

Identification and Evaluation of Vitamin D Levels in Urban Children & Adolescents in Dhaka City, Bangladesh through a Cross Sectional Study

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Abstract

Background: Vitamin D plays a pivotal role in supporting the immune system, helping to reduce the risk of infections and certain autoimmune diseases. Adequate vitamin D levels may be associated with a reduced risk of certain health conditions like pre-eclampsia, gestational diabetes, and postpartum depression. Brittle bones, osteoporosis in the elderly, and osteomalacia in young children are all symptoms of vitamin D insufficiency. Additionally, it contributes to problems linked to gum disease, including an increase in dental cavities, alveolar bone loss around the teeth, and other problems. It could lead to depression, tiredness, and a loss of appetite. In this study, urban children and adolescents in Dhaka city, Bangladesh are examined for vitamin D deficiency, insufficiency, and sufficiency. Methods: The Study was a crosssectional study conducted under Dhaka National Medical College and Hospital, Dhaka and additionally included two other health centers Medinova Medical Services and Monoara General Hospital Service Golap bag, Dhaka from October 2020 to November 2021. The study location was at the 3 (Three) different hospitals which was located in Dhaka City. In this cross-sectional study, Participants will be selected purposively and conveniently based on the age categories from 0 - 19 years of age at the outdoor department of the hospital. The study included the secondary dataset of ambulatory individuals who came to the 3 (three) hospitals, randomly to evaluate serum vitamin D levels on referral from a general out-patient-department (OPD). They were examined for laboratory findings of serum 25 hydroxyvitamin D levels to determine vitamin D deficiency, insufficiency, and sufficiency among children and adolescent groups of both male and female Sex. **Results**: A total of 6394 individuals with a diverse age group were statistically examined for laboratory findings of serum vitamin D levels. Vitamin D deficiency was observed in 40.58% of individuals with a mean log of 1.01 ± 0.18 ng/ml serum vitamin D levels, vitamin D insufficiency in 30.93% of individuals with a mean log of 1.38 ± 0.05 ng/ml serum vitamin D levels and vitamin D sufficiency in 19.49% individuals with a mean log of 1.63 ± 0.12 ng/ml serum vitamin D levels. The highest percentage of individuals deficient in vitamin D were children and adolescents of age ranging between 15 to 19 years. Conclusion: The findings of vitamin D deficiency in children and adolescents direct higher authorities in the public health sector to take immediate steps to screen, intervene and educate high-risk populations incorporating vitamin D supplements to establish preventive and therapeutic measures.

Keywords

25 Hydroxyvitamin D, Serum Vitamin D, Vitamin D Deficiency, Prevalence, Children, Adolescents, Adults

1. Introduction

Vitamin D is a fat-soluble vitamin. Few foods naturally contain vitamin D, though it is often added to others and sold as a dietary supplement [1]. We consume vitamin D as a nutrient, but our bodies also produce it as a hormone. It is a fat-soluble vitamin with a long history of helping the body retain and absorb calcium and phosphorus, both of which are essential for bone development [2]. Retinoid X receptors mediate proteins that signal calcium and phosphate ions absorption, and vitamin D3 is the form of 1.25-dihydroxyvitamin D metabolites conjugated to vitamin D receptors. Additionally, research in the lab demonstrates that vitamin D helps lessen inflammation, manage infections, and slow the growth of cancer cells [3]. Vitamin D deficiency or insufficiency affects one billion people worldwide due to a variety of factors, including decreased sun exposure or inadequate intake [4]. Vitamin D consumption has been linked to a lower risk of several diseases, including type 1 diabetes (T1D) and rheumatoid arthritis (RA), as well as multiple sclerosis (MS) [5]. Although recent studies have provided limited insight, the molecular basis by which vitamin D exerts effects on such diseases remains incomplete, particularly in relation to underlying genetic risk [6]. Vitamin D has strong anti-inflammatory properties, slows the formation of new blood vessels, improves cell differentiation, and inhibits cell proliferation [7]. According to several studies, vitamin D may have a protective effect on the heart by inhibiting the renin-angiotensin system, reducing inflammation, or directly affecting heart and blood vessel cells (T. J. [8]. Regardless of gender, color, or geography, vitamin D deficiency has become an epidemic worldwide in all age groups of individuals. According to estimates, one billion people worldwide are either vitamin D deficient or have relative insufficiency. Only twenty years ago, there was a dearth of information on vitamin D insufficiency in various population groups in Bangladesh. A significant field of research has been focused on vitamin D deficiency or insufficiency over the past few years as a possible public health issue. Age, length of sun exposure, amount of exposed skin, time of day, latitude, atmospheric pollution, season, clothing, melanin pigmentation, usage of sunscreen, use of supplements, dietary, and genetic factors are all linked to vitamin D deficiency. [9]

With a total size of 147,570 km² and a population of 169 million, Bangladesh is the eighth most densely inhabited country in the world. It is located in South Asia. It is situated in a tropical to subtropical temperature zone with enough UV radiation (290 - 315 nm) that stretches from Latitude 200°43' to 260°36'N and Longitude 880°3' to 920°40'E. As a result, it has long been assumed that Bangladeshis get enough vitamin D. However, despite receiving lots of sunlight, a few earlier studies consistently stated that vitamin D insufficiency is a quiet epidemic in Bangladesh [10]. In order to maintain the equilibrium of bone minerals, vitamin D is crucial. A lack of vitamin D can cause rickets in children and osteomalacia and osteoporosis in adults, respectively [11]. In Bangladesh, rickets is a serious public health issue. In some regions of the nation, more than 8% of youngsters have a clinical condition [12]. Osteoporosis is a systemic skeletal illness that is defined by low bone mass and small-scale architectural degeneration of bone tissue. As a result, the bone becomes more brittle and susceptible to fractures later in life. This disease affects women four times more frequently than it does males [10]

Dental caries in the first dentition can be linked to maternal vitamin D deficiency. Supplemental calcium and vitamin D therapy can enhance periodontal health [13]. The specific readings from a blood serum laboratory analysis are used to measure the nutritional status of vitamin D. Vitamin D sufficiency is defined as serum vitamin D concentrations of 30 ng/ml or more, vitamin D deficiency as 20 ng/ml or below, and vitamin D insufficiency as 20 to 29.9 ng/ml [14]. The recommended dosage for treating vitamin D deficiency is 2000 IU of vitamin D per day for maintenance and roughly 5000 IU per day for recovery [15].

2. Rationale for the Study

The average life expectancy in Bangladesh increased dramatically from 46 years in 1974 to 73 years in 2017. There are no data available, however, it's possible that older Bangladeshis have a higher incidence of osteoporosis and fractures due to a very high frequency of vitamin D insufficiency [16]. In addition to maintaining bone health and physiological processes, optimal vitamin D status is linked to a number of chronic illnesses, such as diabetes, cardiovascular diseases (CVD), high blood pressure, various cancers, schizophrenia, multiple sclerosis, dementia, impaired immune function, and infectious diseases like tuberculosis [17]. Numerous studies have drawn attention to the link between poor prenatal vitamin D status and a higher risk of unfavorable neonatal outcomes, including preterm birth, small for gestational age births, low birth weight, and short births [4]. The goal of the current study is to identify populations at high risk of vitamin D deficiency and insufficiency among children and adolescents and to assess the status of vitamin D deficiency, insufficiency, and sufficiency among various age groups and genders by monitoring serum vitamin D levels in the population of urban slum areas in Dhaka, Bangladesh. The main goal of the study is to estimate the prevalence of vitamin D deficiency, insufficiency, and sufficiency in both male and female kids and teenagers. As a result, the study's hypothesis claims that serum vitamin D levels in males and females of all ages do not differ statistically significantly. At a 0.05 p-value, this hypothesis was found to be false.

3. Methods

The study was a cross sectional study conducted under the three hospitals located in Dhaka city from October 2020 to November 2021. For the study on "Identification and evaluation of Vitamin D levels in urban children & adolescents in Dhaka city, Bangladesh through a cross-sectional study," the researchers established specific criteria to select participants. Below are inclusion and exclusion principles that were used for this study:

Inclusion Criteria:

- Age Range: The study included children and adolescents within a specific age range, such as 1 to 18 years old, to focus on the target population.
- Urban Setting: The study was limited to participants residing in urban areas of Dhaka city to explore vitamin D levels in an urban environment.
- Consent: Only participants who or whose parents/legal guardians provided informed consent to participate in the study would be included.
- Blood Sample Availability: Participants who were willing to provide a blood sample for the measurement of vitamin D levels had been included.
- Health Status: The study included participants who were generally healthy and free from severe chronic illnesses or conditions that could significantly affect vitamin D levels.

Exclusion Criteria:

- Age Limit: The study excluded individuals outside the specified age range (e.g., above 18 years old or below 1 year old).
- Rural Residents: Participants residing in rural areas outside Dhaka city were excluded to focus specifically on the urban population.
- Informed Consent: Individuals who did not provide informed consent or lacked the capacity to provide consent (e.g., due to cognitive impairment) were excluded.
- Medical Conditions: Participants with certain medical conditions or diseases that had directly impact vitamin D levels (e.g., chronic kidney disease, malabsorption disorders) had been excluded.
- Medication Use: Participants on specific medications or supplements that

could interfere with vitamin D metabolism or absorption had been excluded.

• Pregnancy or Lactation: Pregnant or lactating individuals had been excluded due to potential changes in vitamin D metabolism during these periods.

In this study, Researchers typically investigated several variables to understand the relationship between vitamin D and various health outcomes or conditions. The key independent variable is Vitamin D levels and Dependable variables as socio demographic information as age, sex, location and exposure to Sunlight was used as independent variable. In this cross sectional study, Participants will be selected purposively and screened based on the age categories from 0 - 19 years of age at the outdoor department of the hospital. The study included the secondary dataset of ambulatory individuals who came to the three hospitals Dhaka National Medical College and Hospital, Medinova Medical Services and Monoara General Hospital, Dhaka, randomly to evaluate serum vitamin D levels on referral from a general out-patient-department (OPD). A questionnaire was developed to collect data from the patients. Written informed consent was obtained from all individuals to use their anonymous information and laboratory results for serum vitamin D levels for research purposes while collecting serum samples at hospitals. Parents or legal guardians signed informed consent for the participating children and adolescents. Ethical approval was obtained from the Institutional Review Board (IRB) of the (Dhaka National Medical College and Hospital along with approval from the medical college authority. laboratory facilities at the three-hospital premises have the capacity to perform daily approximately 200 - 300 tests and it has nearly 2 collections both at the center. Data Collector collected the initial data and during their performing serum Vitamin D level at the diagnostic both. We collected the data set from the laboratories with consent from the individual/guardian/parents of the individual and also followed the medical facilities data protection policies. Therefore, we obtained individuals' representative retrospective laboratory data from October 2020 to November'2021. Patients provided a sample of serum, which was collected in standardized serum collection tubes. For 8 hours at 20°C to 25°C, the separating gel in a standardized tube maintains 25(OH)D stability. With a minimum 3.0 ng/ml detection limit for serum 25(OH)D, centrifugation took place in 2 hours. The laboratory provided data for the study from male and female subjects of all ages who were sick and asymptomatic. Data from those whose age or gender information was missing were not included in the analysis. Therefore, 6394 people made up the final sample size after exclusion. Serum vitamin D levels across the board in males and females of all ages were examined for vitamin D deficiency, insufficiency, and sufficiency. A vitamin D deficient group was defined as people with blood vitamin D levels below 20 ng/ml, a vitamin D insufficient group as people with values between 21 and 29.9 ng/ml, and a vitamin D sufficient group as people with values above 30 ng/ml. Estimating the prevalence of vitamin D deficiency, insufficiency, and sufficiency among male and female children, adolescents was the study's main goal.

Statistical Analysis: SPSS software version 22.0 was used for the statistical analysis, which had a 5% error margin and a 95% confidence interval. For the normal distribution of serum vitamin D levels in the study population, log transformations were used. All demographic data, including age, gender, and location, were subjected to descriptive quantitative analysis. The mean logs of vitamin D deficiency, insufficiency, and sufficiency among males and females of all ages were compared using an analysis of variance and an independent-sample t-test. Statistics were considered significant at P-values of 0.05 or above.

4. Results

A total of 6394 individuals were statistically analyzed for the demographic variables of age and gender correlated with laboratory measurements of serum vitamin D levels. **Table 1** demonstrates descriptive statistics of individuals age categories. It was identified that 28.98% of participants was 15 - 19 years of age, 28.1% of the individual had 10 - 14 years of age, similarly 21.63% was 5 - 9 years and 21.29% was children under 5 years.

Figure 1 demonstrated a higher number of females (62.78%) than males (37.22%) were included in the study.

Based on the age categories, we observed at **Table 2** that more females (17.99%) were engaged in the categories from 10 - 14 years of age as well as 17.89% from 15 - 19 years of age. Most of the male were counted from 15 - 19 years of age categories.

In addition, among the study participants, we found that female participants were found, 14.59% (n = 933) of aged 0 - 4 years, 12.30% (n = 787) of aged 5 - 9 years, 17.99% (n = 1150) of aged 10 - 14 years, 17.89% (n = 1144) of 15 - 19 years of age. Participants from 10 - 14 years were mostly involved. **Table 2** shows also

Table 1. Age wise gender distribution.

Age Categories	Freq.	Percent	Cum.
0 - 4	1361	21.29	21.29
5 - 9	1383	21.63	42.92
10 - 14	1797	28.1	71.02
15 - 19	1853	28.98	100
Total	6394	100	

Table 2. Age wise sex ratio.

Age Categories	Female	Male	Total
0 - 4	933 (14.59%)	428 (6.69%)	1361
5 - 9	787 (12.30%)	596 (9.32%)	1383
10 - 14	1150 (17.99%)	647 (10.12%)	1797
15 - 19	1144 (17.89%)	709 (11.09%)	1853
Total	4014 (62.78%)	2380 (37.22%)	6394

the clear picture of the male participants at the study. It shows that 11.09% (n = 709) male from the aged 15 - 19 years were mostly participated.

Figure 2 Demonstrated that only 19% of the study participants had Vitamin D sufficiency (>30 ng/ml), 40% of the Participants had Vitamin Insufficiency (>20 to 30 ng/ml) and 41% had vitamin D insufficiency.

Figure 3: The study revealed that 42.55% of the female children (n = 1708) have vitamin D deficiency (R1 \leq 20 ng/ml), similarly it was observed that 37.27% of male children (n = 887) have Vitamin D deficiency, Subsequently 39.83% female (n = 1599) and 40.08% of Male children (n = 954) have Vitamin insufficiency (R2 = Vitamin D Insufficiency (>20 to 30 ng/ml)}. At the same time, the study also found 17.61% of female (n = 707) and 22.65% of male children (n = 539) have vitamin D sufficiency.

Table 3 described that 2595 (40.58%) had vitamin D deficiency where 794 (42.85%) children were 15 - 19 years of age and 785 (43.68%) children were 10 - 14 years of age. Similarly, the study revealed that Vitamin D sufficiency had less in aged 10 - 19 years of children.

Figure 4 illustrates details about the aged appropriate serum vitamin D level at the study. Considering age appropriate and gender inclusive data analysis at **Figure 3**, it was revealed that Most of the cases in Female had more Vitamin D deficiency and insufficiency whereas a little difference in Vitamin D sufficiency. We might consider that female needs more vitamin D at the area. It was revealed that more children have vitamin D deficiency and Insufficiency at the age of 10 - 19 Years of age. Most of the children were adolescents.

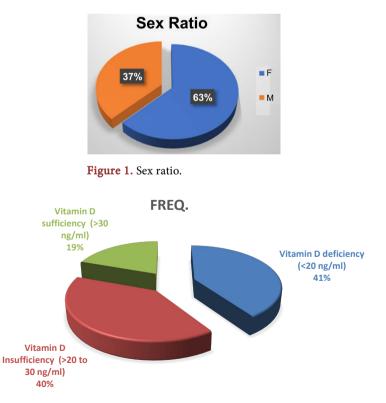


Figure 2. Vitamin D level.

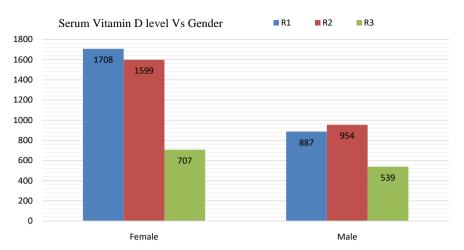


Figure 3. Serum Vitamin D level(R1 \leq 20ng/ml, R2 is more than 20 ng/ml to 30ng/ml, R3 is greater than 30 ng/ml) >versus sex. (F-4014, M-2380).

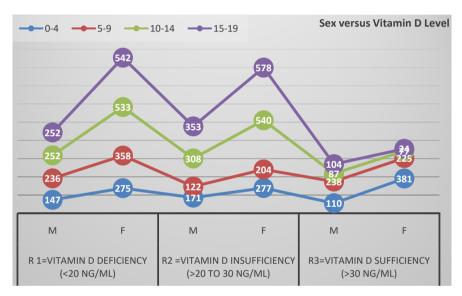


Figure 4. Gender and age marker based vitamin D levels.

Table 3. Comparison between age categories and vitamin D levels.
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Age Categories	Vitamin D deficiency (<20 ng/ml)	Vitamin D Insufficiency (>20 to 30 ng/ml)	Vitamin D sufficiency (>30 ng/ml)	Total
0 - 4	422 (31.0%)	448 (32.92%)	491 (36.08%)	1361
5 - 9	594 (42.95%)	326 (23.57%)	463 (33.48%)	1383
10 - 14	785 (43.68%)	848 (47.19%)	164 (9.13%)	1797
15 - 19	794 (42.85%)	931 (50.24%)	128 (6.91%)	1853
Total	2595 (40.58%)	2553 (39.93%)	1246 (19.49%)	6394

Figure 5 describes the age appropriate Vitamin D levels at the study. The study clearly shows that nearly more Study participants at the age of 10 - 19 years have more vitamin D deficiency and insufficiency compared to the other ages.

Figure 6 shows the exposure to sunlight. The Study revealed that Nearly 1519 children who had confirmed Vitamin D deficiency had exposure to sunlight (n-150) nearly less than 3 minutes (<30 minutes) and 1076 Children had Vitamin D deficiency had more that 30 minutes per day to exposure to the sunlight. Interestingly, 2375 Vitamin insufficiency children had less exposure to sunlight whereas only 178 had more exposure to sunlight. In case of vitamin Sufficiency, nearly 1125 Vitamin Sufficient children had less exposure to sunlight and 121 Vitamin Sufficient children had more exposure to sunlight.

Table 4 described the information of the children who had exposed more that 30 min/day at the sunlight and who had exposed less 30 min/day at the sunlight. The Study found that nearly 1375 children (21.5%) had exposed > 30 min/day at

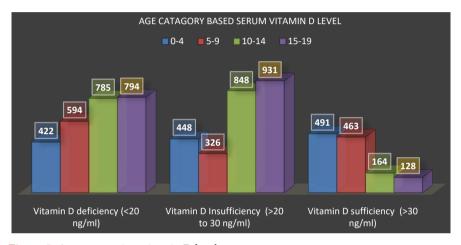
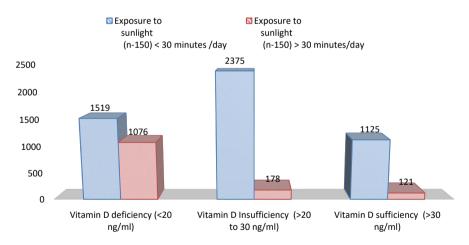


Figure 5. Age-appropriate vitamin D levels.



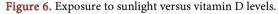


Table 4. Percentage of exposure to sunlight.

Exposure to sunlight (n-150)	Freq.	Percent	Cum.
<30 min/day	5019	78.5	78.5
>30 min/day	1375	21.5	100

the sunlight and nearly 5019 children (78.5%) had exposed < 30 minute/day at the sunlight. There might have a correlation with Sunlight exposure versus vitamin D deficiency.

5. Discussion

Many biological processes depend on vitamin D. Some vitamin D is obtained from dietary sources, but sunshine exposure accounts for the majority. The body must change vitamin D into its active form after ingesting it. More than a billion children and adults worldwide suffer from vitamin D deficiency and insufficiency, which is a global health problem. One cannot underestimate the effects of a vitamin D deficiency. Many acute and chronic ailments, including as preeclampsia, childhood dental caries, periodontitis, autoimmune disorders, infectious diseases, cardiovascular disease, fatal malignancies, type 2 diabetes, and neurological problems have been linked to vitamin D deficiency. Research consistently shows that hypovitaminosis D is extremely common among many population groups. We identified in another study based that The Prevalence of Vitamin D deficiency was higher in older people and women. For infants, kids, and teenagers, hypovitaminosis D varied from 21% to 75%; for premenopausal women, 38% to 100%; for pregnant women, 66% to 94.2%; for adult men, 6% to 91.3%; and for postmenopausal women, 82% to 95.8%.

The goal of the current study was to observe the prevalence of vitamin D deficiency and insufficiency in an urban context by making descriptive observations of serum vitamin D in children and adolescents of both sexes, including both symptomatic and asymptomatic individuals. The current study was also revealed that 6.55% of the study children aged 0 - 4 years have Vitamin D deficiency, similarly 11.16% from 5 - 9 years, 12.28% from 10 - 14 years and 12.48% from 15 -19 years of age. It was identified at the study that 42.47% study population had vitamin D deficiency. We found in another study, where 0 - 16 years of children was study participants and found that 46.75% children had Vitamin D deficiency.

41% of the current study participants were found to have serum vitamin D deficiency. The prevalence of it in females was found to be higher than in males. Around 26.71% of the female participants had serum vitamin D deficiency, with a greater female-to-male ratio whereas 13.87% of male had Serum Vitamin D deficiency. Hence, it can be said that women are more likely than men to be vitamin D deficient or insufficient. Vitamin D deficiency can affect both males and females, but there are certain factors that might contribute to a higher prevalence of vitamin D deficiency in females compared to males. Cultural, societal, and clothing habits can affect sun exposure [18]. In some cultures, females might have more conservative clothing practices that cover more skin, leading to reduced sunlight exposure and consequently lower Vitamin D synthesis. In some societies, there might be more emphasis on the health and well-being of females, leading to increased screening and awareness of health issues, including Vitamin D deficiency [19].

These results can be ascribed to a cohort that is predominately female rather than male. A lobortary-based observational study of Dhaka City in Bangladesh revealed that 68.4% of the female population had vitamin D insufficiency. Lack of education, weekday sunlight exposure of less than 15 minutes, the practice of avoiding sun exposure or covering oneself in sunlight, a lower intake of eggs, milk, or fish for only one or two times a week or no intake at all were all found to contribute to a higher prevalence of vitamin D deficiency in women [20]. In the current study, data from individuals from various socioeconomic backgrounds, age groups, and both sexes were retrospectively analyzed. While sunlight is a natural and efficient way for the body to synthesize Vitamin D, it's important to balance sun exposure with the risk of skin damage. Adequate Vitamin D levels can also be achieved through dietary sources and supplements when necessary. Always consult a healthcare provider to determine the best approach for maintaining healthy Vitamin D levels based on your individual circumstances. The Study revealed that Female had more Vitamin D deficiency and Insufficiency that the male children at the Dhaka City.

Similar lab data-based studies were conducted in nearby nations like Saudi Arabia, Pakistan, and India [21]. In the current study, 40% of participants had insufficiency (serum 25(OH)D 20 - 29.9 ng/mL), whereas 41% had vitamin D deficiency (serum serum 25(OH)D 20 ng/mL). Just 19% of participants had adequate vitamin D levels (serum 25(OH)D 30 ng/mL).

Although females in the current study had a more severe case of hypovitaminosis D than males did, these differences were not statistically significant [22]. Male and female participants in the Indian study had significantly different mean serum 25(OH)D levels. However, such discrepancies were not discovered by the other study [23].

Limitation: The study contains some significant flaws. This study lacked information because it was retrospective and only dependent on laboratory reports. The blood vitamin D status may be influenced by some confounding physiological and pathological factors, such as sun exposure, skin tone, dietary habits, and drugs. It was impossible to determine whether people with dangerous doses of vitamin D were taking it. As a result, the results cannot be broadly generalized. Notwithstanding these drawbacks, the study provides information on the significant prevalence of hypovitaminosis D in a diverse population in the Bangladeshi environment. A well-designed cross-sectional study and a statewide survey should also be conducted as a result of the current research in order to produce representative data on vitamin D insufficiency in Bangladesh, which will help shape future public health policies.

6. Recommendation

To lessen the widespread issue of hypovitaminosis D among vulnerable Bangladeshi people, the following recommendations could be made: 1) Public consciousness increasing public knowledge of the need of sunlight exposure in preventing vitamin D deficiencies, the health effects of vitamin D deficiencies, and the widespread occurrence of hypovitaminosis D in Bangladesh. The knowledge might be shared widely by using a variety of media, including the internet, radio, television, social networking sites (such as Facebook and YouTube), billboards, newspapers, magazines, short films, and literature in the educational system. The government of Bangladesh's healthcare providers may be crucial to the success of this scheme.

2) Solar exposure: Consistent 10 - 15-minute exposure to external sunlight with exposed arm, feet, and face (at least 2 to 3 times per week). When compared to uncovered women or women with lighter complexion, veiled women with brown or dark skin must increase their time spent in the sun by 2 - 3 times (30 - 45 min).

3) Biodiversification of food, particularly with regard to fish and dried mushrooms.

4) Vitamin D food fortification is an effective way to treat vitamin D insufficiency. Foods that are readily available, inexpensive, and widely consumed are frequently utilized as fortification agents. The following foods could be chosen as food carriers for vitamin D fortification: oil, margarine, milk, cheese, and other dairy products (both regular-fat and low-fat), infant formulae, bread, flour (rice, wheat), and orange juice.

5) Supplementation: Community clinics in Bangladesh provide free distribution of supplements (vitamin D, calcium, and several micronutrients) to the population's most vulnerable segments, including children, women, and the elderly.

6) Improving nutrition education: Any attempts to end vitamin D deficiency must take nutrition education into account. To increase understanding of vitamin D sources and the health effects of vitamin D deficiency, active steps must be taken to boost nutrition education programs offered through schools and health facilities.

7) Quick identification of vulnerable individuals: Nurses or doctors can quickly check people's vitamin D status in community health centers so that prompt action can be taken.

8) Rapid diagnostic process: To confirm vitamin D deficiency, persons in the community health centers must have access to simple and affordable laboratory measurement facilities.

9) The government must provide funding for more research to track the results of all efforts to end vitamin D deficiency.

7. Conclusion

The discovery of vitamin D deficiency in children and adolescents compels higher health authorities in both the public and private sectors to act right away to screen and inform the high-risk population and to treat those who are afflicted with vitamin D supplements to establish preventive and therapeutic measures.

Conflicts of Interest

The Authors have no conflict of interest with the research.

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