

Original Research Article

Trial of vitamin D supplementation to prevent asthma exacerbation in children

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ABSTRACT

Background: To assess the level of vitamin D in children with bronchial asthma and to study the effects of vitamin D supplementation in asthmatic children who had vitamin D deficiency in terms of asthma control test score and Number of exacerbations.

Methods: This interventional study was conducted in Department of Paediatrics, KAPV Government medical college, Trichy, Tamil Nadu, India from September 2016 to February 2017. 96 asthmatic children of age group 5-12 years who attended outpatient department and admitted in ward for asthma exacerbation were selected. After assessing their Vitamin D level, Vitamin D supplementation given along with standard treatment for asthma. Outcomes measured were ACTS (Asthma control test score), number of emergency room visits, number of hospital admissions and reliever medication use.

Results: Out of 96 children, 83 (86.4%) children had vitamin D deficiency. There was significant correlation between vitamin D level and absolute eosinophil count (p-value=0.037), asthma severity (p-value<0.001) and asthma control (p-value<0.001). Significant reduction in emergency room visits, (p-value<0.001) reliever medication use (p-value<0.001) and improvement in asthma control test score (p-value=0.008) occurs after vitamin D supplementation.

Conclusions: There is a significant correlation between vitamin D level, asthma severity and its control. Asthma exacerbation in terms of emergency room visits and reliever medication use were further reduced by vitamin D supplementation.

Keywords: Asthma, Children, Exacerbation, Vitamin D, Vitamin D supplementation

INTRODUCTION

Bronchial asthma is the most common chronic respiratory disease in childhood. Worldwide, childhood asthma prevalence appears to be increasing and in India childhood asthma prevalence ranges from 10-25%.^{1,2}

Bronchial asthma is one of the leading causes for emergency room visits, hospital admissions and missed school days in children. Childhood asthma has a great impact on social and economic perspective of the children and their families. Because of loss of sleep at

night due to nocturnal symptoms, it affects child's daytime concentration in school and subsequently school performance.³

Vitamin D, a pro hormone apart from its main role in calcium and bone metabolism it reduces the risk of chronic diseases like auto immune disease, malignancies, cardio vascular and other infectious disease.⁴

Numerous studies have been done recently found the correlation between Vitamin D and bronchial asthma. Studies shows asthmatic children had more vitamin D deficiency compared to control children and strong

correlation between vitamin D level and severity of asthma symptoms.⁵⁻⁸

Bronchial asthma and Vitamin D deficiency both being common in Indian children, we want to study the correlation between Vitamin D level and asthma and also the effects of Vitamin D supplementation in Bronchial asthma.

Aim of the study

- To assess the level of vitamin D in children with bronchial asthma.
- To study the effects of vitamin D supplementation in asthmatic children who had vitamin D deficiency.

Objectives

To study the effects of vitamin D supplementation in terms of

- Asthma control test score
- Number of exacerbations
 - a) Number of Emergency room visits
 - b) Number of hospital admissions
 - c) Reliever medication use

METHODS

Study setting

This study was conducted in Department of Paediatrics, KAPV Government medical college, Trichy, a tertiary care centre in South India. Institutional Ethical committee approval was obtained.

Study period

The study was conducted from September 2016 to February 2017. It was an interventional study.

Study population

Children presented with acute exacerbation of bronchial asthma in Paediatric outpatient department and also children who got admitted for asthmatic exacerbation in Paediatric wards were included in this study. Age group was 5-12 years

Exclusion criteria

Following children were excluded from the study:

- Those on drugs like phenytoin, phenobarbitone
- Impaired renal function
- Obesity
- Chronic liver disease
- Chronic diarrhea
- History of fracture in last 2 years

- Immunotherapy
- Disease of calcium or bone metabolism
- Respiratory tract infection within past 4 weeks
- Parenchyma /pleural disease
- Those on vitamin D supplementation

Written and informed consent were obtained from the parents. Children who met the inclusion criteria were included in the study after the control of asthmatic exacerbation. Risk factors for bronchial asthma were asked in the history. Their weight and height were measured by using weigh scale corrected to 500 grams and stadiometer respectively. Nutritional status were assessed by plotting the BMI (Z score) for age in WHO (World Health Organisation) Growth charts.

Children were classified into four groups as intermittent, mild persistent, moderate persistent and severe persistent asthma based on their severity of symptoms for asthma.

Their control were assessed and categorized in three ways as well controlled, not well controlled and very poorly controlled.

Asthma severity and control were based on The National Asthma Education and Prevention Program's Expert Panel Report 3 (EPR 3) guidelines.

Reliever medication (salbutamol inhaler) for intermittent asthma and controller medication (Inhaled corticosteroids + Montelukast) for persistent asthma were started as per standard treatment protocol by GINA (Global initiative for asthma).

Devices used were MDI (metered dose inhaler) with spacer or Rotahaler. Correct techniques for device usage were taught and the patient were asked to demonstrate the technique after adequate training.

Their asthma control was assessed by using asthma control test score (ACTS), a validated questionnaire approved by GINA, emergency room visits, hospital admission and reliever medication use at 1 month interval for period of 3 months.

At the end of 3 months, Blood for following investigations were taken. Serum calcium, alkaline phosphatase, renal function test (RFT), Liver function test (LFT), absolute eosinophil count (AEC) and 25 Hydroxy Vitamin D.

Children who had deficient Vitamin D level were supplemented with Stoss regimen (intramuscular vitamin D injection 3,00,000-6,00,000 IU over 1-5 days) and oral vitamin D 600 IU and calcium (30-70 mg/kg/day) for period of 3 months along with their asthma treatment. Their asthmatic control for subsequent 3 months was analyzed.

Parents were asked to maintain the following data in their pulmonologist visit follow up and drug note book.

- Day time symptoms
- Night time awakenings
- Number of times they used reliever medication
- Days of absenteeism from school because of asthma

Patients were reviewed once in 15 days when they came to pulmonologist for obtaining drugs. Their drug compliance, adherence and control (by verifying their follow up note book) were checked by returning empty drug container. The data collected were entered into data sheet and statistical analysis was done with the help of SPSS software version 16.0.

Definitions used in this study

Socio economic status

It is determined by using Modified Kuppaswamy’s Socio-Economic Status Scale.²⁷ It has 3 components with 7 sub divisions in each component having individual score for each sub division.

- Education of the head
- Occupation of the head
- Family income per month

Socio economic status score:

- Upper (I) 26-29
- Upper middle (II) 16-25
- Lower middle (III) 11-15
- Upper lower (IV) 5-10
- Lower (V) <5

Nutritional status

It is determined by calculating BMI and plotting BMI value in WHO growth chart 2007. Based on Z score (BMI for age), classified into 5 classes. Separate charts are available for boys and girls.

Table 1: Nutritional status.

| Z score (S.D) | Class |
|----------------|-----------------|
| >2 | Obesity |
| 2 to 1 | Overweight |
| 1 to -2 | Normal |
| -2 to -3 | Thinness |
| >-3 | Severe thinness |

Lab values (normal range)

The below list includes various variable normal value range which are being used in this study.

- Serum calcium: 8.8-10.8 mg/dl
- Alkaline Phosphatase: 145-420 U/L
- AEC: 50-250 cells
- RFT- Urea: 5-18 mg/dl
- Creatinine: 5-10 years- 0.22 -0.59 mg/dl; 10-14 years - 0.31-0.88 mg/dl

LFT

- Total Bilirubin: <1 mg/dl
- Total Protein: 6-8 mg/dl
- Albumin: 3.5 - 5.6 mg/dl
- ALT (SGPT): 5-45 U/L
- AST (SGOT): 10-50 U/L

RESULTS

A total of 104 children were included in the study of which 8 children lost for follow up. Majority of the children 55 (57.3%) belongs to 5-8 years age group. 22 are in 9-10 years (22.9%) and 19 are in 11-12 years age group (19.8%). Male children included in the study were 57 (59.4%) whereas female children were 39 (40.6%). 29 (30.2%) children belong to class III-lower middle socioeconomic status and 67 (69.8%) belongs to class IV-upper lower socioeconomic status. 12 (12.5%) children were overweight, 56 (58.3%) children were in normal nutritional status. 25 (26%) children came under thinness category whereas 3 (3.1%) children came under severe thinness. Majority of children came under mild persistent- 53 (55.2%) followed by Moderate persistent- 23 (24%), intermittent- 12 (12.5%) and severe persistent- 8 (8.3%). Majority of children were not under control group- 70 (72.9%) followed by well control group- 13 (13.5%) and Very poor control group- 13 (13.5%).

Blood parameters

86 (89.6%) children had normal Serum calcium level and 10.4% had S. calcium less than 8.8 mg/dl but not in hypocalcemic range (<8.5 mg/dl). 64 (66.7%) children had abnormal (increased) absolute eosinophil count and 32 (33.3%) had normal AEC. All children (96) had normal renal function test, liver function test and s. alkaline phosphatase level.

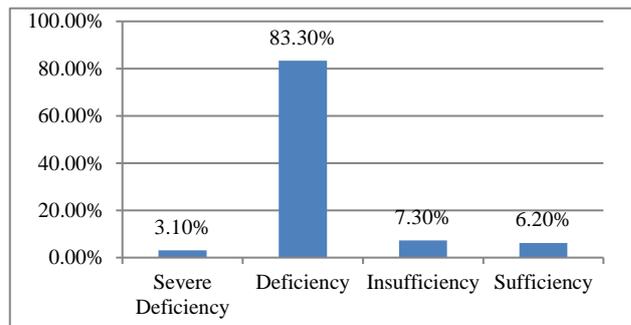


Figure 1: Vitamin D status.

Vitamin D status:

Majority of children were Vitamin D deficient- 80 (83.3%). 7 (7.3%) had insufficient Vitamin D level and 3 (3.1%) had severe Vitamin D deficiency. Only 6 (6.2%) children had normal Vitamin D status.

Statistical analysis

The collected data were analysed by using SPSS software version 16.0. To describe about the data, percentage analysis were used for categorical variables and for

continuous variable the mean and standard deviation were used. To find the significance between vitamin D level and categorical variable, chi square test was used. To find the significance between vitamin D level and categorical variable, paired t test was used. P value of less than 0.05 was considered statistically significant.

Association between demographic status and Vitamin D status

There was no significant correlation between age group, sex, socioeconomic status and Vitamin D status.

Table 2: Association between absolute eosinophil count and vitamin D deficiency.

| Vitamin D level | | Absolute Eosinophil count | Severe deficiency | Deficiency | Insufficiency | Sufficiency | Total |
|-------------------|------------|---------------------------|-------------------|------------|---------------|-------------|-------|
| Normal | Frequency | 0 | 25 | 2 | 5 | 32 | |
| | Percentage | 0% | 78.1% | 6.2% | 15.6% | 100.0% | |
| Abnormal | Frequency | 3 | 55 | 5 | 1 | 64 | |
| | Percentage | 4.7% | 85.9% | 7.8% | 1.6% | 100.0% | |
| Total (Frequency) | | 3 | 80 | 7 | 6 | 96 | |

There is significant correlation between absolute eosinophil count and Vitamin D level (p value-0.037).

Table 3: Association between nutritional status and vitamin D status.

| Vitamin D level | | Nutritional status | Severe deficiency | Deficiency | Insufficiency | Sufficiency | Total |
|-------------------|------------|--------------------|-------------------|------------|---------------|-------------|-------|
| Overweight | Frequency | 1 | 9 | 1 | 1 | 12 | |
| | Percentage | 8.3% | 75.0% | 8.3% | 8.3% | 100.0% | |
| Normal | Frequency | 2 | 46 | 6 | 2 | 56 | |
| | Percentage | 3.6% | 82.1% | 10.7% | 3.6% | 100.0% | |
| Thinness | Frequency | 0 | 22 | 0 | 3 | 25 | |
| | Percentage | 0% | 88.0% | 0% | 12.0% | 100.0% | |
| Severe thinness | Frequency | 0 | 3 | 0 | 0 | 3 | |
| | Percentage | 0% | 100.0% | 0% | 0% | 100.0% | |
| Total (Frequency) | | 3 | 80 | 7 | 6 | 96 | |

There is no statistical significant correlation between nutritional status and vitamin D status (p value-0.59).

Table 4: Association between asthma severity and vitamin D status.

| Vitamin D level | | Asthma severity | Severe deficiency | Deficiency | Insufficiency | Sufficiency | Total |
|---------------------|------------|-----------------|-------------------|------------|---------------|-------------|-------|
| Intermittent | Frequency | 0 | 5 | 2 | 5 | 12 | |
| | Percentage | 0% | 41.7% | 16.7% | 41.7% | 100.0% | |
| Mild Persistent | Frequency | 0 | 50 | 3 | 0 | 53 | |
| | Percentage | 0% | 94.3% | 5.7% | 0% | 100.0% | |
| Moderate Persistent | Frequency | 0 | 20 | 2 | 1 | 23 | |
| | Percentage | 0% | 87.0% | 8.7% | 4.3% | 100.0% | |
| Severe Persistent | Frequency | 3 | 5 | 0 | 0 | 8 | |
| | Percentage | 37.5% | 62.5% | 0% | 0% | 100.0% | |
| Total (Frequency) | | 3 | 80 | 7 | 6 | 96 | |

There is statistically significant correlation between asthma severity and vitamin D status (p value < 0.001)

Table 5: Association between asthma control and vitamin D status.

| Vitamin D level | | Severe deficiency | Deficiency | Insufficiency | Sufficiency | Total |
|------------------------|------------|-------------------|------------|---------------|-------------|--------|
| Well controlled | Frequency | 0 | 6 | 2 | 5 | 13 |
| | Percentage | 0% | 46.2% | 15.4% | 38.5% | 100.0% |
| Not well controlled | Frequency | 1 | 64 | 4 | 1 | 70 |
| | Percentage | 1.4% | 91.4% | 5.7% | 1.4% | 100.0% |
| Very poorly controlled | Frequency | 2 | 10 | 1 | 0 | 13 |
| | Percentage | 15.4% | 76.9% | 7.7% | 0% | 100.0% |
| Total (Frequency) | | 3 | 80 | 7 | 6 | 96 |

There is statistically significant correlation between asthma control and vitamin D status (p value < 0.001).

Outcome measures

The outcome measures were depicted in graphical representation which included children with vitamin D deficiency (80±3). In this measure children with Vitamin D insufficiency (n=7) and Vitamin D sufficiency (n=6) were not included because these two variables had small sample size.

Arrow in the below diagrams indicates period from which Vitamin D supplementation has been started.

Emergency room visits

At the beginning of the study 58 children (69.8%) had 1 visit per month and rest 25 children (30.1%) had 2 visits per month. At the end of 3 months 61 children (73.4%) have not visited even once and 22(26.5%) children had only 1 visit in a month. At the end of 6 months 81 children (97.6%) have not visited even once in a month and 2 children had 1 visit/month (2.4%). The emergency room visits were gradually reduced over a period of 6 months.

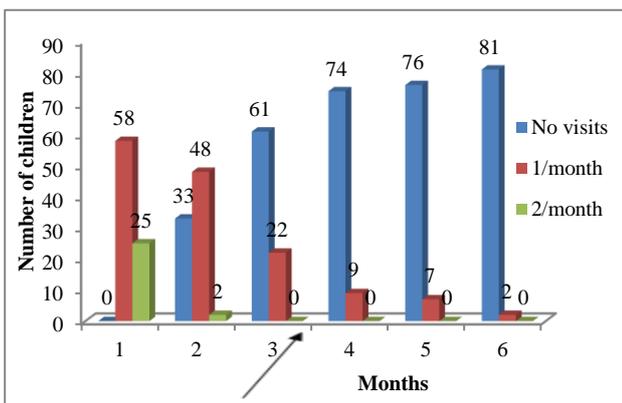


Figure 2: Number of emergency room visits/month.

Hospital admission

At the time of enrolment, 57 children got admitted to hospital only once in a month followed by 14 children with 2 admissions/month and 12 children had not

admitted to hospital even once. From 3rd month onwards, there was no hospital admission for asthma exacerbation.

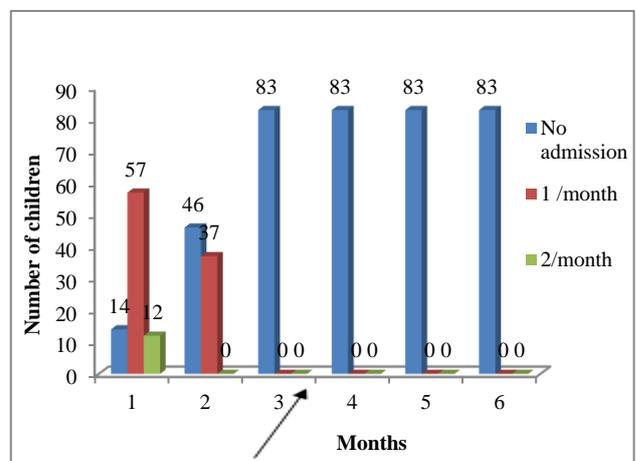


Figure 3: Number of Hospital admission/month.

Reliever medication use

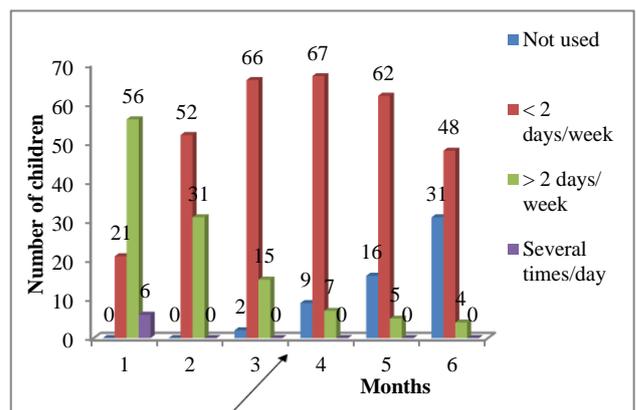


Figure 4: Reliever medication use.

At the end of 1st month, 21 children were using reliever medication for less than or equal to 2 days/week, 56 children were using medications for more than 2 days/week and 6 children were using it several times/day. During 3rd month, 2 children were not at all using reliever medication and 66 children were using it less than or

equal to 2 days/week while 15 children were using it for more than 2 days/week. At the end of 6 months, 31 children were not at all using reliever medications, 48 children were using it for less than or equal to 2 days/week and 4 children were using it for more than 2 days/week.

Asthma control test score

At the time of 1st visit, 78 children may not be under control which is indicated by ACTS score value of less than 19. Same time, 5 children were under control which is indicated by ACTS score range from 20 to 27. At the end of 3 months, 67 may be under control while rest 16 may not be under control. Whereas after 6 months, 77 may be under control and 6 may not be under control.

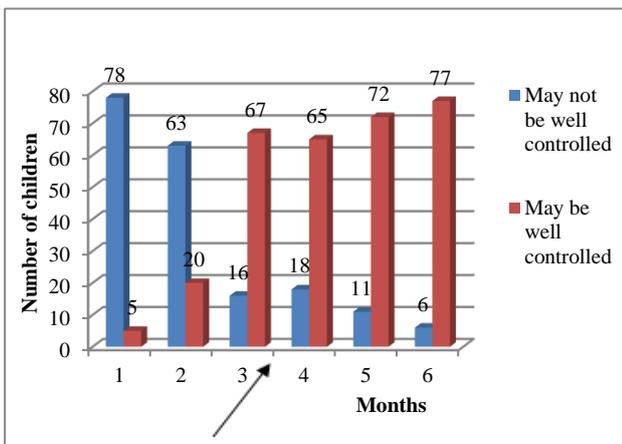


Figure 5: Asthma control test score.

DISCUSSION

Majority of children 55(57.3%) belongs to 5-8 years followed by 22 children of 9-10 yrs age group (22.9%) and in 11-12 yrs age group it was 19 (19.8%). Chhabra et al in his study to find prevalence of asthma in school children aged 4-17 years found highest prevalence in 9-13 years age group.¹² 57 male children (59.4%) and 39 (40.6%) female children were included in the study. Male preponderance in prepubertal age is common and this factor is also

67 (69.8%) children were from class IV - upper lower socio-economic status and 29 (30.2) were from class III - lower middle socioeconomic status. No children were from I, II and V classes. Most of the current study population belongs to lower socio-economic strata. Study by Chhabra et al found no difference in prevalence among socio economic strata whereas study by Goh DY et al found increased prevalence in upper socioeconomic strata.^{12,14,13}

Majority of children were Vitamin D deficient- 80 out of 96 children (83.3%). 3 children (3.1%) had severe Vitamin D deficiency. 7 (7.3%) had insufficient vitamin

D level and only 6 (6.2%) children had normal vitamin D status. The prevalence rate is similar to study by Balasubramanian et al⁴ which ranges from 60-90%.

The correlation between absolute eosinophil count and vitamin D levels was statistically significant (p-value-0.037). Studies by Berhm et al also show the similar findings.⁸ Berhm et al in his study found significant correlation between eosinophil count and Vitamin D level (p-value-0.02) who included 2,714 children.⁸

There was a statistically significant correlation between severity of asthma and vitamin D level (p-value<0.001). It is in line with findings depicted in studies by Majak et al and Gupta A et al.^{7,10} Gupta A et al in his study found that lower vitamin D levels in children with severe asthma compared to control group (p-value<0.001).⁷

Asthma control and vitamin D levels have significant correlation (p-value<0.001). Gupta A et al found children with normal vitamin D level had few exacerbation (p-value<0.001) and better asthma control (p-value<0.001).⁷

Berhm et al in childhood asthma management programme study found that asthmatic children with lower vitamin D had increased rate of hospitalisation and emergency room visits (p-value-0.01).⁶ The study population by Berhm et al was 1024 mild-moderate persistent asthmatic children.⁶ So there was significant correlation between vitamin D level, absolute eosinophil count which is a marker of allergy, asthma severity and control in this study.

The difference at 3rd and 6th month was statistically significant for emergency room visits, reliever medication use and asthma control test score indicated by p-value <0.001, <0.001 and 0.008 respectively.

There was marked reduction in emergency room visits, reliever medication usage over a period of 6 months. There is also a significant improvement in asthma control indicated by ACTS.

Compared with previous studies, asthma exacerbation in the form of emergency room visits and hospital admission were significantly reduced. Urashima et al in their study found that asthma attacks were reduced after vitamin D supplementation (p-value-0.006).⁹

Majak et al in their study found that asthma exacerbation were significantly lower in study group (n=24) compared to control group (n=24) evidenced by p-value-0.029.¹⁰ They found significant difference in ATAQ score before and after vitamin D supplementation (p-value-0.001).

CONCLUSION

There is a significant correlation between vitamin D level, asthma severity and its control. Asthma exacerbation in terms of emergency room visits and reliever medication use were further reduced by vitamin

D supplementation. To confirm this more multicentre randomized control trials involving all categories of children are needed to define the exact role of vitamin D supplementation. More in-depth studies are needed to find vitamin D dosage and duration of supplementation in asthmatic children.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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