



Review Article

Management of lung cancer in Africa: Underdiagnosis and poor access to treatment – A close look at Nigeria and West African Sub-region

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ABSTRACT

Lung cancer is of public health importance and imposes a great deal of socioeconomic and disease burden on the West African subregion and Nigeria in particular. It is one of the most common cancers worldwide and accounts for 11.4% of all new cancers. In this review, we did not find any well-coordinated lung cancer registry in either Nigeria or any other West African country. For us to attain any meaningful level of the interventional plan to address any identifiable deficiencies in the treatment of lung cancer in the West African subregion, it is imperative that a specific regional lung cancer registry with a regular audit of the reporting, is set up. There is an urgent need for further studies on the local risk factors predisposing to lung cancer, especially in the younger age group. Finally, intense pressure must be mounted on the governments within West Africa to implement the 15% GDP allocation to the health budget as agreed in the WHO/Abuja Declaration and to speed up efforts towards universal health insurance.

Keywords: Lung cancer, Lung cancer registry, Risk factors, Underdiagnosis

INTRODUCTION

Lung cancer is of major public health importance and imposes great socioeconomic and disease burden on the world.^[1] It is one of the most common malignancies worldwide and accounts for 11.4% of all new cancers.^[2] In the United States and United Kingdom, it was reported as the third most common malignancy in both sexes.^[3,4] In Ghana, it was reported as the third most common cancers among males (5.3%).^[5] Furthermore, in Ethiopia and Egypt, lung malignancy is one of the most common cancers with crude incidence rate of 1.9% and 0.8%, respectively.^[6,7] However, in Nigeria, with an incidence of 1.4%, lung malignancy ranked 14th overall on the yearly new diagnosed cancer cases.^[8]

In Nigeria, there is no specific lung cancer registry and figures are derived from few institutional all-cancer registry. The other challenge is that the data from these registries are inexact and irregular.^[9]

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In the West African subregion, the mortality from lung cancer remains high as a result of late presentation with an advanced stage of the disease. Some of the reasons earlier reported for this late presentation include delay in achieving diagnosis, limited access to tertiary care facilities and inability to pay out-of-pocket.^[10-12] Furthermore, the facilities for establishing early diagnosis for lung cancer are limited in the subregion.^[10,11] Ogunbiyi^[10] about 20 years ago, advocated for enhancement of facilities for earlier diagnosis in developing countries. Ezemba *et al.*^[11] noted that with an apparent increase in the incidence of lung malignancy and lack of advanced diagnostic modalities, treatment outcome had remained poor.

It is noteworthy that the observed decrease in lung malignancy mortality in the developed countries is largely due to increased awareness of the harmful effect of smoking and exposure to other risk factors and improved treatment modalities.^[13,14] This pattern has not been observed in low- and middle-income countries.

This review presents the current knowledge of lung cancer in Nigeria and the West African subregion; examines modifiable risk factors, awareness, access and availability of treatment options. It also questions the accuracy of regional prevalence of lung cancer with recommendation on what needs to change. This review is tailored towards stimulating the interest of all the health care workers, especially the thoracic surgeons and pulmonologists.

ACCURATE DATA, POOR KNOWLEDGE AND AWARENESS

Accurate epidemiological lung cancer data is essential for any meaningful intervention plan to address deficiencies in the treatment of lung cancer in the West African subregion. This could be achieved through a properly maintained regional or national lung cancer registry. We did not identify any well-coordinated lung cancer registry in either Nigeria or any West African country. The data on lung cancer generally cited came from four institutional general cancer registers; three of which are from the southern part of Nigeria and only one from the North.^[8] Desalu *et al.* in their study of disease awareness across the middle belt of Nigeria noted a very poor state of awareness of the early warning signs and risk factors for lung cancer.^[15] This will appear to be a general trend; even in a developed country like the United Kingdom despite the advanced health care system and higher levels of health literacy.^[16] Inadequate and poorly articulated messaging from public health campaigns may contribute.^[17]

The unfortunate implication is that many people with early symptoms may not recognize the serious implications and therefore delay seeking medical care. Even when they do, their first point is usually their local health center where the facilities and expertise to achieve early diagnosis and effect appropriate

treatment usually are not available. However, there is evidence to show that knowledge may not lead to earlier presentation.^[18]

Some sociocultural practices, language barriers, and stigmatization attached to the disease may also hinder knowledge and awareness.^[19] Lack of awareness of the existence of appropriate medical facility to handle lung cancer has been reported in a study in Tanzania.^[20]

THE INCIDENCE AND AVAILABILITY OF TREATMENT OPPORTUNITIES ACROSS REGIONS

The wide discrepancy in the incidence of lung cancer between countries in Europe, the United States of America; and those in Africa, Asia, Central and South America, is well documented. It is widely reported to be quite high in the former and much lower in the later.^[21] The incidence of lung cancer in the various regions of Africa according to Global Cancer Observatory 2020 is as follows; South Africa is 27.5 and 9.3, North Africa is 19.3 and 3.5, East Africa 4.2 and 3.0, Middle Africa 3.4 and 1.8, and West Africa is 2.8 and 1.8 all per 100,000 for males and females, respectively.^[2] Available data show that both South and North Africa have higher incidence of lung cancer than recorded in East, and West Africa combined. Increasing life expectancy in both North and South African countries may be a contributing factor.^[22] In the West African sub-region, there is no comprehensive and well-administered health insurance scheme hence, health-care financing within the sub-region is mainly out-of-pocket.^[12,23] Misdiagnosis of lung cancer as pulmonary tuberculosis, by health care workers and subsequent non-referral to appropriate medical facility is yet another factor contributing to the underreporting.^[24]

A retrospective review at University College Hospital, Ibadan, by Ogunbiyi found only 142 cases of lung cancer during a 30-year review of all cancers. The male: female ratio was 1.7:1 and interestingly, the peak incidence in females was two decades earlier than in male patients.^[10] It is noteworthy that 60% of patients in this series were heavy smokers. The above study will support the notion that lung cancer is not common in Nigeria. However, a more recent prospective study by Ezemba *et al.* recorded a total of 51 cases over a 30-month period at the University of Nigeria Teaching Hospital, Enugu, Southeast Nigeria.^[11] This was a hospital-based study, and in their series, male: female ratio was 2.4:1, and only 42% of their patients had a history of smoking. In another regional study, Christopher and Charles showed that lung cancer accounted for 2.5% of all cancers seen in the Niger Delta region of Nigeria between 2012 and 2017.^[25] This clearly shows higher incidence of lung cancer when compared to previous studies in Nigeria.

As the standard of living improves across all African countries, it is projected that the number of people over

the age of 65 will quadruple by the year 2050 to about 193 million, approximately 10% of the estimated population.^[26] Therefore, the burden of cancer in is likely to increase.

In general, within the West African sub-region, most patients with lung cancer present very late, with over 90% presenting at the stage when curative treatment is no longer feasible. In the series by Ezemba *et al.*, only 2% of cases were judged to be surgical candidates. Similarly, in another series by Adewole *et al.*, at presentation, 85% of the patients had advanced and extensive disease; limiting treatment to only palliative chemoradiotherapy.^[27]

There is a paucity of surgical treatment options for lung cancer in Nigeria and other West African countries owing to this pattern of presentation with advanced disease. Equally, the outcome of palliative treatment with chemotherapy for these patients, is poor. Newer and more effective drugs and novel therapies are not readily available and are generally too expensive with many patients unable to afford a recommended full chemotherapy cycle. Unfortunately, radiotherapy is equally not readily available; Nwankwo *et al.* in 2013 noted only nine centers with radiotherapy facility for the treatment of cancer in Nigeria with a population of 172 million at that time, most of which were out of function.^[28] The situation has not changed much with only four actively functional cancer radiotherapy units in a 2020 count.

RISK FACTORS AND PREVALENCE IN AFRICA

In spite of global strategies redirecting cancer prevention efforts to the identification of inherent lung cancer risk factors in other to mitigate their carcinogenic effect, there remains a gross paucity of indigenous risk factor data across most regions of Africa unlike what obtains in other regions of the world.^[22,29] Most of the extrapolations for lung cancer risk factors for the African population are based on studies conducted among black sub-populations resident in western countries.^[13,30-33]

The many genetic and environmental factors that are associated with increased susceptibility to lung malignancy include but are not limited to tobacco, exposure to outdoor air pollution, diets, and pre-existing lung disease.^[13,34,35] Furthermore, these risks were observed to have ethnic and racial predilections.^[35,36] In Africa, there is evidence of regional disparities in available literatures on risk factors for lung malignancy.^[22,30,33]

However, recent genealogical susceptibility studies conducted outside Africa^[31,32,37,38] among people of African descent, to determine genetic ancestry and atavism contributing to higher lung malignancy prevalence and poorer outcome and survivorship, examined mutations, and alterations of angiogenic pathway genes such as epidermal growth factor receptor (EGFR) and matrix

metalloproteinase-3 (MMP-3) receptor; both of which are commonly associated with higher risk of lung cancer development and poorer prognosis as well as other commonly reviewed lung cancer receptor genes such as tyrosine kinase/Ras/Raf pathway and KRAS; but found no definite or significant association especially among Africans of West African ancestry. Majority of indigenous African genetic susceptibility studies on lung cancer have origins in North Africa with a few from South Africa and none from Nigeria and the rest of West Africa.^[22] Data from Egypt, Tunisia, and Morocco indicated higher frequency of P53 genetic mutation in lung cancer among North Africans though EGFR and MMP-3 mutations share similarities to their neighboring European countries.^[39-45] However, genetic studies from North Africa cannot be extrapolated to all Africans since the people of North Africa are a genetically diverse, complex and heterogeneous population consisting of an admixture of Middle East Arabs, sub-Saharan Africans (SSAs), European, and autochthonous North Africans.^[46,47]

Cigarette smoking is one of the most studied non-genetic or modifiable lung cancer risk factors in Africans.^[22] There are reports showing a high odds ratio of developing lung cancer associated with heavy smoking among North Africans.^[48,49] The calculated odds were lower in a much older but similar study from Southern Africa^[50] and another from East Africa.^[51] Interestingly, these odds have been reported to be far lower in West Africa by a more recent study conducted in Nigeria.^[52] Across all regions of Africa, miners are the most studied workers group for occupational exposures predisposing to lung cancer with cumulative evidence of lower odds of lung cancer development compared to tobacco. Asbestos exposure^[50] among South African miners and other industrial exposures previously reported to be associated with lung cancer in Africa include chrome, coal, copper, gold, nickel, arsenic, and silica; most of which had relative lower odds compared to tobacco exposure or use.^[53,54] Exposure to petroleum, gas fumes products, and cement dust at building sites, is common across Nigerian urban dwellers and use of protective air filter masks are non-existent providing a fertile ground for researchers to explore work-based associated risks of lung cancer.

Interestingly, environmental risks of lung cancer reported from North and South Africa indicated lower odds with exposure to coal used for domestic and commercial cooking compared to tobacco smoking, outdoor air pollution from emissions, and poor ventilation.^[48,53,55,56] It remains to be determined if current levels of exposure to these carcinogenic risk factors retain low odds as the number of lung cancers occurring in non- and never smokers continue to increase.^[22,57] Infection-associated predisposition has been reported by Sasco *et al.*^[48] and Stein *et al.*,^[58] with human immunodeficiency virus (HIV) infection being highly implicated. However, a pooled analysis

by Akarolo-Anthony *et al.* did not find a significant association between HIV and lung cancer in Nigeria.^[59]

Considering the interplay of genetic and non-genetic risk factors in lung cancer evolution among Africans, genetic polymorphism involving CYP1A1, CYP1A2, CYP2F1, CYP2A6*2, and CYP2A6*9 genes has been described by recent studies from North Africa.^[60-62] These genes alter the rate of byproduct and metabolite detoxification among cigarette smokers, especially those possessing slow metabolizer variants with inherent higher risk of developing lung cancer particularly squamous carcinomas. Furthermore, Hetta *et al.*^[63] recently reported the presence of circulating microRNA-17 and microRNA-22 in North African lung cancer patients which may be useful for routine non-invasive early detection of lung cancer through liquid biopsies.

Prevalence data on lung cancer burden in West Africa and particularly Nigeria relies heavily on Global Cancer Incidence, Mortality, and Prevalence (GLOBOCAN) periodic reports published by the International Agency for Research on Cancer.^[2,22] Country-specific population-based data modeling is done to arrive at the GLOBOCAN figures which are largely based on available national cancer data and population statistics with the validity of data closely tied to in-country data quality and source. As observed in [Figure 1], West Africa posted the lowest global lung cancer incidence and overall, 5-year prevalence among all the regions of the world in the latest GLOBOCAN reports of 2020.^[64,65] These figures may be due to gross cancer under capturing and underreporting. Using Nigeria as an example, the 2020 GLOBOCAN lung cancer estimates captured national data only from four population-based cancer registries most of which are located in the Southern parts of the country; in Ibadan (2015–2017 data), Calabar (2016–2017 data), and Ekiti (2013–2018 data); notwithstanding that Nigeria is a very heterogeneous and multiethnic country. The Nigerian National System of Cancer Registries, though functional, is still limited in capacity due to logistics, legal, and intermittent funding challenges.^[66] Nonetheless, the GLOBOCAN figures may actually mirror the presentation pattern and outcome of cancers in everyday practical scenario within Nigeria and West Africa, due to established poor knowledge and awareness about early symptoms and signs of lung cancer and general poor health-seeking behavior.^[15] Several barriers exist in accessing lung cancer care in many SSA countries which may exclude lung cancer sufferers from formal health-care system and by extension from official cancer registration.^[67] Previously reported barriers to lung cancer care in SSA include patients' lack of knowledge and awareness of symptoms and risk factors for lung cancer,^[68] low level of education,^[22] low socioeconomic status and remote distance to health facility,^[69] ready availability of alternative medicine (medical pluralism),^[70] social stigmatization and language barriers, lack

of lung cancer screening modalities, and a poor and time-consuming referral system.^[19,71]

It is yet unknown the full extent of the impact of the ongoing COVID-19 pandemic in different parts of the world. There are, however, ongoing reports of challenges with cancer diagnosis and treatment occasioned by health services interruptions and deliberate attempt by health authorities to control human traffic particularly at public health institutions as part of containment strategies to minimize disease spread. These could ultimately lead to reduced health-care access with expected short-term decline in reported cancer incidence and formally documented cancer burden followed in the latter years by a rising number of advanced stage diagnoses and cancer mortality.^[72,73] Nevertheless, some good may still come out of the obvious exposure of the inadequacy of health-care facilities seen during COVID-19 surges, as many governments in the subregion are investing into the health-care system.

WHAT NEEDS TO CHANGE?

Recommendations aimed at addressing the underdiagnosis and poor management of lung cancer in West Africa and Nigeria in particular should be aimed at solving the problems of health-care funding and lack of expertise, while bridging the technological gap and addressing challenges in practice. The responsibility to change this narrative lies not only on the government but also more so on the regional postgraduate training colleges and all categories of health practitioners.

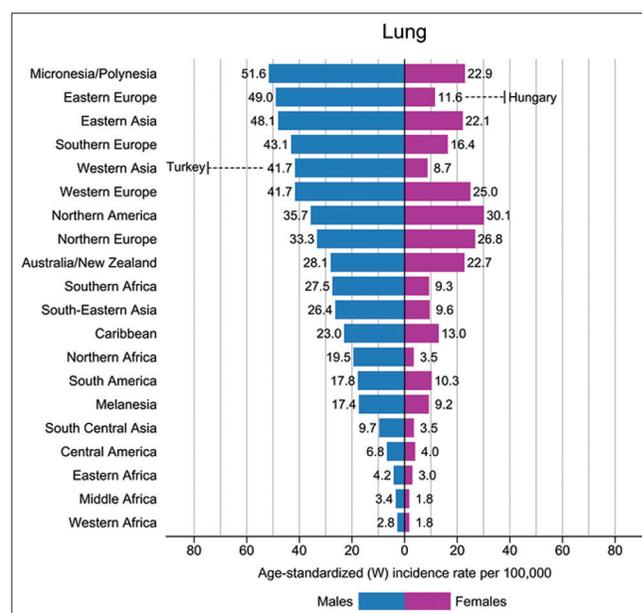


Figure 1: Region-specific incidence age-standardized rates by sex for lung cancer among men and women in 2020. Rates are shown in descending order of the world (w) age-standardized rate in men, and the highest national rates among men and women are superimposed. Source: GLOBOCAN 2020.

There should be an increase in total health expenditure. African countries, as well as donor countries should fulfill the terms of the Abuja Declaration.^[74] The benefit of such investment is multifold because health capital has great potential for improvement of the economic growth and development and healthier workers are physically and mentally more energetic.^[75] Such investment in health should target provision of technology and full implementation of universal health coverage. The Nigerian Cancer Control Plan^[76] is a well thought out plan; it should be funded, and fully implemented and if successful, extended across the entire subregion. Furthermore, stakeholders should develop a culture-focused intervention program that will increase public awareness about the symptoms of the disease and encourage early presentation towards improved treatment outcomes.^[22] The program should be targeted at high-risk population groups in which awareness is particularly lacking, to empower them and change their health-seeking behaviors. It is suggested that the Nigerian Thoracic Society and similar national associations across the subregion, take a lead in these public awareness campaigns. The Nigerian government should also institute comprehensive measures including enacting very strict anti-tobacco laws targeting tobacco production and marketing since the absolute number of active smokers in Nigeria remains high.^[77]

Postgraduate Medical Training Colleges should make efforts to bridge the technological gap in medical practice by making the curriculum fit for the 21st century. It is impossible to train without contemporary technology and expect to get better outcomes. Where cost of acquiring new technology is a problem, it may be prudent to procure medical equipment hardware directly from health facilities in developed economies during their upgrade. Improvements in physicians' education and training as well as adoption of technological advancements should help narrow the gap in providing specialist oncological care for patients with lung cancer.^[78]

Primary and secondary care physicians should be educated on the need for screening for lung cancers in patients with early warning symptoms and signs. The recommended lower thresholds for screening in people of African descent should inform our practice.^[79] Referral pathways and guidelines should be developed, defined, and enforced; and these should be championed by the National Specialty Associations or Societies. Circular migration of skilled physicians should be encouraged as this would improve domestication of expertise. Emphasis on skill development in bronchoscopy and mediastinoscopy should be encouraged. Thoracic themed training in cardiothoracic surgery should be encouraged. There should be a coordinated data capturing platform across all levels of health care. The data capturing from primary and secondary health facilities which is presently limited to communicable diseases should be extended to include non-communicable diseases including cancers.^[80]

Minimally invasive biopsy of lung masses remains the route to diagnosis of lung cancer. These small biopsy or cytology specimens should be routinely subjected to immunohistochemical and molecular testing to identify targetable driver mutations. The amount of information to be gleaned from these small biopsies and cytologic specimens is great and has increased dramatically over the past decade.^[78] Similarly, training in minimally invasive thoracic surgery should be prioritized to improve treatment outcomes since surgical resection remains the main stay for curative treatment of lung cancer.

There should be optimal utilization of nuclear medicine services as these seem to be presently underutilized.^[81] With an average of one bone scan per year and <0.2% of total bone scans in an 11-year period, bone scintigraphy requested for lung cancer.^[82] In the absence of PET/CT imaging, bone scintigraphy still has an important role to play in patients' management and referring physicians are encouraged to embrace this imaging modality. National governments should be sensitized to invest in PET/CT imaging and make them available at some major reference hospitals.

CONCLUSION

Lung cancer is of public health importance with a great degree of socioeconomic burden. Case fatality rate is higher than any other commonly reported cancer. Late presentation is a major factor to the high fatality rate. Well-coordinated and regularly supervised awareness and education campaign championed by the Nigerian Thoracic Society and similar national associations across the West African subregion could help. Campaigns should target the first-line health-care practitioners on the need for early recognition and referral to the appropriate specialist centers.

The apparent underreporting of lung cancer incidence should be addressed by both the respiratory physicians and cardiothoracic surgeons working together to set up specific regional lung cancer registries with regular audit of the reporting. There is an urgent need for further studies on the local risk factor predisposition to lung cancer, especially in the younger age group as recent studies have shown increasing incidence of lung cancer among the younger non-smoking age group, especially women.

Finally, intense pressure should be mounted on the governments to implement the 15% GDP allocation to health-care budget as agreed in the WHO/Abuja Declaration and also hasten the actualization of a truly universal health insurance scheme across the subregion.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Conflicts of interest

There are no conflicts of interest.

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