Determinants of vitamin D deficiency among Bangladeshi children: A hospital based case-control study

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ABSTRACT

Background: Risk factors of vitamin D deficiency among children have been identified in many developed countries but not yet in some developing countries like Bangladesh. Therefore, the aim of this study was to identify the determinants of vitamin D deficiency among Bangladeshi children.
Methods: This case-control study was conducted at 2 paediatric hospitals in Dhaka city from January to June 2017. We recruited 198 vitamin D deficient cases and 198 apparently healthy controls. Data were analyzed using IBM SPSS, where quantitative variables were analyzed using descriptive statistics. The association between vitamin D deficiency with different lifestyle and dietary factors were analyzed by using Chi-square test. A 2-tailed p-value less than 0.05 were considered as statistically significant. Univariate and multivariate logistic regression analysis were performed to confirm the association.
Results: The study revealed that not playing outdoor games (OR=3.09; 95% CI 1.46, 6.54), playing video/TV/mobile games (OR=4.14; 95% CI 1.97-8.67), no sun exposure (OR=2.42; 95% CI 1.25-4.67), no milk consumption (OR=3.01; 95% CI 1.38-6.57), no sea fish consumption (OR=2.20; 95% CI 1.19-4.08) and not exclusively breastfeeding (OR=2.03; 95% CI 1.14-3.63) were significantly associated with vitamin D deficiency.
Conclusion: We concluded that improper lifestyles and nutritional habits are the key determinants of Vitamin D deficiency among Bangladeshi children. Strategy for hypovitaminosis D prevention should be implemented immediately, which includes vitamin D supplementation of breastfed infants and ensuring adequate maternal vitamin D status during pregnancy. Also an awareness program should be initiated to promote a healthy lifestyle and to improve nutritional habits.

Keywords: Determinants, vitamin D deficiency, children, Bangladesh

INTRODUCTION

Even though a pandemic nutritional condition, vitamin D deficiency still remains the most un-diagnosed or under-diagnosed nutritional problem in the whole world [1-3]. Though the treatment is simple and inexpensive,

the risk factors of vitamin D deficiency are not commonly identified. The deficiency may occur in every individuals, irrespective of geography, race, age, gender and socio-economic conditions. Vitamin D is a very crucial content for bone health. It has been found that vitamin D deficiency can lead to rickets and osteomalacia [4-6]. Vitamin D deficiency is also highly associated with osteoporosis and an increased risk of fractures [7-9]. Researchers in the field have also shown that low vitamin D levels are associated with some extra skeletal consequences, including increased risks of cancer, diabetes mellitus, cardiovascular disease, multiple sclerosis, and autoimmune diseases [10].

Bangladesh is a tropical country, located in South Asia, on the Equator which is sunny all year round. The people of Bangladesh receive around 6 to7 hours of sunshine per day. It was thought that exposure to sunlight alone is responsible for vitamin D sufficiency. However, prevalence of vitamin D deficiency is still very high in Bangladesh [11]. Our previous study evaluated vitamin D status among healthy Bangladeshi children, which has shown the high prevalence [11]. Hence, the mystery remains why people living in the sunny regions of the world are still suffering from vitamin D deficiency.

Untill now, researchers have found a variety of risk factors for vitamin D deficiency; which included darker skin pigmentation; working indoors [10]; habitually wearing long-sleeved or protective clothing; staying under the shade; homebound lifestyle [12], individuals who those with not been exclusively breastfed as infants, low calcium intake, dietary restrictions, vegans and obesity [13, 14]. Some studies also mentioned malabsorption syndrome or other conditions, e.g. Crohn's disease, cystic fibrosis, severe liver disease [15]. Some drugs that have interactions with vitamin D, e.g. anticonvulsants, rifampicin, cimetidine, thiazides, corticosteroids [16-17] were also found as risk factors for vitamin D deficiency. However, all of these studies have been conducted in developed country settings and there is a scarcity of studies to evaluate the potential extrinsic risk factors that can affect vitamin D status of Bangladeshi children. Therefore, this study aimed to identify lifestyle and nutritional variables which depict the predictors of vitamin D deficiency among Bangladeshi children.

METHODS

Study site and study population

This case-control study was conducted between January to June 2017 in two paediatric hospitals in Dhaka city, Bangladesh. 198 vitamin D deficient children (aged 1 to 13yrs) were selected as cases from outpatient department conveniently. At the same time, 198 apparently healthy unmatched controls were identified conveniently from the same hospitals who attended with minor symptoms like cough and cold. When a children presented in an outpatient department with symptoms like suspected vitamin D deficiency, they were advised for biochemical test. When the vitamin D level was equal or less than 30 ng/ml (explained details in later section) we have considered it as a case. Our inclusion criteria for case were: level of vitamin D equal or less than 30 ng/ml plus one symptom. Inclusion crietria for control was, the children who have attended those hospitals with minor symptoms during study period. Exclusion criteria were the presence of hepatic, skeletal, renal, or endocrine disorders, and use of medications known to affect vitamin D metabolism during the last 3 months. Additional information was collected by face-to-face interviews with semistructured questionnaires. Written informed consent from the parents/caregivers was obtained before data collection.

Socioeconomic, lifestyles and nutritional data

Socioeconomic data were collected during hospital visits, including age, sex, height, weight, parents' education, parents' occupation, religion, living status, living conditions, etc. Lifestyle and nutritional factors such as playing outdoor games, playing video/television/mobile phone games, sun exposure, schooling, milk consumption, sea fish consumption, egg consumption were also collected. We considered 20 minutes of exposure to sunlight for last 6 months as sun exposure. Children were considered exclusively breastfed if they received only breast milk without any additional food or drinks (not even water) for the first 6 months of their life. We have considered regular milk or egg consumption if child consumed milk/egg 2-3 times in a week for the last 6 months. Sea fish consumption was considered if child consumed fish at least once in a week for the last 6 months.

Laboratory data

A 5 ml blood sample was obtained from each participant. Blood tests were performed in the most well-equipped and modern laboratory in Dhaka city. Circulating levels of 25-hydroxyvitamin D [25(OH)D] were measured by direct enzyme-linked immunosorbent assay, which is the most popular and widely used method in Bangladesh [4]. ARCHITECT plus i1000SR fully automated immunoassay analyzer (USA) was used and standardisation and calibration were done every 2 months. The same batch of test kits was used to test 25-hydroxyvitamin levels for all children. There is no definite cut-off point for optimal levels of 25-hydroxyvitamin D as measured in serum. Most experts defined vitamin D deficiency as a level of 25-hydroxyvitamin D below 50 nmol per liter [17], which is equivalent to 20 ng/ml. In children, due to fewer outcome data, the optimal level

of serum 25(OH)D for general health is not known yet. Moreover, it is more controversial than in adults [18-19]. It is evident that biochemical sequeal of vitamin D deficiency may appear at cut-off levels of 75 nmol/L [20-21]. Expert opinions suggested that the minimal optimal circulating vitamin D level should be increased from 50 nmol/L to 75 nmol/L [22] and levels between 50 nmol/L and 75 nmol/L can be considered as a relative insufficiency of vitamin D in children. In our previous study, we have categorized deficiency as <10 ng/ml, insufficiency as 10-29 ng/ml and sufficiency as 30-100 ng/ml [4]. In this study, based on the researchers' experience and local context, we have defined the case of vitamin D deficiency as only when the level is equal or less than 30 ng/ml.

Statistical analysis

Data were categorized and analysed using the statistical software package IBM SPSS Statistics version 23.0. Distribution of quantitative variables were assessed using descriptive statistics and results were presented as mean±SD, number, and percentage. The association between vitamin D deficiency with different lifestyles and dietary factors were analysed by the Chi-square test. A 2-tailed p-value less than 0.05 were considered as statistically significant [23]. Univariate and multivariate logistic regression analysis were performed to confirm the association. The risks were estimated as odds ratios together with 95% confidence interval.

RESULTS

In total, 198 cases and the same number of unmatched controls were recruited in this case-control study where both groups of children were from similar age ranges of 1 to 13 years with a mean age of 5.0 vs 4.9 years respectively. Table 1 shows that both groups have similarity in all other sociodemographic aspects such as parents' education, parents' occupation, residence status, living status, etc.

Table 2 shows the association of vitamin D deficiency with different lifestyle related factors. We have found that not playing outdoor games is a major risk factor of vitamin D deficiency (p<0.01), whereas the duration of playing outdoor games was not statistically significant (p=0.94). Similarly, playing video/television/mobile phone games had a strong relationship with vitamin D deficiency (p<0.01), now a days which is a very common scenario among children all over the world. Likewise, sun exposure and duration of sun exposure had a strong association with vitamin D deficiency (p=0.01 and p=0.03). But children's schooling was not associated with vitamin D deficiency.

Table 3 shows the association of vitamin D deficiency with certain food habit related factors where we have found that, no milk consumption, no sea fish consumption and not exclusively breastfed were significantly associated (p=0.02, p=0.03, and p=0.02 respectively) with vitamin D deficiency. However, our study did not find any association with the frequency of those food habits.

Table 4 shows the unadjusted and adjusted odds ratio with vitamin D deficiency as the dependent variable. It has shown that, not playing outdoor games was strongly associated with vitamin D deficiency (OR=2.46, 95% CI=1.27-4.74). In the multivariate logistic regression model, after adjustment by age, sex, parents education, parents' occupation, religion, housing status and living status, the relationship became stronger (OR=3.09, 95% CI=1.46-6.54). Similarly, playing video/television/mobile phone games also had a strong relationship with vitamin D deficiency (OR=2.47, 95% CI=1.39-4.38) and after adjustment by the same sociodemographic variables, the relationship became much stronger (OR=4.14, 95% CI=1.97-8.67). The study also found some other factors, such as no sun exposure (OR=1.99, 95% CI=1.11-3.56), not consuming milk regularly (OR=2.12, 95% CI=1.15-3.90), not consuming sea fish (OR=2.01, 95% CI=1.12-3.61) and not being exclusively breastfed (OR=2.02, 95% CI=1.14-3.58) had significant association with vitamin D deficiency. After adjustment by the same sociodemographic variables, those associations remained, and in most of the cases became stronger than pre-adjustment (OR=2.42, 95% CI=1.25-4.67), (OR=3.01, 95% CI=1.38-6.57), (OR=2.20, 95% CI=1.19-4.08) and (OR=2.03, 95% CI=1.14-3.63) respectively.

DISCUSSION

In this case-control study, we have found that vitamin D deficiency was significantly associated with not playing outdoor games. A recently published article explored the status of vitamin D status among adults in Kuwait and found that number of times adolescents walk to schools per week was significantly related to vitamin D deficiency [24], which supports our findings. A study conducted among adult Bangladeshi garment workers indicated that indoor lifestyle is an important factor for vitamin D deficiency [25]. Our study also found playing video/television/mobile phone games was associated with vitamin D deficiency. It is a global concern now-a-days that children and adolescents spend most of their time with electronic gadgets and increasing their gadget depency day-by-day. The scenario in Bangladesh is no different.

We have found that no sun exposure had a 2 times higher chance of vitamin D deficiency. After adjustment in multivariate analysis, the risk remains similar or even stronger. For many decades, it has been well established that sun exposure is an important

TABLE 1. Baseline characteristics of the study participants (both case and control)

VARIABLES		CASE		CONTROL	
		Number (N)	Percentage (%)	Number (N)	Percentage (%)
Gender					
	Male	80	40.4	80	40.4
	Female	118	59.6	118	59.6
Father's education					
	Primary	32	16.2	30	15.2
	Secondary	64	32.3	70	35.4
	Higher secondary	84	42.4	82	41.4
	Graduate and above	18	9.1	16	8.1
Mother's education					
	Primary	48	24.2	46	23.2
	Secondary	90	45.5	94	47.5
	Higher secondary	56	28.3	52	26.3
	Graduate and above	4	2.0	6	3.0
Religion					
	Muslim	166	83.8	172	86.9
	Hindu	22	11.1	18	9.1
	Christian and others	10	5.1	8	4.0
Father's occupation					
	Unemployed	6	3.0	8	4.0
	Business	92	46.5	92	46.5
	Service	100	50.5	98	49.5
Mother's occupation					
	Unemployed	108	54.5	114	57.6
	Business	28	14.1	28	14.1
	Service	62	31.4	56	28.3
Residence status					
	Urban	82	41.4	86	43.4
	Semi-urban	18	9.1	14	7.1
	Rural	98	49.5	98	49.5
Child living with					
	Extended family	126	63.6	130	65.7
	Nuclear family	32	16.2	28	14.1
	Single parent	40	20.2	40	20.2
Age		Mean (Range)	± SD	Mean (Range)	+ SD
		5.00 12 (1.0-13.0)	2.70	4.96 12 (1.0-13.0)	2.77

TABLE 2. Association of vitamin D deficiency with common lifestyle-related factors

VARIABLES		CASE		CONTROL		*p*-value
		Number (N)	Percentage (%)	Number (N)	Percentage (%)	
Play outdoor games						
	Yes	128	64.6	162	81.8	**<0.01**
	No	70	35.4	36	18.2	
	Total	198	100.0	198	100.0	
Hour of play outside						
	<1 hour	32	24.2	44	27.1	0.94
	1-2 hours	70	54.7	86	53.1	
	>2 hours	26	21.1	32	19.8	
	Total	128	100.0	162	100.0	
Playing Video/Tv/Mobile games						
	Yes	126	63.6	80	40.4	**<0.01**
	No	72	36.4	118	59.6	
	Total	198	100.0	198	100.0	
Hour of Video/Tv/Mobile use						
	<1 hour	54	42.9	36	45.0	0.26
	1-2 hours	64	51.6	44	55.0	
	>2 hours	8	6.5	0	0.0	
	Total	126	100.0	80	100.0	
Sun exposure						
	Yes	102	51.5	134	67.7	**0.01**
	No	96	48.5	64	32.3	
	Total	198	100.0	198	100.0	
Hour of sun exposure per day						
	<30 minutes	46	45.1	32	23.9	**0.03**
	30-60 minutes	48	47.0	72	53.7	
	>60 minutes	8	7.9	30	22.4	
	Total	102	100.0	134	100.0	
The child goes to school						
	Yes	130	65.6	126	66.6	0.88
	No	68	34.4	72	36.4	
	Total	198	100.0	198	100.0	
Hour of staying in school						
	<2 hours	22	16.9	24	19.0	0.95
	2-3 hours	60	46.2	56	44.4	
	>3 hours	48	36.9	46	35.6	
	Total	130	100.0	126	100.0	

TABLE 3. Association of vitamin D deficiency with the nutritional habits

VARIABLES		CASE		CONTROL		p-value
		Number (N)	Percentage (%)	Number (N)	Percentage (%)	
Meal per day						
	3-4	162	81.8	154	77.8	0.29
	>5	36	18.2	44	22.2	
	Total	198	100.0	198	100.0	
Regular milk consumption						
	Yes	118	59.6	150	75.8	0.02
	No	80	40.4	48	24.2	
	Total	198	100.0	198	100.0	
Milk consumption per day						
	<200 ml	12	10.2	14	9.2	0.73
	200-300 ml	80	67.8	96	63.2	
	>300 ml	26	22.0	42	27.6	
	Total	118	100.0	152	100.0	
Regular egg consumption						
	Yes	124	62.6	142	71.7	0.23
	No	74	37.4	56	28.3	
	Total	198	100.0	198	100	
Sea fish consumption						
	Yes	58	29.3	90	45.5	0.03
	No	140	70.7	108	54.5	
	Total	198	100.0	198	100.0	
The frequency of sea fish consumption						
	Once a week	28	48.3	42	46.7	0.82
	Twice a week	30	51.7	48	53.3	
	Total	58	100.0	90	100.0	
Exclusive breastfeeding						
	Yes	94	47.5	128	64.6	0.02
	No	104	52.5	70	35.4	
	Total	198	100.0	198	100.0	

TABLE 4. Univariate and multivariate logistic regression analyses with vitamin D deficiency case or control as the dependent variable

Variables	Crude OR	95% CI	Adjusted OR	95% CI
Not play outdoor games	**2.46***	**1.27-4.74**	**3.09***	**1.46-6.54**
Play video/Tv/mobile games	**2.47***	**1.39-4.38**	**4.14***	**1.97-8.67**
No sun exposure	**1.99***	**1.11-3.56**	**2.42***	**1.25-4.67**
Not regular consumption of milk	**2.12***	**1.15-3.90**	**3.01***	**1.38-6.57**
Not consumption of sea fish	**2.01***	**1.12-3.61**	**2.20***	**1.19-4.08**
Not exclusively breastfeeding	**2.02***	**1.14-3.58**	**2.03***	**1.14-3.63**

*OR = odds ratio, CI = Confidence interval, * = Significant*

factor for vitamin D deficiency. It has been again indicated by several recent studies [26-27]. Despite the fact that 67% of the children in this study were school going and have reported daily exposure to the sun, vitamin D deficiency is still prevalent among them because of other lifestyles factors. This finding might be attributed to the fact that although the weather is sunny and hot in Bangladesh, almost all year round, the clothing style and lack of outdoor activities may limit sun exposure and physical activity. A study published in the British Journal of Nutrition long ago (1981) indicated that the greater part of serum 25-OHD is derived from skin synthesis in response to ultra violet irradiation [28].

Our study found that milk consumption rate was potentially less among the cases in comparison to the control group (40.4% vs 24.2%) and also statistically significant (p=0.02, OR=2.12). A recent study conducted among Saudi Arabian children and adults found a strong correlation between dairy product consumption with serum level of vitamin D [29]. In Bangladesh, for the last few years, people were scared to consume dairy products due to food adulteration. That could be a potential reason of decrease in consumption of milk and milk products among thm. There is also an increasing trend of drinking fat-free milk among these population, which might be another reason of vitamin D deficiency. Even though sea fish consumption was not so common among the population in Dhaka city a few years ago, but due to rapid changes in communication and digital marketing, availability of sea fishes are increasing in super shops and online shops. With sea fish becoming more available and affordable among middle-income and upper middle-income group urban population, we have tried to see the sea fish consumption rate and its association with vitamin D deficiency. We have found that sea fish consumption rate is higher among the control group in comparison to the case. It is also statistically significant in both univariate and multivariate analysis. A recently published paper has indicated the relationship between small sea fish with vitamin D deficiency among adult population [30], which is, to some extent, supportive to our study. Another recent case-control study conducted among Bangladeshi garment workers found calcium and alkaline phosphatase had a significant correlation with vitamin D deficiency [31].

Exclusive breastfeeding is a "magic solution" for many nutritional deficiencies and related diseases. In our study, we have found that the rate of exclusive breastfeeding among the case group was less than the control group and also statistically significant. A recent Japanese study has found a significant relationship between exclusive breastfeeding, formula feeding and vitamin D deficiency [32].

Our study had a few limitations. This study includes the patients who have attended only two paediatric hospitals, so that limits our ability to generalize the study results among the whole country. Another limitation is that only a particular age group was considered, so it is difficult to relate whether those factors affect the whole population or not. Lastly, maternal vitamin D status was not measured. Despite having some limitations, the strength of our study was the selected hospitals are very popular and patients from different regions of the country and different socioeconomic backgrounds attending those hospitals, so it may represent the scenarios of the general population of children of Bangladesh.

CONCLUSION

We can conclude that the potential risk factors of vitamin D deficiency among Bangladeshi children may be attributed to lifestyle and nutritional habits. Strategies for hypovitaminosis D prevention should focus on Bangladeshi children. These strategies include vitamin D supplementation of breastfed infants and ensuring adequate maternal vitamin D status during pregnancy. We recommend a strong health awareness program to promote good nutritional habits and healthy lifestyles. For children of school-going age, there must be an allocated time period for sun exposure for about 15-20 minutes, at around 11:00 am -12:00 noon at the school premises, which could be called "Mid-day Sun Bath". The aim of the mid-day sun bath should be to reduce the incidence of Vitamin D deficiency and to promote healthy living. Furthermore, we propose adding vitamin D screening to the national health strategy of the country. There is a need for setting a screening schedule to cover all age groups for early detection and treatment of cases. Lastly, it is important to carry out further intervention studies to confirm the causality and see the effects of vitamin D supplementation.

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Declarations

Ethics approval and consent to participate: This study was approved by the Institutional Review Board of North South University. Informed writted consent was obtained from all parents before data collection.

Consent for publication

Consent for publication of this study results was obtained from the parents of children.

Availability of data and material

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declared that they have no competing interests.

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Authors' contributions

1. Mohammad Delwer Hossain Hawlader, planned and implemented the whole study procedure. He also wrote the first draft of manuscript.
2. Sanjana Zaman supervised the data collection overall as well as revised the final draft of manuscript.
3. Moshiur Rahman contributed to design the research methodology.
4. Mohammad Niaz Morshed Khan analyzed the data.
5. Aazia Hossain analyzed the data and edited the manuscript.
6. Gias Uddin Ahsan edited the final manuscript and provided overall supervision the study work.

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