

# Role of vitamin D in acute Diarrhoea among Bangladeshi children: A single center experience

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## Abstract

**Background:** Acute diarrhoea is a major cause of the infectious disease in Bangladesh especially among infant and young children. Recent studies have demonstrated a relationship between poor vitamin D status and respiratory infections and diarrhoea among young children. Despite South Asia's low latitude and abundant sunshine, low [25(OH)D] has been reported in infants in India, Pakistan, Nepal and Bangladesh, suggesting that the contribution of serum vitamin D3 status to acute diarrhoea risk might be prominent in this region.

**Objective:** To observe the level of vitamin D in cases of acute watery diarrhoea.

**Methods:** Cross sectional study, which was done at the Department of Paediatrics at Mughda Medical College and Hospital, Dhaka from January 2021 through June 2022. Children age between 6 months to 59 months irrespective of sex with acute diarrhoea who were admitted in this hospital were included in this study.

**Result:** Maximum number of patients with diarrhoea aged between 6 to 12 months with preponderance to urban children. Male patient outnumbered the female. Level of vitamin D was found deficient in more than 50% of the patients. More than 50% of patients with deficient vitamin D level having some dehydration. Hospital stay was also longer in vitamin D deficient patients.

**Conclusion:** Vitamin D3 level was found low among the children between 6 months to 5 years with acute diarrhoea. Low vitamin D level was also associated with longer duration of diarrhoea and significant dehydration.

**Keywords:** Acute diarrhoea, Vitamin D, Infants

## Introduction

Diarrhoeal disease is one of the major causes of childhood morbidity and mortality in many developing countries. Diarrhoea remains a leading cause of childhood mortality – out of 1.7 billion episodes recorded globally in children under 5 years of age, approximately 700,000 result in death.<sup>1</sup> Globally, diarrhoea causes 9% of under-5 deaths, most of these are in developing countries.<sup>2</sup> Every year around 10 million children of under 5 age group die: about half of these deaths are associated with under nutrition and about 2 million with diarrhoea (out of a total of 2.5 billion episodes of diarrhoea). Most of the mortality related to diarrhoea occurs in less developed countries, and the highest rates of diarrhoea occur among malnourished children.<sup>3</sup> In Bangladesh, the burden of diarrhoeal diseases is significant among children of <5 years old. The overall diarrhoea prevalence among children of <5 years old was found to be around 44.5%.<sup>4</sup> The evidence suggests that, diarrhoea, measles, fever and acute respiratory diseases account for most of the child deaths in Bangladesh.<sup>5</sup> Vitamin D deficiency is considered to be the most common nutritional deficiency and often one of the undiagnosed medical conditions in the world.<sup>6</sup> It is our general belief that vitamin D deficiency is prevalent only in western countries, but actual condition is reverse. It is surprising that in South Asia, 80% of the apparently healthy population is deficient in vitamin D and up to 40% of the population is severely deficient.<sup>7</sup>

Vitamin D deficiency is highly prevalent in children worldwide, even in equatorial regions where it had not been previously suspected. In Latin America, reported prevalence of vitamin D insufficiency and deficiency among children and adolescents ranges from 28% in Costa Rica<sup>8</sup> to 56% in Bogotá, Colombia<sup>9</sup> and 62% in São Paulo, Brazil.<sup>10</sup> The prevalence of vitamin D

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DOI:

<https://doi.org/10.3329/dshj.v41i1.93358>

Received: 2 April 2025

Revised: 17 April 2025

Accepted: 23 April 2025

deficiency in young children is around 50-90 % in the Indian subcontinent.<sup>11</sup> A recent study showed that 31.88% children of 0-1 year had deficient Vitamin D level and 52.17% children had insufficient level and among 2 - 5 years' group, 38.16% were deficient and 50% were insufficient.<sup>12</sup> In 2020 Sarker Shamim found that deficient serum 25(OH) D level was found in 30.15% infants of up to one year age group, 35% in 2-5 years, and insufficient level was found in 52.38% in infants up to one year, 50% in 2-5 years.<sup>13</sup>

Emerging evidence suggests that the consequences of vitamin D deficiency (VDD) extend beyond its well-known effects on bone metabolism and calcium homeostasis, and also include alterations of specific arms of immunity. Immunomodulatory properties of vitamin D may influence susceptibility to infection.<sup>14</sup> These effects are primarily mediated through the vitamin D receptor (VDR), which is expressed in many cells of the immune system, including T and B lymphocytes, neutrophils, monocytes, macrophages and dendritic cells.<sup>15-19</sup> Recent experimental evidence supports a positive effect of vitamin D on the immunomodulation of infectious disease, which has led to investigate its effect on diarrhoea.<sup>20-22</sup> Study on school age children showed that, sufficient vitamin D had a protective effect on the severity of diarrhoea and vomiting.<sup>23</sup> Cells of the gastrointestinal tract, including epithelial cells and lamina propria macrophages are constantly exposed to luminal bacterium, which play key roles in normal intestinal development and innate immunity. The intestinal Paneth cells are known to secrete antimicrobial peptide, which are regulated by VDR signaling.<sup>24</sup> Vitamin and food supplement should be investigated to reduce illnesses due to diarrhoea. Apart from the immunologic properties of vitamin D, it represents an additional micronutrient that may have a role in the prevention of childhood diarrhoeal diseases.

Acute diarrhoea is a major cause of the infectious disease in Bangladesh especially among infant and young children. Recent studies have demonstrated a relationship between poor vitamin D status and respiratory infections and diarrhoea among young children. Despite South Asia's low latitude and abundant sunshine, low [25(OH)D] has been reported in infants in India, Pakistan, Nepal and Bangladesh, suggesting that the contribution of serum vitamin D3 status to acute diarrhoea risk might be prominent in this region. However, in Bangladesh limited information is available on the vitamin D status of children with acute diarrhoea. Therefore, this study is aimed to gain a preliminary insight of vitamin D status in children with acute diarrhoea and severity of illness.

## Materials and Methods

This study was designed as a cross sectional study, which was done at the Department of Paediatrics at Mughda Medical College and Hospital, Dhaka from January 2021 through June 2022.

Children age between 6 months to 59 months irrespective of sex with acute diarrhoea who were admitted in this hospital were included in this study. Purposive sampling technique was used to collect samples.

Children with 1) Severe acute malnutrition (SAM), malabsorption syndrome, renal disease and hepatic disease 2) who are diagnosed as Rickets 3) history of premature birth, low birth weight (<2500 g) & 4) receiving vitamin D supplementation were excluded from the study.

Though children with diarrhoea with no sign of dehydration can be treated in the ORT corner instead of indoor management, but for parental anxiety of further progression to moderate to severe dehydration, these cases were also admitted in the indoor.

## Procedures of data collection & analysis

Patients who were admitted in Department of Paediatrics of Mughda Medical college Hospital with acute watery diarrhoea were enrolled according to inclusion and exclusion criteria. The detail clinical history regarding duration, type, frequency of diarrhoea was taken. Detailed physical examination and dehydration status was assessed and classified as no dehydration, some dehydration and severe dehydration according to WHO IMCI protocol. Investigations based on clinical background were done. To measure serum 25(OH)D levels in children with acute diarrhoea, 2ml of blood collected by venipuncture, allowed to clot. Serum was separated by centrifugation at room temperature. Estimation of serum level of 25(OH)D vitamin was done by ELISA (Enzyme Linked Immuno-Sorbent Assay) technique. Technique was performed according to manufacturer instructions (DRG international, Inc., USA) All the findings were recorded in a pre-structured questionnaire by the first author himself.

Data were collected, compiled and Statistical analysis was done by SPSS version 20 (Statistical Package for Social Science version 20) for Windows.

## Results

This cross-sectional study was carried out among the total of 100 children (boys 64, girls 36) from 6 month to 59 months old admitted in Mughda Medical college hospital under the department of Paediatrics from January 2021 to June 2022.

In this study we found that 36% children were female and 64% were male. Fifty-Nine (59%) patients were between 6 months to 12 months followed by infants aged between 13 month and 24 months (35%). Mean age was found 14.13±8.20 months (Figure. 1).

We also found that among most of the studied patients 94 (94%) were living in urban area only 6 (6%) patients were living in rural area. Twenty percent patients (20%) belonged

to upper class socioeconomic background and 54% from middle class background. Thirty-two (32%) of the father had secondary level education and 36 (36%) mother had secondary level education. Twenty one percent father and twenty three percent mothers were graduate respectively. Thirty-five (35%) fathers were service holder and 94 (94%) mothers were house wife (Table I).

**Table 1: Socio-demographic characteristics of the study children (N=100)**

| Indicators                                 | No. | %    |
|--------------------------------------------|-----|------|
| <b>Sex</b>                                 |     |      |
| Male                                       | 64  | 64   |
| Female                                     | 36  | 36   |
| <b>Residence</b>                           |     |      |
| Urban                                      | 94  | 94.0 |
| Rural                                      | 6   | 6.0  |
| <b>Socio-economics status<sup>25</sup></b> |     |      |
| Upper Class                                | 20  | 20.0 |
| Middle Class                               | 54  | 54.0 |
| Lower Class                                | 26  | 26.0 |
| <b>Father's education</b>                  |     |      |
| Illiterate                                 | 8   | 8.0  |
| Primary                                    | 24  | 24.0 |
| Secondary                                  | 32  | 32.0 |
| Higher secondary                           | 15  | 15.0 |
| Graduate                                   | 21  | 21.0 |
| <b>Mother's education</b>                  |     |      |
| Illiterate                                 | 11  | 11.0 |
| Primary                                    | 24  | 24.0 |
| Secondary                                  | 36  | 36.0 |
| Higher secondary                           | 6   | 6.0  |
| Graduate                                   | 23  | 23.0 |
| <b>Father's occupation</b>                 |     |      |
| Driver                                     | 15  | 15.0 |
| Shop keeper                                | 3   | 3.0  |
| Business                                   | 18  | 18.0 |
| Garment worker                             | 12  | 12.0 |
| Service                                    | 35  | 35.0 |
| Day labor                                  | 3   | 3.0  |
| Others                                     | 14  | 14.0 |
| <b>Mother's occupation</b>                 |     |      |
| House wife                                 | 94  | 94.0 |
| Student                                    | 3   | 3.0  |
| Service holder                             | 3   | 3.0  |

Among the participants 59% children were 6-12 months old, 35% from 12 months to 24 months and the rest 6% are in the group of >24 months to 59 months (Figure 1).

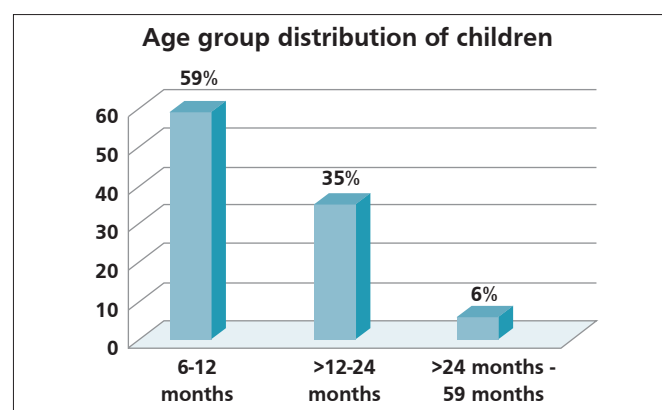


**Figure 1. Distribution of the study children by age group (N=100)**

Sixty-two children completed their immunization till date, 21 children completed and 17 children did not complete their immunization (Table II).

**Table II: Immunization status of the study subjects (N=100)**

| Immunization status | No. | %   |
|---------------------|-----|-----|
| Complete till date  | 62  | 62% |
| Complete            | 21  | 21% |
| Incomplete          | 17  | 17% |

This study shows that 48% had breast feed along with complementary food, 31% had complementary feeding only, and 21% had breast feeding with formula milk. Most of the patients 88% started their complementary feeding after 6 months (Table III).

**Table III: Feeding history of study subjects (N=100)**

| Feeding history                      | No. | %    |
|--------------------------------------|-----|------|
| Breast feed + Complementary food     | 48  | 48.0 |
| Complementary feeding                | 31  | 31.0 |
| Breast feeding+ formula milk         | 21  | 21.0 |
| <b>Complimentary feeding started</b> |     |      |
| 6 months                             | 12  | 12.0 |
| >6 months                            | 88  | 88.0 |

In our study 92% of parents washed their hands before preparing food and used soap after coming from latrine (Table IV).

**Table IV: Distribution of parents based on personal hygiene (N=100)**

| Personal hygiene                   | No. | %    |
|------------------------------------|-----|------|
| Hand washing before preparing food | 92  | 92.0 |
| Use soap after coming from latrine | 92  | 92.0 |

Vomiting or nausea was found in 74 (74%), abdominal pain in 12 (12%) and 65 (65%) children had fever (Table V).

**Table V: Distribution of children by presenting complaints (N=100)**

| Complaints      | No. | %    |
|-----------------|-----|------|
| Vomiting/nausea | 74  | 74.0 |
| Abdominal Pain  | 12  | 12.0 |
| Fever           | 65  | 65.0 |

In this study we found visible blood in the stool in 6 (6%) patients and the rest 94 (94%) children had watery stool. (Table VI)

**Table VI: Distribution of children by nature of the Stool (N=100)**

| Nature of stool | No. | %    |
|-----------------|-----|------|
| Bloody stool    | 6   | 6.0  |
| Watery stool    | 94  | 94.0 |

Regarding hydration status of the participants. Severe dehydration was observed in only 3 (3%) children, and some dehydration in 90 (90%) Children. Seven children with no sign of dehydration were found in this study (Table VII).

**Table VII: Distribution of children by dehydration status (N=100)**

| Dehydration status | No. | %    |
|--------------------|-----|------|
| No dehydration     | 7   | 7.0  |
| Some dehydration   | 90  | 90.0 |
| Severe dehydration | 3   | 3.0  |

Regarding the blood level of Vitamin D3 in the participating children, we found that 56 children (56%) had <20 ng/ml, 38 had 20-29 ng/ml and 6 patients had >30 ng/ml of vitamin D3 level (Table VIII).

**Table VIII: Distribution of children by serum vitamin D3 level (N=100)**

| Vitamin D3 level           | No. | %    |
|----------------------------|-----|------|
| <20 ng/ml (50 nmol/l)      | 56  | 56.0 |
| 20-29 ng/ml (50-75 nmol/L) | 38  | 38.0 |
| >30 ng/ml (>75 nmol/L)     | 6   | 6.0  |

In this study, 50 patients (89.3%) had stool frequency more than 20 times per day who had vitamin D3 level <20 ng/ml in comparison to 14 (36.4%) patient who had vitamin D3 level 20-29 ng/ml. On the contrary none of the patient had stool frequency >20 times per day who had vitamin D3 level >30ng/ml which was statistically significant ( $p<0.001$ ) (Table IX ).

**Table IX: Association of frequency of stool in 24 hours and serum vitamin D3 level (N=100)**

| Frequency of stool      | Vitamin D3 Level |                    |                 | p value |
|-------------------------|------------------|--------------------|-----------------|---------|
|                         | <20 ng/ml (n=56) | 20-29 ng/ml (n=38) | >30 ng/ml (n=6) |         |
|                         | n (%)            | n (%)              | n (%)           |         |
| ≤20 episodes/ 24 hours¶ | 6 (10.7)         | 24 (63.2)          | 6 (100)         | <0.001  |
| >20 episodes/ 24 hours* | 50 (89.3)        | 14 (36.8)          | 0 (00)          | <0.001  |
| Total                   | 56 (100)         | 38 (100)           | 6 (100)         |         |

\*Fisher's exact text, ¶Chi square test.

In this study 51 patients to whom diarrhoea continued for 1-3 days 6 (11.76%), 29 (56.86%), 16 (31.38%) were from vitamin D3 sufficient, insufficient and deficiency group respectively. Whereas among 10 patients to whom diarrhoea continued for >5 days 1 (10) from insufficient group and 9 (90%) form deficient group (Table X).

**Table X: Association of duration of diarrhoea and serum vitamin D3 level (N=100)**

| Duration of diarrhoea | Vitamin D3 level |       |                    |       |                  |       | Total | p value |
|-----------------------|------------------|-------|--------------------|-------|------------------|-------|-------|---------|
|                       | >30 ng/ml (n=6)  |       | 20-29 ng/ml (n=38) |       | <20 ng/ml (n=56) |       |       |         |
|                       | no               | %     | no                 | %     | no               | %     |       |         |
| 1-3 days¶             | 6                | 11.76 | 29                 | 56.86 | 16               | 31.38 | 51    | <0.001  |
| 4-5 days*             | 0                | 00    | 8                  | 20.51 | 31               | 79.49 | 39    | <0.001  |
| >5 days*              | 0                | 00    | 1                  | 10    | 9                | 90    | 10    | <0.001  |

\*Fisher's exact text, ¶Chi square test.

## Discussion

Mortality and morbidity are high among under five years children. About 12.5-15% of world population are in this age group. In developing countries, 25-30% of mortality occurs in this group. Among the major life-threatening infectious diseases diarrhoea is one of the major preventable gastrointestinal health problems. Risk factors for diarrhoea include malnutrition, poor gastrointestinal absorption, poor personal hygiene, environmental sanitation problems, unhygienic food preparation, improper sewage disposal and improper use of latrines, early discontinuation of breastfeeding, and unhygienic bottle-feeding. Prevalence of diarrhoea is quite alarming amongst our children who belong to low socioeconomic status. According to UNICEF and the World Health Organization (WHO), diarrhoea kills more children than any other illness – more than AIDS, malaria and measles combined. Effective interventions to reduce diarrhoea deaths are available, but reach too few children. Reducing child mortality is one of the eight Millennium Development Goals (MDGs).<sup>26</sup>

This study showed majority of (59%) children were between 6 months to 1 year followed by >1 year to 2 years (35%) and >2 years to 6 years (6%). These findings are consistent with Shah et al. They found majority (70%) of patients were below 2 years of age.<sup>27</sup> In this study male child outnumbered female, comprising 64 males and 36 females, the ratio being 1.7:1. Shah et al. found 65% were male and 35% were female in their study.<sup>28</sup> One possibility in our country is that parents are more concerned about their sons than daughters.

Parent's educational qualification is strongly linked to the nutritional status of their children. In this study 66% of the parents had formal primary to secondary education and 36% had completed higher secondary to graduate certificate. In a similar cross-sectional study conducted in

Kushtia Bangladesh they found 40% parents had education background from primary to secondary level.<sup>4</sup> In this study, 86% of the households used tap water and 83% used boiled water for drinking. These findings are also consistent with other studies.<sup>4</sup> In this study 92% of parents practice hand washing before preparation of food and used soap water after coming from the latrine. A similar study conducted by Khatun A found 62% parent washed hand before cooking and 52% used soap water after coming from latrine.<sup>4</sup>

In this study vitamin D status was measured concurrently with disease diagnosis; thus, the potential for reverse causation in which infection may have affected 25 (OH) D concentration cannot be excluded. In this study dehydration status, frequency of stool and duration of diarrhoea were compared with 3 different categories of serum Vitamin D3 level. In this study vitamin D3 deficiency was found in 56%, insufficient in 38 % and sufficient in 6% in studied cases. These findings are consistent with the findings of the other research works.<sup>23,29</sup> Thornton et al. measured 25 (OH) D3 concentration in 475 randomly selected school age children (mean age, 8.9 years) and followed them during an academic year for diarrhoea.<sup>23</sup> In that study, vitamin D deficiency and insufficiency were associated with a higher number of diarrhoea episodes. Severe diarrhoea (frequency of stool >20/24 hours) was significantly higher in vitamin D3 deficient group than vitamin D3 insufficient and sufficient group (p value <0.001). A cross-sectional study of 458 Qatari children reported a significantly higher prevalence of gastroenteritis among those who were vitamin D deficient.<sup>30</sup>

According to dehydration status of the studied children number of some dehydration and severe dehydration cases were higher in vitamin D3 insufficient and deficient group and the difference was found statistically significant. Duration of diarrhoea was longer in vitamin D3 deficient group than vitamin D3 insufficient and sufficient group. The difference was also found statistically significant.

There is scarcity of data regarding the association of vitamin D3 level with dehydration status, frequency of stool and duration of diarrhoea. So further studies are warranted to establish the causal relationship of vitamin D3 and acute diarrhoea and to ascertain whether vitamin D supplementation reduces the risk of gastrointestinal morbidities in children.

### Limitations of the study

The limitation of our study is that a single center study. We did not evaluate geographical variation from multiple centers. Another limitation was that there is no widely accepted national value of serum vitamin D3 level in children so western value was considered as standard.

### Conclusion

Vitamin D3 level was found low among the children between 6 months to 5 years with acute diarrhoea. Frequency of stool was increased and duration of diarrhoea was longer among the vitamin D3 insufficient and deficient children. Dehydration was also significantly noticed among the children with low vitamin D3 level than sufficient vitamin D3 level.

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