How to Cite:
Aravind, C., Loknath, B., & Ragul, B. (2022). Comprehensive assessment of the relation between clinical symptoms, functional parameters and biomarkers of airway inflammation. *International Journal of Health Sciences*, *6*(S2), 4026–4038. https://doi.org/10.53730/ijhs.v6nS2.5889

Comprehensive assessment of the relation between clinical symptoms, functional parameters and biomarkers of airway inflammation

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***Abstract*---**Background: Asthma is a chronic inflammatory disorder of the airways causing bronchial hyper-responsiveness that is characterized by variable and recurring symptoms and airflow obstruction. Asthma is characterized by multiple biomarkers measurable in biological fluids. To become useful, these biomarkers need to be quantifiable by reliable systems, reproducible in the clinical setting, easy to obtain and cost-effective. bjective: The current study aimed to assess the relation between clinical symptoms, functional parameters and biomarkers of airway inflammation. Materials and Methods: This prospective, observational and single-center study carried out in the outpatient and inpatient department of Thoracic medicine, Tirunelveli Medical College Hospital, Tamil Nadu, India from June-2017 to June-2018 was aimed to assess the relation between clinical symptoms, functional parameters and biomarkers of airway inflammation in all stable asthmatic patients of 18–60 years of age. The severity of asthma was assessed according to the GINA criteria, based on clinical symptoms and pulmonary function test. Blood samples were collected for absolute eosinophil count and induced sputum samples for eosinophil count. Data was entered in Microsoft Excel and statistical analysis was performed by t-test. $p<0.05$ was considered statistically significant. Result: In our study, total 101

International Journal of Health Sciences ISSN 2550-6978 E-ISSN 2550-696X © 2022.
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Manuscript submitted: 27 Feb 2022, Manuscript revised: 18 March 2022, Accepted for publication: 05 April 2022

cases were selected, out of them 52% (n=53) were male and 48% (n=48) were female. The distribution of age varied from 20 to 60 years. The overall mean age was 39 years. Maximum patients were found in the 21 to 40 years' age group (56.4 %, n= 57). Around 59.4 % cases were exposed to occupation related risk factor, among them 16.8% were beedi workers. In our study, cases who had a family history, smokers, most of them were severe persistent asthmatics and there was no significant correlation to eosinophil count. Dust and seasonal allergens are the most common triggering factors in our study. Rhinosinusitis was the common co-morbidity of asthma in our study showed a significant correlation with severity of asthma. Conclusion: Prevalence of asthma is more in middle age group with equal sex ratio. Dust and seasonal allergens are the most common triggering factors. Beedi workers were more when compared to other occupations. Risk factors for severe asthma was female sex, environment dust exposure, smoking, who had family history, long duration of symptoms and rhinosinusitis co-morbidity.

***Keywords*---**asthma, severity, rhinosinusitis.

Introduction

It is estimated that approximately 358 million individuals worldwide are affected by asthma, and the global prevalence can vary from 1 to 18%.[1] According to the recent Indian Study on Epidemiology of Asthma, Respiratory Symptoms and Chronic Bronchitis (INSEARCH), the prevalence of asthma in India is estimated to be 2.05% among those aged >15 years and the national burden of asthmatics is estimated to be 18 million.[2]

Chronic inflammation in asthma is a consequence of the participation of several mediators that lead to influx of inflammatory cells and airway remodeling as a consequence of goblet cell metaplasia, excessive subepithelial collagen deposition, airway smooth muscle hyperplasia, and increased vascularity. These characteristic features are orchestrated mainly by Type 2 (Th2) cells and cytokines.[3] Thus, the main goal of asthma treatment is to reduce inflammation in the airways and consequently control the disease and its symptoms. Asthma treatment includes inhaled corticosteroids (ICS) and long-acting bronchodilators (LABA), and, more recently, for severe asthma, biologicals that target Th2 mediators.[4]

The approach to the management of asthma recommended by the International Global Initiative for Asthma (GINA) guidelines continues to be based on the severity of the condition, with drugs added on the basis of asthma control. In the era of the personalized medicine, it is important to define biomarkers able to predict the course of the disease and the response to therapy. Despite the sustained research efforts during the last years focused on the identification of biomarkers applicable in clinical practice for the management of asthma, only a few biomarkers indicative of T2-high asthma have been described (e.g. IgE, eosinophils in blood and/or sputum, Fractional Exhaled Nitric Oxide [FeNO],

periostin), and their utility in diagnosis, prognosis and therapy is still controversial.[5]

Asthma is a heterogenous disease characterized by multiple biomarkers measurable in biological fluids. To become useful, these biomarkers need to be quantifiable by reliable systems, reproducible in the clinical setting, easy to obtain and cost-effective. Using biomarkers to predict asthma outcomes and therapeutic response to targeted therapies has a great clinical significance, particularly in severe asthma. In the last years, significant research has been realized in the identification of valid biomarkers for asthma.[6] However, not much data is available regarding the relation of clinical symptoms and functional parameters to these biomarkers of airway inflammation.

In view of this, this prospective, observational and single-center study carried out in the outpatient and inpatient department of Thoracic medicine, Tirunelveli Medical College Hospital, Tamil Nadu, India from June-2017 to June-2018 was aimed to assess the relation between clinical symptoms, functional parameters and biomarkers of airway inflammation in all stable asthmatic patients of 18–60 years of age.

Method

This prospective, observational and single-center study carried out in the outpatient and inpatient department of Thoracic medicine, Tirunelveli Medical College Hospital, Tamil Nadu, India from June-2017 to June-2018 was aimed to assess the relation between clinical symptoms, functional parameters and biomarkers of airway inflammation in all stable asthmatic patients of 18–60 years of age. Ethics approval was obtained from Tirunelveli Medical College Institutional Ethical Committee (TIREC). Inclusion Criteria involved all stable asthmatic patients of 18–60 years of age. Whereas, patients experiencing Acute exacerbation, patients having Clinical features and spirometry suggestive of chronic obstructive pulmonary disease, patients not willing to give consent, patients not able to perform spirometry correctly, patients with history of recent myocardial infarction and patients on chronic corticosteroid therapy were excluded from our study. After obtaining informed written consent from patients, their demographic status (age, sex, BMI, occupation), history (smoking, clinical symptoms and signs, co morbid conditions) and relevant investigations were recorded. The severity of asthma was assessed according to the GINA criteria.

Spirometry: Patients were subjected to PFT with flow sensing MIR Spirobank II and were assessed for post bronchodilator reversibility after administering 200 µg of inhaled salbutamol by repeating the test after 15 min from the baseline.

Statistical analysis

Data were entered in Microsoft Excel and its analysis was carried out in SPSS software version 16.0. Descriptive analysis was performed on all patient data (means and standard deviations. Statistical analysis was performed by t-test. $p<0.05$ was considered statistically significant.

Results

This prospective, observational and single-center study was carried out in the outpatient and inpatient department of Thoracic medicine, Tirunelveli Medical College Hospital, Tamil Nadu, India from June-2017 to June-2018.

Patient distribution: A total of 120 individuals were assessed for eligibility and 19 were excluded due to alternative diagnosis. Therefore, a total of 101 patients were included in the study.
Gender distribution: Out of total 101 cases, 52% (n=53) were male and 48% (n=48) were female.

Table 1: Tabular representation of distribution of gender among study patients

Gender	Frequency	Percent
Male	53	52.5%
Female	48	47.5%
Total	101	100.0%

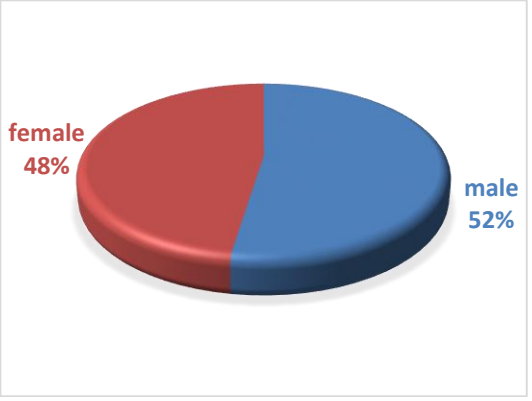

Figure 1: Graphical representation of distribution of gender among study patients

Correlation of gender and severity of asthma

Gender was compared with severity of bronchial asthma and found that most of the females were presented with severe asthma when compared to males showing significant correlation with *p* value of 0.008.

Table 2: Tabular representation of Correlation of gender and severity of asthma

Gender	Severity mild	%	Moderate	%	Severe	%	P value
Male	12	22.64%	18	33.96%	23	43.40%	0.008
Female	7	14.58%	6	12.50%	35	72.92%	
Total	19		24		58		

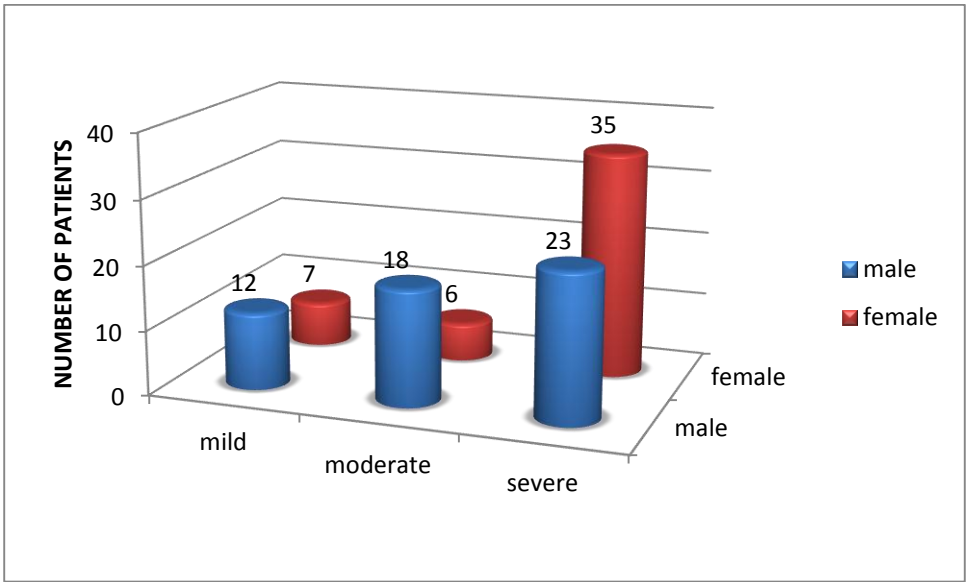

Figure 2: Graphical representation of Correlation of gender and severity of asthma

Gender was compared with sputum and absolute eosinophil showing no significant correlation (p value of 0.576 and 0.943.)
Age distribution: The distribution of age varied from 20 to 60 years. The overall mean age of the study subject was 39 years. Maximum patients were found in the 21 to 40 years age group (56.4%, n= 57) followed by more than 41 to 50 years age group (24.8%, n=25) and least in less than 20 years (5%, n=5)

Table 3: Tabular representation of distribution of age among study patients

Age	Frequency	Percent
18 - 20	5	5.0%
21 - 40	57	56.4%
41 - 50	25	24.8%
50 - 60	14	13.9%
TOTAL	101	100.0%

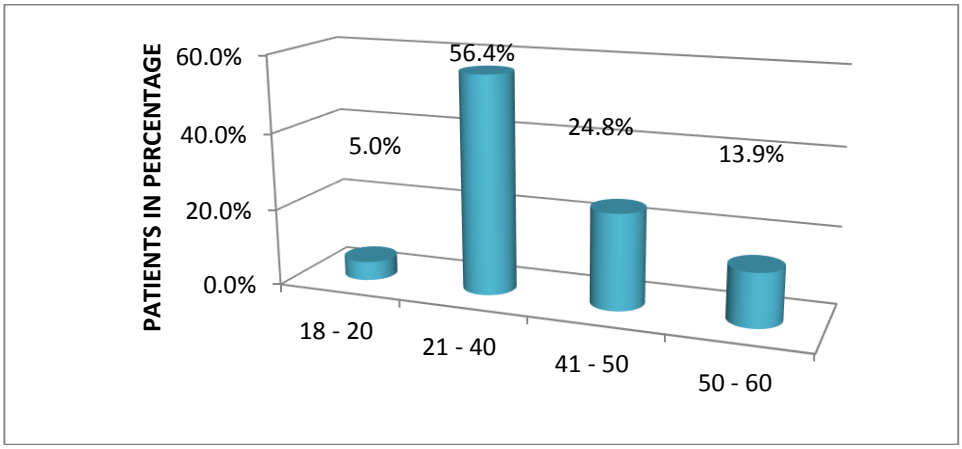

Figure 3: Graphical representation of distribution of age among study patients

Correlation of age group with severity of asthma

Age group was compared with severity of bronchial asthma showing no significant correlation (p value of 0.529.)

Table 4: Tabular representation of Correlation of age and severity of asthma

		Severity			P value
		Mild	Moderate	Severe	
Age group	18 - 20	1	1	2	0.529
	21 - 40	8	19	30	
	41 - 50	6	3	16	
	50 - 60	4	1	9	
Total		19	24	58	

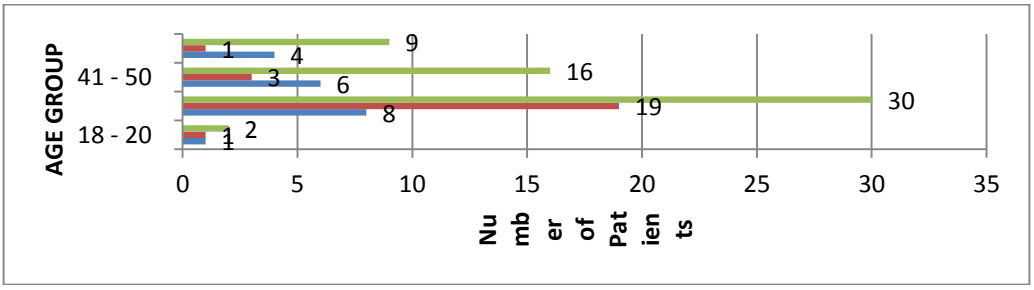

Figure 4: Graphical representation of Correlation of age and severity of asthma

Occupation distribution

Table 5: Tabular representation of occupancy among study patients

Occupation	Frequency	Percent
	60	59.4
Beedi worker	17	16.8%

Construction worker	6	5.9%
Cotton mill worker	4	4.0%
Fire worker	2	2.0%
Other	12	11.9%
Total	101	100.0%

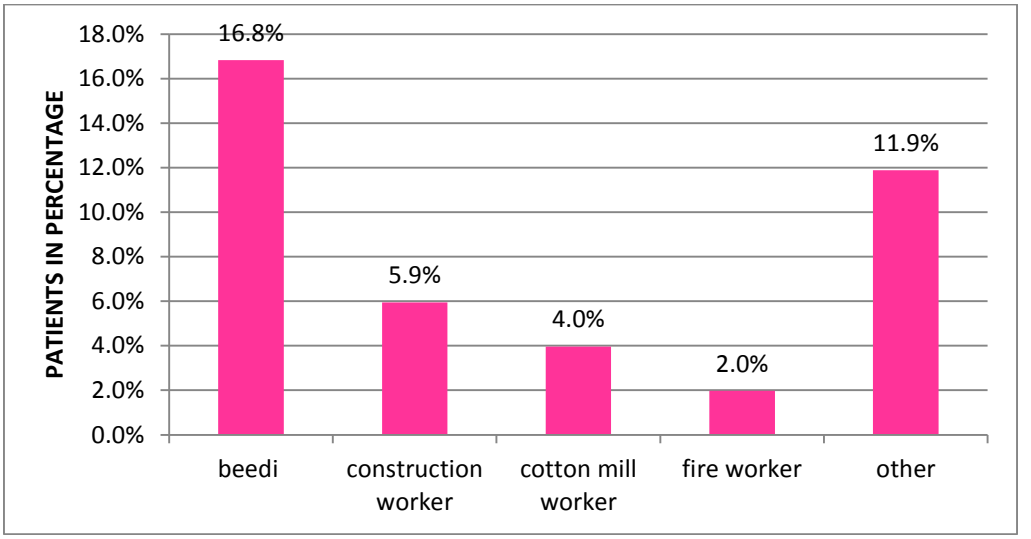

Figure 5: Graphical representation of distribution of occupation among study patients

In our study, 59.4 % cases were exposed to occupation related risk factor among them 16.8% were beedi worker.

Correlation of environmental exposure history and severity of asthma

Table 6: Tabular representation of correlation of environmental exposure history and severity of asthma

		Severity			P value
		Mild	Moderate	Severe	
Environment	No	13	17	30	0.186
	Yes	6	7	28	
Total		19	24	58	

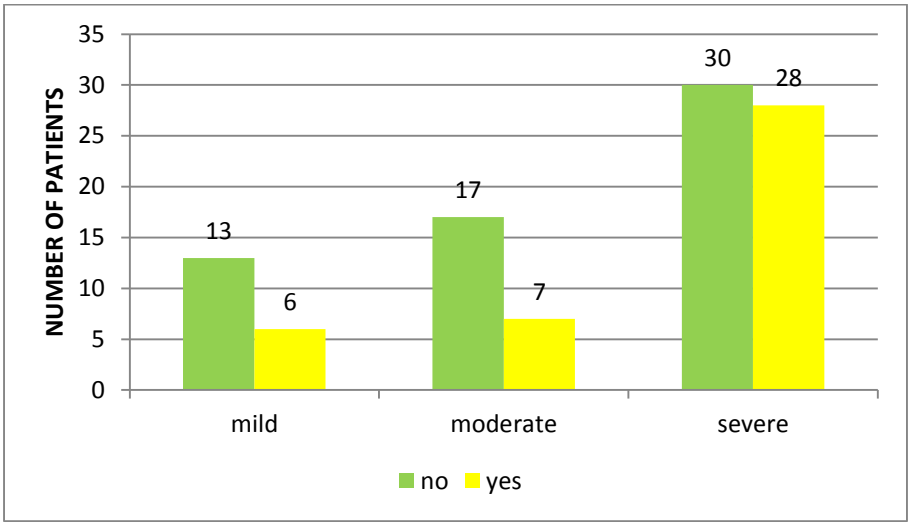

Figure 6: Graphical representation of correlation of environmental exposure history and severity of asthma

In our study, patients who had an environmental exposure history (n=41) correlated with severity of asthma showed no significant correlation (p value of 0.186).

Distribution of smokers

Table 7: Tabular representation of Distribution of smokers

		Severity		
		Mild	Moderate	Severe
Smoker	No	19	23	50
	Yes	0	1	8

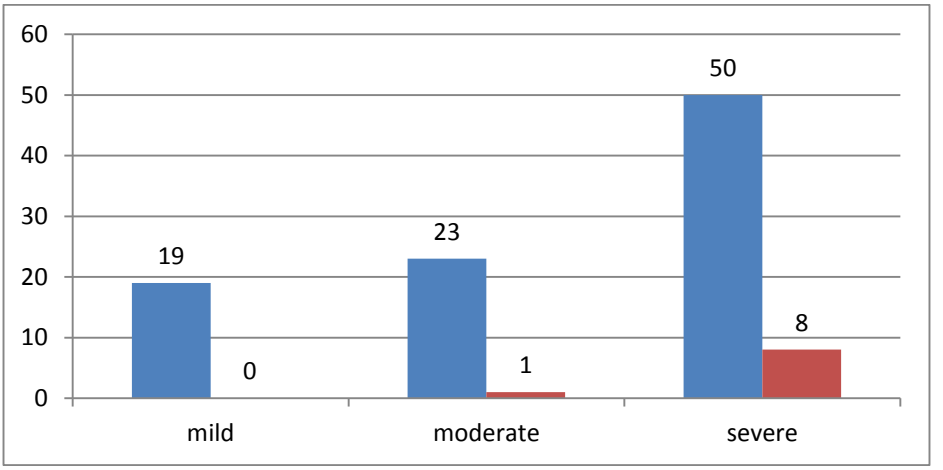

Figure 7: Tabular representation of Distribution of smokers

Total 9 Smokers in our study, out of them 8 were severe asthmatics.

Correlation of family history with severity of asthma

Table 8: Tabular representation of Correlation of family history and severity of asthma

		Severity		
		Mild	Moderate	Severe
Family history	No	5	7	16
	Yes	14	17	42
Total		19	24	58

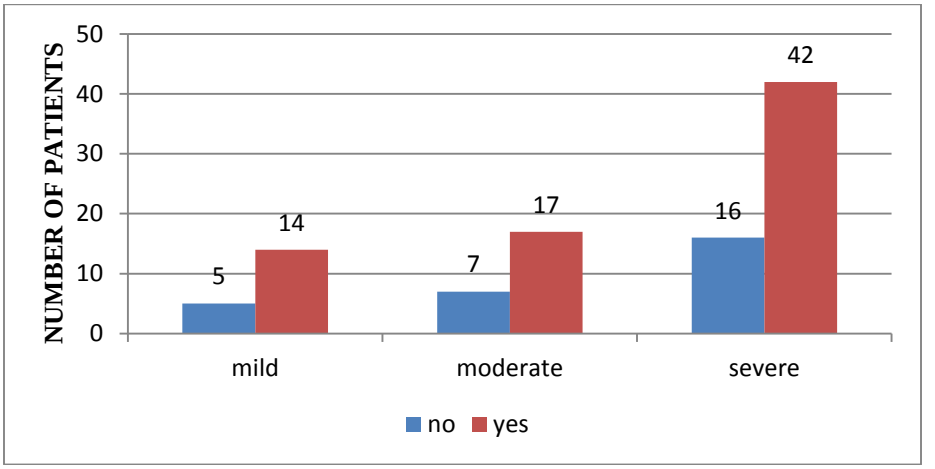

Figure 8: Graphical representation of Correlation of family history and severity of asthma.

Out of 101 cases, 73 cases had a family history and most of them were severe asthmatics.

Correlation of type of allergy with severity of asthma

Table 9: Graphical representation of Correlation of type of allergy with severity of asthma

ALLERGIES	SEVERITY			P VALUE
	MILD	MODERATE	SEVERE	
Dust	19	21	51	0.276
Pollen	0	11	28	0.001
Drugs	0	1	0	0.198
Seasonal	19	22	52	0.349

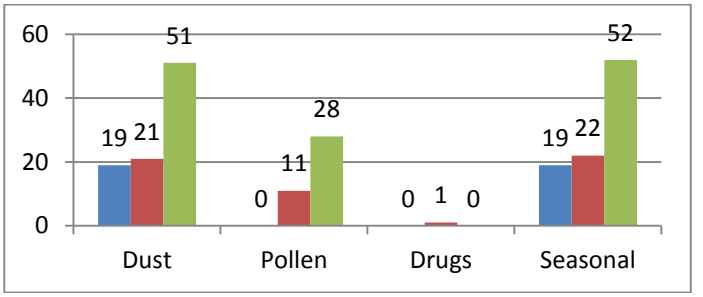

Figure 9: Graphical representation of Correlation of type of allergy with severity of asthma

Among 101 cases, dust and seasonal allergens were the most common triggering factors. Allergens were correlated with severity of asthma, showed no significant correlation except pollen with p value of 0.001.

Correlation of asthma co-morbidity and severity of asthma

Table 10: Tabular representation of asthma co-morbidity and severity of asthma

Co-morbidities	Severity			P value
	Mild	Moderate	Severe	
Depression	2	2	3	.694
Osa	0	0	2	.469
Gerd	4	3	8	.693
Rhinosinusitis	3	5	24	.04

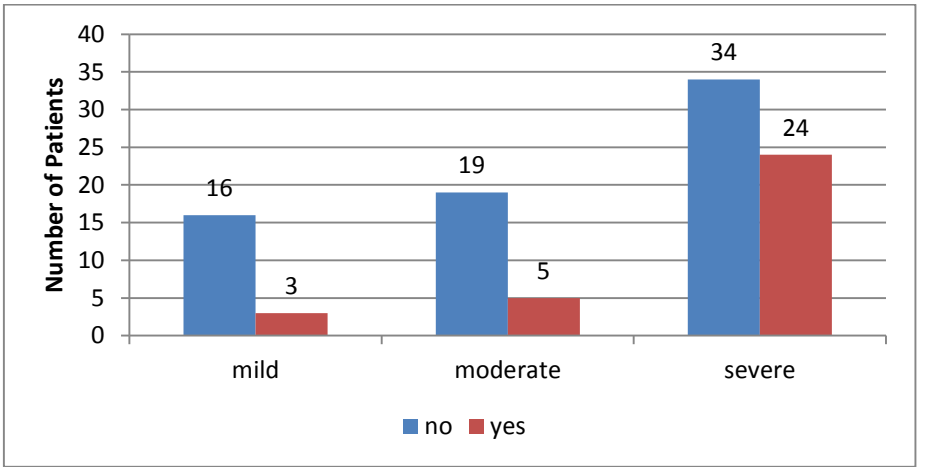

Figure 10: Graphical representation of asthma co-morbidity and severity of asthma

Rhinosinusitis was the common co-morbidity of asthma in our study (n = 32) showed a significant correlation with severity of asthma (p value .04)

Discussion

In our study, total 101 cases were selected, out of them 52% (n=53) were male and 48% (n=48) were female. According to 2012 census (INSEARCH), in India prevalence of asthma is 2.05 % with almost equal sex proportion of male 1.09% and female 0.96%.[2] In United states of America, asthma prevalence was higher among children (9.3%) than adults (8.0%).[7] Overall, females (9.5%) were more than males (7.0%). Although the female-to-male balance changes over development, with asthma less common in females than males during childhood, but more common in females than males during adulthood because of hormonal factors.[8]

Gender were compared with severity of bronchial asthma and found that most of the females were presented with severe asthma when compared to males showing significant correlation (p value 0.008). In various literatures, asthma in women was reported to be more severe and associated with higher health care use. After puberty, a gender switch occurs, and asthma becomes more prevalent and severe in women. Girls who mature early, and pregnant women are likely to be exposed to higher estrogen levels, and greater cumulative hormonal exposure of sex hormones, which place them at higher risk for asthma development later in life. In contrast, oral contraceptive may be protective and decrease the risk of exacerbation in asthmatic women.[9]

In our study, the distribution of age varied from 20 to 60 years. The overall mean age was 39 years. Maximum patients were found in the 21 to 40 years' age group (56.4 %, n= 57) followed by more than 41 to 50 years' age group (24.8%, n=25) and least in less than 20 years (5%, n=5). In most of the studies, common age group prevalence in adult population is between 18 to 40.[10] Asthma is more common in children in the 5 to 14 years' age group. Being a chronic disease, the cumulative prevalence of asthma increases as the age advances.[11,12]

We found 59.4 % cases were exposed to occupation related risk factor, among them 16.8% were beedi workers. According to literatures, a systematic analysis of population attributable risk showed that an estimated 16.3% of all cases of adult-onset asthma are caused by occupational exposure. There was discrepancy between the rates of asthma diagnosed by a health professional as being work related (4.7% of all new asthma cases) and rates that include self-reported cases of work-related asthma (18.2% of all new asthma cases).[13,14]

In our study we found that there was no significant correlation between the environmental exposure population group, severity and eosinophil count. In our study, cases who had a family history, smokers, most of them were severe persistent asthmatics and there was no significant correlation to eosinophil count. In literatures, tobacco Smoking was another important cause of increased asthma morbidity among both children and adults.[15]

Dust and seasonal allergens are the most common triggering factors in our study. Allergens were correlated with severity of asthma showing no significant correlation except pollen with p value of 0.001. Polluted country like India, inhaled substance particle are the strongest risk / triggering factor in developing

asthma. Rhinosinusitis was the common co-morbidity of asthma in our study (n = 32) showed a significant correlation with severity of asthma (p value .04). Currently, the prevalence of allergic rhinitis worldwide is between 20 and 30 %, increased from approximately 10–15 % at the midpoint of the twentieth century. According to literatures,10-40% of patients with allergic rhinitis have asthma, the majority of patients with asthma (70-90%) have allergic rhinits and it is the major risk factor for poor asthma control.[16]

Conclusion

In conclusion, the prevalence of asthma was more in middle age group with equal sex ratio. Dust and seasonal allergens are the most common triggering factors. Beedi workers were more when compared to other occupations. Risk factors for severe asthma was female sex, environment dust exposure, smoking, who had family history, long duration of symptoms and rhinosinusitis co-morbidity.

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