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Recurrent Wheezing In Preschool Children; The Associated Factors. A Cross Sectional Study In Tertiary Care Hospital

Shaista Mumtaz, Farooq Ikram*, Sarah Javed, Asbah Rahman*, Ammara Jamil*, Atif Naseem Abbasi***

Department of Paediatrics, Pak Emirates Military Hospital Rawalpindi / National University of Medical Sciences (NUMS) Pakistan, *Department of Paediatrics, Combined Military Hospital Rawalpindi / National University of Medical Sciences (NUMS) Pakistan, **Department of Pathology, Foundation University Medical College Islamabad Pakistan

ABSTRACT

Objective: To determine associated factors in preschool children presenting with recurrent wheezing to children out patient department.

Study Design: Cross sectional study.

Place and Duration of Study: Pediatrics department, Pak Emirates Military Hospital Rawalpindi from April 2019 to January 2021.

Methodology: 300 children with age 2-5 year presenting with recurrent wheezing to children outpatient department were included in the study. Vitamin D levels were carried out in all of them and levels of <20ng/ml was considered as deficient. Gender, breastfeeding status, serum Ig E levels and socioeconomic status of family were correlated with the presence of Vitamin D deficiency amongst children suffering from recurrent wheezing.

Results: Out of 300 preschool children with recurrent wheeze, 213(71%) showed the presence of vitamin D deficiency while 87(29%) had normal vitamin D levels. 179(59.7%) patients were male and 121(40.3%) patients were female. Mean age of the patients was 3.4±3.211 years. After applying the binary logistic regression, we found that low socioeconomic status and breastfeeding the child for less than 6 months had significant association with the presence of vitamin D deficiency amongst preschool children with recurrent wheeze.

Conclusion: Vitamin D deficiency emerged as a common finding amongst preschool children presenting with recurrent wheeze at our tertiary care hospital in Pakistan. Children who were not adequately breastfed or were from families with low income were more at risk of having vitamin D deficiency in our study.

Keywords: Children; vitamin D; wheeze

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INTRODUCTION

Pakistan is a developing country with a high birthrate and huge population involving children with limited health facilities.[1] Respiratory conditions have been one of the most commonly diagnosed condition in children of all age groups.[2] Wheezing is basically a symptom not a disease and is a musical sound produced when air pass through narrowed respiratory tract. Narrowing of respiratory tract may be due to any infective, inflammatory, immunological or mitotic lesion. Depending upon the cause and management, children with recurrent wheeze may have a high mortality and morbidity.[3]

Vitamin D deficiency is a common problem among the children of developing countries including Pakistan.[4,5] Many medical, neurological and psychiatric illnesses have been linked with vitamin D deficiency. Endocrinopathies, rheumatologic diseases, kidney diseases and mental health problems are some of the diseases linked with the vitamin D deficiency among the individuals of all age groups.[6]Early recognition not only enable the clinician to fix the exact cause of deficiency but also prevent the negative short term and long term consequences of this deficiency.

Relationship of wheezing with vitamin levels has been studied in the past in other parts of the world. Dogru et al.[7] in a study published in 2017 concluded that vitamin D levels were significantly less in cases as compared to controls. Same author with other colleagues in 2014 tried to study relationship of different parameters of asthma and vitamin D levels among children of various age groups. They revealed that vitamin D deficiency was a common finding among patients of asthma and number of exacerbations had a significant relationship with deficient vitamin D levels among their study

Correspondence: Dr Shaista Mumtaz, Department of Paediatrics, Pak Emirates Military Hospital Rawalpindi Pakistan.

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participants.[8] Uysalaol et al. in 2014 did a cross-sectional study and looked for the relationship between recurrence of wheezing and serum levels of vitamin D, zinc, and copper in wheezy children compared with a healthy group.[9] They concluded that the vitamin D and zinc levels were significantly lower and serum copper and copper/zinc ratio was significantly higher in patients with recurrent wheezing. They even coined the idea of using these parameters as biomarkers to assess the severity of wheezing or underlying inflammatory disease causing the recurrent wheezing among the children.

Vitamin D levels have been studied in various population groups of our country. Moorani et al.10in 2019 published data from five big areas of Karachi and concluded that around 60% children were vitamin D deficient, whereas 15% had insufficient vitamin D levels. Socio-economic status had statistically significant relationship with vitamin D deficiency in their target population. Limited data is available with regard to relationship of vitamin D deficiency with other clinical condition in children of preschool age. We therefore planned and conducted this study with the rationale to determine vitamin D deficiency and associated factors in preschool children presenting with recurrent wheezing to children out patient department.

METHODOLOGY

This cross sectional study was conducted at the pediatrics department of Pak Emirates Military hospital Rawalpindi from April 2019 to January 2021. Sample size was calculated by using the WHO sample size calculator by keeping population prevalence proportion of Vitamin D deficiency in children as 76.7%.11Non-probability consecutive sampling technique was used to gather the sample for this study. Screening was performed on all the preschool (2-5 years of age) children presenting with recurrent wheezing episodes evaluated by consultant pediatrician. Exclusion criteria were the patients more than 5 years of age or those whose parents did not consent to or those with a past or current history of any chronic metabolic or hematological illness. Children who had thyroid or parathyroid abnormalities, had rickets or osteomalacia were also excluded. Recurrent wheeze was diagnosed as more than one episode of wheeze within the last 12 months.[12]

Vitamin D deficiency was diagnosed in the study participants if levels were <20ng/dl.[13]

All ethical aspects were catered for the study including the formal ethical approval (via letter number A/28/Ec/222/2020) and formal consent from the parents of children after providing them all the information regarding the study and mentioning them their right to withdraw at any time from the study. The concentration of vitamin D3 in serum was measured by electrochemiluminescence immunoassay on a Roche Elecsys (Roche Diagnosis, Penzberg, Germany). It is a competitive assay in which the binding protein of vitamin D3 is inactivated during incubation. The assay employs a polyclonal antibody directed against vitamin D3. This method can measure the concentration of vitamin D3 in the range of 4–100 ng/mL (10–250 nmol/L). Socio demographic variables of the study participants were also collected.Variables in the study included Gender, breastfeeding status, serum Ig E levels, and socioeconomic status of family. Normal serum IgE levels were considered as100 to 200 I.U and above this range was considered as elevated.[14] Socioeconomic class was classed as more than or equal to outgoing or less than outgoing. It was based on a regular economic survey done in Pakistan.[15]

Descriptive statistics were used in the study to describe the relevant data. Presence and absence of vitamin D deficiency was mentioned by using the percentage and frequency. Patients were divided into two groups group 1 (no vitamin deficiency) and group 2 (vitamin d deficiency). Pearson chi-square was the statistical test applied initially to establish any correlation between the variables and vitamin D deficiency among the preschool children presenting with recurrent wheeze. Extent of correlation was confirmed by using the binary logistic regression. SPSS-23.0 was the software used to process all the data and perform the analysis. Differences between groups were considered significant if *p*-values were less than or equal to 0.05.

RESULTS

A total of 300 preschool children with recurrent wheeze were included in the study after inclusion/exclusion criteria. Mean age of the patients was 3.4±3.211 years. 179(59.7%) patients were male and 121(40.3%) patients were male. Out of these 300 patients, 213(71%) showed the presence of vitamin D deficiency while 87(29%) had normal levels of vitamin D. 179(59.7%) patients were male and 121(40.3%) patients were male. Table I summarized the baseline characteristics of patients and application of Pearson chi-square test. Chi-square established correlation of

socioeconomic status and breastfeeding with recurrent wheeze (p-value<0.05). Table II showed that after applying the binary logistic regression, socioeconomic status and breastfeeding the child for less than 6 months confirmed the significant association with the presence of vitamin D deficiency among the preschool children with recurrent wheeze (p-value<0.05).

Table-I: Associated Factors With Recurrent Wheez

Socio demographic factors	Group-1 (no vitamin D deficiency)	Group-2 (vitamin D deficiency)	*p*-value
Gender			
Male Female	57(65.5%) 30(34.5%)	131(61.5%) 82(38.5%)	0.312
Breastfeeding			
> 6 months < 6 months	73(83.9%) 14(16.1%)	145(68.1%) 68(31.9%)	0.004
Serum IgE levels			
within range Raised	48(55.2%) 39(44.8%)	131(61.5%) 82(38.5%)	0.737
Socioeconomic status			
Income more than outgoing Income less than outgoing	59(67.8%) 28(32.2%)	113(53.1%) 100(46.9%)	0.018

Table-II: The Correlated Factors Relating To Vitamin D Deficiency In Preschool Children With Recurrent Wheeze: The Binary Logistic Regression

Correlated factors	*p*-value	OR (95% CI)
Gender (reference was male child)	0.189	1.432(0.839-2.444)
Breastfeeding (reference was > 6 months)	0.023	2.132(1.110-4.095)
IgE levels (reference was levels within range)	0.193	0.700(0.409-1.198)
Socioeconomic status (reference was income more than outgoing)	0.017	1.968(1.127-2.434)

DISCUSSION

Various nutritional deficiencies in body have usually been characterized in a specific way with set of clinical manifestations. Vitamin D deficiency usually has been related to skeletal abnormalities but this essential nutritional element has multiple functions for human body. Vitamin D deficiency and recurrent wheezing both are common findings among children of growing age in all parts of the world.[3,5] but interestingly a lot of studies done have shown that these two apparently unrelated problems may have a relationship which needs to be explored and understood by the clinicians in order to effectively manage the patient. We therefore conducted this study with the objective to determine vitamin D deficiency and associated factors in preschool children presenting with recurrent wheezing to Children out patient department.

Feketea *et al*.[16] published an interesting paper in 2020 that new biomarkers should be studied for children presenting with recurrent wheeze and as Vitamin D deficiency has been observed in significant number of patients with recurrent wheeze so this can be used as biomarker in such patients. They also emphasized the importance of correcting vitamin D deficiency in such patients and repeating the levels after 6 weeks of administration of Vitamin D. Our results supported their findings as around 70% patients in our study had deficient levels of this important vitamin.

Ozadun *et al*.[17] in 2013 published their data regarding association of Vitamin D levels with recurrent wheeze among children and came up with the findings that there has been no statistically significant association between recurrent wheeze and vitamin D levels when cases of recurrent wheeze were compared with health controls. Ours was not a case control study and we found that most of our preschool children presenting with recurrent wheeze had deficiency of vitamin D with children from low socio-economic status and less duration of breastfeeding more at risk of this deficiency.

Ozdemir *et al*.[18] in 2016 studied this subject with more depth and correlated vitamin D levels with different phenotypes of wheeze among the infants. They concluded that low levels of 25 (OH)D were detected in infants with two different phenotypes of recurrent wheeze. They also suggested that vitamin D deficiency might play a role in the pathogenesis of recurrent wheezing among the infant population. We chose preschool children and our study design was also different but still our findings supported the results generated by Ozdemir *et al*.

Another interesting study was conducted by Stelmach *et al*.[19] in 2015 assessing the associations between cord blood concentration of vitamin D and incidence of wheezing and other form of allergies during the first two years of life. They concluded that cord serum 25[OH]D levels were inversely associated with the risk of multi-triggered wheezing, and especially viral-induced wheezing by the age of 2 years. This highlights the importance of regulation of vitamin levels for infants. We did not study the cord

vitamin D levels but breastfeeding was related to vitamin D deficiency in our study participants.

Limitations of the study include the confounding variables which were not studied like the nutritional status of children and exposure to sunlight etc. Exact cause and effect relationship between vitamin D levels and recurrent wheezing could not be established by cross-sectional study design which we opted therefore future studies with better design can establish exact relationship between the two variables.

CONCLUSION

Vitamin D deficiency emerged as a common finding among the preschool children presenting with recurrent wheeze at a tertiary care hospital of Pakistan. Children who were not adequately breastfed or those who were from families with income less than outgoings were more at risk of having vitamin D deficiency in our study participants.

Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

SM & FI: Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

SJ & AR: Data acquisition, data analysis, approval of the final version to be published.

AJ & ANA: Critical review, concept, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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