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Risk Factors Predicting Hypovitaminosis D in Children in South-East Region of Bangladesh

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Abstract

Background: Hypovitaminosis D (serum concentration of 25(OH)D < 20 ng/ml) has been observed in temperate to tropical zones throughout world. Aim of this study is to determine the prevalence of Hypovitaminosis D among children in South-East region of Bangladesh and also explore its association with socio-demographic profile, weight, feeding pattern, residence, seasonal variation, degree of sun exposure, education type and schooling pattern. **Methods:** This was a cross sectional observational study having conducted at a paediatric clinic in Chittagong Metropolitan City from July, 2012 to December, 2017 including 524 children of 0 - 18 years by convenient sampling. The relevant data were assessed using standard case record form and lab parameter of 25(OH)D assay. Serum level of 25(OH)D of <20 ng/ml was taken as Hypovitaminosis D. Anaemia was defined as Hb level less than 11 gm%. **Results:** The prevalence of Hypovitaminosis D was 50.57%. Compared with the infancy age group the odds of Hypovitaminosis D is 1.36 times more likely in >5 yrs children. The odds of association (odds ratio or OR = 0.19) of rural population with Hypovitaminosis D is lower than urban population. The formula fed children had less chance of association (OR = 0.32) of developing hypovitaminosis D in comparison to exclusively breastfed babies. Occasional Sun exposed group was 1.40 times more likely to develop hypovitaminosis D in comparison to daily sun exposure group. The odds of Hypovitaminosis D were 1.9 times more in winter season than summer season. School going children had double the chance of Hypovitaminosis D than children with no education. Subjects with high weight for age were 3.65 times increased risk of suffering from hypovitaminosis D compared with normal weight for age. Girls had a little bit more chance of hypovitaminosis D than boys. Children coming from family with monthly Income > 10,000 BDT are associated with more Hypovitaminosis D. Among clinical variables only wheeze has significant association (OR = 1.83). **Conclusion:** Hypovitaminosis D (<20 ng/ml) prevails significantly among Infants and children of South-East region of Bangladesh. Age, area of residence, feeding pattern, sun exposure practice, seasons, schooling pattern, weight for age have strong association with Hypovitaminosis D.

Keywords

Hypovitaminosis D, Children, Bangladesh

1. Introduction

Vitamin D plays a pivotal role in health and disease [1]. Hypovitaminosis D is implicated as a risk factor for many diseases right from conception throughout life span [2]. Deficiency of Vitamin D leads to hypocalcaemia and hypophosphataemia with resultant rickets in children and Osteomalacia in adults, but these are rarely seen in areas of abundant sunshine and history of taking Vit D rich Foods. Lack of Vitamin D has its effect on body's Endocrine system, Immune system, Cardio Vascular System and Neuropsychological functioning. Vit D has a potent antioxidant protecting effect against carcinogenesis. Hence hypovitaminosis D is a risk factor for many diseases [2].

Vitamin D deficiency has been reported in Europe, America, Middle East, Africa, and Asia. Even it is more frequent in the sunny Mediterranean, south Asian, and their neighboring countries like China, Japan, and Thailand [3]. Most commonly Hypovitaminosis D in paediatric population is often asymptomatic. In Northern China about 42% of infants with Hypovitaminosis D suffer from Rickets [4]. Vitamin D is mainly derived from sunlight by ultraviolet radiation and only 10% from diet [5]. Vitamin D deficiency is not only prevalent in western country, it is surprising to note that hypovitaminosis D is highly prevalent even in areas with adequate sunshine. [2] [6]. It may be due to skin pigmentation and traditional clothing [7]. Modern day lifestyle changes have significantly reduced the total duration of sun exposure in children. Ultraviolet B, having shorter wavelength, tends to scatter earlier or later in the day. Hence cutaneous vitamin D synthesis is maximum from 10 AM to 3 PM, the time when most of the children are either in school or indoors. Exposure of only face, hands and arms due to clothing versus whole body is associated with marked differences in vitamin D synthesis [8]. Dietary factors like very low calcium intake and high fiber diet may deplete vitamin D stores [9]. Genetic factors like increased 25(OH)D, 24-hydroxylase (leading to degradation of vitamin D) activity in South Asians are also among the various explanations in sunny countries [10].

As vitamin D crosses the placenta and poor vitamin D content of breast milk, maternal vitamin deficiency and exclusive breastfeeding without vitamin D supplement or adequate sunlight exposure are important risk factors for vitamin D deficiency in infants. Fortifying foods with vitamin D remains the only alternative when cutaneous synthesis is inadequate. An Asian would require three times the sun exposure than light skinned person to produce equivalent amount of vitamin D [11]. In the absence of adequate sun exposure, 800 - 1000 IU vitamin D3/day may be needed to achieve this in children [12].

Though there are many studies regarding Hypovitaminosis D in adult population, data is scarce in paediatric population. In India the prevalence in children is 62% [13]. In Northern Pakistan instead of abundant Sun light ricket is prevalent due to malnutrition, lack of awareness and antenatal care [14]. In Japan Hypovitaminosis D is rare due to high sea fish consumption [15]. Vitamin D insufficiency of Children of Australia, Turkey and Lebanon varies between 30% - 50% [16] [17]. The cut off point for Hypovitaminosis D is still controversial. In most of the studies, serum level of 25(OH) of 20 ng/ml is taken as Hypovitaminosis D [18]. Though there are many studies in Bangladesh regarding Hypovitaminosis D in adult population, data is scarce in pediatric population [19] [20] [21]. This study was therefore conducted to find out prevalence and factors associated with Hypovitaminosis D in children in South-East Region of Bangladesh.

2. Methods

This cross sectional study was conducted in a private pediatric outpatient clinic in metropolitan area of Chattogram in south eastern region of Bangladesh over a period of sixty six months from July 2012 to December 2017. Considering the anticipated prevalence of Hypovitaminosis D of 50%, to fall within 5% of true prevalence with 95% confidence, the required sample size was 384 [6]. We included 524 children of 0 - 18 yrs. 25(OH)D level < 20 ng/ml was considered as Hypovitaminosis D. The study protocol was approved by the ethical committee of Department of Statistics, Faculty of Science of Chittagong University. Caregivers were provided with an informed consent or assent in written form. Children with severe malabsorption, taking anticonvulsants, suffering from Nephrotic syndrome, severe Hepatocellular disease and Renal disease were excluded. A case record form exploring socio-demographic profile, feeding habit, life style, schooling and environmental variation was developed. Body weight was measured to the nearest 100 gm up to upto 12 kg infant in MISAKI infant weighing scale. In older child with the subjects wearing no shoes, having light clothing and standing on a portable in RGZ-160 weighing machine to the nearest 0.5 kg then plotting in NCHS percentiles Growth Charts. For measurement of 25-OH Vitamin D, 5 ml venous blood sample was taken for each case by disposable syringe, and was collected in a red capped tube (no anticoagulant) which was sent to centrifuge machine (Rotofix 32 A, 3000 RPM) after 1 hr. of collection in a standard lab in the Metropolitan city under supervision of Medical Biochemistry consultant. With 10 minutes centrifugation the separated serum of sample cup (300 micro liter) was put in the Auto machine (Cobas: Elecsys 2010) for measuring 25(OH)D by Eletro-Chemiluminescence's in ADVIA centaur XP/Elecsys 2010/Immulite 2000 xPi and, the result was provided 24 minutes later. Data were analyzed by Z score calculator for proportion and MedCalc statistical software for Windows. One tailed P value of less than 0.05 was considered statistically significant.

3. Results

A total of 524 children were included in the study. Among the study subjects, hypovitaminosis D (<20 ngm/ml) was noticed in more than half of the case (265, 50.57%). It was observed that Hypovitaminosis D was significantly lower among children in 1 - 5 years compared to the infancy. There was no statistically significant difference between the infant group and >5 years groups (**Table 1**), however there is higher odds of association (1.36) with hypovitaminosis D in age group > 5 years compared to infancy though it is clinically and statistically not significant (p = 0.2675) (**Table 2**).

In the study population boys of hypovitaminosis D were noticed in 166 cases out of 337 (49.25%) whereas 99 out of 187 girls (52.94%) suffered from hypovitaminosis D. There was no significant difference between gender (**Table 1**), although girls had a little significant Association (1.15) (**Table 2**).

Among 265 patients with hypovitaminosis D, a significantly higher proportion of children resides in urban area than rural area (79.90% vs 43.55%) (**Table 1**). Rural children had also lower odds of association with Hypovitaminosis D (OR 0.19) which is both clinically (CI: 0.1264 - 0.2980) and statistically (p = 0.0001) significant (**Table 2**).

There was a statistically significant difference of Hypovitaminosis D and feeding patterns. Formula feeding is significantly less associated with Hypovitaminosis D (p = 0.005) (**Table 1**). **Table 2** revealed that the level of vitamin D was statistically significantly lower among exclusive breast feed children compared to the formula feeding (p = 0.013, OR = 0.32). There was no statistically significant difference between exclusive breast feeding children and the home made feeding children (p = 0.05) (**Table 1**).

Though statistically significant proportion (p = 0.03) of children coming from higher income family suffered from Hypovitaminosis D (**Table 1**) but in multivariate analysis it is not clinically significant (CI = 0.9594 - 2.8318).

Children with low weight for age had less association with Hypovitaminosis D (OR = 0.74) compared with children with normal weight for age (**Table 2**). But in children with high weight for age had significant association (OR = 3.65) but this association is imprecise (CI = 1.19 - 11.16).

Children going to Kindergarten, Primary and higher schools had significant proportion of Hypovitaminosis D compared with children not going to school (**Table 1**). Children going to primary school had both statistically and clinically significant association (OR = 2.19, p = 0.005, CI = 1.41 - 3.41) (**Table 2**).

Table 1. Prevalence of Hypovitaminosis D of participants with respect to socio-demographic, feeding pattern, schooling and seasonal factors (N = 524).

Parameter	Frequency (N = 524)	Hypovitaminosis D (n = 265)†	P-value‡
Age (years)			
Infancy	72	39 (54.16%)	
1 - 5	269	113 (42%)	0.03288
>5	183	113 (61.75%)	0.1335
Gender			
Boy	337	166 (49.25%)	0.208
Girls	187	99 (52.94%)	
Weight for age			
Normal	306	160 (52.29)	
Low	198	89 (44.95%)	0.05
High	20	16 (80%)	0.007
Residence			
Urban	209	167 (79.90%)	0.00001
Rural	225	98 (43.55%)	
Monthly Income (BDT)			
≤10,000	73	31 (42.46%)	0.149
>10,000 - 20,000	177	88 (49.71%)	0.03
>20,000 - 50,000	191	105 (54.97%)	0.192
>50,000	83	41 (49.39%)	
Feeding Pattern			
Exclusive breast feeding	30	20 (66.67%)	
Formula feeding	69	27 (39.13%)	0.005
Homemade feeding	425	218 (51.29%)	0.05
Schooling			
No education	317	142 (44.79%)	
Kindergarten	77	40 (51.95%)	03
Primary	114	73 (64.04%)	0.0002
High	16	10 (62.5%)	0.0002
Sun exposure			
Daily	223	102 (45.74%)	0.02872
Occasionally	301	163 (54.15%)	
Seasonal variation			
Summer	155	74 (28.39%)	
Rainy	79	31 (39.24%)	0.21
Spring	145	68 (46.9%)	0.44
Winter	145	92 (63.45%)	0.003

†Figures within parentheses denote % of children of Hypovitaminosis D in the same category. ‡different categories were compared with 1st category in each parameter.

Children with daily sun exposure less suffered from Hypovitaminosis D than those with occasional sun exposure ($p = 0.02$) and occasional sun exposure is more associated with Hypovitaminosis D (OR = 1.4) (**Table 2**).

Table 2. Multivariate logistic regression analysis of association between Hypovitaminosis D and various socio-demographic and other variables.

Variable	Category	P value	Confidence interval	Odds ratio
Age	Infancy (Ref)			
	1 - 5 years	0.0666	0.3633 - 1.0341	0.6129
	>5 years	0.2675	07872 - 2.3703	1.3659
Residence	Urban (Ref)			
	Rural	<0.0001	0.1264 - 0.2980	0.1941
Feeding History	Exclusive breastfeeding (Ref)			
	Formula feeding	0.0134	0.1307 - 0.7906	0.3214
	Home Made feeding	0.1082	0.2408 - 1.1517	0.5266
Gender	Male (Ref)			
	Female	0.4193	0.8103 - 1.6575	1.1589
Weight for age	Normal (Ref)			
	Low	0.1079	0.5204 - 1.0666	0.7451
	High	0.02	1.1928 - 11.1689	3.65
Schooling type	No education (Ref)			
	Kindergarten	0.2596	0.8090 - 2.1941	1.3323
	Primary	0.0005	1.4104 - 3.4137	2.1943
	Higher	0.1733	0.7289 - 5.7884	2.0540
Socioeconomic condition	≤10,000 (Ref)			
	>10,000 - 20,000	1.042	0.7731 - 2.3213	1.3396
	>20,000 - 50,000	0.0701	0.9595 - 2.8518	1.6542
	>500,000	0.3866	0.7024 - 2.4905	1.3226
Sun Exposure	Daily (Ref)			
	Occasional	0.0572	0.9898 - 1.9836	1.4012
Seasonal	Summer (Ref)			
	Rainy	0.2171	0.4076 - 1.2262	0.7069
	Spring	0.8835	0.6142 - 1.5214	0.9667
	Winter	0.0065	1.1969 - 3.0163	1.90

In Winter season Vit D insufficiency occurs significantly more than summer ($p = 0.003$). Children in Winter season were also statistically and clinically ($p = 0.006$), CI = 1.19 - 3.01) associated with Hypovitaminosis D (OR = 1.9) (Table 1).

Regarding clinical variables only proportion of children with wheeze has significant Hypovitaminosis D ($p = 0.003$) (Table 3). Table 4 revealed that feeding problem, lack of growth and speech problem had lower odds of association with vitamin D insufficiency and all other clinical variables had some association with Vitamin D insufficiency which are not statistically (All p-values are >0.05) and clinically significant (All CI includes 1). Only wheezy children had both statistically and clinically significant association with Hypovitaminosis D (OR = 1.83, $P = 0.007$, CI = 1.17 - 2.84).

Table 3. Proportion of clinical variables in Hypovitaminosis D†.

Variable	Proportion in Hypovitaminosis D‡	Proportion in sufficiency of Vitamin D‡	p-value
Cough	107/265 (40.37%)	100/259 (38.61%)	0.340
Respiratory Distress	32/265 (12.07%)	31/259 (11.96%)	0.484
Feeding Problem	23/265 (08.67%)	34/259 (13.12%)	0.050
Fever	27/265 (10.18%)	22/259 (08.49%)	0.251
Lack of growth	10/265 (03.77%)	14/259 (05.40%)	0.186
Seizure	10/265 (03.77%)	7/259 (02.70%)	0.245
Development Failure	7/265 (02.64%)	4/259 (01.54%)	0.189
Speech Problem	3/265 (01.13%)	8/259 (03.08%)	0.059
Wheeze	65/265 (24.52%)	39/259 (15.05%)	0.003
Anaemia	83/265 (31.32%)	69/259 (26.64%)	0.119

†Only one case had florid skeletal manifestations of rickets. ‡figure in parenthesis denotes percentage.

Table 4. Multiple logistic analyses of clinical variables associated with Hypovitaminosis D.

Variable	P value	Confidence interval	Odds ratio
Cough	0.679	0.7585 - 1.5287	1.07
Respiratory distress	0.970	0.5966 - 1.7103	1.01
Feeding problem	0.104	0.3595 - 1.1005	0.62
Fever	0.505	0.6768 - 2.2068	1.22
Lack of growth	0.374	0.2992 - 1.5742	0.68
Seizure	0.491	0.5291 - 3.7671	1.41
Development failure	0.386	0.5002 - 5.9808	1.72
Speech problem	0.133	0.0942 - 1.3695	0.35
Wheeze	0.0070	1.1798 - 2.8488	1.83
Anaemia	0.238	0.8600 - 1.8336	1.25

4. Discussion

Hypovitaminosis D is found in more than half of children in our study. The similar high prevalence was reported in other Bangladeshi and Indian studies [7] [14]. High Prevalence was also reported in Children of China, Mongolia, Middle East, sub-Saharan area and Latin America [22]. Increased prevalence may be due to higher skin pigmentation, increased pollution impairing Vit D synthesis, higher fibre rich diet which contain more phosphate and phytates that deplete Vitamin D and more 25 hydroxyvitamin D-24-hydroxylase that degrades 25(OH) Vit D to inactive metabolites [8] [23].

In this study (**Table 1** and **Table 2**), Hypovitaminosis D was found more in children > 5 years than those of 1 - 5 yrs. However infants suffered more than children of 1 - 5 years, probably proportion of infants is much lower than that of 1 - 5 years. In each category at least 42% suffered from insufficiency of Vitamin D. Hence in our children Hypovitaminosis D is present from birth. Vitamin D insufficiency was also found higher among American children aged 6 - 11 years (73%) than children aged 1 - 5 years (63%) [24]. The same type of prevalence was also shown in other study in Bangladesh [25]. VitD insufficiency increases with increasing age due to higher mineral demand of their growing bones [26]. Actually in our population Hypovitaminosis D is present from birth which may be due to lower Vitamin intake during pregnancy.

Female children suffered from Hypovitaminosis D more than male (**Table 1**). Same is reported in a study in America (girls vs Boys: 71% vs 67%) [24] (Mansbach, 2009). Though statistically and clinically not significant, still female children a bit at more risk (OR = 1.16) than male (**Table 2**). Probably it is due to more clothing and less outdoor physical activity in case of female children [27].

Regarding feeding pattern it was shown in **Table 2** that the formula fed child is less likely to develop hypovitaminosis D [OR = −0.321] and children taking home made food are also less risk of developing hypovitaminosis D [OR = 0.526], in comparison to exclusive breastfed babies (**Table 2**). It is now established that exclusive breastfeeding without vitamin D supplements or adequate sunlight exposure are important risk factors for vitamin D deficiency in infants [28].

High weight for age children has significantly increased proportion of Vitamin D insufficiency (p = 0.007) (**Table 1**). Logistic regression had shown (**Table 2**) that compared with normal weight for age subjects with low weight for age are at decreased risk (OR = 0.74) and subjects with high weight for age are with increased risk of suffering from hypovitaminosis D [OR = 3.65]. Absoud M, Cummins C, Lim MJ *et al.*, found that there is a association of higher risk of VDI among children who were overweight [29]. It has been suggested that higher body fat causes increased sequestration of Vitamin D [30].

Table 1 showed Hypovitaminosis D is significantly less in rural children than Urban (p = 0.00001). Logistic regression shows that rural populations are 0.194 times less likely to suffer from hypovitaminosis D than urban populations (**Table 2**). In other studies in India, Pakistan and Ethiopia Hypovitaminosis D is also more prevalent in urban population. It is attributable to dress code, occupation and longer duration of exposure to sunlight (long outdoor physical activity) in rural children [31] [32].

Table 1 showed children going to different grades of school had significantly higher proportion of Hypovitaminosis D than children not going to school at al. Logistic regression had shown that all kindergarten, Primary and High school children had increased risk, it is highest in primary school which is significant both statistically (p = 0.0005) and clinically (CI = 1.41 - 3.41) (**Table 2**). The same picture is evident in other studies in Montreal, Afghanistan and other studies [22] [33] [34]. This difference may be r elated to dress code, timing and duration of outdoor sun exposure, in different categories of school education.

Association between sun exposure and vitamin D status **Table 1** had shown that in children with occasional sun exposure hypovitaminosis D was significantly found (p = 0.02). Logistic regression in **Table 2** had shown occasionally sun exposed group were 1.40 times more likely to develop hypovitaminosis D in comparison to daily sun exposure group. In our study, (**Table 1**) among 265 subjects, prevalence of Hypovitaminosis D in Rainy and Spring seasons is not significantly different from Summer but in winter season it is significantly high ($p = 0.03$) Logistic regression (**Table 2**) had shown subjects in winter season are at 1.9 times higher risk in comparison to summer season which is both statistically and clinically significant ($p = 0.006$; CI = 1.196 - 3.016). In many studies vitamin D status of children was found to be related to timing of sun exposure and amount of skin exposed where increased outdoor exposure was found to be positively correlated with increased vitamin D level [35].

The present study (**Table 1**) has shown that children of high socio-economic group significantly suffered from Hypovitaminosis D ($p = 0.03$). Though logistic regression analysis (**Table 2**) showed High socio-economic group is at significant risk (OR > 1), it was not statistically and clinically significant (CI included 1). Linhares *et al.* has also shown that there is no significant difference of Vitamin D level in two groups [36]. Probably low income group had more time of sun exposure (well off children are more engaged in digital games, less outdoor activity, more risk of obesity and less space for outdoor games in urban children [37].

Among the clinical variables only wheeze has significant ($p = 0.003$) occurrence in children with Hypovitaminosis D (**Table 3**). Although feeding problem, lack of growth and speech problem were at less risk of association with vitamin D insufficiency, the significant association (OR > 1) of other clinical parameters excepting Wheeze ($p = 0.007$, CI = 1.179 - 2.848) are statistically and clinically significant. Lower respiratory tract infection with wheeze was also found in north-eastern rural Bangladesh and Turkey but Rahman *et al.* did not find any association of wheeze with Hypovitaminosis D [25] [38].

5. Limitation

Sampling was purposive. Not whole paediatric population of Bangladesh was included. Most of data were by self-reporting of guardians. Besides, type of supplementation, food habit related data and life styles were not addressed.

6. Conclusion and Recommendation

Hypovitaminosis D is highly prevalent in the pediatric population of south-eastern zone of Bangladesh. Age > 5 years, Urban dwellers, female, breast fed infants, high weight for age, Higher socio-economic strata, occasional sun exposure and winter season, school going children and only clinical parameter wheeze had significant association with Vitamin D Insufficiency. Multi-center RCT throughout Bangladesh will give idea about predictors of Hypovitaminosis D in Bangladesh. As it is prevalent from age 0, vitamin D supplementation during antenatal period and awareness of Vitamin D fortification may be ensured.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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