A synopsis of asthma research in Nigeria between 1970 and 2010

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Bronchial asthma is a chronic inflammatory condition that affects about 300 million people world-wide.[1] The prevalence of asthma and other allergic diseases has increased markedly in the last century and asthma now imposes a high disease burden on individuals, the healthcare system, and society.[2] The increase in the prevalence of asthma is closely associated with higher levels of atopic sensitisation, related to urbanisation. Urbanisation rates are projected to grow from 42% to 59% by 2025, with a concomitant rise in the number of asthmatics of 100 million over the same period.[1]

Asthma affects the psychological, physical, and social well-being of affected persons.[3] The disability-adjusted life years (DALYs) lost due to asthma worldwide is about 15 million per year, accounting for about 1% of all DALYs lost from any disease.[1] The quality-adjusted life years (QALYs) of a year with asthma is equivalent to a 0.7 years without asthma symptoms, suggesting a high negative impact on health-related quality of life.[4] It is estimated that asthma accounts for 1 in every 250 deaths worldwide,[1] the majority of which are preventable and are often due to sub-optimal, long-term medical care and delays in obtaining medical help.[5]

Advances in our understanding of the epidemiology, phenotype and clinical characteristics, therapeutic responses, and outcomes have contributed to improving the overall quality of asthma care in developed countries. Asthma research has been ongoing in Nigeria for about four decades, and this review was designed to provide a comprehensive evaluation of the published literature to understand the epidemiology, clinical profile, treatment modalities, and co-morbidities of asthma in Nigeria. The study also aimed to identify gaps in knowledge, and provide guidance for the direction of further studies.

Methodology

A literature search of published data on asthma in Nigeria from 1970 to 2010 was carried out. Data were sourced from PubMed® Medline, African Journals Online (AJOL), and by 'snow-balling'. Additional un-indexed publications

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were also obtained via communications with colleagues via the Nigerian Thoracic Society. The data search was up-to-date as of May 30, 2011. Search terminologies used were: 'asthma and Nigeria', 'bronchial asthma and Nigeria', and 'wheezing and Nigeria', limited to human studies within the time frame 1970–2010. Considering that the *lingua franca* in Nigeria is English, only articles written entirely in English (or published in another language but including a full text of the English translation) were included. For clarity, no articles were published that were solely in any other language.

Selection criteria for the identified publications were specified by subject matter, epidemiology of asthma, clinical profile, co-morbidities, availability and use of diagnostic facilities, treatment modalities and mortality, and knowledge of asthma by healthcare providers. Only original research papers, including conference abstracts, were selected.

Results

The literature search yielded a total of 158 articles comprising 121 publications cited on PubMed ® Medline, an additional 32 articles available from African Journals Online, and 5 non-indexed publications obtained by
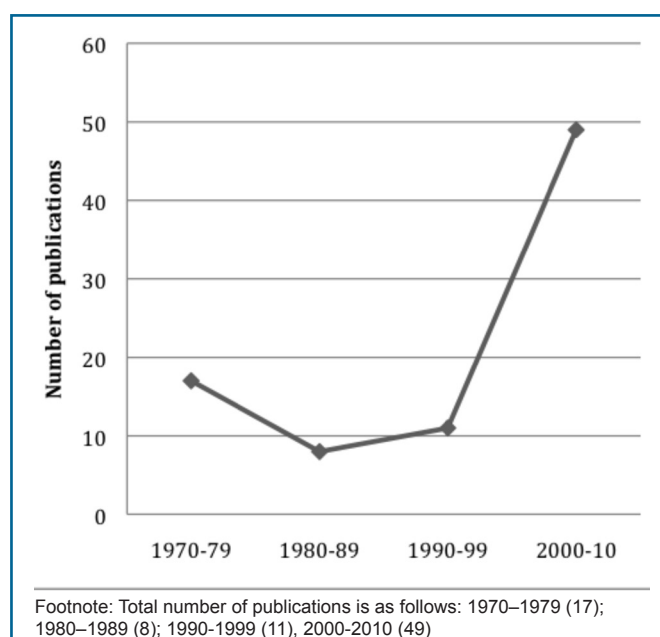

Footnote: Total number of publications is as follows: 1970–1979 (17); 1980–1989 (8); 1990-1999 (11), 2000-2010 (49)

Figure 1 Trend of number of publications on asthma in Nigeria: 1970–2010.

'snow-balling'. All articles referred to by colleagues had been previously identified. Of these, 85 articles meeting the study criteria were selected and reviewed.

Period and context/focus of studies
The 85 articles were sub-divided according to the decade of publication and the focus of the study (see Table 1) and Figure 1 shows a trend of an increase in the number of publications relating to asthma from the initial decade, 1970–1979 (17/decade), to the last period, 2000–2010 (49/decade).

Clinical series
Sofowora (1970) reported an incidence rate of 2.4% from 250 patients seen over 10 years in Ibadan (south-western Nigeria) with a late age of presentation (78% presented between 15 and 45 years.[6] Warrel et al (1975) studied 160 patients in Zaria (northern Nigeria), and corroborated that age of onset was mostly in adulthood (19 years in 69% of patients).[7] Haddock studied 78 patients in Benin (southern Nigeria) and described the acute asthmatic episodes as being severe without permanent respiratory crippling.[8]

Frequencies of hospital visits
Aderele et al (1979) reported a frequency of hospital visits in childhood asthma of 40 per year over two and half years with a slight male preponderance (1.6:1).[9] Asthma was more common in the higher socioeconomic class, 97% of the children were less than 5 years old.[9] Abdurrahman (1982) in Zaria, reported a lower hospital prevalence in children of 22 per year over 4 years.[10] In an adult series (2010), a frequency of hospital visits 6.6% was reported, with a female preponderance (1.5:1).[11] Asthma ranked second (17.5%) to tuberculosis (42.1%) among causes of respiratory morbidity and mortality in a tertiary hospital.[12]

Prevalence
Prevalence studies on asthma have been carried out since 1995 and six of these studies were reviewed.[13–18] Table 2 shows the various studies, highlighting the location, age, prevalence, and diagnostic criteria.

Time trends in the symptoms of asthma among school children in Ibadan were assessed with cross-sectional data from two ISAAC studies conducted 7 years apart (1995–2001/2002). The prevalence of current wheeze increased non-significantly in the 6- to 7-year age group (4.8–5.2%) and significantly in the 13- to 14-year-old age group (10.7–13%).[19]

Impact of asthma on physical, psychological, and social functioning
Oni et al reported that asthma was associated with limitations in performing sporting activities in 84% of their patients, as well as household chores (61%), other physical activities (55%), and social activities (54%); it also affected choice of career (60%). Asthma symptoms disturbed sleep in 53% of the patients, 53% had regular daytime symptoms, and about 50% had been to the emergency room or had been hospitalised as a result of recurrent symptoms.[11]

Risk factors for developing asthma and triggers of asthma exacerbations
Table 3 summarises the various risk factors for developing asthma that have been studied in Nigerians.[20–31] Age, gender, education, and socio-economic status were not significant risk factors.[20] Three studies refuted the hypothesis that parasitic infections (intestinal parasites), high IgE levels, or rural dwelling protected from asthma.[32–34] Several studies have explored triggers of asthma exacerbation.[35–47] The most common triggers identified were house dust and house dust mite.[35–47] Other frequently identified allergens are *Aspergillus fumigatus*, feathers, dog hair, cat fur, grass, pollen, cockroach allergen, damp mouldy rooms, cigarette smoke, mosquito coils, and rodents.[35–47] Reactions to food and pollen allergens were not high. Other triggers include *Ascaris* antigens, infections (frequently viral), psychological factors (e.g. worry, anger), and exercise.[9,48–51] Free running was a more effective trigger of exercise-induced asthma compared with step test or bicycle ergometer.[51]

Clinical profile
Dyspnoea, chest tightness, and cough have been highlighted as prominent presenting symptoms of asthma.[6,9,15,52] Severity of asthma was assessed as mild to moderate in 72% of asthmatics based on a forced expiratory volume in 1 second (FEV_1) greater than 60% of that predicted.[53] Asthma was controlled in 48% (Asthma Control Text (ACT) score ≥20) of patients in a tertiary hospital and a positive correlation was seen between the ACT score and the FEV_1.[54] Aderele reported the presence of precipitating factors for asthma exacerbations in 78% of children[9] and triggers are frequently non-allergic.[8]

Asthma is often associated with other allergic conditions.[9–11,13,14,55,56] This included hay fever (26%), atopic eczema (28%), rhinoconjunctivitis (34%), and other atopic conditions (70%) in children;[13] and allergic rhinitis and rhinosinusitis (80%), pharyngitis (54%), conjunctivitis (54%), and dermatitis (30%) in adults.[11] Nasal symptoms preceded, precipitated, or accompanied asthma exacerbations and treatment of the nasal symptoms improved asthma control in the report by Jarikre et al.[56]

Abnormal mucocilliary clearance, elevations of IgM, IgG, C3a and C5a anaphylatoxins, hyper-viscosity and hyper-fibrinogenaemia have been reported and contribute to disease morbidity and mortality.[57–59]

Co-morbidities in asthma
Psychological disorders are prevalent with a strong impact on asthma symptoms among Nigerians.[49,60–64] The association between asthma and gastro-esophageal reflux disease (GERD), was explored in one study and there was no significant difference in the incidence of GERD

Year of publication	Total number of publications	Prevalence studies				Risk factors	Clinical profile	Co-morbidities	Availability and use of diagnostic facilities	Knowledge by healthcare providers	Treatment	Mortality
		Case series	Hospital-based	Community-based	Total							
1970–1979	17	3	1		4	11	3	1			3	1
1980–1989	8		1		1	6	1				1	
1990–1999	11			2	2	5	2	1				1
2000–2010	49		2	4	7	9	3	9	4	6	16	3
Total	**85**	**3**	**4**	**6**	**14**	**33**	**9**	**11**	**4**	**6**	**20**	**5**

Footnote: Row totals do not add up to total number of publications in each decade as several studies focused on multiple areas.

Table 1 Focus of asthma publications from Nigeria (1970–2010)

Study (year)[13-18]	Location	Age (years)	Study instrument	Prevalence	Diagnostic criteria
Falade et al (1998)	Ibadan (SW)	13–14	ISAAC questionnaire.phase 1	10.7%	Presence of recent wheeze (last 12 months)
Faniran et al (1999)	Lagos (SW)	8–11	Parent completed questionnaire	10.2%	Presence of recent wheeze (last 12 months)
Ibe and Ele (2002)	Onitsha and Nnewi (SE)	10–19	Self completed modified ISAAC questionnaire	14.3%	Diagnosis of asthma based on repeated episodes of two or more asthma symptoms (last 12 months)
Falade et al (2004)	Ibadan (SW)	6–7	ISAAC questionnaire phase 3	5.1%	Presence of recent wheeze (last 12 months)
Erhabor et al (2006)	Ile-Ife (SW)	15–35	Self-completed questionnaire	14%	'Probable asthma' based on presence of three or more symptoms or past diagnosis of asthma
Desalu et al (2009)	Ilorin (SW)	18–65	ECRHS screening questionnaire, spirometry, PEFR variability	15.2%	Diagnosis of asthma based on two or more recurrent asthma symptoms or physician diagnosed asthma or PEF variability $\geq$10%

Footnote: International Study of Asthma and Allergy in Childhood (ISAAC); European Community Respiratory Health Survey (ECRHS); South west Nigeria (SW); South east Nigeria (SE).

Table 2 Studies of asthma prevalence in Nigeria

Risk factor	Study findings
Family history	Three studies reporting positive family history of asthma in 22%,[7] and 80% of asthmatics,[20*] and a family history of allergy in 40%[9] of asthmatics
Alpha 1 antitrypsin	Significantly lower levels in asthmatics,[21,22] higher rates of heterozygous phenotypes (PiMZ, PiMW,PiLM) and positive correlation of heterozygous phenotypes with asthma severity[22]
Vitamin C and minerals	Lower levels of vitamin C,[23,24] uric acid, magnesium and albumin[24,25] in asthmatics. High dose vitamin C lessened the frequency and severity of attacks over 3 months in one randomised controlled trial,[26] and vitamin C supplementation lessened peroxidative damage but did not improve lung function in asthmatics[27]
Occupational asthma	Prevalence of asthma symptoms: wheezing in sawmill workers (4.1%,[28] periodic breathlessness in bakery workers (23.2%),[29] chest tightness (13.3%),[30] and asthma (6.5%) in wood workers[31]

Footnote:
*This study also provided odds ratios for several self-reported risk factors as follows: family history 5.32; allergic rhinitis 5.29; out-door pollutant 3.51; tobacco smoking 3.47;

Table 3 Studies assessing the risk factors for developing asthma

between the asthmatics (36%) and controls (30%).[65]

The frequency of hypertension among 134 stable asthmatics was 37% and transient elevation in blood pressure was also noted during asthma attacks in 12 patients which did not require treatment as it resolved 2 weeks after the attack.[66]

Availability and use of diagnostic facilities

Three studies addressed this issue over the period.[67–69] Erhabor and Adigun retrospectively reported that none of 226 cases reviewed had peak flow monitoring during acute exacerbations and spirometry was unavailable.[67] Ayuk et al assessed asthma management by 285 doctors (68% from tertiary hospitals); spirometry was available to 25% of doctors, and 34% used lung function assessment (peak flow meter in all instances) in making a diagnosis of asthma.[68] Doctors working in non-tertiary hospitals and those >15 years or <5 years post-graduation were less likely to utilise diagnostic tools.[68] Desalu et al, in a study of 321 doctors, corroborated the 25% with access to spirometry,[69] and noted that unavailability was the greatest barrier to the use of spirometry in 62% of doctors and lack of awareness of its usefulness the greatest barrier in 17%.[69] Forty percent of doctors with access to spirometry were confident of interpreting the results.[68,69]

One study demonstrated that response to histamine or methacholine challenge tests was used to aid asthma diagnosis.[70]

Knowledge of asthma management by healthcare professionals

Misdiagnosis rates of asthma range from 70% to 98%.[9,15–18,71] Only 2% of the cohort in the population study by Desalu et al[18] and 24% of the children presenting at a tertiary care hospital,[71] had a previous diagnosis of asthma. Two studies directly assessed knowledge of asthma diagnosis and management.[72,73] Among 170 newly qualified doctors, 32% would use nebulised salbutamol, 83% intravenous aminophylline, 39% steroid inhaler, 55% salbutamol inhaler, and 28% prednisolone in the management of asthma exacerbation.[72] Interestingly, 23% considered diazepam relevant in asthma treatment.[72] A related study in 76 community pharmacists reported a mean knowledge score of 57%, with pharmacists who had recent training on asthma having significantly higher scores.[73] The pharmacists recorded the highest scores in asthma definition (95%) and recognition of symptoms (94%) and their lowest scores in the adequate means of delivering asthma medications (43%) and characteristics of inhaled medications (35%).[73] Desalu et al reported that 64% of doctors obtained knowledge of spirometry from medical school, 27% from continuing medical education (CME), and the rest from internet websites, medical textbooks, and journals.[69] Also, 21% of the doctors had attended a CME in general medicine in the previous year and 6% in the previous 2 to 5 years.[69] Erhabor et al demonstrated the positive impact of CME in improving knowledge of healthcare providers.[74]

Asthma treatment

Sodium cromoglycate, aerosol isoproteronol, and aerosol salbutamol have been shown to improve ventilatory function in asthmatics.[75–77] Several drug trials in Nigeria have demonstrated the effectiveness of the use of inhaled steroids, long-acting beta 2 agonists and leukotriene antagonists in asthma.[78–83] Many asthmatics in Nigeria are treated symptomatically with only oral bronchodilators such as salbutamol and aminophylline – usually under self supervision.[52,67] Spacers and written management plans are not often used and 25% of doctors prescribe antibiotics routinely in the management of acute asthma.[68] There is inadequate documentation of vital information crucial to patient short-term and long-term care, frequent use of aminophylline, and inadequate instructions on discharge medications and follow-up in the emergency room.[67,84] For long-term asthma control, oral steroid was often used (81%).[11] High costs of inhaled steroid, fear of side-effects, and inability to use the inhaler correctly have been shown to contribute to poor adherence.[85] A number of African plants are used in Nigeria for asthma treatment and some have been shown to have anti-inflammatory and/or bronchodilator activities.[86–88] However, there are no randomised controlled clinical trials utilising these therapies.

Asthma mortality

There are no population-based mortality figures, but case fatality rates (CFR) have been provided from hospital-based studies. Elegbeleye reported a CFR of 6% (n=177, between 1965 and 1974)[89] while Erhabor et al (2001) reported a CFR of 4.9% (n=226) over a 10-year period.[67] Salami et al (2004) reported the highest CFR of 7.8% in 103 patients over 5 years in Ilorin.[52] These studies agree that most deaths are preventable and late presentation to the hospital was identified as a very important cause of asthma deaths.[5,52,67,89] Eighty-two percent of the patients in Ilorin presented late (≥48 hours after onset of symptoms).[52] Poor long-term asthma care, inadequate objective assessment of airway function, increasing age, under use of corticosteroids, and dependence on intravenous aminophylline also contributed significantly to mortality.[5,52,67]

Discussion

This review provides a summary of asthma research in Nigeria in the last four decades (1970–2010). A large number of research papers have been published and Nigeria ranks second to South Africa in asthma publications from Africa,[90] although the figures lag significantly behind publications from other continents. The main trend observed is that there has been a significant increase in rates of asthma publication in the last decade, in which more than 50% of all publications have occurred. Secondly, the research focus has shifted from predominantly descriptive to exploratory studies and assessment of psychosocial issues and quality of life and quality of care issues. The studies on prevalence were initially reports

of case series and hospital frequencies but collaborative population-based studies are now being carried out.

The study clearly highlights the fact that opportunities for research are available. These include gaps caused by methodological deficiencies in earlier studies, and research questions that have been entirely unanswered by prior studies, considering recent advances in understanding various aspects of the pathophysiology, genetics, and treatment options for asthma. The studies also provide insight into issues in delivery of care that can inform broad-based interventions targeting healthcare providers and policy makers, such as measures to improve asthma education, strengthen infrastructure for qualitative care, and enhance access to evidence-based diagnostic and therapeutic options.

The main finding in this review is that of the increasing prevalence of asthma, as shown in the trend of current wheeze in Ibadan (1998–2001/2002) of 10.7 to 13%.[19] This increase was corroborated in other parts of the world: South Africa (1995–2002), 16% to 20.3%.[91] Korea (1995–2000), 2.7% to 5.3%,[92] United Kingdom (1995–2002), 20.6% to 25.9%.[93] However, the wide geographic diversity of Nigeria implies that environmental influences may result in differing prevalence rates across the country. Thus population-based studies need to be conducted across the entire country to document prevalence rates and explore any geographic differences that may exist. This variation in prevalence across one country has been demonstrated in the USA.[2] Population-based data will also be useful in determining mortality figures which are currently lacking and are necessary for adequate evaluation of the disease and planning.

Genetic risk factors are currently an important research focus in asthma. Five asthma genes or gene complexes that have been identified by genetic cloning include ADAM33, PHF11, DPP10, GRPA and SPINK5.[94-98] The functions of all these genes are not yet very clear but the expression of DPP10, GRPA and SPINK5 in terminally differentiating epithelium suggests that they deal with damage from the external environment.[99] Other genes identified by candidate gene studies include the IL13 which modifies mucus production, FcERI-ß which modifies allergic triggers on mast cells and microbial pattern recognition receptors of the innate immune system.[99] Genetic findings aid better classification of complex diseases such as asthma and aid development of novel therapies. To enhance the role of genetics in asthma, all genetic polymorphisms need to be examined in representative population samples and in samples of clinical subtypes taken from different parts of the world. It is likely that different genes will react with different environmental variables in different places, with different therapeutic implications. Such genetic studies are lacking in Nigeria and this is an important area for future research.

The low prevalence of food and pollen allergies compared to data from the USA requires further study.[100,101] This may reflect the different dietary and environmental exposures encountered by asthmatics in Nigeria that would require that allergens derived from local plants and foods should be incorporated into the test kits. Methodologically rigorous studies to clearly delineate the impact of occupational exposures in asthma pathogenesis in Nigerians are also required, as earlier studies did not uniformly employ strict diagnostic criteria.

Despite current management guidelines, asthma care is still inadequate in Nigeria and the level of asthma control is not optimal. Infrastructural and manpower development are necessary to improve diagnosis, quality of care and adherence to guidelines. There is need for improvement in the knowledge base of healthcare practitioners. This can be achieved via policies that enforce regular CME making it compulsory for healthcare practitioners to undertake such CME at least once in 2 years. 'Asthma clubs' often supported by pharmaceutical companies is a good forum for patient education and should be organised in as many centres as possible. Diagnostic facilities need to be provided at all levels of healthcare delivery and not limited to tertiary centres. With improvement in the knowledge of healthcare practitioners and patients, there will be increased utilisation of diagnostic facilities, early presentation to the hospital during acute exacerbations, and overall improvement in asthma management and prognosis. The high cost of inhaled steroids contributes to low compliance and we advocate government subsidies for asthma medications. Unfortunately, oral prednisolone and methylxanthines are relatively cheap and can be purchased over the counter. Funding of research to explore the role of traditional plants that have been shown to have anti-inflammatory effects in asthma treatment is imperative.

Co-morbidities such as GERD and obstructive sleep apnoea have not been extensively studied and it is relevant to do so because lack of recognition and treatment often leads to poor asthma control. There are no studies in Nigeria that have assessed the usefulness of exhaled nitric oxide monitoring in patient management and randomised controlled trials on recent and novel treatment options have not been explored.

Conclusion

The total number of asthma publications from Nigeria in the last four decades is quite substantial; however gaps remain in the methodologies, focus, and scope of some studies. The focus of research in the new millennium should include genetic studies as well as studies that explore newer risk factors and co-morbidities. Manpower development and funding are major limitations to research in Nigeria. Access to institutional grants, international collaborations, and sponsorships will improve the quality and scope of asthma research in Nigeria.

Review Article

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