

ORIGINAL ARTICLE

NOTTINGHAM HISTOLOGICAL GRADING OF CASES OF PRIMARY INVASIVE CARCINOMA OF THE BREAST AT LAUTECH TEACHING HOSPITALS, NIGERIA***Oluogun W.A¹, Sabageh D¹, Adelusola K.A¹ and Adedokun K.A²**¹Department of Morbid Anatomy and Histopathology, Faculty of Basic Clinical Sciences, College of Health Sciences, LAUTECH, Ogbomoso, Nigeria²Department of Morbid Anatomy and Forensic Medicine, Faculty of Basic Medical Sciences, College of Health Sciences, Obafemi Awolowo University, Ile-Ife, Nigeria**ABSTRACT****Background**

Breast cancer has since been known to be a global public health problem being the most common malignancy in women worldwide. The incidence in Nigeria is yet to be determined but is said to range from three and a half to thirteen and a half percent in hospital-based reports.

Objective

Our study aimed at grading the cases of primary invasive carcinoma of the breast using the Nottingham Histological System of grading.

Methods

The study was a hospital-based retrospective study carried out at LAUTECH Teaching Hospitals in Osogbo and Ogbomoso with ethical approval being obtained from the research and Ethics Committee of LAUTECH Teaching Hospital Ogbomoso. The original request cards were retrieved, studied and essential clinical details which include age, and the side (right or left) of the breast tumor were extracted. Tissue blocks were also retrieved and fresh sections about 3-5µm were cut from formalin-fixed and paraffin-embedded blocks and stained with Hematoxylin and Eosin dyes for histological analyses. Data obtained was analyzed using both Microsoft Excel and EPI Info statistical software and statistical package for social sciences. The information obtained was reported using frequencies and percentages. Quantitative data were presented as mean $\pm$ SD [Standard Deviation]. A 95% confidence interval was used in this study and a P-value of ≤ 0.05 was considered statistically significant.

Result

Our study revealed the commonest histological variant of primary invasive carcinoma of the female breast to be infiltrating ductal carcinoma, not specified type with 305 cases (88.9%).

Keywords: Nottingham histological grading, primary invasive carcinoma, breast malignancy, global public health problems

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INTRODUCTION

Breast cancer is a global public health problem being the most common malignancy in women worldwide (1, 2). It is 9 times more common in women than in men. It is also the commonest malignant tumour in Nigeria (4). One of every fifteen women in Europe and one of every eight women in the United States of America will develop breast cancer in her lifetime (1, 3). The incidence in Nigeria is yet to be determined but ranges from 3.5% to 13.5% of breast cancer cases in hospital-based reports (5). The diagnosis of breast cancer at earlier stages is associated with a more favourable overall prognosis (6).

The majority of breast cancer cases were of high grade and carried a very poor prognosis because of the late presentation of patients to the hospital (7). Oluwole and his colleagues reviewed cases of breast diseases seen in Ile-Ife between 1977 and 1986 (8). The findings showed 26% had breast cancer. The peak age incidence, histological grade and the stage of presentation of breast cancer in this study were similar to the findings of Chidozie (7).

Infiltrating ductal carcinoma is the most frequently encountered malignant tumour of the breast, accounting for 65 to 80% of all mammary cancers (9). It is termed 'not otherwise specified' because it is not classified into any of the other categories of invasive mammary carcinoma. The relative frequency of some of the other types of breast carcinoma is Intraductal carcinoma 20-30%, medullary carcinoma 1-5% and Invasive lobular carcinoma 5-10%. It has been reported that infiltrating ductal carcinoma, No Special Type (NST) represented 65.7% of breast carcinomas while papillary carcinoma, medullary carcinoma, and tubular carcinoma represented 9%, 4.5% and 4.5% respectively (10).

Survival generally has been related to specific histological types of breast cancer and it was also noted that the relatively uncommon histological types of breast cancer: Medullary, Colloid, Tubular and Adenoid cystic carcinomas tend to be prognostically more favourable (11, 12, 13). Histological grade provides prognostic information in many tumours including breast cancers.

Two main methods have evolved, based either on nuclear factors or a combination of cellular features (nuclear, cytological and architectural) (14). The latter method is the most widely accepted for grading breast cancer and has been refined with the stricter definition of more objective criteria. As a result, the reproducibility of histological grading of breast cancer, previously questioned, has been improved; and recent studies have confirmed that good correlations between pathologists could be obtained if strict criteria are used (14). The currently acceptable grading method is the Nottingham breast cancer grading method, which takes into consideration tubule formation, nuclear size/pleomorphism and mitotic count (14). This is an improvement on Greenough who described a system of grading mammary carcinomas based on three histological components of the tumour cells: the degree of tubule formation; the size, shape and chromatism of the nuclei; and the frequency of mitoses (15). Studies by Black *et al*, as well as Bloom and Richardson show a relationship between the tumour grade and the survival of patients (16, 17). Other investigators have confirmed a similarly close relationship between breast tumour grades and tumour recurrence as well as the overall survival of patients with breast cancer (18).

MATERIALS AND METHODS

This study was carried out at LAUTECH Teaching Hospitals in Osogbo and Ogbomoso. This is a hospital-based retrospective study, which involves the retrieval of archival records, paraffin wax blocks and surgical specimens of cases histologically diagnosed as breast cancer in the histopathology Department of LAUTECH Teaching Hospital between January 2005 and December 2014.

Ethical approval was obtained from the research and Ethics Committee of LAUTECH Teaching Hospital Ogbomoso, Oyo state. The permission of the heads of the Histopathology Department of LAUTECH Teaching Hospitals Osogbo and Ogbomoso was sought and gotten.

This study posed no risk to the patients, their relatives, or the community as it was carried out on archival

tissue samples and patients' clinical records. Data generated during the course of this study were accessible to the investigators only. All information was coded by number and no name was recorded. All data were transferred to a password-protected personal computer.

The original request cards were retrieved, studied and essential clinical details which include age, and the side (right or left) of the breast tumor were extracted.

Tissue blocks were retrieved and fresh sections about 3-5µm were cut from formalin-fixed and paraffin-embedded blocks and stained with Hematoxylin and Eosin dyes for histologic analyses.

Data obtained was analyzed using both Microsoft Excel and EPI Info statistical software [version 3.5.4] and statistical package for social sciences 20 (SPSS version 20). The information obtained was reported using frequencies and percentages. Quantitative data were presented as mean $\pm$ SD [Standard Deviation]. A 95% confidence interval was used in this study and a P-value of ≤ 0.05 was considered statistically significant.

RESULTS

Three hundred and forty-three cases of female breast cancer were seen during the study period.

Breast cancer occurred slightly higher in the left breast with 172 cases (50.1%) recorded while 171 cases (49.9%) were on the right breast.

Two hundred and eighty-nine cases were analyzed for age. This is because some of the histology request cards and the records did not indicate the age of some patients with breast cancer.

The age range was 20 to 89 years (mean=49.70 years). The peak age incidence in the 6th decade (50-59years).

The majority of the cases occurred between the 4th and 7th decades (30-69 years). More than 50% occurred over the age of 50 years. (Figure 1 shows the age distribution of the female breast cancer patients).

The commonest histological variant of female breast cancer seen was infiltrating ductal carcinoma with 305 (88.9%) of the cases. Sixteen cases (4.7%) were invasive lobular carcinoma while only three cases (0.9%) each were metaplastic carcinoma and carcinosarcoma. There were 2 cases (0.6%) each recorded for malignant phyllodes and poorly differentiated carcinoma. There was only 1 case (0.3%) each of apocrine and tubular carcinoma. There were 4 (1%) cases of mucinous carcinoma. (Table 1)

Nottingham histological grade using tubule formation, pleomorphism, and mitosis was used to score 343 cases.

Seventy-five (22.0%) cases were high grade (Grade 3), 244 (71.0%) cases were intermediate grade (Grade 2) and 24 (7.0%) cases were low grade (Grade 1) as depicted in table 3.

DISCUSSION

The total number of female breast cancer cases in this study was three hundred and forty-three (343) which is more than the number and percentage of cases done in Ile-Ife, Osun State by Adelusola and Titiloye *et al* (19) which is 66.7%, and the majority of other centers in Nigeria such as Benin, Calabar, and Zaria with 77%, 74.3% and 64% respectively (7, 20, 21).

The Ladoke Akintola University of Technology Teaching Hospitals Ogbomoso and Osogbo where this study was carried out in a tertiary health institution in the Oyo and Osun states of Nigeria.

In this study, female breast cancer occurrence is slightly more in the left side of the breast than the right side in 50.1% and 49.9% of cases respectively. This is not different from the known pattern of breast cancer occurring slightly more common in the left breast for reasons not known. Adesunkanmi and Oluwole *et al* (8) found that breast cancer occurred slightly more on the left side of the breast in 53.3% and 52.5% respectively of the cases studied (22).

In this study, female breast cancer was observed to occur between 20-89 years with a mean of 49.70 years.

This is in agreement with Adesunkanmi *et al* (22) in a previous study at Ile-Ife, Osun state which put the age range at 23-85 years and a mean of 48 years. Ihekwa also recorded a mean age of 48 years (23). Out *et al* (20) however recorded a lower age range of 21 to 70 years and a mean age of 40 years and this was similar to the result from Adelusola *et al* (24) in a previous study at Ile-Ife, Osun state which recorded a mean age of 49 years. Adelusola *et al* (24) also found two peak age groups of 40-49 years and 60-69 years among the different age groups.

However, the peak age group in the current study was in the 6th decade (50-59) years. This is a decade or two later than the studies already mentioned from other parts of the country. The study of Otu *et al* (22) is of interest as it recorded earlier peak age group occurrence, an early age group of 26-35 years and a later age of 46-50 years. Gukas *et al* (24) in a comparison of the pattern of occurrence of breast cancer in Nigeria and British women noted that the age group seen in African breast cancer is 1 or 2 decades less than that seen in the Caucasians. The age group seen in this study tends towards the pattern of Caucasians. The reason for this might be attributed to an increase in awareness of breast cancer in comparison to what was obtained 10 to 15 years ago. Also standard of living and life expectancy is improving in our society (24).

In this study, out of the primary invasive carcinoma of the female breast, the commonest histological variant seen was infiltrating ductal carcinoma, not specified type with 305 cases (88.9%). The commonest histological variant of breast cancer globally was infiltrating ductal carcinoma, none otherwise specified which other nomenclature put as no special type. Tubular carcinoma and mucinous carcinoma have been documented to have a better prognosis out of invasive breast cancers. Mucinous carcinoma was seen in 1.2 % of cases in this study while tubular carcinoma was seen in only 1 case. This is in agreement with an earlier study by Titiloye *et al* (21) in Ile-Ife. This is probably because the social lifestyle of the patients could be similar since Osogbo and Ile-Ife are located within the same State in Nigeria.

The overall grading of female breast cancer showed that a grade 2 cancer occurs in 71.0% of the cases. This grading is not in agreement with Ikpai *et al* (23) in a study of 300 patients in Calabar, Nigeria where he found 44 to be grade 1, 119 were grade 2 and 137 were grade 3. Studies conducted on blacks in America showed similarity to this study (24).

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Table 1: Frequency distribution of histological types of breast cancers

Type	Frequency (%)
Invasive Ductal carcinoma NST	305(88.9)
Invasive Lobular Carcinoma	16 (4.7)
Medullary carcinoma	6(1.7)
Metaplastic carcinoma	3(0.9)
Mucinous carcinoma	4(1.2)
Malignant Phyllodes tumour	2(0.6)
Apocrine carcinoma	1(0.3)
Carcinosarcoma	3(0.9)
Tubular carcinoma	1(0.3)
Poorly differentiated carcinoma	2(0.6)
Total	343(100.0)

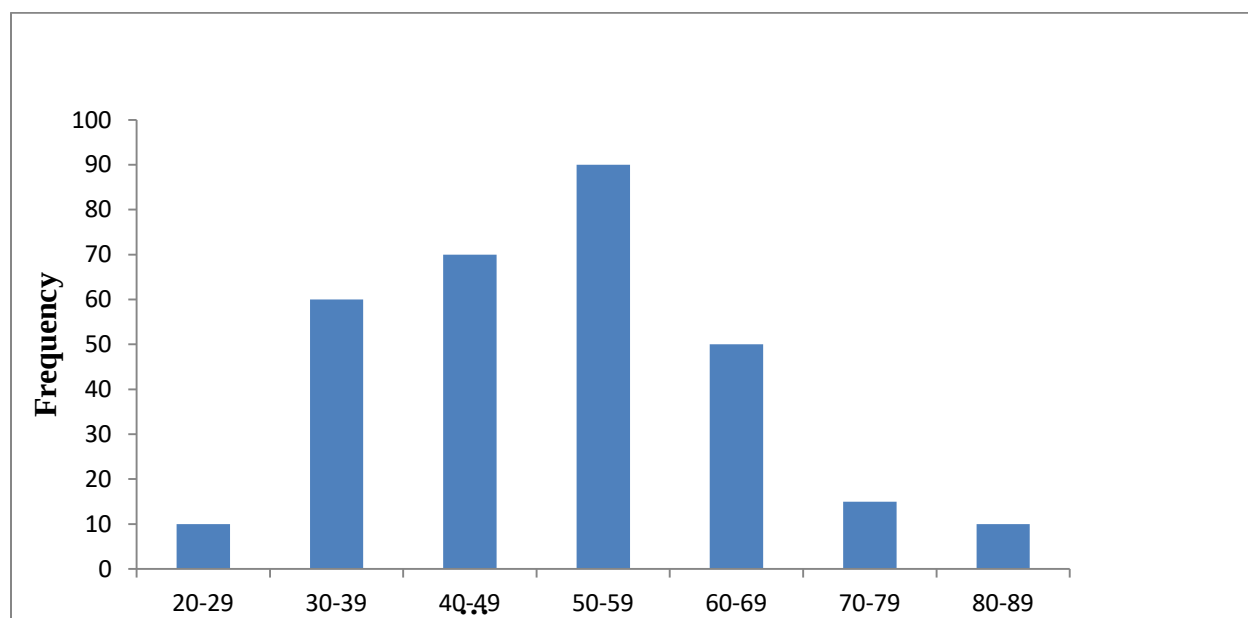


Fig 1: Age distribution of female breast cancer in Ogbomoso and Osogbo, Nigeria

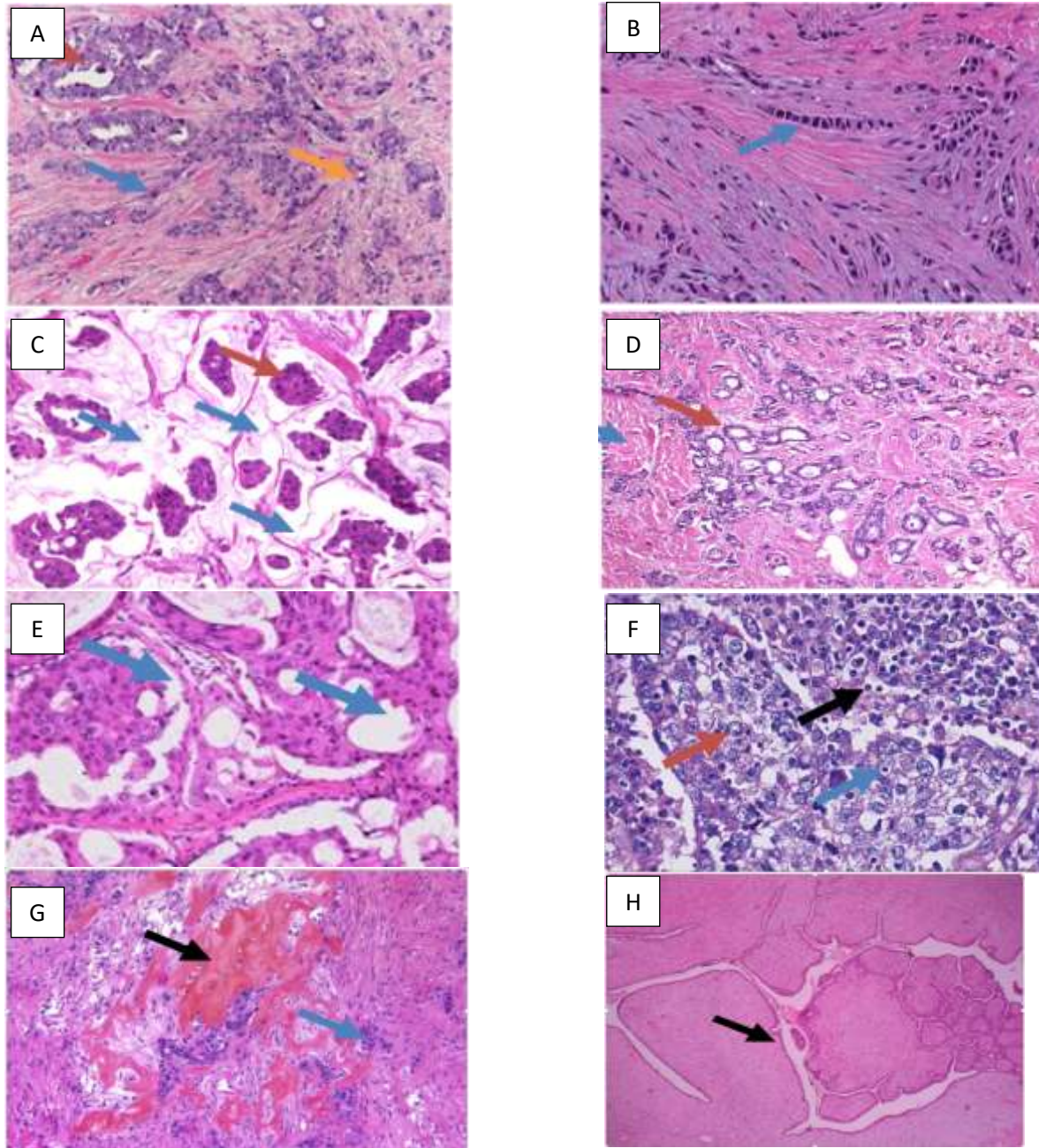


Figure 2: Photomicrograph A-H (H&E x40)

A- Invasive ductal carcinoma (NST); Red arrow indicates tubule formation, Blue arrow indicates high pleomorphism, Orange arrow shows mitotic figure. This case was Nottingham grade 3. Note the number of tubule formation, high pleomorphism and mitotic figure on the picture.

B- Invasive lobular carcinoma; Blue arrow indicates the column of malignant epithelial cells arranged in Indian file pattern.

C- Mucinous Carcinoma; Red arrow indicates the clusters of malignant cells. Blue arrows indicate the pools of extracellular mucin

D- Tubular Carcinoma; Red arrow indicates presence of well-formed tubules lined by single layer of cells with small uniform nuclei. The tumour cells lack myoepithelial cell layers placing the tumour cells in direct contact with the fibrous stroma as shown by the blue arrow

E- Apocrine Carcinoma; Blue arrows indicate the presence of tubules lined by tumour cells that exhibit apocrine metaplasia.

F- Medullary carcinoma; Red arrow indicates the presence of solid, syncytial-like sheets of large cells with vesicular, pleomorphic nuclei with prominent nucleoli. Blue arrow depicts mitotic figure. Black arrow depicts moderate to marked lymphoplasmacytic infiltrate surrounding the tumour.

G- Metaplastic carcinoma; Black arrow indicates the presence of matrix-producing tumour. Blue arrow indicates squamous cell carcinoma.

H- Malignant Phyllodes; Black arrow shows presence of nodules of proliferating stroma covered by epithelium. The tumour has infiltrative borders.