

*East African Medical Journal Vol. 88 No. 4 April 2011*

AETIOPATHOLOGY AND MANAGEMENT CHALLENGES OF LUNG CANCER IN THE DEVELOPING WORLD  
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## AETIOPATHOLOGY AND MANAGEMENT CHALLENGES OF LUNG CANCER IN THE DEVELOPING WORLD

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### ABSTRACT

**Background:** There are newer diagnostic and therapeutic armamentaria for primary lung cancer. Application of molecular genetics in lung cancer management is evolving rapidly. However, the traditional knowledge and practices that were applicable before the 1980s still hold sway in most developing countries.

**Objective:** To highlight the gap in current aetiopathology and management profile of primary lung cancers.

**Design:** Hospital based prospective study.

**Setting:** Metropolitan Lagos University Teaching Hospital which accounts for about 13% of Nigerian population.

**Subjects:** Two hundred and sixty seven patients referred to our centre with lung malignancy as a differential diagnosis.

**Results:** The research lasted 99 months beginning October 1999 during which 267 patients were enlisted. There were 148 males (55.4%) and 119 females (44.5%). Stage IV patients were 183 (68.5%) while only three patients were found at stage I. Histology showed squamous cell carcinoma in 27.7% of cases while adenocarcinoma constituted 64.0%. Curative surgery was performed for 13.1% while non curative surgery was performed for 16.5%. Correlation between smoking and malignancy was stronger among the male than the female patients.

**Conclusion:** There is increasing incidence of primary lung cancers among non-smoking females. Despite the availability of modern diagnostic and therapeutic tools, the developing world is lagging behind in their acquisition and application.

### INTRODUCTION

Tumours of the lung are either benign or malignant. Malignant tumours are either primary or secondary depending on tissue of origin. Primary malignant tumours of the lung are further classified into small cell and non small cell tumours of the lung. All these variants are available worldwide. While no real improvement in the long term survival has been obtained in lung cancer, during this decade, a significant improvement in cancer control has been obtained by biology-driven targeted therapy as with anti EGFR tyrosine kinase (1). Two phases can be described in the knowledge of lung cancer biology: a first phase obtained in the 1980s describing the main molecular anomalies and impaired cell control mechanisms, and a second phase starting in the 2004-2005 giving rise to the therapeutic applications of this knowledge (1). TP53 somatic mutations are frequent in many cancers, and their prognostic and predictive values are currently being assessed in clinical trials.

In fact, TP53 gene therapy is in use in China (2). The implications of these are that, somatic mutations have followed different routes to becoming substances of clinical application and sequencing several genes in human tumours is on the verge of becoming routine clinical practice (2). An important development here is the finding of Paxillin over-expression that occurs during the earliest stages of lung cancer development (3). It is therefore being thought of as an important screening modality for bronchogenic carcinoma in high risk individuals (3). Smoking is a documented risk factor for cancer, especially for lung carcinomas. Nicotine and its derived carcinogenic nitrosamines contribute to lung cancer development and progression through the binding to nicotinic acetylcholine receptors (nAChR) in lung cancer predisposition. The traditional armamentaria for the diagnosis of lung cancers include information from history, clinical features, chest radiographs (including computerised axial tomographic scan), bronchoscopy and cytology/histology amongst others. Beyond

these, there is growing interest in the use of tumour genetics in clinical practice. Even at that, misdiagnoses still occur (5). Hypermethylation of SHOX2 in bronchial aspirates appears to be a clinically useful tumour marker for identifying subjects with lung carcinoma, especially if histological and cytological findings after bronchoscopy are ambiguous (6). This has the tendency to further strengthen the accuracy of diagnosis of bronchogenic carcinoma. Surgery for loco-regional control of tumour offers the best chance of cure especially at early stages. This can be in form of (multi)segmentectomy lobectomy, bi-lobectomy and pneumonectomy. This is often combined with chemotherapy to mop up subclinical metastasis. Radiation therapy offers a lot of support for loco-regional palliation. The available therapeutic armamentaria notwithstanding, there has been no real improvement in the long term survival of lung cancers (1). Various tumour markers are now being used to monitor the progression of the disease. More recently, cytoplasmic HuR expression is known to correlate with angiogenesis, lymphangiogenesis and poor outcome in lung cancer (7). This promises to offer some clinical roles in determining the post-operative prognosis of bronchogenic carcinoma in future.

Despite these widespread developments and applications of molecular genetics in relation to tumorigenesis, diagnosis, treatment and monitoring of treatment, the traditional knowledge and practices that were applicable before the 1980s still hold sway in most places in Africa. There is therefore a wide gap between what is obtainable in most parts of Africa and the developed world.

This research was conducted to highlight the staggering gap in the current aetiopathological and management profile of lung cancer. It is also an assessment of the readiness of the developing world for the challenges of lung cancer management as we enter the new decade.

## MATERIALS AND METHODS

The research took place at the Lagos University Teaching Hospital, Lagos Nigeria. The study period spanned 99 months beginning October 1999. A data book was opened to accommodate the needed data. We included all patients referred to our unit through the clinics and the emergency rooms with suspicion of primary cancer of the lung. In the bio-data section, their ages and sexes were entered as they presented. The states of origin were also noted with smoking history, occupation, exposure to dust over time and history of premalignant lesions. The results of chest radiographs, computerised tomographic scans, sputum cytology, fine needle aspiration cytology, bronchoscopy, pleural biopsy, lung surgical specimens (open biopsy or resected lung biopsy) were noted for diagnosis. We adopted the old method of staging for

uniformity because the research began in 1999.

The treatment modalities were recorded. Those that could not be offered surgery were referred appropriately to the oncology department after tissue diagnosis.

The data were analysed to give various information. We sought correlation between smoking and occurrence of cancer (treating the males and females separately). For the purpose of regional identification of patients, we divided patients into three geopolitical zones (southwest, southeast and south-south zones) and we looked at regional disposition.

We confirmed diagnosis in all cases before the patients were referred to oncology department. Only patients whose staging was concluded were included in the study. We excluded those whom for any reason(s) were not completely staged. Statistical analysis was done manually.

## RESULTS

The research lasted 99 months beginning October 1999 during which 267 patients were enlisted. They comprised of 148 males (55.4%) and 119 females (44.5%). The ages ranged from 37-76 years. A significant proportion of the patients (73.8%) were in the 50-69 year age range. The males constituted 54.3% of the bulk while the females were 45.7% (table I). Stage IV patients were 183 (68.5%) while only three patients were found at stage I of disease. The histology showed squamous cell carcinoma in 27.7% of cases and adenocarcinoma in 64.0%. Among the stage IV group, 64.5% were adenocarcinoma while 25.1% were squamous cell carcinoma.

**Table 1**  
*Age and sex distribution*

| Age      | Male       | Female     | Total       |
|----------|------------|------------|-------------|
| 30-39yrs | 1          | 2          | 3(1.1%)     |
| 40-49yrs | 11         | 4          | 15(5.6%)    |
| 50-59yrs | 52         | 41         | 93(34.8%)   |
| 60-69yr  | 55         | 49         | 104(39.0%)  |
| >69      | 29         | 23         | 52(19.5%)   |
|          | 148(55.4%) | 119(44.5%) | 267(100.0%) |

Within the same group, 169 patients (92.3%) presented with pleural effusion. This constituted 63.3% of the total number of patients studied. Only 24 patients (9.0%) underwent bronchoscopy. Cytology specimens were collected in 191 patients and 89 specimens (46.6%) were positive for malignancy. The remaining 102 cytology negative patients underwent needle biopsies (using Abram's needle). We got 74 positive specimens. A further 21 patients

**Table 2**  
*Staging and Histology*

|                | I       | II        | III       | IV         | Total       |
|----------------|---------|-----------|-----------|------------|-------------|
| Squamous cell  | 1       | 10        | 17        | 46         | 74(27.7%)   |
| Adenocarcinoma | 2       | 21        | 30        | 118        | 171(64.0%)  |
| Others         | -       | 1         | 2         | 19         | 22(8.2%)    |
|                | 3(1.1%) | 32(12.0%) | 49(18.4%) | 183(68.5%) | 267(100.0%) |

had open lung biopsies while the remaining seven patients had exploratory thoracotomy for diagnosis and treatment. Curative surgery was performed for 13.1% while non curative surgery was performed for 16.5%. Seventy nine patients underwent thoracotomy for lung resection. These were 46 lobectomies, six bi-lobectomies and 27 pneumonectomies. There was no segmentectomy or multi-segmentectomy. All the patients were referred to Oncologists for continuation of care. The correlation between smoking and malignancy was stronger among the male than within the female patients. We saw no significant relationship between malignancy and the region of origin of the patients.

## DISCUSSION

There have been a lot of developments in the understanding of lung cancer aetiopathology and its management over the last decade. The causative roles of cigarette smoke have been further clarified as an initiator and promoter of carcinogenesis. Therefore, even without significant change in long term survival of lung cancer victims during the last decade, a significant improvement in cancer control has been obtained by biology-driven targeted therapy (1). In the developing world, there is no properly conducted prospective research on long term survival of lung cancer patients. In fact little is known about the epidemiology and aetiopathogenesis of this very important malignancy. Therefore, there is a clear justification for this research which is about highlighting the aetiopathology of lung cancer and the challenges faced by practitioners in their management in the developing world. It is another channel, opened to compare notes with other international works in the field to determine the gap between what is ideal and what is obtainable in the developing world.

While applying the strict inclusion criteria for this research, we saw 267 patients in 99 months. They were 148 males and 119 females giving a M:F ratio of 1.2:1 (Table 1). Unpublished experience at our centre showed increasing incidence of lung cancer among the female population. It has been difficult to show this trend statistically because there were no baseline figures.

Our youngest patient was 37 years and the oldest 76 years. Stage IV disease was found in 68.5% of the

patients. Within this group, 92.3% presented with pleural effusion. It therefore means that majority of the patients presented late. Only three patients reported with stage I disease. This challenge can only be mitigated by institution of proactive steps directed at routine screening of high risk patients. It has been difficult to do a proper follow up on the patients because they were referred to oncologists after initial surgery and tissue diagnosis. This situation calls for awareness campaigns to educate the populace about the dangers inherent in smoking and the need for routine screening of smokers to detect lung cancers at early stage(s).

There was preponderance of adenocarcinoma in the series. Adenocarcinoma constituted 64.0% of cases seen while squamous cell carcinoma was found in 27.7% of them.

In Nigeria, there are six geopolitical zones with fairly different socio-cultural practices and environmental concerns. Three of these zones are in the south. The south – south and part of the south east are exposed to environmental pollution from oil exploration and mining. South-western people are exposed to agricultural dust and the cosmopolitan Lagos and Ibadan (both in the south west) are highly polluted with human wastes and vehicular hydrocarbons.

These three groups of people are reasonably represented in Lagos metropolis in good proportions. The only universal occurrence in the three groups was the strong correlation between prolonged smoking and malignancy especially among the males. The visibly increasing incidence amongst the females could not be totally explained by their smoking history alone. There are therefore certain (yet to be explained) predisposing factors that will require further studies to elucidate.

The main modalities of treatment included lung resections when the disease is operable, and chemotherapy and radiotherapy as adjuvant. There were 58 lobectomies (12 from bi-lobectomies) and 27 pneumonectomies. Therefore, 79 patients (29.6%) were operable at presentation leaving 69.4% inoperable. No patient was suitable for segmentectomy at presentation. The situation can only be reversed through early presentation of cases. Patients and general practitioners need to be adequately informed about the need for early recognition and referral of

suspected lung cancer cases.

More recently, it is believed that unprecedented and much more cost-effective results can be obtained when targeted agents are administered following appropriate biomarker-driven selection of non small cell lung cancer patients (8). The rapidly developing concept of translating biological development to medical therapy is expected to improve the outlook of primary lung cancers with time.

In conclusion, primary lung cancer might be affecting more females (and the males alike) and there is need to protect them from the known predisposing factors. We also believe that the developing world is dangerously lagging behind in acquisition and deployment of new diagnostic and therapeutic armamentaria for primary lung cancers. Practitioners in the developing world need to face this challenge by acquiring modern diagnostic and therapeutic equipment and drugs to better the lots of their patients.

#### ACKNOWLEDGEMENT

To Tolulope Thomas, Oyindamola Thomas and Oyinlola Thomas for jointly typing the manuscript.

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