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Review Article

Epidemiology and Challenges of Managing COPD in sub-Saharan Africa

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Abstract

There is paucity of data on the burden and specific drivers operative in the pathogenesis of chronic obstructive pulmonary disease (COPD) in the African setting and populations. Lack of awareness and inadequate knowledge on the aetio-pathogenesis of the disease together with inadequate capacity for COPD care contributes to preventive and management challenges. Thus, the majority of patients with COPD are misdiagnosed, misclassified and mismanaged or undertreated. With the struggling improvement in the quality of healthcare in Africa, studies conducted over the last 10 years indicates the rising trends in both the risk factors and the burden of COPD. The role of new risk factors such as indoor pollution, infections with human immunodeficiency virus (HIV) and pulmonary tuberculosis (TB), in the pathogenesis of COPD in Africa is increasingly being recognized. This literature review attempts to collect and synthesize information that could be useful in improving COPD care and informing the governments to take appropriate actions for prevention, diagnosis and management of COPD in Africa.

Keywords: COPD; Prevalence; Risk Factors; Spirometry; Africa

Introduction

Africa is undergoing rapid socio-economic transition characterized by increased economic and population growth, industrialization, urbanization, increased informal settlements and congestion in major cities. Africa lacks capacity and technology to invest in renewable, clean energy options with full dependence on fossil energy and biomass fuel [1]. The use of fossil energy and biomass fuel are potential sources of ambient air and indoor pollution. The effect of air pollution is particularly more dramatic in the setting of poor urban planning with congestion, and poor housing. Prolonged exposure to air pollution has a substantial negative impact on human health particularly the airway system [2]. Cigarette smoking is the major cause of chronic obstructive pulmonary disease (COPD) globally [3]. In addition to cigarette smoking, air pollution, infection with human immunodeficiency virus (HIV), pulmonary tuberculosis (TB) and respiratory infections are increasingly being recognized as an important causes of COPD in Africa. Globally, COPD is the 4th leading causes of deaths, accounting for about 3 million deaths in 2012 [4]. The large proportions of deaths attributed to COPD are highest in low income countries particularly in South Asia and sub-Saharan Africa [3]. Though the burden of COPD is highest in Africa, much of what is known about COPD is imposed on the continent from studies conducted elsewhere. Thus, lack of this locally-relevant knowledge hampers the inadvertent efforts for COPD care in Africa.

Epidemiology of COPD

The incidence and prevalence of COPD is growing globally and regionally albeit with scarce data from Africa [3,5]. In a review based on data prior to 2010, it was revealed that about 227.3 million COPD cases were estimated in the year 1990 corresponding to a global prevalence of 10.7% and the number increased to 384 million in 2010, representing a global prevalence of 11.7% [5]. Pooled data from BOLD and PLATINO studies on spirometry-confirmed COPD cases from 12 countries worldwide reported a prevalence of 10.1% [6]. In a review by Finney., et al. in 2013 reported the prevalence of COPD in Africa to vary between 4% and 25% across countries [7]. However, in a proportion of studies included in these estimates in Africa, COPD cases were not confirmed by spirometry. In another review that included all spirometric-confirmed cases, the prevalence of COPD in Africa was estimated at 13.4% [8].

Selected studies conducted in sub-Saharan Africa over the last 10 years reveal the prevalence of COPD to vary across countries and communities. The COPD prevalence varies from 2.4% to 22% depending on the study population, age of study participants and criteria used for diagnosis as shown in table 1 and figure 1 below. However, it is noteworthy to highlight that there is a universally high rate of missed opportunities for diagnosis of COPD worldwide; with the highest rates recorded in Africa [9]. This under-reporting is contributed partly by lack of awareness and

well-designed studies to determine spirometry-confirmed burden of COPD. Thus, many patients with COPD remains undiagnosed in the communities thus leading to what has been described as an ''incoming storm'' or the ''silent epidemic'' in Africa [10,11]. The burden of COPD is projected to increase over the next decade due to the raising trends in the major risk factors and lack of comprehensive preventive strategies [12].

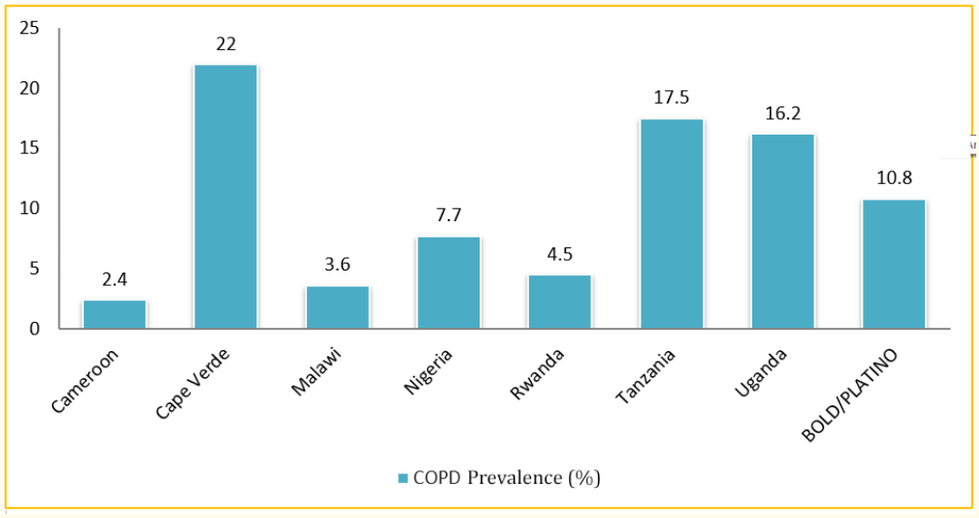

Figure 1: Prevalence of COPD in selected countries in sub-Saharan Africa based on spirometry-defined criteria. The numbers on the bars represent the prevalence of COPD in respective countries.

Country	First Author	Year	Study Design	Setting	Sample Size, n	Age Limit	COPD Diagnostic Criteria	Spirometry	Prev.
Cameroon	Pefura-Yone EW	2014	HB	Urban	922	> 18	FEV_1/FVC < LLN	Yes	5.2%, 5.0%
Cameroon	Pefura-Yone EW	2016	PB	Urban	1287	> 19	FEV_1/FVC < LLN	Yes	2.4%
Cape Verde	Martins, P	2009	HB	Urban	274	> 20	FEV_1 < 80%, FEV_1/FVC < 70%	Yes	22%
Malawi	Meghji, J	2016	PB	Urban	749	> 18	FEV_1 < 80%, FEV_1/FVC < 70%	Yes	3.6%
Malawi	Banda, HT	2017	PB	Rural	3554	> 15	Medical records	No	4.6%
Nigeria	Desalu, OO	2011	PB	Rural	391	> 35	ECSC Questionnaire	No	5.6%
Nigeria	Obaseki, DO	2013	HB	Urban	50	> 40	FEV_1/FVC < LLN	Yes	7.0%
Nigeria	Obaseki, DO	2016	PB	Rural	-	> 40	FEV_1/FVC < LLN	Yes	7.7%
Rwanda	Musafiri, S	2011	PB	Mixed	1824	> 15	FEV_1/FVC < LLN	Yes	4.5%
Tanzania	Zoller, T	2018	HB	Mixed	598	> 18	GOLD, ATS/ERS	Yes	4%, 5%
Tanzania	Magitta, NF	2018	PB	Rural	496	> 35	FEV_1/FVC < 70%	Yes	17.5%
Uganda	van Gemert, F	2015	PB	Rural	588	> 30	FEV_1/FVC < LLN	Yes	16.2%
BOLD and PLATINO	Buist, AS	2008	PB	Mixed	-	> 40	FEV_1/FVC < LLN	Yes	11.8%

Table 1: Study characteristics on the prevalence of COPD in selected countries in sub-Saharan Africa.
FEV1: One Second Forced Expiratory Volume; FVC: Forced Vital Capacity; LLN: Lower Limit of Normal; ATS: American Thoracic Society; ECSC: European Coal and Steel Community; HB: Hospital-based; and PB: Population-based.

Risk factors for COPD

Cigarette smoking and air pollution

Cigarette smoking is the major risk factor for developing and progression of COPD globally [13]. The magnitude of cigarette smoking varies widely in many African countries but the trends are generally increasing [14]. The mechanisms through which smoking causes COPD are not well understood. However, multiple chemical substances and particulate matters present in cigarette smoke triggers complex mechanisms characterized by chronic inflammatory response and increased oxidative stress [15]. Despite the available evidence, the international efforts for combating tobacco use including the limitation on the adverts on tobacco products, prohibition of smoking in public places as well as smoking cessation programs are weakly enforced in the majority of countries in Africa [14].

In Africa, due to cultural taboos, a very small proportion of women particularly in urban setting smoke cigarettes, yet developing ''non-smoking COPD'', indicating that other factors are operative in the pathogenesis [16]. In these patients with non-smoking COPD, exposure to environmental air pollution is probably the major aetiology. Air pollution resulting from industrial and traffic emissions together with use of biomass fuel for cooking and lighting in the context of poor housing ventilation, is an important risk factor for COPD development and progression. The prevailing weak enforcement and poor implementation of preventive strategies for air pollution is likely to drive COPD epidemic in Africa. In rural Africa, over 90% of households and individuals are exposed to biomass fuel, which is normally used for cooking and lighting [17,18]. Women and young children are particularly at a greater risk of exposure to biomass-related indoor pollution while routinely spending long hours in poorly ventilated houses during preparation of food [19].

Africa is currently striving to achieve industrialization which is characterized by heavy investment in fossil fuel–driven machineries together with extensive exploration in petroleum and minerals. The evolving small to medium scale industries and enterprises often operates under very limited safety and health standards. This socioeconomic transition exposes workers to a range of environmental particulate matters, chemical aerosols, and dust, leading to increased risk for developing occupational COPD. Unfortunately, there is weak legal protection and minimal enforcement of health protection for workers in terms of air quality control, use of protection gear and standard screening and treatment for possible occupational-related hazards [20]. A recent survey among hard rock miners in Tanzania revealed exceedingly high levels of air pollution and occupational COPD rates among workers and lack of safety protection standards (Magitta., *et al.* unpublished data).

It is well characterized that only a proportion of cigarette smokers and air pollution-exposed individuals develop COPD. This observation highlights that other factors could contribute to the COPD susceptibility and progression. These additional risk factors include genetic variants, childhood respiratory infections, prematurity and low birth weight, poor diet, malnutrition and low socioeconomic status; which contribute to poor development of lung parenchyma and alteration in the immunological defence mechanisms within the airways [21]. Of recent, infections such as HIV and TB are changing the paradigm in the pathogenesis of COPD in Africa.

Genetic susceptibility

Both the susceptibility and progression of COPD are influenced by genetic variants in the form of single nucleotide polymorphisms (SNPs) in multiple genes. Studies conducted in diverse ethnic populations worldwide have reported SNPs which are associated with COPD. These genetic variants typically tend to fall into five major categories namely; proteinases, anti-proteinases, anti-oxidants, mediators of inflammation and xenobiotic-metabolizing enzymes. However, the results for most of the identified loci have not been replicated in other populations which may be partly explained by genetic heterogeneity [22]. Noteworthy, there are very few studies on genetic variants that have been conducted in sub-Saharan Africa.

Though considered low in sub-Saharan Africa, the prevalence of all the alpha-1 antitrypsin (AAT) deficiency genotypes (PI*ZZ, PI*SS, and PI*SZ) has been estimated to be relatively common from few genotyping surveys. For instance, the prevalence of AAT deficiency genotypes was reported as 54 per 1000 in Angola, 22 per 1000 in Namibia. and 15 per 1000 in Cape Verde [23]. Comparatively, in Tunisian population, AAT deficiency allele (PI*Z, PI*S, and PI*M) were identified to be associated with predisposition and progression of COPD [24]. Likewise, several other Tunisian studies reported multiple SNPs in matrix metalloproteinase (MMP) gene to be associated with increased risk and severity of COPD [25]. Other COPD susceptibility SNPs acting independently or synergistically have been genotyped in glutathione-S-transferase (GSTM1, GSTT1, and GSTP1) and microsomal epoxide hydrolase-1 (mEPHX1) genes [26]. Noteworthy, most of the aforementioned genes are involved in anti-oxidative pathways in the body which is central in the pathogenesis of COPD.

Furthermore, other specific SNPs and haplotypes with increased odds for COPD have been described in phosphodiesterase 4D (PDE4D), IL-1β and C3 complement genes. These genes are typically involved in cellular bio-signalling and inflammation [27]. Another important gene in this category is CLCA1 gene, which play a critical role in the regulation of mucous production in the airway, more importantly during inflammatory states. The expression of CLCA1 is unregulated in situations of airway inflammation such as asthma [22]. Patients with COPD and asthma are characterized by increased airway hyper-responsiveness. Thus, genes which participate in the control of bronchial smooth muscle responsiveness to the agonistic stimuli are likely to play important role in the pathogenesis of COPD. Testing of this hypothesis revealed that genotyping of specific SNPs of β-2 adrenoceptor (ADRB2) gene were associated with susceptibility and severity of COPD [28].

Pulmonary TB, HIV and childhood respiratory infections

Specific infections within the respiratory system increase the risk for developing and progression of COPD. These infections are thought to trigger airway inflammatory response that consequently heals by fibrosis resulting in decreased lung volumes. Of particular importance, pulmonary TB, triggers a chronic inflammatory response characterized by increased oxidative stress, and accelerated deterioration of lung volumes and impaired lung function [29]. As previously alluded to, increased oxidative stress in the airway and lung parenchyma has been demonstrated as key pathological process in the development and progression of COPD [15,30]. Thus, a history of previous pulmonary TB is currently considered as an independent risk factor for developing COPD and could account for a substantial proportion of cases in Africa [29].

HIV infection appears to synergize the damaging effect of smoking through acceleration of inflammatory process and perturbation of airway mucosal immunity [31]. The overall synergy increases the risk of developing COPD and other lung disorders. Global survey of COPD in a population of HIV infected people is estimated at 10.5% [32]. However, even in the absence of tobacco use or smoking, HIV infection has been shown to be an independent predictor for COPD in adults and airflow limitation in the paediatric population [33]. Inadvertently, COPD, smoking and infections such as TB, HIV and respiratory infections interact through poorly understood deleterious and synergistic mechanisms resulting in the clinical phenotype and worsened outcome [34]. In addition, tropical parasitic infections characterized by persistent pulmonary eosinophilia could lead to a subclinical airway inflammation and subtle damage which exposes individual to increased risk of developing COPD and treatment outcome [35].

COPD management challenges

Current recommendations for COPD care

The current Global Initiative for Obstructive Lung Disease (GOLD) guidelines set standard requirements for diagnosis and optimal management of COPD and co-morbidities. The diagnosis of COPD is made based on clinical symptomatology and a history of exposure to risk factors followed by confirmation of persistent airflow limitation using spirometry. The prevention and maintenance therapy of COPD involves strategies for avoidance of exposure to risk factors (e.g. cessation of tobacco smoking and air pollution), tailored pharmacological therapy using appropriate inhaler techniques together with vaccination against influenza and pneumococci. In addition, a proportion of COPD patients may require pulmonary rehabilitation and long-term oxygen therapy in those with resting chronic hypoxaemia. Furthermore, surgical intervention may be indicated for selected patients with advanced emphysema which is refractory to optimized medical care [36].

Moreover, COPD care involves treatment during stable states and exacerbations as well as treatment of co-morbidities. In advanced and intractable disease states, patients with COPD eventually require rehabilitation, education and self-management together with supportive, palliative, end-of-life and hospice care [36].

Inadequate diagnosis and treatment of patients with COPD

Patients with COPD typically present with chronic cough and sputum production with or without dyspnoea. These clinical features of COPD tend to overlap with asthma, hence the term "asthma-COPD overlap syndrome", thus in the absence of appropriate clinical work up, patients are frequently managed as asthma [37]. Moreover, in Africa, this clinical presentation tends to be ignored by patients until they are at advanced stages of disease often after developing intolerable dyspnoea. Regrettably, even at the health facilities, COPD is largely unrecognized and undertreated [38]. Thus, COPD patients might frequently be misdiagnosed and treated for other conditions including heart failure and pulmonary TB.

Myths and disease explanatory models for NCDs in Africa

Africa is characterized by diversity of formal and informal healthcare systems interwoven within social and cultural realm of health explanatory models. The beliefs and perceptual systems towards causation, therapy and prevention of chronic non-communicable diseases (NCD) are tenacious. The existing diverse disease explanatory models are central in shaping the societies' health-seeking behaviour and therefore influencing choices made towards healthcare services or creating a barrier which deter patients from access to trustworthy healthcare services [39]. Of recent, there have been a rising number of multiple informal alternative therapies in Africa with claims to heal and cure NCDs through rituals, prayers, herbs and homeopathy. Thus, it is likely that these informal practitioners could lure patients from seeking relevant medical care for personal financial or popularity gains. It fairly common for patients with COPD and asthma who presents with shortness of breath or dyspnoea and wheezes to be attributed to demonic possessions and therefore, their management sought from sources other than orthodox medicine thereby exposing patients to increased suffering and mortality. Typically, there are no appropriate mechanisms for monitoring of these practices and services.

Inadequate capacity and shortage of resources needed for effective COPD care

The current GOLD recommendations for management of COPD face major limitations when attempted for implementation in Africa [40]. The management of COPD is based on appropriate diagnosis which relies on clinical features, lung function test, and assessment of the presence of exacerbation. However, the majority of health facilities in Africa do not have access to spirometry; the gold standard for diagnosis and grading of severity of COPD as well as planning for appropriate management strategy [41]. Thus, in these settings, COPD diagnosis relies solely on clinical features and patients are offered treatment without spirometric assessment

of disease severity and GOLD stratification [42]. Moreover, there is very little emphasis on COPD care in Africa as reflected by lack of speciality training in respiratory medicine in many institutions and lack of specialized clinics at all levels of care contrary to other chronic diseases [41,43]. This enigma contributes substantially to the low level of knowledge on COPD care and spirometry across all levels of healthcare in Africa [41,44].

Overall, in most African countries, the existing programs for the management of COPD are poorly developed, and the quality of care is often of a low standard with limited availability and access to affordable medicines and diagnostic tests [45]. The current management of COPD requires stepwise administration of bronchodilators and steroids preferably via inhalational routes during stable states and exacerbation. However, these GOLD guidelines are often not adhered to in routine clinical practice in Africa [46]. For instance, there is continued use of ineffective drugs and most drugs are frequently administered through non-recommended routes instead of inhalational route, thus exposing patients to adverse effects, reduced efficacy, frequent exacerbation and poor health-related quality of life. A recent 5-year follow up, BOLD study in South Africa reported a mortality rate of 23% and revealed a substantial level of inappropriate treatment [47].

Healthcare financing for COPD care in Africa

Management of COPD in Africa is a major challenge particularly to the poor who often cannot afford the life-long expensive treatment [45]. There is a well-documented health disparity, inequality and inequity across diverse socio-economic strata in Africa. The majority of poor people are illiterate, not formally employed and thus are not covered by the available health insurance schemes and therefore dependent on out-of-pocket payment for healthcare services. The healthcare cost and expenditure derails the already weakened household income thus exposing affected families to extreme poverty. The overwhelming healthcare cost may affect lifelong adherence and affordability of standard treatment options and thus divert patients to inferior remedies with consequent risk of increased morbidity and mortality [48]. Thus, given these challenges, the most cost-effective method for control of COPD should focus on reduction of risk factors [49]. In most high income countries, there are ongoing efforts for developing integrative pathways and guidelines for comprehensive care of COPD through designing common approaches for prevention, diagnosis, management and rehabilitation [50].

Conclusion

The burden of COPD is grossly underestimated in many countries in Africa. This insufficient information underpins the efforts for planning for prevention and management strategies. The development of a comprehensive package for prevention and control of COPD are hampered by limited resources, lack of access and availability of affordable medicines and diagnostics. There is an urgent need for capacity building through training and deployment of skilled human resources to rural Africa. A focus on reduction of major risk factors for COPD will likely have an appealing impact on the control strategies. Moreover, Africa should partner with international communities for its representation in the global standards of care through surveys, clinical trials and development of treatment guidelines. This integration in the development of healthcare resources and products is particularly critical in this era of precision medicine and tailored healthcare.

Disclosure of Conflict of Interest

The author declares no any conflict of interest.

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