

Correspondence

Family history & the risk for adult onset asthma

Sir,

Asthma is one of the most common chronic disorders worldwide. Epidemiological twin and family studies mainly on childhood asthma have offered evidence for familial aggregation of asthma and atopy. Asthma heritability of as high as > 90 per cent has been reported in separate studies^{1,2}. Segregation analyses on asthma have revealed different modes of inheritance such as polygenic inheritance with major gene involved^{3,4}, co-dominant inheritance⁵, and polygenic/multifactorial influence with a recessive component inheritance⁶. Risk factors for developing asthma in adults, particularly in those who did not have asthma in childhood, are less defined. With an aim to demonstrate the parental effect of asthma and to determine the relative contribution of family history as a potential risk factor in adult onset asthma and its mode of inheritance, and to investigate the effect of consanguinity in adult onset asthma, the present study was undertaken on consecutive patients attending a tertiary care asthma centre (Allergy, Asthma, and Chest Center) in Mysore, Karnataka, India, during 2009-2010.

The laboratory work was performed in the Genomics Laboratory of University of Mysore. The study protocol was approved by the Institutional Human Ethical Committee (IHEC) of the University of Mysore and informed written consent was obtained from cases and controls who participated in the study. Assuming history of maternal and paternal asthma of 20 per cent in cases and 10 per cent in controls with a 1:2 case control ratio, a sample of 195 cases and 390 controls was required to detect the level of significance at 0.05 with a power of 90 %. The sample size of 200 index cases and their family members were selected. Asthma in the index adult was diagnosed according to Global

Initiative for Asthma (GINA) guidelines⁷ and American Thoracic Society Guidelines⁸. The patients with asthma were included only if they had their first respiratory symptoms after the age of 18 yr. A total of 400 families were randomly selected in four administrative wards and these wards were randomly selected from the 30 units that were part of a large epidemiology study on asthma in urban Mysore. Only one adult subject from each family was considered as index control. A genetic register was designed to collect data on demographics, respiratory symptoms, triggers, age of onset of asthma and medications. Also detailed family history that included data in the pedigrees was collected. Adult patients with asthma were asked about the diagnosis of asthma in the first family members including parents, grandparents, siblings, uncle/aunt and their children. Odds ratio and 95 % confidence interval were estimated to quantify the relation between determinants of interest and the risk of asthma. Logistic regression analysis was performed to assess independent association of variables found to be significant in univariate analysis.

The mean age of patients was 40±13 yr and that of controls was 39±13 yr. The male : female ratios were 1:1.35 in cases and 1:1.4 in controls. Family history of asthma was observed in 128 (64%) cases and 52 (13%) controls ($P=0.001$), revealing a significant association of asthma with family history of the disease in univariate analysis (OR = 13.29, 95% CI = 8.77 - 20.14) (Table). Parental consanguinity did not show any effect on adult onset asthma in this study. The independent association of maternal and paternal asthma with adult onset asthma was confirmed with paternal asthma associated with a higher risk of asthma in the offspring (OR = 11.82; $P=0.003$) than the maternal asthma (OR = 10.23; $P=0.03$) (Table). Sibling

Table. Logistic regression analysis of patients with asthma (n=200) and healthy controls (n=400)

Family history (FH)	Patients	Controls	Univariate analysis		Multivariate analysis	
	n (%)	n (%)	OR (95% CI)	P value	OR (95% CI)	P value
Any	128 (64.0)	52 (13.0)	13.29 (8.77-20.14)	0.001	13.35 (8.17-21.81)	0.001
Maternal	41 (20.5)	3 (0.8)	33.08 (10.09-108.47)	0.001	10.23 (1.16-89.63)	0.03
Paternal	46 (23)	4 (1.0)	28.74 (10.16-81.26)	0.001	11.82 (2.25-61.93)	0.003
MGP	18 (9)	3 (0.8)	19.68 (4.51-85.71)	0.001	1.93 (0.22-16.59)	0.54
PGP	28 (14)	5 (1.3)	13.94 (5.31-36.54)	0.001	0.55 (0.05-5.91)	0.62
Sibling	48 (24)	21 (5.3)	6.0 (3.44-10.44)	0.001	6.42 (1.66-24.79)	0.007
AU	28 (14)	15 (3.8)	4.30 (2.20-8.40)	0.001	10.50 (1.20-91.95)	0.03
SD	27 (13.5)	9 (2.3)	6.78 (3.12-14.72)	0.001	2.39 (0.34-16.72)	0.37

OR, odds ratio; CI, confidence interval; MGP, maternal grandparent; PGP, paternal grandparent; AU, aunt/uncle; SD, son/daughter

and aunt/uncle history of asthma was also found to be independently associated with adult onset asthma in our study population. Of the 128 families with asthma patient, the most common mode of asthma inheritance observed was dominant (61%). Of these families, only 6 per cent had consanguineous marriages, indicating null effect of consanguinity in the manifestation of asthma.

In this study, paternal asthma was observed to be more significantly associated with asthma than the maternal asthma. This is in line with another study from India⁹ where the paternal history of asthma was found to confer a greater risk than the maternal asthma. To investigate the role of maternal asthma in the offspring and to determine if a parent-of-origin effect exists, a meta-analysis of multiple studies was performed. It was concluded that maternal asthma predisposed offspring to the disease more than paternal asthma¹⁰.

Limitations of this study include patients being selected from a tertiary care center which may not be reflective of the general population. The control population though identified from the general population was limited to four administrative wards and may not be representative of Mysore city. There are also possibilities of information bias if the index cases and controls did not have a precise knowledge of their family members having asthma.

In conclusion, it was observed that family history of asthma conferred a great risk in developing new

onset asthma in adults. Paternal asthma was observed to be more significantly associated with asthma than the maternal asthma. Further studies on a larger population of adults with new onset of the disease are needed to confirm these findings.

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