

# ALLERGIC CO-MORBIDITIES IN CHILDHOOD ASTHMA IN LAGOS, NIGERIA

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## ABSTRACT

Globally, asthma is the commonest chronic disorder of childhood, with increasing prevalence, especially in developing countries. Asthma severity and persistence is associated with allergic co-morbidities, which in turn are associated with poorer control and quality of life. Knowledge of the burden of co-morbid allergies may guide optimal asthma care. In this study, we evaluated the prevalence and pattern of co-morbid symptomatic allergies, as well as its association with asthma severity, in children with asthma, while assessing them during routine care at the Paediatric Allergy, Dermatology and Pulmonary Medicine Division of Lagos State University Teaching Hospital, Ikeja, Lagos, Nigeria. In this study, asthmatic children were recruited consecutively at our clinic. By means of a structured questionnaire and clinical evaluation, we obtained demographic and clinical data about asthma severity and the presence of co-morbidities: allergic rhinitis, allergic conjunctivitis, atopic dermatitis and food allergy. Eighty children aged between six months and 15 years were recruited. Although most were referred to our unit with a clinical diagnosis of asthma, none of them had been diagnosed with the co-morbidities until presentation in our clinic. Overall, the presence of co-morbidities was not associated with asthma severity. However, the presence of allergic conjunctivitis was significantly associated with asthma severity but only it remained independently associated with persistent asthma. We conclude that allergic co-morbidity, mostly allergic rhinitis, is common among the asthmatic children who attend our clinic.

Keywords: asthma; children; prevalence; co-morbid; allergy; Nigeria

## BACKGROUND

Asthma is now recognised as ‘a heterogeneous disease ... characterised by chronic airway inflammation ... with variable expiratory airflow limitation’.<sup>1</sup> Whereas the prevalence of asthma in adults and children seemed to have plateaued in high-income countries, it is increasing in developing parts of the world such as Africa, including Nigeria.<sup>2–5</sup> This increasing prevalence is attributable to factors such as growing urbanisation, the adoption of a Western lifestyle and a rise in air pollution.<sup>1,6–9</sup>

Although asthma-related death is not commonly reported in our setting, it is associated with significant morbidity, such as hospitalisation for acute exacerbations.<sup>3,10</sup> One of the factors associated with greater asthma severity in childhood is the presence of co-morbid allergies such as allergic rhinitis (AR), allergic conjunctivitis (AC), atopic dermatitis (AD) and food allergy (FA).<sup>5,9,11,12</sup> The co-existence of these allergies with asthma is also associated with poorer control, the higher cost of treatment and more frequent hospital visits.<sup>13–15</sup>

In Nigeria, community- and hospital-based studies have showed that up to 42–80% of children and adolescents with asthma suffer

from concomitant allergic disorders.<sup>5,14,16,17</sup> In many of these patients, however, their co-morbid allergies remain undiagnosed, predisposing them to more severe disease and poorer asthma control and quality of life (QoL).<sup>18–20</sup> The need therefore exists to identify actively and specifically such asthmatic children in order to afford them optimal care.<sup>14,15</sup> In a drive to optimise the care (including a scaling-up of allergy services) of asthmatic children attending an outpatient paediatric asthma clinic at the Lagos State University Teaching Hospital (LASUTH), we prospectively studied the prevalence of co-morbid symptomatic allergies in children with asthma and its association with asthma severity.

## METHODS

### STUDY SITE

LASUTH is a tertiary hospital in South-West Nigeria. The hospital offers basic and tertiary care to patients from the Lagos metropolis and neighbouring states. The Paediatric Allergy, Dermatology & Pulmonary Medicine Division runs a weekly outpatient clinic headed by a consultant paediatric allergologist or dermatologist. The clinic sees 5–10 asthmatic children weekly. It receives referrals not only from public and private health facilities in the Lagos metropolis and neighbouring states, but also from other specialist units in the hospital.

## STUDY POPULATION

The study population comprised all asthmatic children accessing routine outpatient care at the LASUTH clinic. In this clinic, attending clinicians (consultants and senior registrars) diagnose asthma based on the presence of recurrent, episodic wheeze, cough, chest tightness and breathlessness, with clinical evidence of reversible bronchoconstriction (spontaneous reversibility or with salbutamol); diagnostic bronchodilator reversibility was not routinely available during this study. We also routinely assess asthma severity retrospectively, using only the symptom and activity limitation modules of the National Asthma Education and Prevention Programme's (NAEPP's)<sup>21</sup> guidelines. Therefore:

- *intermittent asthma* was defined as daytime symptoms less than three times weekly, night-time awakenings less than three times a month, the use of short-acting beta-agonist (SABA) less than thrice a week, and no interference with activity;
- *mild persistent asthma* was defined as daytime symptoms more than twice weekly but not daily, night-time symptoms of 3–4 times a month, the use of SABA for more than two days weekly but not daily, and minor limitation of activity;
- *moderate persistent asthma* was defined as daily daytime symptoms, night-time symptoms more than once weekly but not nightly, and some limitation of activity;
- *severe persistent asthma* was defined as daytime symptoms occurring throughout the day, night-time symptoms occurring often or nightly, the use of SABA several times daily, and extreme limitation of activity.

We preferably assessed asthma severity at first contact, before the commencement of controller medications. For patients who had been commenced on controller medications before presentation to us, we used their response to such therapy as an adjunct to assessing their severity.<sup>21,22</sup>

## STUDY DESIGN

The study was a pilot cross-sectional study designed to inform a larger prospective study on the epidemiologic, clinical and allergy profile of children with asthma who were accessing routine outpatient care at the unit.

## STUDY DURATION

February–December 2018

## DATA COLLECTION

With the aid of a structured questionnaire, we obtained information on the subjects' demographic data (age, sex), asthma severity, allergies in first-degree relatives and presence of co-morbid allergies (physician-diagnosed or symptoms suggestive of AR, AC, AD or FD) in subjects. The presence of these conditions was corroborated with an examination for physical signs:

- AR (pale, swollen inferior nasal turbinates, clear nasal discharge, cobble-stoning of the posterior pharynx and postnasal drip);
- AC (brownish conjunctiva, cobble-stoning of tarsal conjunctiva and limbal involvement); and
- AD (typical dry, pruritic skin eruptions with characteristic distributions).

## STATISTICAL ANALYSIS

We extracted data from the questionnaires into Microsoft Excel 2013 (Microsoft Inc), from where they were imported into SPSS version 21 for statistical analysis. We assessed the distribution of continuous variables with Kolmogorov-Smirnov and Shapiro-Wilk Tests. Normally distributed continuous variable (age) was expressed as a mean  $\pm$  standard deviation (SD) and categorical variables (sex, asthma severity, atopic co-morbidities, family atopies) as frequency and percentages. Potential association between asthma severity (dichotomised as *intermittent* or *persistent*) with each of age, sex, any allergic co-morbidity and each form of allergic co-morbidity was tested with Fisher's exact test, with or without odds ratio and its 95% confidence interval (CI) (derived from  $2 \times 2$  contingency tables). Variables with a significant association with asthma severity were entered into a binary regression model with asthma severity as dependent variables and the potential factors as independent variables. Independent association was assessed with adjusted OR, its 95% CI and p-value. A variable is retained in the model if it does not violate any of the assumptions for logistic regression.<sup>23</sup> A p-value of 0.05 was considered as statistically significant.

## RESULTS

### DEMOGRAPHIC CHARACTERISTICS

Eighty subjects aged 0.5 to 15.7 years, with mean  $\pm$  SD age  $7.6 \pm 3.6$  years, were recruited during the study period. The youngest subject was diagnosed at six months of age following three episodes of hospitalisation for acute wheezy illness since the second month of life. There was a positive maternal history of asthma. The episodic wheeze usually resolved with salbutamol nebulisation. A diagnosis of asthma was further established after a remarkable resolution of the recurrence of acute wheezy episodes with about a six-week trial of inhaled budesonide. As shown in Table I, more than half of the subjects were aged 5–10 years; two-thirds were boys. The mean age was similar for boys and girls ( $7.58 \pm 3.52$  vs  $7.90 \pm 3.86$ ;  $p = 0.730$ ).

### ASTHMA SEVERITY

The commonest severity of asthma was mild persistent asthma as shown in Figure 1. When recoded into two categories (*intermittent* vs *persistent* asthma), 49 (65.3%) of the subjects had persistent asthma.

**TABLE I: DEMOGRAPHIC CHARACTERISTICS OF SUBJECTS**

| VARIABLE           | N   | %  |
|--------------------|-----|----|
| Age groups (years) |     |    |
| <5                 | 16  | 21 |
| 5–10               | 44  | 58 |
| >10                | 16  | 21 |
| Total              | 76* |    |
| Sex                |     |    |
| Male               | 52  | 67 |
| Female             | 26  | 33 |
| Total              | 78* |    |

N: number of subjects; %: percentage; \* less than  $n = 80$  due to missing data

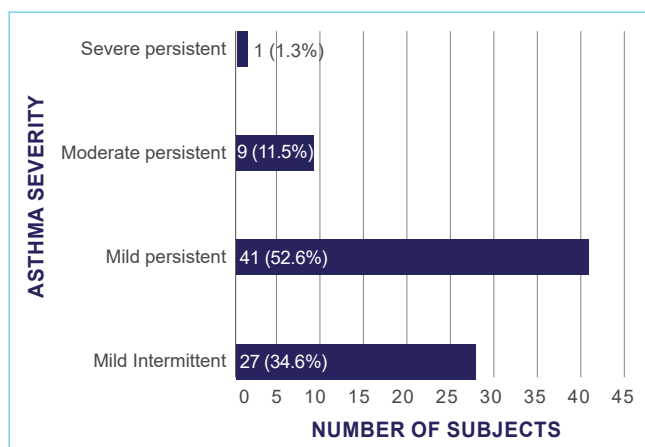


Figure 1: Frequency of asthma severity

#### FAMILY HISTORY OF ATOPY

Nineteen (24%) of the study subjects had a history of allergies in first-degree relatives: mothers (n = 9), fathers (n = 4) and siblings (n = 7).

#### ALLERGIC CO-MORBIDITIES

Three-quarters (n = 62/80, 78%) of our subjects had symptoms of at least one allergic co-morbidity, with the commonest being AR (n = 53/80, 66%); other forms of allergies were AC (n = 23/80, 29%), AD (n = 7/80, 9%) and FA (n = 1/80, 1%). One-third (n = 26/80, 33%) of the subjects had more than one co-morbidity, while 20 (25%) had rhino-conjunctivitis; one subject had three forms of allergy (AR, AC and AD) and one boy had both AD and FA.

#### ASSOCIATION BETWEEN DEMOGRAPHIC CHARACTERISTICS AND ASTHMA SEVERITY

Fisher's exact test revealed that asthma severity was not associated with age (n = 74, df = 2, p = 1.00) or sex (n = 76, df = 1, p = 0.30).

#### ASSOCIATION BETWEEN CO-MORBIDITIES AND ASTHMA SEVERITY

The presence of *any atopic co-morbidity* was not associated with asthma severity (OR = 1.2; 95% CI: 0.4–3.7, p = 0.78) (see Table II). However, the presence of *allergic conjunctivitis* was associated with five-fold increased odds of persistent asthma (OR = 5.2; 95% CI: 1.4–19.4, p = 0.02), whereas the presence

of *atopic dermatitis* was associated with decreased odds of persistent asthma (OR = 0.3; 95% CI: 0.2–0.4, p < 0.0001). However, on entry into a regression model, only the presence of AC remained independently associated with persistent asthma (aOR = 5.2 (1.4, 19.4), p = 0.02) (see Table II).

#### DISCUSSION

Our study sought to determine the burden and spectrum of co-morbid symptomatic allergies and their association with asthma severity in children with asthma while being assessed during routine outpatient care at the Paediatric Allergy clinic of LASUTH. Three-quarters of the children with asthma in our unit had co-morbid allergies; AR was predominant in approximately two-thirds of our cohort. Although the presence of co-morbid allergy was not associated disease severity, AC was independently associated with it.

Approximately three out of four of our subjects had symptoms of other forms of allergy in addition to asthma. This was similar to findings by Uche-Okonkwo et al,<sup>16</sup> who reported that 79% of asthmatic adolescents in a secondary school in South-West Nigeria also had other allergies. In contrast, Ayuk et al<sup>14</sup> reported a lower prevalence of 42% at a paediatric asthma clinic in Enugu, South-East Nigeria. Kim et al<sup>24</sup> also reported a lower prevalence of 64% among Korean pre-school children with asthma.

AR was the commonest form of allergic co-morbidity in our study, a similar finding to that of a previous clinic-based report from South-Eastern Nigeria.<sup>14</sup> The high burden of co-morbid AR in asthmatic children in our study is also in line with data from population-based studies, including the International Study of Asthma and Allergies in Childhood (ISAAC) and the more recent Asthma Insight and Reality (AIR) survey.<sup>5,17,25,26</sup> Our study was conducted in Lagos – a burgeoning, rapidly growing megacity with significant and increasing air and environmental pollution – a strong risk factor for the development of allergies.<sup>9</sup> These studies, including ours, provide child-health stakeholders with data with which to engage policy-makers and government agencies on the need to employ proven eco-friendly infrastructural development technologies that will minimise air pollution.<sup>17</sup>

In contrast to our finding, AC was the commonest form of allergic co-morbidity (33%) in a study of asthmatic children and adolescents by Garba et al<sup>27</sup> in Northern Nigeria. It is not clear

TABLE II: ASSOCIATION BETWEEN ATOPIC CO-MORBIDITY AND ASTHMA SEVERITY

| RISK FACTORS                 | INTERMITTENT | PERSISTENT | OR (95% CI)     | AOR (95% CI)    | P-VALUE |
|------------------------------|--------------|------------|-----------------|-----------------|---------|
| Any atopic co-morbidity      | 21           | 41         | 1.2 (0.4, 3.7)  | N/A             | 0.78    |
| More than one allergy        | 9            | 17         | 1.0 (0.4, 2.7)  | N/A             | 1.00    |
| Allergic rhinitis            | 17           | 36         | 1.4 (0.5, 3.8)  | N/A             | 0.61    |
| Allergic conjunctivitis      | 3            | 20         | 5.2 (1.4, 19.4) | 5.2 (1.4, 19.4) | 0.02*   |
| Allergic rhinoconjunctivitis | 3            | 17         | 4.0 (1.0, 15.2) | N/A             | 0.54    |
| Atopic dermatitis            | 7            | 0          | 0.3 (0.2, 0.4)  | 0.0             | 1.0*    |
| Food allergy                 | 1            | 0          | 0.3 (0.2, 0.5)  | N/A             | 0.35    |

OR: odds ratio; CI: confidence interval; aOR: adjusted OR, derived from a binary logistic regression model; N/A: not applicable (non-significant variables not entered into regression model); \*: p-values from regression model

whether the authors of the Kano study specifically asked for symptoms of AR (such as recurrent sneezing, nasal discharge or congestion), because only 6% and 4% of the subjects had allergic shiners and allergic salute, respectively. The predominance of AC in Northern Nigeria may also be explained by the more arid climate, resulting in persistent eye irritation. Unlike a North American report,<sup>28</sup> where about 10% of a cohort of asthmatic children had FA, only one child in our cohort had symptoms suggestive of FA.

Asthmatics with allergic co-morbidities are at increased risk of more frequent hospitalisation, worse disease severity and poorer asthma control (although we did not assess control).<sup>14,15,19,20</sup> Overall, the presence of allergic co-morbidity was not associated with more severe disease in our study, in contrast to other reports,<sup>12,15</sup> presumably due to our relatively small sample size. Whereas the impact of co-morbid AR (or allergic rhinoconjunctivitis) on asthma severity and control has been extensively reported elsewhere,<sup>12,14,15,29</sup> there is a relative paucity of data on the association between asthma and co-morbid AC.<sup>18,30,31</sup> A rather curious finding in our study was that the presence of allergic conjunctivitis, but not allergic rhinoconjunctivitis, was independently associated with persistent asthma. We noted, however, that all but three of the 23 asthmatic children with AC had persistent asthma. Therefore, the observed significant association with severity may have occurred by chance owing to our small sample size. Nonetheless, does the finding that almost all of our subjects with AC had persistent asthma suggest that AC may be a stronger surrogate of atopy compared to AR? This potential relationship may need evaluation with larger studies that include allergen sensitisation testing. Meanwhile, our data may add to the call that conjunctivitis be considered as part of the 'one-airway' concept.<sup>18,30,32,33</sup>

We observed that, despite having been diagnosed in other referring units outside our centre, these co-morbid allergies were not diagnosed in the majority of our subjects. The treatment of concomitant allergies in asthma improves control and quality of life (QoL).<sup>15,34</sup> It is therefore important for clinicians to evaluate asthmatics specifically for co-morbid allergies, because in most of these children these allergies go undetected, predisposing them to poorer control and outcomes.<sup>18,19</sup>

The current study was essentially preliminary and intended to inform a larger study of the epidemiology of asthma in our unit, as well as the factors that may potentially affect asthma causality, severity and control. Being hospital-based, it may under- or over-estimate the true prevalence of allergic co-morbidities in asthmatic children in the community; it may suffer selection bias and may not be truly representative of the general population of asthmatic children.

We also did not quantify asthma control, which is more objectively quantifiable than asthma severity. Over the years, asthma management has witnessed a change in the evaluation of asthma severity, with recent international guidelines in favour of its assessment 'retrospectively from the level of treatment required to control symptoms and exacerbations'.<sup>1</sup> This approach poses significant challenges in low-resource settings, where the required controller medications are not readily available. Asthma severity may therefore be more easily assessed, in our setting, using symptoms and activity limitation before the commencement of controller medication as recommended by the NAEPP<sup>21</sup> and as adopted by our local asthma guidelines.<sup>22</sup>

The burden of allergic co-morbidities in children with asthma in our unit was high. Whereas the presence of any allergic co-morbidity was not associated with disease severity, isolated AC was independently associated with persistent asthma in our cohort. The need therefore still exists to screen actively for co-morbidities in children with asthma, as their presence can potentially impair asthma control and QoL.<sup>15,18</sup> In addition, our study has provided useful data that may inform local policy in optimising paediatric asthma care in our unit and region.

## CONCLUSION

Allergic co-morbidity, mostly that of AR, is common among asthmatic children in our clinic. There is a need to diagnose and treat co-morbid allergic conditions for optimal asthma care.

## DECLARATION OF CONFLICT OF INTEREST

The authors declare no conflict of interest.

This article has been peer reviewed.

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