A REVIEW OF EPIDEMIOLOGICAL STUDIES OF ASTHMA IN GHANA

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SUMMARY

Context/Background: The last few decades have witnessed a rise in the global prevalence of asthma with a number of risk factors being linked to this increase. Although there is insufficient data on the prevalence of asthma in Ghana, a few studies conducted in this country have shed light on the disease aetiology and associated risk factors.

Evidence Acquisition: The purpose of this review is to explore the literature on epidemiological studies on asthma carried out in Ghana and how these findings fit into the wider context of observations from other countries.

Results: Asthma research in Ghana has focused mainly on children between the ages of 5-16 years with one published study that included adults. Different markers for the disease have been used such as clinician-diagnosed asthma, exercise-induced bronchospasm (EIB) as well as questionnaire-derived symptoms of asthma. Factors found to be associated with asthma in Ghana include atopic sensitisation to environmental allergens, inner-city residence and socioeconomic differences. Other implicated factors are family history of asthma, sib-ship position, breast-feeding duration and helminth infections.

Conclusions: Future research in Ghana must establish the burden of disease among all age-groups as well as clearly differentiate between allergic and non-allergic asthma. Studies are also needed to examine the role of environmental air pollutants on the disease's pathogenesis.

Keywords: Asthma, atopy, allergy, risk factors, urbanisation, Ghana, Sub-Saharan Africa

INTRODUCTION

Burden of Asthma

The World Health Organization (WHO) estimates that there are 300 million people world-wide suffering from asthma[1] with approximately 250,000 asthma-related annual deaths.[2] The last few decades have witnessed a rise in the global incidence of asthma particularly in industrialised nations.[3] This phenomenon, termed the 'asthma epidemic',[4] has come with an enormous economic burden due to the significant health-care utilisation associated with treatment of this condition.[5] The Global Initiative for Asthma (GINA) estimates that the global prevalence of asthma ranges from 1 to 18% of the total population of different countries.[6] Furthermore, studies indicate that asthma is not just a public health problem for high-income countries but is increasingly becoming widespread in the developing world with most asthma-related deaths occurring in low and lower-middle income countries including Sub-Saharan Africa.[1,7,8]

Currently, there is insufficient data on the national burden of asthma in Ghana. The 2005 WHO Ghana Country Office annual report highlighted the fact that data on non-communicable diseases in the country (including asthma) are scattered and not representative.[9] The WHO estimates an asthma country incidence rate of 1.5/1000 per year for Ghana compared to rates as low as 0.3/1000 per year for countries such as Greece and 2.8/1000 per year for Wales and New Zealand.[10]

Disease Aetiology and Risk Factors for Asthma

Asthma is a complex condition with no single biological marker and multiple aetiological causes[11] Its development is seen as an intricate interaction between genetic and environmental factors.[12] Atopy, the genetic tendency to develop Immunoglobulin E (IgE) antibodies in response to an allergen [13] is an important factor in allergic asthma aetiology.[14] During infancy, exposures to house-dust mite, animal dander or pollen in predisposed individuals can increase the risk of developing asthma.[11]

Identified risk factors for asthma include; family history of the disease[15], maternal smoking during pregnancy[16], reduced antioxidant intake [17,18], obesity [19], residence in an inner-city urban area [20], family size [21] and reduced exposure to childhood infections as postulated by the Hygiene Hypothesis.[22] Currently, the link between parasitic infections and asthma is also an active research area.[23]

However, it is estimated that less than 50% of all asthma cases are attributable to allergic mechanisms.[24] Although not well-characterised, non-allergic asthma is thought to be driven by neutrophil cells activated by environmental triggers such as pollutants [25] eventually leading to airway hyperresponsiveness.[26] In non-allergic asthma aetiology, environmental exposures such as bacterial endotoxins, particulate air pollution, ozone and viral infections appear to be important [25] but mechanisms remain unclear.

Epidemiological Studies On Asthma In Ghana

For this review, we conducted a literature search in PubMed (1950 to December 2010) to identify all published epidemiological studies on asthma carried out in Ghana. We also searched conference proceedings and student theses related to the topic.

Atopy and Asthma

The first published asthma investigation conducted in Ghana by Commey and Haddock was a hospital-based study in which asthmatic patients aged between 13-40 years in the city of Accra were skin prick tested for atopic sensitisation to the dustmite *Dermatophagoides farinae.* [27] The investigators found that 33% of individuals with doctor-diagnosed asthma were sensitised to *D. farinae* compared to 4.8% of a non-asthmatic control group.[27]

Addo-Yobo *et al* in 1993 examined the link between asthma and atopic sensitisation among urban as well as rural children aged 9 - 16 years in the Ashanti region. A total of 1095 school-children underwent exercise testing to determine the prevalence of exercise-induced bronchospasm (EIB), after which 916 of these were skin-prick tested for atopic sensitisation. The prevalence of EIB was 3.1% while atopic sensitisation was 4.4% with no significant differences in the prevalence of atopy between children with EIB and those without.[28] This was in contrast to the previous hospital-based study by Commey and Haddock but it was concluded that this could be as a result of inadequate power due to the small number of children with EIB.[28] In a follow-up study, Addo-Yobo *et al* also observed that seasonal change in Ghana had a marked effect on EIB reducing it from 3.1% in the dry season to 1.6% in the rainy season.[29]

In a 10 year follow-up to their 1993 study, Addo-Yobo and colleagues re-examined EIB among 1,848 school-children aged 9 - 16 years and found that EIB prevalence had increased from 3.1% to 5.2% while atopic sensitisation had changed from 4.4% [28] to 13.6%.[30] A notable finding of this later study was that atopic sensitisation was now significantly associated with EIB and was linked to a two-fold increase in the risk of EIB (OR= 2.10, 95% CI 1.29 – 3.42, $p<0.01$).[30] This may imply a transition from largely non-allergic EIB to more allergic EIB within this population over time. Other studies from Africa have made similar observations establishing associations between EIB and allergic sensitisation.[31,32]

Another study that has provided insights into the association between atopy and asthma in Ghana is the multi-centre International Study of Asthma and Allergy in Childhood (ISAAC) Phase II investigation conducted in the rural town of Kintampo in the Brong-Ahafo region [33] using a standardised parental questionnaire on symptoms of asthma among children aged 8 to 12 years and performing skin prick testing for atopic sensitisation. The study collected questionnaire data for 1,354 children of whom 1,322 were skin prick tested.[33] Additionally, a subset of 251 children underwent bronchial challenges using hypertonic saline to assess bronchial responsiveness.[34] They observed that the overall prevalence of reported wheeze in Kintampo was 6.4% while the percentage of those with 'atopic wheeze' (defined by reported wheeze within the past year coupled with a positive skin prick test) was only 0.3%.[33] From bronchial challenges, bronchial hyperreactivity (BHR) was observed among 30.4% (95% CI 23.6–37.3) of children tested all of whom were non-atopic.[34]

Urban-Rural Gradient, Socioeconomic Status Differences and Asthma

Key variations in asthma prevalence between rural and urban areas as well as within urban areas have been noted in epidemiological studies [35]. Addo-Yobo *et al* observed that among children attending an 'urban rich' school, the prevalence of EIB was highest (4.2%) compared to 'urban poor' (1.4%) and rural (2.2%) schools.[28] Ten years later, the EIB prevalence among urban affluent children had doubled to 8.3% [30] while among urban poor children it changed from 1.4% (1993) to 3.0% (2003) and among rural children from 2.2% (1993) to 3.9% (2003). Interestingly, the prevalence of EIB among urban poor was not much different (and even lower) than among rural children indicating that differences in EIB may reflect varying lifestyles and socioeconomic status rather than area of residence.[28] Similar urban-rural trends as well as socioeconomics differences in asthma markers have been observed across Africa.[35,36] In an investigation of 1172 urban and rural Kenyan children (mean age 10.8 years), Odhiambo *et al* found a lower prevalence of questionnaire-derived markers of asthma among rural (3.0%) compared to urban (9.5%) children.[37]

Environmental Risk factors and Asthma

Few studies have examined environmental risk factors for asthma in Sub-Saharan Africa. Addo-Yobo *et al* conducted a case-control study to explore risk factors among 50 asthmatic urban children in Kumasi aged 9 - 16 years who were age and sex-matched to randomly selected healthy controls.[38] Multivariate analysis showed that being asthmatic was significantly associated with sensitisation to house dust-mite allergen (OR=10.4, 95% CI 3.5 – 30.9), cockroach allergen (OR=4.9, 95% CI 1.3 – 18.6, p<0.05), inner-city residence (OR=4.8, 95% CI 1.5 – 15.2, p<0.01) and having a sib ship position less than five (OR=6.3, 95% CI 1.3 – 29.4, p<0.05).[38] Sib ship position was used as a proxy for infection exposure as per the Hygiene Hypothesis.

In the afore-mentioned study, the investigators postulated that inner-city residence as a risk factor for asthma in an African city may be related to pollution from automobile fumes, over-crowding, dampness, modern buildings and furnishings that promote indoor allergens.[38] However, they did note that their proxy measures for over-crowding were not associated with asthma. The exact meaning of 'inner-city residence' in the Kumasi context was not clearly defined and traffic-related pollutants were not measured. Residence in an inner-city environment has long been associated with asthma particularly in relation to urban areas of the United States [20] where there is likely to be greater exposure to irritants (e.g. tobacco-smoke), air pollutants (such as diesel-related particles) and indoor allergens.[39] With regards to indoor allergen levels, house dust mite allergens were abundant in both the homes of cases and controls but were significantly higher among asthmatics compared to controls (p<0.05).[38] This observation, along with the fact that there was greater atopic sensitisation to dust-mites among asthmatics demonstrates the importance of house dust mites in asthma aetiology in Ghana.

Research done on the distribution and abundance of house dust mite species in homes in the Greater Accra Region of Ghana complement these observations.[40-42] Surveys conducted found high house dust mite densities within homes especially in stuffed furniture and carpets. These house dust mites were predominantly of the *Dermatophagoides* mite species [40-42] that have been implicated in asthma pathogenesis world-wide.[43] Although these mite distribution studies did not explore asthma prevalence, they do provide some indications of elevated levels of indoor allergens that may be associated with asthma within Ghanaian homes.

One environmental factor that was not found to be linked to increased risk of asthma from the Kumasi study was exposure to allergens from pets.[38] A meta-analysis of studies from across the globe found that dog ownership increased the risk of asthma (OR=1.14, 95% CI 1.01-1.29) while cohort studies showed that cat ownership exerted a slight protective effect against asthma (OR=0.72, 95% CI 0.55 - 0.93).[44] Moreover, a study by Woodcock *et al* observed that although cat and / or dog ownership rates in Ghana and the UK were similar, levels of pet allergens within Ghanaian homes with pets were 75-fold lower for dogs and 275-fold lower for cats compared to UK homes with pets.[45] Hence, low levels of exposure to pet allergens in Ghanaian homes would explain the lack of significance of pet allergens as a risk factor.

Heredity, Early Life Risk Factors and Asthma

Research studies have reported a strong correlation between family history of asthma and increased risk of the disease. [11] A cross-sectional study on risk factors for asthma among 421 children aged between 5-16 years living in urban and rural communities of the Greater Accra Region of Ghana examined family history of the disease and some early-life factors.[46] A questionnaire adapted from the ISAAC Phase II study modules [47] was used to determine the prevalence of reported asthma. After adjusting for confounders and taking clustering within families into account, asthma was strongly associated with reported maternal asthma (OR=3.57, 95% CI 1.67 - 7.66, p<0.01) as well as breastfeeding duration for less than 6 months (OR=6.34, 95% CI 1.79 - 22.40, p<0.01).[46] Maternal asthma is known to significantly increase the risk of asthma in off-spring but the mechanisms involved are not well-defined.[48] The role of breastfeeding duration in asthma aetiology remains controversial with studies showing contradicting findings. Some report no effect of prolonged breastfeeding on asthma [49] while others point to a protective effect [50,51]. A few investigations have also demonstrated an increased asthma risk associated with longer breastfeeding. [52,53]

Parasitic Infections and Asthma

Few publications from Ghana have examined the link between parasitic infections and asthma. Commey and Haddock reported that 14% of their participants had intestinal helminths but did not explore this further. [27] Addo-Yobo *et al* found the number of intestinal helminth positive stool samples too low to be of significance.[38]

A meta-analysis of global findings examining current parasitic infection and risk of asthma or wheeze observed that from 17 pooled studies, there was a significant association between clinician-diagnosed asthma and 'any current intestinal helminth infection' (pooled adjusted OR = 1.47, 95% CI 1.02 – 2.12).[54]

Moreover, current hookworm infection had an overall protective effect against asthma while roundworm (*Ascaris lumbricoides)* infection increased asthma risk.[54]
The authors hypothesised that increased asthma risk with *A. lumbricoides* could be related to the relatively high allergenicity associated with this helminth since it is also recognised as the cause of tropical pulmonary eosinophilia unlike the hookworm parasite.[54]

Currently, elucidating the role of different helminths in immune pathways in asthma aetiology is an important area of research. Hartgers *et al* observed that among 120 school-children aged 5-14 years residing in a rural part of the Greater Accra Region, *Schistosoma haematobium* infection suppressed Toll-like receptor-2 (*TLR-2*) and Suppressor of cytokine signalling-3 (*SOCS-3*) genes which are both linked to asthma.[55] Specifically, *TLR-2* gene polymorphisms have been associated with reduced asthma prevalence[56] and murine models link *SOCS-3* expression to multiple pathological features of asthma in an airway hypersensitivity model system.[57] These findings suggest that helminth infections may suppress specific genes that are involved in asthma aetiology and may lower the incidence of the disease among populations in helminth-endemic areas.

CONCLUSIONS

Despite the limited number of studies exploring asthma in Ghana, some significant risk factors for the disease have been identified. Research has demonstrated that atopic sensitisation to environmental allergens such as house dust-mite and cockroach is strongly associated with asthma symptoms with this effect being greatest among urban compared to rural Ghanaian children. Other factors involved in asthma pathogenesis include heredity and early-life determinants such as breastfeeding. Helminth infections have been implicated in the suppression of allergic sensitisation and could be involved in the inhibition of asthma symptoms. Most asthma studies conducted in Ghana place an emphasis on atopy as the major risk factor for the disease which has been the accepted paradigm for many years.[25] Recent global observations indicate that non-allergic asthma may be equally important and further investigation into the role environmental pollutants in Ghana including volatile organic compounds (VOC) is needed.

Most studies have focused on asthma among individuals aged 5 to 16 years and therefore, very little information on risk factors associated with asthma among adults in Ghana is known. Currently, there is a need for large well-designed epidemiological studies exploring the prevalence of asthma in Ghana and associated risk factors among children as well as adults. Socio-clinical studies examining patient care, perceptions, psychosocial factors surrounding asthma and possible interventions to improve asthma management are also needed. Furthermore, a quantitative analysis of the economic burden of asthma on individuals as well as the Ghanaian economy is also essential. Such analyses are vital as the country strives towards universal health coverage under the National Health Insurance Scheme (NHIS). These initiatives alongside surveys on risk factors for the disease are imperative if we are to avert an asthma epidemic in a rapidly urbanising country such as Ghana.

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