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A Study of Propensity for Development of Bronchial Asthma in Preadolescents with Family History of Asthma by Spirometry and Body Mass Index.

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ABSTRACT

Hereditary occurrence of Bronchial asthma has been long been postulated and several studies gave useful information in support of this. Therefore family history of hypersensitivity and asthma is an important factor in the prediction, diagnosis, prevention and /or treatment of Asthma. We studied the young school children (10-11 years; n=150 in groups of 50 each) without any history of Bronchial asthma and those with history of bronchial asthma and those having parents with asthma, in three separate groups. The parameters studied were Forced Vital capacity (FVC), FEV_1 (Timed vital capacity), FEV_1/FVC Ratio, Peak Expiratory Flow Rate measurements and Correlated with BMI. Comparison of the parameters by ANOVA revealed that there were significantly lower values in parameters between the asthmatic children than controls ($p<0.001$). The Body Mass Index (BMI) of asthmatic children was also found higher than normal controls. Similarly, those children with family history of Asthma also showed a trend suggesting decreased values of pulmonary function tests. But there were no significant differences in the parameters among the groups with asthma and those with family history of asthma. From the results it appears that those who are hereditarily linked to asthmatic parents show decline in the respiratory parameters apart from asthmatics. This study throws further light into the well-known belief that the children of asthma patients are more vulnerable and need extra care should be taken to reduce their exposure to the predisposing environment.

Keywords: Preadolescent asthma, Timed vital capacity, BMI.

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INTRODUCTION

Bronchial asthma is a major public health concern, affecting 100-150 million people worldwide and accounts for an estimated 1,80,000 deaths per year [1]. In developing countries, there is a rising incidence of asthma that appears to be associated with increased urbanization. The prevalence of atopy and other allergic diseases has also increased over the same time, suggesting that the reasons for the increase are likely to be systemic rather than confined to the lungs and could possibly have a genetic predisposition [2]. The prevalence of asthma has risen in affluent countries over the last 30 years but now appears to have stabilized, with ~10–12% of adults and 15% of children affected by the disease [2]. In the absence of genetic markers, parental history of asthma, personal history of eczema, peripheral eosinophilia, are the better indicators of the development of asthma in children and infants [3]. A predictive value of family history has been also suggested [4].

Bronchial asthma is a chronic inflammatory disorder of the airways associated with many symptoms [5-8]. Asthma is both common and frequently complicated by the effects of smoking on the lungs; hence, it is difficult to be certain about the natural history of the disease in adults. Asthma can present at any age with a peak age of 3 years. In childhood, twice as many males as females are asthmatic, but by adulthood the sex ratio has equalized. Adults with asthma, including those with onset during adulthood rarely become permanently asymptomatic. Deaths from asthma are uncommon and have been steadily declining in many developed countries over the last decade [2]. Atopy is a genetic predisposition to produce increased amounts of IgE antibodies to common allergens, suggesting that some other environmental or genetic factor(s) predispose to the development of asthma in atopic individuals [2].

The considerable variability between symptoms and degree of airway obstruction is probably due to change in lung volume, rate of broncho-constriction, anxiety level, duration of asthma and age, attitudes, expectations and personality traits [9]. The lung function declines over a period of time in untreated or improperly treated asthma. This is because permanent changes take place in the lungs, especially in the airways due to ongoing inflammation. Fletcher et. Al [10] described the “horse racing effect” which is a relation between the level of FEV1 and FVC and the ratio declines over time. The fall in FEV1 in patients with extrinsic asthma depends on the initial level of FEV1, FEV1/FVC and control of asthma by medication [11-13]. The familial association of asthma and a high degree of concordance for asthma in identical twins indicate a genetic predisposition to the disease. It now seems likely that different genes may also contribute to asthma including severity [14].

Genetic screens indicate that asthma is polygenic. The most consistent findings have been association with polymorphisms of genes on chromosome 5q, including the T helper 2 (T_H2) cell interleukin (IL) 4, IL-5, IL-9, and IL-13, which are associated with atopy. Novel genes that have been associated with asthma, including ADAM-33, DPP-10, and GPRA [2].

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Shiigai N showed that asthma occurred more often in children with family history than otherwise. Child has more asthma when either father or mother has asthma than allergic rhinitis [15]. He concluded that family history of allergic diseases especially asthma is asthmogenic and environmental factors work as aggravating but not asthmogenic factors. This is also agreed by other authors [4].

Limitation of airflow is due mainly to bronchoconstriction, but airway edema, vascular congestion, and luminal occlusion with exudate may also contribute. This results in a reduction in forced expiratory volume in 1 s (FEV_1), FEV_1/forced vital capacity (FVC) ratio, and peak expiratory flow (PEF), as well as an increase in airway resistance. Measurement of these parameters by simple spirometry confirms airflow limitation. Measurements of PEF twice daily may confirm the diurnal variations in airflow obstruction. And a FEV1/FVC ratio of <80 % of Normal is a good predictor of Obstructive lung disease like asthma. Further lung function tests are rarely necessary [2].

Very few studies have been done till date which unequivocally shows a definite correlation between family history of bronchial asthma and predisposition to overt disease in pre-adolescent age group in South Asian population. Hence the study was undertaken to investigate whether the family history of asthma and one or both of allergic rhinitis & atopic dermatitis, can be used as a predictor of development of future overt disease in apparently healthy pre-adolescents. The parameters used for the purpose of this study were Spirometric measurements, PEFR values, Total eosinophil count and an additional parameter BMI was also taken into account.

MATERIALS AND METHODS

The study was conducted in India over a period of two years three months between May 2008 and August 2010. Total 150 subjects were studied. 150 pre-adolescent children (aged10-11 years). These subjects are either had a history of Asthma attacks or had a family history of Asthma, Atopic dermatitis & Allergic rhinitis. At the outset, each of the participants in this study was thoroughly briefed about the procedure and a written informed consent was obtained from parents of the juvenile subjects. The pre-adolescent group was subdivided into 3 sub-groups which consisted of both males and females (n=50).

Group **1(n=50)** (Pre-adolescent, Control): This group consisted of individuals who neither have any family history nor were asthmatics themselves by definition.

Group **2(n=50)** (Pre-adolescent cases): Those who had family history of bronchial asthma and one or both of allergic rhinitis and atopic dermatitis. The subjects themselves were asthmatics diagnosed elsewhere by post-bronchodilator airway obstruction reversibility of > 20%

Group **3(n=50)** (Pre-adolescents with family history of Bronchial asthma): Those who were apparently healthy themselves with no episodes of wheeze in the past 2 years.

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The study on pre-adolescent children was carried out at St. Luke's Day school, Kolkota (with a student population of more than 1000), in India. Spirometry was done with Microlab™ portable spirometer. It is designed to take the best of 3 attempts. The machine was calibrated. Pre-test instructions were given to the subjects. The nasal prong was attached to the subject's nose and the subject was made to expire with maximum force into the mouth piece of the instrument after a maximal inspiration. The process was repeated till a Sharp peak of flow-volume curve was obtained and expiratory effort was more than 4 seconds in the volume-time curve.

FEV1, FVC, FEV1/FVC Ratio and PEFR values were noted. Best value for each parameter as determined by the Microlab spirometer was taken for the purpose of statistical analysis.

Height was measured using a standard scale and weight was measured using an electronic pre-calibrated weighing scale. BMI was calculated from the height and weight obtained using the standard formula.

Statistical analysis was done by ANOVA (Fisher's F Test) & Inter sub-group comparisons were done by using TUKEY'S Test. ($P<0.05$ is accepted as significant).

RESULTS

FVC, FEV_1, FEV1/FVC Ratio, PEFR and BMI values of Control group and Asthmatic subjects are represented in (*Table 1)*. Comparison between the groups by ANOVA showed highly significantly lower values in asthmatics ($p<0.001$). PEFR in asthmatic children was down to half the normal children.

Table 1: Comparison between Group1(controls) and Group 2(Asthma cases)

Parameters	Group1(controls) n=50	Group2(Asthma cases) n=50	p value
FVC (ml)	3490.000±731.297	3096.000±557.311	<0.001**
FEV1(ml)	3024.000±634.890	2426.000±479.289	<0.001**
FEV1/FVC	86.438±2.585	79.274±7.472	<0.001**
PEFR (L/min)	600.000±49.744	300.000±41.020	<0.001**
BMI	19.840±2.207	22.000±1.841	<0.001**

Values given as mean± SD
P**=very highly significant

The mean FVC value was significantly lower in asthmatic cases as compared to controls. The mean FEV_1 value was also significantly lower in asthmatic cases as compared to control as was mean FEV_1/FVC Ratio and mean PEFR values ($p<0.001$). BMI was also compared between asthmatic cases and controls. The mean BMI was significantly higher in asthmatic cases ($p<0.001$).

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Table 2:Comparison between Group1(controls) and Group 3(Study group with family history of asthma)

Parameters	Group1(controls) n=50	Group3(study group with family h/o asthma) n=50	p value
FVC (ml)	3490.000±731.297	3194.000±329.755	<0.001**
FEV1(ml)	3024.000±634.890	2630.000±275.718	<0.001**
FEV1/FVC	86.438±2.585	80.507±8.175	<0.001**
PEFR (L/min)	600.000±49.744	320.000±24.516	<0.001**
BMI	19.840±2.207	21.960±2.563	<0.01**

Values given as mean± SD
P**=very highly significant

Table 2 shows a comparison between Control group and study group with family history of asthma. ANOVA done to compare between the groups showed high significance ($p<0.001$). On comparison between the two groups, the mean FVC value, FEV1, FEV1/FVC Ratio and PEFR was found to be significantly lower in study group with family history of asthma as compared to controls($p<0.001$). The mean BMI on the other hand was significantly higher in study group with family history of asthma($p<0.001$).

The comparison between mean FVC, FEV1, FEV1/FVC Ratio, PEFR and BMI values in Cases and study group with family history of asthma is shown in *Table 3.* Inter-group comparison by ANOVA showed highly significant variations and the values in the children with family history of Asthma had lowed measures as far as the parameters are concerned ($p<0.001$).

Table 3: Comparison between Group2(cases) and Group 3(Study group with family history of asthma)

Parameters	Group 2(cases) n=50	Group3(study group with family h/o asthma) n=50	p value
FVC (ml)	3096.000±557.311	3194.000±329.755	0.004*
FEV1(ml)	2426.000±479.289	2630.000±275.718	0.613
FEV1/FVC	79.274±7.472	80.507±8.175	0.983
PEFR (L/min)	300.000±41.020	320.000±24.516	0.976
BMI	22.000±1.841	21.960±2.563	0.976

Values given as mean± SD
P*= statistically significant

When the above parameters were compared between the groups 2 and 3, there was no significant difference and the values were similar. (Table 3).

DISCUSSION

Asthma has far reaching implications both on the paediatric and adult population and if detected and treated at an earlier age could have positive outcome on prognosis of the disease.

The most definite parameters in diagnosing asthma are- FEV_1, FEV_1/FVC Ratio, and PEFR values. Significant changes in one or more of these parameters are strongly suggestive of asthma [2].

Our results show, that there is a significant reduction in FEV1, FEV_1/FVC ratio, and PEFR values in the asthmatic subjects and study groups with family history of bronchial asthma, as compared to the controls. Also was no significant difference between the asthmatic subjects and the study group with family history of asthma, when the above parameters are considered. This implies that there is definite correlation between family history of Bronchial asthma and chances of development of Bronchial asthma in Paediatric populations. The results suggest that the development of asthma is early onset. They also suggest a role for genetic predisposition of Bronchial asthma in both the populations but more strongly and evidently in the Paediatric group which is in agreement with other obeservations [2].

Kuiper S et.al. and Carlsen K et.al. showed that genetic studies have identified genes associated with asthma, and some other studies provided evidence of a major susceptibility locus located on chromosome 2p [16,17]. This is supported by reports of Burke W, Fesinmeyer M, Reed K et al., suggesting family history of asthma in one or more first-degree relatives was consistently identified as a risk factor for asthma [4]. The results obtained from our study were in agreement with most of the similar studies done in western populations.

Another interesting finding from our study was a statistically significant increase in BMI, in cases as well as the study groups with family history of bronchial asthma, as compared to the controls. This finding is supported by the study done by Litonjua AA et.al. where they found that being overweight, especially obese (a body mass index greater than or equal to 30), is a risk factor for developing asthma [18]. In addition, asthmatics that are obese are likely to have more severe asthma than those who are not obese. Moreover, obese asthmatics can have significant improvement of their asthma with weight loss. Asthmatics subjects who are severely overweight and later lose weight, either through diet or surgical methods (such as bariatric surgery) improve their asthma symptoms, with less medication needs, less hospitalizations and better lung function [19]. Therefore increased BMI can itself be an independent risk factor for predisposition to asthma.

Obesity could be an effect of asthma medications like steroids which are frequently used by the asthmatics. This would explain the cases but not the study group with only family history of asthma. Other reasons that can be put forward as to why obesity worsens asthma such as smaller lung capacity in obese, which causes the muscles around the lung airways to contract more, resulting in more asthma symptoms and smaller airways causing less oxygen exchange in these airways. Obesity appears to cause chronic inflammation in the body, which in asthmatics resulting in worsening asthma and also increases risk for gastro-esophageal reflux disease and sleep apnea, both of which can worsen asthma. Therefore more detailed studies are required to investigate the correlation between the two.

Key points:

From our study we concluded that, the propensity for developing asthma is much more in the population with family history of bronchial asthma, as compared to the control population.

Also, obesity increases the chances of subsequent development of asthma in both pre-adolescent and young adult population.

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