SERUM MAGNESIUM AND VITAMIN D LEVELS AS INDICATORS OF ASTHMA SEVERITY

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Abstract:

Background
The concentration of vitamin D in the blood is affected by the magnesium serum level that affects immunity of the human body. The pathogenesis of asthma is dependent on the concentration of magnesium and vitamin D. Asthma is not common in adults, but a deficiency of vitamin D and serum magnesium level is prominent in asthmatic patients and lack of these levels causes severe asthma attacks, respiratory infection and poor response to bronchodilators in case of severe exacerbation.

Objective
The main purpose of this article is to check the deficiencies of vitamin D and serum magnesium level in the blood and relate these with severity of asthma.

Material and Methods
A cross sectional case control study, which includes 60% asthmatic patients and 60% healthy volunteers and then clinical and systemic examination have been done and serum magnesium level, 25-hydroxycholecalciferol [25(OH)D] and Vitamin D levels are measured.

Results
Severe hypomagnesaemia and deficiency of Vitamin D is observed that causes severe asthmatic attacks. But calcium levels remain constant.

Conclusion
The deficiency of Vitamin D and lack of Magnesium level is highly observed in asthmatic patients. And with the deficiency of one or both can cause severe breathing problems, severe exacerbation of respiratory distress and asthma severity. Serum 25(OH) D levels and magnesium concentration are highly important markers of Asthma severity.

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Please cite this article in press Zain ul Hassan et al. Serum Magnesium And Vitamin D Levels As Indicators Of Asthma Severity, Indo Am. J. P. Sci, 2020; 07(12).
INTRODUCTION:
A Chronic disease which causes recurrent bronchospasm that result in bronchial hyperresponsiveness does not cause such spasm in individuals but produces in response to a stimulus. [1] 334 million people are affected from bronchial spasm because it is worldwide condition. 10-12% adults and 15% of children is suffering from this social impact and it can occur at any stage. [2]

Vitamin D deficiency is an issue of public health because of its deficiency plays an important role in the prevention of respiratory problems. Vitamin D has a main function to regulate calcium and phosphorus levels. The factors that respond to calcium, magnesium and phosphorus level regulate Vitamin D metabolism. Secretion of insulin, inhibition of interleukin production by T-lymphocytes and immunoglobulin’s produced by B-lymphocytes, monocytes differentiation, and cell proliferation modulation. [3] 1,25-hydroxylase can also be expressed by dendritic cells that proposes the conversion of 25-hydroxycholecalciferol (calcidiol) to its active form (calcitriol) and its supports immune system. [4] and vitamin D has a major role in initiating of Immune response against microbial attacks. So Vitamin D is an important marker of Immunity and if its deficiency can occur, it can cause severe breathing problems, risk of asthma, allergies and exacerbation of diseases.[5,6]

Increased tracheobronchial hyperactivity, pulmonary vascular drag, and ventricular arrhythmia are associated with deficiency of Magnesium level. [7,8] if treated with 

B2- agonists, the level of magnesium are reduced by urinary loss. Dilatation and relaxation of bronchial muscles are caused by Magnesium. So in turn, if magnesium level is lowered, then bronchial spasm can occur. Moreover, magnesium is 2nd most important cation and for the synthesis and metabolism of vitamin D, it has a major role in bone mineralization.[9] Magnesium lower levels in serum can cause Hypovitaminosis D. Hypomagnesaemia and Hypovitaminosis can cause exacerbation of respiratory problems that leads to severe clinical conditions. [9,10]

MATERIAL AND METHOD:
Study Design:
A Cross sectional study involved 60 cases of Community I recurrent controlled asthma and 60 obese patients. The study omitted patients with hepatitis or some other related viral infection, undertaking diuretic treatment, and <18 years of age. The personal history of all individuals involved in the study, including prescription, was taken. Blood samples were taken within aseptic conditions in a single vacuity to test serum levels of magnesium, vitamin D (25(OH) D) and serum calcium. Audiometric testing of pulmonary function (PFT) was conducted in each case to gain forced expiratory volume (FEV1), FVC, and PEF to assess the seriousness (or stage) of asthma. The Chemiluminescent Immunoassay (CLIA) on Beckman Coulter, Access-2 tool, assessed serum 25 (OH) D levels. A two production binding immuno-enzymatic assay is a research package. 25 (OH) D that bonds to the set monoclonal anti-25 (OH) D is released by DBP. Lumi-Phos 530 competes with set monoclonal anti-25 (OH) D for binding. In a gravity force, compounds attached to paramagnetic particles collect when unbound materials are swept free. Using the fully automatic ERBA-EM200 analyzer and ERBA reagents, serum magnesium and overall calcium levels were calculated spectrophotometrically.

Analytical Methods:
Serum magnesium reference range: 1.7-2.5 mg/dL
Serum calcium reference range: 8.6-10.3 mg/dL

Effects were computed on the MS excel sheet and the following techniques were used to conduct statistical analyses

Statistical Methods:
Descriptive figures were used: the mean (x) and standard deviation (SD) were measured for the continuous variable set, and the proportion and percentage were collected for categorical variables. The 2-sample Z-test was used to compare two sample proportions, and P values were determined.

RESULTS:
An ANOVA test was used to evaluate variables from three or more classes. The demographics of both classes are seen. Disease severity was categorized according to the 2016 GINA recommendations. 14 (23.3%) had mild persistent asthma, 27 (45%) had moderate persisted. Findings suggest a phase-wise drop in serum levels of both vitamin D and magnesium, with a rise in asthma incidence. There was a negative association between serum vitamin D and magnesium levels with asthma intensity grades. No substantial association between asthmatic patients and controls in serum calcium levels. 63.3% of the patients had vitamin D deficiency and 100% had insufficiency. 50% had abnormality and 0% had shortage among the samples.
Table 1: Distribution of Patients and Control groups

|                      | GROUP 1 N=60 PATIENTS | GROUP 2 N=60 CONTROL |
|----------------------|------------------------|----------------------|
| Gender               |                        |                      |
| Male                 | 22 (36.7%)             | 30 (75%)             |
| **Severity of asthma** |                        |                      |
| Mild                 | 4 (18.2%)              |                      |
| Moderate             | 10 (45.5%)             |                      |
| Severe               | 8 (36.4%)              |                      |
| Females              | 38 (63.3%)             | 10 (25%)             |
| **Severity of asthma** |                        |                      |
| Mild                 | 10 (26.3%)             |                      |
| Moderate             | 17 (44.7%)             |                      |
| Severe               | 11 (28.9%)             |                      |
| Age (years)          | 40 ± 13                | 41 ± 10              |
| BMI                  | 23 ± 3.6               | 22 ± 1.4             |
| History of asthma (years) | 24 ± 7.2              |                      |
| Familial history of asthma | 12 (20%)             |                      |
| Atopy                | 54 (90%)               | None                 |

Table 2: Serum 25 (OH) D and Magnesium levels in Patients and Controls

|                          | Patients       | Controls       | Z value | P value |
|--------------------------|----------------|----------------|---------|---------|
| Serum 25(OH)D            |                |                |         |         |
| Deficient (<50 nmol/L)   | 38 (63.3%)     | 0 (0%)         | 6.4     | <0.001  |
| Insufficient (<75 nmol/L)| 60 (100%)      | 30 (50%)       | 6.1     |         |
| Magnesium                |                |                |         |         |
| Normal                   | 25 (41.2%)     | 57 (95%)       | 5.5     | <0.001  |
| Hypomagnesemia (<1.7 mg/dL) | 35 (58.8%) | 3 (5%)         | 5.5     |         |

Table 3: Prevalence of Hypomagnesemia and Hypovitaminosis D in the Different Grades of Asthma Severity

| Grades of asthma | Hypomagnesemia (<1.7 mg/dL) | Hypovitaminosis D Deficiency | Insufficiency | Both (hypomagnesemia + vitamin D deficiency) |
|------------------|------------------------------|------------------------------|---------------|--------------------------------------------|
| Mild (n = 14)    | 5 (14.3%)                    | 3 (21.4%)                    | 14 (100%)     | 1 (7.1%)                                   |
| Moderate (n = 27)| 13 (48.1%)                   | 16 (59.2%)                   | 27 (100%)     | 10 (37%)                                   |
| Severe (n = 19)  | 13 (68.4%)                   | 19 (100%)                    | 19 (100%)     | 13 (68.4%)                                 |
| Total (60)       | 31 (51.7%)                   | 38 (63.3%)                   | 60 (100%)     | 24 (40%)                                   |

**DISCUSSION:**

The mean 25 (OH) D level was slightly lower in Group I asthma patients (44.9%) than in Group II controls (86.3%). Vitamin D status has been studied by several studies in asthma patients. 79 percent of elderly asthmatic participants had lower than average serum vitamin D at baseline, Colombo revealed. Vitamin D deficiency and insufficiency are extremely common in elderly patients with asthma and respiratory disease. Vitamin D has also been shown to play a crucial role in the immune response against different pathogenic bacteria. Vitamin D up regulates toxic effects on aquatic and antigen synthesis. This would possibly be the plausible cause for the
therapeutic effects of sunshine on malaria. Magnesium (Mg) deficiency is associated with increased tracheobronchial hyperreactivity, pulmonary vascular drag, and ventricular arrhythmias. Beta 2-agonist therapy can reduce serum magnesium levels by intracellular change or urinary loss. In comparison, bronchoconstriction can be produced by hypomagnesemia. In such people, it can interrupt the muscle fibers to such a degree that lung tremors can result. [13]

Properties similar (active vitamin D form) is engaged in glucose metabolism, induction of T-lymphocyte development of interleukin and B-lymphocyte antibody, separation of myeloid embryonic cells and cell duplication regulation. Vitamin D receptors (VDRs) [3] are expressed by immune system cells, such as T-lymphocytes, activated B-lymphocytes, and dendritic cells. 1, alpha-hydroxylase is also expressed by dendritic cells, indicating that 25-hydroxycholecalciferol (Calcidiol) may be directly transformed to its active component (Calcitriol) and is thus involved in the immune system. Vitamin D has also been shown to play a crucial role in the immune response against different pathogenic bacteria. [14] Vitamin D upregulates toxic effects on aquatic and antigen synthesis. This would possibly be the plausible cause for the therapeutic effects of sunshine on malaria. Magnesium (Mg) deficiency is associated with increased tracheobronchial hyperreactivity, pulmonary vascular drag, and ventricular arrhythmias. Beta 2-agonist therapy can reduce serum magnesium levels by intracellular change or urinary loss. [15] In comparison, bronchoconstriction can be produced by hypomagnesemia. In such people, it can interrupt the muscle fibers to such a degree that lung tremors can result. [16]

The reasons for widespread vitamin D deficiencies in various populations are not completely understood. Western lifestyle may contribute to vitamin D deficiency, which increases susceptibility to allergic diseases including bronchial asthma. In the present study, patients had lower serum magnesium levels relative to controls. Hypomagnesemia is triggered by excessive use of β2-agonist inhalation. [17] A link involving vitamin D deficiency, hypomagnesemia, and asthma severity is seen in the later studies. In asthmatic patients, this was shown in serum 25(OH)D levels. Brehm et al and Sandhu and Casale stated that hypovitaminosis D raises the likelihood of significant asthma exacerbation. [18] Study shows hypomagnesemia prevalence in different asthma grades. Magnesium and 25-OH-D increased serum decline with the rise in the severity of symptoms. Their amounts are maximum in moderate asthma and minimum in chronic pain asthma. Vitamin D deficiency is prevalent in asthmatic patients. [19] The levels of serum 25(OH)D and magnesium may serve as asthma severity markers. Vitamin D deficiency and magnesium deficiency can cause larger asthma magnitude and poor asthma control. [20]

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