

2010-01-01

Atopy in US-Mexico Border Elementary School Children: A Pilot Study

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ATOPY IN U.S. - MEXICO BORDER
ELEMENTARY SCHOOL CHILDREN: A PILOT STUDY

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Julia Laura Alvarez

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DEDICATION

This work is dedicated to my dearly loved sons Paul and Mark who have been a constant inspiration to continue my education journey, once again God gave the opportunity to teach my children by setting examples; this is also dedicated to my children's father who always showed a steady solidarity and gave me motivation to persist with my dream. I want to thank my mother, sisters, and rest of my family for their constant support and for believing with me that great dreams may come true.

I would like to thank to the TIES students for their data collection used in this study, thank you Alejandra, Ximena, and Oscar; thanks to Juan and my friends, classmates, and co-workers who bear with me during both: good and bad times. Finally, thanks too to all my Mexican colleagues because you were the original inspiration to pursue a professional degree in Public Health.

Thank you very much to all of you!

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By

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THESIS

Presented to the Faculty of the Graduate School of
The University of Texas at El Paso
in Partial Fulfillment
of the Requirements
for the Degree of

MASTER OF PUBLIC HEALTH

Department of Public Health Sciences
THE UNIVERSITY OF TEXAS AT EL PASO

May 2010

ACKNOWLEDGMENTS

I would like to express my most sincere thanks to the professors and mentors who helped me to achieve my goals. Thank you Dr. Weigel for your invaluable guidance and for being patient with me, thank you Dr. Armijos for your support and for sharing your experience with me, and thank you Dr. Staines for your time and expert input. As well, I would like to thank to all the professors in the Public Health Sciences Department of UTEP College of Health Sciences.

Study funding was provided by The Center for Border Health Research (CBHR), an Initiative of the Paso del Norte Health Foundation (Dr. MM Weigel, PI).

ABSTRACT

Background and Significance. Atopy is a hypersensitivity disorder that mainly affects the mucous membranes and the skin. It is reported to be the most prevalent type of clinical allergy syndrome. Persons who have atopy suffer from various combinations of asthma, rhinoconjunctivitis and/or eczema. Atopy is defined as an inherited predisposition to generate IgE against common environmental allergens. Atopy is a type I hypersensitivity condition mediated by IgE immune response, while allergy is any excessive immune response to a foreign antigen. Thus, all atopic disorders are allergic response but some allergic conditions are not atopic per se.

The etiology of pediatric allergic diseases is complex; it involves multiple phenotypes that are influenced by a variety of genetic, host, and environmental factors. The scientific literature also suggests that certain environmental factors may act to either promote or protect against the development of allergic diseases, depending upon when exposure occurs such as in the prenatal period, early infancy, or later childhood. While some of these such as exposure to tobacco smoke and other indoor and outdoor ambient air pollutants are well documented, the evidence for others is less certain. It is important to investigate these other environmental influences in order to better understand the potential for allergic disease and ways to reduce risk in children. There are no published data the prevalence of childhood atopy in the U.S.-Mexico border region.

Objectives. The major objectives of the current study were to investigate the prevalence and environmental factors associated with the development of childhood atopy in young Mexican schoolchildren. These included familial allergy history, size at birth, respiratory infection history, overweight/obesity, breastfeeding, early weaning, type of weaning foods, and parasitic infections).

Hypothesis. It was hypothesized that the combination of a positive familial allergy history, a proxy for genetic background, in concert with early exposure to certain environmental allergens alters Th1-Th2 immune profile and increases the risk for developing atopy during childhood. It also was hypothesized that overweight/obesity causes chronic inflammation (generated in adipocytes) thereby increasing the risk for childhood atopy by elevating cytokine tumor necrosis factor α (TNF α) from adipose tissue, from interleukins 1 and 6 and leptin.

Methods. The survey was carried out in a public elementary school in Ciudad Juarez, Mexico. A total of 175 children attending the school who were enrolled in grades 1-4 completed the study. Only one child per family was allowed to participate to prevent oversampling by household. Data were collected from the student participants using a structured questionnaire containing closed and open-ended questions on child and household characteristics (sociodemographic, housing and living conditions, and child health history). Participants also underwent a comprehensive physical examination and anthropometric assessment. Serial fecal samples (3) were collected and analyzed for protozoal and helminth infections. The descriptive data were analyzed as number and percent or as means \pm S.D. Two by two contingency table analysis with corrected X^2 or Fisher's exact test, were used as appropriate to assess the bivariate categorical data. Students' independent t-test or one-way ANOVA was used to analyze continuous data, as appropriate. Multiple logistic regression analysis was employed to further analyze variables identified as significant (> 0.05) in the bivariate analyses.

Results. Slightly more than one-fifth (17.1%; 30) of the 175 child participants had one or more atopic conditions. Six children (2.9%) had asthma and 14.3% (25) had other conditions such as rhinoconjunctivitis (hay fever) and atopic dermatitis. Five of the six children (80%) with asthma also had other atopies. The children were reported to have several different types of

allergy triggers. These included dust/soil, pollen, mold, furred animal dander, foods (i.e., avocado, pizza, tunafish, peach, egg, and fried meat), drug (penicillin, sulfa drugs), and stuffed animal toys. Children with a familial history of atopy (34.8%; 16) were more likely than those without (10.9%; 14) to develop asthma or other atopic conditions during childhood (OR= 4.38, 95% C.I. = 1.93, 9.97; P < 0.0001). Children who were fed with any artificial formula during the first 3-4 months (13.2%; 7) were not at increased risk than others (18.9%; 23) to develop atopy (OR=1.53; 0.62, 3.81. Children who were exclusively fed with breast milk for the first six months after birth (3.2%; 1) had a marginally reduced risk than others (20.1%; 29) for developing atopy (OR= 0.13; 95% CI= 0.17, 1.01). It was not possible to assess the contribution of intestinal helminth infection to childhood atopy due to the absence of these in any serial stool samples.

The environmental factors identified as significant in the bivariate analyses included current obesity, early solid food introduction (≤ 4 mos. of age), meat/fish introduction (≤ 12 mos. of age) and a positive history for severe respiratory infection history. The results of the multiple regression analysis revealed that childhood obesity (AOR=2.78; 95% C.I.= 1.11, 6.96), early solid food introduction (AOR=3.66; 95% C.I.= 1.43, 9.33), and meat/fish introduction before the first year of life (AOR=3.15; 95% C.I.= 1.24, 8.02) remained significant even when controlling for the influence of the other variables in the model. However, the contribution of severe respiratory infection history was no longer apparent and was dropped from the model (AOR=3.36; 95% C.I.= 0.95, 12.0).

Conclusions and Recommendations. The study results confirmed that young children with history of family allergy are at very high risk for developing atopy compared to others. The three environmental factors (i.e., premature introduction of solid food and foreign animal

proteins, and child obesity) associated with an increased risk for atopy are all potentially modifiable through dietary and physical activity education/promotion.

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CHAPTER 1

BACKGROUND AND SIGNIFICANCE

Atopy is a hypersensitivity disorder that mainly affects the mucous membranes and the skin. It is reported to be the most prevalent type of clinical allergy syndrome. Persons who have atopy suffer from various combinations of asthma, rhino-conjunctivitis and/or eczema (Galli et al. 2008; Hopkin, 2009). The etiology of pediatric allergic diseases is complex. It involves multiple phenotypes that are influenced by a variety of genetic, host, and environmental factors (Sly et al., 2008; Subbararo et al., 2009).

Overview of Childhood Atopy

Atopy or Allergic Disease

Atopy comes from *atopos*, a Greek word for "out of place", placelessness, special, or unusual. Atopy is defined as "the inherited predisposition to generate IgE against common environmental allergens" (Holgate, 2010). The terms atopy and allergy are often used interchangeably. However, atopy is a type I hypersensitivity condition mediated by IgE immune response while allergy is any excessive immune response to a foreign antigen. Thus, all atopic disorders are allergic response but some allergic conditions are not atopic per se (Merck Manual, 2010).

The term "atopy" is often used to describe conditions such as asthma, eczema, and hay fever. Atopy may also be quantified in regards of the number and size of positive skin prick tests (Carroll, 2006). In genetically susceptible children, there appears to be a tight link between atopy and asthma (Gaffin, 2009). Atopic sensitization is thought to be a major risk factor for childhood asthma although not all authors agree as to the robustness of the reported association (Pearce et

al., 1999; von Mutius, 2002). In addition, as Weinmayr and associates (2007) have pointed out, the majority of the evidence that supports a strong association between atopic sensitization and asthma development has been collected in more developed countries (Weinmayr, 2007). Recent results from Kenya, Ethiopia, China, and other less developed countries suggest that the relationship between the two may not be as simple as was once assumed (Weinmayr, 2007).

Immunology of Atopy

Atopic disease arises when the immune system is non-regulated producing an allergic inflammation characterized by IgE antibodies. Such dysregulation and the development of an atopic disease is mediated by genetic and environmental factors (Gold, 2005). Unhygienic environmental conditions may be a factor providing protection against atopic disorders by inducing not only Th1 responses but also producing additional immunologic regulatory complexes (von Hertzen, 2004).

Atopic diseases also include rhinoconjunctivitis and eczema in addition to asthma. The “atopic march,” refers to the progression from eczema, the first atopic disease that is usually manifested early in infancy, to asthma and/or rhino-conjunctivitis (Gold, 2005). Atopic diseases in children are usually diagnosed using ISAAC parameters (Wördemann, 2006). Atopy is tested using a skin prick test (RAST) to determine IgE antibodies specific to common environmental allergens (Tariq, 1998; Gold, 2005).

Epidemiology of Atopy and Asthma

Atopy Prevalence

The global ISAAC study surveyed the prevalence of allergic rhino-conjunctivitis and atopic eczema symptoms in a sample of approximately one-half million subjects living in 56

countries (Asher et al., 2006; Williams et al., 1999; von Hertzen, 2004; Beasley et al., 1998). They identified wide variations in the population prevalence of these two allergic conditions among the various countries in the study during study phases I and III similar to that seen in the case of asthma (Asher et al., 2006). In Latin America, allergic rhino-conjunctivitis symptoms in children aged 6-7 years were most prevalent in Costa Rica (11.6-15.9%) and Brazil (12-12.5%) and somewhat less so in Panama (7.1-11.7%) and Chile (8.2-12.3%).

The atopy prevalence recorded for Mexico was lower, i.e., 8.6-7.2%, compared to other countries surveyed in the region. The prevalence of eczema symptoms for the Latin American countries participating in the survey was ranged from 10.9-12.9% in Chile and 7.9-14.4% in Panama to a low of 4-4.9% in Mexico (Asher et al., 2006). A more recent study carried out in Mexico City by Lopez-Perez and colleagues (2009) confirmed that 42.6% of 8,000 persons surveyed had at least one symptom of allergic diseases. Allergic rhinitis was the most frequent condition identified and children were the most affected group.

Asthma Prevalence

The prevention and control of asthma is ranked as a public health problem of major global significance. The most recent estimate from the World Health Organization (2010) indicates that approximately 300 million people worldwide suffer from asthma. Asthma is the most common chronic disease found in among children. Approximately 255,000 die annually from asthma-related causes. Most asthma-related deaths are reported to occur in low and middle income countries. The World Health Organization projects that asthma-related deaths will increase by one-fifth during the next decade if public health authorities do not take immediate action (WHO, 2010).

The prevalence of asthma appears to be increasing in populations around the world especially those in more developed regions. However, it is uncertain whether this because the true prevalence is higher or because health care access is better and cases are more likely to be reported in more compared to less developed countries. Estimates range from 32.2% (in United Kingdom) to 1.7% (in Ethiopia) worldwide for children aged 10 to 19 years old (Patel, 2008).

The Centers for Disease Control and Prevention (CDC, 2010) estimates that the prevalence of asthma in the U.S. population is 22.2 million or 7.7% of the population (CDC, 2010). Children are especially affected by asthma. The disease reported to be the most frequent cause of chronic illness among children living in the United States (CDC, 2008). Surveillance data collected by the CDC over the past three decades also suggests that the national prevalence of asthma has been steadily increasing and is now estimated to affect 7-15% of all U. S. children (CDC, 2010). Childhood asthma is reported to be the third leading cause of hospitalizations in kids and also accounts for 14 million missed schooldays annually (CDC, 2008).

The prevalence of asthma and asthma-related morbidity and mortality is especially high among African-American children and those of Hispanic descent especially Puerto Rican- and Cuban-Americans (CDC, 2008; Canino, 2006; Wördemann, 2006). However, the reported population prevalence is reported as lower in Mexican-American children including those living in U.S.-Mexican Border States (Svendsen, 2009). Grineski and associates (2007) reported that in Texas, asthma-related hospitalizations averaged 29.0/10,000 inhabitants. However, it was slightly lower in border areas (i.e., 21.2/10,000 inhabitants). Estimates of the population prevalence of childhood asthma in the El Paso area vary between 5-15% (Neas et al. 2004; Alexander et al. 2000; Dr. Maria Amaya, (unpublished data).

The International Study of Asthma and Allergies in Childhood (ISAAC) reported that the prevalence of wheezing among children aged 6-7 years in Latin America varies by country. For example, Asher and associates (2006) have reported the population prevalence of wheezing in Chile (17.9-18.2%), Brazil (21.3-24.4%), and Panama (22.7-23.5%) identified in Phase I and III of the ISAAC study is comparable to that reported in the United States or Canada (Neffen, 2005; Patel, 2008) but is much higher in Costa Rica (32.1-37.6%). In contrast, Mexico had one of the lowest recorded population prevalence recorded for the Americas region by the ISAAC study, i.e., 8.4-8.6% (ibid). Similar prevalence rates were reported for adolescents aged 13-14 living in the same countries (ibid).

Other studies have recorded even lower asthma prevalence estimates for the country, i.e., 3.3% (GINA, 2004). On the other hand, asthma prevalence appears to depend on location. The results of a study conducted by Del Rio-Navarro (2007) and associates revealed that 19.4% of 4,106 children aged 6-7 years who had lived in Mexico City since birth had asthma symptoms. Information on the prevalence on the northern Mexican side of the U.S.-Mexico border is scant. The results of a 1996 survey conducted in the “sister cities” of Nogales, Arizona and Nogales, Sonora among elementary school students (n=631) revealed a comparable prevalence on both sides of the border, i.e., 7.6% in Arizona vs. 6.9% in the Sonora side (Stephen, 2003). A survey conducted in Ciudad Juarez estimated the prevalence of wheezing at 20% and medically diagnosed asthma at 6.8% (Barraza-Villareal et al., 2003).

Risk Factors for Allergic Disease

The etiology of pediatric allergic diseases is complex. It involves multiple phenotypes that are influenced by a variety of genetic, host, and environmental factors (Sly et al., 2008). For

example, three of the most common pediatric asthma phenotypes include transient wheezing, late-onset wheezing, and persistent wheezing (Subbarao et al., 2009). Some of the risk factors hypothesized to increase or protect against asthma and atopy in children include familial history, child sex/gender, prenatal and early postnatal exposure, breastfeeding and weaning patterns, overweight/obesity, respiratory/other infections and antibiotics, exposure environmental tobacco smoke, other air pollutants, and aeroallergens.

Familial History

The results of familial linkage, monozygotic twin, and other studies conducted over the past several decades indicate that genetics plays an important role in the pathogenesis of asthma and other allergic diseases (Subbarao et al., 2009). For example, parental asthma is strongly linked with increased asthma susceptibility in offspring (Gelfand 2009). Previous studies have documented that the risk for a child developing asthma is increased by 40% if one of their parents suffers from allergic disease. The risk for the condition is nearly doubled (70%) if two parents have allergies (COMPEDIA, 2008). The evidence also indicates that family history appears to be the single most important risk factor associated with the development of other allergic conditions. For example, the results of a study conducted by Tariq (1998) revealed that the offspring of asthmatic mothers were approximately three times as likely to develop asthma or allergic rhinitis compared to children without such a family history.

Recent studies have identified the existence of modest to robust associations between a number of different genes and genomic regions and the risk for asthma and allergy (ibid). For example, Weidinger et al. (2008) have reported that genetic mutations linked with certain skin genes were associated with a substantially increased for several allergic conditions including eczema, allergic rhinitis, and asthma in infants with atopic dermatitis. Moffatt and associates

(2007) have reported that the ORMDL3 gene was highly associated with asthma. However, since the results of many studies vary by population, it has been suggested these distinctions may be the result of two factors: genetic heterogeneity related to asthma and allergy and gene-environment interactions. (Subbarao et al., 2009).

Child Sex/Gender

Previous studies have shown that the prevalence and incidence of asthma and atopy is much higher among male compared to female children from birth until puberty when the pattern is reversed (Subbarao et al., 2009; Sears et al. 2002). Boys also are more likely to exhibit airway hyper-responsiveness (le Souf et al., 1995), more clinically severe asthma and to be hospitalized more for asthma-related problems than girls (ibid). The reason for this is unknown but it has been hypothesized that the influence of some environmental allergens may be modified by sex (Oryszcyn et al., 2007).

Prenatal Exposure

Emerging evidence also suggests that certain epigenetic factors may cause immunological changes that could increase the risk of a fetus to develop atopic disease later in life (Hersoug et al., 2007). It also indicates that exposure to certain nutrients (Litonjua, 2008), fatty acids (Chatzi, 2008), and other substances in the maternal diet (Miller, 2008) as well as those in early postnatal life appear to influence the development of childhood asthma and allergic disease (Robinson, 2010; Kumar, 2008). For example, the results of several studies suggest that the infants of women with higher prenatal intakes of fresh fish or fish oil were at apparent decreased risk for eczema and atopic wheeze (Willers et al., 2007; Romieu et al., 2007). Other observational study results also suggest that higher maternal vitamin E and zinc concentrations

appears to protect against wheezing in kids as long as for five years after birth (Devereaux et al., 2006; Litonjua et al., 2006; Martindale et al., 2005). In contrast, dietary restriction of eggs, milk and other common food allergens during pregnancy did not appear to reduce the risk for later allergic disease development in children (Subbarao et al., 2009). Other studies have reported that the children of mothers who consumed a diet rich in n-6-poly-unsaturated fatty acids (PUFA's) during pregnancy are more likely to have eczema by age two years (Pali-Scholl et al., 2009).

Previous studies have also shown that development of fetal immune response is modifiable by allergens inhaled by the pregnant mother. This promotes initial T-helper2 (Th-2) immune response which is then subsequently modified to a non-allergic T-helper1 (Th-1) response after birth (Barret, 2008). Prenatal cigarette smoking significantly increases the risk for food allergy and wheezing development during early childhood (Subbarao et al., 2009). Prior studies have demonstrated a dose-response effect between prenatal exposure to cigarette smoke and reduced airway function in young children. It also appears that in high risk infants, prenatal alcohol consumption may increase IgE levels and the risk for developing pediatric atopic dermatitis according to Gold and associates (2005) who studied the issue in a Danish national child cohort.

Early Postnatal Exposure

Many potentially modifiable post-natal environmental influences are documented to play important roles. The common allergens reported to act as triggers to provoke asthma or allergic disease include foods such as peanuts, seafood, wine, dried fruits treated with sulfites, plant pollens, and furred animal dander, dust mite, cockroach and other insect allergens. Changes in humidity and exposure to air pollutants (cigarette smoke, dust storm events, indoor and outdoor particulate matter and pollutant gases), physical exercise, emotional stressors and anxiety, and

certain medications (e.g., penicillin, aspirin) also can serve as asthma and atopic disease episode (Kim et al., 2008; Drake 2008; Karmaus, 2008; COMPEDIA, 2008; Ho et al., 2007; ALA, 2007; NHLBI, 2007; English, 1998; Cookson, 2009). However, emerging evidence also suggests that some dietary factors such as adherence to a Mediterranean-type diet may exert protective effects against persistent wheeze, atopic wheeze, or atopy in children (Chatzi, 2008).

Breastfeeding

Human breast milk is documented to contain a number of different immune-related compounds with the potential to affect the immune system of the nursing child such as: IgA, T-lymphocytes, IFN-gamma, and cytokines, among others (Schack-Nielsen & Michaelsen, 2007). These play critical roles in protecting against certain types of infectious pathogens. Investigators also have hypothesized that breast-feeding may act to speed up immune system maturation by stimulating the development of Th-1 type cells (ibid). Skewing of the Th1-Th2 type cell ratio in favor of Th1 is associated with a decreased risk for the development of allergies (ref).

However, the role of breastfeeding in the development of atopic diseases is controversial. Results from diverse observational and clinical studies differ regarding as to whether or not breastfeeding protects against or increases the risk for the development of allergic diseases and if so, for which specific conditions (Greer et al., 2008; van Odijk et. al., 2003; Duncan & Sears, 2008; Halken, 2004; Gdalevich et al., 2001; Purvis et al. 2005; Bergman et al., 2002). Other questions remain regarding whether breastfeeding is protective only for children with a genetic predisposition (Laubereau et al., 2004; Benn et al., 2004; van Odijk et. al., 2003), the length of time it confers protection (Kramer & Kakuma, 2002) and whether the specific macronutrient composition of breast milk or other constituents that may be responsible (Schack-Nielsen & Michaelsen, 2007; Laurite et al., 2005).

Oddy and collaborators (1999) reported that breastfeeding appears to be protective against severe asthma by age six years in children, even after adjustment for covariates such as sex, gestational age, history of infections, overweight, parental smoking, and maternal history of allergies/asthma. Likewise, Hidalgo and associates (2009) found that children who were not breastfed at least 3-6 months and/or those who were weaned before the age of 4-6 months had an elevated risk for food allergy (Hidalgo, 2009). It has also been reported that children who were fed with infant formula rather than breastfed before the age of three years had a risk that was almost doubled for asthma by the age of four years compared to others (Tariq, 1998). Siltanen and colleagues (2003) also have reported that breastfeeding appeared to have significant protective effects in children with inherited atopy against allergic rhino-conjunctivitis and furred animal sensitization. However, in children whose atopy was not inherited, it was associated with a significantly elevated risk for atopy symptoms and serum IgE values (ibid).

A cohort study conducted by Sears et al. (2002) examined a group of 1,037 newborns to analyze the potential benefits of extended breastfeeding on reducing childhood atopy and asthma development. Their results indicated that breastfeeding did not appear to protect against atopy or asthma. They also found that breastfeeding for ≥ 4 weeks was associated with an increased risk of having a positive skin prick tests to common allergens (Sears, 2002). The reason for this is unknown but could be due to sensitization to allergens present in maternal breastmilk. In contrast a study of 14,000 pregnant women participating in the Avon Longitudinal Study of Parents and Children (ALSPAC) concluded that breastfeeding does not increase the risk of asthma or atopy even when the mothers themselves are asthmatic (Elliot, 2008).

Weaning Foods

The American Association of Pediatrics (AAP, 2004) and the European Academy of Allergology and Clinical Immunology (Muraro, 2004) have both recommended the delay of complementary food introduction until after 4-6 months of age in children. The AAP (2004) also recommends that cow's milk be delayed until after 12 months in infants. The two academies based their recommendations upon several earlier studies (Greer et al., 2008). However, the results of more recent studies differ as to the allergenic effects of early weaning and those of specific weaning foods on childhood asthma and asthma (Poole et al., 2006; Nafsted et al., 2003; Zutavern et al., 2008; Morgan et al., 2004). In addition, the potential benefits of dietary interventions designed to prevent or delay the onset of atopic disease are mostly restricted to infants with a high asthma risk, particularly those with at least one first-degree relative afflicted with allergic disease.

Wilson and colleagues (1998) reported that children weaned before 4 months of age had a significantly increased risk for developing atopy. However, Greer and associates (2008) reported that delaying the timing of complementary food introduction beyond 4 to 6 months of age does not appear to prevent atopic disease from occurring. However, Zutavern and colleagues (2008) reported that the observed prevalence of eczema, asthma, and allergic rhinitis was comparable in children regardless of whether they were first introduced to solid foods at ≤ 4 months of age, 4-6 months of age, and ≥ 6 months.

Nafsted and coauthors (1996) reported that the introduction of fish during the first year of life appeared to lower the risk for asthma and allergic rhinitis in Norwegian children (n=2531), a population with frequent fish consumption. The results of their multivariate study indicated that early dietary fish introduction was associated with a significantly reduced risk for

allergic rhinitis (AOR=0.45, 95% CI= 0.28, 0.74) and asthma during childhood (AOR=0.84, 95% CI = 0.57, 1.22). Poole et al. (2006) reported that the early introduction of cereal grains, i.e., ≤ 6 months vs. > 6 months, were protected from developing wheat allergies as measured by wheat-specific IgE.

Environmental Exposure to Tobacco and other Ambient Air Pollutants

Early postnatal exposure to maternal and other sources of second-hand tobacco smoke has been linked with a significantly increased risk for the development of wheezing (Stein et al., 2008; Desautaux et al., 1999) and asthma in children (Karmaus, 2008). The risk is reported to be especially elevated in cases where the mother also smoked during pregnancy (Subbarao et al., 2009). This relationship has also been confirmed in U.S.-Mexico border children. For example, a study of 6,174 school-aged children living in Ciudad Juarez revealed that those with a positive history for second-hand tobacco smoke exposure as an infant increased their risk for the subsequent development of wheezing by more than one-third (Barraza, 2003).

Exposure to Animals

The results of studies investigating the effects of childhood exposure to domestic cats and dogs on the risk for asthma and atopy are equivocal. For example, Almqvist and co-authors (2003) have reported that children who are exposed to cats are more likely to present with allergic sensitization but other authors either showed no difference in risk for a higher risk for allergic sensitization (Hendriksen et al., 2001; Huss et al., 2001). In addition, some studies have reported that children who are exposed to dogs early in life exhibit decreased sensitization to dog dander as well as other allergens and asthma (Alqvist et al., 2003; Huss et al., 2001). The evidence from early studies has suggested that children who are exposed to farm animals at an

early age appear to be less likely to develop allergic disease later in life (Subbarao et al., 2009).

Size at Birth and Gestational Age

A meta-analysis of size at birth as measured by a high ponderal index (wt/ht^3) or elevated birthweight revealed a relative risk of 1.2 (95% CI= 1.1-1.3) for the future development of childhood asthma and in some cases, wheezing (Flaherman & Rutherford, 2006). Low birth weight has been linked with a reduced risk for childhood development of atopic dermatitis in some studies (Buhrer et al., 1999). However, Liem and co-authors were unable to identify any significant associations between the development of childhood food allergies in low birth weight infants and those born prematurely (Liem and associates, 2007).

Respiratory Infections and Antibiotics

Severe lower respiratory tract viral infections have been linked with chronic wheezing, asthma and atopy in both clinical and animal studies (Subbarao et al., 2009; Karmaus, 2008; Walton & Johnston, 2008). It has been estimated that at least one-fifth of all children in their first year experience lower respiratory tract infections caused by viral infections accompanied by wheezing (Sly et al., 2008). The viruses identified as most likely to induce these conditions are human rhinovirus, respiratory syncytial virus, and parainfluenza viruses (Sly et al., 2008; Walton & Johnston, 2008). In addition, adenoviruses, human metapneumovirus, and influenza virus have been implicated but to a lesser degree (Sly et al., 2008).

It remains, however, unclear as to whether sensitization occurs in genetically susceptible infants who were previously sensitized to allergens. This could result in skewing toward a Th2-type immune response leading to asthma or other atopic conditions (Subbarao et al., 2009). It is

also unclear as to whether the hypothesized effects are virus-specific or if repeated and synergistic allergen exposures are able to induce Th2 immune responses in children who do not have genetic vulnerability to allergic disease (ibid). The available evidence suggests that although lower respiratory tract infections appear to promote sensitization to aeroallergens and asthma in some children, in others they may actually play a protective role (Subbarao et al., 2009). In addition, the potential role of exposure to antibiotic drugs during early life in causing allergic disease is controversial. The use of antibiotics was linked to an increased risk for early allergic sensitization such as childhood wheezing and asthma by recent authors (Alm et al., 2008; Kozyrsky et al., 2007; Kummeling et al., 2007). However, it could be proxy for frequent lower respiratory illnesses caused by viruses or bacteria, both of which are frequently treated with antibiotic drugs at the insistence of parents.

Parasitic Infections

It has also been hypothesized that exposure to parasitic infections early in life may act to reduce asthma and allergy. Specifically, the “hygiene hypothesis” suggests that in populations such as those in more developed countries (MDC’s), cleaner environmental conditions, use of antibiotics, and vaccinations, decreases the probability of children being exposed and contracting infectious diseases early in life. This, in turn, increases the risk for the development of allergic disease such as atopy in susceptible persons through the effects on Th1 response. It is hypothesized that exposure to certain parasites, especially helminths, in early life may prevent immune diseases since these may promote healthy immunomodulation (Carvalho et al.; 2006). The inverse relationship between helminth infection and atopy has been demonstrated by a number of prior studies (Hagel et al., 1993; Lynch et al., 1993; Cooper et al., 2003; 2004; Carlswell et al., 1976). However, the results of some other studies suggest helminth infection can

result in exacerbation of asthma symptoms (Palmer et al., 2002; Kayhan et al., 1978; Guement 1973) and eczema (Cooper et al., 2004).

Overweight and Obesity in Infancy and Childhood

The global prevalence of obesity has been steadily increasing among all age, ethnic, gender, and socioeconomic groups in both more- and less-developed countries (WHO, 2000; Speiser et al, 2005). This continued increase in prevalence makes obesity a problem of epidemic proportions, with a behavior that is comparable to the characteristics of infectious diseases (WHO, 2000). The global increase in the overweight/obesity has paralleled that of asthma (Ayres, 2009) and atopic diseases (Bodner, 1998). The epidemiologic evidence generally suggests that children who are overweight are at increased risk for asthma. Oddy and associates (2004) reported that high BMI (kg)/ [height (m)]², was a risk factor for asthma even after adjustment for most known risk factors. However, the risk for atopy development in children was not associated with BMI (Oddy, 2004). Another study conducted by Schachter (2003) found that although a BMI of 85-95th percentile in boys significantly increased the risk for wheeze and cough, it was not associated with either recent asthma episode or increased airway elevated sensitivity. In contrast, higher BMI in girls was associated with significantly increased risk for atopy, wheeze and cough (ibid).

Another randomized, double blind clinical trial study (n=1005, mean age: 9.0 years) found that children at risk for overweight were more likely than their peers to have mild-to-moderate asthma (Bender, 2007). The results of the bivariate analysis for a study conducted by Beuther and associates (2006) found a positive association between child BMI and the risk for asthma and atopy using NHANES III data (n= 5984). However, after adjustment for confounders, only the previously identified contribution of BMI remained significant only for asthma. In contrast,

other studies suggest that overweight children are more likely than those that are normal weight to develop atopy (Nathan, 2008).

Although the precise mechanism responsible for the apparent association between high BMI (overweight/obesity) and asthma and atopic disease development is not known, the emerging evidence suggests that the relationship is mediated by chronic low grade inflammation. Obesity in animal models is strongly linked with inflammation due to overexpression and subsequent elevation of the cytokine tumor necrosis factor (TNS) - α from adipose tissue (Hotamisligil, 1995). In obese individuals, CRP is regulated by substances secreted by adipose tissue such as cytokine tumor necrosis factor α (TNS), interleukins 1 and 6, and leptin (Economou, 2005; Nathan, 2008).

Study Rationale

The available evidence suggests that gene-environment interactions are most likely responsible for worldwide variance in the prevalence of pediatric allergy and asthma. The scientific literature also suggests that certain environmental factors may act to either promote or protect against the development of allergic diseases, depending upon when exposure occurs such as in the prenatal period, early infancy, or later childhood. While some of these such as exposure to tobacco smoke and other indoor and outdoor ambient air pollutants are well documented, the evidence for others is less certain. It is important to investigate these other environmental influences in order to better understand the potential for allergic disease and ways to reduce risk in children.

Published data reporting on the prevalence of asthma and atopy in Mexican populations is scant, particularly for those living along the U.S.-Mexico border including the Paso del Norte area. Data collected using active surveillance methods suggests the prevalence of medically

diagnosed asthma may be much higher than previously realized (M. Amaya, unpublished data). There are no published data the prevalence of atopic disease in the border region.

The prevalence of childhood overweight is reported to be elevated and growing among the predominantly Hispanic (i.e., Mexican descent) groups that inhabit both sides of the U.S.-Mexico border in the Paso del Norte region. However, the relationship between overweight and asthma has not been investigated in this population groups on either side of the border. In addition, little is known about the breastfeeding, weaning, and early introduction of foods in the northern Mexico border area. These have the potential allergenic potential that could predispose children to develop asthma and atopy.

CHAPTER 2

STUDY OBJECTIVES AND HYPOTHESIS

Major Objective

The major objective of the proposed study is to investigate the prevalence and factors associated with the development of childhood atopy in young Mexican schoolchildren.

Specific Objectives

1. To investigate the prevalence of atopy in a group of Mexican public elementary schoolchildren.
2. To examine the role of the hypothesized risk factors for atopy. These include familial allergy history (a proxy for genetic atopy inheritance), and environmental factors such as size and gestational age at birth, respiratory infection history, overweight/obesity, breastfeeding, early weaning and type of weaning foods, and parasitic infections.

Hypothesis

It is hypothesized that the combination of a positive familial allergy history, a proxy for genetic background, in concert with early exposure to certain inhaled, dermatologic, and ingested allergens (i.e., meat, fish, tobacco smoke, infections, and pet dander) alters Th1-Th2 immune profile and increases the risk for developing atopy. It also is hypothesized that overweight/obesity causes chronic inflammation (generated in adipocytes) which increases the risk for childhood atopy by elevating the cytokine tumor necrosis factor α (TNF α) from adipose tissue, from interleukins 1 and 6 and leptin.

CHAPTER 3

METHODS AND MATERIALS

Study Design and Research Site

The cross-sectional study was carried out in a working class neighborhood in the Mexican city of Ciudad Juarez at the “Francisco I. Madero” public elementary school. It was selected pursuant to discussions with Mexican colleagues at the Universidad Autónoma de Ciudad Juarez and after meeting with the school’s administration and the parents/guardians of the child students. The majority of the homes in which the school is located have potable water, adequate sewage and solid waste disposal, and paved roads. The neighborhood has good transportation services facilitated by the city’s public transportation system.

Sample Selection and Informed Consent

One-hundred eighty-one children attending the school were selected to participate in the study. A total of 175 participants completed the study. Prospective participants were eligible to participate if they were currently enrolled in grades 1-4. In order to minimize the possibility of over-sampling, only one child per family was eligible for study participation. The study protocol was approved by both the University of Texas at El Paso and the Universidad Autónoma de Ciudad Juárez, Instituto de Ciencias Biomédicas institutional review boards (IRB). The written informed consent and assent processes were carried, respectively, with for the study parents/guardians and child participants. This occurred previous to enrolling any of these in the study.

Study Protocol

The data were collected from the participants in a vacant schoolroom at the school during morning class hours. The study data were gathered by the trained interviewers in Spanish from the participant parents/guardians using a structured questionnaire containing closed- and open-ended questions on child and household sociodemographic characteristics/housing/living conditions and a child health history. The physician-administered clinical examination of the child participants focused on the identification of objective indicators and subjective signs and symptoms of chronic and infectious illness. Subsequently, the anthropometric assessments of the child participants were performed. The children donated a 6 mL sample of fasting venous blood into a heparinized blood collection container. The blood samples were immediately placed in a cool box and transported to the Quest Laboratory outlet in Cd. Juarez for subsequent analysis. In addition, the participants donated three serial stool samples in sterile fecal sample collection vials provided to them. These were also transported to the Quest Labs in Cd. Juarez after being given to the study team by the participant's parents. At the lab, they were analyzed for the presence/absence of protozoal and helminths.

The child participants were each provided with snacks immediately after completing their data collection session. They also received a monetary incentive which was given to the child participant families who participated in the study for the purpose of compensating them for their time and trouble. Twenty dollars cash compensation was given to each parent/guardian-child pair who completed the interview, health history, physical, anthropometric, and laboratory study portions of the study. They also were given two dollars for each stool sample that they submitted for the analyses for a total of six dollars. Furthermore, all parents/guardians were informed verbally and in written form about the results of their children's clinical, lab, and

anthropometric exams. Each also had their children's results interpreted for them. In addition, they were given their written referrals and recommendations for those children who were detected to have conditions that required intervention.

Data Collection Instruments

Household Characteristics Questionnaire

The structured questionnaire containing open- and close-ended questions was used to collect data on child participant and sociodemographic, housing, lifestyle and other characteristics. This Spanish-language instrument was previously developed for use local border residents by the study P.I. (Weigel et al., 2006).

Child Health History

A modified version of the main health history portion of the California Farmworker Health Survey CAWHS was used to collect information on recent and current illnesses of child subjects (CIRS, 2002). The CAWHS was previously validated for use in Mexican and U.S. Mexican populations (Mines et al., 2001). The instrument was administered by the study team during interviews with the parents/guardians of the child participants. The CAWHS instrument used open- and closed-ended items to question parents/guardians about the history and timing of recent and current conditions that their child may have experienced. These included gastrointestinal respiratory and other infections (e.g., colds, measles, TB, HIV, varicella), chronic (e.g., diabetes) and allergic diseases (e.g., asthma, eczema, rhinoconjunctivitis). Additional questions on physician-diagnosed conditions, hospitalization events, vaccination history, and the use of conventional and traditional remedies to treat illnesses were also asked.

Clinical Examination

Each child participant received a comprehensive physical examination. The licensed medical physicians on the study team performed examination of the heart, lung, skin, central nervous system (CNS) and other organ systems. The exam also concentrated on the child's general appearance, eyes, nose, throat, lymph, cardiac, abdomen, pulmonary, neurological, spine and extremities. In addition, the physicians measured cardiac frequency rate (b/min) and blood pressure using a manual sphygmomanometer (System 5, Multicuff BP system) with a child cuff size(s).

Anthropometric Assessment

Standardized protocols (Gibson, 2005) were used to collect the anthropometric measurements on each child: body weight, standing height, mid-upper arm circumference, and triceps skinfold, and mid-upper-arm fat area. Body weight was measured to the nearest 0.5 kg using a calibrated portable scale (Detecto, USA). The scale was recalibrated after each subject was weighed. Standing height was measured to the nearest 0.1cm using a portable stadiometer (Detecto, USA). All shoes, coats, hats and other headwear were removed from the children prior to taking their weight and height measurements. Subject MUAC was measured to the nearest 0.1 mm using a semi-flexible insertion tape measure (Ross Labs-USA). Triceps skin fold was measured using a Lange skin fold caliper (Beta Technologies, MA). The triceps skin fold and MUAC was used to calculate mid-upper arm muscle area and mid-upper arm fat areas and then compared with reference standards (Gibson, 2005). Mid-upper arm fat area (MUFA) is reported to provide a better estimate of total body fat than a single skinfold at the same site (Gibson 2005). Subject body mass index (BMI) was compared to the 2000 International Obesity Task Force recommendations (Cole, 2000).

Fecal Samples

Three fecal samples were collected during 3 consecutive days in containers provided to the parents; the parents were instructed on the proper method for its collection. Subsequently, the samples were examined within 24 to 72 hours by parasitologic techniques for detection of protozoal and helminth infections. All fecal samples were processed at Quest Laboratories in Cd. Juarez.

Data Analysis and Interpretation

The data was entered into a SPSS database (SPSS, version 17). Descriptive data was presented as number (percent) or means \pm S.D. Bivariate analysis of the differences between proportions was assessed using 2 x 2 contingency table, analyses with corrected X^2 or Fisher's exact test, as appropriate. Students' independent t-test or one-way ANOVA were used to analyze mean differences. Simple linear regression was employed to analyze the association of continuous independent and dependent variables. Multivariate analysis was used to further analyze variables identified as significant (> 0.05) in the bivariate analyses. These used multiple logistic regression with adjustment for potential confounders.

Sample Size & Power

The effect size reported by prior studies for the major atopy predictors of interest ranged from approximately 0.15-0.25. With a setting of the statistical power of 0.8 (β) at the 0.05 level (α) and with an estimated effect size of 15%, the sample size of 175 was found to be sufficient to establish statistical significance for the desired power and the effect size.

CHAPTER 4

STUDY RESULTS

Participant Characteristics

All of 175 children in the study were Mexican nationals from working class families. The mean age of participants was 8.3 ± 1.3 years. All attended grades 1-4 at the Francisco I. Madero public elementary school in Ciudad Juarez. Fifty-six percent (97) were female.

Atopy Prevalence

Slightly more than one-fifth (17.1%; 30) of the 175 participants had one or more atopic conditions. Six children (2.9%) had asthma and 14.3% (25) had other conditions such as rhinoconjunctivitis (hay fever) and atopic dermatitis. Five of the six children (80%) with asthma also had other atopies. The children were reported to have several different types of allergy triggers. These included dust/soil, pollen, mold, furred animal dander, foods (i.e., avocado, pizza, tunafish, peach, egg, and fried meat), drug (penicillin, sulfa drugs), and stuffed animal toys.

Atopy Risk Factors

Familial Allergy History

Participants with a familial history of atopy (34.8%; 16) were more likely than those without (10.9%; 14) to develop asthma or other atopic conditions during childhood (OR= 4.38, 95% C.I. = 1.93, 9.97; $P < 0.0001$).

Size at Birth

The results of the bivariate analyses did not identify any statistically significant associations between the birth characteristics of the participants and their risk for childhood

atopy. The average weight (3.4 ± 0.63 kg vs. 3.4 ± 0.68 kg; $t=0.08$; $P=0.94$), crown-heel length (52.1 ± 3.3 cm vs. 51 ± 4.3 cm; $t= -1.0$; $P= 0.32$), ponderal index (24.3 ± 4.8 vs. 27.1 ± 8.6 ; $t=1.3$; $P=0.19$) and gestational age (40 ± 1.02 vs. 39.4 ± 1.8 ; $t= -1.5$; $P= 0.13$) at birth of the children who later developed childhood atopy was similar to those who did not develop atopy. Likewise, the proportion of children with low birthweight (13.3% vs. 19.2%; Fisher's exact test $P= 0.91$) and premature delivery (0% vs. 17.6% Fisher's exact test $P= 0.42$) was comparable between those who did and did not develop atopy by the time of the study.

Nutritional Factors

Infant Feeding History

For the first several months of life, approximately one-third (30.3%; 53) were breastfed exclusively, 24% (42) received artificial infant formula, and 45.7% (80) were fed with a combination of breastmilk and formula. Only 17.7% (31) of the infants were breastfed exclusively for at least six months. Children who were fed with any artificial formula during the first 3-4 months (13.2%; 7) were not at increased risk than others (18.9%; 23) to develop atopy (OR=1.53; 0.62, 3.81; $P=0.49$). Children who were exclusively fed with breast milk for the first six months after birth (3.2%; 1) had a marginally reduced risk than others (20.1%; 29) for developing atopy (OR= 0.13; 95% CI= 0.17, 1.01; $P=0.045$).

Vegetables were one of the most common first solid foods given to infants (58.3%; 102). These were fed in mashed or soup form and included green leafy vegetables, squash, carrots, beets, and potatoes. Mashed or pureed fruits such as apple, pear, melon, papaya, peaches, and banana also were a common first food (49.7%; 87). Cereals such as rice and oats (24.6%; 43), finely ground or shredded meats (e.g., chicken, turkey, pork) and fish (22.3%; 39), whole or egg yolks (16.6%; 29) or legumes such as mashed/soupy lentils, beans, green peas (12%; 21) were

less frequently given as first foods compared to vegetables and fruits. Only one child (0.6%) received a dairy product (yogurt) as one of their first foods.

The bivariate analysis results revealed that the average age at which children were introduced to their first solid food was reduced in children who later developed atopy compared to those who did not develop atopy (4.1 ± 1.7 months vs. 5.9 ± 2.7 months; $t= 3.4$; $P= 0.001$).

The results also showed that the risk for atopy was increased almost five-fold among children who were fed any type of solid food before the age of four months compared to others (30%; 21 vs. 8.1%; 8; OR= 4.88; 95% C.I.=2.01, 11.8). Children who were given meat/fish in their diet before the age of 12 months (33.3%; 13/30 vs. 12.5%; 17) also were at 3.5 times the risk for developing atopy compared to other kids (OR=3.50; 95% C.I.=1.52, 8.09; $P=0.005$).

Anthropometric Indicators

One-third (34.9%) of the Mexican children in the study were classified as being either overweight (17.8%; 31) or obese (17.2%; 30) according to the International Task Force on Obesity classification. One fifth (20.2%; 35) of the children also had a mid-upper arm fat area that was ≥ 2 standard deviations above the mean for their age and sex. Close to one-tenth (9.7%; 17) showed evidence of linear growth retardation (growth stunting).

The results of the bivariate analyses indicated that children with atopy had a higher average body mass index compared to those without atopy (19.7 ± 0.8 vs. 17.9 ± 0.3 ; $t=2.4$; $P=0.016$). they also were nearly four times as likely to be classified as obese by IOTC standards compared to non-obese children. The risk for atopy among child participants with mid-upper arm fat areas that were ≥ 2 standard deviations above the mean for their age and sex was only marginally increased compared to their other counterparts in the study (28.6%; 10 vs. 14.5%; 20; OR=2.36; 95% C.I.= 0.99, 5.65; $P= 0.086$).

Infectious Factors

Respiratory System Infection History

None of the child study participants were reported to have a positive history for serious respiratory infections such as pulmonary tuberculosis, whooping cough or diphtheria. However, a number of children were reported to have experienced other respiratory infections such as pneumonia, severe bronchitis, and chronic sinus infections. Twelve percent (21) of the children had a history of hospitalization for severe respiratory infections including pneumonia (4.5%; 8), severe bronchitis (5.1%; 9), and asthma (2.3%; 4). Children with a history of severe respiratory infections were at increased risk for developing atopy compared to other children (46.7%; 7 vs. 14.4%; 23; OR= 5.21; 95% C.I. = 1.72, 15.8; $P= 0.005$).

Intestinal Parasitic Infections

The prevalence of laboratory-diagnosed intestinal parasitic infections among the sample was low. Fewer than five percent had one or more stool samples that were positive for a pathogenic protozoal parasite, i.e., *Giardia intestinalis* (4.6%; 8) or *Amoeba histolytica* (2.6%; 4). None of the children were found to have adult or larvae from helminths in their stool samples. No difference in the risk for atopy was seen among children with intestinal protozoal infections compared to those without (16.7%; 2 vs. 17.2%; 28; OR=0.96; 95% C.I.= (0.20, 4.64). It was not possible to investigate the potential association between intestinal helminth infection and atopic conditions.

Multivariate Analysis of Atopy Risk Factors

The factors previously identified as significant in the bivariate analyses included current obesity, early solid food introduction, meat/fish introduction ≤ 12 months of age and positive

history for severe respiratory history. The table shows the results of the multiple regression analysis that investigated the association of these factors with the risk for childhood atopy. As is indicated, the first three factors (obesity, early solid food introduction, meat/fish introduction before age 12 months) remained significant even when controlling for the influence of the other variables in the model. However, the contribution of severe respiratory history was no longer apparent and was dropped from the model.

CHAPTER 5

DISCUSSION

To the best of knowledge, the present study is the first to investigate the prevalence and factors associated with the atopy development in a U.S-Mexico border pediatric population. The results showed that atopy was common among the child border group studied since slightly more than one-fifth of the 175 participants had one or more atopic conditions. Medically diagnosed asthma was less common than other atopies such as rhinoconjunctivitis (hay fever) and atopic dermatitis. Consistent with previous reports from other global populations, almost all of the children with asthma also had other atopies. The different types of triggers for asthma and other atopic episodes were also congruent with the literature, i.e., dust/soil, pollen, mold, furred animal dander, specific types of foods, penicillin, and sulfa drugs. Children with a familial history of atopy had a fourfold increase in their risk for developing atopic conditions during childhood. The present study results are consistent with those finding that family history is the single most important risk factor associated with atopy development (Gefand, 2009; Tariq, 1998; COMPEDIA, 2008). Wilson et al., 1998 reported that kids weaned at 4 months or younger age had an increased risk for atopy development. Nathan (2008) reported that overweight kids have an increased risk for atopy, which is similar to our study results.

Baranowski et al. (1990) studied the relationship between ethnicity, infant-feeding practices and adiposity in the childhood, finding a weak relationship between the duration of breastfeeding and the children's body weight. Infants' breastfed during 12 months or more compared to formula-fed were leaner in a study that researched growth patterns for weight, length, head circumference, and body composition (Dewey, 1992). School age children aged 5 and 6 years who were exclusively breastfed during 2 to 12 months were less likely to be

overweight or obese. Breastfeeding was found to be a consistent and protective factor, not attributable to social classes or lifestyle (Von Kries, 1999).

Hediger et al. found similar results to those previously reported by the National Health and Nutrition Examination Survey III (NHANES 1988-1994): children of Mexican-American origin had an increased risk of become overweight when compared with non-Hispanic white children, he also found that the delay in introduction to solid foods may reduced the risk of become overweight at ages 3 to 5 years (Hediger, 2001). This author's second finding is an important foundation to our study results (by combining both, overweight and early childhood food introduction).

In conclusion, the study results confirmed that young children with history of family allergy are at very high risk for developing atopy compared to others. The three environmental factors (i.e., premature introduction of solid food and foreign animal proteins, and child obesity) associated with an increased risk for atopy is all potentially modifiable through dietary and physical activity education/promotion. Future studies with larger samples sizes and a greater age range of children should be conducted in Mexican and US- Mexico border population to fully investigate potential roles and interactions of prenatal and postnatal risk factors.

Study Limitations

Every study has strengths and limitations. Both should be considered when interpreting their results. This study major strength was the use of objective clinical, anthropometric, and laboratory indicators that minimizes potential systematic error, and the use of multivariate analytic techniques that controlled for possible confounding sources. Other strength was that the participants' parents or guardians were supplied with their children tests results and

recommendations in case that any alteration were found in their children; this point is especially important because many of the participants had none or limited access to proper medical care. Another possible limitation was the use of only one overweight and obesity classification (International Task Force on Obesity) that disallowed the comparison between two or more classifications.

Some of the limitations of the study were the use of a relatively small sample size of 175 participants who completed all the study stages, with a narrow child age range; it was a pilot study with convenience sampling. Other limitation to take in consideration is the lack of an objective test to determine the participant's atopic response as expected if uses a prick-test (gold standard) to document allergy or sensitization. The use of self-reported questionnaires may affect the results by increasing memory bias since mothers or respondents may forget important information about their children (mainly related to dates, weaning information, food given to children, and/or childhood diseases). Atopy and asthma are self-reported conditions. Finally this research did not investigate the role of maternal prenatal factors, such as tobacco use or tobacco smoke exposure, maternal infections, diet during pregnancy, antibiotics or other medication use, etc.

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GLOSSARY

Child Overweight and Obesity Classification. Body Mass Index (BMI) or Quetelet's Index is a formula to calculate the body fatness. BMI is calculated from a person by dividing the body weight by height; in other words, weight in kilograms divided by height in meters squared (CDC, 2009). Body mass index (BMI) is the most widely accepted standard method for classifying adult overweight and obesity in both individuals and populations (WHO, 1995; CDC, 2007). Two of the most widely used child BMI classification systems are the Centers for Disease Control and Prevention (CDC) and the International Obesity Task Force (IOTF) classification standards, since it does not exist an accepted international standard for classifying children BMI.

Eczema. Term used for a group of medical conditions that causes the skin to become irritated, itchy, or inflamed.

International Task Force on Obesity (IOTF) definition of overweight and obesity. The IOTD percentile recommendations for children are based on the adult BMI cut-off points of 25 and 30 that were adopted by WHO, reflecting values in children which track to future adult overweight and obesity (Troiano & Flegal, 1998; Cole et al., 2000; Flegal et al., 2001).

Rhinoconjunctivitis. Combination of allergic nasal and ocular symptoms.

TABLES

Table 1. Results of the Multiple Logistic Regression Analysis Showing the Association of Environmental Risk Factors with Childhood Atopy (n=175)

	No. (%)	OR (95% C.I.)	<i>P</i>	AOR (95% C.I.)	<i>P</i>
Current body mass index					
Obese	14 (34.1)	3.82 (1.67, 8.77)	0.002	2.78 (1.11, 6.96)	0.029
Non-obese	16 (11.9)	1.00 (reference)		1.00 (reference)	
Early solid food introduction (< 4 mos.)					
Yes	21 (30.0)	4.88 (2.01, 11.8)	0.007	3.66 (1.43, 9.33)	0.007
No	8 (8.1)	1.00 (reference)		1.00 (reference)	
Meat/fish introduction before age of 12 mos.					
Yes	13 (33.3)	3.50 (1.52, 8.09)	0.005	3.15 (1.24, 8.02)	0.016
No	17 (12.5)	1.00 (reference)		1.00 (reference)	
History of respiratory tract infection					
Yes	7 (46.7)	5.21 (1.72, 15.8)	0.005	3.36 (0.95, 12.0)	0.062
No	23 (14.4)	1.00 (reference)		1.00 (reference)	

Homer-Lemeshow goodness of fit $X^2=6.111$; $P=0.191$

CURRICULUM VITA

Laura Alvarez was born in the northern part of Mexico in the state of Chihuahua. She was the first child of a family with 3 daughters. She graduated from the Facultad de Medicina in the city of Chihuahua in May of 1992. After graduated from Medical School, Laura moved to U.S. where she worked as Physician's Assistant in a Correctional Facility. Then, Laura moved back to Mexico where she worked with the Mexican Health Secretariat at the State Epidemiology Department. In 2003 Laura returned to US to work with the UT-Houston School of Public Health; while pursuing her Master in Public Health she worked with the University of Texas at El Paso and for the City of El Paso at the Department of Public Health – Epidemiology Department, where she currently works as Disease Surveillance Specialist. Her practicum (internship) was carried out at the US- Mexico Border Office of the Pan-American Health Organization (PAHO).