Original Articles

CONTRIBUTOXY FACTORS IN BRONCHIAL ASTHMA AMONG THE KARACHIITES

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Abstract

A study on 50 consecutive patients attending chest OPD of Jinnah Postgraduate Medical Centre, Karachi has been done during the year 1974-75 to assess the important contributory factors in asthma among the local population. Various laboratory investigations and skin tests were done. Their importance in the diagnosis and treatment of asthma has ben evaluated. The epidemiological data has also been compared with other published reports.

Introduction

The incidence of asthma in particular and small airway disease in general appears to be high in Karachi than at other places in Pakistan. The prevalence of this chronic condition among factory workers represents public health problem of staggering proportions. The present study was undertaken to find out the pattern of disease in Karachi and to evaluate the various factors contributing to this condition and to assess their importance in diagnosis and treatment of asthma.

Reckemann (1940) has classified asthma on etiological grounds into 'extrinsic' non infective asthma with positive skin test to external allergens and the 'intrinsic' infective type where asthma is normally associated with bacterial, fungal or viral infection without skin sensitivity. The extrinsic type normally occurs in younger patients who have family history of allergy. Eosinophilia of blood and/or sputum is also found in this type. A third type 'mixed asthma' has been described by others where both the infection and the external allergens are the contributing agents. The patients may have positive skin sensitivity reaction to the allergens, but the other laboratory findings i.e., eosinophilia of blood and/or sputum may be masked by polymorphonuclear leukocytosis. The culture of sputum is often found positive due to superadded infection.

Material and Methods

Asthma was defined as a disease characterized by narrowing of the intrathoracic airways and clinically manifested by dyspnea or wheezing. Fifty consecutive patients attending chest OPD of Jinnah Postgraduate Medical Centre, during the year 1974-75 and satisfying this definition of asthma, were selected for the study.

The following procedures were carried out on them:

1. Physical examination was done to exclude any other associated disease.
2. A questionnaire covering the clinical features of asthma was completed. Information was sought about family history of atopic disease, age of onset, severity and frequency of attacks, and history of hypersensitivity to external allergens.
3. Skin tests were performed by prick test method (Pepys 1972). A drop of fluid containing the allergen was placed on the volar surface of fore arm, the skin was pricked through the fluid with No. 20 needle as superficially as possible to minimize non-specific reaction. The tests were read after 15 minutes and any weal bigger than the control test reaction was taken as positive. All the patients had been asked to stop any medicine containing corticosteroids or antihistamines at least one day before the test.

Results and Discussion

Table I shows the age of onset in males and females when the symptoms of asthma appeared first. More than half of the patients experienced their first attack between 10-40 years of age. Figures from different sources are in agreement with our results regarding the age of onset. The earlier the age of onset of atopic disease the higher the proportion of subjects that gave type I reaction to prick test (McCarthy and Pepys, 1971). According to Tuft (cited by Banszky 1959) the maximum number of asthmatics experience their first attack between 10-40 years of age. The age and sex distribution of patients with asthma is shown in table II. Fifty six percent of patients belonged to 10-40 years of age. Twice as many males were found to have asthma as females. Most investigators agree on the preponderance of males as compared to females suffering from asthma.

Table I: Age of Onset of Asthma

Age Group	*M*	*F*	*Total*	*Percentage*
≤10	2	1	3	6.0
10-40	14	14	28	56.0
>40	16	3	19	38.0
Total	32	18	50	100.0

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Table II: Age and Sex Distribution of Patients

Age Group	*M*	*F*	*Total*	*Percentage*
≤20	1	2	2	4.0
20-40	14	12	26	52.0
41-60	15	4	19	38.0
>60	3	—	3	6.0
Total	32	18	50	100.0

The age of onset of asthmatic symptoms is strongly dependent on the factor of inheritence. If both parents have allergies, the asthma usually begins in early life, if only one parent has allergy the occurrence is considerably less and the onset is apt to be later; if neither parent is affected, the percentage is much less and the symptoms often do not appear until adult age (Derbes and Engelhardt, 1946). Tai and Chinn (1975) recorded an incidence of family history in 41% of asthmatics. Only 16% of our total cases gave history of atopic disease in family and that also in one parent only (Table III). This lowered level of overall percentage may be due to preponderance of adults in this study, as in the few cases among the younger age group two out of three had family history of atopic disease.

Table III: Relationship of Age of Onset and Family History

Age of onset (years)	*Total cases*	*Cases with family history*	*Percentage*
≤10	3	2	66.6
10-40	28	3	21.4
>40	19	3	15.8
Total	50	8	100.0

Haemoglobin was estimated in all cases to exclude anemia or emphysema. Diagnosis of anemia is important as it may contribute to dyspnea, while emphysema is a known complication of asthma. Neither of the above conditions is a common accompaniment of asthma is further substantiated by this study (Table IV). Eighty six percent had haemoglobin levels in the normal range (Hb 11-16 gm%). Eight percent, all males, were in polycythemic group (Hb, >16 gm%) and six percent, all females, were anemic (Hb ≤ 11 gm%). Total leukocyte count was under normal range in 90% of cases (i.e. 3000-12000 cells/cmm), while in 10% of cases it was high up to 15,000 cells/cmm.

Blood eosinophilia is increased in allergic states including asthma of allergic origin except when the disease is in quiescent state, or during secondary infection. In our study 24% had significantly high eosinophil absolute count (Table V). As all the cases were symptomatic and none was on cortisone group of drugs,

Table IV: Haemoglobin Levels in Patients

Haemoglobin	*M*	*F*	*Percentage*
≤11 gm%	—	3	6
11-16 gm%	28	15	86
>16 gm%	4	—	8

secondary infection might be responsible for the low eosinophil count in majority of cases. However, blood neutrophil absolute count did not reveal any case with abnormally high or low counts. Relation between eosinophilia in blood and sputum is shown in figure 1. Sputum eosinophilia was regarded as present where the proportion of eosinophils estimated from the stained smears was greater than 20% of the white cells. It was recorded in 32% of cases. However not all the cases which had high blood eosinophil count had sputum eosinophilia or vice versa. Only 18% had both sputum and blood eosinophilia. Pulmonary eosinophilia has been considered to be of importance in differential diagnosis of asthma (Crofton 1952). Lately however, their diagnostic significance has been disputed (McCarthy and Pepys, 1973).

Table V: Blood Eosinophil Count

Blood Eosinophil (absolute count)	*Total cases*	*Percentage*
≤200/cm	9	18.0
200-500/cm	29	58.0
>500/cm	12	24.0
Total	50	100.0

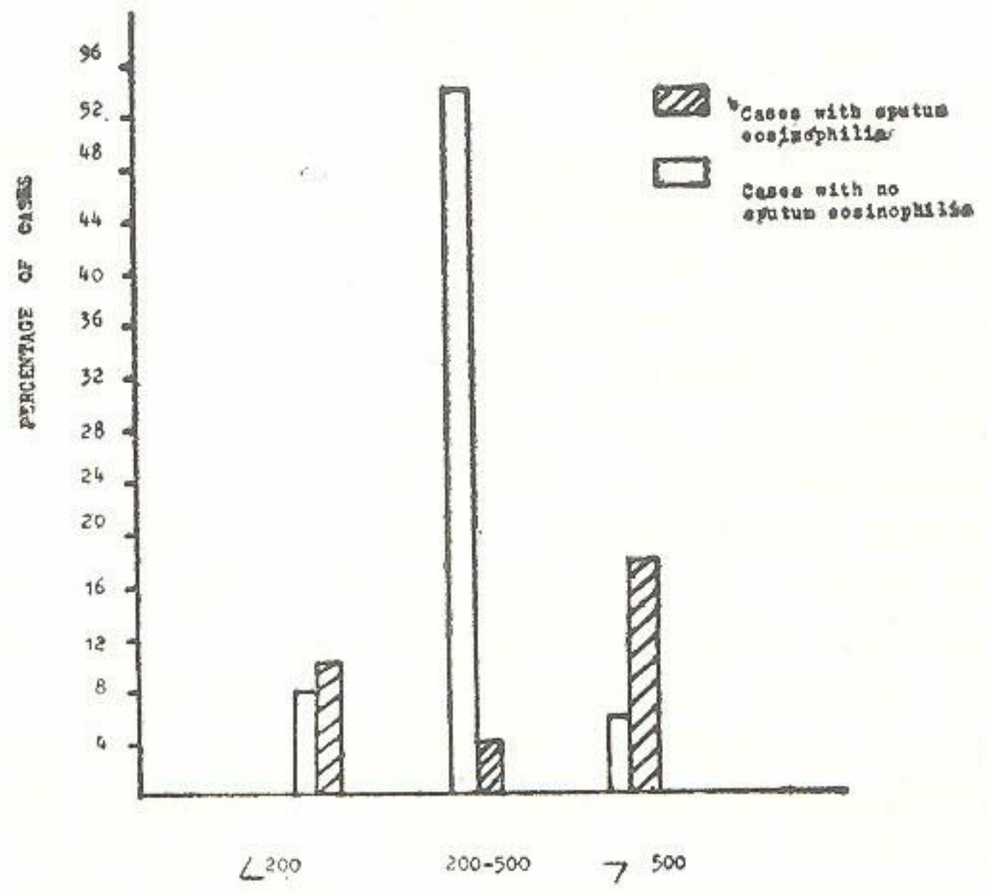

Fig. 1: Relationship of Cases with Sputum Eosinophilia and Blood Eosinophil Count.

Prick test was done for 19 allergens and all of the fifty asthmatics were found to be positive for one or more of the allergens indicating that atopy was present in all the patients and that the allergens in question may be the contributory

factors of asthma. The results of skin sensitivity are presented in figure 2. Among the inhalants, the order of frequency was house dust, mattress dust, fungi, chicken feather, tobacco smoke, cotton and cat hair. Half of the cases were found positive to house dust and in almost all of them the sensitivity overlapped with many other environmental agents. Sensitivity to mattress dust was detected in 30% of cases. All but four of these cases were associated with house dust allergy, suggesting that some common allergen, possibly house dust mite of Dermatophagoides genus, is present in both the types of dusts. The reported incidence of house dust sensitization as found by scratch test has varied from 45% to 79% (Derbes and Engelhardt, 1946). Behrendt (1962) reported house dust to be the commonest offending allergen among the environmental agents, especially in adults.

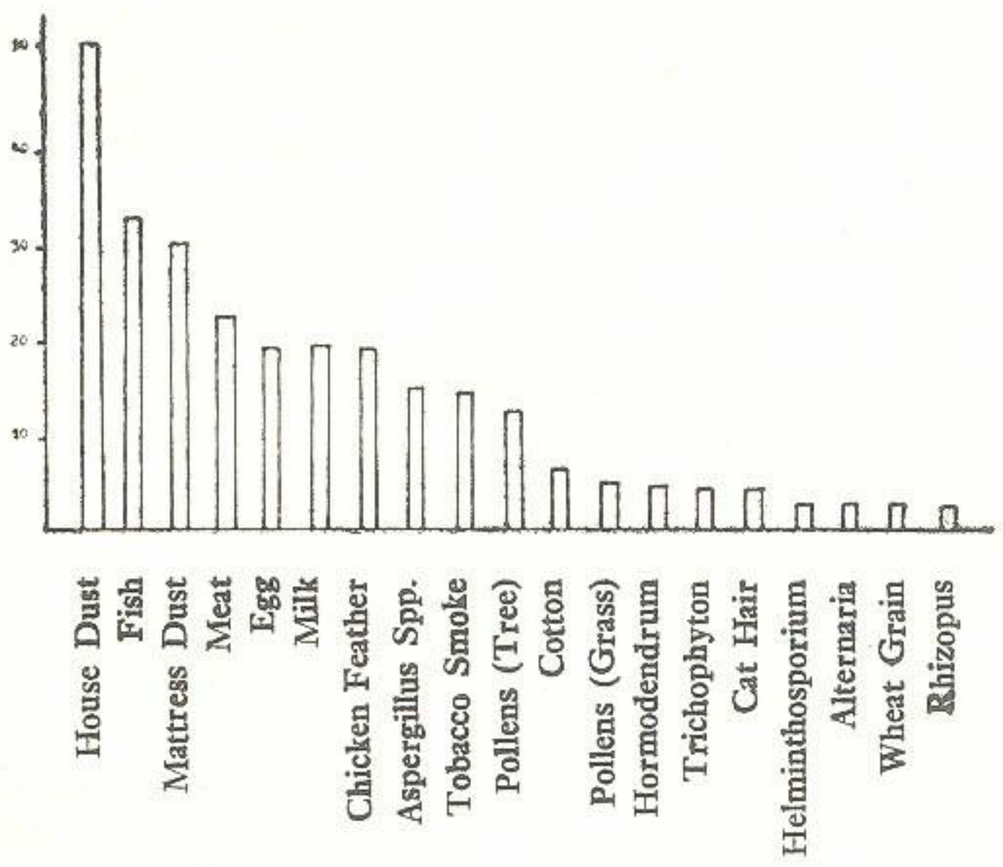

Fig. 2 : Prick Test to Different Allergens.

Allergy to fungi was demonstrated in 22% of cases, more than half of which were sensitive to Aspergillus species alone or in combination. Allergic bronchopulmonary aspergillosis has been reported to be the commonest form of asthma and pulmonary eosinophilia in Britain (Longbottom and Pepys, 1964). Whether these fungi are the primary cause of asthma in our cases also cannot be comitted at this stage, as no precipitins were looked for these fungi in patients sera, neither these fungi were looked for in patients environment. However, because of their ubiquitous nature, it is highly suggestive that these fungi are also one of the important factors in causing or precipitating symptoms of asthma in our country.

Though fish and sea food are not uncommon causes of asthma and rhinitis, more frequently they cause other allergic manifestations, e.g., angioneurotic edema, eczema, gastrointestinal allergy, and urticaria, migrain (Unger 1946). In the present study sensitivity to fish ranked second (32%) in order of frequency. This is much high in contrast to the reported figure of 7.7% (Rower cited by Unger 1946). Similarly meat sensitivity was demonstrated in much higher proportion of our cases (22%). Egg and milk have been recorded as important food allergens, causing more symptoms in children (Behrendt 1962). In our study 18% had allergy to egg and a similar percentage of cases had allergy to milk. Chicken feather allergy was not of much significance in our patients, probably because they are not being commonly used in pillows and mattresses in our country. Tobacco smoke which accounted for 14% of cases in this study, has been recognized as a frequent precipitant of asthmatic attacks, sometimes as an allergen and sometimes as a nonspecific irritant.

Conclusion

This study has shown that while all the cases did give positive prick test to one or more of the common allergens, only few of them could qualify to be labelled as classical cases of extrinsic asthma, because family history of allergy was positive in 16% only, blood eosinophilia was present in 24% of cases, pulmonary eosinophilia was present in 32% of cases. The majority of our cases seem to be of mixed type and it is suggested that therapeutic measures should be directed against both the offending allergen and the infection.

Apart from house dust sensitivity cases, none of them admitted to the allergen giving positive skin test to have precipitated an acute attack of asthma. The provocative tests could not be done, as all these cases came during acute episode. On the other hand there was supportive evidence from their history that secondary infection had precipitated an attack of bronchospasm. The laboratory report did not give much of information in this regard, except leukocytosis in 10% of cases.

Acknowledgements

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LIVER FUNCTION PROFILE IN PATIENTS TAKING METHYLDOPA

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Abstract

Liver function tests were done in 100 patients who had taken methyldopa for a variable period and 96 hypertensives taking other anti-hypertensive agents who served as controls. The groups were approximately comparable in regard to the intake of other drugs. The frequency of abnormal SGPT and SGOT values was higher in the methyldopa group (27-32%) as compared with the controls (11%). Of those showing abnormal transaminases values amongst the methyldopa group, the rise was mild (<70 i.u.), in nearly three fourth with a general tendency to revert to normal levels inspite of continued drug administration. In a small group the transaminases values tended to deteriorate. A small prospective study also showed a mild rise of transaminases in a significant number following administration of methyldopa. No evidence of clinical liver disease or overt hepatotoxicity possibly related to drug was observed. Methyldopa remains a useful drug but should be avoided in those with evidence of liver disease. The study also highlights the importance of drug history in the interpretation of liver function tests.

Introduction

Methyldopa is a potent anti-hypertensive agent and is widely used in clinical practice. The drug is generally well tolerated and is free from serious side effects. On rare occasions liver dysfunction has occurred following its use (Gillespie 1960; Elkington et al., 1969; Irvine et al., 1962). Most reports have described a picture simulating hepatitis which is reversible on withdrawal of the drug (Elkington te al., 1969; Tysell and Knauer, 1971; Cannon and Laragh, 1963), but on rare occasions deaths from hepatic damage have also occurred (Hoyumpa and Connell, 1973; Rehman et al., 1973). The other rare hepatic syndromes associated with methyldopa include chronic active hepatitis (Goldstein et al., 1973), granulomatous hepatitis (Miller and Reid, 1976) and cholestatic jaundice (Hoffbrand et al., 1974).

In this country some studies have documented liver dysfunction in a small but sizeable percentage of apparently normal subjects (Ahmad and Quraishi, 1975; Haider et al., 1975). In view of the widespread use of methyldopa in clinical practice and its propensity to cause hepatic dysfunction in some, we studied the liver function profile in hypertensive patients taking methyldopa.

Material and Methods

In the first part of the study, liver function profile was studied in 100 hypertensives attending the Hypertension Clinic of PMRC Unit at Lahore. These patients had been taking methyldopa for a variable period ranging between 6 months to 1-1/2 year. For the sake of comparison 96 hypertensives, who were taking drugs other than methyldopa were also investigated. A detailed drug history was taken on each visit to document the intake of any other potentially hepatotoxic drug. In all patients, special attention was paid to inquire about past history of liver disease as well as any prodromal symptoms of impending liver damage such as fever, rash, abdominal pain, malaise and discoloration of urine etc.

In the second part of the study, which was designed to be prospective, liver function profile was studied in 25 patients before starting methyldopa. The tests were repeated in 14 patients after they had taken methyldopa for a period ranging between 3-12 months.

The serum transaminases were expressed as Karman units, (normal: SGOT 8-40 units; SGPT 5-35 units) and alkaline phosphatase as K.A. units (normal 3-13 units). The other biochemical investigations which included serum bilirubin, serum protein, albumin: globulin ratio were done according to methods described by King and Wooten (1964).

Results

A. Random Study (Table I):

The abnormality in transaminases was

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