Bronchial asthma is an inflammatory disease of the airways causing reversible airflow obstruction, airway hyper responsiveness, mucous hyper secretion and airway wall remodelling. Incidence of allergic asthma has increased in the past few years due to urbanisation. The disease has affected more than 300 million people worldwide with around 250,000 annual deaths. Prevalence of asthma among atopic subjects is 12.9%. The strongest risk factor for asthma is atopy which is the genetic propensity to develop IgE antibodies in response to exposure to allergen. Allergens and allergen-specific IgE antibody assays are assessed by skin prick test (SPT). Prevalence of asthma among atopic subjects is 12.9%. There is an increase in the global prevalence and economic burden of allergic diseases. Population based studies have shown a definitive relationship between serum total immunoglobulin E (IgE) and asthma.

Bronchial hyper responsiveness is a fundamental feature of asthma and thought to have a heritable component. Studies in both humans and animals have revealed a genetic propensity to bronchial hyper responsiveness. A greater concordance for this trait among monozygotic twins than among dizygotic twins has been observed. In children with no history or symptoms of atopy or asthma, bronchial hyper responsiveness is strongly associated with elevated serum IgE levels. Population studies clearly reveal a very strong association between atopy and bronchial hyper responsiveness.

Major locus regulating serum IgE levels is on chromosomes 5q31-q33. This chromosomal region is rich in candidate genes, and many of them regulate IgE production either directly or indirectly and affect the activation and proliferation of cells involved in inflammatory processes associated with bronchial hyper responsiveness, allergy and asthma.

It has been reported that IgE production is tightly controlled by a balance between T helper type1 (Th1) and T helper type2 (Th2) cytokines, interleukin (IL) 4 and 13 being involved in the immunological switching towards
IgE production. Th17 and Th9 cell subtypes are known to contribute to the inflammation or enhancing smooth muscle contraction or stimulating mast cells.\textsuperscript{1}

Published studies have revealed the association between airway hyper responsiveness and the number of allergen sensitisations.\textsuperscript{4,7} A study reported that the development of sensitisation to perennial allergens early in life (<3 years of age) combined with exposure to high allergen levels was predictive of chronic asthma and reduced lung function at the age of 13 years.\textsuperscript{3} In South Korea, house dust mites (HDMs) are the primary inhalant allergens with about 60% of the population sensitised to HDMs\textsuperscript{18} whereas its sensitisation in asthmatics is around 40-80% in many parts of Asia.\textsuperscript{7,19}

The sensitisation rate among cats was reported to be 15.5%, which is comparable to 20.4% for dogs in pet-owners.\textsuperscript{20}

Allergic asthma and aeroallergen sensitisation is relatively less explored in the local population. The current study was planned to assess the frequency of allergic asthma among local patients of bronchial asthma and to highlight the importance of common causative aeroallergens in allergic asthma.

**Patients and Method**

This descriptive cross-sectional study was conducted at the Department of Immunology, Armed Forces Institute of Pathology (AFIP), Rawalpindi, Pakistan, from March 2014 to March 2016. After approval was obtained from the institutional ethics committee, clinically-diagnosed male and female patients attending the pulmonology clinic for bronchial asthma, referred from various hospitals of Rawalpindi and Islamabad, were included in the study. Sample size was determined using World Health Organisation (WHO) sample size calculator.\textsuperscript{21} Confidence interval was set at 95%. Absolute precision required was 6.5% with an anticipated population proportion of 12.9%.\textsuperscript{5}

The subjects were included on the basis of signs and symptoms and a decreased forced expiratory volume first (FEV1)/Forced vital capacity (FVC) ratio below 70%. Patients with signs and symptoms of chronic obstructive pulmonary disease (COPD) and those on systemic steroid therapy were excluded. There was representation from all provinces of Pakistan except Baluchistan.

Whole blood samples were obtained from each patient in plain serum collection tubes. Serum total IgE antibody levels were determined in patient serum using a commercially available enzyme-linked immunosorbent assay (ELISA) kit (Amgenix, UK).

SPT was performed using allergen extracts of 18 common aeroallergens. The test was performed by placing a drop of the allergen extract on the skin. Insulin syringe was used to puncture the skin and the results were checked in 15-20 minutes. A negative saline control was also included in each test. SPT are regarded positive if the mean wheal diameter is >3mm at the SPT.\textsuperscript{9} Allergen extracts for SPT were procured from abroad (Greerlabs, USA) and included allergens of HDMs, paper mulberry, grass, mixed pollen, neem and eucalyptus, cannabis, dandelion, ragweed, bottle brush, cockroach, cat and dog hair, wasp and pigeon feathers, Candida albicans, Alternaria alternata and Aspergillus fumigatus.

Frequency and percentages were calculated for gender, atopic asthma and allergen sensitisation. Mean and Standard Deviation (SD) were calculated for numerical data like age and serum total IgE using SPSS 20. Significance of association of raised serum total IgE with development of allergic asthma was calculated using Chi square test. Level of significance was set at 0.05. Odds ratio (OR) was calculated at 95% confidence interval (CI) for which upper limit was set at 15.7 and the lower limit at 2.81.

**Results**

Of the 105 patients, 62 (59.05%) were males and 43 (40.95%) were females. The mean age was 29.9±10.2 years (range: 18-53 years) for males, and 28.7±7.0 (range: 19-43 years) for females.

Overall mean serum total IgE of the patients was 285.01±241.39IU/ml (Table-1) which was compared with the cut-off value for adult patients which is 150 IU/L.

SPT (SPT) was performed on all the patients (Table-2).

<table>
<thead>
<tr>
<th>Range (IU/L)</th>
<th>Mean (IU/L)</th>
<th>SD</th>
<th>Patients with raised total IgE</th>
<th>Patients with normal total IgE</th>
</tr>
</thead>
<tbody>
<tr>
<td>25-860</td>
<td>285.01</td>
<td>±241.39</td>
<td>60 (57.14%)</td>
<td>45 (42.86%)</td>
</tr>
</tbody>
</table>

IgE: Immunoglobulin E.
There is an increase in the global prevalence and economic burden of allergic diseases. Environmental factors are considered to play a more important role than genetic factors for the recent increment in the prevalence of allergic diseases. Environmental factors such as smoking, lifestyle, obesity, pets, diet, and air pollution are considered causative or aggravating factors for allergic diseases. Therefore it is very important to accurately investigate the prevalence of allergic diseases and the level of exposure to indoor and outdoor allergens.

IgE-mediated allergic reactions to environmental allergens play a very significant role in the pathophysiology of asthma. Atopic persons have high levels of IgE which is reactive against one or more specific environmental allergens and they also often have increased plasma total IgE concentrations. Also, the prevalence of asthma is quite closely related to serum IgE levels standardised for age and gender. Our results indicated that patients with raised total IgE have 6.6 times more chance of developing asthma which is in accordance with international data.

Frequency of allergic asthma in our patients was 57.2% and HDM was the main inhalant allergen causing the highest sensitisation in 35(33.1%) patients, which is in accordance with other regional and international studies.

One study revealed that prevalence of asthma and atopy were 25.5% and 56% respectively in Korean population. HDM was the most common aeroallergen in 60% population followed by cockroach (23.6%), mugwort (22.9%), oak (22.9%), ragweed (10%), Japanese hop (9.1%), dog dander (8.2%), and cat dander, birch, rye grass and Alternaria (5.5%).

A study conducted on Pakistani population revealed that the prevalence of allergic asthma was 19.36%. Sensitisation of various inhalant allergens was: pollen 20.3%, HDM 20.3%, paper mulberry 20.3%, thresher 20.2% and raw cotton 17%.

Sensitisation to animal allergens is a very important risk factor for developing allergic diseases like asthma, rhinitis, and atopic dermatitis, especially in occupationally exposed workers. Our results revealed that frequency of sensitisation to cat and dog allergens was 20(19%) and 15(14.3%) respectively.

An American study reported the prevalence of...
atopic/allergic asthma to be 56.3% with highest sensitisation to cat allergen (29.3%), followed by positive responses to Alternaria (21.1%), white oak (20.9%), dust mite (10.1%), and cockroach (7.6%).

A pan European study revealed that 27% of patients referred to an allergy centre were sensitised to cat and/or dog related allergens. Another study reported that among asthmatic patients 43.9% were sensitised to dog allergens, 41.7% to cat allergens and 38.9% to rabbit allergens.

A study reported that sensitisation to cat allergens was a more potent risk factor in adults for developing asthma than was cat ownership, suggesting that sensitisation to cat allergens can develop regardless of cat ownership.

One study reported that the prevalence of atopic asthma in Indian asthmatics was 55.6% with highest sensitisation to housefly antigen in 31.1% patients and lowest to HDM which was only in 7.8% patients. This difference in sensitisation of aeroallergens can be due to regional and environmental differences in indoor and outdoor settings.

The most important implication of diagnosing allergic sensitisation in patients with asthma or other allergic diseases is the treatment modification in these patients. Specific allergen immunotherapy (SIT) is a unique therapy with an ability to change the natural evolution of allergic diseases. In this treatment modality, allergens are given to patients in repeated and gradually increasing doses to provide immune tolerance. The efficacy of both subcutaneous (SCIT) and sublingual (SLIT) immunotherapy is documented for perennial and seasonal allergic respiratory diseases by systematic reviews and meta-analyses. SIT should be considered in the management of asthmatic patients who experience adverse effects of medications, to reduce or avoid long-term pharmacotherapy and the increasing economic burden of medications and in the presence of allergic rhinitis or other comorbid allergic conditions.

Avoidance of allergens is another important tool in the prevention of allergic asthma and asthma-like symptoms.

The patients included in the study were from almost all parts of Pakistan and they were selected according to a well-defined inclusion and exclusion criteria, adding to the strength of the study. However, most patients belonged to Rawalpindi and Islamabad only which means there was a relatively uneven area representation from different parts of Pakistan, which is a limitation of the study.

Conclusion
The prevalence of allergic asthma was high at 56.2% and the most common allergen causing highest sensitisation was HDM. Identifying causative allergen can be very helpful in the management of patients. Environmental control of allergens, their avoidance and use of SIT are important management tools.

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Conflict of Interest: None.

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References


