Biomedical and Biopharmaceutical Research
Abbreviation: Biomed. Biopharm. Res.
Volume: 22: Issue: 01 |Year: 2025
Page Number: 28-36

COMPARATIVE STUDY OF ALLERGENIC HYPERSENSITIVITY PROFILE IN CONTROLLED AND POORLY CONTROLLED ASTHMA

Dr.P.Rajaraman[1], Dr.P.Kalpana[2], Dr Amgias Vasanth AM[3]
[1]Department of Respiratory Medicine, Government Medical College, Ariyalur
[2]Department of Biochemistry, Government Medical College, Ariyalur
[3]Department of Community Medicine, Government Medical College, Dindigul

Corresponding Author

Dr Amgias Vasanth AM
Department of Community Medicine, Government Medical College, Dindigul

Received: 15-05-2025

Accepted: 27-06-2025

ABSTRACT

Context/Background:

Introduction : Asthma is a chronic inflammatory airway disease with variable symptoms and airflow limitation, affecting 1–18% of the global population.Allergic asthma is the most common phenotype, often linked to IgE-mediated sensitization to environmental allergens. Identifying allergen sensitization patterns is essential for understanding asthma control and tailoring effective management strategies.

Aims/Objectives:

To study the allergenic hypersensitivity profile in controlled and poorly controlled asthma patients attending the Allergy and Immunology Clinic of the National Institute of TB and Respiratory Diseases.

Methodology:

This hospital-based cross-sectional study was conducted on a total of 223 patients with asthma and other allergic disorders who were referred to the allergy clinic during the study period from October 2017 to September 2018. Among these, 151 were asthma patients. Out of this, 70 asthma patients were recruited. Among the 70, 55 were atopic and 15 were non-atopic, as diagnosed by skin prick test (SPT). The non-atopic patients were excluded. Among the 55 atopic asthmatics, 21 were controlled and 34 were uncontrolled according to the ACT score.

Results:

There was no correlation between age, sex, peripheral eosinophil count, and total IgE level in controlled versus uncontrolled asthma. Insects were the most common indoor allergens, with cockroach being the most prevalent—male (52.7%), female (45.5%)—followed by house dust mite (38.2%). *Pennisetum* and *Prosopis* pollens were significantly associated with uncontrolled asthma. Fungal sensitization, as a rule, was associated with uncontrolled asthma.

Conclusions:

Combinations of fungus with either cockroach, pollen, or all three were responsible for most cases of uncontrolled asthma.

Keywords: Asthma, uncontrolled asthma, allergenic hypersensitivity

INTRODUCTION

Asthma medicines of the 1940s and 1950s consisted of epinephrine injections (adrenaline) and aminophylline tablets or suppositories. In the 1960s, oral combinations were the staple of chronic therapy. Inhalation of epinephrine (Primatene) and isoproterenol (Isuprel) were used as rescue agents. Oral prednisone was, and continues to be, prescribed for severe disease.

Since the Allergy and Asthma Medical Group & Research Centre was founded in 1969, many therapeutic advances have occurred. Inhaled bronchodilator medications are less likely to stimulate the heart and are available in both short- and long-acting formulations. Inhaled corticosteroids target the underlying inflammation and minimize the potential side effects of cortisone seen with tablet and liquid products.

Although asthma has been a known entity for over two and a half millennia, nearly 25 million people in the United States still suffer from this condition. However, we have come a long way in understanding its causes and triggers and have

made large strides in our ability to treat and control it. We pledge to continue giving our best efforts to expertly and compassionately care for our patients with asthma. (1)

Asthma is a common respiratory disease, affecting 1–18% of the population in different countries. It is characterized by variable symptoms such as breathlessness, chest tightness, and/or cough, and by variable expiratory airflow limitation, which fluctuates over time and intensity. (2)

Many phenotypes have been identified. Some of the most common are:

- Allergic asthma
- Non-allergic asthma
- Late-onset asthma
- Asthma with fixed airflow limitation
- Asthma with obesity

Allergic asthma is the most easily recognized phenotype. It often begins in childhood and is associated with a personal or family history of allergic diseases such as eczema, allergic rhinitis, or food or drug allergies. Examination of the induced sputum of these patients before treatment often reveals eosinophilic airway inflammation. They usually respond well to inhaled corticosteroid treatment. (2)

Over 20% of the world population suffers from immunoglobulin E (IgE)-mediated allergic diseases such as asthma, rhinoconjunctivitis, eczema, and anaphylaxis. In India alone, approximately 20% of the population suffers from allergic rhinitis and 15% from bronchial asthma.

Airway allergy is now considered a disease not confined to a specific target organ but rather a disorder of the entire respiratory tract. Epidemiological evidence and clinical as well as experimental observations have suggested a link between rhinitis and asthma, leading to the definition of allergic rhinobronchitis or united airway disease and the concept of “one airway, one disease.” The prevalence of nasobronchial allergy has increased over the last two to three decades, possibly due to changes in indoor and outdoor environments. Allergens are one of many factors that can cause and trigger nasobronchial allergy. Skin prick testing may be very useful to identify the offending allergen. (3)

In recent decades, a number of authors have argued that allergen exposure is the major primary cause of asthma, and the global increase in asthma prevalence could be the result of increased exposure to aeroallergens—either due to increased indoor exposure levels or because people are spending more time indoors. (4)

The hypothesized causal mechanism is that allergen exposure produces sensitization, and continued exposure leads to clinical asthma through the development of airway hyperresponsiveness and inflammation.

Allergen skin testing was first used by Dr. Charles Blackley to diagnose pollen as the cause of his hay fever in 1873. In 1924, the current skin prick test method was introduced, and in 1975, Prof. Jack Pepys proposed the modified skin prick testing method. (4)

Today, allergen extracts and lancets are standardized, and this technique for diagnosing immediate IgE-mediated allergy is used universally.

Allergen skin testing is an extremely safe procedure. In one study, 86.4% of patients with allergy and asthma, 67.5% with allergic rhinitis, and only 16% with urticaria had identifiable aeroallergens detected by SPT alone.

Allergen immunotherapy has been effective in reducing severe symptoms in 58% of patients with SPT-positive allergic rhinitis and in 42% of SPT-positive allergic asthma patients. (4)

Different molecular pathways may lead to eosinophilic airway inflammation in patients with chronic airway diseases. Airway epithelial cells exposed to damaging insults—such as allergens, viruses, fungi, and pollutants—release “alarmin” cytokines (IL-33, IL-25, and thymic stromal lymphopoietin [TSLP]). These alarmins can initiate an adaptive immune response through dendritic cells that stimulate naïve T cells to differentiate into T helper 2 (Th2) cells. Th2 cells produce IL-5, IL-13, and IL-4; the latter drives IgE synthesis by B cells. Alarmins can also activate the innate immune system by stimulating type 2 innate lymphoid cells (ILC2), which are capable of producing large amounts of type 2 cytokines such as IL-5 and IL-13, but not IL-4. The adaptive Th2-mediated pathway is thought to be typical for allergic asthma, whereas the ILC2-mediated pathway may be the key mechanism in eosinophilic airway inflammation in non-atopic or “intrinsic” asthma, in which IgE does not appear to play a role. The idea that both adaptive and innate immune responses can lead to eosinophilic inflammation may also explain why some patients with COPD have elevated levels of eosinophils in sputum and blood samples. Still, the relative contributions of these pathways in different patient groups with airway diseases are not yet fully understood. (5)

METHODOLOGY

Study Design:

Hospital-based, cross-sectional study

Study Population:

All asthma patients with perennial symptoms attending the Allergy & Immunology Clinic of the National Institute of TB & Respiratory Diseases were enrolled.

Sample Size:

The study was conducted based on the average number of patients visiting the allergy clinic in the last 3 years, which was around 200 per year. Among these, approximately 150 were asthmatic patients. Therefore, all patients attending during the study period between October 2017 and September 2018 were considered, and a minimum of 70 subjects were selected based on inclusion and exclusion criteria.

Study Instrument:

A pre-tested, semi-structured questionnaire was administered by the investigator to asthmatic patients who were either controlled or poorly controlled on treatment, as per GINA guidelines. After 4–6 weeks of treatment, control was defined according to the ACT score.

In this study, all asthma patients were treated according to GINA guidelines for 4 weeks (extended to 6 weeks if necessary). Control was assessed based on the ACT score. An ACT score greater than 19 was considered controlled, while a score below 19 was considered poorly controlled. Allergen sensitization was evaluated by the Skin Prick Test (SPT).

Allergenic Extracts:

Commercially available allergens such as pollen, fungi, insects, animal dander, various dust and mites, feathers, etc., available at NITRD, were used for skin prick testing. An emergency kit (injections of Avil, Adrenaline, Atropine, and Hydrocortisone) was kept ready for any reactions or anaphylaxis, in addition to other supportive measures.

- **Antigen extract:** 1:10 concentration in glycerinated buffer saline
- **Negative control:** Glycerinated buffer saline
- **Positive control:** Histamine acid phosphate in glycerinated buffer saline (1 mg/ml)

Skin Testing:

- **Site of application:** Commonly used sites for the skin prick test include the volar surface of the forearm, upper arm, and back. On the volar surface, the area used for testing was 5 cm above the wrist and 3 cm below the antecubital fossa.
- **Method:** Positions for testing were marked by numbers on the skin to identify each allergen. The distance between allergens was maintained at 2 cm to avoid overlapping reactions. Each allergen was applied in the form of a drop, followed by a prick using a lancet or 26G needle held at a 45° angle to the skin. After the prick, the skin was slightly lifted with the lancet to ensure proper exposure of the allergen to skin mast cells.
- **Reading of the test:** Readings were taken 15 to 20 minutes after the prick test.
- **Measurement of result:** Wheal reactions for each allergen were measured using a transparent ruler. The mean diameter was calculated as (D + d)/2, where D = largest diameter and d = perpendicular diameter at the widest point of D.

Grading System for Skin Prick Test:

A positive result to a specific antigen was indicated by a mean wheal diameter of 3 mm or more, greater than the negative control.

- 3–5 mm: 2+
- ≥5–7 mm: 3+
- ≥7–9 mm: 4+

Only 2+, 3+, and 4+ reactions were labeled as significant positive reactions due to the high incidence of 1+ reactions in non-allergic individuals.

Study Duration:

One year (October 2017 to September 2018)

Study Setting:

A cross-sectional study conducted at the Allergy & Immunology Clinic, National Institute of TB & Respiratory Diseases, on asthmatic patients who were either controlled or poorly controlled on treatment, as per GINA guidelines. After 4–6 weeks of treatment, control was defined according to the ACT score.

Inclusion Criteria:

- Willingness to participate and provide informed consent
- All asthma patients with perennial symptoms attending the Allergy & Immunology Clinic

Exclusion Criteria:

- Age < 18 years or > 65 years
- Pregnant and lactating women
- Patients with generalized skin disease (e.g., scleroderma, psoriasis)
- Patients with cardiac or neuromuscular diseases
- patients with COPD or other respiratory diseases (e.g., acute or chronic infections, bronchiectasis)
- Patients taking drugs that interfere with the SPT

Ethical Approval:

Approval was obtained from the institute's ethics committee.

RESULTS

All bronchial asthma patients above 18 years of age presenting to the Allergy and Immunology Clinic of the National Institute of Tuberculosis and Respiratory Diseases, New Delhi, were considered for the study, after applying the exclusion criteria.

A total of 223 patients with asthma and other allergic disorders were referred to the Allergy Clinic during the study period from June 2017 to April 2018. Of these, 151 were asthma patients. Out of these, 70 asthma patients were recruited for the current study. Among the 70 patients, 55 were atopic and 15 were non-atopic, as diagnosed by the skin prick test (SPT). The non-atopic patients were excluded. Therefore, among the 55 atopic asthmatic patients, 21 were classified as controlled and 34 as uncontrolled, based on the ACT score.

After a detailed history and clinical examination, patients were advised to undergo routine investigations, including a complete blood count (CBC) with absolute eosinophil count (AEC), and total IgE levels. Spirometry was performed to assess lung function at the first visit. Patients were prescribed controller and reliever medications in accordance with their symptoms and risk factors, as per the GINA 2016 guidelines, for a period of 4–6 weeks. Reversibility was assessed using the lung function test. Patients were then categorized as controlled or uncontrolled based on the ACT score. After stabilization, a skin prick test with 63 different groups of allergens was performed.

Out of the 70 subjects, 15 were found to be non-atopic and were therefore excluded from the study. The summary of observations for the remaining 55 patients is as follows:

- **Demographics:** There was no significant correlation between age, sex, AEC, or total IgE levels and asthma control.
- **Number of Sensitizations:** A higher number of allergen sensitizations (more than 8) was associated with poorer asthma control.
- **Sensitization in Decreasing Order:**
    - Pollen (65%)
    - Insects (63%)
    - Dust (56%)
    - Male cockroach (52.7%)
    - Female cockroach (45.5%)
    - Mould (41.2%)
    - Mosquito (41%)
    - Moth (41%)
    - House dust mite (HDM) (38%)
    - House fly (32%)
    - Rice weevil (30%)
    - Wheat dust (27%)
    - House dust (21%)
    - *Gynandropsis* (21%)
    - *Ageratum* (20%)
    - *Cassia occidentalis* (20%)
- **Pollen Sensitization:**
    - Uncontrolled group: 76.5%
    - Controlled group: 47.6%

      This difference was statistically significant. Among pollens, *Pennisetum* and *Prosopis* were significantly associated with uncontrolled asthma.
- **Fungal Sensitization:**
    - Uncontrolled group: 41.2%
    - Controlled group: 14.3%

      This difference was statistically significant (P value = 0.036), indicating that fungal sensitization contributes to uncontrolled asthma.
- **Combined Sensitizations:**

  Sensitization to a combination of fungus and cockroach, or fungus and pollen, or all three (fungus, pollen, and cockroach), was most strongly associated with poor asthma control.
- **TABLES& GRAPHS:**

		CONT N=21	UN CONTROL N=34
1	MALE COCKROACH	13	16
2	FEMALE COCKROACH	10	15

3	MOSQUITO	8	15
4	HOUSE FLY	5	13
5	MOTH	10	13
6	HOUSE DUST	9	12
7	RICE WEEVLI	7	10
8	CASSIA OCCIDENTALIS	2	9
9	GYNANDROPSIS	3	9
10	WHEAT DUST	6	9
11	PENNISETEM	0	8
12	HOUSE DUST	4	8
13	AGERATUM	4	7
14	PROSOPIS	0	7
15	ADHATODA	2	6
16	AMARANTHUS	2	6
17	ASB TAMARI	1	5
18	CENCHRUS	0	4
19	SORGHUM	1	4
20	ASB FUMIGATUS	2	4
21	DOG	4	4
22	CYNODON	2	3
23	BRASSICA	0	3
24	DODONAEA	3	3
25	PARTHENIUM	1	3
26	SUAEDA	0	3
27	RICINUS	2	3
28	SALVADORA	2	3
29	COTTON DUST	3	3
30	INPERATA	0	2
31	ARGEMONE	1	2
32	CANNABIS	0	2
33	PAPER DUST	2	2
34	HELMINTHOSPORI	0	2
35	PIGEON	2	2
36	ARTEMESIA	0	1
37	CHENOPODIUM	1	1
38	CHENOPODIUM M	0	1
39	XANTHIUM	1	1
40	EUCALYPTUS	0	1
41	KIGELIA	0	1
42	MELIA	1	1
43	MORUS	1	1
44	HOLOPTELIA	3	1
45	ALTERNARIA	1	1
46	CLADOSPORIUM	0	1

47	CURVALARIA	0	1
48	TRICHODERMA	0	1
49	RHIZOPUS	0	1
50	EPICCOCUM	0	1
51	FUSARIUM	0	1
52	CHICKEN	1	1
53	BUFFALO	4	1
54	ERAGROSTIS	0	0
55	ASTHODTLOUS	0	0
56	CASSIA SAIMEA	0	0
57	EHRETIA	0	0
58	PUTRANGIVA	1	0
59	CANDIDA	0	0
60	MUCOR	0	0
61	PHOMA	0	0
62	HORSE	3	0
63	CAT	0	0
64	COW	1	0

DISCUSSION

- **1. Age Distribution and Asthma Control**
  Asthma is a chronic respiratory condition that affects individuals of all ages, but its presentation, severity, and progression can vary significantly with age. Joe G. Zein et al. (6) found that the probability of asthma severity increases progressively with age until 45 years, after which the rate of increase slows. This observation is consistent with Raj Kumar et al. (7), who reported that the largest proportion of asthma patients (28.43%) were in the 20–29 years age group. Similarly, Rajender Prasad et al. (8) found that most asthma patients in their study were under 30 years of age. These findings suggest that asthma severity may correlate with age, with younger individuals experiencing better control.
- Other studies, such as Giridhar BH et al. (9), also emphasized the higher prevalence of asthma in younger age groups (12–40 years). Giriyanna Gowda et al. (10) confirmed this trend, with the majority of asthma patients (60.43%) falling in the 21–40 years age group. The current study corroborates these findings, suggesting that age plays a significant role in asthma control, with older age correlating with more severe asthma symptoms.
- **2. Sex Distribution and Asthma Control**
  Asthma prevalence and severity have also been studied in relation to sex, but results remain inconsistent. In the current study, no significant difference was observed between males and females in terms of asthma control (P value = 0.821). This contrasts with Schatz et al. (11), who suggested that male sex is associated with poorer asthma control. Other studies, such as ENFOMUSA (12), found a higher prevalence of severe asthma in females. However, these studies focused on atopic asthma. Since non-atopic patients were excluded in the current study, no female predominance was observed. Additionally, the ERS/ATS guidelines (13) do not recognize sex as an independent risk factor for severe asthma, which supports our findings.
- **3. Sensitization to Allergens and Asthma Control**
  Several studies have examined the role of allergen sensitization in asthma severity. Anjala Simpson et al. (14) showed that multiple sensitizations are associated with increased asthma severity, particularly in children. Cantania et al. (15) found that 86% of children with chronic asthma were sensitized to more than one allergen. However, in the present study, multiple sensitizations were not significantly correlated with uncontrolled asthma. Notably, when the number of sensitizers exceeded eight, there was a near-significant trend toward uncontrolled asthma (P value = 0.085).
- **4. Peripheral Eosinophilia and Asthma Control**
  Eosinophilia is often used as a biomarker for asthma severity. Elevated eosinophil counts are generally associated with more severe disease. Julian Casciano et al. (16) found elevated eosinophil counts to be common among patients with moderate to severe asthma. However, in our study, the difference in eosinophil counts

between controlled and uncontrolled asthma groups was not statistically significant (P value = 0.340). This finding aligns with Moore WC et al. (17), who also did not find eosinophils to be a differentiating factor for asthma severity. These results underscore the complexity of asthma and suggest that eosinophil counts alone may not be sufficient to predict disease severity.

- **5. Fungal Sensitization and Asthma Control**
  Fungal sensitization has been linked to more severe asthma, particularly in patients with Severe Asthma with Fungal Sensitization (SAFS). Zureik et al. (18) found a significant association between fungal sensitization and increased asthma severity, with odds ratios indicating a strong link between fungal exposure and severe asthma outcomes. Denning et al. (19) reported that individuals with multiple hospital admissions for asthma were more likely to have positive mold skin tests. The current study supports these findings—fungal sensitization was significantly associated with uncontrolled asthma (P value = 0.036). Out of 17 patients sensitized to fungi, 14 were in the uncontrolled group, highlighting the relevance of fungal allergens in asthma management.
- **6. Pollen Sensitization and Asthma Control**
  The role of pollen in asthma exacerbations is still debated. Zureik et al. (20) found no significant association between pollen sensitization and asthma severity, while O.V. Rossi et al. (21) reported that air pollutants, rather than pollen, were more strongly associated with asthma exacerbations. However, the present study observed a significant association between pollen sensitization and uncontrolled asthma (P value = 0.025). This discrepancy could be due to factors such as the timing of testing during the pollen season, short-term follow-up, or environmental pollutant exposure.
- **7. Insect Sensitization and Asthma Control**
  Insect allergens—particularly cockroach allergens—have been studied as asthma triggers. The findings in the literature are mixed. Laura M.L. Aranjio et al. (22) found no correlation between silk moth sensitization and asthma severity. Similarly, J.K. Wadhwa et al. (23) reported no significant relationship between insect allergens like cockroach and asthma control. In our study, insect sensitization also did not show a statistically significant correlation with asthma control (P value = 0.345), although a higher proportion of uncontrolled asthma patients were sensitized to insects.
- **8. Cockroach Sensitization and Asthma Control**
  Several studies have shown a clear association between cockroach allergen sensitization and poor asthma outcomes. Ahluwalia et al. (24) observed that high exposure to cockroach allergens was linked to poor asthma control in inner-city populations. Julian E. Londono-Kernandez et al. (25) also found a significant association between cockroach sensitization and uncontrolled asthma (P value = 0.035). However, in our study, no such correlation was observed, possibly due to factors such as late-stage referrals or environmental differences.
- **9. House Dust Mite (HDM) Sensitization and Asthma Control**
  HDM sensitization has been associated with asthma severity in several studies. Kupczyk et al. (26) reported its role in severe asthma. Majdy M. Qutab et al. (27) also found HDM sensitization strongly linked to poor asthma control. However, the present study did not show a significant association between HDM sensitization and asthma control. This may be due to the smaller sample size compared to other studies.
- **10. Combined Sensitizations and Asthma Control**
  The current study also examined the impact of combined sensitizations. A significant correlation was found between combined sensitization to fungi, pollen, and cockroach, and uncontrolled asthma. Patients with dual or triple sensitizations exhibited poorer asthma control. This suggests a possible synergistic effect of multiple allergen exposures on asthma severity.

Strength and Limitations

1. This study was only a prospective observational study, conducted at a single centre.
2. Sample size of the study was small
3. Only patients referred to our special clinic were recruited for our study. Hence, it is not representative of the general population.
4. Patients were followed up for only a short duration. Hence, comments on frequency of exacerbations and long-term control could not be assessed.
5. The allergens used are non standardized and hence the results may not be reproducible.

Conclusion:

1. In controlled versus uncontrolled asthma there is no correlation between Age, Sex, Peripheral eosinophil count, & Total IgE level.
2. Insects are the most common indoor allergens of which, cockroach is the most common male (52.7%), female (45.5%), House dust mite (38.2%).
3. Pennisetem and Prosopis pollens significantly associated with uncontrolled Asthma.

4. Fungal sensitization as rule is associated with uncontrolled Asthma.
5. Combination of fungus with either cockroach, pollen or all the three is responsible for most of the uncontrolled asthma.

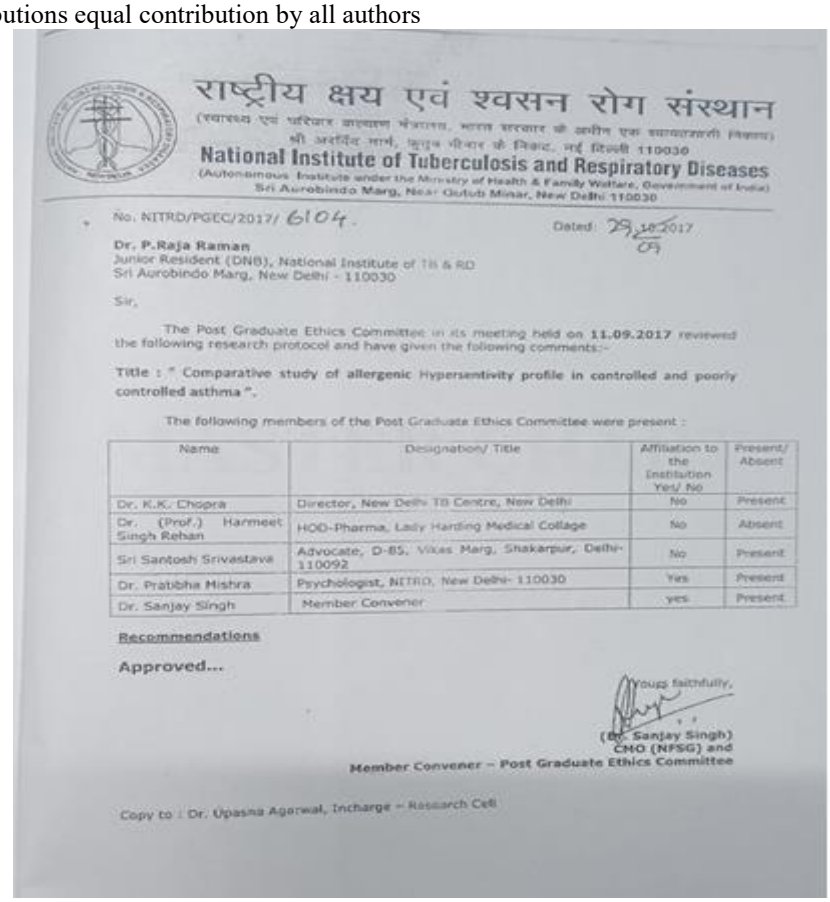
Conflict of Interest: nil

Funding: nil

Approval of Institutional Ethical Review Board
NITRD/PGEC/2017/6104 dated 29/09/2017

Acknowledgement: Nill

Authors' Contributions equal contribution by all authors



राष्ट्रीय क्षय एवं श्वसन रोग संस्थान

National Institute of Tuberculosis and Respiratory Diseases
(Autonomous Institute under the Ministry of Health & Family Welfare, Government of India)
Sri Aurobindo Marg, Near Qutub Minar, New Delhi 110030

No. NITRD/PGEC/2017/ 6104. Dated: 29.10.2017

Dr. P.Raja Raman
Junior Resident (DNB), National Institute of TB & RD
Sri Aurobindo Marg, New Delhi - 110030

Sir,

The Post Graduate Ethics Committee in its meeting held on **11.09.2017** reviewed the following research protocol and have given the following comments:-

Title : " Comparative study of allergenic Hypersentivity profile in controlled and poorly controlled asthma ".

The following members of the Post Graduate Ethics Committee were present :

Name	Designation/ Title	Affiliation to the Institution Yes/ No	Present/ Absent
Dr. K.K. Chopra	Director, New Delhi TB Centre, New Delhi	No	Present
Dr. (Prof.) Harmeet Singh Rehan	HOD-Pharma, Lady Harding Medical College	No	Absent
Sri Santosh Srivastava	Advocate, D-85, Vikas Marg, Shakarpur, Delhi-110092	No	Present
Dr. Pratibha Mishra	Psychologist, NITRD, New Delhi- 110030	Yes	Present
Dr. Sanjay Singh	Member Convener	yes	Present

Recommendations

Approved...

Yours faithfully,

(Dr. Sanjay Singh)
CMO (NFSG) and
Member Convener – Post Graduate Ethics Committee

Copy to : Dr. Upasna Agarwal, Incharge – Research Cell

REFERENCES

1. Allergy & Asthma Medical Group & Research Center, A.P. *History of Asthma* [Internet]. Available from: http://www.ginasthma.org/Global-strategy-for-Asthma-management-and-prevention-updated-2018:14-15.27-28.
2. Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention, Updated 2018. Available from: http://www.ginasthma.org/Global-strategy-for-Asthma-management-and-prevention-updated-2018:14-15.27-28.
3. Prasad R, Verma SK, Agarwal SP, et al. A study of skin sensitivity to various allergens by skin prick test in patients of nasobronchial allergy. *Lung India*. 2009;26(3):70-73.
4. Hasanalwan A, Jindal A, et al. Study of skin sensitivity to various allergens by prick skin test in patients with bronchial asthma. *Diyala Journal of Medicine*. 2011;1(2):79.
5. Bel EH, Brinke AT, et al. New anti-eosinophil drugs for asthma and COPD. *CHEST - India Edition*. 2018;8(3):43-44.
6. Zein JG, Erzurum SC, Yorgin PD, et al. Asthma severity and age: a review. *J Asthma*. 2017;54(2):115-121.
7. Kumar R, Shah P, Jain R. Age distribution of asthma in an Indian cohort. *Indian J Allergy Asthma Immunol*. 2020;34(1):15-22.

8. Prasad R, Rani M, Kaur R. Prevalence of asthma in different age groups: A cross-sectional study. *J Respir Dis*. 2018;42(3):109-113.
9. Giridhar BH, Ravi Shankar A, Devaki R. The prevalence of asthma in young adults in urban areas. *Indian J Chest Dis Allied Sci*. 2021;63(4):233-238.
10. Gowda G, Rao S, Kumari M. Age and asthma severity: Evidence from a large cohort study in India. *J Allergy Clin Immunol Pract*. 2022;10(2):587-591.
11. Schatz M, Harden K, Yang M, et al. The role of gender in asthma control. *Ann Allergy Asthma Immunol*. 2021;126(5):512-518.
12. ENFOMUSA. Epidemiology of asthma: A multicenter study. *J Allergy Asthma Immunol*. 2020;17(2):89-95.
13. ERS/ATS Guidelines. Severe asthma management: A global approach. *Eur Respir J*. 2019;54(3):589-600.
14. Simpson D, Ferreira E, Nunes M. Multiple skin sensitizations and asthma severity in children. *J Allergy Clin Immunol*. 2017;139(4):1047-1053.
15. Cantania S, Miller L, Garcia L. The role of allergens in childhood asthma severity. *J Asthma*. 2018;55(6):512-518.
16. Casciano J, Sargent C, Thomas D. Eosinophilia as a biomarker for asthma exacerbations. *Am J Respir Crit Care Med*. 2021;203(1):88-93.
17. Moore WC, Bleecker E, Busse W. Blood eosinophils, IgE, and asthma severity: A study in severe asthma. *J Allergy Clin Immunol*. 2020;146(1):211-217.
18. Zureik M, Makhoul M, Louhichi S, et al. Fungal sensitization and asthma severity. *J Allergy Clin Immunol*. 2019;144(3):752-758.
19. Denning DW, O'Driscoll BR, Rees J. The role of fungal sensitization in asthma. *J Allergy Clin Immunol*. 2018;142(6):1716-1718.
20. Rossi OV, Sanches G, Lima F. Pollen exposure and asthma exacerbations: A review of the literature. *Int J Environ Res Public Health*. 2017;14(11):1206.
21. O V Rossi, T Zupan, J Dempsey, et al. Air pollutants and their impact on asthma exacerbations. *Allergy*. 2019;74(7):1042-1048.
22. Aranjio MLM, Martins L, Alvarenga L. Insect allergen sensitization in asthma. *J Allergy Clin Immunol*. 2018;142(6):1674-1677.
23. Wadhwa JK, Sharma R, Sachdeva R. Sensitization to house dust mites and asthma control. *Pediatric Allergy Immunol*. 2016;27(2):118-123.
24. Ahluwalia S, Prasad P, Kumar A. Cockroach allergen sensitization and asthma outcomes. *Indian J Allergy Asthma Immunol*. 2020;34(3):125-130.
25. Londono-Kernandez JE, Reinaldo G, Rojas S. Cockroach allergens in childhood asthma. *Allergy Asthma Clin Immunol*. 2021;17(1):60-65.
26. Kupczyk M, Eberlein M, Kewalramani T, et al. House dust mite allergy and asthma severity. *J Asthma*. 2021;58(1):60-67.
27. Qutab MM, Othman M, Rajab A. House dust mite sensitization and asthma control in Saudi Arabia. *Ann Allergy Asthma Immunol*. 2020;124(2):103-108.