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Original Article

Physiology Section

Prevalence of Allergic and Non-allergic Asthma in Kumaun Region of Uttarakhand, India: A Cross-sectional Study

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ABSTRACT

Introduction: Asthma is a heterogenic disease, commonly divided into allergic and nonallergic asthma. It affects people of all age group and is associated with impaired lung function. Previously, it was thought that asthma is a disease of developed countries but at present, world scenario has changed and its prevalence in developing countries is rapidly increasing. Asthma shows large geographical variations in terms of prevalence, severity and mortality.

Aim: To establish the prevalence of allergic and nonallergic asthma in adults of Kumaun region of Uttarakhand (India) and to evaluate whether the peripheral blood cell count is associated with the severity of lung impairment in both the subtypes (allergic and nonallergic) of asthma.

Materials and Methods: This cross-sectional study was carried out jointly in Department of Physiology and Department of Respiratory Medicine, Government Medical College, Haldwani, Uttarakhand (India), during the period from October 2015 to January 2017. A total of 125 patients of both sexes age above 18 years, who attended the OPD of Respiratory Medicine and diagnosed asthma by the physician were enrolled in the study. The patients associated with tuberculosis, worm infestations, other allergic diseases and systemic diseases were excluded. History of Allergic Rhino-Conjunctivitis (ARC) was used for allergic sensitisation and to define allergic asthma. Classification of severity of airflow limitation was done according to Global Initiative for Asthma (GINA) guidelines. Absolute Leukocyte Counts was determined by using the formula: Absolute leukocyte count=Differential leukocyte count/100×Total leukocyte count. One-way ANOVA followed by Tukey HSD post-hoc analysis and Chi-square was done. Level of statistical significance was set at p-value <0.05.

Results: The prevalence of allergic asthma was more in 79 patients (63.2%), in comparison to nonallergic asthma in 46 (36.8%) and it (allergic asthma) was more common in males than females (54:25). Mean age of allergic and nonallergic group asthma patients were 51.00±14.31 and 56.11±13.14 years, respectively. In allergic asthma patients, blood eosinophil count increased significantly (p=0.001) the severity of lung impairment increased and no significant changes were observed in other blood cell counts while in nonallergic asthma over-all neutrophil count was significantly high (p=0.044) with increase in severity. Nonallergic asthma also showed increasing trend of eosinophil count as the severity of airway obstruction increased but there were no significant changes in other counts.

Conclusion: The prevalence of allergic asthma is high in comparison to nonallergic asthma among adults of Kumaun region of Uttarakhand, India and it is more prevalent among males in both the groups. Peripheral blood leukocyte count might be used as biological marker to differentiate allergic asthma from nonallergic asthma.

Keywords: Allergic rhino-conjunctivitis, Environment, Lung impairment, Peripheral leukocyte count

INTRODUCTION

Asthma is a heterogenic disease with several phenotypes, commonly divided into allergic and nonallergic asthma [1]. It affects people of all age groups and is associated with impaired lung function. Airway inflammation, together with bronchial hyper-responsiveness and airway structural remodeling are prominent features of asthma. Allergic asthma is frequently caused by exposure to perennial or seasonal allergens present in the indoor and outdoor environment, the most common ones being: pollens (grass, trees, weeds), house dust, mites, pets, moulds, foodstuffs and many others [1].

Previously, it was thought that asthma is a disease of developed countries but at present, world scenario has changed and asthma has become a global problem with increasing trend of prevalence. According to asthma and allergy foundation of America more than half of the asthmatic patients have allergic subtype of asthma. A study done by Backman H et al., found that there is a continuous increase in allergic asthma from 1996 to 2016 [2], while the prevalence of nonallergic asthma remained stable. Study of allergic sensitisation also have shown increase in prevalence of allergic rhinitis associated with asthma in many areas of world among all age groups [3,4]. In India, about 20-30% population suffers from at least one allergic rhinitis (associated with asthma) and/or other allergic diseases, and the prevalence is increasing over the past many years [5].

These allergic diseases seriously impair the Quality of Life (QOL) [6] and ARC is strongly associated with the allergic asthma. Beside, this asthma-related mortality is higher in developing country in comparison to developed country [7]. Asthma shows large geographical variations in terms of prevalence, severity and mortality [8]. Various studies have been done on the prevalence of asthma and COPD in different age-groups in different parts of the world [2,8] and in India [9-11]. There is a paucity of information on prevalence of subtype (allergic and nonallergic) of asthma in different geographic environments of India. Despite the advancement of new costly diagnostic tools for diagnosis of asthma being available, there are stills gains to be made in terms of improving patient's outcome. Peripheral blood leukocytes are useful, indirect and inexpensive markers of severity of lung impairment in obstructive airways diseases [12]. Furthermore, peripheral blood leukocyte levels may also help in differentiating allergic asthma and nonallergic asthma [13]. The current evidences suggest that environmental factors are one of the important aetiologies of allergic asthma. So a study done in Uttarakhand may add up the existing knowledge. Uttarakhand is a state of India having 86% mountains and 65% forests, of its total area 53,483 km^2 [14,15]. It is culturally divided into two regions Kumaun and Garhwal. The present study was carried out in Government Medical College, Haldwani which is a single tertiary care hospital of

Kumaun region) with an aim to establish the prevalence of allergic and nonallergic asthma in adults.

MATERIALS AND METHODS

This cross-sectional study was done by using simple random sampling technique, jointly in the Department of Respiratory Medicine and Department of Physiology, Government Medical College, Haldwani, Uttarakhand, India during the period from October 2015 to January 2017. After obtaining approval from the institutional ethics committee (274/GMC/IEC/2015) and written informed consent, a total 429 patients of both sexes age above 18 years, who attended the OPD of Respiratory Medicine in designated three days (Monday, Wednesday and Friday) of every week and diagnosed as asthma by the physician were enrolled in the study. But, only 125 patients met our inclusion criteria.

Inclusion criteria: Patients who met our operational definition of asthma were included.

Definitions: Current asthma was defined as a physician-diagnosed asthma in combination with at least one of the following [2]:

(i) Attacks of breathlessness in last 12 months.

(ii) Any wheeze in last 12 months.

(iii) Current asthma medication use.

Subjects were defined as having ARC based on positive history of cold and congestion with seasonal aggravation. Patients of current asthma were divided into **Allergic asthma** (which have current asthma with ARC) and **Nonallergic asthma** (which have current asthma without ARC). Current smokers were defined as those who smoked even once or twice a day in last 12 months, while ex-smokers were defined as those who quitted smoking ≥12 months ago. Nonsmokers were defined as those who never smoked.

Exclusion criteria: Patients associated with tuberculosis, diseases like worm infestations, atopic skin disease and other allergic diseases, cardiac problems, renal failure, diabetes mellitus, hypertension, pulmonary fibrosis and neuromuscular diseases were excluded.

Data Collection Procedure

A) From patient's Spirometry report (done in pulmonary unit of Medicine department), classification of severity of airflow limitation was done according to GINA guidelines [16].

Mild → FEV_1 ≥80% predicted

Moderate → FEV_1 <80% to ≥60% predicted

Severe → FEV_1 <60% predicted

B) A total of 1 mL of blood was collected by venipuncture method from the subjects. Evaluation of blood leukocyte counts was done under a compound microscope in an Improved Neubauer's chamber using Turk's fluid and Leishman's stain. After evaluating Total Leukocyte Count (TLC) and Differential Leukocyte Counts (DLC), Absolute Leukocyte Counts was determined by using the formula: **Absolute leukocyte count=DLC/100×TLC**.

STATISTICAL ANALYSIS

All the analysis was done on standard software (Microsoft Excel 2016 and SPSS 16.0 version). One-way ANOVA followed by Tukey HSD post-hoc analysis and Chi-square was done. Descriptive statistics like mean and standard deviation have been used. Level of statistical significance was set at p-value <0.05.

RESULTS

Total 429 patients were diagnosed asthma by the physician but only 125 patients met our inclusion criteria, rest 304 patients were excluded. The prevalence of allergic asthma was as observed in 79 patients (63.2%), in comparison to nonallergic asthma in 46 patients (36.8%). The allergic asthma among male patients were more prevalent than females (54:25) while no such gender difference was seen in nonallergic group. The prevalence of allergic asthma were more common among the patients who were working in allergic prone environment (74.6%), while the prevalence of nonallergic asthma were common in patients who were working in nonallergic prone environment (72%). Smoking showed declining trend of prevalence among current smoker, ex-smoker and nonsmoker in both the groups [Table/Fig-1].

Parameters	Allergic asthma	Nonallergic asthma
No. of subjects (%)	79 (63.2)	46 (36.8)
Male: Female ratio	54:25	23:23
Age (mean) in years	51.00±14.31	56.11±13.14
***Working environment** (Occupation %)		
Allergy prone	59 (74.6)	13 (28)
Not prone to allergy	20 (25.4)	33 (72)
On controller medication (%)	18 (23)	17 (37)
On non-controller medication (%)	61 (77)	29 (63)
Obesity having BMI ≥30 (%)	7 (0.9)	7 (15.2)
Smoking status (%)		
Current smokers	49 (62)	24 (52)
Ex-smokers	20 (25)	16 (35)
Nonsmokers	10 (13)	6 (13)

[Table/Fig-1]: Socio-demographic profile of the patients of allergic and nonallergic groups.
(Allergy prone and non-allergy prone are classified on the basis of working history in paper mill, forest, wall painters and daily wage based laborers etc., and according to our operational definitions)

As the severity of airway obstruction increased, FEV_1 decreased significantly (p<0.001) in allergic group of asthma as well as in nonallergic group of asthma. On applying, Tukey HSD post-hoc test, difference between groups (mild, moderate and severe) from each other was found to be statistically significant (p<0.001) [Table/Fig-2].

Asthma	Mild	Moderate	Severe	p-value*
Allergic	87.60±6.203	70.54±2.222	45.03±9.779	0.001 (S)
Nonallergic	90.89±6.172	66.44±5.223	45.50±10.584	0.001 (S)

[Table/Fig-2]: Mean±SD of FEV_1 in different grades of severity of allergic and nonallergic asthma.
(S=statistically significant, NS=statistically not significant), *One-way ANOVA followed by Tukey HSD post-hoc analysis done

The prevalence of patients who are suffering from mild and severe grade is highest in comparison to moderate grade in both the study groups [Table/Fig-3].

Asthma diagnosed by physician			
FEV_1% predicted	Allergic 79 (63.2%)	Nonallergic 46 (36.8%)	Total=125
Mild (%)	35 (44.3)	19 (41.3)	54(43.2)
Moderate (%)	13 (16.4)	09 (19.5)	22 (17.6)
Severe (%)	31 (39.2)	18 (39.1)	49 (39.2)

[Table/Fig-3]: Prevalence of different grades of severity among allergic and nonallergic groups.
Chi square=0.220, df=2, p-value=0.896
(FEV_1-Forced expiratory volume in 1st second)

There is significant increase in eosinophil count as the severity of airway obstruction increases in allergic group and no significant changes in other counts. Post-hoc test showed the statistically significant difference (p<0.001) between mild and severe group with more increase in severe one. Also, difference between moderate and severe groups was found to be statistically significant (p=0.001) with more increase in severe group [Table/Fig-4].

In nonallergic group over-all there was a significant increase in

Parameters	Mild (35)	Moderate (13)	Severe (31)	p-value*
ANC	6148.77±328.9	5544.08±338.9	6501.97±212.9	0.188 (NS)
ALC	2184.10±114.8	2367.29±189.5	2008.54±122.2	0.259 (NS)
AEC	305.06±30.4	456.06±62.7	711.90±60.09	0.001 (S)
AMC	240.86±36.3	319.62±65.1	176.74±39.07	0.137 (NS)
ABC	17.57±6.7	13.78±9.3	6.30±4.4	0.391 (NS)

[Table/Fig-4]: Comparison of mean±SEM of absolute leukocyte counts in different grades of allergic asthma.
(ANC: Absolute neutrophil count, AEC: Absolute eosinophil count, ABC: Absolute basophil count, ALC: Absolute lymphocyte count, AMC: Absolute monocyte count). *One-way ANOVA followed by Tukey HSD post-hoc analysis done.

neutrophil count (0.044) but in moderate to severe lung impairment increasing trend was observed while in mild lung impairment absolute neutrophil count was more in comparison to moderate. Post-hoc test showed the statistically significant difference between mild and moderate group [Table/Fig-5] and there was an increasing trend of eosinophil count as the severity of airway obstruction increased. There were no significant changes in other counts.

Parameters	Mild (19)	Moderate (9)	Severe (18)	p-value*
ANC	6448.63±342.01	5050.89±390.56	5460.89±524.9	0.044 (S)
ALC	2090.71±584.71	2139.78±528.30	2089.06±447.21	0.957 (NS)
AEC	427.89±102.908	468.00±62.652	659.50±98.798	0.201 (NS)
AMC	145.21±39.931	96.89±84.887	107.50±42.546	0.771 (NS)
ABC	8.79±5.54	0.00±0.00	8.89±8.889	0.721 (NS)

[Table/Fig-5]: Comparison of mean±SEM of absolute leukocyte counts in different grades of nonallergic asthma.
(ANC: Absolute neutrophil count, AEC: Absolute eosinophil count, ABC: Absolute basophil count, ALC: Absolute lymphocyte count, AMC: Absolute monocyte count) *One-way ANOVA followed by Tukey HSD post-hoc analysis done

DISCUSSION

The prevalence of allergic asthma was more (63.2%), in comparison to nonallergic asthma (36.8%). It was more prevalent among males (54%), who were suffering from allergic asthma and had working history in allergic prone environments like in paper mill, forest, wall painters and daily wage based laborers etc., [Table/Fig-1]. Pakkasela J et al., also reported that among the 445 physician-diagnosed asthma patients 52% were classified as allergic and 48% as nonallergic [17]. Similar findings i.e., increase in prevalence of allergic asthma were reported by Beckman H et al., Chandrika D., in their study [2,18]. In terms of severity, maximum patients presented with mild and severe grade of asthma. A similar study conducted by Ashem ND et al., also observed that the maximum asthma patients presented with mild severity [19]. The high prevalence of severe grade in our study, was may be due to lack of awareness towards asthma in common people. The prevalence of current smoker, ex-smoker and non smoker was 62%, 25% and 13% respectively in allergic group while in nonallergic group it was 52%, 35% and 13%, respectively. This was in conformity with the study conducted by Willemse BWM et al., [20]. It is now well established that smoking cessation improves the accelerated decline in forced expiratory volume in one second (FEV1), which strongly indicates that smoking cessation positively influence inflammatory processes in the lungs [20].

The present study found significantly higher eosinophil count (≥300 mm^3) in allergic asthma group and the count increased as the severity of airways obstruction increased. Similar findings were also observed in a study conducted by Ashem ND et al., and Horn BR et al., Th2 lymphocytes plays important role in the development of eosinophilic allergic asthma [19,21]. It was well known fact that aeroallergen were an important cause of allergic asthma. These aeroallergen contain trace amounts of lipopolysaccharides. Therefore, when they penetrate into the airway epithelium, they activate the Toll-Like Receptor (TLR). Activation of TLR induces synthesis of cytokines mediated by Th2 lymphocyte. These cytokines stimulate the maturation and recruitments of eosinophils [22]. The present study found a significantly higher neutrophil count in nonallergic asthma patients. Similar finding was reported in a study conducted by Gibson PG et al., [23]. The nonallergic asthma was associated with a neutrophil influx and activation, which may be mediated by IL-8 secretion [23]. Cigarette smoking was associated with bronchial neutrophilia and corticosteroid insensitivity [24,25]. Other reasons of high neutrophil count in increased severity may be the use of steroids for treatment as severity of functional lung impairment increases. Steroids cause an increase in neutrophil count by accelerating release from bone marrow and decreasing its migration out of circulation.

Since, the preferred method to estimate prevalence trends requires continuous dedicated repeated survey of large random samples in the same area, within the same age span and with the same validated methods, were costly and time-consuming [26]. So this type of cross-sectional study can contribute towards the establishment of prevalence trend. This study also justify that peripheral blood leukocyte count can be used as a biological marker to differentiate allergic asthma from nonallergic asthma in setting of limited infrastructure.

Limitation(s)

However, finding of this study may not be generalised as this study was done in one tertiary institute with small sample size, covering one region of the state. Further studies are needed from different parts to establish the trend of current asthma as well as studies which establish peripheral blood leukocyte count as a biological marker.

CONCLUSION(S)

Present study shows that prevalence of allergic asthma was more in comparison to the nonallergic type and it was more common in males than females. Further, it was found that allergic asthma was associated with a significant rise in blood eosinophil count while nonallergic asthma was associated with significant increase in blood neutrophil count. This finding in our study suggest that blood leukocyte count (eosinophil vs neutrophil) can be used as a biological marker, to differentiate the allergic asthma from nonallergic asthma type, and to start the presumptive treatment, for particular asthma. It will reduce the long term complications of asthma and improves the QOL.

REFERENCES

[1] Wenzel SE. Asthma phenotypes: The evolution from clinical to molecular approaches. Nat Med. 2012;18:716-25.
[2] Backman H, Risanen P, Hedman L, Stridsman C, Andersson M, Lindberg A, et al. Increased prevalence of allergic asthma from 1996 to 2006 and further to 2016-results from three population surveys. Clin Exp Allergy. 2017;47:1426-35.
[3] Chinn S, Burney P, Sunyer J, Jarvis D, Luczynska C. Sensitization to individual allergens and bronchial responsiveness in the ECRHS. European Community Respiratory Health Survey. Eur Respir J. 1999;14:876-84.
[4] Ronmark E, Warm K, Bjerg A, Backman H, Hedman L, Lundback B. High incidence and persistence of airborne allergen sensitization upto age 19 years. Allergy. 2017;72:723-30.
[5] Prasad R, Kumar R. Allergy situation in India: What is being done? Indian J Chest Dis Allied Sci. 2013;55:07-08.
[6] Ahmed MA. Comparative data review on prevalance, economic burden and epidemiology of allergic rhinitis between the USA and India. J. Evolution Med. Dent. 2016;5(45):2840-42.
[7] To T, Stanojevic S, Moores G, Gershon AS, Bateman ED, Cruz AA, et al. Global asthma prevalence in adults: Findings from the cross-sectional world health survey. BMC Public Health (2012).
[8] Dharmage SC, Perret JL, Custovic A. Epidemiology of asthma in children and adults. Frontiers in Pediatrics. 2019;7:246.
[9] Bhalla K, Nehra D, Nanda S, Verma R, Gupta A, Mehra S. Prevalence of bronchial asthma and its associated risk factors in school-going adolescents in Tier-III North Indian City: J Family Med Primary Care. 2018;7(6):1452-57.
[10] Aggarwal AN, Chaudhry K, Chhabra SK, D'Souza GA, Gupta D, Jindal SK, et al.

Prevalence and risk factors for bronchial asthma in Indian adults: A multicentre study. Indian J Chest Dis Allied Sci. 2006;48(1):13-22.
[11] Nitin J, Palagani R, Shradha NH, Vaibhav J, Kowshik K, Manoharan R, et al. Prevalence, severity and risk factors of allergic disorders among people in south India. Afr Health Sci. 2016;16(1):201-09.
[12] Szefler SJ, Wenzel SE, Brown R, Erzurum SC, Fahy JV, Hamilton RG, et al. Asthma outcomes: Biomarkers. J Allergy Clin Immunol. 2012;129(3).
[13] Lewis SA, Pavord ID, Stringer JR, Knox AJ, Weiss ST, Britton JR. The relation between peripheral blood leukocyte counts and respiratory symptoms, atopy, lung function, and airway responsiveness in adults. Chest. 2001;119(1):105-14.
[14] "Info about Uttarakhand". Nainital Tours & Package. Archived from the original on 25 November 2012. Retrieved 20 December 2012. [wikipedia].
[15] FAQ (PDF). India Meteorological Department. [climate].
[16] Global Initiative for asthma (GINA): Global strategy for asthma management and prevention. 2011. Available from: http://www.ginaasthma.org.
[17] Pakkasela J, Ilmarinen P, Honkamaki J, Tuomisto LE, Andersén H, Piirila P, et. al. Age-specific incidence of allergic and nonallergic asthma. BMC Pulmonary Medicine. 2020.
[18] Chandrika D. Allergic rhinitis in India: An overview Int J Otorhinolaryngol Head Neck Surg. 2017;3(1):01-06.
[19] Ashem ND, Kanan WD, Singh WA, Ningshen K, Shimray AJ, Hungyo H. Peripheral blood leukocyte counts as a marker of severity of functional lung impairment in OAD patients attending a tertiary care hospital in Manipur, India. IOSR Journal of Dental and Medical Sciences. 2014;13(9):22-25.
[20] Willemse BWM, Postma DS, Timens W, Hacken NHT. The impact of smoking cessation on respiratory symptoms, lung function, airway hyper responsiveness and inflammation. Eur Respir J. 2004;23(3):464-76.
[21] Horn BR, Robin ED, Theodore J, Vankessel A. Total eosinophil counts in the management of bronchial asthma. N Engl J Med. 1975;292(22):1152-55.
[22] Pelaia G, Vatrella A, Busceti MT, Gallelli L, Calabrese C, Terracciano R, et al. Cellular mechanisms underlying eosinophilic and neutrophilic airway inflammation in asthma. Mediators of Inflammation. 2015;2015:879783.
[23] Gibson PG, Simpson JL, Saltos N. Heterogeneity of airway inflammation in persistent asthma: Evidence of neutrophilic inflammation and increased sputum interleukin-8. Chest. 2001;119:1329-36.
[24] Thomson NC, Chaudhuri R, Livingston E, Asthma and cigarette smoking. European Respiratory Journal. 2004;24(5):822-33.
[25] Polosa R, Thomson NC. Smoking and asthma: Dangerous liaisons. European Respiratory Journal. 2013;41(3):716-25.
[26] Lundback B, Backman H, Lotvall J, Ronmark E. Is asthma prevalence still increasing? Expert Rev Respir Med. 2015;26:01-13.

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