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Introduction

Asthma is a chronic respiratory condition characterized by recurrent attacks of reversible airway obstruction resulting in breathlessness and wheezing that varies in severity and frequency among individuals (World Health Organization, 2011; American Lung Association, 2012). The condition is increasing in prevalence across the United States and is considered one of the most common chronic disorders among children (American Lung Association, 2012; Kaslovsky, Sondike, & Cummings, 2010; WHO, 2011) with 10 % of children younger than eighteen years of age having a current diagnosis of asthma (United States Department of Health and Human Services, 2012). The Centers for Disease Control and Prevention (CDC) reports that one in 12 (~8%) people had asthma in 2009 (2011a), a value that has been increasing by about 1.2 % annually since 2001 (Akinbami, Moorman, & Liu, 2011). While asthma is can be a serious chronic condition to live with, death related to asthma is rare in children; however, it "is the third leading cause of hospitalization among children younger than the age of 15" (American Lung Association, 2012).

Asthma is a public health problem affecting people of all ages, races, genders, and socioeconomic statuses. However, it does seem to occur at disproportionately higher rates among some races and socioeconomic levels (American Lung Association, 2010). Among children, boys are affected more than girls (15.4 % to 12.9 % respectively) while women are more likely to be affected in the adult population (USDHS, 2012; CDC, 2011a). There appears to be a higher prevalence among non-Hispanic African Americans younger than 18 than any other race with 16.4 % of those having current asthma symptoms (USDHS, 2012). In fact, "the greatest rise in asthma rates was among black children (almost a 50 % increase) from 2001 to 2009" (CDC,

2011a). Additionally, children from a lower socioeconomic bracket tend to have higher prevalence of asthma. For example, children in poor families are more likely to have had an asthma diagnosis in the past (17.6 %) and currently have asthma symptoms (12.8 %) (USDHS, 2012).

There is increasing prevalence with asthma symptoms among persons that are overweight or obese, yet the pathology is unclear according to the Global Initiative for Asthma (GINA, 2012). In fact, a report from GINA states "asthma is more frequently observed in obese subjects and is more difficult to control" (p. 5).

Obesity is a condition that has become more prevalent in the United States with more than one-third of adults (CDC, 2011a) and 17% of children and adolescents being obese. In children, obesity is defined as having BMI that is greater than the ninety-fifth (95^{th}) percentile for age (Kaslovsky, Sondike, & Cummings, 2010). It is associated with the risk of developing many other acute and/or chronic conditions such as cardiovascular disease, diabetes, and cancer (ten Hacken, 2009, p. 663). Obesity has also been associated with gastroesophageal reflux disease (GERD), depression, and respiratory conditions such as sleep apnea (Lugogo, Kraft, & Dixon, 2009, p. 730).

Obesity often "precedes the development of asthma" and literature reviews suggest a higher prevalence of asthma in the obese population can be found (Marugan & Sharma, 2008; Sutherland, 2008). Weight can have an effect on the well being of those diagnosed with asthma, as well as a possible influence on the diagnosis of asthma. Burgess et al. (2007) suggests childhood obesity increases the risk of the development of asthma or obtaining a diagnosis of asthma in adulthood. Ho et al. (2011) found that the risk of being diagnosed with asthma increased with the presence of obesity among adolescent girls. Asthma in these individuals may

not be caused by airway inflammation, but by changes in lung mechanics (Juel, Ali, Nilas, & Ulrik, 2012). Scholtens et al. (2009) found that children with a high body mass index (BMI) were more likely to exhibit asthma-like symptoms. But, they also concluded that children with a high BMI at an early age but returned to a normal BMI by age eight did not experience asthma type symptoms. And Aaron et al. (2008) found that nearly one-third of the patients carrying a physician's diagnosis of asthma had no evidence of asthma. The misdiagnosis of asthma may occur more often in obese non-asthmatic children who experience obesity related respiratory symptoms (Lang, Feng, & Lima, 2009).

The purpose of this paper is to provide a review of the current literature to determine if obese children are at an increased risk of obtaining a diagnosis of asthma when compared to normal weight children.

Definition and Diagnosis

Asthma can be defined as a chronic inflammatory disorder of the airways associated with reversible airway obstruction caused by airway hyperresponsiveness leading to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing (GINA, 2012). These episodes are commonly experienced at night or early in the morning. In order to diagnose asthma in a pediatric patient, several key indicators must be present including a history of a cough, wheeze, difficulty breathing, or chest tightness (Guilbert, Moss, & Lemanske, 2009). These key indicator symptoms may occur or worsen in the presence of exercise, inhaled allergens or irritants, changes in weather, stress, etc. Several, but not all, key indicators must be present to increase the probability of childhood asthma and would warrant further testing.

A chest radiograph is often obtained, and in the presence of mild asthma, will most likely be normal (Guilbert et al., 2009). Lung function tests can confirm or exclude asthma as a

diagnosis. Examples of these tests may include spirometry measurements, lung volume measurements, and bronchodilator response tests (Stewart, 2008). Diagnosis of asthma can be made when there is documented improvement (by 12 percent) in the forced expiratory volume in the first second (FEV1) after inhalation of albuterol (Stewart, 2008; Guilbert et al., 2009).

Theoretical Framework

The theoretical framework utilized in this study is the Neuman's systems model due to its wholistic, wellness orientation and it is based on stress and the body's reaction to that stress. According to Neuman (2011), stressors are the environmental forces that impact a client's health. In the Neuman Systems Model, the person is viewed as a client system "represented by a series of concentric rings surrounding" the central core (Neuman, 2011, p. 16). The central core contains the five client system variables – physiological, psychological, sociocultural, developmental, and spiritual – and their interactions. The concentric circles – known as the flexible line of defense, normal line of defense, and lines of resistance – serve as protective mechanisms to the central core (Neuman, 2011).

Using Neuman's model, obesity can be considered a stressor to the body. In response to that stressor, a restrictive pattern of breathing develops creating asthma-like symptoms. Upon loss of weight, studies have shown improvement in lung function (Aaron, Fergusson, et al., 2004) and asthma symptoms (Stenius-Aarniala et al., 2000).

Methods

A series of systematic searches were carried out utilizing the databases MedLine, PubMed, CINAHL, MDConsult, Sage Premier, and Google Scholar via the Southern Adventist University library as well as the National Institutes of Health. The general search terms included "asthma and obesity", then "asthma" and "obesity" separately. The search was repeated with

adding the following search terms: children, adolescents, body mass index, overweight, weight loss, pathogenesis, and overdiagnosis. Additional systematic reviews pertinent to providing information were utilized. Manual assessment of reference lists accompanying those utilized systematic reviews aided in the supplementation of the citation pool provided the information was pertinent to the above search terms.

Pathogenesis

Asthma is defined by the U.S. Department of Health and Human Services (USDHS, 2011) as "a chronic inflammatory disorder of the airways characterized by episodes of reversible breathing problems due to airway narrowing and obstruction." Obesity is defined as having a body mass index (BMI) of 30 or greater and overweight is defined as having a BMI of 25 to 29.9 (CDC, 2010b). For children, obesity is defined as having BMI that is greater than the ninety-fifth (95^{th}) percentile for age (Kaslovsky, Sondike, & Cummings, 2010). Over the past few decades, prevalence of asthma and obesity has increased suggesting a possible relationship in the two (Murugan & Sharma, 2008).

Multiple theories exist to the pathophysiology of coexisting asthma and obesity. Some explain that asthma develops first while a majority of the literature suggests obesity develops first. Figueroa-Munoz, Chinn, and Rona (2001) suggest obesity as a possible etiological factor to the development of asthma, but that "asthma may be a risk factor for obesity as many parents believe that a child with asthma should not exercise" (p. 136). While there are good explanations and reasoning for both, this paper focuses on how obesity may affect a diagnosis (or misdiagnosis) of asthma possibly leading to over-diagnosis, specifically in children.

Lung Function

Obesity affects lung function by a variety of mechanisms but primarily due to the excessive mass on or around the chest wall. It leads to "alterations in respiratory mechanics, airway resistance, pattern of breathing, respiratory drive, and gas exchange" (Murugan & Sharma, 2008). Obesity causes a decrease in forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), tidal volume (TV) and occasionally residual volume (RV), which usually remains unchanged (Zammit et al., 2010; Boulet, 2012; Peroni, Pietrobelli, & Boner, 2010). Reduced expiratory reserve volume (ERV) and functional residual capacity (FRC) are the most notable changes seen with obesity (Boulet, 2012). Additionally, obesity is associated with a restricted pattern of breathing evidenced by decreased lung volumes on spirometry (Zammit et al., 2010) and an elevated FEV_1/FVC ratio to forced vital capacity (West, Burton, & Bell, 2011).

Canoz et al. found "no correlation…between BMI and asthma" (p. E375); however, obese asthmatic patients demonstrated higher waist circumference, hip circumference, and waist-hip ratio ($P < 0.01$) than an obese control group ($P < 0.001$). "Excess weight on the anterior chest wall due to obesity lowers chest wall compliance and respiratory muscle endurance with increase in work of breathing and airway resistance" (Zammit et al., p. 336). Abdominal and intra-abdominal adipose tissue impedes diaphragmatic movement thus diminishing lung expansion during inspiration (Boulet, 2012) resulting in decreased lung volumes.

Ho et al. (2011) found that the risk of being diagnosed with asthma increased with the presence of obesity. Girls with higher BMIs were at greater risk of having a physician diagnosis of asthma one year later (Ho et al.). Ho et al. did not find similar results in boys in their study; however, Oddy et al. (2004) found a correlation between BMI and asthma among breastfed children "were significant only in boys ($r=0.111$; $P<0.01$)" (p. 1533) although the relationship is weak (as shown). Lang et al. (2012) found obese males to experience airflow obstruction and

obese females to exhibit improved lung function while West, Burton, & Bell (2011) found a restrictive pulmonary function results in obese females and not males. And Beuther and Sutherland (2007) found higher asthma prevalence among overweight and obese subjects with no differences among genders. Therefore, gender bias cannot readily be determined with such differing results and more research in this area is suggested.

Genetic Influences

When discussing pathologies and etiologies of coexisting asthma and obesity, genetic involvement should be considered (if any). Twin studies may provide the strongest evidence of any genetic influences in regards to asthma and obesity. Hallstrand et al. (2005) studied monozygotic and dizygotic twins. Monozygotic, or identical twins, have identical genotypes, and dizygotic , or fraternal twins, share half of their genes (Hallstrand et al.). Hallstrand et al. report a genetic association between asthma and obesity but that the magnitude of that association is modest at best. Thomsen et al. (2007) found a "significant relationship between obesity and asthma that was most pronounced in" female twins ($OR=1.04$, $P\leq0.001$). Hallstrand et al. also found a significant prevalence in female twins ($P<0.001$) while in men, the association was not as significant ($P=0.07$).

Barnes (2011) reports several genes have been identified that are associated with asthma and, more specifically, the gene *ORMDL3* has been identified for childhood induced asthma after reviewing the genome-wide association study (GWAS). Additionally, several other obesity related genes were identified by Su et al. (2012). In a study to analyze genetic factors between obesity and asthma in children, Melen et al. (2010) were unable to find "convincing evidence" that the obesity and asthma traits share genes (p. 6). It is possible that certain genes (such as those associated with asthma) could be activated when presented in the circumstance of a chronic

condition (i.e. obesity). Su et al. proposed that genetic modification occurs when children live in a damp environment. Additionally, Su et al. found interaction between three genes: an inflammatory gene (*IL4Ra*), an obesity gene (*INSIG2*), and an antioxidative gene (*GSTP1*). So, given these findings, it is possible to suggest that the chronic inflammatory state presented by a state of obesity (discussed below) may alter or "turn on" asthma genes.

Systemic Inflammation

Obesity is thought to be a "pro-inflammatory" state in which various inflammatory mediators are chronically increased (Boulet, 2012). The various cytokines and mediators include tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), C-reactive protein (CRP), and leptin and have been associated with both asthmatic and obese individuals. It has been suggested that the chronic inflammatory state of obesity may contribute to the development of asthma. Ford (2003) suggests adults with asthma are more likely to have elevated levels of CRP and that adults with asthma are more likely to be obese. Canoz, Erdenen, Uzum, Muderrisoglu, and Aydin (2008) studied 54 obese asthmatic women and found a correlation between asthma and elevated levels of IL-6, TNF-α, and leptin. These inflammatory mediators contribute to the production of immunoglobulin E (IgE), subepithelial fibrosis, and airway remodeling: the primary pathogenesis of asthma. Thus, obesity aids in increasing remodeling in the airways due to the constant inflammation (Canoz et al., 2008).

Scholtens et al. (2009) found an association between elevated BMI at age 6 to 7 years of age and a resultant finding of bronchial hyperresponsiveness at age eight. These same children with an elevated BMI were not found to have allergic sensitizations or allergy induced asthma symptoms suggesting chronic inflammation as a result of obesity is the cause of the bronchial hyperresponsiveness.

Effects of Weight Loss

Weight loss in obese individuals improves "lung function, oxygenation, respiratory muscle function, exercise tolerance, gas exchange, sleep quality, and daytime sleepiness" (Murugan & Sharma, 2008, p. 237-238). Stenius-Aarniala et al. (2000) and Aaron et al. (2004) studied a weight-loss program and its effect on asthma. Each found that weight loss in obese individuals improves lung function, health status and asthma symptoms. However, Aaron et al. found that bronchial reactivity did not improve with weight loss indicating the improvement in symptoms was a result of the reduction in body mass. In a systematic review, Juel et al. reports that regardless of whether the weight loss is obtained by diet and exercise or bariatric surgery, the weight loss improves symptoms and control of asthma (2012). Therefore, it is plausible that the improvement in asthma symptoms were caused by a reduction of mass loading on the respiratory system. However, levels of the anti-inflammatory hormone adiponectin have been found to increase with weight loss inhibiting the production of the abovementioned inflammatory mediators (Boulet, 2012); thus possibly decreasing asthmatic symptoms via an anti-inflammatory process. Therefore, weight reduction is highly encouraged as "even a modest weight loss is associated with significant improvement of asthma and a reduced need for medication" (Boulet, p. 15).

Over-diagnosis

Several studies imply a potential over-diagnosis of asthma in obese patients (West & Burton, 2009). It has been suggested that many people receive a diagnosis of asthma with no diagnostic testing (Stanbrook & Kaplan, 2008), rather by history and physical alone resulting in not only an over-diagnosis but a misdiagnosis of asthma and a resultant mistreatment for that particular patient such as inappropriate use of "short-acting bronchodilators or corticosteroids in

persons who are short of breath for obesity-related dyspnea that does not represent reversible airway obstruction" (Schwartzstein & Gold, 2009, p. 1319). Aaron et al. (2008) found that nearly one-third of adult patients with a diagnosis of asthma had no physical evidence of asthma. "The use of symptoms alone is not an effective diagnostic method for asthma in obesity" (West & Burton, p. 30). Pulmonary function testing should be utilized for a correct diagnosis of asthma, especially in obese individuals.

Lang, Feng, & Lima (2009) studied how and if obesity-related respiratory symptoms lead to the misdiagnosis of asthma in obese children. These authors did not find evidence of misdiagnosis or over-diagnosis of asthma in obese children; instead, they found evidence confirming the association between obesity and asthma.

Discussion

To date, there is mounting evidence supporting an association between asthma and obesity. Children are the most affected by asthma and with childhood obesity rates and asthma rates climbing across the nation and worldwide, it is easy to assume a causal factor or an inappropriate diagnosis. To begin this study, the question was asked: are obese children are at an increased risk of obtaining a diagnosis of asthma when compared to normal weight children? While studies report misdiagnosis of asthma in obese adults, children are a different story. The literature does not suggest misdiagnosis of asthma in children; which is possibly due to primary care providers being diligent and performing the pulmonary function testing necessary.

Obesity may cause asthma by three potential mechanisms: shear mass (especially abdominal), inflammation, and genetic interactions; although, the literature remains unclear or uncertain as to the physiology behind the relationship. More research is definitely required in this area as there is much to learn about how genetics affects asthma and obesity together.

Additionally, there seems to be a gender bias with many studies reporting the greater association of asthma and obesity among females.

Limitations of this study include a possibility that not all articles pertinent to the subject were identified. Retrospectively, more articles were needed regarding mis- or over-diagnosis of children. Additionally, more studies discussing genetics may have made the subject more clear and provided a better understanding of how gene interaction occurs. However, these articles were not identified via the databases utilized.

In conclusion, this paper provides a background to asthma and obesity, explored obesity as a possible causal factor of asthma, and discussed how weight loss affects asthma. Additionally, this paper discussed over-diagnosis of asthma among the obese persons and children. Given that asthma is seen more often in the overweight and obese population, a change is needed in the approach to treating asthmatics that are overweight or obese. It is important to begin a weight reduction program as research shows that decreased weight actually improves symptoms, possibly even reducing medication usage. For those patients that are obese without a diagnosis of asthma, beginning a weight reduction program is important to prevent a future diagnosis of any chronic condition. Most chronic conditions are preventable and are easier to prevent than to treat or cure.

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