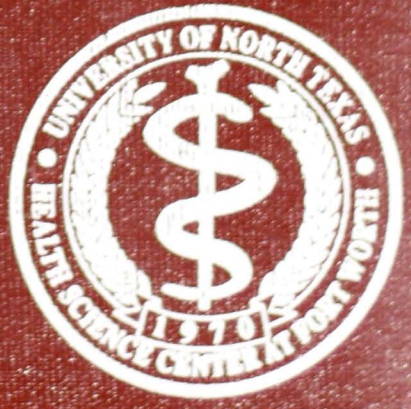
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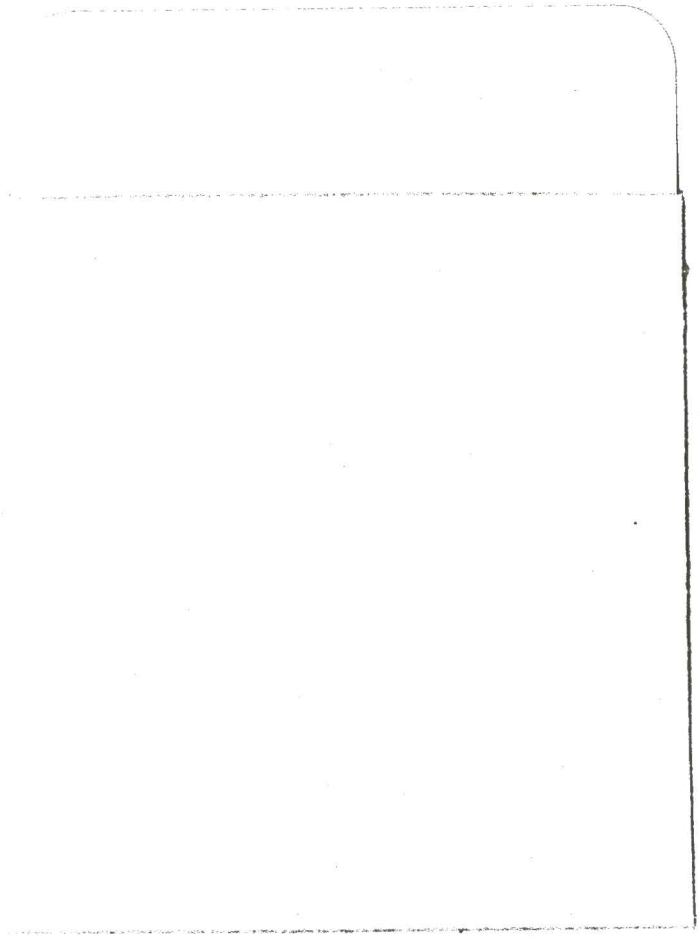

Alvarez-Garriga, Carolina, Risk Factors for Childhood Asthma in the United States: A Cross-Sectional Study Based on NHANES 1999-2000 Data. Doctor of Public Health (Epidemiology), May 2005, 114 pp., 18 tables, 4 figures, bibliography, 93 titles.

The purpose of this study was to identify and assess risk factors for childhood asthma. A total of 158 asthmatics were compared to 1,104 non-asthmatics regarding selected factors by using the multiple logistic regression adjusted odds ratio as a measure of association. A 2.3 times higher prevalence (13.8 per 100) was found for the U.S. than that reported in the previous national survey (NHANES III) during 1994 (5.9 per 100). Males and all race/ethnic minorities showed higher probability to have asthma. Income was inversely related to having asthma, and, among other results, renting a house, low birthweight, hay fever, chickenpox, learning disabilities, ear infections, trouble seeing even with glasses, and not covered by private insurance had higher chance of having asthma. Childhood asthma is still alarmingly increasing, and results from this study about high-risk groups and modifiable factors can be used for public health interventions.

RISK FACTORS FOR CHILDHOOD ASTHMA IN THE UNITED STATES: A CROSS-SECTIONAL STUDY BASED ON NHANES 1999-2000 DATA

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RISK FACTORS FOR CHILDHOOD ASTHMA IN THE UNITED STATES: A CROSS-SECTIONAL STUDY BASED ON NHANES 1999-2000 DATA

DISSERTATION

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for the Degree of

Doctor of Public Health

By

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CHAPTER I

INTRODUCTION TO THE STUDY

Asthma is a public health problem, as it is particularly severe and could be fatal during childhood and in the elderly (Redd, 2002). At the end of the 1990s, childhood asthma was reported to be the most common chronic disease in that age group (Hu et al., 1997; Pearce, Beasley, Burgess, & Crane, 1998). The prevalence, incidence, severity and mortality of childhood asthma is increasing. Studies show that an incidence rate of 5 per 100 increased per year from 1995 until the year 2000, representing 500,000 new cases every year (Weiss, 2001). Asthma prevalence increased as much as 74% from 1980 to 1995 and during that same time period increased 163% in children aged 0 to 4 years (Chulada, Arbes, Dunson, & Zeldin, 2003). The Centers for Disease Control and Prevention (CDC) reported that from 1980 to 2000, asthma cases have increased more than two times, from 6.8 million in 1980 to 17.3 million in 1998 (Weiss, 2001). The prevalence of asthma was reported during year 2001 to be highest in the younger age groups, with children ages one to four years, accounting for up to 50% of all emergency visits where the most frequent diagnosis was asthma (Dell & To, 2001). During year 2000, asthma was estimated to affect 15 million people in the United States; five million

of whom were under 18 years of age (Schwab, Cullen, & Schwartz, 2000). During 1997, asthma was estimated to affect five to nine percent of children whose ages were six months to eleven years in the United States (Nelson et al., 1997). In the United States, during 1999, 9 - 16% of children use medication for asthma regularly and 0.4% (4 per 1,000 cases) were hospitalized for asthma annually (Peat & Li, 1999). The morbidity of childhood asthma is a significant source of health care costs for young children (1 to 4 years of age). During year 2000, asthma was estimated to cost the U.S. economy $11 billion dollars in health care expenditures, as well as significant lost of productivity each year (Schwab et al., 2000). During 2001, asthma was the number one cause of hospitalization in children and the number one cause for missed school days (Weiss, 2001).

The International Study of Asthma and Allergy in Children, ISAAC, evaluated a series of studies on the prevalence of asthma in several participating countries during 1999. This study rated the United States as second in prevalence of asthma behind the United Kingdom (Peat & Li, 1999). The United States, Brazil, Canada, and Peru had prevalence rates of 25 per 100 population and Australia, Ireland, New Zealand, (list their stats here), whereas the United Kingdom had prevalence rates as high as 30 per 100 population (Peat & Li, 1999). Developed nations have consistently higher asthma rates than developing nations. This has been attributed to many different factors. Differences between developing and developed nations include the following: urban environments,

high body mass indices (BMIs), overuse of antibiotics, high fat processed food, lack of parasites, low levels of endotoxins, and low particulate air pollution (Weiss, 2001).

Many hypotheses have been made to explain the dramatic increase and differences between nations. One hypothesis asserts that the typical westernized diet usually lacks adequate levels of antioxidants. This may produce a weaker host response to allergens and therefore, increases the risk of asthma (Pearce et al., 1998). Other studies have suggested that the increase is due to global changes in exposure to infectious organisms through improved sanitation (asthma has been associated with improved sanitation) and widespread use of antibiotics (Wright, Sherill, Holberg, Halonen, & Martinez, 1999). The increase in asthma is also hypothesized to be directly proportional to the increases in outdoor and indoor pollution, familial factors, and in how asthma is diagnosed (Pearce et al., 1998). When examining the difference between the U.S. and Australia in 1999, it was discovered that in Australia and New Zealand, who had lower asthma rates than the United States, 50% of infants were breastfed for more than four months and 25% for more than six months. In contrast, in the United States, only 27% of infants were breastfeed for their first month of life and 13% until their third month (Peat, 1998; Raisler, Alexander, & O'Campo, 1999). These remarkable findings encourage more research on infant diet in the first months of life and the relationship with asthma rates. In addition, there is growing interest in the potential protective effects that breastfeeding may have on conditions other than asthma; such as otitis media and

necrotizing enterocolitis to childhood asthma (Wright, Bauer, Naylor, Sutcliffe, & Clark, 1998).

Many studies have shown that exposures to asthma triggers early in childhood may contribute to the development of asthma. Early life preventive measures, such as breastfeeding and avoidance of asthma triggers, could possibly decrease the prevalence and severity of asthma and save in health care costs. It is biologically plausible that breastfeeding may offer some protection against the occurrence of asthma by decreasing allergic sensitization and/or improve the infant's immune system (Dell & To, 2001). However, in the United States, Raisler et al. (1999) found that only 27% of mothers breastfed their children in the first month, 13% in the third month, and only 2% of mothers breastfed at 6 months in 1988. This study also observed that lower incidence of breastfeeding was found in black, poor, young and less educated mothers (Raisler et al., 1999).

It is clear that childhood asthma is a serious problem. Identifying and assessing specific risk factors that are associated with this disease is important not only for predicting the probability of developing of disease, but also the likelihood of having it for a lifetime (Randi, Altieri, Chatenoud, Chiaffarino, & La Vecchia, 2004). The purpose of this research was to identify and assess childhood asthma's risk factors as they were related individually and combined.

CHAPTER II

BACKGROUND AND RATIONALE

Medical Background

Asthma is defined as a chronic inflammatory disease of airways that is characterized by increased responsiveness of the tracheobronchial tree to a multiplicity of stimuli. This produces widespread narrowing of the airways that, in turn, produces symptoms (Harrison, 2005). It is considered to be the most common chronic disease in childhood (Lowe, Custovic, & Woodcock, 2003). The pathophysiology of asthma has complicated pathways. Asthma is clinically characterized by three factors: reversible bronchial airway inflammation, increased mucous production and airway hyper-responsiveness (Knight, Stewart, & Thompson, 1994).

Natural History of Asthma

The process that leads to the development of asthma is varied and involves a number of factors. According to medical textbooks, the "nature" of asthma can be classified into two broad groups namely allergic and idiosyncratic. Allergic asthma is often associated with a personal or family history of allergic diseases such as rhinitis, urticaria, and eczema. They have a positive skin reaction (allergic skin test) to intradermally injection of extracts of airborne antigens and increased levels of IgE in the serum with a positive response to provocation tests involving the inhalation of specific antigens (Busse & Holgate, 2000). All of these characteristics can be compiled with the name "atopy". Atopy is define as "a genetic predisposition toward the development of immediate (type I) hypersensitivity reactions against common environmental antigens (atopy allergy)". The most common clinical manifestations include allergic rhinitis, atopic dermatitis and asthma (Dorland's, 1994). It has been seen that atopy is the single most important risk factor for asthma development. This could be considered the strongest evidence for the genetic predisposition and asthma is classified according to such genetic predisposition (AAAI, 2005). The other groups of patients that are classified under idiosyncratic asthma have no personal or family history of the disease. They also have normal levels of IgE and negative allergy skin tests. In general, asthma that has its onset in early life tends to have a strong allergic component, whereas asthma that develops late tends to be non-allergic or to have a mixed etiology (Harrison, 2005).

The stimuli that interact with airway responsiveness and trigger acute episodes of asthma can also be grouped into seven major categories: allergenic, pharmacologic, environmental, occupational, infectious, exercise-related, and emotional (Harrison, 2005).

Pathophysiology

The main pathophysiologic characteristic of asthma is a reduction in airway diameter produced by contraction of smooth muscle, vascular congestion, edema of the bronchial wall, and thick, profuse secretions. This results in an increase in airway resistance, a decrease in forced expiratory volumes and flow rates, hyperinflation of the lungs and thorax, increased work of breathing, alterations in respiratory muscle function, abnormal distribution of both ventilation and pulmonary blood flow, and altered arterial blood gas concentrations. Most asthma patients have a Forced Vital Capacity (FVC) of less than 50%. In acutely ill patients, residual volume (RV) frequently approaches 400% of normal, while functional residual capacity doubles. The typical findings seen in an asthmatic are hypoxia, hypocapnia and respiratory alkalosis (Busse & Holgate, 2000).

The basis for the development of allergic asthma is due to the inherent hypersensitivity to allergens or any other stimuli in the tracheobronchial tree. In both normal and asthmatic individuals, airway reactivity rises after viral infections of the respiratory tract and exposure to oxidant air pollutants such as ozone and nitrogen dioxide. Viral infections have more profound consequences and airway responsiveness may remain elevated for many weeks after a seemingly trivial upper respiratory tract infection. Allergens can cause airway responsiveness to rise within minutes and to remain elevated for weeks. If the dose of antigen is high enough, acute episodes of obstruction may occur daily for a prolonged period after a single exposure. Presently, the most popular hypothesis for the pathogenesis of asthma is that it derives from a state of persistent sub acute inflammation of the airways. The airways become edematous and are infiltrated by inflammatory cells such as neutrophils, lymphocytes and eosinophils along with glandular hypertrophy. These cells release mediators like leukotrienes C, D, and E; platelet-activating factor; and prostaglandin's (PGs) E_2, $F_2\alpha$, and D_2, which produce an intense, immediate inflammatory reaction causing bronchoconstriction, vascular congestion and edema formation. The leukotrines are also responsible for mucus production and impaired mucociliary transport (Gershwin & Naguwa, 2005).

Cytokine production is another central component of the inflammation of asthma. They are synthesized and released from many of the inflammatory cells mentioned above, as well as from epithelial cells, fibroblasts, endothelial cells and airway smooth

muscle. They activate specific cell-surface receptors that are coupled to signal transduction pathways, which often result in alterations of gene regulation and enzyme production. The cytokines that are particularly relevant to asthma are secreted by T lymphocytes and include IL-3 IL-4 and IL-13 (switching of B lymphocytes to IgE production and expression of adhesion molecules), and IL-5 (differentiation and enhanced survival of eosinophils). Other cytokines, such as IL-1B, IL-6, IL-11, tumor necrosis factor α(TNF-α) and GM-CSF are proinflammatory and may amplify the inflammatory response. There has also been evidence that show a very strong genetic link that is responsible for the symptoms in few cases. The high levels of IgE and atopy have been observed on 5q, 11q and 12q (Gershwin & Naguwa, 2005).

Clinical Features

The clinical triad of asthma includes dyspnea, cough and wheezing. The symptoms are generally episodic and the patients usually experiences chest discomfort, along with tachycardia, tachypnea and mild systolic hypertension. In severe cases, the patient may experience high pitched wheezing and also use accessory muscles to breathe. The cough is productive and copious (Harrison, 2005).

The severity of asthma symptoms can be classified in four categories:

1) Mild intermittent - Includes attacks no more than twice a week and nighttime attacks no more than twice a month. Attacks last no more than a few hours to days. Severity of attacks varies, but there are no symptoms between attacks.
2) Mild persistent - Includes attacks more than twice a week but not every day, and nighttime symptoms more than twice a month. Attacks are sometimes severe enough to interrupt regular activities.
3) Moderate persistent - Includes daily attacks and nighttime symptoms more than once a week. More severe attacks occur at least twice a week and may last days. Attacks require daily use of quick-relief (rescue) medication and changes in daily activities.
4) Severe persistent - Includes frequent severe attacks, continual daytime symptoms, and frequent nighttime symptoms. Symptoms limit daily activities (Slavin & Reisman, 2002).

Diagnosis of Asthma

The diagnosis of asthma is established by demonstrating reversible airway obstruction. Reversibility is traditionally defined as a 15% or greater increase in forced expiratory volume (FEV_1) after two puffs of a beta-adrenergic agonist treatment. When the spirometry results are normal, the diagnosis can be made by showing heightened

airway responsiveness to challenges with histamine, methacholine, or isocapnic hyperventilation of cold air. Once the diagnosis is confirmed, the course of the illness and the effectiveness of therapy can be followed by measuring peak expiratory flow rates (PEFRs) at home and/or the FEV_1 in the laboratory. Positive wheal-and-flare allergic reactions to skin tests can be demonstrated to various allergens, but such findings do not necessarily correlate with the intrapulmonary events. Sputum and blood eosinophilia and measurement of serum IgE levels are also helpful but are not specific for asthma. Chest x-rays showing hyperinflation are also nondiagnostic(Harrison, 2005).

The best treatment of asthma is to eliminate the causative agent from the environment. Desensitization or immunotherapy can also be used, but with limited success. The drug treatment involves use of a number of different agents to control the symptoms. They include short term agents which are used to control the immediate symptoms and the long term agents which prevent recurrent attacks (Busse & Holgate, 2000).

The following medications are used for the treatment of asthma:

Cromolyn Sodium – is a solution available as a spray and a nebulizer. It is an anti-inflammatory medication which is relatively free of side effects. It may cause some throat irritation and, as with all inhalation medications, may provoke cough or wheezing.

Nedocromil – is available as a spray. This medication is very similar to cromolyn. It is a more potent anti-inflammatory than cromolyn. It is relatively side effect free. The main side effects are headache and nausea.

Zafirlukast – is available as a tablet. It is one of the newest asthma medications. It is a completely different type of anti-inflammatory known as a leukotriene inhibitor. Adverse reactions include headaches, infections, nausea, and diarrhea. The main advantage of this anti-inflammatory medication is that it can be used by patients who can not use sprays. It is not recommended for young children.

Montelukast- is available as a tablet and chewable tablet. It is the newest leukotriene antagonist and is similar to Zafirlukast. However, unlike Zafirlukast, this medication has been approved for treating children 6 years and older and is taken once daily. Its use can decrease or even avoid the use of systemic or inhaled steroids. It is also useful for patients who prefer tablets over sprays or children who have not yet mastered the use of sprays. Reactions to the medication may include diarrhea, laryngitis, pharyngitis, nausea, otitis media, sinusitis, and viral infection.

Inhaled Steroids- are available as sprays. Steroids are used for their potent anti-inflammatory effect. The current recommendations and guidelines from the U.S. Federal Government are to use high potency inhaled steroids for treating severe asthma, but until

recently, there was no high potency spray available in the U.S. They include beclomethasone, flunisolide, triamcinolone, fluticasone, and budesonide.
All inhaled steroids have essentially the same side effects which include thrush (a yeast infection in the mouth), hoarseness, dry throat, irritated throat, and dry mouth. The risk of thrush can be minimized by using a spacer which increases the amount of medication deposited in the lungs and decreases the amount deposited in the mouth and throat. Rinsing the mouth after each use can also decrease the risk of thrush.

Inhaled steroids are the most potent available anti-inflammatory drugs available for the treatment of asthma, other than oral steroids. They are excellent medications for the long term management and control of moderate to severe asthma. In general, they do not cause the side effects of systemic (oral, intravenous, or injected) steroids, but they are absorbed to some extent, and in high enough doses, can suppress the normal production of steroids by the body. Because of the possibility of systemic absorption of inhaled steroids, patients treated with these drugs should be observed carefully for any evidence of systemic steroid effects including suppression of growth in children. The degree, to which inhaled steroids suppress growth, if at all, is currently under study. They also blunt the immune response. While there are no reports of serious problems with infection in children who use sprays, caution is advised if susceptible children on these sprays are exposed to chickenpox or measles. Because of all these cautions, inhaled steroids are generally not first line drugs. They are reserved for more severe asthma (Busse & Holgate, 2000).

Systemic Steroids - Systemic means taken into the body rather than put directly into the lungs as with a spray or nebulizer. Children who are sick enough to be hospitalized for asthma generally get steroids intravenously. Systemic steroids have a much more potent anti-inflammatory effect on the inflamed airways than inhaled steroids, and they have a much more rapid onset of action than inhaled steroids. They also have a much greater risk of side effects. Initial side effects such as stomach irritation and mood changes are dose related. The most serious side effects are related to prolonged use. Prolonged use of steroids can cause growth retardation, osteoporosis, cataracts, a rounded face, increased body fat, fluid retention, muscle weakness, peptic ulcer, menstrual irregularities, aggravation of diabetes mellitus, impaired wound healing, and decreased immunity response. In addition, systemic steroids taken for more than two weeks causes sufficient suppression of normal adrenal gland function and the steroids must be tapered rather than abruptly withdrawn (Slavin & Reisman, 2002).

Albuterol –It is available as tablets. It provides prolonged bronchodilation. Side effects include hyperactivity, shakiness and rapid heart rate.

Salmeterol –It is available as a spray and is a bronchodilator. Salmeterol is similar to albuterol, but its duration of action is longer and its onset of action is slower. Side effects are similar to albuterol, although sprays generally have fewer systemic side effects than medicines taken by mouth.

Ipratropium bromide- It is available as a spray and is useful for the prevention of bronchospasm. Unlike other bronchodilators, Ipratropium bromide blocks the reflexes that cause bronchospasm. It can be used in combination with the bronchodilators that cause bronchial relaxation to achieve better control. Ipratropium bromide is used more often for chronic bronchitis and emphysema, than for asthma. The most common side effects are dry mouth and cough.

Methylxanthines- These include aminophylline and theophyllines. These drugs are stimulants which act as bronchodilators. The intravenous aminophylline and theophylline have a relatively rapid onset of action. The others are long acting medications primarily useful for chronic management (Harrison, 2005).

Childhood Asthma Epidemiology

Introduction

Important progress has been made in the understanding of factors that are associated with the development of childhood asthma (Naspitz, Szefler, Tinkelman, & Warner, 2001). These include: genetics, gender, maternal effects, atopy, respiratory infections, and microbial burden. Some of these factors are classified as inception factors

and are recognized in epidemiology as risk factors for the development of asthma. Progression factors, also called prognostic factors, are known to trigger asthma attacks and increase the likelihood of chronic, severe, and fatal asthma (Naspitz et al., 2001).

Demographics and Socio-Economic Status

Many studies have identified "high-risk" children for the development of asthma. These children share the following characteristics: family history or genetic markers (parental history of asthma), similar ethnicity, socioeconomic status, gender, and birth order (Peat & Li, 1999). Within socioeconomic status, many studies consider maternal age, maternal education, and family income level to be significant in whether or not a child will develop asthma. An ecological study was conducted in 1988 in the state of Maryland, using 9,041 hospital asthma discharges of children, ages 1-19. After adjusting for social and economic status, researchers concluded that African American children were at increased risk of hospitalization for asthma, but noted that some or all of this increase was related to poverty, rather than to race (Wissow, Gittelsohn, Szklo, Starfield, & Mussman, 1988). A more recent ecological study using U.S. mortality records obtained from the National Center for Health Statistics from 1991 to 1996, Grant et al. (2000) studied the relationship between socioeconomic factors and race/ethnicity as risk factors for asthma mortality. Higher standardized mortality ratios were seen for African

Americans (SMR = 3.34) as compared to Caucasians (Whites) (SMR = 0.65), low (SMR = 1.51) in contrast to high educational level (SMR = 0.69), and low (SMR = 1.46) as compared to high income (SMR = 0.71). Excess mortality for African Americans was reported when compared to Whites in the highest and lowest quintiles of median county income and educational level. The disparity in asthma mortality rates, according to median county income and education, remained after controlling for race/ethnicity. The authors concluded that income strongly influences mortality due to asthma, but African American race/ethnicity appears to be associated, independently from low income and low education, with an elevated risk for asthma mortality (Grant, Lyttle, & Weiss, 2000). Nicholas et al. (2005) in a community intervention study in central Harlem called "The Harlem Children's Zone Asthma Initiative" in New York City found that childhood asthma is as high as 28.5 per 100 when the national estimates are 7 per 100 for thegeneral population 0 – 12 years of age and 8 per 100 for African American children (Nicholas et al., 2005). Lindbaek et al. (2003) conducted a cohort study that evaluated the effect of socioeconomic factors on a child's asthma status. This study examined children between the ages of 4 -5 in Norway. This study indicated that a higher percentage of asthmatic children had less than five rooms in their home, at least one parent with a chronic disease (most likely asthma), a higher frequency of having a single parent, and a low level of parental education (Lindbaek, Wefring, Grangard, & Ovsthus, 2003). A cumulative prevalence of asthma was 8.7 per 100 in this study in children ages 4 -5 years.

Gender and race/ethnicity have also been considered two of the identifiers of high risk children (Naspitz et al., 2001). In a study of a homogeneous suburban areas by Nelson et al. (1997), the lifetime prevalence of asthma was 9.5% (12% for African Americans and 6% for Whites) being higher in boys (14%) than in girls (5%) (Nelson et al., 1997). Another study by Hu et al. (1997), found boys to be 1.7 times more likely to have physician diagnosed asthma than girls. The findings of Hu et al. (1997) study were similar to previous studies concerning differences in racial and socioeconomic status. According to Hu et al. one possible mechanism is the amount of IgE an individual produces. Similar studies have found a strong correlation between serum IgE levels and the prevalence of asthma. These other studies, according to Hu et al., also suggest that African Americans have a higher IgE level than Whites and that males have higher levels than females. A second possible explanation for variation between males and females is anatomic differences. First; boys tend to have smaller airways at any given lung size than girls. Second; boys tend to have greater bronchial lability, and third; boys tend to have higher incidence of lower and upper tract respiratory infections (Hu et al., 1997).

Tobacco Use and other Prenatal Factors associated with Asthma

A prenatal factor that contributes to childhood asthma is maternal smoking during pregnancy. The Hu et al. study also reported maternal smoking during pregnancy as significantly associated with childhood asthma (adjusted OR = 1.9; 95% CI 1.1 to 3.5).

This study also found that cord blood IgE concentrations were significantly elevated in infants whose mothers smoked during pregnancy, predisposing infants to subsequent sensitization and allergy. It has also been suggested that intrauterine exposure to smoking could cause changes in pulmonary structure and function. According to Dell and To (2001), prenatal and postnatal household smoking were strongly correlated ($r = 0.53$, $p < 0.001$). This population-based cross-sectional study found that children who were exposed prenatally to smoke were 96% more likely to develop asthma, when compared to children who were not exposed. Dell & To (2001) also reported that exposure to postnatal smoke was a statistically significant contributor of childhood asthma (OR = 1.5). The effect of parental smoking on wheezing and asthma in children under 5 years of age showed that the odds ratio for children who wheeze or have asthma if their parents smoke is fairly consistent between 1.3 and 2.4. This study was conducted by Peat et al. (1998).

Gilliland et al. (2003) studied the effects of in utero exposure to cigarette smoking in a retrospective cohort study, which examined lung functions in 5,933 children. Their research demonstrated a lower FEV1/FVC in children with in utero exposure to tobacco and a history of family asthma. This research suggests that the "in utero" exposure during critical periods of fetal lung development could permanently alter the lung structure and cause an increase risk of asthma development. However, this study showed that in utero exposure to household smoke and maternal smoking increased the risk of

developing childhood asthma, but environmental exposure to cigarette smoke did not (Guilliland, Berhane, Li, Rappaport, & Peters, 2003).

Family History of Asthma, Perinatal Infections and Other Perinatal Factors

Other factors related with asthma etiology that are identified with the development of asthma include: infections in early life and perinatal factors; such as low birth weight and disproportionate fetal growth (Seidman, Laor, Gale, Stevenson, & Danon, 1991). The presence of these factors during fetal development may indicate direct causal mechanisms at a cellular level according to (Peat & Li, 1999).

Due to the increasing prevalence of childhood asthma, a multitude of studies have examined potential opportunities for primary and secondary prevention. Reducing indoor allergens, such as dust mites, is considered a possible intervention. Others include: educating and reducing the percentage of parental smoking, both pre and postnatal, and supplementing infant diets with Omega-3 fatty acids (Peat & Li, 1999).

Yet another factor is genetic predisposition, such as the presence of maternal asthma. The role that parental asthma plays in the development of childhood asthma has always been considered a major risk factor (Peat & Li, 1999). However, some research suggests that asthmatic mothers should breastfeed their children to reduce the likelihood

of their children developing asthma. Oddy et al. (2002) examined a cohort of 2,602 Australian children in a prospective cohort study. At age 6, 17% of children developed asthma, 22% had wheezing in the previous year, and 31% had physician-diagnosed asthma. Fifteen percent of the mothers from this cohort had current asthma. The risk did not change when adjusted for maternal asthma status (Oddy, Peat, & deKlerk, 2002).

Asthmatic mothers may represent a population bias by reporting and being more diligent in the treatment and ascertainment of a diagnosis of asthma. Asthmatic mothers may also use medications during pregnancy that would influence the immune system (Wright, Holberg, Taussig, & Martinez, 2001). In a study that compared familial history of asthma and the risk of developing asthma, ORs ranged from 1.7 to 6.8 (Burke, Fesinmeyer, Reed, Hampson, & Carlsten, 2003).

Daycare Attendance

Early-life experiences and environmental exposures have been associated with childhood asthma (Naspitz et al., 2001). Salam et al. (2004) investigated whether the timing of such experiences and exposures was associated with the occurrence of asthma by 5 years of age. The authors conducted a matched case-control study nested within the Children's Health Study, a population-based study of more than 4,000 school-aged

children in 12 southern California communities. Asthma diagnosis before 5 years of age was associated with day care attendance within the first 4 months (OR = 2.4; 95% CI, 1.3-4.6) (Salam, Li, Langholz, & Gilliland, 2004). However, day care attendance in early life has been found to be inversely associated with asthma at school age. Celedon et al. (2003) studied the association between day care in the first year of life and asthma. Day care attendance in early life was associated with a 70% decreased risk of asthma (OR = 0.3, 95% CI = 0.1-0.7) at the age of 6 years among children without maternal history of asthma. The "hygiene hypothesis" may be the basis for this theory. This hypothesis suggests that exposure to other children and exposure to mild infections can create allergen sensitization and tolerance resulting in less asthma symptoms (Celedon et al., 2003). However, among children with maternal history of asthma, day care in early life had no protective effect on asthma (Liu & Murphy, 2003).

Along with other socioeconomic factors, day care attendance has been known to be a predictive factor for asthma. One explanation could be an increase in respiratory infections in children who attend day care. Children who attend day care are more likely to develop infections with respiratory synscitial virus (RSV) and hepatitis A infections (Infante-Rivard, Amre, Gautrin, & Malo, 2001). These infections are known to promote asthma in childhood but may be protective later in life(Oddy et al., 2002).

Prematurity and low birth weight were strongly correlated with the development of asthma (OR = 3.6, $p < 0.001$;(Dell & To, 2001). In the first cohort study that

examined low birth weight (< 2500 g) and asthma, Seidman et al. (1991) reported a positive correlation. They examined 20,312 subjects and observed an OR = 1.4 (95% CI; 0.8 – 2.6), indicating that prematurity contributes to lower respiratory infections that lead to a history of asthma later in life. However, this study did not adjust for the observation that most low birth weight infants are from families with low socioeconomic status (Seidman et al., 1991).

A more recent cohort study examined the relationship between asthma and low birth weight (LBW) within the African American population. African Americans were found at a higher risk for both low birth weight (16.6% vs. 3.9%) and asthma (12.5% vs. 5.3%; (Joseph, Ownby, Peterson, & Johnson, 2002). This study found low birth weight and asthma to be associated. After adjusting for race and gender, a strong relationship is still observed between low birth weight and asthma (OR= 4.8; 95% CI 0.7 – 31.1).

Attention Deficit Disorder and other Learning Disabilities

Attention deficit disorder with or without hyperactivity is characterized by the person's inability to pay attention in non-selective activities, hyperactivity that is difficult to inhibit, impulsiveness with failure to control their reactions, and an unstable personality. These characteristics make learning and working more difficult. Even leisure

activities may become challenging when social settings are unstructured. Valdizan (2004) conducted a study of 170 children with attention deficit disorder finding that a third of them presented associated pathologies such as: allergic rhinitis, asthma, allergies and dermatitis, with no differences between genders (Valdizan, 2004). A review article of the evidence regarding the impact of chronic or intermittent hypoxia on cognition related conditions in childhood was performed by Bass et al. (2004), using both a systematic review of published reports and a critical evaluation of the causality criteria. A Medline search was conducted from 1966 to 2000 by using the OVID interface. Both English and non-English language citations were included. Significant articles identified by the reviewers up to 2003 were also included. A total of 788 literature citations were screened. For the final analysis, 55 articles met the criteria for inclusion in the direct evidence. One of their conclusions stated that adverse impacts of chronic or intermittent hypoxia on development, behavior, and academic achievement have been reported in many well-designed and controlled studies in children, and hypoxia could be caused by asthma(Bass et al., 2004). In a case series study by Rosenfield et al. (1994), medically evaluated three asthmatic children who otherwise were fluent in their speech. These children developed speech dysfluency following administration of theophylline. Language dysfluency came to an end in all three, following discontinuation of the asthma medication. Theophylline was re-instituted in two of the three patients, prompting return of dysfluency in both of them (Rosenfield, McCarthy, McKinney, Viswanath, & Nudelman, 1994).

Visual acuity could be affected by asthma treatment as well. Inhalation steroid therapy can cause ocular hypertension or open angle glaucoma. Desnoeck M, Casteels I, and Casteels K. (2001) described the case of a young girl who presented raised intraocular pressure and headaches, due to the prolonged administration of nasal and inhalation steroids (Desnoeck, Casteels, & Casteels, 2001).

Obesity and Physical Activity

Obesity has recently being considered a condition of public health importance not only in the U.S., but worldwide (WHO, 2005). It is a very significant cause of morbidity, mortality, and health care expenditures, accounting for approximately 300,000 deaths each year. Further more, it accounts for about 7% of the nationwide health care budget, with an economic impact greater than $100 billion dollars annually in the United States (CDC, 2005). Obesity and its complications such as cardiovascular disease, diabetes, arthritis and some cancer types have been on the rise (CDC, 2005). The parallel time trend with an increasing prevalence of asthma has induced a lively debate about a potential link between both conditions. Schaub and Mutius (2005) conducted a review of selected prospective cohort studies and concluded that gaining weight can be related to the development of asthma. Effect modification by gender may be present because some studies have shown effects of body mass index on asthma, but only among females.

Several hypotheses have been developed to explain this epidemiological association including, alterations in airway mechanics, different immune responses, hormonal influences and, genetic factors. However, the mechanisms underlying this relationship are unclear. Nevertheless, regarding causality, it has been shown that weight reduction among asthmatics has a direct impact improving lung function (Schaub & von Mutius, 2005).

Childhood asthma may be affected by changes in the diet and increments in the body mass related to a sedentary lifestyle. However, as mentioned above, the mechanisms are poorly understood. Romieu et al. (2004) in a cross-sectional study using NHANES III reported that after studying 7,904 children and controlling for dietary intake, physical activity, and sociodemographic variables, asthma risk was three times higher for children aged 6-16 years in the highest percentiles of BMI (> 95th percentile), when compared to children in percentiles 25-49 (OR = 3.4; 95% CI, 1.5-8.0). However, this increment was no important or statistically significant in children aged 2-5 years (Romieu, Mannino, Redd, & McGeehin, 2004). In a cross-sectional study by Epstein et al. (2000) based on NHANES III data studied factors that modified the relationship between asthma and pediatric body mass index. Television watching and maternal body mass index had synergistic interactions increasing the association of child body mass index and asthma(Epstein, Wu, Paluch, Cerny, & Dorn, 2000).

Schachter et al (2003) reported an analysis of cross-sectional data in a 5,993 Caucasian Australian children aged from 7 to 12 years. The study aim was to determine if increased body weight, as measured by body mass index, is associated with a higher prevalence of asthma or atopy or with an increase in airway obstruction or airway responsiveness to histamine. They also examined whether the association between body weight, atopy, and symptoms of asthma was different between girls and boys. After adjusting for atopy, gender, age, smoking and family history, the authors found that body mass index was associated with wheezing and cough in girls only, but was not associated for recent asthma or airway hyper-responsiveness in neither boys nor girls (Schachter, Peat, & Salome, 2003).

Breastfeeding and Diet in Early Life

Human milk macrophages can produce IL-1alpha, IL-1beta, IL-1ra, IL-6, IL-8 and IL-10 (Hanson, 1998). It is estimated that on average, two billion polymorphonuclear leukocytes (PMNs) and mononuclear cells are ingested during the first four days by the breastfed baby (Pabst, 1997). Lactoferrin is a protein that is also found in human milk. Lactoferrin has many beneficial properties such as lymphostimulatory, anti-inflammatory, bactericidal, viricidal and fungicidal properties (Xanthou, Bines, & Walker, 1995). Its main function is to carry iron. However,

lactoferrin suppresses production of certain cytokines, IL-6, IL-8 and TNF-alpha (Cruse & Lewis, 1999), which can result in anti-inflammatory actions. Lactoferrin prevents the recruitment and activation of leukocytes to sites of inflammation (Xanthou et al., 1995). Oligosaccharides are also found in human milk in large numbers. Human milk is rich in long chain fatty acids that are thought to prevent allergic responses by preventing inflammation developing in the airways (Peat & Li, 1999). Other factors include complement, C3 and C4, lysozome (bactericidal) and fibronectin (important in inflammation and wound healing).

IgE (1% of the immunoglobulins) is the immunoglobulin that acts in the anaphylactic hypersensitivity response (Cruse & Lewis, 1999). IgE may act to stimulate the infant's immune system towards antimicrobial (TH1), rather than allergic (TH2) response (Wright et al., 1999). IgE may also act to develop the intestinal colonization to develop the TH1 response. Another suggested pathway for protective effect of breastfeeding is the decreased exposure of the infant to external antigens during exclusive breastfeeding, which reduces the risk of sensitization (Gdalevich, Mimouni, & Minnouni, 2001).

The specific anti-inflammatory properties of human milk are as follows: IgA in human milk does not activate complement, but protects by interfering with the binding of bacteria and bacterial toxins to epithelial cells (2) the biochemical pathways that produce mediators of inflammation such as complement

coagulation factors are poorly represented in human milk and (3) human milk contains many anti-inflammatory factors in and of itself, such as enzymes that degrade mediators of inflammation, scavengers of oxygen-radicals, and cytokines that down regulate inflammation (Xanthou et al., 1995).

Multiple studies conducted in the past have shown a link between breastfeeding as the primary mode of nutrition for infants and reduction in atopy, allergy and other childhood illnesses. This demonstrates the immunological strengthening ability of human milk. In the Dundee infant feeding study (Wilson et al., 1998), a cohort of children were followed prospectively for feeding habits and demographics for the first seven years of their life. This study concluded that the probability of respiratory illness occurring at any time during childhood is significantly reduced if the child is fed breast milk exclusively for at least 15 weeks, and no solid foods are introduced during this time (Wilson et al., 1998). A second aspect of this study examines whether the benefits of breast-feeding extend past infancy into childhood. This study did not conclude significant findings between asthma and breastfeeding; however, introduction of solids before 4 months was associated with a history of wheezing. Due to similarities in the immune response for allergy and asthma, this study showed a positive protective factor between breastfeeding and reduction in respiratory illness (Wilson et al., 1998).

A cross-sectional study by Raisler et al. (1999), using the National Maternal and Infant Health Survey (NMIHS) including 7,092 infants demonstrated that sick baby visits

were 30% less frequent in children who were fully breastfed. They reported a dose-response relationship with exclusive breastfeeding (Raisler et al., 1999). Bloch, et al. (2002) conducted a meta-analysis of prospective studies with the subject of breastfeeding and allergic rhinitis (AR). This systematic review of breastfeeding was assessed for the first three months of life. The summary odds ratio of 0.7 (95% CI 0.5-1.01) showed a modest protective effect of breastfeeding with a borderline significant level (Bloch, Mimouni, Mimouni, & Gdalevich, 2002). Adjusting for family history of atopy an OR = 0.87 (95% CI 0.48-1.58) was found. The findings of this study extend past the primary premise of breastfeeding's protective effects.

In 1998, a population based cohort study conducted by Wright et al. (1998) in a Navajo community, concluded that an increase in the proportion of infants in a community that are exclusively breastfed resulted in an overall decrease in infant illness, including: wheezing, lower respiratory tract illnesses, pneumonia, upper respiratory tract disease, otitis media, gastroenteritis, meningitis and necrotizing enterocolitis (Wright et al., 1998). One possible explanation for this finding was that breastfeeding reduces the incidence of viral and bacterial illnesses, which in turn, reduce the prevalence of respiratory infections associated with asthma. Similar results and conclusions were published by Burr et al (1993) in a prospective cohort study (Burr et al., 1993). In a systematic review of twelve prospective studies (Gdalevich et al., 2001), exclusive breastfeeding was found to lower asthma rates during childhood. The summary odds ratio for the protective effect of breastfeeding was 0.7 (95% CI 0.6 - 0.8).

In a prospective cohort study by Oddy et al. (1999), the association between duration of exclusive breast-feeding and development of asthma by age six was examined. Some factors that Oddy examined were: being male, low birth weight, preterm birth, young maternal age, maternal smoking, and early cessation of exclusively breast feeding (Oddy et al., 1999). The cumulative incidence of both asthma ($p= 0.001$) and wheezing ($p < 0.001$) was higher if other milk was introduced before 4 months of age (Oddy et al., 1999). If the infant was introduced to non-breast milk before 4 months of age, the infant was more likely to wheeze and have asthma; instead of having symptoms as a result of the duration of breastfeeding. Giovannini et al. (2004) reported from a study of 25, 767 children that solid food introduced or even the introduction of cow's milk prior to four months of age could promote childhood asthma (Giovannini et al., 2004).

Immunizations and Asthma

Pershagen (2000) reported in a literature review that changing patterns of infections may be of importance for the increase in prevalence of asthma and other allergic diseases. According to Pershagen, the inverse relation between number of siblings and atopy observed in several studies could be related to a protective role of infections. For example, positive tuberculin responses in schoolchildren correlated with a lower prevalence of atopic disorders. However, other studies did not find a relation between BCG vaccination and allergic disease or sensitization. Transient production of

IgE antibodies to pertussis toxin has been demonstrated after pertussis immunization, while randomized clinical trials involving both whole cell and acellular pertussis vaccines have failed to show any enhancement of atopic manifestations in children. Epidemiologic investigations indicate that viral infections may either promote (RSV) or inhibit (hepatitis A, measles) atopy, although data are scarce. As a conclusion of this literature review by Pershagen, evidence is scarce, regarding a direct role of vaccinations for development of atopic manifestations. However, some infections may offer protection in relation to allergic disorders. Therefore, vaccination could then result in an increased risk (Pershagen, 2000).

Wickens et al (2001) examined the risk factors for asthma in children aged 7-9 by using a case-control study, in which 233 cases and 241 controls were randomly selected from participants in the Wellington arm of the International Study of Asthma and Allergies in Childhood (ISAAC). After controlling for confounders, there was a strong association, though insignificant, between having polio vaccination (OR=2.5, 95% CI 0.8-7.4) and asthma. Weaker and non-statistically significant associations were found with hepatitis B vaccination (OR=0.7, 95% CI 0.4-1.04), or measles/mumps/rubella vaccination (OR=1.4, 95% CI 0.95-2.4), and asthma (Wickens et al., 2001). Similar results were found by DeStefano et al. (2002) in their large cohort study where the weak associations of asthma for hepatitis B and *Haemophilus influenzae* type b (Hib) vaccines could be explained by information bias and disparities in health care utilization. Vaccines were not found associated with an increase risk of asthma in the report by (Maher,

Mullooly, Drew, & DeStefano, 2004) from a retrospective cohort study. In contrast, Benke et al. (2004) in a cross-sectional and retrospective study of young adults found a strong association (RR = 3.3, 95%CI: 0.5-21.3) of asthma for polio vaccine, and a weak but not statistically significant association with hepatitis B immunization. Nevertheless, subjects reporting a full immunization were found to be at a higher risk to asthma (RR = 1.5, 95% CI 1.1 – 2.1) (Benke, Abramson, Raven, Thien, & Walters, 2004).

McIntire et al. (2003) found that infection by hepatitis A virus (HAV) may protect individuals from atopy if they carry a particular variant of the gene that encodes TIM-1 (also known as HAVcr-1) — the cell-surface receptor used by HAV to infect human cells. Exposure to HAV is associated with poor hygiene, large family size and day-care center attendance. All of these factors are also inversely associated with atopy. The authors found in a series of experiments, an interaction between HAV and TIM-1 genotype that may contribute to the basis for the etiology of atopic diseases, providing a mechanism to explain the hygiene hypothesis (McIntire et al., 2003).

The present study is an epidemiological survey identifying risk and protective factors for childhood asthma based on current knowledge and aiming at confirming the association of known factors and exploring new ones by using NHANES 99-00 data.

Rationale

During 2001, approximately 80 - 90% of all childhood asthma was diagnosed by the age of 6 years (Weiss, 2001). Thus, there is evidence of a possible link to exposures in early childhood and in utero. It is known that genetics play a large role in the development of asthma (Gershwin & Naguwa, 2005). Genetic susceptibility of asthma has been widely recognized as the key element to determine susceptibility to develop asthma (Harrison, 2005). A child with one asthmatic parent has approximately a 30 - 40% probability of developing asthma, whereas a child whose parents are not asthmatic has a 15 - 20% probability (Naspitz et al., 2001). The challenging epidemiological questions are: how to characterize high risk groups, the identification of risk factors that trigger asthma, and the protective factors that can be used in control programs to prevent asthma. The present study is an attempt to identify high risk groups and factors that modify the likelihood to develop asthma in the United States by using the National Health and Nutrition Survey (NHANES), conducted in 1999-2000 (CDC, 2003). A number of factors already known to be associated with childhood asthma are: demographics, newborn care and daycare, breastfeeding, hepatitis A and B immunizations, obesity/overweight, attention deficit disorder, stuttering/stammering, tobacco and respiratory diseases, were included in this study to learn their relative importance and explore their potential interaction with each other. Factors that have never been reported as being directly related to asthma include: type of drinking water

(private/public well vs. private/public water; water treatment devices), learning disabilities, deficient visual acuity, and anemia.

CHAPTER III

AIMS AND METHODS

Purpose

The purpose of this study is to identify and assess factors for childhood asthma. The National Health and Nutrition Survey (NHANES) data for 1999-2000 was used to achieve this objective. Overall Hypothesis: There are factors that influence the likelihood of having childhood asthma in the U.S. that can be identified and assessed by using the NHANES 1999-2000 data.

Hypotheses and Aims

Hypothesis 1: The prevalence rate of childhood asthma in the United States does not differ by age, gender, or race and ethnicity.

1. Assess the prevalence rate of childhood asthma by age, gender, ethnicity, race and other relevant variables by using frequency distributions and cross tabulation of the NHANES data 1999-2000.

Hypothesis 2. There is no difference between children with asthma and children without asthma regarding family history of asthma, demographics, perinatal factors, passive smoking, selected food items, attending daycare or pre-school, selected indoor environmental factors, and income.

2. Identify and assess individual risk and protective factors for childhood asthma by comparing children with asthma with children without asthma regarding selected variables included in the NHANES data 1999-2000.

Hypothesis 3. Family history of asthma, demographics, perinatal factors, passive smoking, selected food items, attending daycare or pre-school, selected indoor environmental factors, and income are the best predictors of childhood asthma.

3. Identify and assess different combinations of risk and protective factors for childhood asthma by comparing children with asthma and children without asthma regarding combinations of selected variables included in the NHANES data 1999-2000.

Study Design

This is a cross-sectional study based on a large national survey (NHANES) conducted during 1999-2000. This dataset was collected by using probabilistic, complex sampling procedures that guarantee a good representation of the whole United States (Centers for Disease Control, 2003).

Study Population and Sample Size

The study population was composed of respondents to the National Health and Nutrition Examination Survey (NHANES), 1999-2000. NHANES is an effort of the National Center for Health Statistics (NCHS). The 99-00 data contains information collected between March 1999 and December 2000 throughout the United States. The total number of individuals surveyed during this time period equaled 9,965.

The original population of 9,965 individuals was reduced to a usable 1,266 individuals when age limits were introduced to the use the Household Youth Questionnaire. This portion of the survey limited the age range to those 15 years of age and younger (Centers for Disease Control, 2003). However, in order to include perinatal variables such as pregnancy issues and breastfeeding practices, only children under seven years of age could be included in the study because only the mothers of children from 0

to 6 years (72 months) of age were interviewed regarding these variables. Of those respondents to the Youth Questionnaire (3, 449), only 1,266 were within this age range.

Of the 1, 266 survey participants, 679 were males (53.8%) and 583 were females (46.2%). Ethnicity was divided into five categories. Mexican Americans consisted of 37.5% (n = 475) of the population; 81 were other Hispanics (6.4%); 333 were non-Hispanic white (26.3%); 306 were non-Hispanic black (24.2%) and 71 were multi-racial (5.6%). All races and ethnicities will be included in this study.

NHANES 1999-2000 Sampling Procedures

NHANES 1999-2000 is a complex, stratified, multi-stage probability sample of the civilian non-institutionalized population of the United States (Centers for Disease Control, 2003). The survey collects information on diet, activity levels, medication usage, hospital and clinic utilization. The 1999 – 2000 public use data set came from information collected over a two-year period. Previous NHANES surveys were conducted in 15 U.S. locations per year, surveying approximately 5,000 persons annually. The 1999-2000 survey was designed to give statistical data annually that represents the nation. The 1999-2000 survey only contains two years worth of data and not six years like in past available NHANES data sets. This constitutes a smaller sample size in which fewer geographic locations were surveyed. The participants for the NHANES survey were selected with the use of 1990 census data. NHANES has divided cities into

communities and these communities into neighborhoods. From these neighborhoods, certain households selected at random were approached for eligibility into the survey.

Sample Size

A total of 1,266 children were included in the study: 158 with asthma and 1,104 without asthma. This sample size allowed the calculation of the prevalence of asthma (12.5 per 100 approximately) with a 2% precision and 95% confidence level and allowed exploration of odds ratios 2.0 or larger for factors that were 10% or more frequently found among children without asthma (type I error: 0.05, and type II error 0.20 or 80% power) (Dean et al., 1995; Fleiss, 1981).

Study Data

Outcome Definition

The study individuals were those whose mothers answered NHANES questionnaire data item MCQ010 (Has a doctor or other health professional ever told you that you have asthma?). Through the NHANES questionnaire, cases of asthma were identified as those who answered "yes" to data item MCQ010, and these cases were compared to individuals who answered "no" to the same question. Those who answered

"Don't know" were excluded. Past studies have used varying definitions of asthma. Most published studies based on NHANES data use the self-referred questionnaire because it is known to have high levels of sensitivity and specificity (Abramson, Hensley, Saunders, & Wlodarczyk, 1991; F. Montealegre, & Bayona, M., 1996). There is no gold standard for definition of asthma in asthma research. For the present study, physician diagnosed asthma will be used as a definitive diagnosis. This definition was also utilized as a definitive definition in other studies that examined childhood factors for asthma with NHANES III data (Chulada et al., 2003; Rust, 2001).

Exposures

Variables analyzed in this study were based solely on questions available in the Youth NHANES questionnaire (1999-2000). The following are the variables included in the study identified as "exposures":

Gender

Age at Screening

Race/Ethnicity

Annual Household Income

Mother's age when born

Mother smoked when pregnant

Receive newborn care at health facility

Weight at birth in pounds

Ever attend day care or preschool

Now attend day care or preschool

Now attend Headstart

Hours spent away from home/weekday day

Taking treatment for anemia/past 3 mos*

Told have attention deficit disorder?

Doctor ever said you were overweight

Ever told you have learning disability*

Ever had chickenpox*

Ever tested for lead poisoning*

Had hay fever in past year

Had 3 or more ear infections/past year

Had frequent/severe headaches/past yr*

Stuttering/Stammering in past year

Trouble seeing even with glass/contacts*

Received hepatitis A vaccine series

Received hepatitis B 3 dose series

Covered by health insurance

Covered by private insurance

Covered by Medicaid/CHIP

Covered by other government insurance

Dental coverage included*

Time when no insurance in past year?

How long since last insured

Ever breastfed or fed breastmilk

Age stopped breastfeeding (days)

Age first fed milk daily basis (days)

Type of milk first fed - whole milk

Type of milk first fed - 2% milk

Age started eating solid foods(days)

Type of salt used at table*

How often add salt to food at table*

You drink whole or regular milk

You drink 2% fat milk

You drink 1% fat milk

Attend kindergarten

School serves school lunches*

School serves complete breakfast each day*

Does anyone smoke in the home

Total number of smokers in home

Total # of cigarette smokers in home

Type of home

How many years family lived in home

Home owned, bought, rented, other

Source of tap water*

Water treatment devices used or not*

Home painted in last 12 months*

Old paint scraped when home painted?*

Paint peeling, flaking, chipping inside*

Outside paint peeling/flaking/chipping*

Pest control in home in past month?

Rooms treated for pests?

Non-professional treated home with pesticides?*

Professional treated home with pesticides?*

* According to current literature, these are variables being explored for association with asthma for the first time.

Variables to be evaluated in this study include family history of asthma, demographics, perinatal factors, passive smoking, selected food items, attending daycare or pre-school, selected indoor environmental factors, and annual income.

In order to evaluate consistency with other investigations, the selection of variables was made following previous research both in NHANES and other published studies referred in the background of this dissertation, such as maternal smoking (Guilliland et al., 2003), day care attendance (Infante-Rivard et al., 2001), and received

newborn care in a hospital facility (W. H. Oddy et al., 2002). A total of 23 variables included in this study have never being reported related to asthma.

Ethical Issues

The proposal for this research was submitted to and approved by University of North Texas Health Science Center Institutional Review Board before data processing started. The present study used NHANES 1999-2000 publicly available data from the National Center of Health Statistics. No names or other identifiers were included. No individual informed consent was necessary.

Data Processing and Data Analysis

Data Processing and Analysis

In order to achieve the three specific aims of the study, data processing and analysis was performed by using Stata statistical package (Stata, 2005). NHANES 99-00 included a complex multistage sample design including a combination of stratified and cluster sampling. Appropriate sampling weights were needed to estimate prevalence, means, medians, and other statistics. Sampling weights were used to produce correct population estimates because each sampled person does not have an equal probability of

selection. The sampling weights incorporated the differential probabilities of selection and included adjustments for noncoverage and nonresponse (Ezzati, Massey, Waksberg, Chu, & Maurer, 1992; Ezzati-Rice & Murphy, 1995). Therefore, sample weights were used for the accurate calculation of estimates and their variance for each variable. Data analysis included three different parts:

(First specific aim) In order to assess the prevalence rate of childhood asthma per 100 by age, gender, ethnicity, race and other relevant variables, the frequency distribution of the variables of interest, cross-tabulation and percentage of the outcome, namely asthma by each of these variables was carried out (Rosner, 2000).

(Second specific aim) In order to identify and assess individual risk and protective factors for childhood asthma, children with asthma were compared to children without asthma, regarding selected variables included in the NHANES data 1999-2000. The data analysis was divided in two phases:

The first phase assessed the crude and multiple logistic regression adjusted association of each selected risk factor and asthma. This was accomplished by comparing cases of asthma with non-cases regarding individual selected exposures adjusting for all confounders simultaneously. The odds ratio was used as a measure of association between each variable and the outcome, namely childhood asthma.

During crude analysis, continuous variables; such as age and weight at birth, were analyzed as continuous variables. The mean difference was used as a measure of association or difference between children with asthma as compared to children without asthma (Rosner, 2000). In order to assess the precision of the mean difference estimate, the 95% confidence intervals for the mean difference was calculated by using the normal approximation (Rosner, 2000). The independent samples Student's t-test and the Wilcoxon's test were used to assess the statistical significance of the mean difference (Rosner, 2000). After this step, for stratified analysis, continuous variables were categorized by using percentiles as cut-off points (Szklo & Nieto, 2000).

The odds ratio was used as a measure of association for categorical variables (Rothman & Greenland, 1998). The exact 95% confidence intervals were used to assess the precision of the odds ratio estimate (Rosner, 2000).

Stratified analysis was conducted to identify and assess potential confounding and effect modification or interaction effects. Children with asthma were compared to children without asthma regarding each exposure included in this study. Confounding effects were evaluated by comparing the crude and the Mantel-Haenszel adjusted odds ratio (Szklo & Nieto, 2000). If a 15% difference between the crude and the stratified (adjusted) odds ratio was found, confounding was considered to be present. Effect modification and interaction were explored by comparing the stratum specific odds ratios. The Breslow and Day test for homogeneity of the odds ratios was used to assess the

statistical significance of the interaction (Woodward, 1999). If there was an important difference between or among strata, effect modification was considered to be present. If such difference was statistically significant as measured by the Breslow and Day test ($p < 0.10$), a statistical interaction was considered to be present. Whenever an important effect modification or interaction was present, further analysis was stratified by the categories of the interacting variable (Rothman & Greenland, 1998; Szklo & Nieto, 2000).

After stratified analysis, multiple adjustment procedures were carried out to assess the association of each variable controlling for all confounders simultaneously by using multiple logistic regression (Rosner, 2000; Szklo & Nieto, 2000).

(Third specific aim) For the identification and assessment of different combinations of risk and protective factors for childhood asthma, children with asthma were compared to children without asthma regarding combinations of selected variables included in the NHANES data 1999-2000. Combinations of two or more factors were explored to find the best models that predicted the presence of childhood asthma. The factors studied in this phase were those that were found with important associations with the outcome, namely asthma, during the second phase of the study. Multiple logistic regression modeling was use in this phase. The Cox and Snell R-square was used as a measure of predictability (Kleinbaum, Kupper, Muller, & Azhar, 1998). The selection of variables to be combined was conducted by manually entering each variable found associated during

the second phase of the analysis. In order to determine if a certain combination of variables was better than other combinations, the Cox and Snell R-squared was used. The larger the R-squared value, the better predictability (ibid).

CHAPTER IV

RESULTS

The study sample consisted of 1,266 children who were included in the analysis from newborn (0-1) to six years of age. The mean age of this sample was 3.2 years of age.

Table 1 shows selected characteristics among asthmatic children. It was found that among the158 children with asthma, 68% still had asthma at survey time during the previous year; (1) 73% had an asthma attack, (2) 47% had emergency care, (3) 61% wheezing in chest, (4) 71% wheezing disturb sleep during the previous year, (5) 47% had wheezing during exercise, (6) and 26% had wheezing severe enough to limit speech. Those who received medical attention for wheezing attacks were 76% of the total, and children who limit usual activities due to wheezing were 65%. The average number of wheezing attacks during the previous year was 4.4.

Table 1: Selected Characteristics of Asthma in NHANES 99-00

Characteristic	Present/Yes No. (%)	Absent/No No. (%)	Total No.
Still have asthma at survey time	106 (67.9)	50 (32.1)	156
Had asthma attack previous year	77 (72.6)	29 (27.4)	106
Emergency care previous year	36 (46.8)	41 (53.2)	77
Wheezing in chest previous year	97 (61.4)	61 (38.6)	158
Wheezing disturb sleep previous year	69 (71.1)	28 (28.9)	97
Chest sound wheezy during exercise	45 (46.9)	51 (53.1)	96
Wheezing severe enough to limit speech	19 (25.7)	55 (74.3)	74
Got medical attention for wheezing attack	59 (75.6)	19 (24.4)	78
Limit usual activities due to wheezing	51(64.6)	28 (35.4)	79
Average number of wheezing attacks previous year			4.35
Age when first had asthma			
One	104 (65.8)		
Two	20 (12.7)		
Three	18 (11.4)		
Four	7 (4.4)		
Five	5 (3.2)		
Six	4 (2.5)		
	158 (100)		

Figure 1: Age when first had asthma: NHANES data 1999-2000

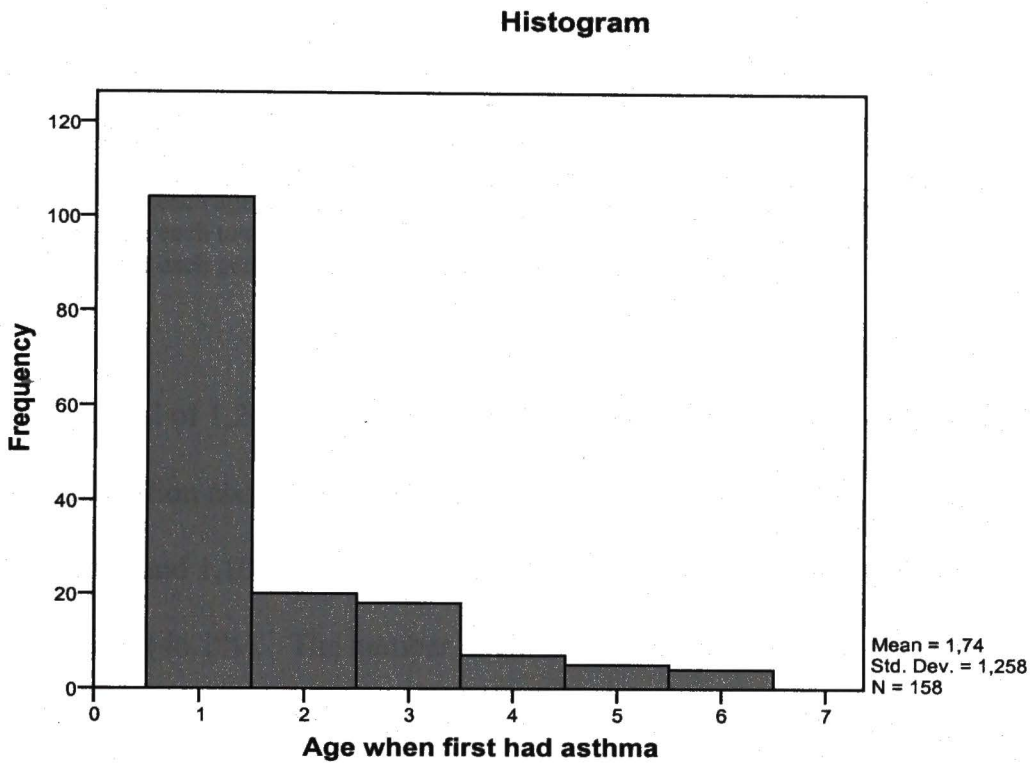


Figure 1 depicts the age when "first had asthma" among the asthmatic children included in the NHANES survey. Clearly, the largest age group when first had asthma was 0-1 years of age with a total of 104 children representing 65.8%. A decreasing trend in the number of asthma cases by age can also be seen.

Table 2: Age and Gender Distribution of Asthma in Children 6 years of age and younger: NHANES 1999-2000

	Males			Females			TOTAL
Age	**Asthmatic**	**Non-Asthmatic**	**Total**	**Asthmatic**	**Non-Asthmatic**	**Total**	
One	11 (10.6)[1]	146 (25.4)[1]	157 (23.1)[1]	5 (9.3)[1]	100 (18.9)[1]	105 (18.0)[1]	262 (20.8)[1]
Two	19 (18.3)	118 (20.5)	137 (20.2)	9 (17.6)	114(21.6)	123 (21.1)	260 (20.6)
Three	18 (17.3)	90 (15.7)	108 (15.9)	10 (18.5)	70 (13.2)	80 (13.7)	188 (14.9)
Four	28 (26.9)	76 (13.2)	104 (15.3)	12 (22.2)	82 (15.5)	94 (16.1)	198 (15.7)
Five	7 (6.7)	65 (11.3)	72 (10.6)	11 (20.4)	90 (17.0)	101 (17.3)	173 (13.7)
Six	21 (20.2)	80 (13.9)	101 (14.9)	7 (13.0)	73 (13.8)	80 (13.7)	181 (14.3)
Total	104 (15.3)[2]	575 (84.7)[2]	679 (53.8)[3]	54 (9.3)[2]	529 (90.7)[2]	583 (46.2)[3]	1262 (100)

[1] Percentage for each age group out of the total number of children for each column.
[2] Percentage for each total group out of total number of children of each gender.
[3] Percentage for each gender out of total number of children in the study.

A total of 1,266 children were included in the study, but four children did not have information about asthma. Therefore, the total sample included 1,262 children; 158 with asthma and 1,104 without asthma. Males (53.8%) were slightly more numerous than females (46.2%). The number of children decreased from 20.8% in the first age group (0-1) to 14.9% in the third age group (3), slightly increased to 15.7% in the fourth age group (4), and decreased again to 13.7% in the fifth group (5), slightly increasing again to 14.3% in the last age group (6).

Figure 2: Age Distribution of Asthmatic children 6 years of age and younger: NHANES data 1999-2000

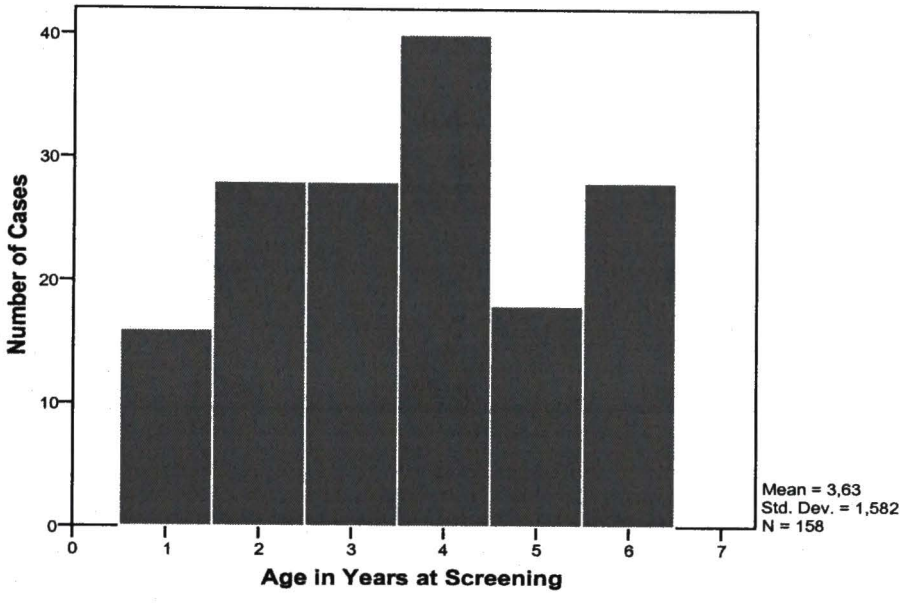
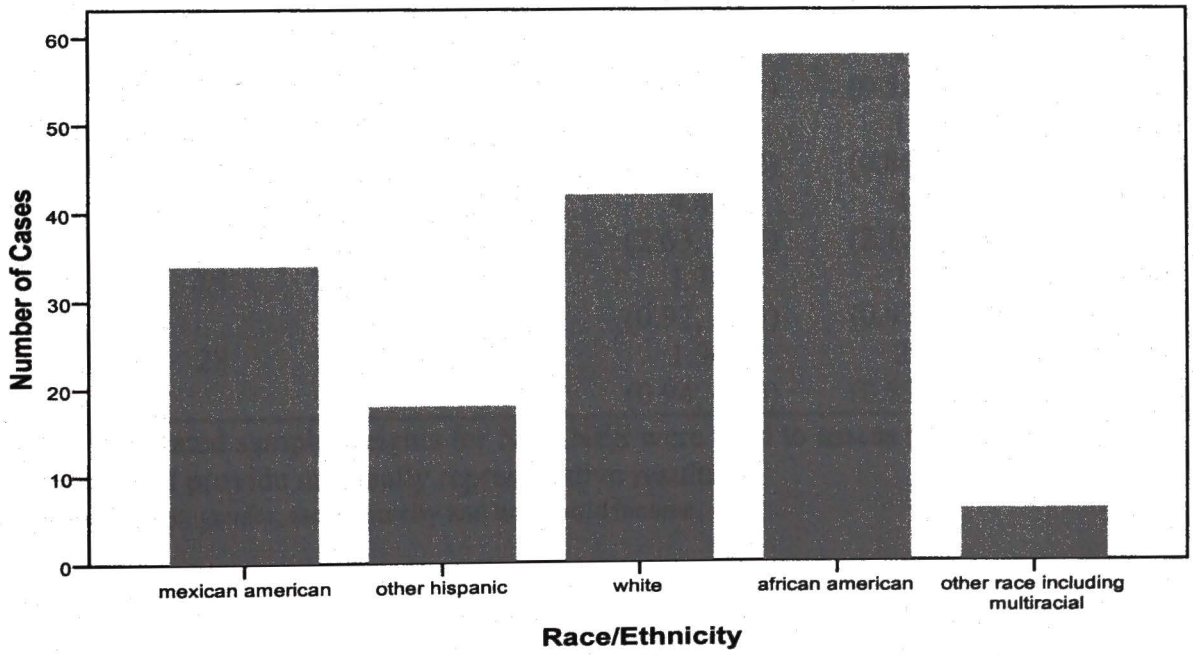


Figure 2 illustrates the age distribution of asthmatic children included in the study (age at the time of the survey). The number of cases increased up to four years of age. After age four prevalence decreased and slightly increased again in the oldest age group.

Table 3. Race and Ethnicity Distribution within the population and Percentage with Asthma for NHANES 99-00

	Total Children Surveyed		Children with Asthma	
Variable Race/Ethnicity	**Number**	**Percent**	**Number**	**Percent**
Mexican American	475	37.5	34	21.5
Other Hispanic	81	6.4	18	11.4
White	333	26.3	42	26.6
African American	306	24.2	58	36.7
Other- including multi racial	71	5.6	6	3.8
Total	1,266	100.0	158	100.0

Figure 3: Race/Ethnicity Distribution of Asthmatic children 6 years of age and younger: NHANES data 1999-2000 (N=158)



The racial/ethnic composition is represented in Table 3 and Figure 3. The largest proportion of the population in this study was the one of the Mexican-Americans including 38% of the surveyed sample; 6.4% were other Hispanics; 26% were white; 24% were non-Hispanic black, and 6% were multi-racial. All races and ethnicities were included in this study.

Table 4: Association between asthma and age and gender in children age 6 and younger: NHANES 1999-2000

Variable	Cases	Non - Cases	Prevalence per 100[1]	Crude OR[1] & 95% CI	Adjusted OR[1,2] & 95% CI	p-value[1,2]
Gender						
Male	104	575	17.4	1.00	1.00	
Female	54	529	9.7	0.51 (0.34, 0.78)	0.45 (0.24, 0.85)	0.017
Total	158	1,104	13.8			
Age						
One	16	246	6.9	1.00	1.00	
Two	28	232	10.6	1.60 (0.60, 4.31)	1.60 (0.52, 4.89)	0.384
Three	28	160	14.8	2.36 (1.09, 5.12)	1.97 (0.86, 4.51)	0.102
Four	40	158	24.5	4.40 (2.63, 7.37)	4.31 (2.12, 8.74)	0.001
Five	18	155	11.5	1.76 (0.97, 3.23)	1.99 (0.97, 4.11)	0.060
Six	28	153	12.5	1.94 (0.94, 4.00)	2.07 (0.83, 5.15)	0.109

[1] NCHS generated sample weights for NHANES were used to assess the estimates, the variance, and provide nationally representative results.

[2] Adjusted for age, gender, race/ethnicity and household income.

Table 4 shows the prevalence of asthma by age and gender, and the associations of gender and age with the outcome, asthma. The prevalence in females was 9.7 per 100 and 17.4 per 100 for males. Females were found to be less likely to develop asthma than males. After adjusting for confounders, such as age, race/ethnicity and household income, females were 55% less likely to develop asthma ($p = 0.017$). The overall prevalence of asthma was 13.8 per 100. Asthma prevalence increased with age, from 6.9 per 100 in the first age group, to 24.5 per 100 in the four years old group. After four years of age, prevalence decreased to 11.5 per 100 and increased again in the oldest age group to 12.5 per 100. For each year of increase in age from one to four, a child's chance of having asthma increased. This dose-response relationship was not as clear for children five years of age, because the association dropped from OR = 4.3 (four years old) to OR = 2.0 (five years old), when comparing them to the 0-1 year age group (the reference group). The association of the last age group, six years of age, asthma slightly increased from OR = 2.0 in the fifth age group to OR = 2.07. In spite of this imperfect dose-response relationship, the linear trend was statistically significant ($p=0.002$).

Figure 4: Gender Distribution of Asthmatic children 6 years of age and younger: NHANES data 1999-2000 (N=158)

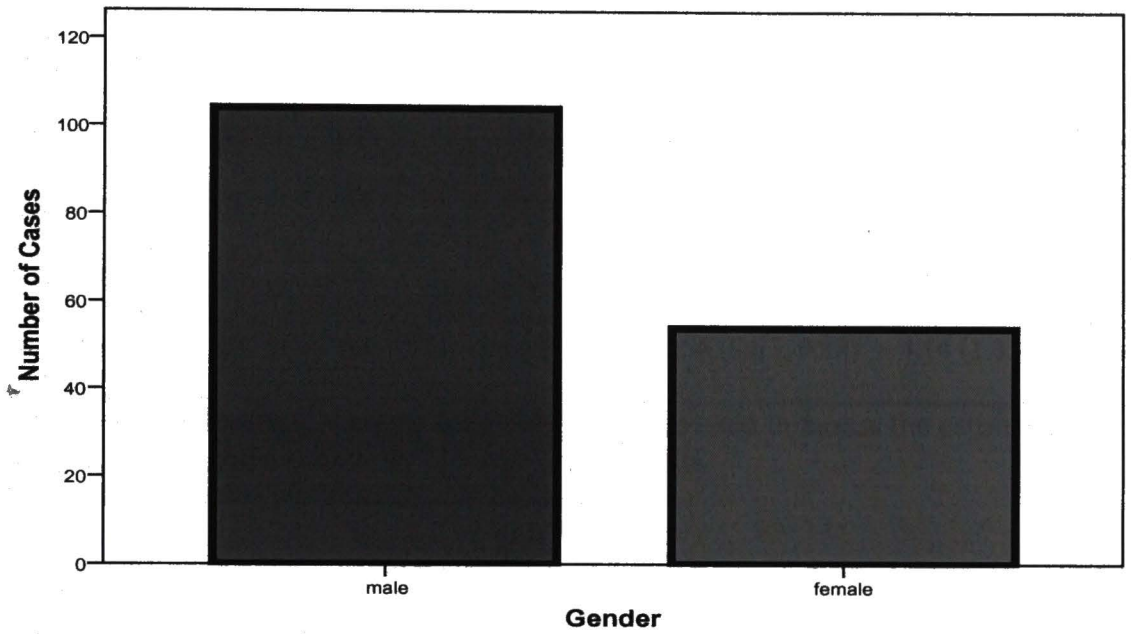


Figure 4 shows the distribution by gender of asthmatic children under study.

Males were 104 cases (65.8%) and females 54 cases (34.2%).

Table 5. Association between asthma and race/ethnicity and income in children age 6 and younger: NHANES 1999-2000

Variable	Cases	Non - Cases	Prevalence per 100[1]	Crude OR[1] & 95% CI	Adjusted OR[1,2] & 95% CI	p-value[1,2]
Race						
White	42	290	6.5	1.00	1.00	
African American	58	248	18.4	3.26 (1.45, 7.33)	3.88 (1.41, 10.65)	0.012
Mixed Race	6	63	13.4	2.23 (0.93, 5.36)	2.72 (1.18, 6.28)	0.022
Mexican American	34	441	19.3	3.47 (1.99, 6.05)	3.90 (2.25, 6.77)	< 0.001
Hispanic (other)	18	62	15.0	2.54 (0.67, 9.58)	4.14 (1.35, 12.71)	0.017

[1] NCHS generated sample weights for NHANES were used to assess the estimates, the variance, and provide nationally representative results.

[2] Adjusted for age, gender, race/ethnicity and household income.

Table 5 shows the prevalence and associations between asthma and race/ethnicity. African Americans, mixed race, Mexican Americans and Hispanics were compared with Whites who were used as a reference group. The prevalence for Whites was 6.5 per 100, 18.4 per 100 for African Americans, 13.4 per 100 for mixed race, 19.3 per 100 for Mexican Americans, and 15.0 per 100 for Hispanics. When analyzing these categories, similar findings were observed before and after adjustment for confounders except in the Hispanic group, where the crude odds ratio was 2.5, and after adjustment was 4.1. Hispanics had the largest difference with the reference group. Mexican Americans and African Americans had similar differences with the reference group. Mixed race was 2.7 times more likely to have asthma than the reference White group. All of these associations were found to be statistically significant ($p < 0.05$).

Table 6: Association between asthma and household and family income in children age 6 and younger: NHANES 1999-2000

Variable	Cases	Non - Cases	Crude OR[1] & 95% CI	Adjusted OR[1,2] & 95% CI	p-value[1,2]
Household Income					
0 – 14,999	33	200	1.00	1.00	
15,000 – 34,999	52	303	1.06 (0.53, 2.09)	0.89 (0.46, 1.71)	0.714
35,000 – 54,999	22	137	0.80 (0.48, 1.33)	0.76 (0.45, 1.27)	0.270
55,000 +	28	236	0.67 (0.26, 1.71)	0.57 (0.25, 1.32)	0.173
Family Income					
0 – 14,999	54	286	1.00	1.00	
15,000 – 34,999	47	318	0.64 (0.35, 1.18)	0.51 (0.25, 1.03)	0.059
35,000 – 54,999	19	133	0.63 (0.37, 1.09)	0.58 (0.30, 1.09)	0.088
55,000 +	22	208	0.55 (0.25, 1.24)	0.44 (0.21, 0.91)	0.030

[1] NCHS generated sample weights for NHANES were used to assess the estimates, the variance, and provide nationally representative results.

[2] Adjusted for age, gender, race/ethnicity and household income.

Table 6 shows the associations between income and asthma. Variables were divided in four categories: (1) from 0 to $ 14,999, (2) from $ 15,000 to $ 34,999, (3) from $ 35,000 to $ 54,999, and (4) from $ 55,000 and more. The first category was used as a reference group (0 to $ 14,999). As household income increased, the likelihood to have asthma decreased from 11% to 43%. However, none of these associations or the trend were found to be statistically significant ($p > 0.05$). Similar results were discovered when

analyzing family income, decreasing the risk of having asthma, from 49% to 56%. These associations were of borderline statistical significance. However, the linear trend of the crude associations was statistically significant ($p = 0.033$).

Table 7a shows the associations of asthma and nourishments, mother's age when child was born, newborn care, and low birth weight. Babies who were not breastfed had an increased chance of having asthma by 19%. This association was not statistically significant ($p = 0.479$). Whenever other than whole milk was used first to feed the child, the likelihood of having asthma was decreased by 28%. However, this association was not statistically significant ($p = 0.279$). A 54% increased likelihood of having asthma was found in those that were fed with milk other than 2% fat. This association was not statistically significant ($p = 0.203$). Starting solid foods before four months into the infant's diet increased the probability to have asthma by 51%; and before six months, the probability increased by 16%. However, these associations were not statistically significant ($p > 0.05$). The analysis shows a statistically significant decrease in the probability to have asthma if the mother's age is 23 years of age or older. Mothers 23 to 28 years of age were 51% less likely to have a child with asthma, and mothers 29 to 45 years of age had 53% less likelihood to have a child with asthma. Both of these associations were statistically significant ($p < 0.05$). Not receiving newborn care (defined as: intensive care unit, premature nursery, or other special care facility) was shown to decrease the chance to have asthma by 62% ($p = 0.001$), and normal birthweight as

compared to low birthweight decreased the probability to have asthma by 53% (p = 0.030).

Table 7b includes exposure to attending day care, Headstart, kindergarten, hours spent away from home, and the outcome, having asthma. If the child never attended day care or preschool, the likelihood of having asthma decreased by 27%. This association was not statistically significant (p = 0.124). However, if the child was currently attending day care or pre school at the time of the survey, he or she was 71% more likely to have asthma. This association was not statistically significant (p = 0.201). If the child attended the Headstart program, the likelihood to have asthma increased 81%, with a borderline statistical significance (p = 0.075). Not attending kindergarten was associated with 26% increased likelihood of having asthma. This association was not statistically significant (p = 0.723). If a child spent up to 4 hours away from home, the odds of having asthma doubled, but this association not statistically significant (p-value = 0.115).

Table 7a: Association of asthma with nourishments, mother's age, newborn care and low birth weight in children age 6 and younger: NHANES 1999-2000

Variable	Cases	Non - Cases	Crude OR[1] & 95% CI	Adjusted OR[1,2] & 95% CI	p-value[1,2]
Breastfed					
Yes	76	670	1.00	1.00	
No	82	428	1.41 (0.87, 2.27)	1.19 (0.71, 2.01)	0.479
Type of milk first fed					
Whole or regular	129	877	1.00	1.00	
Other	29	224	0.70 (0.43, 1.13)	0.72 (0.40, 1.34)	0.279
Type of milk first fed					
2% fat milk	22	149	1.00	1.00	
Other	136	955	1.47 (0.82, 2.64)	1.54 (0.77, 3.09)	0.203
Started solid foods					
> 4 months	35	200	1.00	1.00	
< 4 months	121	894	1.46 (0.91, 2.36)	1.51 (0.85, 2.67)	0.146
Started solid foods					
> 6 months	80	517	1.00	1.00	
< 6 months	76	577	1.08 (0.67, 1.76)	1.16 (0.68, 1.97)	0.568
Mother's age when born					
14 – 22 years of age	61	365	1.00	1.00	
23 – 28 years of age	51	340	0.49 (0.27, 0.88)	0.49 (0.28, 0.88)	0.020
29 – 45 years of age	46	399	0.52 (0.34, 0.79)	0.47 (0.26, 0.85)	0.017
Newborn care					
Yes	32	117	1.00	1.00	
No	126	981	0.34 (0.19, 0.63)	0.38 (0.23, 0.63)	0.001
Low birth weight					
Less than 2.5 Kg	29	94	1.00	1.00	
Equal or more than 2.5 Kg	127	961	0.43 (0.21, 0.87)	0.47 (0.24, 0.92)	0.030

[1] NCHS generated sample weights for NHANES were used to assess the estimates, the variance, and provide nationally representative results.

[2] Adjusted for age, gender, race/ethnicity and household income.

Table 7b: Association of asthma with exposure to attending day care, headstar, kindergarten and hours spent away from home in children age 6 and younger: NHANES 1999-2000

Variable	Cases	Non – Cases	Crude OR[1] & 95% CI	Adjusted OR[1,2] & 95% CI	p-value[1,2]
Ever attended Day Care or Preschool					
Yes	98	552	1.00	1.00	
No	60	551	0.76 (0.52, 1.13)	0.73 (0.48, 1.10)	0.124
Now attending Day Care or Preschool					
Yes	53	323	1.00	1.00	
No	29	129	1.37 (0.73, 2.57)	1.71 (0.73, 4.01)	0.201
Now attend Headstart					
No	17	81	1.00	1.00	
Yes	113	866	0.80 (0.36, 1.77)	1.81 (0.93, 3.50)	0.075
Attend kindergarten					
Yes	51	288	1.00	1.00	
No	35	178	1.91 (1.04, 3.52)	1.26 (0.33, 4.85)	0.723
Hours spent away from home					
5 +	57	437	1.00	1.00	
0 – 4	73	513	1.52 (0.67, 3.48)	2.03 (0.82, 4.99)	0.115

[1] NCHS generated sample weights for NHANES were used to assess the estimates, the variance, and provide nationally representative results.

[2] Adjusted for age, gender, race/ethnicity and household income.

Table 8 shows the association of asthma and tobacco-related variables. Not smoking during pregnancy decreased the likelihood of having asthma by 26% (p = 0.452), though not significantly. The probability to have asthma decreased if nobody smoked at home. In contrast, whenever two or more smokers or cigarette smokers were present at home, as compared to only have one, children had 8.9 times more likelihood of having asthma (p = 0.001).

Table 8: Association of asthma with tobacco related variables in children age 6 and younger: NHANES 1999-2000

Variable	Cases	Non - Cases	Crude OR[1] & 95% CI	Adjusted OR[1,2] & 95% CI	p-value[1,2]
Mother smoked when pregnant					
Yes	34	131	1.00	1.00	
No	124	964	0.57 (0.29, 1.14)	0.74 (0.33, 1.69)	0.452
Does anyone smoke in the home					
Yes	32	185	1.00	1.00	
No	124	897	0.91 (0.45, 1.81)	1.14 (0.48, 2.72)	0.752
Total number of smokers in home					
1	13	131	1.00	1.00	
2 or more	19	54	5.51 (2.73, 11.12)	8.92 (3.02, 26.35)	0.001
Total number of cigarette smokers in home					
1	12	129	1.00	1.00	
2 or more	19	54	5.85 (2.91, 11.75)	8.92 (3.02, 26.35)	0.001

[1] NCHS generated sample weights for NHANES were used to assess the estimates, the variance, and provide nationally representative results.

[2] Adjusted for age, gender, race/ethnicity and household income.

Table 9 shows the association of asthma with selected dietary and nutritional habits. Not drinking whole or regular milk was associated with 45% less likelihood to develop asthma. This result was not statistically significant ($p = 0.192$). Currently drinking other than 2% fat milk was not associated with the probability of having asthma. In contrast, currently drinking other than 1% fat milk increased 3.5 times the probability of having asthma. However, this association was not statistically significant ($p = 0.138$). Often consuming milk products during the previous month was associated with 21% less likelihood of having asthma. However, this association was not statistically significant ($p = 0.607$). Not serving breakfast or lunch at the school were associated with a 27% and 60% less probability to have asthma, respectively. Neither of these two last associations were statistically significant ($p > 0.05$). Not using salt at the table, increased the probability of having asthma by 21% ($p = 0.027$). On the other hand, children that rarely add salt to food at the table had 47% less likelihood to develop the outcome. However, this last association was not statistically significant after adjusting for age, gender and race/ethnicity ($p = 0.362$).

Table 9: Association of asthma with selected dietary and nutritional habits variables in children age 6 and younger: NHANES 1999-2000

Variable	Cases	Non - Cases	Crude OR[1] & 95% CI	Adjusted OR[1,2] & 95% CI	p-value[1,2]
You drink whole or regular milk					
Whole regular	113	743	1.00	1.00	
Other	45	359	0.56 (0.33, 0.95)	0.55 (0.21, 1.40)	0.192
You drink 2% fat milk					
2% fat milk	42	253	1.00	1.00	
Other	116	851	1.02 (0.58, 1.81)	0.97 (0.44, 2.16)	0.937
You drink 1% fat milk					
1% fat milk	5	46	1.00	1.00	
Other	153	1058	3.15 (0.49, 20.12)	3.53 (0.63, 19.69)	0.138
Past 30 day milk product consumption					
Not often	135	966	1.00	1.00	
Often	21	133	0.94 (0.45, 1.94)	0.79 (0.30, 2.08)	0.607
School serve complete breakfast each day					
Yes	43	213	1.00	1.00	
No	8	71	0.65 (0.21, 1.99)	0.73 (0.27, 2.00)	0.518
School serves lunches					
Yes	47	254	1.00	1.00	
No	3	34	0.38 (0.06, 2.25)	0.40 (0.08, 1.82)	0.219
Type of salt used at table					
Ordinary salt	35	247	1.00	1.00	
Does not use or add salt	121	846	1.31 (0.75, 2.28)	1.21 (1.02, 1.42)	0.027
How often add salt to food at table					
Occasionally or very often	13	85	1.00	1.00	
Rarely	22	162	0.86 (0.27, 2.71)	0.53 [3] (0.12, 2.27) [3]	0.362[3]

[1] NCHS generated sample weights for NHANES were used to assess the estimates, the variance, and provide nationally representative results.
[2] Adjusted for age, gender, race/ethnicity and household income. [3] Adjusted for age, gender and race/ethnicity.

Table 10 shows the association of asthma with selected home conditions. Those who had a mobile home or trailer were used as a reference group. Children that lived in a one family house were 49% less likely to have asthma, those that lived in a townhouse were 22% less likely to have asthma, and those that lived in an apartment, had 17% more likelihood to have asthma. None of these associations was statistically significant ($p > 0.05$). The number of years living in the current home was slightly associated with a not statistically significant decreased likelihood of having asthma. Renting as compared to owning a home was associated with 2.3 times more likelihood of presenting asthma ($p = 0.007$). The probability of having asthma was 2.1 times higher if the house was not painted in the last 12 months, as compared to children that lived in a house that was painted in the last 12 months ($p = 0.030$). A 46% less likelihood of having asthma was present whenever the old paint was not scraped when the home was painted. However, this association was not statistically significant ($p = 0.265$). If paint was peeling, flaking or chipping inside the house, the chance of having asthma increased 75%. This association was not statistically significant ($p = 0.116$). In contrast, if paint was peeling, flaking or chipping outside the house, the chance of having asthma decreased 17%. This association was not statistically significant ($p = 0.616$).

Table 10: Association of asthma with selected home conditions in children age 6 and younger: NHANES 1999-2000

Variable	Cases	Non - Cases	Crude OR[1] & 95% CI	Adjusted OR[1,2] & 95% CI	p-value[1,2]
Type of home					
A mobile home or trailer	9	98	1.00	1.00	
A one family house detached from any other house	71	587	0.71 (0.24, 2.08)	0.51 (0.22, 1.18)	0.107
A one family house attached to one or more (townhouse)	18	101	1.13 (0.43, 2.98)	0.78 (0.26, 2.34)	0.631
An apartment	56	294	1.68 (0.54, 5.25)	1.17 (0.42, 3.21)	0.748
How many years family lived in home					
Less than one year	30	217	1.00	1.00	
1 – 2 years	58	288	0.84 (0.38, 1.86)	1.04 (0.56, 1.95)	0.887
3 – 5 years	36	318	0.57 (0.30, 1.08)	0.68 (0.36, 1.29)	0.218
6 – 10 years	15	169	0.47 (0.19, 1.20)	0.74 (0.31, 1.77)	0.469
> than 10 years	17	90	1.04 (0.33, 3.22)	0.82 (0.21, 3.14)	0.756
Home owned, bought, rented, other					
Owned or being bought	56	542	1.00	1.00	
Rented	97	523	2.42 (1.47, 3.96)	2.34 (1.32, 4.15)	0.007
Home painted in last 12 months					
Yes	42	381	1.00	1.00	
No	83	537	2.14 (1.26, 3.60)	2.09 (1.08, 4.02)	0.030
Old paint scraped when home painted					
Yes	14	76	1.00	1.00	
No	24	262	0.71 (0.18, 2.76)	0.54 (0.17, 1.69)	0.265
Paint peeling/ flaking/ chipping inside					
Yes	20	195	1.00	1.00	
No	107	734	1.97 (1.01, 3.85)	1.75 (0.86, 3.57)	0.116
Outside paint peeling/ flaking/chipping					
Yes	22	162	1.00	1.00	0.616
No	105	760	0.96 (0.42, 2.17)	0.83 (0.39, 1.80)	

[1] NCHS generated sample weights for NHANES were used to assess the estimates, the variance, and provide nationally representative results.

[2] Adjusted for age, gender, race/ethnicity and household income.

Table 11: Association of asthma with selected pest control and water supply variables in children age 6 and younger: NHANES 1999-2000

Variable	Cases	Non - Cases	Crude OR[1] & 95% CI	Adjusted OR[1,2] & 95% CI	p-value[1,2]
Pest control in home in past month?					
Yes	39	268	1.00	1.00	
No	116	803	0.96 (0.37, 2.50)	0.85 (0.34, 2.17)	0.722
Rooms treated for pets?					
Not Entire Home	23	134	1.00	1.00	
Entire Home	14	116	0.65 (0.22, 1.97)	0.56 (0.22, 1.41)	0.198
Non-professional treated home?					
Yes	19	172	1.00	1.00	
No	20	93	2.27 (1.12, 4.60)	2.19 (1.11, 4.33)	0.027
Professional treated home?					
Yes	20	105	1.00	1.00	
No	19	162	0.38 (0.12, 1.21)	0.35 (0.11, 1.16)	0.082
Source of tap water					
Private/public Water company	146	981	1.00	1.00	
Private/ public well	6	76	0.83 (0.37, 1.86)	0.90 (0.47, 1.73)	0.735
Water treatment devices used or not					
Yes	23	207	1.00	1.00	
No	133	872	1.67 (0.75, 3.74)	1.44 (0.67, 3.08)	0.321

[1] NCHS generated sample weights for NHANES were used to assess the estimates, the variance, and provide nationally representative results.

[2] Adjusted for age, gender, race/ethnicity and household income.

Table 11 illustrates the association of asthma with selected pest control and water supply variables. Whenever pest control was not used during the previous month, a 15% less probability of having asthma was found, though not statistically significant. If the entire home was treated with pesticides, the chance of presenting asthma was not significantly reduced by 44% ($p = 0.198$). A 2.2 times more likelihood of having asthma was seen if a non-professional treated the home with pesticides ($p = 0.027$). If the home was treated by a professional, a 65% decreased probability of having asthma was found ($p = 0.082$). Regarding the source of tap water, those with private or public well had a non-significant 10% less likelihood of having asthma as compared to those that had private or public water company ($p = 0.735$). If the home did not use any kind of water treatment device, the chance of developing asthma increased by 44%. These findings were not statistically significant ($p = 0.321$).

Table 12a: Association of asthma with selected medical conditions in children age 6 and younger: NHANES 1999-2000

Variable	Cases	Non - Cases	Crude OR[1] & 95% CI	Adjusted OR[1,2] & 95% CI	p-value[1,2]
Taking treatment for anemia/past 3 months					
Yes	8	40	1.00	1.00	0.352
No	150	1064	0.69 (0.31, 1.52)	0.59 (0.19, 1.89)	
Told have attention deficit disorder					
Yes	3	9	1.00	1.00	0.633
No	83	455	0.50 (0.12, 2.12)	0.61 (0.07, 5.38)	
Doctor ever said you were overweight					
Yes	13	39	1.00	1.00	0.493
No	129	818	0.68 (0.32, 1.46)	0.65 (0.17, 2.45)	
Ever told you have a learning disability					
Yes	8	21	1.00	1.00	0.097
No	78	445	0.33 (0.11, 1.02)	0.41 (0.14, 1.20)	
Ever had chickenpox					
Yes	9	100	1.00	1.00	0.007
No	19	51	3.47 (1.13, 10.69)	6.41 (1.84, 22.36)	
Ever tested for lead poisoning					
Yes	52	290	1.00	1.00	0.912
No	76	600	0.88 (0.58, 1.33)	0.98 (0.64, 1.50)	
Had hay fever in past year					
Yes	22	68	1.00	1.00	0.017
No	133	1026	0.37 (0.21, 0.64)	0.38 (0.18, 0.82)	

[1] NCHS generated sample weights for NHANES were used to assess the estimates, the variance, and provide nationally representative results.

[2] Adjusted for age, gender, race/ethnicity and household income.

Table 12b: Association of asthma with selected medical conditions in children age 6 and younger: NHANES 1999-2000

Variable	Cases	Non - Cases	Crude OR[1] & 95% CI	Adjusted OR[1,2] & 95% CI	p-value[1,2]
Had 3 or more ear infections past year					
Yes	40	163	1.00	1.00	0.001
No	118	939	0.48 (0.26, 0.86)	0.32 (0.18, 0.56)	
Had frequent severe headaches past year					
Yes	5	13	1.00	1.00	0.237
No	80	452	0.43 (0.08, 2.21)	0.34 (0.05, 2.21)	
Stuttering/ Stammering in past year					
Yes	7	29	1.00	1.00	0.128
No	79	435	0.31 (0.07, 1.48)	0.36 (0.09, 1.40)	
Problems with coughing in past year					
Yes	62	160	1.00	1.00	< 0.001
No	96	944	0.23 (0.14, 0.39)	0.19 (0.11, 0.33)	
Had dry cough at night in past year					
Yes	9	24	1.00	1.00	0.086
No	149	1080	0.49 (0.18, 1.38)	0.36 (0.11, 1.18)	
Trouble seeing even with glasses					
Yes	11	25	1.00	1.00	0.062
No	130	830	0.29 (0.06, 1.31)	0.18 (0.03,1.11)	
Received Hep. A Vaccine Series					
Yes	17	111	1.00	1.00	0.634
No	115	699	1.23 (0.63, 2.40)	1.34 (0.37, 4.88)	
Received Hep. B Vaccine Series					
Yes	128	865	1.00	1.00	0.656
No	23	157	1.12 (0.52, 2.40)	0.80 (0.27, 2.33)	

[1] NCHS generated sample weights for NHANES were used to assess the estimates, the variance, and provide nationally representative results.[2] Adjusted for age, gender, race/ethnicity and household income.

Table 12a and 12b contain the association of asthma with selected medical conditions. Receiving treatment for anemia increased (non-significantly) the likelihood of having asthma by 69%. A non-significant 64% increased chance of having asthma was found among those with attention deficit disorder. Being overweight was associated with a 54% increased probability of having asthma. However this association was not statistically significant ($p = 0.453$). Children with learning disabilities had 2.4 times more likelihood of having asthma, but this association was borderline significant ($p = 0.097$). Those that had chickenpox were 84% less likely to have asthma ($p=0.007$). Testing for lead poisoning was not associated with asthma. Having had high fever during the past year increased 2.6 times the likelihood of having asthma ($p=0.017$). Whenever the child had three or more ear infections during the previous year, the likelihood of asthma increased 3.1 times ($p =0.001$). Frequent and severe headaches during the previous year were associated with a 2.9 times increased likelihood of having asthma, but this association was not statistically significant. Children stuttering/stammering in the previous year had 2.8 times more chance of having asthma. However, this association was not statistically significant ($p = 0.128$). A 5.3 times more likelihood of having asthma was found in children having problems with coughing in the previous year ($p < 0.001$). Children who had dry cough at night in the past year were 2.8 times more likely to present asthma but this association was of borderline significance ($p =0.086$). Those who had trouble seeing even with glasses had 5.6 times more probability of having asthma. This association was of borderline significance ($p = 0.062$). Receiving hepatitis A vaccine series was associated with a non-significant 25% less likelihood of having asthma ($p =$

0.634). In contrast, those receiving hepatitis B vaccine series were 25% more likely to have asthma but this association was not statistically significant (p = 0.656).

Table 13 includes the association of asthma with selected health insurance coverage variables. Those that were not covered by health insurance had a non-significant 15% more likelihood of having asthma (p = 0.639). Those that had private insurance were 58% less likely to have asthma (p = 0.003). On the other hand, those covered by Medicaid/CHIP were 3.7 times more likely to have asthma (p = 0.001). Those covered by other government insurance had a slightly and non-significant 18% less likelihood of having asthma (p = 0.687). Children whose dental coverage was part of their health insurance were 64% more likely to have asthma, but this association was not statistically significant (p = 0.450). A slight and non-significant 25% increased likelihood of having asthma was seeing in those that had time with no insurance during the previous year (p = 0.439). Children who were less than 3 years since last insurance coverage were 5.8 times more likely to have asthma but this association was not statistically significant (p =0.182).

Table 13: Association of asthma with selected health insurance coverage variables in children age 6 and younger: NHANES 1999-2000

Variable	Cases	Non - Cases	Crude OR[1] & 95% CI	Adjusted OR[1,2] & 95% CI	p-value[1,2]
Covered by health insurance					
Yes	137	893	1.00	1.00	0.639
No	19	186	0.83 (0.45, 1.56)	1.15 (0.61, 2.18)	
Covered by private insurance					
Yes	66	522	1.00	1.00	0.003
No	68	365	1.97 (1.16, 3.32)	2.40 (1.43, 4.02)	
Covered by Medicaid/CHIP					
Yes	64	305	1.00	1.00	0.001
No	70	582	0.44 (0.28, 0.69)	0.27 (0.13, 0.54)	
Covered by other government insurance					
Yes	11	70	1.00	1.00	0.687
No	123	817	0.88 (0.32, 2.38)	1.22 (0.44, 3.37)	
Dental coverage included					
Yes	116	695	1.00	1.00	0.450
No	14	162	0.66 (0.21, 2.09)	0.61 (0.16, 2.38)	
Time when no insurance in past year?					
Yes	8	70	1.00	1.00	0.439
No	126	816	0.95 (0.49, 1.85)	0.80 (0.44, 1.46)	
How long since last insured					
More than 3 years and never	4	95	1.00	1.00	0.182
Less than 3 years	15	84	2.63 (0.73, 9.50)	5.78 (0.39, 84.85)	

[1] NCHS generated sample weights for NHANES were used to assess the estimates, the variance, and provide nationally representative results.

[2] Adjusted for age, gender, race/ethnicity and household income.

Tables 14 to 18 include five different predictive models that were built based on the results of the above individual variable analysis. Table 14 has a predictive model in which all variables were tried until the maximum pseudo R^2 of 0.2151 was achieved. The combination of the variables included in this general predictive model therefore explained 21.5% of asthma in the study population. Table 15 shows a demographic and birth related predictive model in which 6.11% of the outcome is explained by the combination of seven variables. Table 16 includes a demographic and tobacco related predictive model in which 8.4% of asthma can be explained by the combination of seven different variables. Table 17 includes a demographic and insurance related predictive model. This model predicts 6.2% of the outcome with a combination of eight variables. Table 18 shows a demographic and medical conditions related predictive model in which 30.5% of the outcome is explained.

Table 14: General Predictive Model

Variable	Adjusted OR	95% CI		p-value
Gender	0.30	0.13	0.71	0.006
Age	0.49	0.20	1.24	0.133
Mother smoked when pregnant	0.27	0.10	0.74	0.011
Low birth weight	0.35	0.12	1.06	0.063
Now Day Care or Preschool Attendance	2.31	0.90	5.94	0.083
Now attend headstart	1.26	0.41	3.94	0.686
Taking treatment for anemia/ past 3 months	0.61	0.08	4.79	0.640
Told have attention deficit disorder?	4.03	0.13	129.11	0.431
Ever told you have a learning disability	0.11	0.02	0.79	0.028
Had hay fever in past year	0.50	0.17	1.48	0.211
Had 3 or more ear infections past year	0.33	0.10	1.04	0.059
Had frequent severe headaches past year	1.45	0.11	19.39	0.777
Stuttering/ Stammering in past year	2.45	0.52	11.63	0.258
Problems with coughing in past year	0.20	0.07	0.54	0.002
Trouble seeing even with glass/ contacts	0.31	0.04	2.31	0.251
You drink whole or regular milk	1.12	0.46	2.72	0.801

Log likelihood = -86.59513
Number of observations = 235
LR chi^2 (16) = 47.45
Prob > chi^2 = 0.0001
Pseudo R^2 = 0.2151

Table 15: Demographic and Birth Related Predictive Model

Variable	Adjusted OR	95% CI		p-value
Gender	0.49	0.33	0.72	< 0.001
Age	1.19	1.07	1.33	0.001
Race/Ethnicity	1.26	1.09	1.46	0.002
Household Income	0.95	0.89	1.02	0.151
Low birth weight	0.60	0.33	1.07	0.085
Mother's age when born	0.84	0.66	1.07	0.160
Newborn care	0.58	0.34	0.99	0.045

Log likelihood = -366.16214
Number of observations = 973
LR chi^2 (16) = 47.63
Prob > chi^2 = 0.0000
Pseudo R^2 = 0.0611

Table 16: Demographic and Tobacco Related Predictive Model

Variable	Adjusted OR	95% CI		p-value
Gender	0.60	0.24	1.54	0.291
Age	1.04	0.80	1.37	0.751
Race/Ethnicity	1.47	0.98	2.22	0.063
Household Income	0.99	0.82	1.18	0.878
Mother smoked when pregnant	0.71	0.26	1.93	0.498
Total number of smokers in home	2.97	1.15	7.62	0.024
Total number of cigarettes smoked at home	1.92	0.51	7.19	0.334

Log likelihood = -63.413089
Number of observations = 170
LR chi^2 (16) = 11.59
Prob > chi^2 = 0.1150
Pseudo R^2 = 0.0837

Table 17. Demographic and Insurance Related Predictive Model

Variable	Adjusted OR	95% CI		p-value
Gender	0.52	0.34	0.79	0.002
Age	1.22	1.09	1.37	0.001
Race/Ethnicity	1.25	1.06	1.46	0.006
Household Income	1.02	0.94	1.10	0.701
Covered by private insurance	0.63	0.24	1.66	0.353
Covered by Medicaid/CHIP	0.25	0.09	0.67	0.006
Covered by other government insurance	0.58	0.17	2.00	0.385
Time when no insurance in past year?	1.14	0.52	2.53	0.739

Log likelihood = -321.5738
Number of observations = 866
LR chi^2 (16) = 42.68
Prob > chi^2 = 0.0000
Pseudo R^2 = 0.0622

Table 18: Demographic and Medical Conditions Related Predictive Model

Variable	Adjusted OR	95% CI		p-value
Gender	0.28	0.08	0.97	0.044
Race/Ethnicity	1.41	0.89	2.24	0.149
Household Income	1.17	0.95	1.44	0.136
Told have attention deficit disorder?	1.12	0.05	27.22	0.944
Doctor ever said you were overweight	0.14	0.02	0.89	0.037
Ever told you have a learning disability	0.72	0.10	5.44	0.750
Ever had chickenpox	4.48	1.42	14.06	0.010
Had hay fever in past year	0.98	0.19	5.20	0.984
Had 3 or more ear infections past year	0.32	0.06	1.73	0.187
Problems with coughing in past year	0.07	0.02	0.30	< 0.001
Stuttering/ Stammering in past year	0.61	0.09	4.00	0.603

Log likelihood = -44.448321
Number of observations = 139
LR chi^2 (16) = 39.01
Prob > chi^2 = 0.0001
Pseudo R^2 = 0.3050

CHAPTER V

DISCUSSION AND CONCLUSIONS

The results of this study are reported regardless statistical significance due to the epidemiological importance of the associations.

This study presents an extensive analysis of variables included in NHANES in children six years of age and younger. The purpose was to identify and assess predictors of childhood asthma. A total of 1,262 children were included in the analysis; 158 with asthma and 1,104 without asthma. The overall prevalence of asthma was 13.8 per 100, while it was 5.9 per 100 in 1994, when analyzing NHANES III (Chulada et al., 2003). An alarming 2.3 times increase in prevalence was found between the two NHANES surveys.

The prevalence in females was 9.7 per 100 and 17.4 per 100 for males. Therefore, females were found to be less likely to develop asthma than males. (Hu et al., 1997) found boys to be 1.7 times more likely to have asthma than girls in a cross-sectional study of 705 school children in Chicago by using the ISAAC standardized questionnaire.

Prevalence in females was also lower than that of males in the analysis of NHANES III, reported by (Chulada et al., 2003), in which they reported 5.0 per 100 for females and 6.7 per 100 for males. However, no less alarming 1.9 times increase of the prevalence was found for females and 2.6 times for males between the two NHANES surveys.
In the present study, asthma prevalence increased with age with a statistically significant linear trend. Asthma is a chronic disease with acute exacerbations. Once it is diagnosed, the patient is considered asthmatic until exacerbations or other suggestive symptomatology disappears for more than two years (Harrison, 2005; Koh et al., 2005).

Therefore, prevalence will accumulate in the population under study but this is not necessarily indicative of higher risk by age in children under seven years of age.

Regarding race/ethnicity; the prevalence for Whites was 6.5 per 100, 18.4 per 100 for African Americans, 13.4 per 100 for mixed race, 19.3 per 100 for Mexican Americans and 15.0 per 100 for Hispanics. When analyzing race/ethnicity, Mexican Americans and African Americans had similar differences with Whites. Mixed race was 2.7 times more likely to have asthma than the reference White group. These results agreed with previously published research, including studies conducted using NHANES III (1988-1994), (Chulada et al., 2003; Raisler et al., 1999; Roberts, 2002; Rust, 2001) and HHANES (82-84) (Carter-Pokras & Gergen, 1993). However, the prevalence in a new NHANES category "Other Hispanics" of the present study resulted much higher than the one of African Americans and Whites. This new finding has never been published before

as this new race/ethnicity category was included for the first time in NHANES 1999-2000. The only publication indicating a somewhat similar finding was the one from (Carter-Pokras & Gergen, 1993), analyzing the Hispanic NHANES 1982-84 survey (HHANES). They reported the highest prevalence rate in Puerto Rican Children. A possible explanation for this disparity could be inadequate accessibility to health education and health care. In a recent publication by (Brotanek, Halterman, Auinger, & Weitzman, 2005) using cross-sectional data from a nationally representative sample of children with asthma 2-17 years of age from the 1999 National Health Interview Survey, found, after adjusting for gender, insurance, poverty, and race/ethnicity, that Spanish-speaking families were 69% less likely to have a usual health care provider and continuity of care. The authors concluded that this evidence might contribute to inadequate asthma management and maintenance therapy among these children.

As family income increased, the likelihood to have asthma decreased consistently. This association and their potential linear trend were statistically significant. Similar trends have been reported in the United States and elsewhere (Grant et al., 2000; Nicholas et al., 2005; Wissow et al., 1988). For example, (Benicio, Ferreira, Cardoso, Konno, & Monteiro, 2004) reported low income as a risk factor for asthma after analyzing a population-based, cross-sectional survey of 1,132 children aged 6-59 months, in Sao Paulo, Brazil. Their findings included significant results using four different income levels and a statistically significant linear trend.

In the present study, breastfeeding and other type of nourishments were not statistically significant except using salt at the table. Breastfeeding had a protective effect. Whenever other than whole milk was used first to feed the child, it decreased the likelihood of having asthma. An increased likelihood of 54% of having asthma was found for those that were fed with milk other than 2% fat. Starting solid foods before six or four months into the infant's diet, increased the probability to have asthma. Not drinking whole or regular milk was associated with less likelihood to develop asthma. Currently drinking other than, 2% fat milk was not associated with the probability of having asthma. In contrast, currently drinking other than 1% fat milk increased 3.5 times the probability of having asthma. Often consuming milk products during the previous month was associated with a decreased likelihood of having asthma. Not serving breakfast or lunch at the school was associated with a 27% and 60% less probability to have asthma, respectively. Children that rarely add salt to food at the table had 47% less likelihood to develop the outcome. Not using salt at the table, increased the probability of having asthma by 21%. Breastfeeding has been reported in several studies as a protective factor that is not always statistically significant, (Chulada et al., 2003; Gdalevich et al., 2001; Oddy et al., 1999)), (Dell & To, 2001). Chulada et al. (2003) analyzing NHANES III showed a protective effect that was decreased after adjusting for potential confounders. In contrast, Oddy et al. (1999) in a prospective cohort study of 2,187 children adjusted by gender, gestational age, smoking and day care, and when breastfeeding ended, found a borderline statistical significant association as a risk factor (OR = 1.25, 95%CI 1.02, 1.52). Nevertheless, Gdalevich et al. (2001) in a systematic

review with meta-analysis of prospective studies reported a summary odds ratio of 0.70 (95% CI 0.60, 0.81). Dell and To (2001) using the baseline data from the National Longitudinal Survey of Children and Youth, conducted a population-based cross-sectional study of child health and well-being in Canada, including a weighted sample of 331,100 children between the ages of 12 and 24 months. This study reported a dose-response protective effect up to nine months of breastfeeding.

(Becker, Watson, Ferguson, Dimich-Ward, & Chan-Yeung, 2004), conducted an intervention trial in 545 high-risk infants with immediate family history of asthma. Families were randomized into intervention or control groups. Intervention measures included avoidance of house dust mite, pet allergen, and environmental tobacco smoke. Breast-feeding was encouraged with formula supplementation if necessary, and introduction of solid foods was delayed. Significantly fewer children had asthma in the intervention group compared with in the control group (16.3% vs 23.0%), with 60% less persistent asthma at two years of age. (Morisset et al., 2003), in another intervention study, showed an increased risk of asthma to sesame and peanut and for patients who were allergic to egg, peanut and milk, the skin allergy test increased sensitivity with food challenges.

In the present study, babies were less likely to have asthma if their mothers were at least 23 years of age. This finding was determined to be statistically significant. No literature has reported an association between asthma in newborn babies and mother's

age. Surprisingly, several research studies have included this variable, but failed to report any association. However, a recent prospective cohort study in 184 atopic mothers and their neonates conducted by (van Gool et al., 2004) reported that lower maternal age was associated with higher neonatal IgE level (atopy).

Receiving newborn care at hospital facility was shown to increase significantly the chance to have asthma in the present study. It was also found that receiving newborn care was associated with a 10% lower rate of breastfeeding. In this regard, (W. H. Oddy et al., 2002) in their prospective cohort study found that children who were in medical facilities had more chance to have low birthweight, respiratory problems for being premature with underdeveloped lungs, have more congenital anomalies, and an increased risk for respiratory infections due to intubation and mechanical ventilators. These findings might explain the association found in the present study.

In the present study, normal birthweight decreased the probability to have asthma when compared to low birth weight. As explained above, low birthweight is associated with prematurity, an increased risk for respiratory infections, and lower breastfeeding rates. The association of low birthweight and asthma has also been reported by several authors (Dell & To, 2001; Joseph et al., 2002; W. H. Oddy et al., 2002; Seidman et al., 1991).

In the present study, if the child never attended day care or preschool, the likelihood of having asthma decreased. In contrast, if the child was currently attending day care or Pre School at the time of the survey, he or she was more likely to have asthma. None of these two associations were statistically significant. Early-life exposures to asthma triggers have been associated with childhood asthma (Naspitz et al., 2001). (Salam et al., 2004), investigated whether the timing of such experiences and exposures were associated with the occurrence of asthma in children 0-5 years of age. Asthma was associated with day care attendance within the first 4 months (OR = 2.4; 95% CI, 1.3-4.6). However, day care attendance in early life is inversely associated with asthma at school age. (Celedon et al., 2003) reported that day care attendance in early life was associated with a decreased risk of asthma (OR = 0.3, 95% CI = 0.1-0.7). The hygiene hypothesis may be the basis for this theory. This hypothesis suggests that exposure to other children and exposure to mild infections can create allergen sensitization and tolerance, resulting in fewer asthma symptoms (Liu & Murphy, 2003). However, among children with maternal history of asthma, day care in early life had no protective effect on asthma. If attended the Headstart program, the likelihood to have asthma increased with a borderline statistical significance. Not attending kindergarten was associated with a non-significant increased likelihood of having asthma. To spend up to 4 hours away from home was found associated with a two times greater odds of having asthma, but this association was not statistically significant. These associations have never been reported in the literature. However, the "hygiene hypothesis" could possibly explain these associations, at least partly.

In the present study, not smoking during pregnancy decreased the chances of having asthma and a slight increased chance of having asthma was found if nobody smoked at home. None of these two associations were statistically significant. These lifestyle factors are difficult to study in cross-sectional studies of asthma due to the impossibility to study the time sequence of cause and effect relationship. Smoking habits may change because the patient or her/his relatives have asthma (Bayona, Montealegre, Gomes de Andrade, & Trevino, 2002). In contrast, whenever two or more smokers or cigarette smokers were present at home, as compared to have only one, children had 8.9 times more likelihood of having asthma. The present study was unable to asses a potential temporal relationship, however. Hu et al. (1997) reported that maternal smoking during pregnancy significantly increases the chance to have asthma. This study also found that cord blood IgE concentrations were significantly elevated in infants whose mothers smoked during pregnancy, predisposing infants to subsequent sensitization and allergy. It has also been suggested that intrauterine exposure to smoking could cause changes in pulmonary structure and function. Research conducted by Dell and To (2001) showed that exposure to postnatal smoke was a contributor to childhood asthma (OR = 1.5). These findings were statistically significant and consistent with those published by (J. K. Peat, 1998). (Guilliland et al., 2003) reported lower FEV1/FVC in children with in utero exposure to tobacco and a history of family asthma, suggesting that the "in utero" exposure during critical periods of fetal lung development could permanently alter the lung structure and cause an increase risk of asthma development. However, this study showed that in utero exposure to household smoke

and maternal smoking increased the risk of developing childhood asthma, but environmental exposure to cigarette smoke did not.

In the present study, three populations were compared to children who lived in a mobile home and their risk of having asthma was analyzed. The first group lived in a one family home. The second group lived in a townhouse and the third group resided in an apartment. The results: 49% reduced risk, 22% reduced risk, and 17% increased risk, respectively. None of these associations were statistically significant. The number of years living in the current home was slightly associated with a non-statistically significant decreased likelihood of having asthma. Renting as compared to owning a home was associated with an increased likelihood of presenting asthma. The probability of having asthma was 2.1 times higher if the house was not painted in the last 12 months, as compared to children that lived in a house that was painted in the last 12 months. These results could be partially explained by socio-economic status. Income in NHANES is a categorical variable divided into $ 5000 levels, and residual confounding may be present. No research in the literature reports studying the association of asthma and these variables.

In the present study, there was a 46% reduced likelihood of having asthma whenever the paint was not scraped, when the home was was painted. If the paint was peeling, flaking or chipping inside the house, the chance of having asthma increased. In contrast, if the paint was peeling, flaking or chipping outside the house, the chance of

having asthma decreased 17%. These last three associations were not statistically significant. Paint scrapes, peeling, flaking or chipping could contain allergens from cockroach and dust mites that are known asthma triggers. No literature was found reporting these types of associations.

In the present study, whenever pest control was used during the previous month of taking the survey, the risk of having asthma increased by 18%, although no statistical significance was found. If the entire home was treated with pesticides in the previous 12 months, the chance of presenting asthma was reduced by 44%. ($p > 0.05$). A 2.2 times more likelihood of having asthma was seen if a non-professional treated the home with pesticides; whereas if it was treated by a professional, a 65% decreased probability of having asthma was found with a borderline statistical significance. Pesticides eliminate insects such as cockroaches and some arthropods, including mites. Therefore, an effective elimination of allergen-producing pests could reduce the risk of asthma. No studies have reported these findings.

In the present study, those with a private or public water well had a non-significant and 10% less likelihood of having asthma, as compared to those who used a private or public water company. If no water treatment devices were used at home, a non-significant 44% increased chance of having asthma was found. The contents of chlorine and other water disinfectants are typically lower in private or public wells, as compared to those from private or public companies. Chlorine exposure in swimming pools have

been associated with asthma. For example, (Thickett, McCoach, Gerber, Sadhra, & Burge, 2002) reported an increase risk of asthma among indoor swimming-pool workers during an outbreak investigation. This increase was due to exposure to airborne nitrogen trichloride.

The present study showed that taking treatment for anemia increased non-significantly the likelihood of having asthma. No evidence was found in the literature indicating this association.

In the present study, a non-significant 64% increased chance of having asthma was found among those with attention deficit disorder. (Valdizan, 2004), conducted a study of 170 children with attention deficit disorder. This research found that one third of them presented associated pathologies such as: allergic rhinitis, asthma, allergies, and dermatitis. An article conducted by (Bass et al., 2004) reviewed the evidence regarding the impact of chronic or intermittent hypoxia on cognition-related conditions in childhood during 1966 and 2003. This article included a systemic review of published reports and a critical evaluation of the causality criteria. One of their conclusions was that adverse impacts of chronic or intermittent hypoxia on development, behavior, and academic achievement have been reported in many well-designed and controlled studies in children. The authors of this review noted that hypoxia could be caused by asthma.

In the present study, children with learning disabilities had more likelihood of having asthma, but this association was borderline significant. Children stuttering/stammering in the previous year had an increased chance of having asthma. However, this association was not statistically significant. (Rosenfield et al., 1994) in a case series study, medically evaluated three asthmatic children who otherwise were fluent in their speech. These children developed speech dysfluency following administration of theophylline. Interestingly, language dysfluency came to an end in all three, following discontinuation of the asthma medication. Theophylline was re-instituted in two of the three patients, prompting the return of normal speech patterns in both of them.

In the present study, being overweight was associated with a non-significant increased probability of having asthma. The parallel time trend with an increasing prevalence of asthma has created an important debate about the biological plausibility of the link between both conditions. (Schaub & von Mutius, 2005) conducted a review of selected prospective cohort studies showing that gaining weight can be related to the development of asthma. Effect modification by gender may be present because some studies have shown effects of body mass index on asthma only among females. In the present study, the association of obesity and asthma was stronger among females. However, this effect modification was not very important or statistically significant. In the literature, several hypotheses have been developed to explain this epidemiological association, including alterations in airway mechanics, different immune responses, hormonal influences and genetic factors. However, the mechanisms underlying this

relationship are unclear. Nevertheless, regarding causality; it has been shown that weight reduction among asthmatics has a direct impact in the improvement of lung function. Childhood asthma may be affected by changes in the diet and increments in the body mass related to a sedentary lifestyle. However, as mentioned above, the mechanisms are poorly understood. (Romieu et al., 2004) in a cross-sectional study using NHANES III, reported that after studying 7,904 children and controlling for dietary intake, physical activity, and sociodemographic variables; asthma risk was three times higher for children ages 6-16 years in the highest percentiles of BMI (> 95th percentile) when compared to children in percentiles 25-49 (OR = 3.4; 95% CI, 1.5-8.0). However, an increased risk was noticed in children ages 2-5 years, although the findings were insignificant. (Epstein et al., 2000) in a cross-sectional study based on NHANES III data, studied factors that modified the relationship between asthma and pediatric body mass index. Watching television and maternal body mass index had synergistic interactions with the association of child body mass index and asthma.

In the present study, those that had chickenpox were 84% less likely to have asthma. No literature was found regarding this association.

In the present study, testing for lead poisoning was not associated with asthma and it has not been reported in the literature either.

In the present study, as expected, having had hay fever during the past year increased the likelihood of asthma. Hay fever is a common manifestation of atopy and innumerable studies have shown the association of asthma and this condition. For example, (F. Montealegre et al., 2004), reported similar prevalence of sensitization to common allergens between people with atopy and asthma.

In the present study, whenever the child had three or more ear infections during the previous year, the likelihood of asthma increased considerably. Many studies have demonstrated the strong association between asthma and this medical condition. This information can be found in medical text books, such as Harrison, 2005. Furthermore, ear infections are frequently associated with upper respiratory infections and are known to be important predictors of asthma. For example, (Nguyen et al., 2004) discovered that the middle ear may be part of the united airway in an atopic individual.

In the present study, frequent and severe headaches during the previous year were associated with an important increased likelihood of having asthma, but this association was not statistically significant. Currently, there is no literature that links asthma with headaches. Upper respiratory infections are accompanied by conditions, such as: fever that includes hyperthermia and fever that includes malaise (Harrison, 2005). Ear infections are often associated with headaches; which explains the association of headaches and asthma in the present study.

In the present study, a 5.3 times increased risk of having asthma was found in children who had problems with coughing in the previous year. Children who had dry cough at night in the past year were 2.8 times more likely to present asthma, but this association was of borderline significance. Coughing is part of the typical symptomatology of asthma. Furthermore, coughing is present in most respiratory infections that in turn, are strongly associated with asthma (Harrison, 2005).

In the present study, those who had trouble seeing even with glasses had 5.6 times more probability of having asthma, but this association was of borderline significance due to the small number of children with this condition. No literature was available to show vision impairment as a predictor of asthma. However, it is well-known that intranasal steroid treatment is associated with increased intraocular pressure. As a result, this pressure will produce visual acuity problems that cannot be corrected with glasses. This is caused by an inflammation of the optic nerve, not because of refractory errors (Desnoeck et al., 2001; Haimovici, Gragoudas, Duker, Sjaarda, & Eliott, 1997).

In the present study, receiving the hepatitis A vaccine series was associated with a non-significant 25% less likelihood of having asthma. In contrast, those receiving the hepatitis B vaccine series were 25% more likely to have asthma but this association was not statistically significant. No reports have been published regarding the association of

asthma and the hepatitis A vaccine. (Pershagen, 2000) reported in a literature review that epidemiologic investigations indicate that viral infections may either promote (RSV) or inhibit (hepatitis A, measles) atopy; although there is insufficient data. Pershagen's literature review concluded that not enough evidence exists regarding a direct role of vaccinations for the development of atopic manifestations. However, some infections may offer protection in relation to allergic disorders. Therefore, vaccination could result in an increased risk. (Wickens et al., 2001) examined the risk factors for asthma in children ages 7-9 by using a case-control study in which 233 cases and 241 controls were randomly selected from participants in the Wellington arm of the International Study of Asthma and Allergies in Childhood (ISAAC). After controlling for confounders, there was a strong association that was not statistically significant between having polio vaccination (OR=2.5, 95% CI 0.8-7.4) and asthma. Weaker and non-statistically significant associations were found with the hepatitis B vaccination (OR=0.7, 95% CI 0.4-1.04) or the measles/mumps/rubella vaccination (OR=1.4, 95% CI 0.95-2.4) and asthma. Similar results were found by (DeStefano et al., 2002) in their large cohort study, where the weak associations of asthma for the hepatitis B and *Haemophilus influenzae* type b (Hib) vaccines could be explained by information bias and disparities in health care utilization. Vaccines were not associated with an increase risk of asthma in the retrospective cohort study by (Maher et al., 2004). In contrast, (Benke et al., 2004) in a cross-sectional and retrospective study of young adults, found a strong association (RR = 3.3, 95%CI: 0.5-21.3) of asthma with polio vaccine, and a weak and but a non-statistically significant association with hepatitis B immunization. Subjects fully

immunized were found to be at a higher risk to asthma (RR = 1.5, 95% CI 1.1 – 2.1). (McIntire et al., 2003) found that infection by the hepatitis A virus (HAV) may protect individuals from atopy if they carry a particular variant of the gene that encodes TIM-1 (also known as HAVcr-1) — the cell-surface receptor used by HAV to infect human cells. Exposure to HAV is associated with poor hygiene, large family size and day-care center attendance. All of these factors are also inversely associated with atopy. McIntre et al. also found, in a series of experiments, an interaction between HAV and TIM-1 genotype that may contribute to the basis for the etiology of atopic diseases providing a mechanism to explain the hygiene hypothesis.

In the present study, those that were not covered by health insurance had a non-significant more likelihood of having asthma. Those that had private insurance were less likely to have asthma. On the other hand, those covered by Medicaid/CHIP were 3.7 times more likely to have asthma. A slight but non-significant increased likelihood of having asthma was observed in those that had time with no insurance during the previous year. Children who were less than three years of age since last insurance coverage were 5.8 times more likely to have asthma but this association was not statistically significant due to the very small number of children in this category. These associations could be explained by socioeconomic status; including lower health coverage that has been associated with lack of appropriate management of respiratory diseases and asthma prevention including indoor environmental control. This data was found in a cross-sectional dataset from the Childhood Asthma Management Program

by (Cabana et al., 2004), where 896 parents of asthmatic children were assessed.

In the present study, the variables that were strongly associated to the outcome were added, one by one, to each logistical model. This process was conducted until the maximum pseudo R^2 was achieved. As a result, several predictive models were developed. Several considerations were made during the analysis. Specifically, it was considered adding and dropping a number of variables in the models.

1) The first consideration was the strength of the association (odds ratio) of each single variable with the outcome and its statistical significance ($p<0.05$).
2) The second consideration was the contribution of the predictive ability to the model as measured by an important increase of the pseudo R^2 x 100 (percent of the presence of the outcome that can be predicted by the model.

These two considerations were also influenced by trying the least reduction of sample size while keeping statistical significance of the log likelihood chi square measuring the significance of predicting the presence of the outcome with the variables included in the model as compared to not having such variables in the model.

The first predictive model "General Predictive Model" was developed using all variables in different combinations until a pseudo R^2 predicting 21.5 % of the outcome was achieved with a total of 16 variables. However, the usefulness of such a model for

public health purposes was difficult to determine with such diversity and large number of variables. For public health applicability purposes, four more models were built. All of them included the demographic variables as they were found to be good predictors of the outcome. Also, important associations with the rest of the variables were included (i.e., gender, age, race/ethnicity and household income). The additional models included four different combinations of variables selected by topic: birth characteristics, tobacco related, insurance coverage, and medical conditions.

The birth characteristics model only explained 6.1% of the outcome. It included low birthweight, mother's age when born, and newborn care. The tobacco related model achieved an 8.4% predictability, but the log likelihood chi square was not statistically significant. It included the following: mother smoke while pregnant, total number of smokers in the home, and the total number of cigarettes smoked at home. The insurance coverage model predicted 6.2% of the outcome. This model included the variables: "covered by private insurance", covered by Medicaid/CHIP, covered by other government insurance, and time without insurance in the previous year. The model that included medical conditions achieved the best predictability with 30.5% of the outcome, which was explained by this combination of variables. This model included: attention deficit disorder, being overweight, learning disabilities, chickenpox, fever in the previous year, three or more ear infections in the previous year, problems with coughing in the previous year, and stuttering/stammering in the previous year. No asthma epidemiologic predictive models have been published until now. A study in which predictive models

were used for asthma was conducted by (Sun, Burstin, & Brennan, 2003). The purpose was to identify predictors of selected outcomes for frequent emergency department users. This study was based on a cross-sectional survey, medical chart reviews, and telephone follow-up interviews of 2,333 individuals. Multivariate logistic regression identified predictors of frequent emergency department (ED) visitors from five domains (demographics, health status, health access, health care preference, and severity of acute illness). Associations between high use and selected outcomes were assessed with logistic regression models. Demographics predicting frequent ED use included the following: being a single parent, single or divorced marital status, high school education or less, and income of less than $10,000. Health status predictors included: hospitalization in the preceding three months, high ratings of psychological distress, and asthma. They concluded that frequent ED visits are associated with socioeconomic distress, chronic illness; including asthma and frequent use of other health resources. Another study by (Chey, Jalaludin, Hanson, & Leeder, 1999) investigated the validity of a predictive model for asthma hospital admission in children asking the question: "how accurate is it for predicting admissions?" Chey et al. studied 364 index presentations to the ED of a children's hospital with a diagnosis of asthma. The admission rate for this group of children was about 31%. A parsimonious multiple logistic regression model was developed to predict asthma-related hospital admission, based on asthma severity indicators. The model's predictive ability was assessed using two methods of cross-validation, using the same sample that was used for the predictive model, and using data from a split sample. The logistic regression model had a predictive accuracy of 90%

(95% confidence interval 85-95%). The sensitivity and specificity were 86% and 88%, respectively. Cross-validation models confirmed that the predictive ability of the model was stable. (Mrazek et al., 1999) conducted a study that predicts the early-onset of asthma in genetically at-risk children. This study prospectively examined children who were considered at a genetically increased risk for the development of asthma. The respective contributions of 11 potential risk factors, both environmental and biological, were assessed in order to determine their relative roles in affecting the early onset of asthma. Frequent illness, IgE levels at age 6 months, parenting difficulties, and early eczema were significantly associated with the onset of asthma. Only frequent illness, elevated serum IgE levels, and parenting difficulties entered a predictive model where they were independently related to the development of asthma. In order to assess the simultaneous effects of selected risk factors on the occurrence of disease (Mrazek et al., 1999) used multiple logistic regression the log of the odds of getting the disease.

Limitations

Some of the limitations of this study are inherent to the study design and the study population. This research was conducted on a pre-existing dataset that does not include all potential confounders of the associations under study. This study was a cross-sectional survey. However, some questions were retrospectively recorded; such as breastfeeding history and mother's smoking habit during pregnancy. For the rest of the variables, the most important limitation was how to elucidate the temporal relationship between

exposure and outcome. Therefore, it is possible to say that for some study participants, the correct sequence of exposure to outcome occurred. However, for some others, the outcome may have preceded the exposure. In the present study, infants with early asthma had newborn care more often than those without asthma. Therefore, the outcome in some of these children may have preceded the exposure. Recall bias may be a problem for variables recorded in the past. However, the present study only included individuals under the age of six. This short period reduces the potential recall bias. Furthermore, the age of the children under study ranged from 0 to 6 years of age.

Another important limitation was that the present study is a secondary analysis of a data set. Some variables that are known predictors of asthma could not be analyzed due to the lack of available data. For example, there was no information on mother's weight, family history of asthma, and asthma status during pregnancy. These questions had no responses listed for the infants who were included in the NHANES data set. Family history is a known predictor of asthma status in previous studies (Celedon et al., 2003; Wright et al., 1999).

There is a possibility that many of the covariates in the present study were found to be significantly associated with asthma and are interrelated with variables that were not available. For example, many factors such as maternal smoking, low birth weight, and race may be directly or indirectly associated with socioeconomic status (Lindbaek et al., 2003).

Other factors that influence the development of asthma in children that were not analyzed in this study include environmental factors have been shown to be important predictors for asthma. Other variables that were unavailable included education and overall maternal health. An increase in maternal age and education is associated with lower asthma rates (Chulada et al., 2003). These are also indicators of socioeconomic status. Other limitations include potential responder's bias and survival bias that may be present in all or most variables from this study.

Conclusions

The present study explored a number of potential risk and protective factors by analyzing data from NHANES 1999-2000 in children below seven years of age.

The results include the assessment of an alarming increase in the prevalence of childhood asthma from the last NHANES survey in 1996, and the identification and assessment of risk factors that may identify modifiable risk factors and high-risk groups in which preventive measures should be emphasized. Therefore, this research will hopefully contribute to the current knowledge of the epidemiology of asthma and can be used as a base for control interventions in children, the most vulnerable population affected by this disease.

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