CHAPTER ONE

INTRODUCTION

1.0 Background Information

Allergic diseases such as asthma, rhinitis and atopic eczema are among the most prevalent chronic conditions in paediatric populations in the Western industrialized world (1). Moreover, asthma, which tends to be the most common of these diseases, is also a significant cause of morbidity and mortality (1, 2). In Africa, the health priorities have been on infectious diseases such as malaria, human immunodeficiency virus (HIV) and tuberculosis, whilst allergic diseases continue to receive little attention (3). Reports of some early studies indicate that until the late 1970s, childhood asthma was considered rare in Africa (4, 5). This point is further reinforced by the fact that most languages did not even have words in the local dialect for asthma or wheeze (5, 6). Moreover, some early studies suggested that the onset of asthma was in the second decade of life (7). Findings from recent studies however indicate that childhood allergies, which were considered as relatively uncommon, are an emerging public health problem for the African continent (3, 5).

The International Study of Asthma and Allergies in Childhood (ISAAC), which employs a standardized methodology to describe the prevalence and severity of childhood allergies, has shown an increase in the prevalence of these conditions in African countries. Results of the ISAAC Phase III study which enrolled 22 centres in sixteen African countries indicate that the prevalence of symptoms of asthma among children aged 13-14 years in centres such as Cape Town (20.3%), Polokwane (18.0%), Reunion Island (21.5%), Brazzaville (19.9%), Nairobi (18.0%), urban Ivory Coast (19.3%) and Conakry (18.6%) is similar to that of Western Europe (3). Moreover, the prevalence of rhinoconjuctivitis was above 20 % in all but four centres whilst the prevalence of atopic eczema ranged from 4.7% in Khartoum to 23% in

Casablanca (3). Cross-sectional studies which have used exercise-induced bronchospasm (EIB) as a marker for asthma have also shown that childhood asthma is becoming common in Africa (5, 8).

But perhaps the best evidence of the increased prevalence has come from studies which have compared the time trend in the prevalence of allergies. In a comparison of the results of the ISAAC Phases I and III for Cape Town (South Africa), Zar et al. (9) showed that a significant increase in the prevalence of symptoms of asthma (16.1% vs. 20.3%), allergic rhinitis (30.4% vs. 38.5%) and atopic eczema (11.8% vs.19.4%) had occurred over the seven year period among children (aged 13-14 years). In another such study, Addo-Yobo et al. (5) found that the prevalence of EIB and atopic sensitization in children (aged 9-16 years) had nearly doubled over a ten year period from 3.1% to 5.2% and 7.6% to 13.6% respectively in Kumasi, the second largest city in Ghana. The most significant feature of these studies is that the observed prevalence of allergies was considerably higher than what had been reported by previous studies (10).

However, the high burden of infectious agents in Africa means that the results of symptoms of allergies must be treated with caution (3). Symptoms such as wheezing may occur as a result of infections rather than asthma whilst itchy runny nose or itchy rash, which is a typical symptom of allergic rhinitis, might be the results of infection with virus, bacteria or fungi (11). Furthermore, the protocols followed by many studies which have used EIB as a marker for asthma were established mainly for populations in the Western industrialized countries. It might therefore be important to determine if the reference values of the populations they were developed for are applicable to populations in Africa (11).

1.1.0 Rural-urban Gradient in the Prevalence of Allergies

As in other parts of the world, studies have shown a variation in the prevalence of allergies between countries and between different geographical areas within countries in Africa. A rural-urban gradient has been observed in almost all studies on allergies (3, 6, 8, 10). The prevalence of current wheeze, which was used for assessing the prevalence of asthma symptoms in the ISAAC study, was found to be higher in the more urbanized centres of all countries in which more than one centre had participated. Examples of such variations were observed in Morocco (Casablanca: 16% vs. Marrakech: 4.4%), Tunisia (Grand Tunis: 15.4% vs. Sousse: 11.9%), Kenya (Nairobi: 18.0% vs. Eldoret: 13.8%) and South Africa (Cape Town: 20.3% vs. Polokwane: 18.0%). Moreover, the highest prevalence of asthma and rhinoconjuctivitis occurred in Cape Town (20.3% vs. 20.7%) and Reunion Island (21.5% vs. 27.3%) where the standard of living is higher compared to the other African centres (3).

Individual cross-sectional studies have also shown that a higher prevalence of exercise-induced bronchospasm and atopic sensitization exists among children living in urban than rural areas in Ghana, Kenya and South Africa (5, 8, 12). This raises the question as to whether the rural-urban gradient in the prevalence of allergies is due to environmental changes resulting from urban residence or if urban populations are just becoming prone to allergies. Whilst the reasons for this observed gradient still remain to be fully explained, findings of more recent studies indicate that the rural-urban gradient is becoming narrower (10).

Even though literature on the effect of migration within non-industrialized countries is lacking, findings from several international migrant studies indicate that migration from developing countries to industrialized countries is associated with an increased prevalence of allergies. Moreover, a comparison of migrants to indigenous populations (in their countries of origin) has shown that a higher prevalence of allergies occur in the former group (11). In the face of the rapid drift in the rural-urban migration on the African continent and the fact that children under the age of 15 years, who are worst affected, constitute about 50 percent of the population in developing countries (10), it is important to understand the mechanisms and factors which determine this rural-urban gradient in the prevalence of childhood allergies.

1.2 Risk Factors for Allergies

The genetic determinants of allergies cannot explain the trends in prevalence over time (13). Rather, environmental factors such as the adoption of a westernized lifestyle have been implicated in the differential prevalence of allergies between rural and urban areas (10). Hence, most studies which have examined the risk factors for allergies have concentrated on environmental factors which are associated with a more industrialized and urban living. The most important risk factors which have been identified to date include exposure to indoor allergens, childhood infections and pollution (7, 8, 11, 14).

1.2.1 Exposure to Allergens

Allergens refer to substances which the immune system recognizes as foreign and dangerous in some people but cause no response in others (15). Most studies in Africa have identified house dust mite and cockroach allergens as the most common indoor allergens (6) and sensitization to these allergens is normally prevalent among children with asthma (7). Exposure to allergens is a major risk factor for the development of allergy (11). The genetic predisposition of some individuals to develop immunoglobulin (Ig) E antibodies in response to allergen exposure is known as atopy (16). Atopy, which is assessed by skin prick testing or total allergen specific IgE in the serum (16) normally precedes the development of allergic diseases (17) and is considered an important risk factor for allergy (18). Atopic individuals usually exhibit clinical syndromes such as atopic eczema, food allergy, allergic rhinitis and asthma (19). However, whereas some of these syndromes such as peanut allergy are predominantly atopic, others like asthma may or may not be atopic (16). Some recent systematic reviews (20, 21, 22, 23) have observed that the role of atopy in the development of asthma, rhinitis and eczema may have been overemphasized in most studies. Using available evidence at the time, these reviews suggested that atopic mechanisms may account for just about 50% of all asthma, rhinitis and eczema cases whilst the remaining cases could be attributed to non-atopic mechanisms. In Africa, findings from previous studies suggested that non-atopic mechanisms may account for asthma. However, a study in Ghana identified atopy as a major risk factor for childhood asthma (7). Moreover, findings from the ISAAC Phase II study indicate that the link between atopy and childhood allergies such asthma and eczema tend to increase with the economic development of countries (24, 25). This notwithstanding, the role of atopy in the development of childhood allergies remains important but the factors which influence its development are not fully understood (18).

1.2.2 Childhood Infections

The relationship between childhood infections and allergies has remained contentious. The hygiene hypothesis proposed the concept that the declining microbial exposure in industrialized countries might account for the increased prevalence of childhood allergies (26). However, studies have shown that the highest prevalence of allergic asthma cases occur in inner-city residences (7, 18). In Africa, the low prevalence of childhood allergies reported by earlier studies was attributed to infection with intestinal helminths such as *Ascaris lumbricoides* (10) whilst treatment of intestinal helminths was associated with an increased risk of atopy in Venezuela (27). The proposed mechanism was that the increased levels of IgE antibodies during helminth infections competed with allergen-specific IgE in occupying mast cell Fc receptor sites and hence resulted in the blocking of hypersensitive reactions (10, 28). Infection with malarial parasites is also thought to be associated with a modulation of the immune system of the infected host and a study in Gabon suggested *Plasmodium* parasites could have an additional negative effect on skin-test reactivity in helminth-infected children (28). However, more recent studies have suggested that the effect of helminth infections may vary depending on the intensity of infection. In most cases, heavy chronic infections are associated with a decreased risk of allergic sensitization whilst light acute infections have been implicated with an increased risk of developing allergic diseases (11, 29).

1.2.3 Pollution

Indoor air pollution such as passive smoking and domestic fuel has also been associated with respiratory allergies (11). However, even though studies on the effect of passive smoking in Africa have yielded inconclusive results, a study in Ethiopia by Venn et al. (30) found a significant association between the use of modern fuels (such as kerosene and gas) and atopic sensitization [OR: 1.78. 95% CI: 1.06-2.97]. They also found a positive association between the use of modern fuels and rhinitis [OR: 2.06, 95% CI: 1.46-2.91], wheeze [OR: 1.07, 95% CI: 2.26] and eczema [OR: 2.82, 95% CI: 1.61-4.96].

However, despite all the environmental risk factors which have been studied to date, the increased prevalence of childhood allergies and the factors which influence the development of atopy still remain to be fully explained (18, 31, 32, 33) in Africa or elsewhere in the world.

1.3 Diet, Obesity and Allergies

Studies which have investigated the role of diet on the development of allergies in developed countries have speculated that changes in dietary patterns may have contributed to the increased prevalence of allergic diseases (34). The increased intake of omega-6 polyunsaturated fatty acids (PUFAs) such as in margarine and vegetable oil derivatives as well as a decreased intake of oily fish (rich in omega-3 PUFAs) and antioxidants (fruits and vegetables) have been implicated in the increased prevalence of allergic diseases (13). In a recent study in South Africa, Hooper et al. (35) found a positive association between the consumption of a more urban diet and atopy in children. The role of breast-feeding has however remained controversial with various studies producing contradictory results. Moreover, the effect of probiotics in producing an anti-atopic effect has also been explored (34).

The health and nutritional status of populations around the world, more especially, populations in developing countries have been influenced by the rapid changes in diet and lifestyle which have occurred along with industrialization, urbanization, economic development and market globalization (36). Consistent with findings in developed countries, the prevalence of obesity is increasing in developing countries. Within these settings however, obesity has usually been associated with urban residence, higher levels of education and higher socio-economic status (37, 38). The burden however shifts towards the poor as economic development increases (37).

The body mass index (BMI) is the most widely used method for measuring obesity in both children and adults. Studies have shown that adiposity varies with age, sex and ethnicity and the BMI is useful for measuring adiposity, regardless of the fact that it may be imprecise (37). In adults, obesity is classified as BMI > 30. In children however, the varying weight with height which accompanies growth complicates the definition of obesity. Hence, different methods (such as the Centers for Disease Control and Prevention (CDC) 2000 growth charts and the Cole reference) have been employed in standardizing BMI-for-age and sex (37). However, these methods do not usually give the same results (39).

In Ghana, findings from the 2003 World Health Survey (40) indicate that the prevalence of obesity in adults was 5.5% but varied between males (2.8%) and females (7.9%) as well as across the ten administrative regions (Table 1.1). This compares with the WHO age-standardized estimates (41) for other African countries (Table 1.2). Though data on the prevalence of obesity is readily available for adults and children under 5 years of age, there is scanty information on children aged 5 years and over in African countries. However, studies in different parts of Africa which have measured anthropometric indices in school children have reported an increased prevalence of obesity in this population as well (5, 42). In Africa, the increased prevalence of obesity has resulted in the adding on of chronic diseases such as cardiovascular disease, cancer and Type II diabetes (43) to the infectious disease burden. In paediatric populations however, obesity is normally associated with high blood pressure and higher levels of serum lipids (39).

Table 1.1: Prevalence of obesity in the administrative regions in Ghana

Region	Prevalence of obesity (%)
Western	5.1
Central	5.0
Greater Accra	16.1
Volta	3.4
Eastern	7.0
Ashanti	5.4
Brong-Ahafo	3.4
Northern	1.5
Upper East	-
Upper West	2.2

Source: (40)

Table 1.2: Prevalence of age-standardized estimates for obesity in some African countries

Country	Prevalence of obesity (%)	
	Females	Males
Togo	5.3	0.9
Burkina Faso	1.1	0.4
Cote d'Ivoire	5.4	0.2
Nigeria	6.0	2.0
Senegal	9.2	1.3
Sierra Leone	12.7	2.4
Egypt	45.5	22.0
Sudan	5.1	1.2
Cameroun	10.8	7.5
Gabon	15.5	2.3
South Africa	35.2	6.7
Botswana	14.6	5.4

Source: (41)

The role of obesity on the development of allergic diseases has also been the subject of much debate in recent times. Following the concurrent increase in the prevalence of asthma and obesity in developed countries, some investigators began to speculate that the two epidemics might be linked and indeed, most studies which have investigated the obesity-asthma association have emphasized that the prevalence of asthma is increased in obese individuals (44, 45, 46). However, even though the obesity-asthma association has been observed in both adults' and paediatric populations using cross-sectional, aetiological and even interventional studies (44), the relationship between obesity and atopy, which is a major risk factor for allergies, is not clearly established (33). In view of the fact that atopy is highly prevalent in asthmatic children, determining the role of obesity on the atopic status of individuals might help explain the observed association between obesity and asthma (47).

In Africa, the findings of some early studies in Kenya (48) and Zimbabwe indicated that children living in rural areas, where the prevalence of atopy is usually low, were shorter and lighter than their urban counterparts (12). A cross-sectional survey in Ghana, which assessed the time trend in the prevalence of EIB and atopy over a ten year period among children in urban rich, urban poor and rural schools also reported that the children in the urban rich schools were 'heaviest and tallest' whilst those in the rural schools were 'lightest and shortest' (5). What remains unclear though is whether there is an association between increasing body weight and atopic sensitization among children living in rural and urban areas.

1.4.0 LITERATURE REVIEW

1.4.1 Association between Obesity and Atopy in Cross-Sectional Studies

The relationship between increasing body weight and atopy has been investigated in cross-sectional studies in Taiwan, Australia and the US. However, the results of these studies have been inconsistent. In a study of 1,459 Taiwanese teenagers (aged 13-15 years) attending junior high schools in Taipei city as well as some towns and rural areas, Huang et al. (47) found high body mass index (BMI) to be an independent risk factor for atopic sensitization in girls. They reported that girls in the highest BMI quintile compared to those in the middle quintiles had a higher risk of being atopic [OR: 1.77, 95% CI: 1.15-2.73]. High BMI was also found to be associated with a greater number of positive skin test reactivity in girls. A higher prevalence of atopy was however observed in males than females (42% vs. 27%).

Moreover, Schachter et al. (49) observed a significant association between BMI and atopy among girls [χ^2 =7.9, p=0.005] when they investigated the relationship between obesity and atopy using pooled data from seven epidemiological studies of 5,993 Caucasian Australian children (aged 7-12 years). In the US National Health and Nutrition Examination Study (NHANES) III however, von Mutius et al. (50) reported that atopy was only significantly associated with increasing BMI before adjusting for confounding among 7,505 children (aged

4-17 years). The association disappeared after controlling for confounding factors such as age, sex, ethnicity, household size, study area and passive smoke exposure.

1.4.2 Association between Obesity and Atopy in Case-Control Studies

Two case-control studies in Sweden and South Africa have also investigated the association between BMI and atopy. In the Swedish study, Mai et al. (51) reported that BMI was not significantly associated with atopy in two groups of children (aged 12 years); those with wheeze and their controls [OR: 1.3, 95% CI: 0.6-2.7] as well as those without wheeze and their controls [OR: 0.7, 95% CI: 0.4-1.4]. On the other hand, Calvert & Burney (12) found high BMI to be associated with the highest risk of atopic sensitization among 380 South African children (aged 8-12 years) with EIB and their 393 controls living in Kentani district (rural Eastern Cape) and Khayelitsha (an informal urban settlement in Western Cape).

1.4.3 Association between Obesity and Atopy in Cohort Studies

In a birth cohort of 1,037 children who were followed into adulthood in New Zealand, Hancox et al. (52) found BMI to be significantly associated with atopy in females [OR: 1.14, 95% CI: 1.01-1.30] but not in males [OR:1.0, 95% CI: 0.84-1.19].

1.5.0 Biological Plausibility of the Association between Obesity and Atopy

Adipocytes secrete hormones such as leptin and adiponectin as well as cytokines (Figure 1.1) such as tumor necrosis factor α (TNFα), interleukin-6 (IL-6) and interleukin-10 (IL-10). The increased adiposity in the obese state results in an elevated production of leptin, TNFα and IL-6 whilst the plasma concentration of adiponectin decreases. Hence, the secretion of IL-10 is decreased in obese individuals whilst the regulatory effect of Treg cells is also down-regulated. However, the elevated levels of TNFα in the obese state results in an increase in the production of T- helper lymphocyte type 2 (Th2) cytokines such as interleukin-4 (IL-4) and interleukin-5 (IL-5). It has been hypothesized that these changes in the immune system increases allergy susceptibility in obese individuals (33).

Moreover, much of the observed association between obesity and atopy has been restricted to adolescent girls (47, 49) and sexually matured females (18, 52). This observation has led to hypotheses that the atopic predisposition in females may be associated with menarche and an elevated production of the major female sex hormone, 17 β-estradiol. Studies have shown that the insulin resistance which develops along with increased adiposity (in the obese state) suppresses the hepatic production of the sex hormone binding globulin, a process which results in an increase in free 17 β-estradiol. Hence, the concentration and biological availability of this hormone is higher in obese than in non-obese females. The expression and secretion of interleukin-4 (IL-4), one of the primary signals for activating an immune response towards atopy, has been shown to be up-regulated by 17 β-estradiol (18).

1.6.0 Confounding Factors

The reviewed studies which have investigated the obesity-atopy association controlled for the effect of age and sex (12, 47, 49, 50, 51). Other factors such as parental level of education, area of residence (12, 47), family history of asthma (47, 49, 52), number of siblings, birth weight, household size, passive smoke exposure, breast feeding, infection with *Ascaris* (12) were adjusted for. However, none of the studies controlled for the effect of diet.

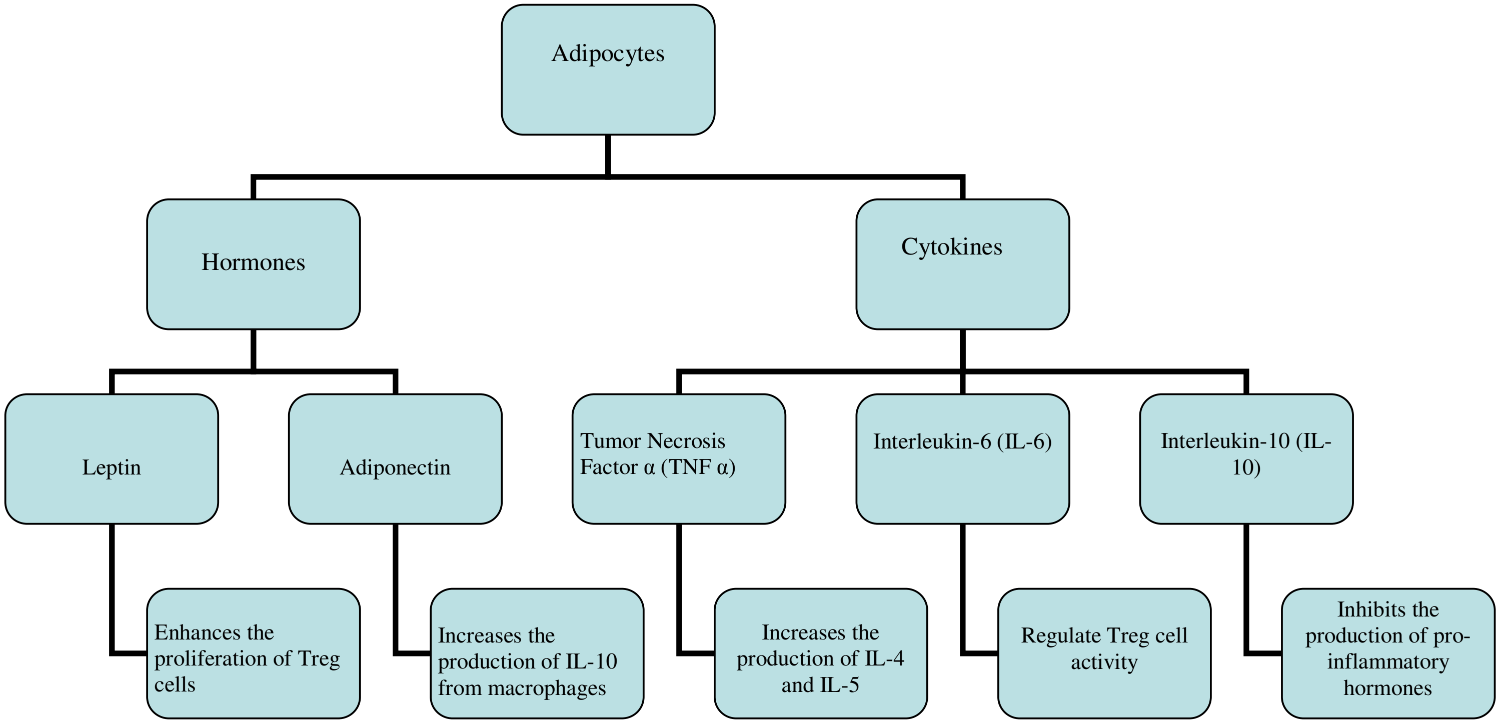


Figure 1.1: Major hormones and cytokines secreted by adipocytes and their functions in the immune system

1.7.0 Measurement of Outcome

Except for two studies which assessed atopy by both skin prick testing (SPT) and total serum IgE (12, 40), SPT was generally used for measuring atopy. The allergens used are shown in Table 1.3. However, different cut-off points were used for defining positive reactions in each study (Table 1.3). The lack of a standard cut-off point makes it impossible to compare these studies. Moreover, the use of low cut-off points in some studies (12, 47, 52) could have introduced false positive results for participants with dermatographism (sensitivity to touch and pressure). These false positives may have introduced non-differential misclassification and an underestimation of the strength of the association between obesity and atopy.

The sensitivity and specificity of SPT also varies with the type of device which is used in pricking (53). In the studies mentioned in Table 1.3, two studies used plain lancets (12, 51) whilst the others used 25 gauge BD needles (50) and the DermaPIK system (47). Other factors such as racial differences in skin thickness are also likely have an effect on the results (11).

Table 1.3: Allergens and diagnostic criteria for atopy

Study	Allergens	Allergen source	Testing site	Controls used	Time	Diagnosis
Huang et al. (47)	*Dermatophagoides pteronyssinus** *D. farinae** American cockroach *Aspergillus* mix Ragweed mix Shellfish mix	Geer Laboratories, Lenoir, NC, USA	Forearm	Histamine and Buffer	15 minutes	When wheal diameter is at least 2mm larger than buffer.
Schachter et al. (49)	8 aeroallergens	-	-	-	-	-
von Mutius et al. (50)	*Alternaria* Bermuda grass Rye grass Ragweed Russian thistle White oak Cat German cockroach Mites Peanut	-	Arm	Histamine and Phosphate buffered saline	20 minutes	When mean wheal diameter is at least 3mm after deducting the reaction to the buffer.

* House dust mite species. **-** Not stated.

Table 1.3: (Continued)

Study	Allergens	Allergen source	Testing site	Controls used	Time	Diagnosis
Calvert (12)	*D. pteronyssinus** *D. farinae** *Blomia tropicalis** Cockroach Timothy grass Bermuda grass *Aspergillus* *Cladosporium* *Alternaria* Cat Dog	Fernandez-Caldas Allergy Therapeutics, Worthing, UK	-	Histamine and saline	-	The presence of any skin wheal greater than 0 after deducting reaction for saline.
Mai et al.. (51)	Birch pollen Grass pollen Cat dander Dog dander Horse dander *D. pteronyssinus* *D. farinae* *Alternaria*	ALK, Horsholm, Denmark	Forearms	Histamine and 50% glycerine	-	A mean diameter of at least 3mm of the duplicate wheals (tests were performed in duplicate).

* House dust mite species. – Not stated.

Table 1.3: (Continued)

Study	**Allergens**	**Allergen source**	**Testing site**	**Controls used**	**Time**	**Diagnosis**
Hancox et al. (52)	*D. pteronyssinus* Grass Cat Dog Horse Kapok Wool *Aspergillus fumigatus* *Alternaria* *Penicillium* *Cladosporium*	-	-	Saline	-	A wheal diameter 2mm greater than saline control

1.8.0 Positive Predictive Value of Skin Prick Testing

Clinical studies have indicated that reactivity to environmental allergens in skin prick testing is over 80 percent in asthmatic children (38). On the population level, the positive predictive value of skin prick testing tends to be higher for children in the Western industrialized countries compared to those in developing countries. In industrialized countries, the positive predictive value for skin prick testing ranges between 30 – 50 % whilst in developing countries like Indonesia, the predictive value is about 15 % (11). However, there have been some studies in Africa which have shown a high predictive value for skin prick testing (7).

1.9.0 Rationale

Although infectious diseases are major public health problems for most parts of Africa, and may continue to be for years to come, non-infectious and chronic diseases such as obesity is gradually being added on to the health burden. Moreover, the rise in the prevalence of non-infectious diseases has been shown to be occurring at a much faster rate in developing countries than it did in industrialized countries (36). Obesity, which is a major health problem in both children and adults, is associated with chronic diseases such as diabetes and cardiovascular disease (36, 43). Reports of studies in industrialized countries have also implicated obesity in the development of allergies such as asthma (44). However, the relationship between obesity and atopy has not been clearly established (33). Though some previous studies in Africa have indicated that the prevalence of childhood atopy is low in rural areas where children are normally shorter and lighter than their urban counterparts, few studies have explored the association between obesity and allergies in Africa. This study therefore aims to investigate the association between obesity and atopy in children living in rural and urban areas in Ghana.

1.9.1 Research question:

Is childhood obesity an independent risk factor for atopy among 6-15 years old children living in rural and urban areas in Ghana in 2006?

1.9.2 Study objectives

- To determine the prevalence of atopy in children living in rural and urban areas in Ghana.
- To determine the distribution of BMI percentiles in children living in rural and urban areas in Ghana.
- To investigate the association between childhood obesity and atopy in children living in rural and urban areas in Ghana.

CHAPTER TWO

METHODOLOGY

2.0 Introduction

In this chapter, the design of the study, selection of study sites and study population are discussed. The different methods of measurements used and the criteria for defining exposure and outcome are also explained. The chapter ends with a detailed description of the data management and analysis techniques used and the ethical considerations in this study.

2.1.0 Study Design

This study was a secondary data analysis of the Global View of Food Allergy (GLOFAL) study which was conducted in 2006 in Ghana. A cross-sectional analytic design was employed in the GLOFAL study to investigate the effect of parasitic infections, diet and dust mite allergies on immune response in asthma and other allergic disorders among children living in rural and urban areas in the Greater Accra Region of Ghana.

2.1.1 Selection of Study Sites

In order to compare the rural-urban differences in the prevalence of childhood allergies, the two most urbanized and the least urbanized districts in the Greater Accra Region were selected as study sites. In Ghana, localities with populations of five thousand people or more are classified as urban. Compared to rural areas, urban areas are more developed in terms of basic infrastructure and lifestyle. The rural site was selected on the basis of the prevalence of helminth infections. A pilot survey was conducted in three targeted rural sites to determine the prevalence of helminth infections and to collect information on schools where children had not received any school-based mass deworming in the five years preceding the study.

2.2.0 Study Sites

The Greater Accra Region, which occupies a total area of 3, 245 square kilometers, is the smallest of the ten administrative regions in Ghana (Figure A1). As of 2000, it was the second most densely populated region in the country, accounting for 15.4 % of Ghana's population. Records available from the 2000 National Population Census indicate that 33 % of the region's population was under the age of 15 years. Under the local government administration system, the Greater Accra Region is divided into five districts namely; Accra Metropolitan Area, Tema Municipal Area, Ga District, Dangme West District and Dangme East District. Participants in the GLOFAL study were recruited from three of these districts namely; Accra Metropolitan Area, Ga District and the Dangme East District. The first two districts were rated as urban settlements whilst the Dangme East District which is approximately 70 km from Accra, the national capital, was rated as a rural settlement.

2.2.1 Accra Metropolitan Area

The Accra Metropolitan Area, which is entirely urban, is the largest and the most diverse city in Ghana (42). It is also one of the most developed districts in the Greater Accra Region and the second largest industrial centre in Ghana. Records available from the 2000 National Population Census indicate that it had a population of 1,695, 135 million, which constituted 57.2 % of the regional population. This, together with its estimated annual growth rate of 3.36 %, makes it one of the fastest growing and most densely populated metropolises in Africa. In 2000, 31.6 percent of the population in this district was under the age of 15 years (54).

2.2.2 The Ga District

The Ga District is the second most urbanized and populated district in the Greater Accra Region after the Accra Metropolitan Area. In 2000, an estimated 88 % of the population in this district lived in urban areas.

2.2.3 Dangme East District

The Dangme East District occupies 28 % of the total area of the Greater Accra Region. It is located in the eastern part of the region and occurs within Latitudes 5^0 45 south and $6^{\ 0}$ 00 north and from Longitude 0^0 20 west to 0^0 35 east. In addition to being the least populated district (constituting 3.2 percent of the regional population) in the Greater Accra Region, it is also largely rural with 82 % of its population living in rural areas. It is estimated that three out of every four people in the district live in a rural area. As of 2000, 42.4 percent of the district's population was under the age of 15 years. Data collected on socio-economic indicators at the time of the 2000 National Population Census show that 75 % households in the district used kerosene lamp as the main source of lighting. Moreover, pipe borne water was available to 24.4 % households in the district (54).

2.2.3.1 Economic Activities in the Dangme East District

The major economic activities in the district are agriculture and salt mining. Crop production, fishing, livestock production and Agro-forestry are the major agricultural activities in the district and 51% of the adult population is employed in this sector; either directly or in the marketing and distribution of farm produce (54). The district is also home to a salt mining complex which covers an area of 12,500 acres around the Songor Lagoon (Figure A1). This salt mining project produces about 90, 000 metric tones of salt annually which is sold locally and for export to neighbouring countries such as Burkina Faso, Togo, Mali and Nigeria. There are also individual miners and cooperative mining groups around the lagoon. However, since these groups depend entirely on the evaporation process, they go out of business in the rainy season (between March and September). An estimated 10 % of the active population in the district is employed in the salt mining sector (54).

2.3.0 Study Population

The study population comprised school children living in the three selected districts in the Greater Accra Region who fell within the age range of 6-15 years at the commencement of the study. Under the educational reform system in Ghana, children receive six years of primary education followed by three years in the junior high school. These constitute basic education. Even though basic education is tuition-free in public schools, it is not mandatory. Most children begin their six years of primary education at age six. Participants in the GLOFAL study were recruited from the basic school level in mixed day schools.

Inclusion Criteria:

- Children attending private and public schools in the two urban sites.
- Children attending public schools in the rural site.

Exclusion Criteria:

- School children who were outside the age range for the study.
- Children who were not enrolled in school

2.3.1 Sample Population

Eight private and four public schools were randomly selected from the urban sites to participate in the study. Of these, seven schools; four private and three public schools were eventually recruited after the school authorities and parents had consented to the children's participation. Based on the results of the pilot study in the rural site, five schools (four in the Sege educational circuit and one in the Kasseh East circuit) were selected. The criteria for selection were; a *Schistosomiasis haematobium* (urinary bilharzia) or intestinal helminths prevalence of ≥ 35 percent and the absence of school-based mass deworming in the five years preceding the study. All selected schools in the rural site agreed to participate in the study. The locations of these schools are indicated in Figure A1.

2.3.2 Sample Size

The sample size for the original study was 2000 school children; 1000 from the urban sites and 1000 from the rural site. The calculation of the sample size was based on the prevalence of helminth infection and skin test reactivity. It was estimated that 2000 participants would provide a 90 percent power to detect the odds ratios for helminth infection in relation to skin reactivity at 5 % significance.

2.3.3 Study Sample

The study sample consisted of all children aged 6 – 15 years in the selected schools whose parents or guardians consented to their participation by signing or thumb printing a consent form. Consent was received for a total of 1,926 children (1,111 from the urban site and 815 from the rural site).

2.3.4 Participation Rate

The participation rates for the rural and urban sites were 67.9 % and 28.7 % respectively. In the site, the participation rate was considerably higher for public schools compared to private schools (Figure 2.1).

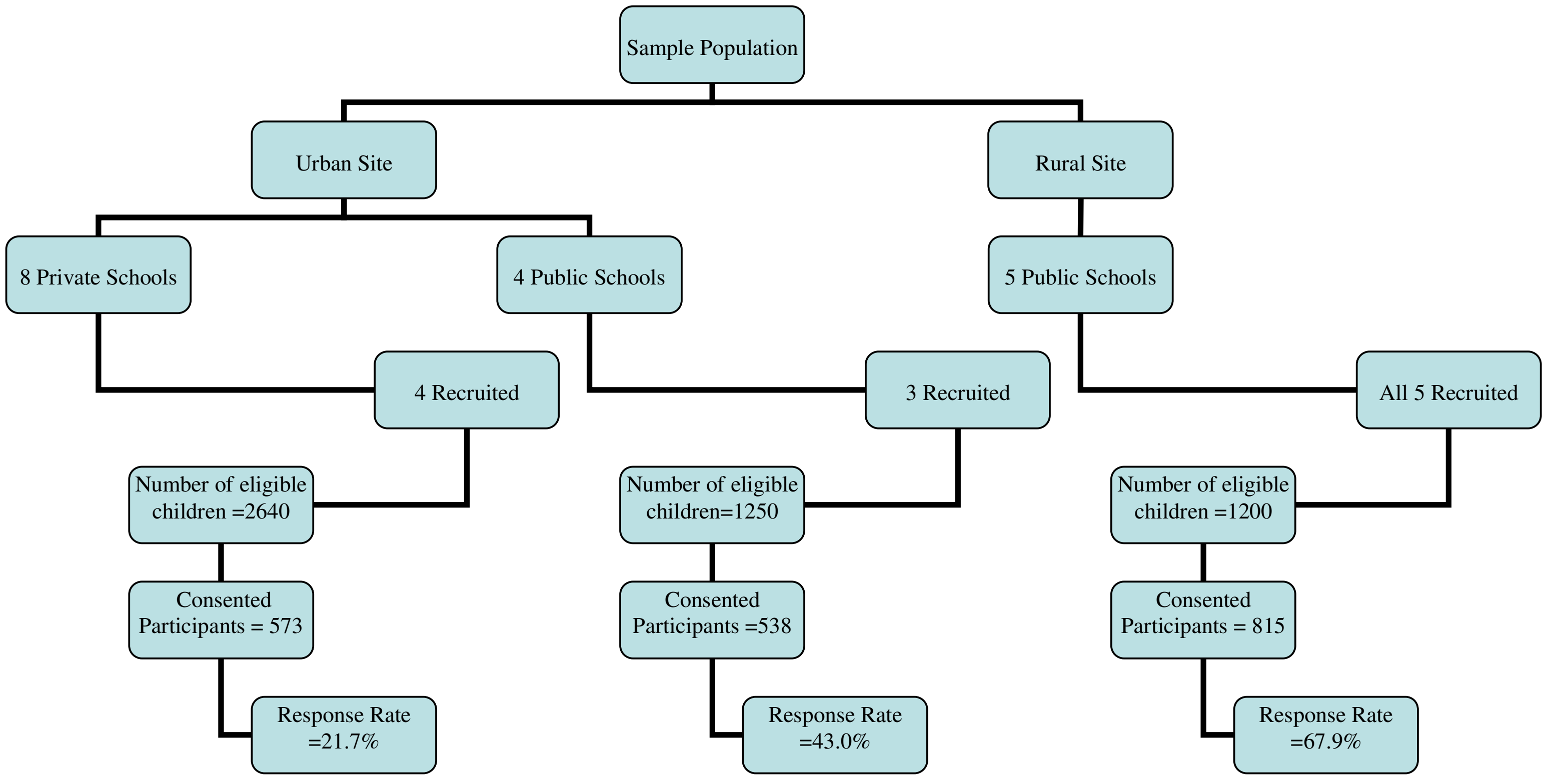


Figure 2.1: Recruited schools and their relative contribution to the sample size

2.4.0 Measurement

2.4.1 Skin Prick Testing

Participants in the study underwent skin prick testing (SPT) to a panel of two common aero-allergens and seven food allergens. The allergens were house dust mite mix (*Dermatophagoides* sp), cockroach (*Blatella germenica*), peanut, papaya, pineapple, apple, mango, orange and banana. Histamine and diluent (ALK-Abello, Denmark) were respectively used as positive and negative controls. The tests were performed by four investigators who had been trained in a standardized way.

2.4.1.1 Testing Procedure

The tests were performed on the volar aspect of the right and left forearms, between the elbow and the wrist. The forearms were first cleaned with rubbing alcohol and allowed to dry. The sites where the individual allergens were going to be tested were marked with a felt-tipped marker. Since sensitivity differs by two folds between the elbow and the wrist, the marks were at least 5 cm from the wrist and 3 cm from the elbow crease (55). In order to prevent reactions from overlapping, an interval of 2 to 3 centimeters was allowed between the marks.

For the aero-allergens (dust mite and cockroach) and peanut, one drop of the standardized allergen extracts (ALK-Abello, Denmark) was placed beside the marked spots on the forearms. A separate one millimeter pointed-tip sterile lancet (HAL Allergy) was used in pricking vertically through each drop of allergen with firm pressure. In the case of the fruits, the prick - prick procedure which involves dipping the tip of the lancet into a cut portion of the fresh fruit and then pricking the skin with the fruit residue was used. A different lancet was used for each fruit. The tests were performed between 09:00 and 13:00 hours. As sensitivity of SPT could vary for different points on the forearm, participants were randomized to be pricked with specific allergens at different points on the forearm. Normally, the first child in the participant list for each school was pricked with the allergen arrangement of Sheet A whilst subsequent participants were assigned to Sheets B, C and D (Tables B1-B4). The procedure was repeated after every fourth participant on the list.

Clean absorbent tissue paper was placed on both forearms to blot drops of excess allergens on the skin immediately after the last prick. Results of the test were read 15 minutes after pricking. A reaction to any of the tested allergens was characterized by a flat elevation on the skin (wheal). The wheal was outlined with a felt-tipped marker and transferred onto a record sheet (Appendix B) by means of transparent tape.

2.4.1.2 Diagnosis of a Positive Reaction

The controls (histamine and diluent) were used for assessing the normal skin reactivity to the test. Under normal circumstances, the negative control (diluent) should not produce any wheal unless the participant has dermatographism (sensitivity to touch and pressure). The positive control (histamine) should however produce a wheal with an average diameter which is ≥3 mm. Wheals < 3 mm or an absence altogether may indicate interference by concomitant medication such as antihistamines or topical steroids (55).

The wheal corresponding to a particular allergen was read as positive if the mean of its longest diameter and the diameter perpendicular to it at its mid-point was at least 3 millimeters greater than the wheal produced by diluent, in the presence of a positive reaction to histamine. A transparent plastic ruler was used in measuring the diameters of the wheal. Measurements were recorded to the nearest 0.5 mm.

2.4.1.3 Sensitivity of Skin Prick Testing

Sensitivity of SPT increases with the potency of the allergen extract, the pressure applied with the lancet and the time of the day when the test is performed. There is a circadian variability in skin responses; normally, skin sensitivity is lower in the morning and higher in the afternoon. Moreover, the thickening of the skin in people who spend much time outdoors may restrict the detection of reactions (56).

2.4.2 Anthropometric Measurements

The standing height (in centimeters) and weight (in kilograms) of participants were measured with a portable free-standing stadiometre and an electronic scale (BS-8001, capacity: 130 kg) respectively. The study participants were measured wearing their school uniforms and no shoes. In measuring weight, each participant was made to stand still in an upright position on the scale. The readings on the scale were allowed to stabilize before being recorded. Weight was recorded to the nearest 0.1 kg whilst height was recorded to the nearest 0.5 cm.

2.4.3 Parasitological Survey

In each school, participants were asked to submit urine samples between 11:00 and 13:00 hours where maximum shedding of schistosome eggs occurs in humans. Participants were also given specimen bottles to collect fresh stool samples in the morning before coming to school.

2.4.3.1 Laboratory Analysis of Parasitological Samples

The urine samples were examined for the presence of haematuria (blood in urine), proteinuria (proteins in urine), and glucose using urine reagent strips (Combur 10 Test®, Roche). The proteinuria and haematuria were classified into the following categories: negative, +, ++, +++

and ++++. To determine infection with *S. haematobium*, 10 ml urine was filtered through a filter (Millipore® filter membrane, pore size 12 μm). The residue was examined under a microscope (Olympus CX21) at a magnification of x10 for the presence and number of *S. haematobium* eggs. The intensity of infection for positive samples was expressed in number of eggs per 10 ml urine.

The Kato-Katz technique (57) was used in processing stool samples to determine the presence of intestinal parasites such as *S. mansoni* (intestinal schistosomes), *Necator sp* (hookworm), *Ascaris lumbricoides* (round worm) and *Trichuris tricuria* (whip worm). The intensity of infection for each species was expressed in number of eggs per gram of faeces.

2.4.4 Questionnaire Survey

Information on early life factors such as duration of exclusive breast feeding as well as diet, socio-economic status, family history of asthma, source of domestic fuel and exposure to passive cigarette smoke was obtained through an interviewer administered questionnaire survey which targeted parents or guardians of the children in the study. The interviews, which occurred in the homes of study participants, were conducted in languages such as English, Akan [ж], Ga* and Ga-Adangme*. Information on participants' date of birth and birth weight was obtained from their antenatal record cards. The highest educational level and occupation of the person who provided financially for the child were used as proxy measures for socio-economic status (Appendix C).

[ж] The most widely spoken local language in Ghana

* Local languages spoken in the Greater Accra Region of Ghana

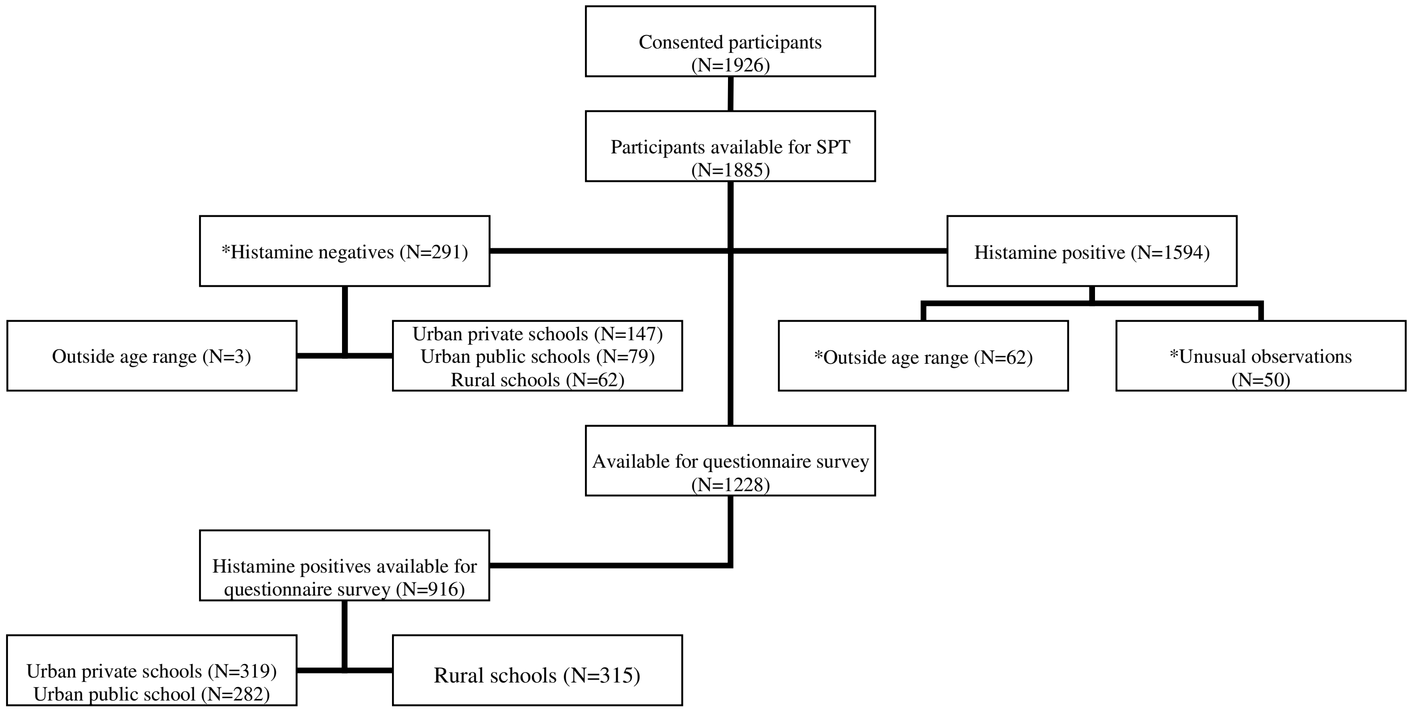
2.5.0 Data Management and Analysis

Data in the original study were entered in a Microsoft Access database. The variables of interest for this study were exported from Access as text files. The text files were then read into Stata version 9.2 (Stata Corp., College Station, TX, USA) using the “insheet” command.

The analysis in this study was restricted to a total of 1,885 participants who had data on skin prick testing (the outcome variable). The individual Stata files for the exposure variable (BMI percentiles for age and sex) and confounding variables were merged unto the file for the outcome variable. Numeric variables in the original database which were interpreted as string variables by Stata were converted into numeric variables using the “destring” command.

2.5.1 Data Editing

Scatter plots were used to examine the distribution of BMI for outliers whilst summary statistics was used in examining the distribution of each variable and to check for unusual values. Non-plausible observations were set to missing. Using 3 millimeters as cut-off for a positive reaction to an allergen or control, 291 participants (3 of whom were outside the age range for the study) tested negative to histamine, the positive control. 42 (14.43%) of the 291 participants who tested negative to histamine had a mean histamine wheal size of 0 whilst the remaining 249 (85.57%) had mean histamine wheal sizes ranging between 1 - 2.75 mm. These values were set to missing and excluded from the analysis. Among the participants who tested positive to histamine, the mean wheal size was 4.45 mm with a standard deviation of 1.04 (range: 3.0 mm - 8.5 mm). After limiting the data to the age range for the study, 65 observations fell outside the required age range of 6-15 years (47 were above 15 years whilst 18 fell below 6 years). These observations were also set to missing and excluded from the analysis. The final analysis was limited to 1,482 observations (Figure 2.2).



* Excluded from analysis

Figure 2.2: Varying participation rates and final sample size used in the analysis

2.5.2 Definition of Atopy (outcome variable)

Positive and negative reactions to any of the tested allergens and the controls were coded as 1 and 0 respectively. Atopy was defined at two levels; sensitization to at least one of the nine tested allergens was defined as 1 whilst 0 represented no sensitization to any of the tested allergens.

2.5.3 Definition of Childhood Obesity (exposure variable)

Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m). NutStat, a programme in Epi-Info version 3.3.2 (CDC, Atlanta, Ga., USA) was used in computing the standardized BMI percentiles for age and sex. This data was then read into the analysis program in Epi-Info and written into a text file. The text file was read into Stata using the 'insheet' command. The calculation of BMI percentiles for age and sex in NutStat was based on the CDC growth charts which were released in 2000 (46). The CDC charts were used because they are widely used for assessing growth in children older than 5 years of age.

Using 85th percentile as cut-off point, the exposure variable was defined at three levels based on the CDC growth reference (58);

- Normal weight (coded 1): BMI ≥ 5th percentile and < 85th percentile
- Underweight (coded 2): BMI <5th percentile
- Overweight or obese (coded 3): BMI ≥ 85th percentile

2.5.4 Categorization of Confounding Variables

Variables such as age, sex, residence, duration of exclusive breast feeding, exposure to tobacco smoke, parental education, parental occupation, family history of asthma (measured as doctor diagnosed asthma), dietary intake, source of domestic fuel and helminth infections were regarded as potential confounding variables in this study. Categories were generated for each of these variables. The occupation given by most parents in the rural site was more than one. This was mainly because most of them did salt winning in the dry season and farming in the raining season. Moreover, the majority of the parents who were into fishing also cultivated crops. Parents in the former group were categorized as traders whilst those in the latter group were categorized as farmers. In order to allow for adequate control of confounding in the analysis, the categories for each of these variables were restricted to a maximum of five. Open-ended categories were also avoided in order to control residual confounding. In order to allow all observations to be used in estimating the effect of non-missing observations in the analysis, dummy values were generated for missing observations of each variable.

2.5.5 Descriptive Statistics

Analysis of variance (ANOVA) was used in testing the differences in the mean of height, weight and BMI in the rural and urban sites, whilst adjusting for the effect of age. Categorical variables were tabulated to determine the frequency of observations which occurred within the various categories. The information provided by these contingency tables was used to determine the relation between variables and also to determine if the observations were adequate for a logistic regression analysis.

2.5.6 Model Building

Since the outcome (atopy) was dichotomous, logistic regression analysis was used in investigating the effect of the exposure and confounding variables on the outcome. The "all possible models approach" was used in selecting which explanatory variables to include in the multivariate model. Univariate logistic regression analysis was performed to investigate associations between explanatory and outcome variables. A variable was retained in the multivariate model if the p-value corresponding to the unadjusted odds ratio was ≤ 0.150. Each of these separate analyses was stratified by sex, age and residence. Since age and sex are associated with a wide range of outcomes and are related to the level of many exposures, they would have been adjusted for in the multivariate model even if they had not met the required criteria for inclusion in the model.

2.5.7 Final Model

The final model was adjusted in a stepwise manner for all the variables which were found to be associated with atopy in univariate analysis at $p \leq 0.150$. The "estimate store" command and the "lrtest" were used in testing whether the inclusion of each variable significantly increased the likelihood of the model.

2.6.0 Ethical Consideration

The original study was approved by the Institutional Review Board of the Noguchi Memorial Institute for Medical Research, University of Ghana (Figure D1). The Human Research Ethics Committee of the University of the Witwatersrand reviewed and approved the secondary data analysis (Figure D2). Informed consent was also obtained from the parents or guardians of the study participants.

CHAPTER THREE

RESULTS

3.0 Introduction

The demographic characteristics of the study population, distribution of BMI in the study population and the prevalence of obesity and atopy are presented in this chapter. The factors associated with obesity in the urban and rural sites and the associations between atopy and childhood obesity as well as potential confounding factors in univariate and multivariate analysis are also presented in this chapter.

3.1.0 Description of the Study Population

The demographic characteristics of the study population are presented in Tables 3.1-3.2. 1,482 participants were included in the final analysis. Of these, females constituted 52.36%. The mean age for the study population was 10.51 (±2.29) years and was significantly higher for urban [11.07, 95% CI: (10.90-11.25)] than rural [9.95, 95% CI: (9.80-10.09)] participants. After adjusting for the effect of age, the mean height and weight for the study population differed significantly by residence with participants in the urban site being taller and heavier. In spite of this, participants in the rural site generally had a higher BMI and prevalence of obesity. The prevalence of intestinal parasite infections was also higher in the rural site. The few parasite infections which were recorded in the urban site occurred mainly among participants in two public schools. Although the response rate was higher in the rural than the urban site, it was much more difficult to contact parents in the rural site for questionnaire administration. This is reflected in the high number of missing observations in the rural site (Table 3.3).

Table 3.1: Distribution of height, weight and BMI in school children aged 6-15 years in urban and rural areas in the Greater Accra Region of Ghana

	Mean Height in m (95% CI) of Male Participants			**Mean Height in m (95% CI) of Female Participants**		
Age (years)	**Urban**	**Rural**	**p-value***	**Urban**	**Rural**	**p-value***
6 - 8	126. 08 (124.05-128.11)	121.09 (119.57-122.61)	0.4263	124.87 (123.07-126.67)	120.82 (119.47-122.17)	0.2147
9 - 11	136.51 (135.10-137.91)	131.47 (130.31-132.62)	0.0392	139.49 (137.83-141.14)	133.69 (132.45-134.93)	0.0445
12 -15	150.15 (148.60-151.69)	139.35 (137.95-140.75)	0.0869	152.04 (150.82-153.26)	140.80 (139.16-142.44)	0.0003
Age (years)	**Mean Weight in kg (95% CI) of Male Participants**			**Mean Weight in kg (95% CI) of Female Participants**		
	Urban	**Rural**	**p-value***	**Urban**	**Rural**	**p-value***
6 - 8	24.95 (23.75-26.16)	25.07 (24.24-25.90)	0.3616	24.62 (23.19-26.05)	24.32 (23.48-25.16)	0.3028
9 - 11	29.96 (28.84-31.08)	30.21 (29.41-31.00)	0.0139	33.18 (31.81-34.55)	31.85 (30.85-32.84)	0.0427
12 -15	40.22 (38.74-41.69)	36.79 (35.58-37.99)	< 0.0001	44.77 (43.26-46.29)	37.10 (35.62-38.58)	0.0000
Age (years)	**Mean BMI in kg/m^2 (95% CI) of Male Participants**			**Mean BMI in kg/m^2 (95% CI) of Female Participants**		
	Urban	**Rural**	**p-value***	**Urban**	**Rural**	**p-value***
6 - 8	15.56 (15.17-15.95)	17.03 (16.68-17.39)	0.1477	15.62 (15.05-16.19)	16.62 (16.17-17.07)	0.1126
9 - 11	15.93 (15.56-16.29)	17.38 (17.11-17.65)	0.5394	16.84 (16.40-17.27)	17.65 (17.32-17.99)	0.7393
12 -15	17.63 (17.24-18.00)	18.86 (18.44-19.28)	0.0445	19.18 (18.70-19.66)	18.61 (18.06-19.17)	0.0645

*Difference in mean height, weight and BMI between urban and rural participants were compared by ANOVA adjusted for age

Table 3.2: Demographic characteristics of 1,482 school children aged 6-15 years in urban and rural areas of the Greater Accra Region of Ghana

Variable	Urban (%)	Rural (%)	Total
All	**742**	**740**	**1,482**
Sex			
Males	347 (46.77)	359 (48.51)	706 (47.64)
Females	395 (53.23)	381 (51.49)	776 (52.36)
Age§			
6-8 years	133 (17.92)	191 (25.81)	324 (21.86)
9-11 years	261 (35.18)	347 (46.89)	608 (41.03)
12-15 years	348 (46.90)	202 (27.30)	550 (37.11)
***Nutritional status indicators**§			
Normal weight	568 (76.55)	599 (80.95)	1,167 (78.74)
Under weight	94 (12.67)	23 (3.11)	117 (7.89)
Obese	80 (10.78)	118 (15.95)	198 (13.36)
Atopy Ψ			
Non-atopic	610 (82.21)	554 (74.86)	1164 (78.54)
Atopic	132 (17.79)	186 (25.14)	318 (21.46)
***S. haematobium* infection**§			
Not infected	714 (96.23)	630 (85.14)	1,344 (90.69)
Infected	20 (2.70)	70 (9.46)	90 (6.07)
Missing observations	8 (1.08)	40 (5.41)	48 (3.24)
Intestinal parasites infection§			
Not infected	659 (88.81)	434 (58.65)	1, 093 (73.75)
Hookworm	13 (1.75)	76 (10.27)	89 (6.10)
Trichuris	2 (0.27)	16 (2.16)	18 (1.21)
Ascaris	0 (0.00)	93 (12.57)	93 (6.28)
Co-infected⁂	3 (0.40)	21 (2.84)	24 (1.62)
Missing observations	65 (8.76)	100 (13.51)	165 (11.13)

* Normal weight defined as BMI ≥ 5 and < 85 percentile
Underweight defined as BMI < 5 percentile
Obese defined as BMI ≥ 85 percentile

⁂ Infected with two or more intestinal helminths
§ Difference between urban and rural sites (p< 0.000)
Ψ Difference between urban and rural sites (p=0.001)

3.2.0 Home Environment Characteristics of Study Population

Use of Liquefied Petroleum Gas (LPG) as the main source of fuel for cooking was reported for the majority of the urban homes (49.60%) whilst firewood was more commonly used in the rural homes (26.89%). Electricity served as the main source of fuel for cooking in 6 homes (5 urban and 1 rural). Since these observations were few, they were combined with observations in the adjacent stratum (i.e. LPG use).

Table 3.3: Home environment characteristics of 1,482 school children aged 6-15 years in the urban and rural study sites in the Greater Accra Region

Variable	Urban (%)	Rural (%)	Total
All	**742**	**740**	**1,482**
***Source of domestic fuel§**			
Liquefied Petroleum Gas (LPG)	368 (49.60)	5 (0.68)	373 (25.17)
Charcoal	184 (24.80)	111 (15.00)	295 (19.91)
Firewood	50 (6.74)	199 (26.89)	249 (16.80)
Missing observations	140 (18.87)	425 (57.43)	565 (38.12)
Passive smoking§			
Non-exposed	398 (53.64)	218 (29.46)	616 (41.57)
Exposed	203 (27.36)	96 (12.97)	299 (20.18)
Missing observations	141 (19.00)	426 (57.57)	567 (38.26)
Family history of asthma§			
No	352 (47.44)	174 (23.51)	526 (35.49)
Yes	170 (22.91)	105 (14.19)	275 (18.56)
No idea	72 (9.70)	36 (4.86)	108 (7.29)
Missing observations	148 (19.95)	425 (57.43)	573 (38.66)
Exclusive breast feeding§			
None	74 (9.97)	48 (6.49)	122 (8.23)
1-6 months	280 (37.74)	360 (48.65)	640 (43.18)
6-12 months	52 (7.01)	54 (7.30)	106 (7.15)
Missing observations	336 (45.28)	278 (37.57)	614 (41.43)
Educational level of parent Ψ			
No formal education	124 (16.71)	148 (20.00)	272 (18.35)
7 –9 years education	178 (23.99)	165 (22.30)	343 (23.14)
10-15 years education	68 (9.16)	108 (14.59)	176 (11.88)
Tertiary education	82 (11.05)	70 (9.46)	152 (10.26)
Missing observations	290 (39.08)	249 (33.65)	539 (36.37)
Occupation of parent			
Unemployed	16 (2.16)	14 (1.89)	30 (2.02)
Trader	76 (10.24)	139 (18.78)	215 (14.51)
Farmer	95 (12.80)	83 (11.22)	178 (12.01)
Public servant	168 (22.64)	169 (22.84)	337 (22.74)
Business	94 (12.67)	84 (11.35)	178 (12.01)
Missing observations	293 (39.49)	251 (33.92)	544 (36.71)
Means of transportation to school§			
Walk	289 (38.95)	313 (42.30)	602 (40.62)
Bus/Taxi	197 (26.55)	2 (0.27)	199 (13.43)
Private car	115 (15.50)	0 (0.00)	115 (7.76)
Missing observations	141 (19.00)	425 (57.43)	566 (38.19)

*Source of domestic fuel refers to fuel used for cooking at home
§ Difference between urban and rural sites ($p< 0.000$)
Ψ Difference between urban and rural sites ($p =0.003$)

Exposure to passive cigarette smoke and family history of asthma were more frequently reported for urban than rural participants (Table 3.3). However, more rural (48.65%) than urban (37.74%) participants were reported as having been exclusively breastfed for at least 6 months. Despite the higher proportion of parents with no formal education in the rural site, there were slightly more unemployed parents in the urban than the rural site (Table 3.3).

3.3.0 Distribution of BMI in the Study Population

The mean BMI for the study population was 17.46 kg/m^2. Figures 3.1-3.2 show the distribution of the standardized BMI-for-age in the study population based on the CDC growth reference charts which were released in 2000.

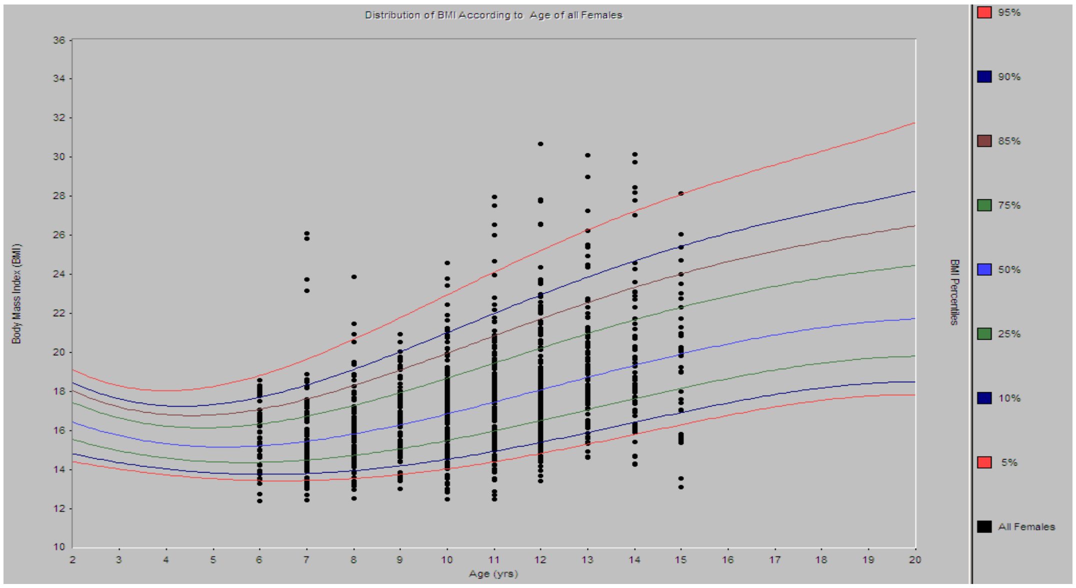


Figure 3.1: Distribution of age-standardized BMI in females aged 6-15 years in the urban and rural sites in the Greater Accra Region of Ghana

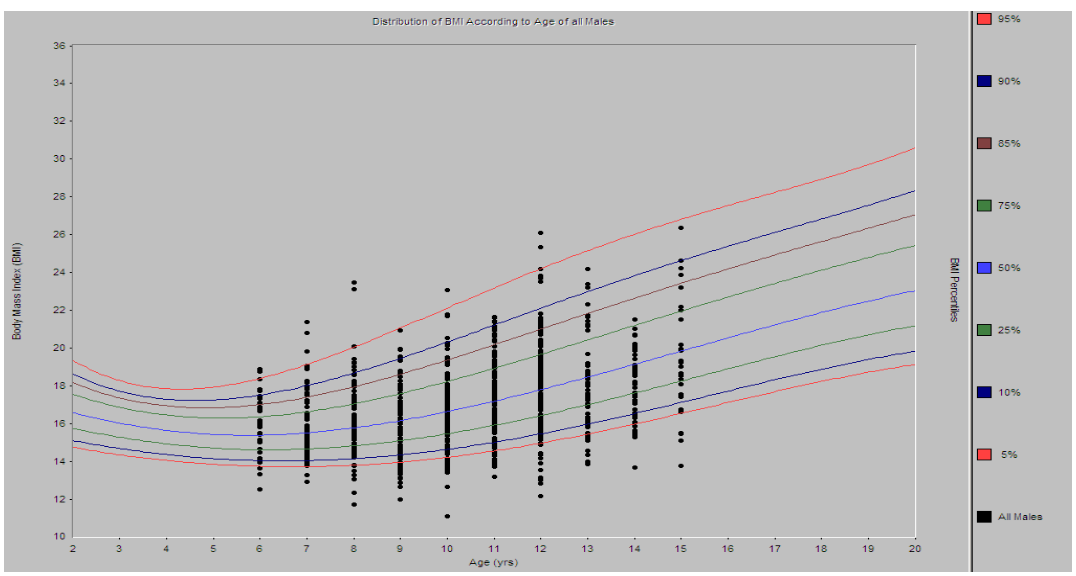


Figure 3.2: Distribution of age-standardized BMI in males aged 6-15 years in the urban and rural sites in the Greater Accra Region of Ghana

3.4.0 Prevalence of Obesity

Values of the standardized BMI-for-age and sex were used in estimating the prevalence of obesity in the study population. The overall prevalence of obesity was 13.36% (198/1482) and was significantly higher in the rural than the urban site (15.95% vs. 10.78%). The proportion of obese females in the study population was not significantly different from that of males. However, whereas the prevalence of obesity was higher among females in the urban site, the converse was observed in the rural site. The highest proportion of obese participants occurred in the youngest age group (6-8 years) in both the urban and rural sites (Table 3.4).

Table 3.4: Prevalence of obesity in 1,482 school children aged 6-15 years in urban and rural areas in the Greater Accra Region of Ghana

	Urban (%) n= 742	**Rural (%)** n=740	**Total** N= 1,482
Obese participants	80 (10.78)	118 (15.95)	198 (13.36)
Sex			
Males	27 (7.78)	66 (18.38)	93 (13.17)
Females	53 (13.42)	52 (13.65)	105 (13.53)
Age			
6 -8 years	16 (12.03)	58 (30.37)	74 (22.84)
9 -11 years	28 (10.73)	36 (10.37)	64 (10.53)
12 -15 years	36 (10.34)	24 (11.88)	60 (10.91)

3.4.1 Factors Associated with Obesity

The factors associated with obesity in this study are presented in Table E1. In univariate analysis, obesity was negatively associated with male sex in the urban site [OR: 0.54, 95% CI: 0.33-0.89], older age in the rural site [OR: 0.27, 95% CI: 0.18-0.42] and passive smoking in the urban site [OR: 0.51, 95% CI: 0.27-0.97]. The effect of sex [OR: 1.72, 95% CI: 1.14-2.57], age and passive smoking [OR: 0.52, 95% CI: 0.30-0.91] on obesity increased slightly after multivariate adjustment. Despite the higher prevalence of helminth infection in the rural site, there was no statistically significant effect between helminth infection and obesity. Dietary intake in the rural and urban sites seemed to follow a trend; whereas the consumption of fresh vegetables, maize and cassava was common in the rural site, rice and fresh fruits were common in the daily diets of the urban participants. Moreover, though fish was commonly consumed in both the urban and rural sites, meat (beef and chevron) was more common in the diet of the rural participants (Table F1). However, the high number of missing observations in the rural site (47.03%) prevented any further exploration of the effect of diet on obesity in this study. Though children in the urban and rural sites may have differed considerably in terms of physical activity levels, the nature of this study (secondary data analysis) restricted the analysis to only one proxy measure of physical activity, the means by which participants got to school. Despite the profound differences between rural and urban participants with respect to this proxy measure (Table 3.3), no effect was observed between it and obesity. However, the effect of missing observations was significant, indicating the possibility that missing observations in the rural site contributed to the lack of effect.

3.5.0 Prevalence of Sensitization to Specific Allergens

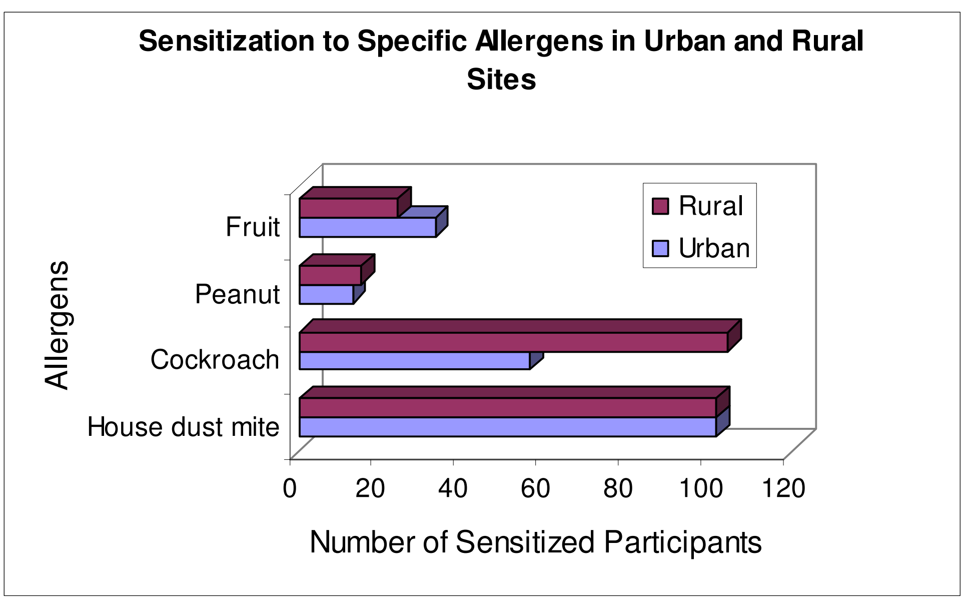


Figure 3.3: Sensitization of urban and rural participants aged 6-15 years in the Greater Accra Region of Ghana to specific allergens

13.63% (202/1,482) of the study population was sensitized to house dust mite, making it the most prevalent allergen in the study population. Cockroach, to which 10.80% (160/1,482) of the study population was sensitized, was more prevalent in the rural site (Figure 3.3). The prevalence of sensitization to at least one fruit (i.e. pineapple, orange, mango, banana, papaya or apple) was 3.85% (57/1,482). However, this was higher in the urban site. Pineapple was the most prevalent fruit allergen whilst apple was the least prevalent. Multiple sensitizations to cockroach and mite allergens in the urban and rural sites were 5.53% and 6.03% respectively.

3.5.1 Prevalence of Atopy

21.46% (318/1,482) of the study population was atopic. The prevalence of atopy was significantly higher in the rural than the urban site (Table 3.5). Compared to females, males were more likely to be atopic in both the urban and rural sites. The prevalence of atopy increased considerably with age in the study population. However, the increasing prevalence of atopy with age was more profound among participants in the urban site. The highest proportion of atopic participants in the urban site occurred in three private schools.

Table 3.5: Prevalence of atopy in 1,482 school children aged 6-15 years in urban and rural areas in the Greater Accra Region of Ghana

	Urban (%) **n = 742**	**Rural (%)** **n=740**	**Total** **N=1,482**
Atopic participants	132 (17.79)	186 (25.14)	318 (21.46)
Sex			
Males	79 (22.77)	104 (28.97)	183 (25. 92)
Females	53 (13.42)	82 (21.52)	135 (17.40)
Age			
6 -8 years	18 (13.53)	43 (22.51)	61 (18.83)
9 -11 years	39 (14.94)	87 (25.07)	126 (20.72)
12 -15 years	75 (21.55)	56 (27.72)	131 (23.82)

* Atopy defined as a positive reaction to at least one of the nine tested allergens

3.6.0 Factors Associated with Atopy

No significant association was observed between obesity and atopy in the study population. However, there did appear to be a trend between underweight and atopy in the urban site but this was not significant. In both the urban [OR: 1.90, 95% CI: 1.30-2.79] and rural [OR: 1.49, 95% CI: 1.06-2.08] sites, males had an increased likelihood of developing atopy compared to females. After multivariate adjustment, the effect of sex on atopy increased in the urban site [OR: 2.10, 95% CI: 1.41-3.42] but became slightly attenuated in the rural site [OR: 1.45, 95% CI: 1.03-2.04]. The risk of atopy was also increased in older children [OR: 1.76, 95% CI: 1.00-3.07] and those with a family history of asthma [OR: 1.58, 95% CI: 1.01-2.47] in the urban site. On stratifying by sex, the effect of older age on atopy remained significant only among males (Table G1). Though the increased risk of atopy in older urban children persisted after multivariate adjustment [OR: 1.89, 95% CI: 1.05-3.42], the effect of family history of asthma became slightly attenuated [OR: 1.54, 95% CI: 0.97-2.46].

No regular trend was observed across the levels of parent's occupation and atopy in univariate analysis. On recoding parent's occupation into a binary variable (unemployed and employed) however, the risk of atopy was observed to be decreased [OR: 0.33, 95% CI: 0.12-0.93] in urban participants with an employed parent. Stratified analysis showed this effect to be present only in females (Table G1). In the rural site, co-infection with two or more intestinal parasites was also associated with an increased odds of atopy [OR: 2.47, 95% CI: 1.01-6.04]. This effect was however attenuated after multivariate adjustment [OR: 2.23, 95% CI: 0.80-5.58].

Table 3.6: Factors associated with atopy in univariate and multivariate analysis among children aged 6-15 years living urban and rural areas in the Greater Accra Region of Ghana

	Univariate Analysis						Multivariate Analysis			
Variable	**Combined OR (95% CI)**	**p-value**	**Urban OR (95% CI)**	**p-value**	**Rural OR (95% CI)**	**p-value**	**Urban OR (95% CI)**	**p-value**	**Rural OR* (95% CI)**	**p-value**
Sex										
Female	1		1		1		1		1	
Male	1.66 (1.29-2.13)	< 0.001	1.90 (1.30-2.79)	< 0.001	1.49 (1.06-2.08)	0.020	2.10 (1.41-3.42)	< 0.000	1.45 (1.03-2.04)	0.032
Age										
6 – 8 years	1		1		1		1		1	
9 – 11 years	1.13 (0.80-1.58)	0.491	1.12 (0.61-2.05)	0.707	1.15 (0.76-1.75)	0.507	1.19 (0.63-2.24)	0.591	1.18 (0.76-1.82)	0.462
12 – 15 years	1.35 (0.96-1.90)	0.086	1.76 (1.00-3.07)	0.048	1.32 (0.83-2.09)	0.235	1.89 (1.05-3.42)	0.035	1.28 (0.79-2.07)	0.319
Passive smoking										
Non-exposed	1		1		1		-		1	
Exposed	1.00 (0.71-1.42)	0.969	0.78 (0.50-1.23)	0.285	1.54 (0.89-2.66)	0.122			1.56 (0.89-2.72)	0.121
Family history of asthma										
No	1		1		1		1		1	
Yes	1.57 (1.10-2.23)	0.012	1.58 (1.01-2.47)	0.046	1.52 (0.86-2.67)	0.150	1.54 (0.97-2.46)	0.070	1.41 (0.79-2.53)	0.243
No idea	1.04 (0.61-1.78)	0.873	0.80 (0.39-1.65)	0.548	1.53 (0.67-3.46)	0.310	0.68 (0.32-1.43)	0.311	1.56 (0.68-3.60)	0.292
Source of domestic fuel										
LPG	1		1		1					
Charcoal	0.78 (0.53-1.16)	0.228	0.75 (0.47-1.19)	0.223	0.88 (0.09-8.29)	0.910				
Firewood	1.19 (0.81-1.75)	0.367	0.52 (0.22-1.28)	0.154	1.45 (0.16-13.29)	0.741				

Table 3.6: continued

	Univariate Analysis						Multivariate Analysis			
Variable	**Combined OR (95% CI)**	**p-value**	**Urban OR (95% CI)**	**p-value**	**Rural OR (95% CI)**	**p-value**	**Urban OR* (95% CI)**	**p-value**	**Rural OR* (95% CI)**	**p-value**
Intestinal parasite infection										
Not infected	1		1		1		-		1	
Hookworm	1.66 (1.02-2.68)	0.039	1.39 (0.38-5.13)	0.621	1.43 (0.84-2.45)	0.192			1.34 (0.77-2.33)	0.303
Trichuris	1.54 (0.54-4.28)	0.414	-		1.50 (0.51-4.41)	0.463			1.50 (0.50-4.50)	0.466
Ascaris	1.03 (0.61-1.74)	0.911	-		0.85 (0.49-1.47)	0.553			0.77 (0.45-1.38)	0.401
Co-infected	2.41 (1.04-5.58)	0.040	-		2.47 (1.01-6.04)	0.047			2.23 (0.80-5.58)	0.085
***S. haematobium* infection**										
No	1		1		1					
Yes	1.04 (0.62-1.74)	0.886	0.81 (0.23-2.80)	0.736	0.93 (0.52-1.65)	0.795				
Occupational status of parent										
Unemployed	1		1		1		1		-	
Employed	0.59 (0.27-1.31)	0.193	0.33 (0.12-0.93)	0.036	1.13 (0.31-4.12)	0.852	0.33 (0.11-1.00)	0.050		
Educational level of parent										
No formal education	1		1		1					
7-9 years education	0.92 (0.62-1.36)	0.662	0.76 (0.43-1.37)	0.366	1.09 (0.64-1.87)	0.752				
10-15 years education	0.94 (0.58-1.50)	0.784	0.43 (0.18-1.06)	0.066	1.32 (0.74-2.37)	0.351				
Tertiary education	1.09 (0.67-1.76)	0.734	0.78 (0.38-1.59)	0.490	1.51 (0.79-2.90)	0.216				
Nutritional status indicators										
Normal weight	1		1		1		1		1	
Underweight	0.61 (0.36-1.04)	0.070	0.58 (0.30-1.12)	0.105	1.08 (0.42-2.78)	0.880	0.52 (0.26-1.02)	0.057	1.07 (0.40-2.83)	0.894
Obese	1.12 (0.78-1.60)	0.536	1.00 (0.55-1.83)	0.985	1.13 (0.73-1.77)	0.581	1.23 (0.66-2.29)	0.512	1.17 (0.73-1.87)	0.517

3.7.0 Effect of missing observations

In order to investigate the effect of missing observations on the outcome, the model containing atopy, age, sex and nutritional status indicators was adjusted for each confounding variable in a stepwise manner. The p-value corresponding to the dummy values of missing observations was then examined for significance at the level of 5%. In the rural site, the p-values for passive smoking, parasite infection and family history of asthma in the adjusted models were 0.159, 0.309 and 0.110 respectively. The p-values for family history of asthma, educational level of parent and occupation of parent in the urban site were respectively 0.475, 0.432 and 0.067. This implies missing observations of the adjusted variables did not influence the results of the analysis in this study.

CHAPTER FOUR

DISCUSSION

This study sought to determine the prevalence of atopy and BMI percentiles as well as investigate the association between childhood obesity and atopy in a population of Ghanaian school children living in rural and urban areas in the Greater Accra Region. The main findings of the study are that the prevalence of atopy and obesity were higher in the rural than the urban sites and there was no association between childhood obesity and atopy. However, univariate analysis showed significant associations between atopy and male sex, older age, family history of asthma and occupational status of parents in the urban site, whilst male sex and co-infection with intestinal parasites were significantly associated with atopy in the rural site. The effect of these variables was only slightly altered after multivariate adjustment.

Previous studies investigating the risk factors for atopy suggested that urbanization may have an important role in the expression of the atopic phenotype; a conclusion which was reached mainly after observing the high prevalence of allergic asthma cases among inner city residents (7,19). Hence, the focus of most studies has been on identifying the features of urban lifestyle that allows the expression of the atopic phenotype (19). Rural areas on the other hand, were generally considered to be 'protective' as far as the risk of allergen sensitization was concerned (7, 8). The observation of a higher prevalence of atopy among rural participants in this study therefore contradicts the findings of previous studies in Ghana (5) and other parts of Africa (8, 12) and the reasons for this are not directly obvious.

The lower levels of atopic sensitization observed by previous studies in rural areas were mainly attributed to factors such as helminth infections (10). More recent studies have also implicated differences in diet as a possible reason for the rural-urban difference in the prevalence of atopy (35). In this study, co-infection with intestinal helminths was positively associated with atopy in univariate analysis; a finding which is in line with previous studies which have reported a positive association between light acute helminth infections and atopic sensitization (29). Though the effect of diet on atopy could not be explored in this study, there was some trend in the frequency and pattern of diet consumption. Further studies on diet taking factors such as the quantity and frequency of consumption into account may be helpful.

Factors such as higher socio-economic status and exposure to modern sources of domestic fuel have also been implicated with higher levels of atopic sensitization (19, 30). In this study, common markers of socioeconomic status such as educational levels and occupation of parents as well as type of domestic fuel were used to assess socio-economic levels. Moreover, the recruitment of participants from rural and urban areas was supposed to reflect the different socio-economic backgrounds of the study participants. Though occupational status of parents was found to be negatively associated with atopy among females in the urban site, domestic fuel and educational level of parents did not have any significant effect on atopy. However, it is possible that these factors did not reflect the actual socio-economic levels of the study population. Despite the differences in basic infrastructure and lifestyles in the urban and rural sites, the rural participants were also involved in several economic activities and it is possible that the gains from these improved their socio-economic levels considerably. Therefore, further studies into the markers of socio-economic status specific to the Ghanaian society are required.

Consistent with the findings of other studies, male sex was observed to be positively associated with atopy (47). Moreover, a family history of asthma increases susceptibility to atopy whilst the risk of atopy also increases in older children (7, 19). The allergens to which participants were most sensitized (cockroach and dust mite) are also consistent with the findings of previous studies (7). Whereas the prevalence of dust mite sensitization was the same in the rural and urban sites, cockroach sensitization was higher in the rural site. In previous studies, dust mite sensitization was often more common in urban areas whilst cockroach allergen has been associated with participants from lower socio-economic levels (7, 10).

Previous studies on obesity have mostly reported higher prevalence in urban settings (37). In this study however, a higher prevalence of obesity was observed in the rural site. Moreover, male sex and passive smoking (in the urban site) as well as older age (in the rural site) were found to be negatively associated with obesity. Though dietary factors and sedentary lifestyles have been implicated in obesity (37), the effect of these factors could not be assessed in the current study. Rural residence in Africa is normally associated with traditional lifestyles such as the consumption of a more traditional diet compared to urban residence. Though energy-dense and fatty foods have been associated with obesity in some studies, the difficulty in measuring diet limits studies on the role of diet on obesity (37). Moreover, the potential for reverse causality in such studies is usually high. In this study, the information collected on dietary intake could not be used in the analysis; hence the effect of diet on obesity could not be determined in the study population.

Lower levels of physical activity are also associated with obesity. In this study however, one would rather have expected children in the rural site to have higher levels of physical activity. The rural site was a coastal community where most people were involved in agricultural activities (such as farming and fishing) and salt mining. In rural settings, children are normally expected to contribute to the work in the household which includes helping parents on the farm, fetching water from the riverside and even joining their fathers on fishing expeditions. Moreover, most children in rural areas walk over long distances to school. Hence the negative association between older age and obesity in the rural site might be due to higher levels of physical activity in older children. Regardless of this, no effect was observed between the proxy measure of physical activity in this study and obesity. A more detailed study measuring the physical activity levels among rural and urban residents is required.

Since children in the rural site were generally shorter than their urban counterparts, there is the possibility that they suffered from chronic malnutrition (which could be caused by helminth infections). It is also possible that there had been an improvement in food supply, which would result in an increase in body weight but not height. This notwithstanding, it is noteworthy that statistical rather than biological grounds are used in estimating obesity in children (37) and it is a measure of excess weight rather than excess body fat. However, there is the possibility that the higher prevalence of obesity in the rural site could have been due to ethnic differences in weight or an indication of economic development. Studies have shown that in developing countries, the burden of obesity tends to shift towards the poor as economic development increases (37). The negative association between male sex as well as passive smoking and obesity are also consistent with the findings of previous studies (44). Studies which investigated the relationship between cigarette smoking and body weight have shown that smoking is inversely associated with obesity; an observation which has been attributed to the effect of nicotine on neurotransmitters. Inhalation of nicotine in cigarette smoke has been shown to induce an acute elevation of the concentration of neurotransmitters such as dopamine and serotonin (which are appetite suppressants). Hence, there is loss of appetite in smokers (59). It is possible that the observed inverse association between passive smoking and obesity in this study could be due to the same mechanism.

Results of studies which have investigated the association between anthropometric indicators and atopy have been inconsistent. Whereas some studies observed a positive association between obesity and atopy (47, 49), other studies found no effect (50, 51). In cases where an association was observed, there was often effect modification by sex. In the current study, no association was observed between obesity and atopy. Though the reasons for this observation are not directly obvious, it is possible that confounding by certain underlying factors which were not measured in this study may have accounted for the lack of effect.

The major strengths of the current study include the standardization of skin prick testing which could have reduced the individual variation in the performance of the test. Moreover, racial variation in skin test responses to histamine and allergens has been suggested by some studies although; this has not been studied in detail (11). Hence, the high number of negative skin test responses to histamine might have been due to factors other than anti-histamine medication use. The use of a high cut-off point in defining atopy could also have reduced the potential for misclassification of participants with dermatographism. The use of a standardized questionnaire and the training of interviewers to administer the questionnaires in a standardized way is also a strength of this study.

This study is however limited by factors such as the low response rate in the urban site, the high number of missing observations in the rural site and the use of secondary data. Possible reasons for the low response rate include the fact that whereas parents from lower socio-economic levels regard research as an easier means of getting free access to health care, parents in high socio-economic levels, who already have easy access to health care do not easily consent for their wards to participate in research programmes. Hence participants who were recruited from the urban private schools were more likely to be the wards of parents who were really interested in the study. It is therefore possible that the observed prevalence of obesity and atopy in the urban site did not reflect the true prevalence of these conditions and that associations observed between obesity and atopy might be biased.

Moreover, since this study could only use information collected in the original study, it was limited with respect to certain information; the levels of physical activity of participants were not measured in the original study. Though information on the frequency of dietary intake was collected in the original study, the quantity of dietary intake was not measured. Hence, it was not possible to assess more thorough reasons potentially explaining the observed difference in the prevalence of obesity between the rural and urban participants.

Conclusion

This study indicates that obesity is not associated with atopy in a population of Ghanaian school children. However, the burden of obesity and atopy may not be limited to urban areas. It is possible that the burden of these health problems is shifting towards the poor.

Recommendations

Future studies investigating the association between obesity and atopy in Ghana should aim to

- Employ/ develop methods ensuring representative recruiting across the population, i.e. increase participation rate in urban affluent settings where people do not easily participate in research programmes.
- Include measures of important confounders and risk factors for obesity such as level of physical as well as the frequency and quantity of dietary intake.
- Develop specific markers for measuring socio-economic levels
- Develop more specific measures of obesity which can indicate body fat and not just body weight.
- Develop methods with a high sensitivity and specificity to assess atopy in developing country settings, to determine factors associated with the predictive value of atopy in and between developing countries and assess racial and geographical differences in skin test reactivity to histamine and allergens.

Moreover, hygienic conditions in homes and schools should be improved in order to minimize exposure to cockroaches and dust mites.

APPENDIX A

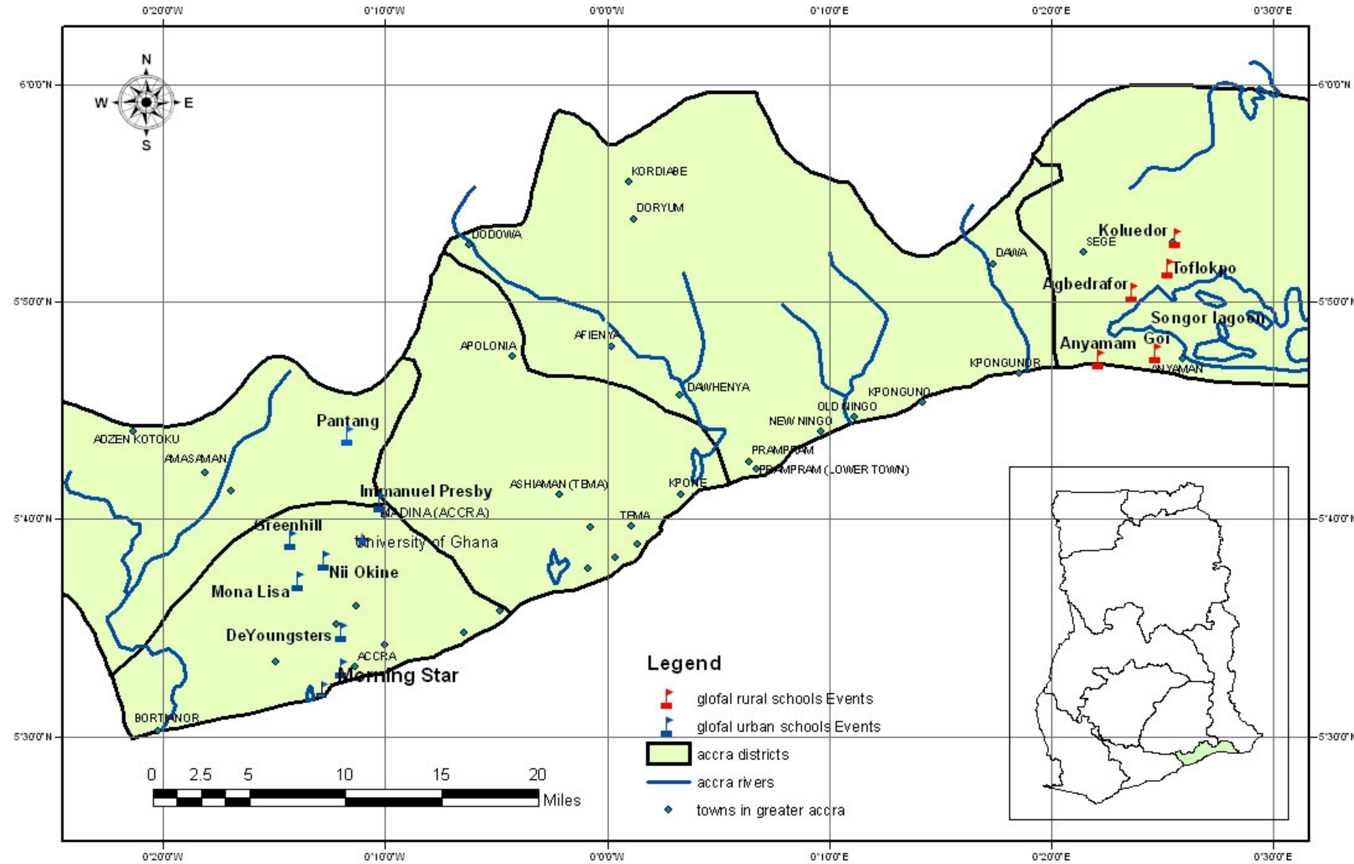


Figure A1: Map of the Greater Accra Region showing the recruited schools in the urban and rural sites

APPENDIX B

Table B1: Skin Prick Testing Record Sheet A

Subject ID:	Date of Test:
Subject Age:	Initials of Pricker:
Subject Sex :	Initials of Reader
Time (Start):	Time (End):

Negative Control	Pawpaw
Peanut (ALK)	Orange
Mango	Cockroach
Banana	Mite Mix
Pineapple	Histamine (ALK)
Apple	

Table B2: Skin Prick Testing Record Sheet B

Subject ID:	Date of Test:
Subject Age:	Initials of Pricker:
Subject Sex :	Initials of Reader
Time (Start):	Time (End):

Negative Control
Pawpaw
Orange
Mango
Banana
Pineapple
Apple

Peanut (ALK)
Cockroach
Mite Mix
Histamine (ALK)

Table B3: Skin Prick Testing Record Sheet C

Subject ID:	Date of Test:
Subject Age:	Initials of Pricker:
Subject Sex :	Initials of Reader
Time (Start):	Time (End):

Negative Control
Peanut (ALK)
Mango
Banana
Cockroach
Mite Mix

Pawpaw
Orange
Pineapple
Apple
Histamine (ALK)

Table B4: Skin Prick Testing Record Sheet D

Subject ID:	Date of Test:
Subject Age:	Initials of Pricker:
Subject Sex :	Initials of Reader
Time (Start):	Time (End):

Negative Control
Peanut (ALK)
Mango
Banana
Pineapple
Apple

Histamine (ALK)
Cockroach
Mite Mix
Pawpaw
Orange

APPENDIX C

GLOFAL
Questionnaire for Allergic Diseases
Multi-Centre Study

Date : __ __/ __ __/ __ __ __ __ **Country:** *GHANA*

Name of interviewer : __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __

Name of Recorder : __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __

A. Child's Details

1. Name / ID number :__ __ __ __ __ __ __ __ __ __ __ __ __ __/ __ __ __ __ __
2. Date of birth / Age : __ __/ __ __/ __ __ __ __ [ ] years
3. Place of Birth (including Region): __ __ __ __ __ __ __ __ __ __ __ __ __ __ __

   [Indicate Country of Birth IF NOT Ghana]: __ __ __ __ __ __ __ __ __ __ __ __
4. Ethnicity **:** __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __

   [Indicate Country of Origin IF NOT Ghana**]**
5. Sex : [ ] Male [ ] Female
6. What is the position of this child in sib-ship? : __ __ __ __ of __ __ __ children
7. School information
   Class : __ __ __ __ __ __ __ __
   Name of school : __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __ __
8. House information
   House Number : __ __ __ __ __ __ __ __
   Suburb/ Area : __ __ __ __ __ __ __ __
   Telephone : __ __ __ __ __ __ __ __

   GPS Readings
   a. Latitude : __ __ __ __ __ __ __ __
   b. Longitude : __ __ __ __ __ __ __ __
   c. Altitude : __ __ __ __ __ __ __ __
9. How far is the school from home (GPS reading)? : __ __ __ __ __ __ __ Km

10. How does the child get to school most of the time?
    - [ ] walk
    - [ ] bicycle
    - [ ] Taxi
    - [ ] Bus / Trotro
    - [ ] Private Car
    - [ ] Other, please specify __ __ __ __ __ __ __ __ __ __

B. Health Concerns

1. Is there any smoker in your house **[ ]Yes [ ]No**

2. If you answered "yes" to question 1, does this person smoke in the presence of the child?
   [ ] Yes [ ] No

3. Is this child exposed to tobacco smoke outside your home?
   [ ] Yes [ ] No [ ] No idea

4. Has any member of this child's family ever had asthma?
   [ ] Yes [ ] No [ ] No idea

5. If you answered "yes" to question 4, indicate relationship to child (*tick all that apply*)
   - [ ] Father
   - [ ] Mother
   - [ ] Brother or Sister
   - [ ] Father's __ __ __ __ __ __ __ __ __ (family member e.g. sister, father)
   - [ ] Mother's __ __ __ __ __ __ __ __ __(family member e.g. sister, father)

C. Early Life Factors

For the following questions please ask to see the ***child's weighing card***.

Is the child's weighing card available? [ ] Yes [ ] No

1. What was your child's weight at birth? _________ kg. Date Recorded ____/____/____

2. After birth, when did your child START breastfeeding:
   [ ] After Hours [ ] After Days [ ] After Weeks

3. For how long was your child breast-fed? Duration________ (in months)

4. For how long was your child fed with ONLY breast-milk? Duration ____ (in months)

D. Socio-economic status

1. Who provides financially for this child?
   [ ] Father and mother
   [ ] Father
   [ ] Mother
   [ ] Other, please specify: __ __ __ __ __ __ __ __ __ __ __ __ __

2. Occupation of person in question number 1: __ __ __ __ __ __ __ __ __ __ __ __ __

   Occupation of the spouse of this person: __ __ __ __ __ __ __ __ __ __ __ __ __ __

3. What is the highest level of formal education completed by person (in question 1)
   [ ] primary/elementary
   [ ] middle school
   [ ] JSS
   [ ] SSS
   [ ] O'level
   [ ] A'level
   [ ] vocational/ commercial
   [ ] Training College
   [ ] Polytechnic/University [ ] other, please specify__ __ __ __ __ __ __ __

4. What is the highest level of formal education completed by the spouse of this person:
   [ ] primary/elementary
   [ ] middle school
   [ ] JSS
   [ ] SSS
   [ ] O'level
   [ ] A'level
   [ ] vocational/ commercial
   [ ] Training College
   [ ] Polytechnic/University [ ] other, please specify__ __ __ __ __ __ __ __

5. The fuel mostly used at home for cooking is*(tick all that apply):*
   [ ] LPG [ ] Electricity [ ] Charcoal [ ] Firewood

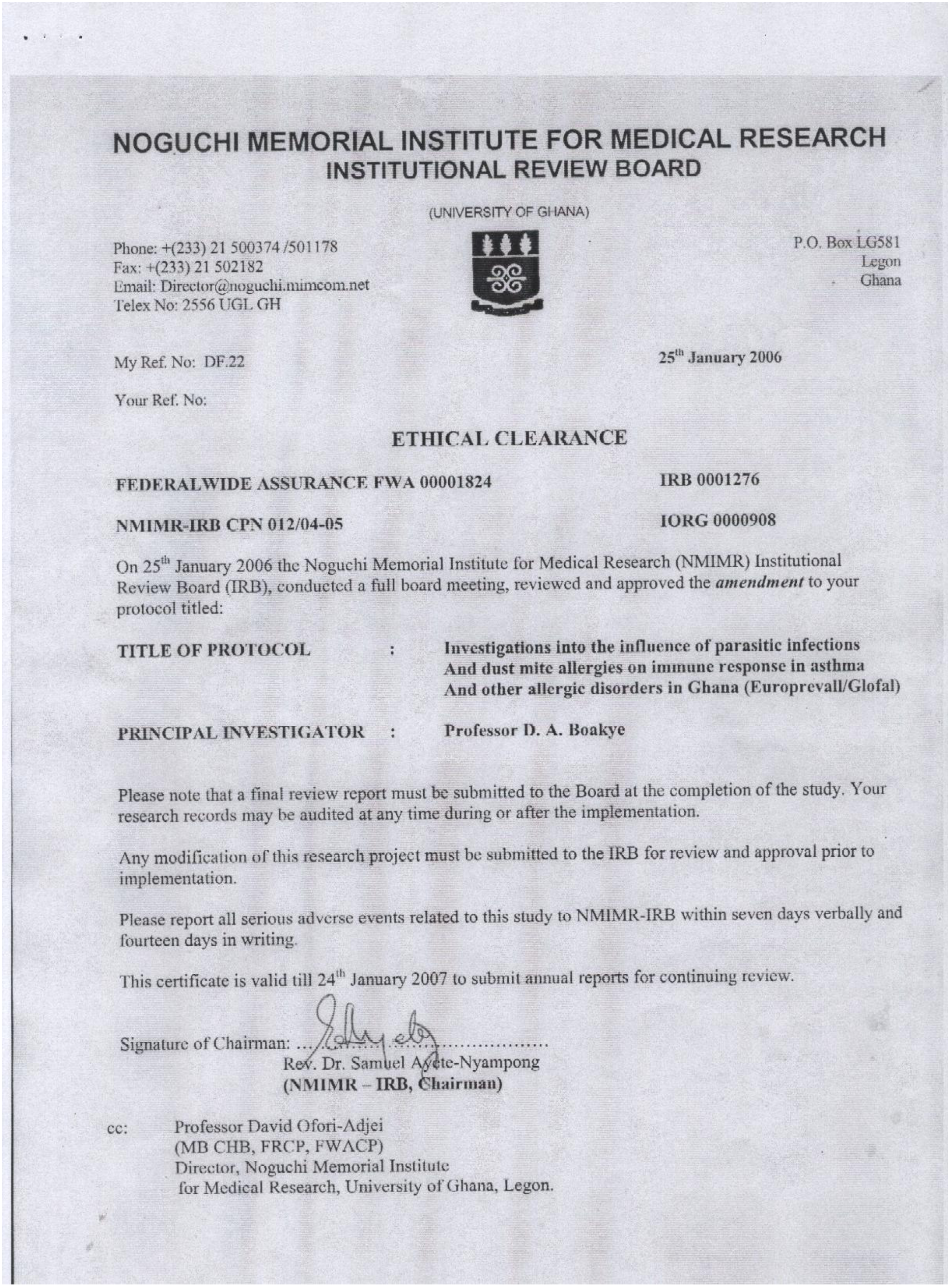
   [ ] Kerosene [ ] other, please specify__ __ __ __ __ __ ____ __ __

APPENDIX C

E. Diet

Food Item	Frequency of Consumption				
	Daily	***1x weekly (at least***	***1x monthly (at least)***	***Every half year (at least***	**Never**
Staples					
Maize/ Corn	[ ]	[ ]	[ ]	[ ]	[ ]
Cassava	[ ]	[ ]	[ ]	[ ]	[ ]
Yam	[ ]	[ ]	[ ]	[ ]	[ ]
Rice	[ ]	[ ]	[ ]	[ ]	[ ]
Plantain	[ ]	[ ]	[ ]	[ ]	[ ]
Other____	[ ]	[ ]	[ ]	[ ]	[ ]
Meat/Protein Source					
Fish	[ ]	[ ]	[ ]	[ ]	[ ]
Chicken	[ ]	[ ]	[ ]	[ ]	[ ]
Mutton	[ ]	[ ]	[ ]	[ ]	[ ]
Beef	[ ]	[ ]	[ ]	[ ]	[ ]
Chevron	[ ]	[ ]	[ ]	[ ]	[ ]
Shellfish	[ ]	[ ]	[ ]	[ ]	[ ]
Other______	[ ]	[ ]	[ ]	[ ]	[ ]
Fresh Fruits					
Orange	[ ]	[ ]	[ ]	[ ]	[ ]
Mango	[ ]	[ ]	[ ]	[ ]	[ ]
Pawpaw	[ ]	[ ]	[ ]	[ ]	[ ]
Pineapple	[ ]	[ ]	[ ]	[ ]	[ ]
Banana	[ ]	[ ]	[ ]	[ ]	[ ]
Apple	[ ]	[ ]	[ ]	[ ]	[ ]
Other______	[ ]	[ ]	[ ]	[ ]	[ ]
Fresh Vegetables					
Pepper	[ ]	[ ]	[ ]	[ ]	[ ]
Salads	[ ]	[ ]	[ ]	[ ]	[ ]

APPENDIX D



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Telex No: 2556 UGL GH

P.O. Box LG581
Legon
Ghana

My Ref. No: DF.22

25th January 2006

Your Ref. No:

ETHICAL CLEARANCE

FEDERALWIDE ASSURANCE FWA 00001824 **IRB 0001276**

NMIMR-IRB CPN 012/04-05 **IORG 0000908**

On 25th January 2006 the Noguchi Memorial Institute for Medical Research (NMIMR) Institutional Review Board (IRB), conducted a full board meeting, reviewed and approved the ***amendment*** to your protocol titled:

TITLE OF PROTOCOL : **Investigations into the influence of parasitic infections And dust mite allergies on immune response in asthma And other allergic disorders in Ghana (Europrevall/Glofal)**

PRINCIPAL INVESTIGATOR : **Professor D. A. Boakye**

Please note that a final review report must be submitted to the Board at the completion of the study. Your research records may be audited at any time during or after the implementation.

Any modification of this research project must be submitted to the IRB for review and approval prior to implementation.

Please report all serious adverse events related to this study to NMIMR-IRB within seven days verbally and fourteen days in writing.

This certificate is valid till 24th January 2007 to submit annual reports for continuing review.

Signature of Chairman: ....
Rev. Dr. Samuel Ayete-Nyampong
(NMIMR – IRB, Chairman)

cc: Professor David Ofori-Adjei
(MB CHB, FRCP, FWACP)
Director, Noguchi Memorial Institute
for Medical Research, University of Ghana, Legon.

Figure D1: Ethics clearance certificate for the original study

APPENDIX D

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Larbi

CLEARANCE CERTIFICATE **PROTOCOL NUMBER M071145**

PROJECT Association between Childhood Obesity and Atopy among School Children aged 6-15 Years Living in Rural & Urban areas in Ghana 2006

INVESTIGATORS Miss IA Larbi

DEPARTMENT School of Public Health

DATE CONSIDERED 07.11.30

DECISION OF THE COMMITTEE* APPROVED SUBJECT TO: State for what degree this is

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 07.12.07 **CHAIRPERSON** ....
(Professors PE Cleaton-Jones, A Dhai, M Vorster, C Feldman, A Woodiwiss)

*Guidelines for written 'informed consent' attached where applicable

cc: Supervisor : Prof KK Grobusch

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10005, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Figure D2: Ethics clearance certificate for secondary data analysis

APPENDIX E

Table E1: Factors associated with obesity in univariate and multivariate analysis in school children aged 6-15 years in rural and urban areas in the Greater Accra Region of Ghana

	Univariate Analysis			Multivariate Analysis	
Variable	**Combined OR (95% CI) p-value**	**Urban OR (95% CI) p-value**	**Rural OR (95% CI) p-value**	**Urban OR (95% CI) p-value**	**Rural OR (95% CI) p-value**
Sex					
Female	1	1	1	1	1
Male	0.97 (0.72-1.31) 0.840	0.54 (0.33-0.89) 0.015	1.43 (0.96-2.12) 0.080	0.60 (0.39-0.92) 0.020	1.72 (1.14-2.57) 0.008
Age					
6 – 8 years	1	1	1	1	1
9 – 11 years	0.40 (0.28-0.57) < 0.000	0.88 (0.46-1.69) 0.698	0.27 (0.18-0.42) < 0.000	1.05 (0.58-1.89) 0.880	0.30 (0.19-0.47) < 0.000
12 – 15 years	0.41 (0.28-0.60) < 0.000	0.84 (0.45-1.58) 0.595	0.31 (0.18-0.52) < 0.000	1.21 (0.69-2.12) 0.513	0.32 (0.19-0.55) <0.000
Passive smoking					
Non-exposed	1	1	1	1	1
Exposed	0.52 (0.32-0.86) 0.011	0.51 (0.27-0.97) 0.039	0.55 (0.24-1.24) 0.150	0.52 (0.30-0.91) 0.022	0.58 (0.26-1.30) 0.184
Exclusive Breast feeding					
None	1	1	1		
1-6 months	0.93 (0.55-1.58) 0.797	0.96 (0.44-2.12) 0.929	0.76 (0.37-1.56) 0.447		
6-12 months	0.78 (0.37-1.62) 0.501	0.44 (0.11-1.72) 0.239	0.86 (0.33-2.21) 0.755		
Family History of asthma					
No	1	1	1		1
Yes	1.05 (0.66-1.66) 0.851	0.65 (0.34-1.24) 0.190	1.91 (0.94-3.90) 0.075		1.84 (0.90-3.76) 0.095
No idea	1.03 (0.53-2.00) 0.933	0.98 (0.44-2.18) 0.951	1.15 (0.36-3.66) 0.807		1.00 (0.30-3.13) 0.966

Table E1: continued

	Univariate Analysis						Multivariate Analysis			
Variable	**Combined** OR (95% CI)	p-value	**Urban** OR (95% CI)	p-value	**Rural** OR (95% CI)	p-value	**Urban** OR (95% CI)	p-value	**Rural** OR (95% CI)	p-value
***S. haematobium* infection**										
No	1		1		1				1	
Yes	0.71 (0.35-1.44)	0.341	1.46 (0.42-5.10)	0.553	0.47 (0.20-1.11)	0.085			0.57 (0.25-1.31)	0.183
Intestinal parasite infection										
Not infected	1		1		1				1	
Hookworm	0.59 (0.27-1.29)	0.186	0.69 (0.88-5.39)	0.724	0.46 (0.19-1.10)	0.082			0.50 (0.20-1.21)	0.124
Trichuris	1.37 (0.39-4.80)	0.620	-		1.24 (0.34-4.48)	0.740			1.32 (0.35-5.00)	0.687
Ascaris	2.00 (1.19-3.36)	0.009	-		1.57 (0.91-2.72)	0.108			1.26 (0.71-2.24)	0.423
Co-infected	1.37 (0.46-4.08)	0.568	-		1.27 (0.41-3.88)	0.679			1.52 (0.46-5.01)	0.488
Means of transportation to school										
Walking	1		1		1					
Bus/Taxi	0.99 (0.60-1.65)	0.977	1.07 (0.59-1.94)	0.824	-					
Private car	0.84 (0.43-1.65)	0.622	0.95 (0.46-1.97)	0.887	7.24 (0.44-118.1)	0.165				
Occupational status of parents										
Unemployed	1		1		1					
Employed	1.17 (0.40-3.42)	0.767	2.00 (0.26-15.48)	0.506	0.83 (0.23-3.05)	0.784				
Educational level of parent										
No education	1		1		1					
7-9 years	1.19 (0.76-1.85)	0.439	1.08 (0.54-2.16)	0.832	1.34 (0.75-2.39)	0.319				
10-15 years	0.90 (0.52-1.56)	0.704	0.70 (0.26-1.91)	0.489	0.97 (0.49-1.90)	0.918				
Tertiary	1.18 (0.68-2.03)	0.561	0.90 (0.37-2.16)	0.806	1.53 (0.75-3.10)	0.239				

Table F1: Frequency of dietary intake among school children aged 6-15 years in rural and urban areas in the Greater Accra Region of Ghana

Diet	Urban Site				Rural Site			
	Frequency of Dietary Intake, n (%)				Frequency of Dietary Intake, n (%)			
	Daily	**Weekly**	**Monthly**	**Missing observations**	**Daily**	**Weekly**	**Monthly**	**Missing observations**
Fresh fruits	263 (35.44)	295 (39.76)	44 (5.99)	140 (18.87)	203 (27.43)	153 (20.68)	36 (4.86)	348 (47.08)
Fresh vegetables	102 (13.75)	316 (42.59)	184 (24.80)	140 (18.87)	246 (33.24)	91 (12.30)	55 (7.43)	348 (47.03)
Sources of Protein								
Fish	487 (65.63)	89 (11.99)	26 (3.50)	140 (18.87)	383 (51.76)	0 (0.00)	9 (1.22)	348 (47.03)
Chicken	60 (8.09)	346 (46.63)	196 (26.42)	140 (18.87)	53 (7.16)	150 (20.27)	189 (25.54)	348 (47.03)
Mutton	0 (0.00)	57 (7.68)	545 (73.45)	140 (18.87)	5 (0.68)	34 (4.59)	353 (47.70)	348 (47.03)
Beef	37 (4.99)	244 (36.93)	291 (39.22)	140 (18.87)	47 (6.35)	128 (17.30)	217 (29.32)	348 (47.03)
Chevron	1 (0.13)	91 (12.26)	510 (68.73)	140 (18.87)	8 (1.08)	52 (7.03)	332 (44.86)	348 (47.03)
Staples								
Maize	144 (19.14)	414 (55.80)	44 (5.93)	140 (18.87)	364 (49.19)	20 (2.70)	8 (1.08)	348 (47.03)
Cassava*	60 (8.09)	467 (62.94)	75 (10.11)	140 (18.87)	322 (43.51)	45 (6.08)	25(3.38)	348 (47.03)
Yam	17 (2.29)	447 (60.24)	138 (18.60)	140 (18.87)	22 (2.97)	134 (18.11)	236 (31.89)	348 (47.03)
Rice	319 (42.99)	271 (36.52)	12 (1.62)	140 (18.87)	215 (29.05)	146 (19.73)	31 (4.19)	348 (47.03)
Plantain*	58 (7.82)	460 (61.99)	84 (11.32)	140 (18.87)	26 (3.51)	134 (18.11)	232 (31.35)	348 (47.03)

*Cassava: *Manihot esculenta*; * Plantain: *Musa paradisiaca*

APPENDIX G

Table G1: Factors associated with atopy in univariate analysis in children aged 6-15 years in urban and rural areas in the Greater Accra Region of Ghana

Variable	**Urban Site OR (95 % CI) p-value**						**Rural Site OR (95 % CI) p-value**					
	Males		**Females**		**Total**		**Males**		**Females**		**Total**	
Nutritional status												
Normal weight	1		1		1		1		1		1	
Under weight	0.48(0.22-1.07)	0.073	0.59(0.17-2.02)	0.402	0.58(0.30-1.12)	0.105	1.54(0.36-6.58)	0.562	0.90(0.25-3.30)	0.879	1.08(0.42-2.78)	0.880
Obese	1.08(0.44-2.67)	0.872	1.12(0.49-2.55)	0.784	1.00(0.55-1.83)	0.985	1.20(0.67-2.13)	0.545	0.97(0.47-2.00)	0.935	1.13(0.73-1.77)	0.581
Age												
6 – 8 years	1		1		1		1		1		1	
9 – 11 years	1.35(0.60-3.01)	0.466	0.88(0.35-2.20)	0.777	1.12(0.61-2.05)	0.707	1.45(0.82-2.58)	0.204	0.90(0.49-1.67)	0.747	1.15(0.76-1.75)	0.507
12 – 15 years	2.18(1.02-4.66)	0.044	1.44(0.62-3.30)	0.395	1.76(1.00-3.07)	0.048	1.16(0.61-2.19)	0.645	1.50(0.78-2.92)	0.227	1.32(0.83-2.09)	0.235
Passive smoking												
Non-exposed	1		1		1		1		1		1	
Exposed	0.87(0.48-1.55)	0.628	0.64(0.31-1.33)	0.232	0.78 (0.50-1.22)	0.285	1.64(0.75-3.60)	0.215	1.46(0.68-3.13)	0.334	1.54(0.89-2.66)	0.122
Exclusive breast feeding												
None	1		1		1		1		1		1	
1-6 months	1.00(0.39-2.55)	0.998	1.91(0.54-6.79)	0.316	1.29(0.62-2.70)	0.497	1.00(0.40-2.53)	0.994	1.04(0.36-3.01)	0.937	1.01(0.51-2.03)	0.967
6 -12 months	0.89(0.26-3.00)	0.851	2.18(0.40-11.92)	0.370	1.34(0.50-3.57)	0.559	0.27(0.05-1.47)	0.130	0.77(0.20-2.94)	0.700	0.52(0.19-1.41)	0.200
Family history of asthma												
No	1		1		1		1		1		1	
Yes	1.52(0.84-2.74)	0.169	1.47(0.72-3.00)	0.290	1.58(1.01-2.47)	0.046	1.57(0.70-3.51)	0.273	1.46(0.66-3.24)	0.353	1.52(0.86-2.67)	0.150
No idea	0.51(0.18-1.41)	0.192	1.24(0.44-3.51)	0.681	0.80(0.39-1.65)	0.548	1.57(0.49-5.07)	0.452	1.49(0.47-4.67)	0.496	1.53(0.67-3.46)	0.310
Source of domestic fuel												
LPG	1		1		1		1		1		1	
Charcoal	0.70(0.37-1.33)	0.278	0.90(0.45-1.80)	0.760	0.75(0.47-1.19)	0.223	-		-		0.88(0.09-8.29)	0.910
Firewood	0.50(0.14-1.80)	0.289	0.64(0.18-2.25)	0.485	0.52(0.22-1.28)	0.154	-		-		1.45(0.16-13.27)	0.741

Table G1: continued

Variable	Urban Site OR (95 % CI) p-value Males	Females	Total	Rural Site OR (95 % CI) p-value Males	Females	Total
Highest educational level of parent						
No formal education	1	1	1	1	1	1
7-9 years	0.83(0.39-1.75) 0.625	0.69(0.26-1.83) 0.460	0.76(0.43-1.37) 0.366	0.45(0.20-1.01) 0.054	2.68(1.17-6.15)< 0.020	1.09(0.64-1.87)0.752
10-15 years	0.34(0.09-1.27) 0.108	0.62(0.18-2.16) 0.451	0.43(0.18-1.06) 0.066	1.13(0.51-2.49) 0.763	1.93(0.76-4.87) 0.167	1.32(0.74-2.37)0.351
Tertiary	0.68(0.26-1.77) 0.434	0.95(0.31-2.92) 0.932	0.78(0.38-1.59) 0.490	0.64(0.26-1.55) 0.320	4.89(1.73-13.80)<0.003	1.51(0.79-2.90)0.216
Occupational status of parent						
Unemployed	1	1	1	1	1	1
Employed	0.45 (0.10-1.94) 0.282	0.22(0.05-0.99) 0.048	0.33(0.12-0.93) 0.036	1.29(0.09-6.89) 0.749	0.89(0.09-8.68) 0.917	1.13(0.31-4.12)0.852
Intestinal parasites infection						
Not infected	1	1	1	1	1	1
Hookworm	1.39 (0.35-5.51) 0.641	-	1.39(0.38-5.13) 0.621	1.08(0.53-2.18) 0.839	1.84(0.79-4.25) 0.156	1.43(0.84-2.44)0.192
Trichuris	-	-	-	0.46(0.05-4.03) 0.484	3.13(0.85-11.57) 0.088	1.50(0.51-4.41)0.463
Ascaris	-	-	-	0.44(0.18-1.03) 0.060	1.52(0.73-3.16) 0.261	0.85(0.49-1.47)0.553
Co-infection	-	-	-	1.32(0.37-4.67) 0.670	4.69(1.30-16.93) 0.018	2.47(1.01-6.04)0.047
S. haematobium infection						
No	1	1	1	1	1	1
Yes	0.60 (0.13-2.80) 0.515	1.08(0.13-9.17) 0.943	0.81(0.23-2.80) 0.736	0.99(0.44-2.24) 0.982	0.90(0.39-2.04) 0.793	0.93(0.52-1.65)0.795
Means of transportation to school						
Walking	1	1	1	1	1	1
Bus/Taxi	0.83(0.49-1.57) 0.561	1.52(0.74-3.14) 0.255	1.07(0.67-1.71) 0.783	-	3.56(0.22-58.26) 0.374	
Private car	1.45(0.71-2.96) 0.302	1.47(0.63-3.40) 0.374	1.40(0.82-2.38) 0.219	-	0.94(0.57-1.54) 0.810	-

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