)	18 (7.5)	.396
Father education	≥Secondary level	60 (58.3)	166 (68.9)	
	<Secondary level	43 (41.7)	75 (31.1)	.063
Vitamin D deficiency	No	47 (45.6)	127 (52.7)	.241
	Yes	56 (54.4)	114 (47.3)	

distributed. The non-normally distributed data were expressed as medians (interquartile range; IQR). The 2 groups (with and without symptoms of pica) were compared by chi-square and Mann–Whitney *U* as applicable. Simple linear analysis was performed with 25(OH)D as the dependent variable and sociodemographics (age, gender, BMI, educational level, and symptoms of pica as the independent variables. Variables with $P < .20$ in the simple linear analysis were entered in multiple linear regression. The adjusted coefficient and 95% CIs were calculated. A two-sided *P*-value of <.05 was considered statistically significant.

Ethical Approval

The current work was conducted per the Declaration of Helsinki. This study has received ethical approval from the Research Ethics Committee of the Faculty of Medicine, University of Khartoum, Sudan, with reference number: 9, 2021. The authors followed all measures to ensure the privacy and confidentiality of participants, such as excluding personal identifiers during data collection. All participants and their legally authorized representative (parents/guardians) signed written informed consent.

Results

Of the 344 enrolled adolescents, 161 (46.8%) and 183 (53.2%) were male and female, respectively. The IQR medians of age and BMI Z-score were 15.1 (14.0-16.3) years and −0.6 (−1.6 to 0.3), respectively. While 50 (14.5%) adolescents had thinness/underweight (BMIZ < –2 SD), 2 (0.5%) of the adolescents were overweight (BMIZ > +1 SD), and 8 (2.3%) of the adolescents were obese (BMIZ > + 2 SD). Around two-thirds of the parents had education equal to or higher than the secondary level (65.7% of the fathers and 62.2% of the mothers). Of the 344 mothers, 91.6% were housewives. Of the students, 103 (29.9%) had symptoms of pica. The median (IQR) of 25(OH)D level was 20.0 (8.9–30.8), and 170 (49.4%) of them had vitamin D deficiency (25(OH)D level < 20 ng/mL).

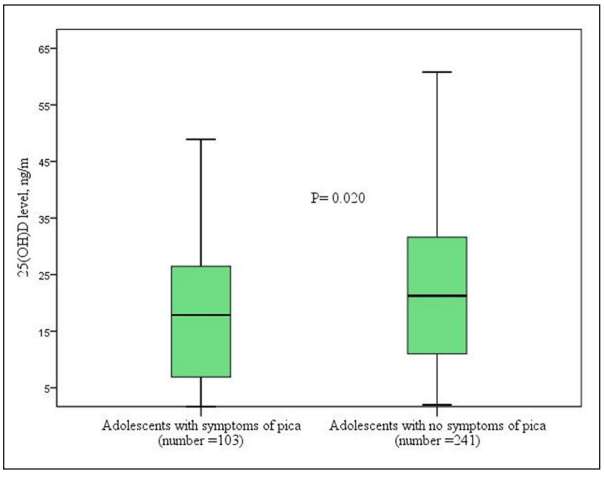

Figure 1. Comparison of 25(OH)D level in the adolescents with and without symptoms of pica.

The median (IQR) of 25(OH)D level was significantly lower in adolescents with symptoms of pica than in those without (17.8 [6.8–26.0] vs 21.2 [10.8–31.9], $P = .020$), as shown in Table 1 and Figure 1. There was

Table 2. Simple and Multiple Linear Regression Analysis of the Factors Associated With 25(OH)D Level in the Adolescents.

Variables		Simple linear regression analysis		Multiple linear regression analysis	
		Coefficients (95% confidence interval)	*P*	Coefficients (95% confidence interval)	*P*
Age, years		0.6 (−0.3−1.8)	.197	1.1 (1.5−2.0)	.023
Body mass *Z*-score		0.1 (−0.9−1.2)	.817		
Sex	Male	Reference			
	Female	−7.3 (−10.1 to −4.4)	<.001	−7.5 (−10.5 to −4.5)	<.001
Mother education	≥Secondary level	Reference		Reference	
	<Secondary level	0.8 (−2.2 to 3.9)	.583		
Mother occupation	Housewife	Reference			
	Employed	1.7 (−3.6 to 7.0)	.532		
Father education	≥Secondary level	Reference			
	<Secondary level	−1.0 (−4.2 to 2.0)	.493		
Symptoms of pica	No	Reference		Reference	
	Yes	−3.3(−6.6 to −1.3)	.041	−3.5 (−6.7 to −0.29)	.032

no difference in the prevalence of vitamin D deficiency between participants with or without pica symptoms (56/103 [54.4%] vs 114/241 [47.3%], $P=.241$), as shown in Table 1. A significantly higher number of females had symptoms of pica (29/103 [28.2%] vs 132/241 [54.8%], $P<.001$). There was no significant difference in age, BMI Z-score, or parents' education between adolescents with and without pica symptoms (Table 1).

Female sex (coefficient=−7.3, 95% CI=−10.1 to −4.4, $P<.001$) and symptoms of pica (coefficient=−3.3, 95% CI=−6.6 to −1.3, $P=.041$) were inversely associated with 25(OH)D level in simple linear regression. In simple linear regression, age, BMI *Z*-score, and parents' education were not associated with 25(OH)D levels. Multiple linear regression analysis showed that, while age (coefficient=1.1, 95% CI=1.5-2.0, $P=.023$) was positively associated with 25(OH)D level, female sex (coefficient=−7.5, 95% CI=−10.5 to −4.5, $P<.001$), and pica symptoms (coefficient=−3.5, 95% CI=−6.7 to −0.29, $P=.032$) were negatively associated with 25(OH)D levels (Table 2).

Discussion

The main findings of the current study are that 25(OH) D level is significantly lower in adolescents with symptoms of pica than in those without. That pica (coefficient=−3.5) is associated with 25(OH)D level. As mentioned above, to the best of our knowledge, there is no published data on pica and vitamin D status. Previous studies have shown that individuals displaying the impulsive behaviors that are characteristic of patients with eating disorders,[5] specifically anorexia nervosa,[9] have lower levels of 25(OH)D. In their study, Barron et al[6] observed that patients with anorexia nervosa and bulimia nervosa have lower 25(OH)D levels. Likewise, Modan-Moses et al[7] found a higher prevalence of vitamin D deficiency in adolescents with eating disorders. In a recent meta-analysis, 25(OH)D level was significantly lower in patients with anorexia nervosa as compared with healthy controls.[9] Patients with pica sometimes have micronutrient deficiencies, mainly iron[25] and zinc.[18] Miao et al[18] included 43 studies in their meta-analysis, involving 6407 individuals with pica and 10 277 controls without, and reported a significant association between pica and lower zinc levels.[18]

Although our study showed a lower 25(OH)D level in adolescents with symptoms of pica than in those without, there was no significant difference in the prevalence of vitamin D deficiency between these groups. The current study was conducted to detect differences in 25(OH) D levels between participants with and without symptoms of pica with optimum power (80.0%); it was not conducted to detect differences in vitamin D status or vitamin deficiency. A sample of 2443 adolescents (with 80.0% power) would be needed to analyze vitamin D status if the exact proportions of vitamin deficiency were assumed, namely 54.4% and 47.3% in individuals with and without pica symptoms.[24] Different definitions or cut-off points are suggested as appropriate for evaluating vitamin D status, and we adopted <20 ng/mL as denoting vitamin D deficiency for this study, as outlined in The Endocrine Society's guidelines.[26]

There is no obvious explanation for the association between pica and nutrient deficiency, although some plausible explanations have been proposed. Ingested materials may bind to the gastrointestinal tract's mucosal

layer, interfering with micronutrient absorption.[27,28] These materials, such as clay or starch, may themselves absorb micronutrients from ingested food, preventing them from metabolizing further.[27,28] Furthermore, central actions in brain function that might affect the ingestion of particular nutrients, such as vitamin D, have been reported to play a role in the production of serotonin.[29]

Our results showed that age was positively associated with 25(OH)D level, and female sex was negatively associated with 25(OH)D level. Recently, Baranoglu Kilinc and Bolu[30] reported that 25(OH)D level was significantly lower in girls and in the 10 to 18-year age group compared with the other age groups.

This study has some limitations. The questionnaire used in the current study was not validated. The DSM-5 criteria were not followed in diagnosing pica,[10] and other sociocultural influences and mental or medical conditions were not looked for. Several other aspects that could influence 25(OH)D levels, such as dietary factors, sun exposure, and inflammatory factors, were also not investigated. Moreover, other elements such as calcium level, phosphorus, and parathyroid hormone were not assessed in the current study.

Clinical Implications

25(OH)D level and vitamin D deficiency are to be considered among adolescents with pica.

Further research on vitamin D status and eating disorders are needed.

Correction of vitamin D among adolescents with pica is needed.

Conclusion

This study highlights those adolescents with symptoms of pica had a lower 25(OH)D level. However, the current study did not investigate calcium level, phosphorus and parathyroid hormone. Screening for 25(OH)D level may be an important part of clinical care for adolescents with symptoms of pica and other eating disorders. Further larger studies are needed to explore the association between 25(OH)D level and pica and may recommend vitamin D supplements to ameliorate symptoms of pica. More studies that elaborate on pica and other factors that could influence vitamin D status are needed.

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Author Contributions

MAA and IA conceived the study; AA and AA supervised the work, guided the analysis and critically reviewed the manuscript; MAA and IA prepared the analysis plan, performed the data analysis, and wrote the first draft of the paper; and AA and AA supervised data collection. All authors reviewed and approved the final manuscript.

Availability of Data and Material

The datasets generated and analyzed during the current study are not publicly available (because the manuscript is still under the peer review process) but are available from the corresponding author upon reasonable request.

Declaration of Conflicting Interests

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Supplemental Material

Supplemental material for this article is available online.

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