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RESEARCH ARTICLE

STUDY OF VITAMIN D LEVELS IN RELATION TO BRONCHIAL ASTHMA

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Abstract

Background: Vitamin D has a significant role in the metabolism of calcium and bone. Therefore, its deficiency leads to rickets in growing children and osteomalacia in adults. The classical functions of Vitamin D in bone metabolism and calciumphosphorus homeostasis is well established. The non-classical functions of Vit D as an immunomodulatory and growth-promoting factor influencing the overall well being in general and respiratory health, in particular, is the subject of current interest. It is reported that vitamin D plays a crucial role in foetal lung's proper growth and maturity. In many children with steroid-resistant asthma, vitamin D supplements may increase the responsiveness to steroids. Vitamin D deficiency states were reported to be associated with an increased risk of acute exacerbations of bronchial Asthma. Our study is conducted to determine serum levels of vitamin D in asthmatic children and association of vit D deficiency with asthma.

Aim of The Study: To determine the serum levels of vitamin D in asthmatic children.

Objective: To Study the relation between vitamin D levels and

1. The severity of asthma
2. Frequency of asthma exacerbation

Study Design: It is cross sectional study.

Methods: 100 children who got admitted to the pediatric ward (or) PICU of MIMS, of whom 40 were known asthmatics and 60 age and sex-matched controls were considered to do a comparative study of the variables under consideration. "Study of vitamin D levels in relation to bronchial asthma in children" has been carried out as an analytical case-control study for 18 months.

Results: 60% of the study participants were vitamin D deficient. Whereas 15% had insufficient levels, and sufficient vitamin D levels are observed only in 25% of the participants. A statistically significant difference in vitamin D levels and the severity of illness has been observed among the study participants. Moderate persistent Asthma has been seen more in patients who are deficient in vitamin D. A high statistically significant association has been observed between exacerbations of Asthma and levels of vitamin D.

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Conclusion: A statistically significant difference in vitamin D levels and the severity of illness among the study participants are observed. Moderate persistent Asthma has been seen more in patients who are deficient in vitamin D. A high statistically significant association has been observed between exacerbations of Asthma and levels of vitamin D.

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Introduction:-

Vitamin D is the generic term that denotes metabolically active compounds such as cholecalciferol (Vitamin D3) and ergocalciferol (Vitamin D2). Vitamin D has a significant role in the metabolism of calcium and bone. Therefore, its deficiency leads to rickets in growing children and osteomalacia in adults or the older population. The classical functions of Vitamin D in bone metabolism and calcium-phosphorus homeostasis is well established. The non-classical functions of Vit D as an immunomodulatory and growth-promoting factor influencing the overall wellbeing in general and respiratory health, in particular, is the subject of current interest. Research into its genomic functions has explored the presence of 1000 to 2000 Vitamin D Receptor (VDR) genes in the body that mediate the non-skeletal (non-classical) manifestations of Vit d. It is reported that vitamin D plays a crucial role in fetal lung's proper growth and maturity. Some studies suggest that maternal intake of vitamin D in appropriate doses is associated with a lowered risk of recurrent respiratory tract infections and childhood asthma. In many children with steroid-resistant asthma, vitamin D supplements may increase the responsiveness to steroids. Vitamin D deficiency states were reported to be associated with an increased risk of acute exacerbations of bronchial asthma.

Bronchial Asthma:-

It is related to increased airway inflammation, hyper airway responsiveness, and airflow obstruction in response to specific triggers leading to repeated wheezing episodes, dyspnoea, a feeling of tightness in the chest, and cough. These episodes are usually associated with a bronchial obstruction that resolves spontaneously or after treatment. Varied aetiological factors and changing factors such as atmospheric pollution, dietary changes, allergens, and lifestyle changes may increase asthma prevalence. Impaired immunogenic tolerance and interplay between cells and inflammatory mediators may ultimately promote airway obstruction associated with the disorder. A potential role of Vitamin-D in tuberculosis, pneumonia, influenza, and respiratory infections has been proposed. The existence of associations of vitamin-D with Asthma and allergy remains uncertain. While some studies found hypovitaminosis D more prevalent amongst asthmatics, others suggest that vitamin D supplementation may increase allergy risk. Hence the present study was conducted to determine serum levels of vitamin D in asthmatic children and the association of vitamin d deficiency with asthma.

Vitamin D and Asthma:-

Since most of the population spends time indoors away from sun exposure, it leads to vitamin D deficiency. Several researchers have found that vitamin D has an inhibitory effect on the Th17 response. Th17 cells are thought to play a significant role in childhood asthma etiopathogenesis. Few cross-sectional surveys have indicated a possible correlation between asthma and vitamin D. Studies have concluded that decreased serum 25(OH)D is associated with increased prevalence, hospitalization, increased emergency visits, reduced lung function, and increased airway hyperresponsiveness in asthmatic children. Recent clinical trials have shown that vitamin D supplementation has a beneficial effect in asthmatic patients. Also, increased consumption of vitamin D during pregnancy has an impact on Asthma in children and adults. Evidence from the research concludes that asthma exacerbations and resistance to standard therapies are significant challenges to reducing asthma-related morbidity and mortality. Studies supported the role of vitamin D in both these aspects.

Evidence from clinical trials have shown that vitamin D has a beneficial function to play against exacerbations of Asthma. A randomized, double-blind, 6-month clinical trial performed by Majak et al. found that children receiving 500 IU/d of additional vitamin D had a lower risk of asthma exacerbations due to acute respiratory infections. Another randomized, double-blind, parallel-arm clinical trial performed by Urashima et al. in 217 school children showed a reduced risk of asthma exacerbations following vitamin D3 supplementation.

Materials And Methods:-

It is a cross sectional study. Asthmatic children who attended in paediatric OPD and admitted in ward or PICU of MIMS, Nellimarla were taken as study subjects. For controls children were enrolled from well-baby clinics, immunization clinics, school camps and children attending OPD, of other departments at MIMS. Out of the 100 children, 40 were known asthmatics, and 60 were age and sex-matched controls. Study period was December 2018-May 2020.

Inclusion Criteria:-

1. Children with Asthma aged one year to 14 years diagnosed according to the NAEPP, Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma.12.
2. parents who are willing to register their children with Asthma in this study.
3. Documented reversibility with bronchodilators.
3. History of taking asthma medications in the last six months.
4. Children presented to other OPDs like ENT, Dermatology also in school camps, immunization clinics, etc. as control.

Exclusion Criteria:-

1. Those who are on long term steroids for other causes than Asthma.
2. History of respiratory distress or ventilator care in the neonatal period or later.
3. Those who are on vitamin D therapy for skeletal features of deficiency.

Methods:-

Consent was taken from the Parents, detailed history taken using a structured questionnaire, the clinical examination done, and the parents were advised to maintain an asthma diary that was evaluated during regular follow-ups. An information sheet providing the details of the study was provided. Enrollment was done after obtaining written informed consent from parents/guardians. Approval of the institutional ethics committee was taken before the start of this study.

Procedure of sample collecting:-

Five millilitres of blood was drawn from a convenient peripheral vein into plain and EDTA tubes. The tubes were labelled and placed in a cool box containing icepacks. The samples were always protected from light using sheets of black plastic. They were transported to the laboratory of the Maharajah's Institute of Medical sciences. Standard measures were taken, and quality is ensured while drawing and analysing samples. The time of collection of pieces was documented on samples of both groups for reference. Collected blood samples were analysed for CBC, Serum Vit D2, Se IgE levels. CBP was measured by an automated 5-part analyser (Celltac). Age and sex-matched controls were selected. In controls that satisfy the inclusion criteria, blood samples were collected and analyzed for vitamin D. Peak Expiratory Flow Rate (PEFR) and spirometry were done wherever possible.

Vitamin D estimation:-

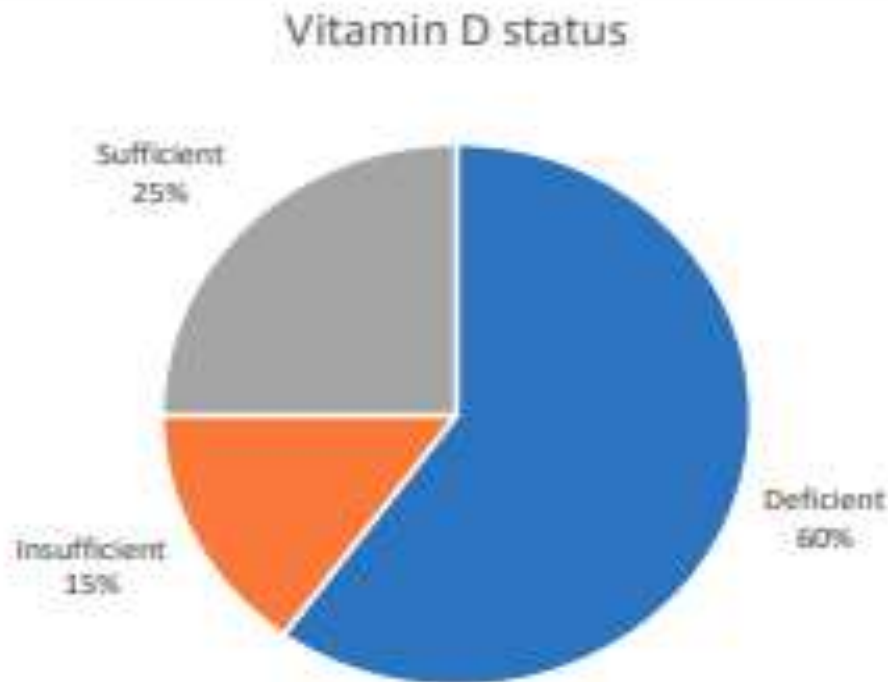
After collecting a venous sample of 4ml with proper aseptic measures, 25(OH)D3 was assayed by two methods. One is by Electro Chemiluminescence Immunoassay (ELISA). The kit was vitamin D Total COBAS, Analyzer-COBAS E411. Most Indian reports suggest ELISA, Chemiluminescence, or RIA as methods of assessment. Although many other studies recommend TMS, very few centres in India have this facility.

Results:-

Table 1:- Vitamin D status of study population.

Vitamin D Status	Frequency (%)
Deficient	24 (60%)
Insufficient	6(15%)
Sufficient	10(25%)
Total	40(100%)

65% of the study participants were vitamin D deficient, whereas 15% had insufficient levels, and sufficient vitamin D levels are observed only in 25% of the participants.

Fig:1:- Vitamin D Status.**Table 2:- Association between severity of asthma and vitamin D levels.**

Severity of Asthma	Deficient	Insufficient	Sufficient
Intermittent	2 (5%)	3 (7.5%)	1 (2.5%)
Mild Persistent	9 (22.5%)	2 (5%)	8 (20%)
Moderate Persistent	13 (32.5%)	1 (2.5%)	1 (2.5%)
Total	24 (60%)	6 (15%)	10 (25%)

Chi-square = 13.24, p=0.01* (Statistically significant)

A statistically significant difference in vitamin D levels and the severity of illness has been observed among the study participants. Moderate persistent Asthma has been seen more in patients who are deficient in vitamin D.

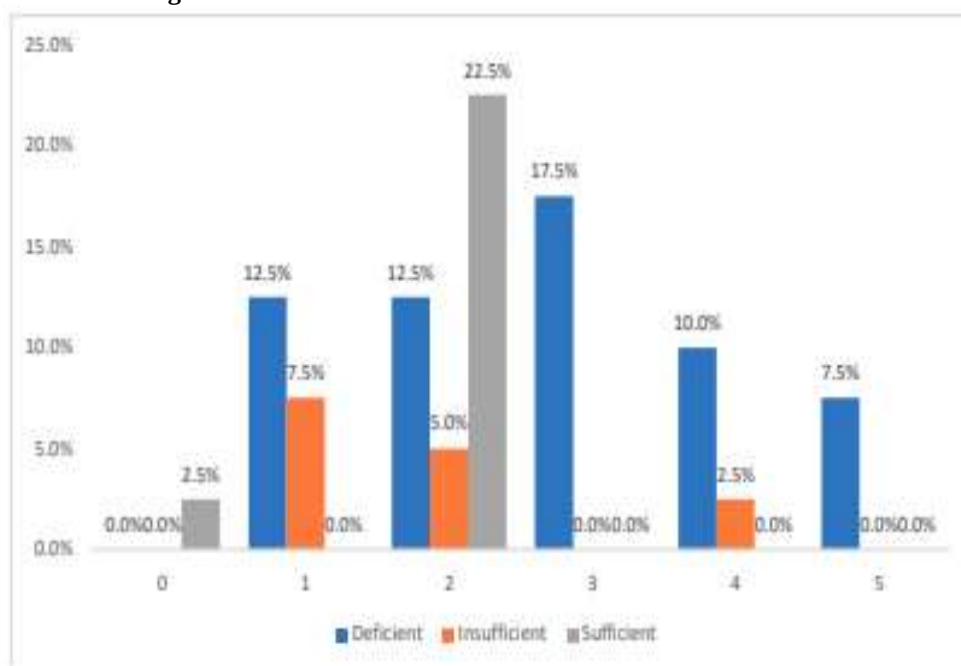
Table 3:- Association between exacerbations and vitamin D levels.

No of Episodes	Deficient	Insufficient	Sufficient	Total
0	0 (0%)	0 (0%)	1 (2.5%)	1 (2.5%)
1	5 (12.5%)	3 (7.5%)	0 (0%)	8 (20.0%)
2	5 (12.5%)	2 (5.0%)	9 (22.5%)	16 (40.0%)
3	7 (17.5%)	0 (0%)	0 (0%)	7 (17.5%)
4	4 (10.0%)	1 (2.5%)	0 (0%)	5 (12.5%)
5	3 (7.5%)	0 (0%)	0 (0%)	3 (7.5%)

Chi-square Test = 24.6, p=0.006* (Statistically Significant)

A high statistically significant association has been observed between exacerbations of Asthma and levels of vitamin D.

Fig:2:- Association between exacerbations and vitamin D levels.



Discussion:-

Asthma is one of the most common chronic respiratory diseases in childhood. It is characterized by chronic airway inflammation with a history of recurrent respiratory symptoms such as wheeze, breathlessness, chest tightness, and cough. Asthma in children is different from an adult with a lot of versatility in causation and presentation. Most of the times, Asthma is under-diagnosed and under-treated in children, which results in the poor quality of life in children in terms of wasted school days, hospitalization, and in their parents in terms of psychological as well as socio-economic impact due to direct treatment cost as well indirect costs in terms loss of wages due to accompany the child to the hospital. Of the varied aetiologies in the causation of Asthma, vitamin D deficiency was found to be of great importance. Its prevalence has been increasing worldwide, and its deficit is attributed to be causative or contributive in the pathogenesis of various other systemic illnesses. Its role in the development, pathogenesis, and associations with the disease severity still need to be studied extensively. In the present study, study participants are evenly distributed through the age under consideration and followed a normal distribution. The mean age of the study participants were 8.15 ± 3.02 years, where majority of the study participants belonged to the age group of 6-10 years. There was no statistically significant difference has been observed in the distribution of study participants in the groups based on age. Such similar sort of observation has been made in the studies done by Fahad Aleem et al. Gupta A et al.

Vitamin D and Asthma: Vitamin D is a fat-soluble nutrient produced in the human body from 7-dehydrocholesterol after exposure to sunlight's ultraviolet rays. It acts as a modulator of calcium absorption and bone health. However, it can be formed naturally in the body. 70-90% Indian general population had vitamin D at a subnormal level. The possible reasons for this deficiency can be attributed to lack of food fortification of commonly consumed foods with Vitamin D, prevailing religious and socio-cultural customs in India which are limiting the adequate exposure to Sun, thus negating potential benefits of sunshine which helps in the natural production of vitamin D. Because of these probable reasons a subclinical vitamin D deficiency was highly prevalent in both urban and rural settings, and across all socio-economic and geographic strata. Though there is ample knowledge of Vitamin D deficiency's ill effects, there are no specific guidelines on optimum serum 25OHD. However, vitamin D deficiency is defined as a 25OHD level of less than 50 nmol/L (20 ng per milliliter). When the levels are between 50 and 75nmol/L (20–30 ng per milliliter) it is considered to be vitamin D insufficiency, and stations between 75 nmol/L (30 ng per milliliter) to 100 nmol/L are deemed to be normal vitamin D levels and serum levels more than 150ng/ml will be considered as vitamin D intoxication. Few Indian data suggests taking 20ng/ml (50nmol/L) as serum 25(OH)D level since it coincides with the level that covers 97.5% of the population. Hence, they consider concentration 20ng/ml as sufficient. In the present study, 60% of the study participants were vitamin D deficient, whereas 15% had insufficient

levels, and sufficient vitamin D levels are observed only in 25% of the participants. Inadequate dietary intake and exposure to Sun have been thought to be the probable causes of vitamin deficiency. Karnam S et al. conducted a cross-sectional study among 60 children with Asthma to know the relationship between serum vitamin D levels and severity of Asthma and found that children with well-controlled Asthma had higher serum levels of 25 (O.H.) D than children with partially controlled or uncontrolled Asthma. Guru H et al observed that Vitamin D deficiency was highly prevalent in asthmatic patients, and there was a direct and a significant relationship between serum vitamin D levels, the severity of Asthma, control of Asthma, serum IgE levels, sputum eosinophils, and lung function and similar findings were observed in this present study as well. Our study shows A statistically significant difference in vitamin D levels and the severity of illness has been observed among the study participants. Moderate persistent Asthma has been seen more in patients who are deficient in vitamin D. A high statistically significant association has been observed between exacerbations of Asthma and levels of vitamin D

Conclusion:-

A statistically significant difference in vitamin D levels and the severity of illness among the study participants are observed. Moderate persistent Asthma has been seen more in patients who are deficient in vitamin D. A high statistically significant association has been observed between exacerbations of Asthma and levels of vitamin D. A significant association observed between vitamin D levels and IgE levels The significant association observed between vitamin D levels and AEC levels.

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