Global Academic Journal of Medical Sciences

Available online at www.gajrc.com
**DOI:** 10.36348/gajms. 2023.v05i01.003

OPEN ACCESS

ISSN: 2706-9036 (P)
ISSN: 2707-2533 (O)

**Original Research Article**

# Effect of Vitamin D Supplementation in Children with Severe Acute Malnutrition

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**Article History**
Received: 13.11.2022
Accepted: 19.12.2022
Published: 11.01.2023

**Abstract:** ***Background:*** Malnutrition accounts for about 35% of under-five mortality, of which 4.4% is specifically because of severe wasting. Prevalence of vitamin D deficiency in malnourished children ranges from 31% to 61%. Addition of high dose vitamin D supplementation in children with severe acute malnutrition would be effective in elevating serum vitamin D concentration and thus improve weight gain. The association of vitamin D and malnutrition is well recognized but data are scarce. ***Objectives:*** To see the effect of vitamin D in the treatment of severe acute malnourished children. ***Methods*:** This prospective randomized controlled trial study was conducted among children 6 months to 5 years old with a diagnosis of SAM in the pediatric ward of Dhaka Shishu (Children) Hospital in Bangladesh from July 2018 to January 2020.Sample was collected through simple random sampling then randomized into two groups by lottery method. Finally, 50 patients were included in the study, among them 25 patients received 6 lac IU vitamin D orally in day 1 in addition to the standard treatment of SAM and the other 25 patients received only the standard treatment of SAM. Demographic data and other related information regarding clinical feature, laboratory feature, outcome variables were recorded and anthropometric measurement and Z-scoring was done to assess malnutrition. Collected data was checked manually and analyzed by computer-based program SPSS for Windows (version 20.0). ***Outcomes were:*** Length of hospital stay and average weight gain between the two groups. Comparison of parameters among the group were done by unpaired t-test and chi-square test. ***Results:*** There were no statistically significant difference in length of hospital stay (16.24 ±3.29 versus 15.34±2.64) days, p=0.291 but there was statistically significant difference in average weight gain (9.08±2.99 versus 7.52±2.06) gm/kg/day, p=0.037 and wasting (weight for height z score) improved significantly on follow ups (p=0.241 on first, p=0.039 on 2nd, p=0.009 on 3rd and p=<0.001 on 4th follow up). ***Conclusions:*** Vitamin D supplementation causes significant weight gain in children with severe acute malnutrition.

**Keywords:** Acute Malnutrition, Vitamin D supplementation, Prevalence of vitamin D deficiency.



**Citation:** Shahrina Afroze Tisha, Syed Shafi Ahmed, Md. Kamrul Hasan, Saiful Islam, Md. Naim Hossain Ratan, Nazmul Hasan, Kanta Halder (2023). Effect of Vitamin D Supplementation in Children with Severe Acute Malnutrition. *Glob Acad J Med Sci*; Vol-5, Iss-1 pp- 12-20.

## INTRODUCTION

Severe acute malnutrition is the most extreme and visible form of undernutrition. Affected children have very low weight for their height and severe muscle wasting. Nearly half of all deaths in children under 5 are attributable to undernutrition. Undernutrition puts children at greater risk of dying from common infections and also increases the frequency and severity of such infections and delays recovery. About 20 million children are affected worldwide mainly in Asia and Africa where it is a major cause of death. Children with severe acute malnutrition commonly have low levels of vitamin D. This micronutrient plays an important role for muscle and bone health and for maintaining a healthy immune system but the standard treatment contains relatively modest amounts of this vital micronutrients. And somewhat, surprisingly the effects of adding high dose vitamin D to the standard treatment of SAM have not previously been studied. Vitamin D deficiency associates with severe wasting in malnourished children. Vitamin D supplementation has been shown to enhance weight gain in low birth weight infants [1]. Vitamin D has also been shown to have favorable effects on skeletal muscle function, neurodevelopment and immune function [2-4], due to its anti-inflammatory and antimicrobial actions it might enhance the response to standard therapy for severe acute malnutrition because severe acute malnutrition is a condition in which both increased systemic inflammation and infections are associated with adverse outcome [5, 6]. Acute malnutrition, which is also known as 'wasting', occurs when there is recent rapid weight loss or a failure to gain weight. This is most often caused by insufficient food, disease, inappropriate childcare practices or a combination of these factors. Malnutrition accounts for about 35% of under-five mortalities, of which 4.4% is specifically because of severe wasting. Severe wasting is estimated to account for around 400,000 childhood deaths each year [7]. In India, the prevalence of severe acute malnutrition in children between 6 months to 5 years is 6.4%. [8] Vitamin D deficiency (VDD) is prevalent in children worldwide which is a major public health problem [9]. Among the nutritional deficiency vitamin D deficiency is considered to be the most common. [10] Vitamin D deficiency is highly prevalent in all age groups in all populations around the globe [11]. It is estimated that about 1 billion people worldwide have vitamin D deficiency or insufficiency [12]. The prevalence of vitamin D deficiency in Indian children is 50-90% [13]. In low and middle income countries VDD ranging from 28-62% [14]. Prevalence of vitamin D deficiency in malnourished children ranges from 31% to 61% [15]. A survey of vitamin D deficiency among malnourished children showed a prevalence of 28% in sub-Saharan Africa from 2012 to 2014 [16]. The association of vitamin D and malnutrition is well recognized but data are scarce. A study in Pakistan found that 33.6% of severely malnourished children had rickets. As F-75 and F-100 contains insignificant amount of vitamin D, so this source may not be sufficient to consistently elevate circulating concentration of 25-hydroxyvitamin D [25(OH)D] into the optimal range in children with severe acute malnutrition, given the high prevalence of vitamin D deficiency in this group and the presence of a systemic inflammatory response that may disregulate vitamin D metabolism and increase vitamin D requirements [17]. So the addition of high dose of vitamin D supplementation to the standard treatment of severe acute malnutrition would be effective in elevating serum 25(OH)D concentrations into the high physiologic range in children with severe acute malnutrition and this would improve weight gain over the initial 8 weeks of treatment. Since children with severe acute malnutrition have a high rate of vitamin D deficiency and as this child may develop severe complications so the study has been done to see the effect of vitamin D supplementation in children with severe acute malnutrition and to compare the outcome indicators between two groups of children with severe acute malnutrition with or without vitamin D supplementation.

## OBJECTIVES

**General objectives:**

General objective of this study was to compare the effect of vitamin D supplementation in children with severe acute malnutrition.

**Specific Objectives:**

- To assess the weight, gain in child with vitamin D supplementation.
- To assess the weight, gain in child without vitamin D supplementation.
- To compare the weight, gain between two group with or without vitamin D supplementation.

## METHODOLOGY

It was single blinded, parallel group randomized controlled study, from July 2018 to January 2020, children with severe acute malnutrition with ages between 6 months to 59 months admitted in the Bangladesh Shishu Hospital & Institute, Dhaka. Bangladesh. A total of 50 patients were included in the study, among them 25 patients received 6 lac IU vitamin D orally in day 1 in addition to the standard treatment of SAM and the

other 25 patients received only the standard treatment of SAM.

**Inclusion criteria:**

A children aged 6-59 months, diagnosed as Severe acute malnutrition defined by WHO [children with a MUAC of <115 mm, a weight for height z score < -3 or bilateral pedal edema.

**Exclusion criteria:**

- Children with underlying chronic disease (chronic renal failure, chronic liver disease, Cholestasis).
- Cerebral palsy with mental retardation/developmental delay.
- Any medical transfer cause, unstable vital parameters.
- Any underlying cause for lack of weight gain other than malnutrition.
- Frank signs and symptoms of rickets.

**Study procedure**

After admission in to hospital children who met the inclusion criteria and whose parents gave consent to participate underwent the following baseline assessment. A structured questionnaire was given to capture information on participant's demographic details, parental occupation, education, monthly income and detailed feeding history like exclusive breast feeding, time of initiation of complimentary feeding, preparation of food etc, birth history, developmental history, any history of chronic disease. A thorough physical examination was done. Anthropometric measurements were conducted by trained personal. MUAC was measured with color labeled MUAC tape at the midpoint between the olecranon process and the acromion process. Weight for height z score was calculated according to the WHO child growth standards. All baseline investigations including 25(OH)D level was done during admission using the ARCHITECT system from Abbott Laboratories and expressed in ng/ml and labeled as children with vitamin D levels of <10 ng/ml are vitamin D deficient, 10-29 ng/ml are insufficient and 30-100 ng/ml are sufficient. The children were randomized into two groups by lottery. Both the groups were treated by the fully trained staff according to the recommendation given by WHO for admitted patient's management of children with severe acute malnutrition. Participants randomly assigned to the intervention arm of the trial additionally received high dose (6 lakh IU) vitamin D orally on day 1 along with standard treatment of SAM and the other group got only the standard treatment of SAM. The outcome indicators average length of stay and average weight gain were determined at the time of discharge. The patients who were discharged followed at every 15 days for 4 times and their W/H, Height for age (H/A), MUAC were recorded.

**Data processing and data analysis**

Statistical analysis was carried out using the Statistical Package for Social Sciences version 23.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Chi square test was used to determine any significant association between vitamin D supplementation and outcome indicators and Unpaired Student T test was used to analyze the quantitative variables. P values <0.05 were considered as statistically significant.

**Ethical issue:**

Informed written consent was taken from parents or legal guardian. Ethical clearance was taken from the Ethical Review Committee of Bangladesh Shishu Hospital & Institute.

## RESULTS

**Table-1: Comparison of age between two groups, (N=50)**

| Age (in months) | Case (n=25) n (%) | Control (n=25) n (%) | P value |
|---|---|---|---|
| 6-12 months | 10(40.0%) | 8(32.0%) | 0.131 |
| 12-36 months | 14(56.0%) | 16(64.0%) | |
| 36-60 months | 1(4.0%) | 1(4.0%) | |
| Mean ±SD | 15.8±8.6 | 19.9±10.3 | |
| Range | (6-39) months | (6-60) months | |

Table 1 showed, majority patients belonged to age 12-36 months in both groups, which was 14(56.0%) in cases and 16(64.0%) in control. The mean age was found 15.8±8.6 months in cases and 19.9±10.3 months in control. The mean difference was not statistically significant (p>0.05) between the groups.

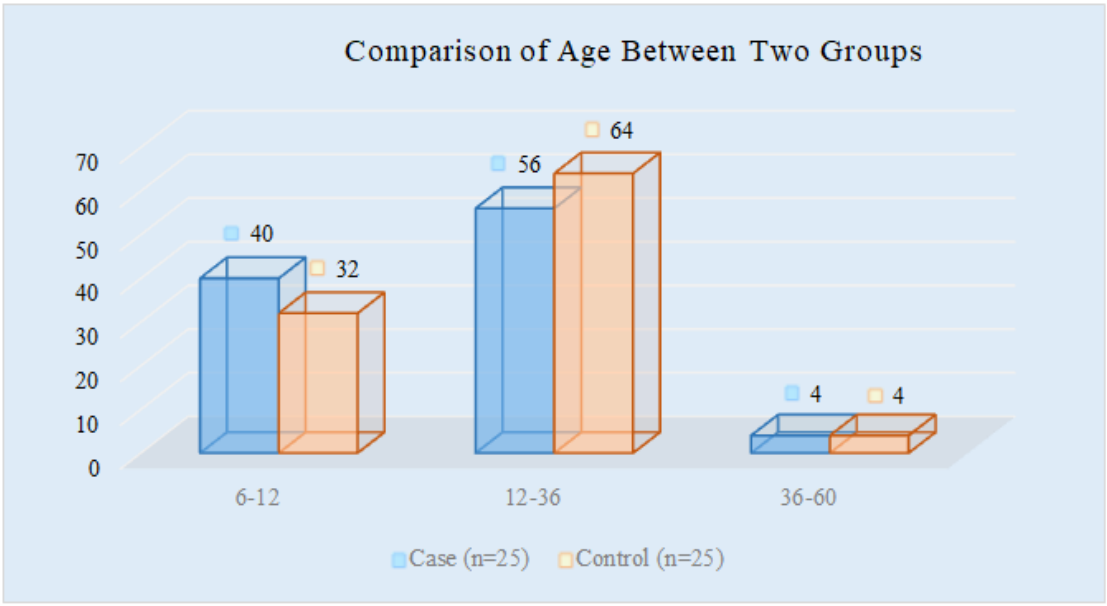


**Figure I: Bar chart showed comparison of age between two groups, (N=50)**

**Table-2: Distribution of the study patients by sex, (N=50)**

| Sex | Case (n=25) n (%) | Control (n=25) n (%) | P value |
|---|---|---|---|
| Male | 18(72.0%) | 16(64.0%) | 0.544 |
| Female | 7(28.0%) | 9(36.0%) | |
| Male: Female ratio | 2.6:1 | 1.8:1 | |

Table 2 showed, majority patients were males among the groups, 18(72.0%) in case and 16(64%) in control. Females were 7(28.0%) in case and 9(36.0%) in control. The difference was not statistically significant (p>0.05) between the groups.

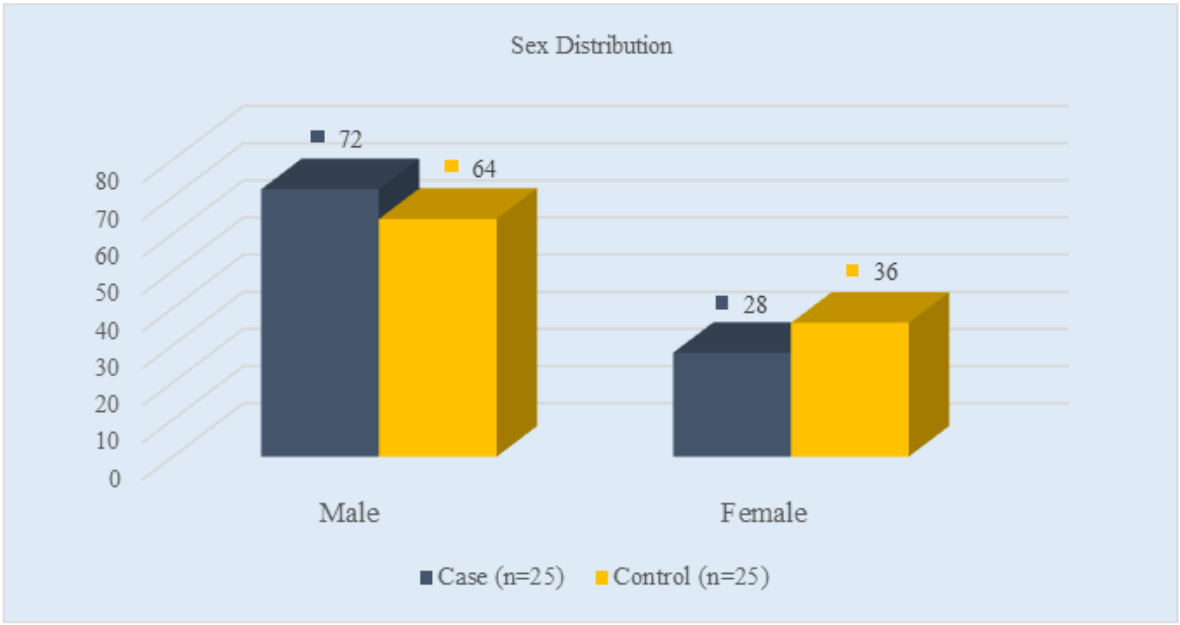


**Figure II: Bar chart showed group wise sex distribution of the Patients, (N=50)**

**Table-3: Others symptoms of the patients, (N=50)**

| Sex | Case (n=25) n (%) | Control (n=25) n (%) | P value |
|---|---|---|---|
| Fever | 16(64.0%) | 12(48.0%) | 0.254 |
| Pneumonia | 18(72.0%) | 15(60.0%) | 0.370 |
| Watery diarrhea | 13(52.0%) | 16(64.0%) | 0.390 |
| Dermatitis | 10(40.0%) | 8(32.0%) | 0.556 |
| Anemia | 9(36.0%) | 8(32.0%) | 0.765 |
| Acute gastritis | 4(16.0%) | 5(20.0%) | 0.713 |
| Others | 10(40.0%) | 12(48.0%) | 0.689 |

Table 3 showed, regarding others symptoms, fever was found 16(64.0%) in case and 12(48.0%) in control. Pneumonia was found 18(72.0%) in case and 15(60.0%) in control. Acute watery diarrhea was found 13(52.0%) in case and 16(64.0%) in control. No symptom shows any statistically significant (p>0.05) between the groups.

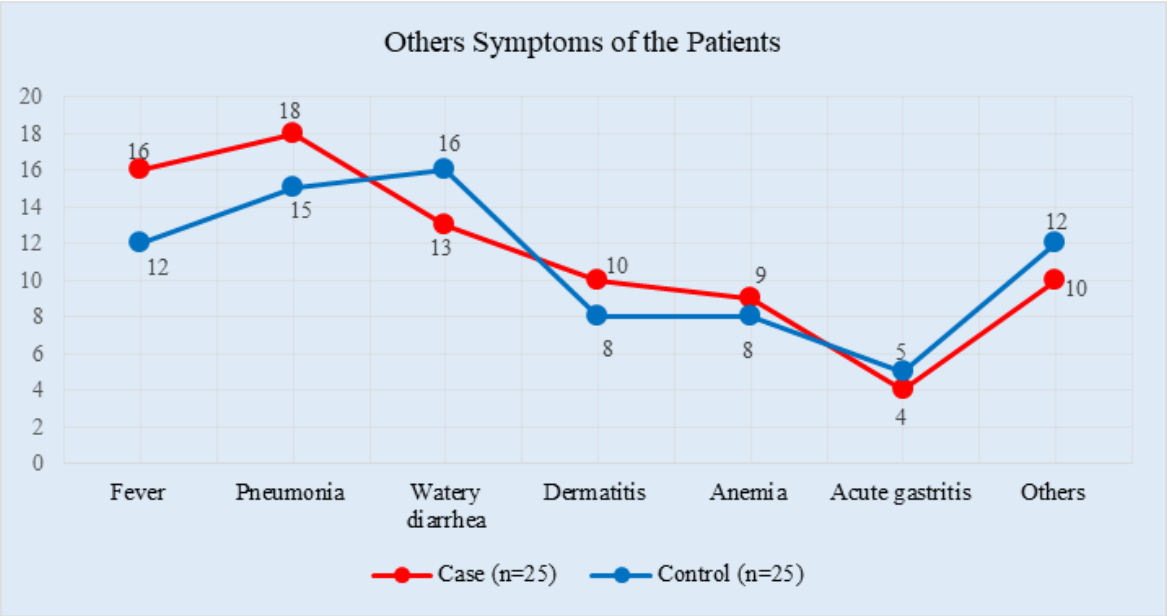


**Figure III: Bar chart showed others symptoms among the Patients, (N=50)**

**Table-4: Baseline characteristics of randomized groups, (N=50)**

| Baseline characteristics | Case (n=25) n (%) | Control (n=25) n (%) | P value |
|---|---|---|---|
| Age (months) | 15.8±8.6 | 19.9±10.3 | 0.131 |
| Male | 18(72.0%) | 16(64.0%) | 0.544 |
| Female | 7(28.0%) | 9(36.0%) | |
| Edema | 14(56.0%) | 11(44.0%) | 0.396 |
| Exclusive breast feeding | 10(40.0%) | 13(52.0%) | 0.395 |
| Timely initiation of complementary feeding | 6(24.0%) | 4(16.0%) | 0.480 |
| Anthropometric measurement | | | |
| Mean weight on admission | 6.64±2.56 | 7.67±2.93 | 0.193 |
| Weight for age | -3.78±1.71 | -3.14±2.03 | 0.237 |
| Weight for height | -4.06±0.95 | -3.84±0.69 | 0.362 |
| Height for age | -1.09±3.39 | -0.92±3.28 | 0.858 |
| MUAC (cm) | 10.33±0.79 | 10.40±0.75 | 0.742 |
| Serum 25(OH)D | 17.77±5.76 | 18.54±7.44 | 0.683 |

Table 4 showed, oedema was present in 14(56.0%) in case and 11(44.0%) in control. Exclusive breast fed child were 10(40.0%) in case and 13(52.0%) in control. Timely initiation of complimentary feeding was present in 6(24.0%) in case and 4(16.0%) in control. These findings showed no statistically significant difference between groups. Anthropometric measurements like mean weight, weight for age, weight for height, height for age and MUAC showed no significant difference between the groups. Serum 25(OH)D level was 17.77±5.76 in case and 18.54±7.44 in control which also showed no significant difference between the groups.

**Table-5: Comparison of outcome between two groups, (N=50)**

| Outcome | Case (n=25) n (%) | Control (n=25) n (%) | P value |
|---|---|---|---|
| Length of hospital stay (days) | 16.24±3.29 | 15.34±2.64 | 0.291 |
| Average weight gain (gm/kg/d) | 9.08±2.99 | 7.52±2.06 | 0.037* |

Table 5 showed, the length of hospital stay was 16.24±3.29 days in case and 15.34±2.64 days in control which was not statistically significant between the group. Average weight gain was 9.08±2.99 gm/kg/d in case and 7.52±2.06 gm/kg/d in control and the result is statistically significant ($p<0.05$) between the group.

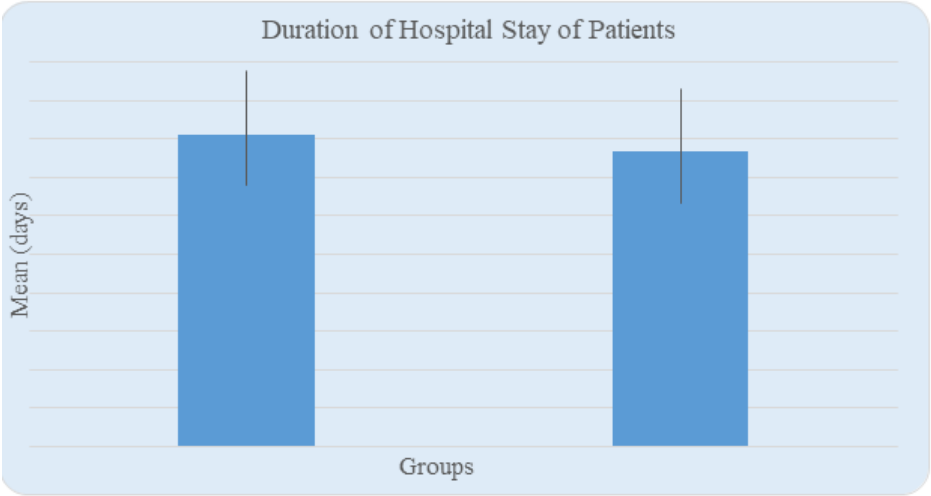


**Figure IV: Bar chart showing the duration hospital stay of Patients, (N=50)**

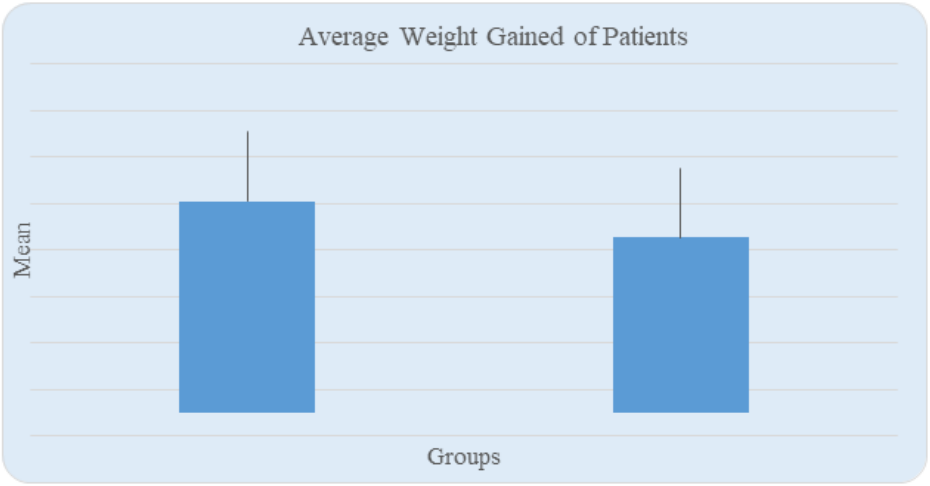


**Figure V: Bar diagram showing average weight gain between two groups. (N=50)**

**Table-6: Weight for height comparison at admission, discharge and follow up between two groups, (N=50)**

| Weight for height | Case (n=25) n (%) | Control (n=25) n (%) | P value |
|---|---|---|---|
| During admission | -3.99±0.92 | -3.71±0.62 | 0.212 |
| During discharge | -2.50±1.03 | -2.92±1.33 | 0.223 |
| 1st follow up | -2.43±1.13 | -2.84±1.31 | 0.241 |
| 2nd follow up | -2.06±0.94 | -2.73±1.25 | 0.039* |
| 3rd follow up | -1.78±0.78 | -2.54±1.15 | 0.009* |
| 4th follow up | -0.96±0.82 | -2.38±1.09 | <0.001* |

Table 6 showed, weight for height during admission, during discharge and during 1st follow up showed no significant difference between two groups. But during 2nd follow up the mean weight for height was -2.06±0.94 in case and -2.73±1.25 in control, during 3rd follow up mean weight for height was -1.78±0.78 in case and -2.54±1.15 in control and during 4th follow up mean weight for height was -0.96±0.82 in case and -2.38±1.09 in control. The results during 2nd, 3rd and 4th follow up showed significant difference between two groups. P value is highly significant.

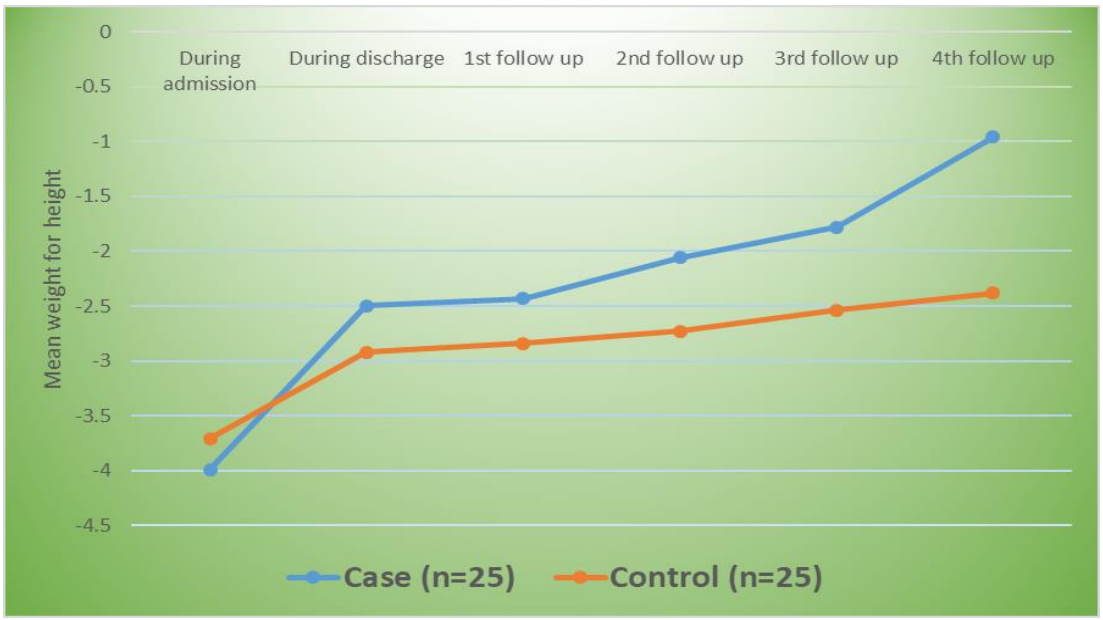


**Figure VI: Line diagram showed the comparison of weight & height between two groups, (N=50)**

## DISCUSSION

In this study, majority patients belonged to age 12 months to 36 months. The mean age was found 19.9±10.3 months in control group, 15.8±8.6 months in case group. The mean difference was not statistically significant (p>0.05) among two groups. Maurya *et al*., (2018) the mean age was found 16.44±9.97 months in control group and 17.52±9.48 months in case group [18]. Javeria *et al*., (2018) reported the mean age was found 15.0±9.6 months in placebo group and 15.7±10.8 months in Vitamin D group [19]. Overall the mean age was 15.4 months. The difference was not statistically significant (p>0.05) between two groups. In Nahida Z *et al*., (2017) study out of 134 patient's majority were of age group 9-24 months. [20] In this study we observed that the majority patients were males in both groups, 18(72.0%) in case, 16(64.0%) in control group. Females were 7(28.0%) in case, 9(36.0%) in control group. The difference was not statistically significant (p>0.05) among groups. Maurya *et al*., (2018) observed a slight male preponderance Male: Female 1.91:1 in control group and 1.69:1 in case group [18]. Nahida *et al*., (2017) study found male preponderance in severe acute malnourished children with 56.7% male and 43.3% female [20]. Javeria *et al*., (2018) reported females were found 54.8% in vitamin D group and 57.6% in placebo group [19]. The high incidence in males as compared to females may be due to greater health care seeking attitude of parents towards the male child. In this study, Mean weight was 6.64±2.56 in case group and 7.67±2.93 in control group. Mean Height was, mean MUAC was 10.33±0.79 cm in case and 10.40±0.75 cm in control group and mean weight for height -4.06±0.95 in case group and -3.84±0.69 in control group. The difference was not statistically significant (p>0.05) between groups.

Maurya *et al.,* (2018) reported that their mean weight on admission was 6.23±1.58 kg, mean height was 69.53±7.48 cm, MUAC was 106.05±12.08 cm [18]. Javeria *et al*., reported Mean weight was 5.5kg, Mean MUAC was 10.2 cm and Mean weight for height z score -3.9. Fever, pneumonia and acute watery diarrhoea were the most common complications affecting 56%, 66% and 58% children respectively [19]. Other complications are severe anemia, different stages of dermatitis, etc. Maurya *et al*., showed Acute gastroenteritis and pneumonia were the most common complication affecting 33.3% and 12.5% children [18]. In our study 46% children were exclusively breast fed, only 20% children had timely initiation of complimentary feeding. Nahida Z *et al*., study showed only 12(9%) children were exclusively breast fed, 51(41%) children had timely initiation of complimentary feeding [20]. Maurya *et al*., reported 25(34.7%) children were exclusively breast fed and 24(33.3%) children had timely introduction of complimentary feeding [18]. In our study 50% children had oedema during admission, 3(6.0%) had vitamin A deficiency and serum 25(OH)D level was 17.77±5.76 in case group and 18.54±7.44 in control group which signifies that almost all children were vitamin D insufficient. The result was not statistically significant between two groups. In this study mean hospital stay was found 16.24±3.29 days in case and 15.34±2.64 days in control which is not significant (p>0.05) between two groups. Maurya *et al*., reported mean hospital stay was 19.26±8.22 days in cases and 19.96±9.20 days in control which is similar to present study [18]. In our study, average weight gain is 9.08±2.99 gm/kg/d in cases and 7.52±2.06 in control group and the result is statistically (P=0.037) significant who were supplemented with high dose of vitamin D as compared to control group. In this study, mean weight for height during (W/H) 1st, 2nd, 3rd and 4th follow ups are -2.43±1.13, -2.06±0.94, -1.78±0.78 and -0.96±0.82 in cases respectively and -2.84±1.31, -2.73±1.35, -2.54±1.15 and -2.38±1.09 in control respectively. Result showed significant improvement in wasting (W/H) in vitamin D supplemented group than in control group after discharge in 2nd, 3rd and 4th follow ups suggestive some role of vitamin D in long term management of severe acute malnutrition. Maurya *et al*., In their study, they found significant improvement in wasting in vitamin D supplemented group after discharge in first 2 months follow ups which is similar to present study [18].

### ETHICAL CONSIDERATION

Informed written consent was taken from parents or legal guardian. This study procedure did not hamper the treatment procedure. Study didn't burden much extra cost upon patient. Confidentiality was strictly maintained regarding all data. The participant could withdraw him any time from the study. Ethical clearance was taken from the ethical review committee of Bangladesh Shishu Hospital & institute.

## LIMITATIONS

The study population was selected from one selected hospital in Dhaka city, so that the results of the study may not reflect the exact picture of the entire country. We didn't conduct a dose response study; therefore it remains unclear whether a lower dose would be sufficient to boost weight gain to a similar extent or not. Serum 25(OH)D level couldn't be checked at the end of the study due to financial constrain. For that we couldn't decide further supplementation of vitamin D is needed or not. As the children received high dose of vitamin D irrespective of serum 25(OH)D level, the possibility of side effects with high dose cannot be ignored. The study duration was relatively short. So further assessment is needed whether this early benefits is sustained and translated into long term benefits on growth or not.

## CONCLUSION & RECOMMENDATION

Addition of vitamin D supplementation in the treatment of severe acute malnutrition improve weight gain. Further ulticentre studies can be undertaken by including large number of patients.

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