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ORIGINAL ARTICLE

Environmental exposures and family history of asthmaShahid I. Sheikh, MD^{1,2}, Judy Pitts, ANP², Nancy A. Ryan-Wenger, PhD, RN^{1,2}, Karen S. McCoy, MD^{1,2}, and Don Hayes, Jr., MD, MS^{1,2,3}¹Department of Pediatrics, The Ohio State University College of Medicine, ²Section of Pulmonary Medicine, Nationwide Children's Hospital, and³Department of Internal Medicine, The Ohio State University College of Medicine, Columbus, OH, USA**Abstract**

Background: Asthma pathogenesis is a complex interaction of genetic, ethnic, environmental and social/life style risk factors. **Aim:** The goal of this study was to identify associations, if any, in children with asthma, between environmental risk factors (exposure to second-hand tobacco smoke (STS), pet ownership, race and a family history of asthma). **Methods:** After IRB approval, from June 2011 to December 2014, 823 children with asthma were enrolled in this prospective cross sectional study. At the initial visit, families completed a questionnaire with information on family history of asthma, having a pet at home and exposure to STS by parents at home. Chi square analyses were calculated, with alpha level of significance ≤ 0.05 . **Results:** History of asthma in parents, siblings or grandparents was reported by 575 (69.8%) patients including father ($n=154$, 17.8%) and mother ($n=235$, 26.5%). Children with family history of asthma ($n=575$) were significantly more likely to have a pet at home and exposure to STS ($n=347$, 60.3% and $n=198$, 34.4%, respectively) compared to families without a history of asthma ($n=124$, 50%, $p=0.006$ and $n=44$, 17.7%, $p<0.001$, respectively). Similarly, asthmatic children with exposure to STS ($n=241$) were significantly more likely to have a pet at home and a family history of asthma ($n=153$, 63.5% and $n=197$, 81.7%, respectively) compared to children with no STS exposure ($n=315$, 55.5%, $p=0.034$ and $n=371$, 65.3%, $p<0.001$ respectively). **Conclusions:** Significantly more asthmatic children with immediate relatives with a history of asthma have a pet at home and experience STS exposure compared to children without relatives with a history of asthma, suggesting association between life style choices/environmental exposures and family history of asthma.

Keywords

Asthma, children, family history of asthma, race, smoking, STS, pets

History

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Introduction

Asthma is a common, heterogeneous chronic respiratory disease affecting all age groups, which results from interactions of multiple environmental, social, genetic and psychological factors. Despite heterogeneity, there are significant racial/ethnic disparities associated with asthma prevalence [1–4]. History of asthma in close relatives is a well-known risk factor for asthma [5] leading to a recent emphasis on identifying genetic origins of asthma. Currently, more than 110 genes have been identified which may be associated with asthma, but none have been linked to every ethnic group [6,7], suggesting either genetic modifiers and/or important confounding factors such as environmental or social/psychological factors may play a role. It is feasible that genetic markers may represent susceptibility for physiological responses in asthma for some individuals, but phenotypic expression requires a secondary exposure that is

environmental, social or psychological, such as environmental allergens, viral exposures, anxiety, exposure to pets or cigarette smoke. It is not clear whether asthma in families is because of a specific genetic risk or if it is merely an expression of chronic exposure to confounding risk factors within the same family, including environmental exposures (allergens, pet exposure), social life style choices (STS, obesity) or psychological issues (anxiety, depression).

The goal of the current study was to identify exposure of non-genetic risk factors (second hand tobacco smoke exposure, pet ownership) in children with asthma and to evaluate the relationship of these factors with race and the presence or absence of family history of asthma. Our hypothesis was that exposure to environmental risk factors may be more common in asthmatic children with a positive family history of asthma suggesting association between genetic and environmental risk factors in asthmatic children.

Methods**Study cohort**

After local IRB approval (IRB11-00174), 850 children with asthma referred to the Pediatric Asthma Center between June

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2011 and December 2014 were enrolled into the study. Inclusion criteria were all children with physician-diagnosed asthma referred to pediatric asthma center. Written consent was waived by IRB. Families or patients were not compensated for study participation. The design was a prospective, cross-sectional observational study with completion of a survey (questionnaire) at the initial clinic visit. The survey was self-administered by the parents. Information collected from parents included demographics such as age, gender, race, history of asthma in immediate family relatives (parents, siblings or grandparents), the presence of a pet at home and exposure to second hand tobacco smoke (STS) at home. Eight hundred and twenty three families completed the questionnaire (823/850, 97%). Asthma severity was classified according to the guidelines for the diagnosis and management of asthma (EPR-3) [8]. A small sample of Asian children ($n=14$) were removed only from race related analysis as number of children in this group were very small. All other analyses are based on total sample of 823 children.

Statistical analysis

Comparisons among asthma risk factors were conducted with SPSS version 19 (IBM, Armonk, NY). Demographic, clinical and asthma risk factors were reported as frequencies, percentages, means and standard deviations as appropriate. Comparison of factors between the four racial groups (Caucasian, African American, Hispanic and biracial with one Caucasian parent) was conducted with chi-square analyses and z -tests with Bonferroni adjustments of p value, and one-way analysis of variance (ANOVA) depending upon the level of measurement. Alpha level of significance was set at ≤ 0.05 .

Results

Of 823 children, 477 (58%) were males and 346 (42%) were females, ranging in age from 1 to 20 years (mean 6.9 ± 4.4) years. The mean age at the time of diagnosis was 2.5 ± 2.4 years with mean duration of symptoms of 4.4 ± 3.8 years. Among them, there were 540 (65.6%) Caucasians, 195 (23.9%) African Americans, 42 (5.7%) Hispanic and 26 (3.2%) were biracial. The majority of the cohort had moderate asthma ($n=490$, 69.2%) based on current accepted diagnostic guidelines (Table 1). Of the 823 subjects participated in this study, 174 were siblings living in the same household.

A family history of asthma was reported for 69.8% ($n=575$) children. Exposure to STS by parents was reported in 29.8% ($n=241$). More than half of the families had at least one pet in the home ($n=468$, 58.5%). Dogs were in 45.5% of households, while cats were in 20.8% (Table 1).

Gender

Females were significantly older than males at their first clinic visit (7.5 versus 6.5 years, $p=0.001$) and at diagnosis of asthma (2.9 versus 2.3 years, $p=0.001$). Moreover, females had experienced asthma symptoms for a longer period of time, but this difference was not statistically different (4.7 versus 4.2 years, $p=0.054$; Table 2). A comparison of demographic and asthma risk factors between males and females found no significant differences in race or asthma

Table 1. Demographic and asthma risk factors for the total group of children diagnosed with asthma ($N=823$).

	Total sample	
	<i>n</i>	%
Gender		
Male	477	58.0
Female	346	42.0
Ethnicity		
White	540	65.6
Black	195	23.7
Hispanic	42	5.1
Biracial	26	3.2
Asthma severity		
Intermittent	11	1.6
Mild persistent	187	26.4
Moderate	490	69.2
Severe	20	2.5
Family history of asthma	575	69.8
Mother	235	28.5
Father	154	18.7
Both parents	116	14
sibling	137	17
Grandmother	115	14.2
Grandfather	54	6.5
Both grandparents	27	3.3
Smoke exposure	241	29.8
Mother	128	15.5
Father	102	12.3
Both parents	49	5.9
Pets	468	58.5
Dog	367	45.5
Cat	167	20.8
Both dog & cat	118	14.7
Other pets	51	6.3

Table 2. Comparison between males and females.

	Mean $\pm$ SD			<i>F</i>	<i>p</i>
	Total sample ($N=823$)	Male ($n=477$)	Female ($n=346$)		
Age	6.9 ± 4.4	6.5 ± 4.1	7.5 ± 4.8	10.16	0.001
Age at diagnosis	2.5 ± 2.4	2.3 ± 2.1	2.9 ± 2.9	10.81	0.001
Symptom duration	4.4 ± 3.8	4.2 ± 3.5	4.7 ± 4.0	3.74	0.054

severity ($p=0.289$ – 0.853). A family history of asthma was reported in 71.4% of males and 73.8% of females. Among family members with a history of asthma, no significant differences were noted between male and female children for mothers, fathers, siblings or grandfathers ($p=0.155$ – 0.912). However, grandmothers with a history of asthma were more frequently noted for females ($n=65$, 19.1%) compared to males ($n=115$, 14.2%, $p=0.001$). There were no significant differences between genders noted for the presence of dogs, cats or other pets in the household ($p=0.167$ – 0.932) or among mothers, fathers or grandparents who smoked ($p=0.250$ – 0.868).

Family history of asthma

A family history of asthma was reported by 575 (71.4%) patients, including history of asthma in fathers ($n=154$, 18.7%) and mothers ($n=235$, 28.5%). Asthmatic children of families with a history of asthma were more likely to have a pet at home compared to asthmatic children of families

without a family history of asthma ($n=347$, 60.3% and $n=124$, 50%, $p=0.006$, respectively) with significance was noted for either dog or cat (Table 3). Asthmatic children of families with a history of asthma were also more likely to be exposed to STS ($n=198$, 34.4 and $n=44$ 17.7%, $p<0.001$, respectively) and significance was noted for either mother or father or if both parents smoke (Table 3). In families with an asthmatic mother ($n=235$), children were more likely to be exposed to STS and more likely to have either mother or both parents who smoke ($p=0.012$, <0.001 and $=0.003$, respectively, and were also more likely to have a dog at home ($p=0.040$) compared to families without maternal asthma (Table 3). Similarly in families with an asthmatic father ($n=154$), children were more likely to be exposed to STS and more likely to have a dog at home ($p=0.022$ and 0.027 , respectively; Table 3). Family history of asthma was not significantly different in different racial groups.

Exposure to second-hand tobacco smoke

Exposure to STS was reported by 241 (29.8%) families, including maternal source of smoking in 128 (15.5%), paternal smoking in 102 (12.3%), both parents 49 (5.9%; Table 4).

Asthmatic children of families with exposure to STS were more likely to have a family history of asthma compared to asthmatic children of families without exposure ($n=197$, 81.7% and $n=371$, 65.3%, $p<0.001$, respectively) and significance was noted if either mother, father, or both parents had asthma ($p=0.018$, 0.025 and 0.022 , respectively). Similarly, asthmatic children of families with exposure to STS were also more likely to have a pet, dog or especially cat at home ($p=0.034$ and 0.008 , respectively) compared to children without exposure to smoking (Table 4). STS exposure was not significantly different in different racial groups.

In families with maternal smoking ($n=128$), children were more likely to have a family history of asthma, especially maternal asthma ($p<0.001$ for both). In families with paternal smoking ($n=102$), children were still more likely to have a family history of asthma ($p<0.001$; Table 4).

Table 3. Family history of asthma compared to other risk factors.

	Family history of asthma ($n=575$)		No family history of asthma ($n=248$)		<i>p</i>
	<i>n</i>	%	<i>n</i>	%	
Smoke exposure	$n=198$	34.4%	$n=44$	17.7%	<0.001
Mothers who smoked	$n=108$	18.8%	$n=20$	8.1%	<0.001
Fathers who smoked	$n=86$	15%	$n=17$	6.9%	0.001
Both parents smoked	$n=43$	7.5%	$n=6$	2.4%	0.005
Pets in the home	$n=347$	60.3%	$n=124$	50%	0.006
Cats in the home	$n=128$	22.3%	$n=39$	15.7%	0.032
Dogs in the home	$n=271$	47.1%	$n=96$	38.7%	0.026
	Mothers with history of asthma ($n=235$)		Mothers without history of asthma ($n=588$)		
Smoke exposure	$n=84$	35.7%	$n=158$	26.9%	0.012
Mothers who smoked	$n=55$	23.4%	$n=73$	12.4%	<0.001
Both parents smoked	$n=23$	9.8%	$n=26$	4.4%	0.003
Dogs in the home	$n=118$	50.2%	$n=249$	42.3%	0.040
	Fathers with a history of asthma ($n=154$)		Fathers without a history of asthma ($n=669$)		
Smoke exposure	$n=57$	34.4%	$n=185$	27.7%	0.022
Dogs in the home	$n=81$	52.6%	$n=286$	42.8%	0.027

Pet at home

Pet exposure/ownership at home was significantly different in different racial groups. More Caucasian (376, 70%) and biracial families (18, 72%) had a pet (cat, dog or both) in the home compared to 53 (27%) African American and 21 (44%) Hispanic families ($p<0.001$).

Pet exposure/ownership was reported by 468 (58.5%) patients, including dog ownership in 366 (45.5%), cat ownership in 167 (20.8%) and both cat and dog in 118 (14.7%).

Asthmatic children with pet exposure/ownership were more likely to have family history of asthma, a sibling with asthma and exposure to STS compared to asthmatic children without exposure/ownership of pet ($p=0.006$, 0.049 and 0.025 , respectively). Families with cat exposure/ownership ($n=167$) were also more likely to have family history of asthma, a sibling with asthma and STS exposure ($p=0.032$, 0.041 and 0.008 , respectively; Table 5). Families with only dog exposure/ownership ($n=367$) were also more likely to have family history of asthma, maternal asthma and paternal asthma ($p=0.026$, 0.040 and 0.027 , respectively; Table 5). Families with exposure/ownership of both cats and dogs ($n=118$) were also more likely to have STS exposure ($p=0.025$; Table 5).

Chi-square comparisons between asthma severity levels and demographic characteristics of the sample revealed no significant differences for race ($\chi^2=7.140$, $p=0.623$), gender ($\chi^2=1.452$, $p=0.693$), family history of asthma ($\chi^2=2.676$, $p=0.444$), STS ($\chi^2=3.826$, $p=0.281$), pets in the home ($\chi^2=0.5126$, $p=0.916$), cat in the home ($\chi^2=4.347$, $p=0.226$), dog in the home ($\chi^2=6.512$, $p=0.089$) or both dogs and cats in the home ($\chi^2=0.1956$, $p=0.0978$).

Discussion

The most important finding of the current study is that significantly more asthmatic children with family history of asthma in immediate relatives (parents, siblings or grandparents) have a pet at home and are also exposed to STS compared to children without family history of asthma,

Table 4. Exposure to cigarette smoke compared with other risk factors.

Smoke exposure	Exposed to smoke (n = 241)		Not exposed to smoke (n = 568)		p
	n	%	n	%	
History of asthma in family	197	81.7	371	65.3	<0.001
Mother with history of asthma	84	34.9	151	26.6	0.018
Father with history of asthma	57	23.7	96	16.9	0.025
Brother with history of asthma	29	12	42	7.4	0.033
Pets in the home	153	63.5	315	55.5	0.034
Cat in the home	63	26.1	102	18	0.008
Both parents have a history of asthma	45	18.7	71	12.5	0.022
	Mother smokes (n = 128)		Mother does not smoke (n = 681)		
History of asthma in family	108	84.4	460	67.5	<0.001
Mother with history of asthma	55	43	180	26.4	<0.001
	Father smokes (n = 102)		Father does not smoke (n = 707)		
Family history of asthma	85	83.3	483	68.3	<0.001
	Both parents smoke (n = 49)		Both parents do not smoke (n = 760)		
Family history of asthma	43	87.8	525	69.1	0.006
Mother with history of asthma	23	49	212	27.9	0.004
	Grandparents smoke (n = 40)		Grandparents do not smoke (n = 769)		
Grandmother have a history of asthma	11	27.5	113	14.7	0.028
Cat in the home	16	40	149	19.4	0.002
Both parents have a history of asthma	11	27.5	105	13.7	0.015

Table 5. Pets in the family compared to other risk factors.

	Pets in the home (n = 468)		No pets in the home (n = 341)		
	n	%	n	%	
Family history of asthma	347	73.7	228	64.8	0.006
Sibling with history of asthma	68	14.4	69	19.6	0.049
Smoke exposure	153	32.5	89	25.3	0.025
	Cats in the home (n = 167)		No cats in the home (n = 656)		
Family history of asthma	128	76.6	447	68.1	0.032
Sibling with history of asthma	19	13.9	118	18	0.041
Smoke exposure	63	37.7	179	27.3	0.008
	Dogs in the home (n = 367)		No dogs in the home (n = 456)		
Family history of asthma	271	73.8	304	66.7	0.026
Mother with history of asthma	118	32.2	117	25.7	0.040
Father with history of asthma	81	22.1	73	16	0.027
	Both dogs and cats in home (n = 118)		Both dogs and cats not in the home (n = 705)		
Smoke exposure	45	38.1	197	27.9	0.025

suggesting significant associations between environmental and genetic risk factors. It supports the concept, that environmental factors (STS, pets) play a role in the development of asthma, particularly if there is a family history of asthma.

It was also noted that parental smoking or family history of asthma was not significantly different across racial groups, suggesting a common susceptibility. Among male children with family history of asthma, gender of the parents, siblings or grandparents was not a risk factor; however, for female children with asthma, significantly more grandmothers were noted to have a history of asthma. An accepted concept is the tendency for asthma to be common in families, but it is unknown if propensities for asthma regarding gender exist.

Our data revealed that if such risk exists, it is more likely to be in females but more studies are needed to confirm our observation.

Several environmental factors, such as exposure to STS have been associated with asthma [9]. It is well known that maternal cigarette smoking is associated with high risk of asthma prevalence in early childhood [10,11]. Our data suggest that asthmatic children with exposure to parental smoking were also more likely to have history of asthma in either or both parents and were also more likely to have a cat or dog at home compared to children without exposure to STS suggesting a possible connection between environmental factors and history of asthma in same families. Some environmental factors may even help developing immune

systems to develop in a balanced and well-regulated manner as some studies suggest that pet exposure in early life may have such effect in some children [12–17]. Thus, environmental factors can either be protective against asthma or may be responsible in causing asthma or a reason for acute flare up in known asthmatics. A family history of asthma is a strong predictor of asthma risk [5] but how genetics or race play a role in asthma in families is not well understood. It is suggested that responses to environmental factors associated with asthma may vary by race, ethnicity or social class as smoking rates vary by race and ethnicity [18]. Racial and ethnic differences in nicotine uptake and metabolism are well documented, which may explain differences in smoking habits [19–21]. We noted more Caucasian families have pet at home compared to minorities, but there was no racial difference noted in smoking exposure and family history of asthma.

Previous studies have suggested that in asthmatics with known genetic risk, environmental factors can influence risk and phenotypic features [22]. Underlying mechanisms are not clear but the presence or absence of certain genes and/or varying levels of endotoxin exposure are the suggested mechanisms [23,24]. It is known that certain environmental factors, such as exposure to STS and dog ownership, are associated with high levels of endotoxin exposure and race/ethnicity may play a role [25]. In our study, significantly more children with immediate relatives with asthma were also exposed to STS and had a pet at home compared to those without family history of asthma, suggesting those patients with a high likelihood of a genetic risk for asthma also had a high prevalence of confounding environmental factors. Racial disparity was only observed for pet ownership (Caucasians were more likely to have pet ownership compared with African American and Hispanic families with asthma) but not with smoking exposure.

Current literature suggests that asthma is considered a complex disease in which multiple genetic factors pre-dispose individuals to clinical disease especially when exposed to environmental stresses. Such responses may be secondary to immune modulation or reflection of the manner in which airways respond to the stresses which may be environmental in nature [26]. Family history of asthma is common in asthmatics suggesting it can be used as a risk factor to identify at risk patients [5,27]. It appears that in individuals with genetic pre-disposition certain environmental exposures and/or life style changes may lead to immune modulation resulting in increased risk of altered physiological changes including asthma [5,25,27]. Genetic pre-disposition may vary in each individual and so can modifiers such as environmental exposures (such as allergens or pets), life style choices (such as STS exposure or obesity) or psychological stresses (anxiety or depression). Race/ethnicity may alter both genetic pre-disposition [28–32] and co-morbidities related to environmental exposures [9,24] making it more complex.

There are several limitations of the current study. The reliance on information provided by the family is a concern. More importantly, there was no control group without asthma for comparison. Socio-economic and household income data were not collected. Finally, a single institutional study can introduce bias. Despite these deficiencies, the current study

has a large cohort with the majority of the cohort completing the questionnaire.

History of asthma in immediate relatives is a known risk factor for asthma. Its correlations with exposure to environmental factors were noted in our cohort. It is not clear from our study if environmental exposure or life style choices have impacted genetic pre-disposition or if chronic exposure to these environmental/life style exposures in these families by itself have resulted in chronic symptoms. This information can be useful in asthma education and risk determination which can help in behavior modification to minimize environmental exposures. Thus, it may be important that in children with history of asthma in immediate relatives, avoidance of cigarette smoke may decrease their chances of environmental stresses which could increase their risk of developing asthma. Exposure to pets is a more complex issue, as in some children pets may have a protective effect. More longitudinal studies with larger cohorts would be very informative.

Conclusion

More asthmatic children with history of asthma in immediate relatives have a pet at home and are exposed to parental smoking compared to children without history of asthma in close relatives suggesting significant associations between environmental exposures (STS, pets) and genetic risk factors (family history of asthma). This information is helpful to clinicians caring for children in these clinical settings for early intervention and risk reduction. Counseling for lifestyle modifications would be important for children with family history of asthma who appear to be pre-disposed for asthma.

Declaration of interest

The authors report no conflicts of interests and have no relevant disclosures.

Author contributions

Dr Sheikh contributed to the study design, study conduct, data collection and manuscript preparation. He had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis and serves as the guarantor of the manuscript. Judy Pitts contributed to the study design, study conduct, data collection and manuscript preparation. Dr Nancy Ryan-Wenger contributed to the study conduct and data analysis, interpretation and manuscript preparation. Dr Hayes contributed to the study design, study conduct, data collection and manuscript preparation. Dr McCoy contributed to the study design, study conduct, data collection and manuscript preparation.

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