

# Association between Childhood Atopic Disease and Parental Atopic Disease in a Population with High Consanguinity

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## ABSTRACT

*The aim of the study was to investigate the association between asthma, allergic rhinitis, and eczema in Qatari schoolchildren with allergic conditions in their parents. A cross-sectional study was conducted among 3500 Qatari schoolchildren aged 6–14 years in period: February, 2003–February, 2004. A questionnaire was used to collect the clinical history of asthma and allergic rhinitis in their parents and siblings. It was found that 21.6% of asthmatic children had mothers with asthma and 18.2% fathers with asthma. This contrasted with 6.8% of non-asthmatic children who had fathers with asthma and 9.4% mothers with asthma. As for allergic rhinitis, 26.5% of asthmatic children had mothers with allergic rhinitis and 25.3% fathers with allergic rhinitis. The frequency of either parent of the asthmatic children having allergic rhinitis was 41.8% and for both parents was 10.0%. The frequency of siblings having asthma was 36.6%, allergic rhinitis 16.4%, and eczema 29.1%. The present study revealed a strong association between respiratory allergies and eczema in parents, and their asthmatic children.*

**Key words:** asthma, allergic diseases, school children, parental asthma, hereditary, State of Qatar

## Introduction

The prevalence rate of childhood asthma, allergic rhinitis and eczema showed variation and increase worldwide through the latter half of the 20<sup>th</sup> Century<sup>1–3</sup>. Possible causes of asthma have been the focus of several studies with genetic factors being seen as playing an important part. It is difficult to find a cause and the relationship between asthma and environmental and genetic causes ascribed to it. Figures for the prevalence of asthma and allergic rhinitis changes from one country to another.

The prevalence studies in different geographical areas are often difficult to compare because of variations in methodology, culture, genetics and environment. Many of these difficulties have been overcome by the protocol developed for the International Study of Asthma and Allergies in Childhood (ISAAC), which standardizes both methodology and terminology. Several authors have reported the strong association between asthma, allergic rhinitis and eczema<sup>4–8</sup>. It is reasonably well documented from family and twin studies that asthma has a hereditary basis.

The objective of this study was to investigate the prevalence of asthma in Qatari schoolchildren and analyses the association of atopic disease in particular asthma in children aged 6–14 years and their parents.

## Subjects and Methods

### Population

The studied school children were the subjects of a cross-sectional population study which was conducted in both urban and rural areas of the State of Qatar. The survey was performed to study the prevalence of asthma and allergic symptoms in Qatari national schoolchildren aged 6–14 years between February 2003 and February 2004 and to find its association with allergic rhinitis and eczema in subjects, parents and their siblings.

### Questionnaires, sampling and data collection

The methods selected included the use of International ISAAC protocol and standardized questionnaires

have been described in details<sup>9,10</sup> to survey. A multi-stage sampling technique was used and the schoolchildren were selected randomly. Stratification allowed both urban and rural areas to be proportionally represented. The list of names of government schools was obtained from the office of Director of General Education in the Ministry of Education. Government schools in Doha are segregated according to sex. There are 104 schools in 21 districts with 56 schools for boys and 48 for girls. Out of these, 30 schools were selected which have majority of Qatari national students. Again, we have divided these schools in equal proportion for boys and girls. Similarly, the classrooms and school children were selected in the second and third stages using the same simple random sampling procedure that resulted in the selection of 3,500 students (determined minimum sample size by ISAAC) who proportionally represented the study population.

The questionnaires with a letter of explanation were distributed to the parents of these children, who were Qatari nationals, and lived in either urban or rural areas of Qatar. The questionnaires and administration team were the same for both urban and rural areas. The data obtained were based on the information provided by the parents of these children. The self-administered questionnaire was completed by the parents of each child and returned to the school. A qualified pre-trained nurse interviewed both parents. In some occasions, they contacted the parent over the phone to complete the Questionnaire. All were biological parents. Although the sample population included only children aged 6 to 14 years, we did not impose any age limit for the children when parents were asked about the history of allergic condition in their children. The question concerning the diagnosis of asthma was »Has the child ever been diagnosed as having asthma by a doctor?« »what was the age at which asthma was first diagnosed?« and »has the child ever needed treatment or hospital admission due to asthma?«. »Were you ever told that the frequent upper respiratory symptoms were due to allergy (allergic rhinitis)?« As for eczema, »were you ever told by physician that your child had eczema?«

### Statistical analysis

Fisher exact and  $\chi^2$  test were performed to ascertain the association between two or more categorical variables. Student's-t test was used to determine the significance of difference between two continuous variables, and  $p < 0.05$  was considered as the cut-off value for significance. The relative risk (RR) and their confidence intervals (CI) were obtained by using Mantel-Haenszel test. Logistic regression analysis was used to adjust for potential confounders and to rank the risk factors (determinants) for asthma. The level  $p < 0.05$  was considered as cut-off value for significance.

Approval for the study was obtained from the Medical Ethics Committee of the Hamad Medical Corporation. A signed consent form was obtained from the parents of each child after the explanation of aims and the nature of the study.

## Results

Questionnaires with a letter of explanation were distributed to the parents of 3,500 children living in urban and rural areas. Parents of 3,283 children (93.8%) gave their consent for the study. The age range of the children studied was 6–14 years, with a mean of 9.02 years and standard deviation of 1.99 years; 52.3% were males, and 47.7% females. The measurements of repeatability used to assess the degree of reproducibility of the questionnaire were kappa values, average correct classification rates and the proportion in agreement. Response to the questionnaire administered on two occasions by the same people, showed a high degree of repeatability between the first and second samples. The questions concerning diagnosed asthma (88%), and allergic rhinitis (83%) showed excellent agreement.

The overall prevalence rate of asthma in this population was 19.8%. 439 boys and 210 girls had asthma giving a sex ratio of 2.1:1. (sex ratio of total population studied was 1.09:1). 649 children had asthma out of 3283 children studied giving a prevalence rate of 19.8%. Of these asthmatic children, 227 children had either the fathers or mothers were affected with asthma (35%). When we considered any one of the allergies; asthma, eczema or allergic rhinitis in the children, we found 1,579 out of 3,283 children had at least one of the above conditions. Of these 1,579 children, 1,016 had at least one parent (64.3%) suffering from any one of these conditions and (relative risk 1.8 (95% confidence intervals 1.7–2.0),  $p < 0.0001$ ).

Whereas the prevalence of asthma in fathers of non-asthmatic children was 6.8%, it reached 18.2% among asthmatic children (relative risk 2.2, 95% CI 1.9–2.6). Similar values were observed for asthma in mothers (Table 1). It was found that 35.0% had either parents with the above condition and this contrasted with 14.8% of non-asthmatic children who had either parents with asthma and the difference being statistically significant ( $p < 0.0001$ ). A similar pattern was seen when parent-child association of allergic rhinitis symptoms was investigated, with 25.3% and 26.5% of asthmatic children had fathers and mothers with allergic rhinitis respectively. It was also found that 41.8% of asthmatic children had either parents with allergic rhinitis, and 10.0% of asthmatic children had both parents with allergic rhinitis. The prevalence rates of eczema in fathers, mothers, either parents and both parents of children who were asthmatic were 17.7%, 19.6%, 31.6% and 5.4% respectively. There were 1001 children who had allergic rhinitis and 721 with eczema. The frequency of occurrence of the conditions in the children and their parents are presented in Table 2.

Table 3 shows the Multivariate stepwise logistic regression to predict Asthma with socio-demographic and other atopic conditions among children and parents.

Figure 1 shows the Venn diagram of asthma overlapping with allergic rhinitis and eczema. The prevalence of asthma, allergic rhinitis and eczema overlapped to a

**TABLE 1**  
RELATIONSHIP OF PARENTAL ASTHMA, ALLERGIC RHINITIS AND ECZEMA TO CHILDREN'S ASTHMA

	Father		Mother		Either parent		Both parent	
	Asthmatic	Non asthmatic	Asthmatic	Non asthmatic	Asthmatic	non asthmatic	Asthmatic	Non asthmatic
	Relative risk (95% CI)	Relative risk (95% CI)	Relative risk (95% CI)	Relative risk (95% CI)	Relative risk (95% CI)	Relative risk (95% CI)	Relative risk (95% CI)	Relative risk (95% CI)
Asthma	118 (18.2)	179 (6.8)	140 (21.6)	248 (9.4)	227 (35.0)	390 (14.8)	31 (4.8)	37 (1.4)
		2.2 (1.9–2.6)*		2.1 (1.8–3.4)*		2.3 (2.0–2.7)*		2.4 (1.8–3.1)*
Allergic rhinitis	164 (25.3)	411 (15.6)	172 (26.5)	436 (16.6)	271 (41.8)	728 (27.6)	65 (10.0)	119 (4.5)
		1.6 (1.4–1.9)*		1.6 (1.4–1.8)*		1.6 (1.4–1.9)*		1.9 (1.5–2.3)*
Eczeema	115 (17.7)	329 (12.5)	127 (19.6)	359 (13.6)	205 (31.6)	583 (22.1)	35 (5.4)	104 (3.9)
		1.4 (1.2–1.6)*		1.4 (1.2–1.7)*		1.5 (1.3–1.7)*		1.3 (0.9–1.8)†

\* p<0.001, † not significant, CI – confidence interval

**TABLE 2**  
PREVALENCE OF ALLERGIC CONDITIONS IN CHILDREN STUDIED AND OCCURRENCE OF SAME CONIDITON IN PATIENTS

	Father		Mother		Either parent		Both parent	
	Frequency (%)	Relative risk (95% CI)	Frequency (%)	Relative risk (95% CI)	Frequency (%)	Relative risk (95% CI)	Frequency (%)	Relative risk (95% CI)
Asthma	118 (18.2)	2.2 (1.9–2.6)*	140 (21.6)	2.1 (1.8–2.4)*	227 (35.0)	2.3 (2.0–2.7)*	31 (4.8)	2.4 (1.8–3.1)*
Allergic rhinitis	286 (28.6)	1.9 (1.7–2.1)*	329 (32.9)	2.2 (2.0–2.4)*	495 (49.5)	2.2 (2.0–2.5)*	120 (12.0)	2.3 (2.0–2.6)*
Eczeema	159 (21.5)	1.8 (1.5–2.0)*	165 (22.4)	1.7 (1.4–1.9)*	268 (36.3)	1.8 (1.6–2.1)*	54 (7.3)	1.8 (1.4–2.2)*
Asthma or allergic rhinitis	454 (36.0)	1.9 (1.7–2.0)*	475 (37.7)	1.8 (1.6–1.9)*	716 (56.8)	2.0 (1.8–2.2)*	213 (16.9)	2.0 (1.8–2.2)*
Asthma or eczeema	328 (28.7)	1.6 (1.4–1.7)*	390 (34.2)	1.6 (1.4–1.8)*	577 (50.5)	1.8 (1.6–2.0)*	276 (24.2)	1.6 (1.5–1.8)*
Asthma or allergic rhinitis or eczeema	682 (43.2)	1.6 (1.5–1.8)*	721 (45.7)	1.6 (1.5–1.7)*	1016 (64.3)	1.8 (1.7–2.0)*	387 (24.5)	1.7 (1.6–1.8)*

\* p<0.001, CI – confidence interval

**TABLE 3**  
 MULTIVARIATE STEPWISE LOGISTIC REGRESSION TO  
 PREDICT ASTHMA WITH SOCIO-DEMOGRAPHIC AND OTHER  
 ATOPIC CONDITIONS AMONG CHILD'S PARENTS

Independent variables	Odds ratio	95% confidence interval	p value
Number of people sharing the room	1.17	1.04–1.31	0.009
Allergic to food	2.78	2.01–3.84	<0.001
Allergic to medicine	2.08	1.13–3.86	0.019
Father has asthma	2.44	1.81–3.28	<0.001
Father has allergic rhinitis	1.46	1.14–1.87	0.002
Mother has asthma	2.26	1.69–3.00	<0.001
Mother has allergic rhinitis	1.34	1.05–1.71	0.020
Father smoker	1.39	1.10–1.75	0.005

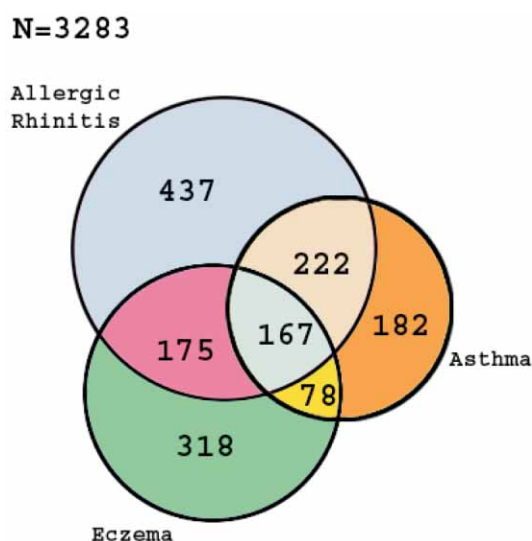


Fig. 1. Venn Diagram showing the overlapping of Asthma with Allergic rhinitis and Eczema (N=3,283, asthma=649, eczema=738, allergic rhinitis=1,001).

high degree in this study. 649 patients had asthma, 738 patients had eczema and 1,001 patients had allergic rhinitis out of the total 3,283. About 71.9% percent of the children who had asthma had either accompanying allergic rhinitis or eczema. 167 subjects had all the three disorders and 1,704 subjects had neither of them.

### Discussion

Our finding of a higher prevalence of asthma among offspring's of parents with allergic respiratory diseases strongly supports the hypothesis that asthma is inherited as reported previously<sup>7,9–11</sup>. The finding of this study of the occurrence of asthma, allergic rhinitis and eczema in parents and asthma in children suggest that these diseases share a common genetic defect. The prev-

alence of atopic disease in parents of children with atopic disease is 64%, whereas the prevalence in parents of the healthy children was 36.1%. The association of asthma, allergic rhinitis and eczema in the same patient has been reported in other studies<sup>1–6,12–15</sup>.

We have found a significant relationship between parental history of asthma, allergic rhinitis and eczema, and asthma in children. Although there were efforts to exclude bias from the study, the possibility that biased reporting of the disorder by the family could have taken place cannot be ruled out. Reporting may depend on whether they had relatives with an allergic condition and therefore it would have been more likely to recognise the condition in their offspring than those who did not have such relatives.

Other family studies have shown that parental history of allergic diseases clearly influences the presence or absence of their children's symptoms<sup>6–8,16</sup>. Familial propensity for the condition has been reported in other studies. A shared environment which is constant for families gives strong support to the general acceptance by workers in the field of the genetic basis of the association between parents and children's respiratory allergies. However, twin studies are necessary to distinguish between genetic and environmental effects. One large study of twins<sup>17</sup> showed a greater incidence of concordance in monozygotic (19%) than dizygotic twins (4.8%). The data in our study revealed that from the 65 children in whom both parents were asthmatic, 31 (47.7%) had a history of asthma. This was read to be consistent with a genetic etiology of asthma. Our study has shown a definite link, as others have, between the occurrence of allergic conditions in the parents and in their children with statistically significant differences in prevalence rates between asthmatic children with asthmatic parents and non-asthmatic children with asthmatic parents. In this study, an interesting feature was that asthma, eczema and allergic rhinitis in mothers gave comparable odds ratios (Table 1), but that was not the case for these features in the fathers in whom the asthma odds ratio was slightly lower. There is no plausible explanation for this occurrence, except that a sex influence on the atopic condition is a possibility, where a maternal modification of developing immune responses may occur<sup>6–8</sup>.

A study of 344 families<sup>16</sup> showed that the risk of developing asthma was 6.5% in children of parents who were not asthmatic. This risk increased to 19.7% if one parent was affected and 63.6% if both were affected. In our study, there is a similar increase in risk not only in children of parents with asthma but also those with allergic rhinitis and eczema. An Australian study<sup>17</sup> analysis gave a strong support to the general acceptance by workers in the field of the genetic basis of the association between parents' and children's respiratory allergies. An interesting finding in our study was that children with asthma were more likely to have mothers with allergic rhinitis and eczema than fathers with allergic rhinitis and eczema. It could be speculated that



perhaps it is related to genomic imprinting<sup>18</sup> wherein the differential expression of genetic material at either a chromosomal or allelic level, depend on whether the genetic material has come from the male or the female. There was no perceived sex difference in the heredity of either eczema or asthma but a definite significant increase in the frequency of allergic rhinitis existed in the maternal line. Cookson et al.<sup>19</sup> showed that sibling pairs affected by atopy shared the maternal 11q13 allele in 62% of the cases while only 46% of the paternally derived alleles were shared. The shared maternal allele differed significantly ( $p=0.001$ ) from the expected distribution, while paternally derived alleles were not significantly different from the expected ratio.

The problems with comparing studies of this type are that differences in definition, age groups studied and sampling methods complicate the issues. A sampling method recently described using prescriptions were found to be very effective in identifying asthmatic patients in the community<sup>6,8</sup> Most of the family studies show that asthma has a considerable genetic component<sup>6,15</sup>. Also, there is much evidence that the occurrence of asthma in first-degree relatives of asthmatics is significantly higher than in the relatives of normal controls<sup>10</sup>. However, the mode of inheritance has yet to be determined. Some classic examples of closed communities where prevalence of asthma is in the region of

20–30% imply strongly that genetic factors are important. At the same time, studies on migrating populations have shown a rise of prevalence of asthma in the same community, which migrate from a low prevalence area to a high prevalence area. This suggests also a major role of environmental factors. What these factors are, are yet to be determined.

Qatar boasts one of the highest rates of consanguinity (54%) in the world with 34.8% of marriages between first cousins and 13.4% between those related more distantly<sup>20</sup>. Whether this has any bearing on the prevalence of asthma would depend on the mode of inheritance of the trait. Therefore, in conclusion, although etiology of asthma is most probably multifactorial, the present study has shown that there is a great likelihood of a genetic component being an important factor in that. There is a greater risk of a child developing asthma if either of his parents or siblings have asthma or other allergies. The genetic expression of the disease could depend on the sex of the affected parent.

### Acknowledgement

This work was supported and funded by the research Committee of Hamad Medical Corporation, Grant No. 227-HMC, Doha, the State of Qatar.

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## **POVEZANOST IZMEĐU DJEČJIH I RODITELJSKIH ATOPČNIH BOLESTI U POPULACIJI S VISOKIM SRODSTVOM**

### **S A Ž E T A K**

Cilj ovog istraživanja je istražiti povezanost između astme, alergijskog rinitisa i ekcema u školske djece iz Katara i alergija njihovih roditelja. Presječna studija provedena je među 3,500 školske djece u dobi od 6 do 14 godina u periodu od Veljače 2003 do Veljače 2004. Sastavljen je upitnik u cilju sakupljanja podataka o kliničkoj povijesti astme i alergijskog rinitisa kod roditelja te braće i sestara. Utvrđeno je da 21.6% astmatične djece ima majke s astmom te da 18.2% astmatične djece ima očeve s astmom. Ovi podaci bili su oprečni podacima da samo 6.8% djece koja nemaju astmu imaju očeve s astmom i da 9.4% djece koja ne boluju od astme ima majke s astmom. U slučaju alergijskog rinitisa, 26.5% astmatične djece imalo je majke, a 25.3 % očeve s alergijskim rinitisom. Frekvencija barem jednog od roditelja astmatičnog djeteta koji ima alergijski rinitis bila je 41.8% a za oba roditelja frekvencija je 10.0%. Učestalost astme kod braće ili sestara astmatične djece bila je 36.6%, alergijskog rinitisa 16.4% i ekcema 29.1%. Istraživanje je pokazalo jaku povezanost između astme u djece i respiratornih alergija i ekcema u roditelja.