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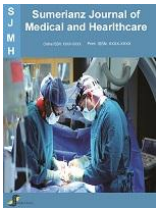

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Histopathological Characteristics of Breast Carcinoma in a Tertiary Health Facility in Subsaharan Africa

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Abstract

Background: Breast cancer is the commonest cancer in the female and histopathologic features beside the molecular subtype is a very useful prognostic factor in the clinical management of breast cancer patients. The most useful histopathological prognostic factors include tumour size. Lymph node involvement, lymphovascular invasion and grade of the cancer, **Aims and Objective:** The study aim to describe the histopathological characteristics and social demographic variables of breast carcinoma at University of Calabar Teaching Hospital (UCTH), Calabar. **Method:** This is a retrospective descriptive study of histopathologic characteristics of breast carcinoma in UCTH. The records of cases diagnosed as breast cancer in a five year period (2010-2014) in the department of Histopathology. The demographic variables and the histopathologic characteristics like the side tumour is located, tumour site, tumour size, histologic types, histologic subtypes, histologic grade, stage and number of lymph nodes involved are collated and analyzed. The findings were presented in tables and charts and statistical significance of variables tested. **Result:** One hundred and forty seven (147) cases of breast cancer samples were analysed. The mean age at diagnosis was 46.31+/-12.75 years old. The age ranged from 21-80 years old, the modal and median ages were 40 and 45 years respectively. Ninety eight percent (98%) were female and 2.0% male. All the males had invasive ductal carcinoma not otherwise specified. The right breast was involved in 54.42%of cases, left was 45.58% of cases and none had bilateral breast cancer. Mastectomy was the surgical treatment for 63.95% and lumpectomy in 36.05% of cases. Ninety nine percent (99%) were ductal carcinoma while lobular carcinoma was 1%. Invasive ductal carcinoma not otherwise specified (92.52%) was the commonest histologic subtype while special types was only a minor fraction of 3.40%. The majority (75.51%) has a tumour size of 2-5cm and moderately differentiated grade 2 was the most common accounting for 48.57%. **Conclusion:** Breast cancer is commoner in the premenopausal women. Invasive ductal carcinoma not otherwise specified is the commonest histologic subtype, the special type accounted for only a small fraction. The moderately differentiated breast cancer is the commonest. Breast cancer is commonest in female while the male breast cancer is just a fraction. The majority of the cancer has size 2-5cm but larger tumour size is associated with breast cancer in the young less than 40 years.

Keywords: Histologic type; Ductal; Lobular; Histologic grade; Tumour.

1. Introduction

Breast cancer is a heterogenous disease with varied morphological appearance, molecular features, behaviour and response to therapy. It arises from ductal epithelium in 90% of cases and originate from lobular epithelium in 10%. It occurs more often in the left breast than the right and is bilateral in about 4% of cases. The incidence of bilaterality in invasive breast carcinoma is about five times that of the general population and is even higher if there is a family history of breast carcinoma. [1]. It is particularly high in lobular carcinoma in situ, reaching figures of 25% to 50% in some studies. The tumours may be synchronous or metachronous. Juan [2] They may result either from intra-mammary spread or from independent events; the latter mechanism seems the most frequent. Anatomically, upper outer quadrant is the site of tumour in 50% of cases, followed in frequency by central portion and equally in the remaining both lower and the upper quadrants. Breast cancer can be multi-centric (presence of carcinoma in other quadrant other than the one containing the dominant mass). The other mass may be a smaller foci of invasions or in situ carcinoma and clonal analysis studies suggests that these tumour have a single primary origin with spread throughout the breast. Multi-centricity is commoner in lobular than in ductal carcinomas. [3]

1.1. Histopathologic Classification of Breast Carcinoma

Microscopically, the two major determinants in the classification of breast cancer are: (1) whether the tumour is confined to the glandular component of the organ (in situ carcinoma) or whether it has invaded the stroma (invasive carcinoma) and (2) whether it is of ductal or lobular type. The term ductal carcinoma may be taken to imply that the tumour is either arising from or involving a duct and preferentially involve with the appearance of a duct, in the

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same vein, lobular carcinoma implies tumour arising from the lobules or involving it and are preferentially located in the lobules. However, numerous exceptions in location of the tumours exist in both directions. Both tumour types arise from the same segment of the mammary gland (i.e; the Terminal Duct Lobular Unit (TDLU). Be that as it may, it should be made clear that it is the type of tumour as defined by cytoarchitectural features that establish its identity rather than its precise location within the breast.

1.1.1. In-situ Carcinoma

In-situ carcinoma accounts for 15-30% of breast carcinoma (DCIS- 80% and LCIS- 20%).The tumour cells in in-situ carcinomas remain confined within the ducts or lobules, also known as non-invasive carcinoma because the basement membrane is intact and no spread of tumour cells to the stroma. It can be ductal and lobular.

1.1.1a. Ductal Carcinoma In-situ (DCIS)

The diagnosis of DCIS rapidly increased from fewer than 5% of all carcinomas to 15% to 30% of carcinomas in well-screened populations with the advent of mammographic screening; and 10% to 20% of cases of DCIS are bilateral. Several morphologic variants of DCIS exist: papillary, comedocarcinoma, solid, cribriform, micropapillary, clinging, and cystic hypersecretory. A recent proposal that regards these tumours as part of a continuum has been suggested. This divides DCIS into three-grade system largely on the basis of cytological criteria. These are: the classic comedocarcinoma as grade 3 DCIS (having large pleomorphic cells with necrosis), the classic solid/cribriform/micropapillary lesions as grade 1 DCIS (small uniform cells without necrosis), and those showing intermediate cytological features are reported as grade 2 DCIS. Other rare additional morphologic variations of DCIS include cases with signet ring cells with apocrine-type cytology, and those with evidence of endocrine differentiation.

1. Papillary

Papillary carcinoma is a very distinct type, thought to arise from large ducts. Papillary carcinoma makes up only a small percentage of breast carcinomas. Grossly, it may present as a well circumscribed mass or it may ramify within several ducts to involve an entire breast segment. In the variant known as intra-cystic papillary carcinoma, the tumour appears as a mural nodule within a large cystic space representing a dilated duct. Papillary carcinomas occur in an older age group. Microscopically, the epithelial cells are uniform in size and shape. The epithelial cells may be round, oval, or spindle, the latter arranged perpendicularly to the duct axis. There is only one cell layer with the myoepithelial cells lacking, this is demonstrated by actin stain which highlight its presence or absence; there is nuclear hyperchromasia and high nucleocytoplasmic ratio, high mitotic activity, lack of apocrine metaplasia, cribriform and trabecular patterns. The stroma may be scanty or absent, and lack of benign proliferative disease in the adjacent breast. The presence of scattered large pale eosinophilic cells (known as clear or globoid cells) concentrated in the basilar portion; these cells can be mistaken for myoepithelial cells.

2. Comedocarcinoma

It originates from terminal ductal lobular unit (TDLU). Comedocarcinoma may reach a relatively large size and become palpable. It may be 2 to 5cm in diameter. Majority of these tumours are centrally located. It may be multicentricity in 32% to 33% of cases and bilaterality in 10% of cases. The gross morphology of the tumour presents as a cluster of thick-walled ducts with normal breast parenchyma between them. These ducts when compressed show plugs of necrotic tumour reminiscent grossly of those seen in comedos extrude from them, hence the name comedocarcinoma. If the duct walls are not thickened, the tumour may not be apparent grossly. Microscopically, the ducts show a solid growth of large pleomorphic tumour cells accompanied by generally abundant mitotic activity and lacking connective tissue support. Necrosis which may be in form of large central focus or of individual tumour cells is always present and constitutes an important diagnostic sign. Coarse calcification often supervenes in these necrotic areas, and this can be identified by mammography. Myoepithelial cells are usually absent in ducts involved by comedocarcinoma, but their presence in no way invalidates the diagnosis. The stroma around the involved ducts shows a characteristic concentric fibrosis accompanied by a mild to moderate mononuclear inflammatory reaction. Tumours with the classical comedocarcinoma appearance are characterized by aneuploidy, negativity for hormone receptors, metallothionein expression, c-*erb*B-2 over-expression, and a high frequency of p53 mutations. The tumour cells can spread to the nipple resulting in Paget disease or there may be stromal invasion in about 21% of cases. Comedocarcinoma has the highest possibility amongst all the DCIS of having invasion of the stroma.

3. Solid Variant

This also arises from the terminal duct lobular unit. In this form of DCIS, the glandular lumen is filled by the proliferation of medium-sized cells, which are larger than those of LCIS but smaller and more uniform than those of comedocarcinoma. The cells have sharp edges and a pale cytoplasm. Cribriform variant: in this variety, a neat punched out fenestration are seen in intra-ductal tumour. The punched out fenestrations (spaces) are regular in terms of distribution, size, and shape; and this regularity is a feature of it being malignant. These spaces are often associated with two formations of similar pathogenesis, designated as trabecular bars and Roman bridges, respectively. Trabecular bars are rigid rows of cells with their long axes arranged more or less perpendicular (or at least not parallel) to the long axis of the bar; these should be distinguished from partial detachments of the duct lining. Roman bridges are curvilinear trabecular bars connecting two portions of the epithelial lining.

4. Micropapillary Variant

The micropapillary shows elongated epithelial projections projecting into the glandular lumen; these lack connective tissue support, may have a cavity at the base, and often show a bulbous expansion at the tip. This variant is more likely than others to involve multiple quadrants of the breast.

5. Clinging Variant

Clinging carcinoma shows one or two layers of malignant cells lining a glandular formation with a large empty lumen. In the more easily recognizable cases, the tumour cells are large, highly atypical, and associated with individual cell necrosis, these features suggesting a link with comedocarcinoma. In other instances, the tumour cells are smaller and more regular; these have been interpreted as being related to the "noncomedo" form of intraductal carcinoma, particularly the micropapillary variety and is thus referred to as "flat" variant of micropapillary in situ carcinoma by some authors.

6. Cystic Hypersecretory Variant

The cystic hypersecretory form is a variation of DCIS characterized by the cystic formations induced by the abundant secretory material present; it is though hardly a distinct entity.

1.1.1b. Lobular Carcinoma In-situ

Lobular carcinoma in situ (LCIS), is also known as lobular neoplasia. LCIS has an incidence of 1% to 6% of all breast carcinomas and this has not been affected by the introduction of mammographic screening because it is not associated with calcification or increased density. LCIS is more common in young women, with 80% to 90% of cases occurring before menopause. Grossly, it has no distinguishing features and is usually found accidentally in breasts removed for other reasons like fibroadenoma and sclerosing adenosis. It is multicentric in about 70% of the cases and bilateral in about 30% to 40%. Most cases are found within 5 cm of the nipple from the skin surface in the outer and inner upper quadrants. Residual tumour foci are found in 60% of breasts removed following a diagnosis of LCIS made from a biopsy specimen. Microscopically, the lobules are distended and completely filled by relatively uniform, round, small to medium-sized cells with round and normochromatic (or only mildly hyperchromatic) nuclei. In general, atypia, pleomorphism, mitotic activity, and necrosis are minimal or absent. However, some cases can have minor morphologic variations, singly or in combination: moderate nuclear pleomorphism, larger nuclear size, loss of cohesiveness, appreciable mitotic activity, scattered signet ring cells (relatively common), apocrine changes (exceptional), focal necrosis, and variations in the shape of the involved lobules. The neighbouring terminal ducts often exhibit proliferation of cells similar to those involving the lobules. These cells may form a continuous row beneath the secretory epithelium, a pattern that has been referred to as mural or pagetoid; they can also grow in a solid, cribriform, or micropapillary fashion. Although occasionally this change extends to larger (lactiferous) ducts, true Paget's disease of the nipple has not been reported as a result of lobular carcinoma. LCIS has the probability of developing invasive carcinoma following a biopsy diagnosis of LCIS without additional therapy (in about 20% to 30%). This increased risk applies to both breasts, although it is greater on the side of the biopsy; and the invasive carcinoma may be of either lobular or ductal type.

1.1.2. Invasive Carcinoma

Invasive carcinoma accounts for 70-85% of breast carcinoma (79%-classical, lobular-10%, tubular/cribriform-6%, mucinous-2%, medullary-2%, papillary-1% and metaplastic -<1%). Invasive carcinoma are tumours in which stromal invasion is detectable, whether an in situ component is identifiable or not and regardless of the relative proportion of the two components. These tumours can be divided into two major categories— ductal type and lobular type— acknowledging the existence of mixed and undetermined forms. The type of invasive carcinoma is determined from its appearance, rather than deduced from the type of in situ component present, if any.

The classification of invasive breast carcinoma is done using a wide range of criteria, such as cell type (as in apocrine carcinoma), type and amount of secretion (as in mucinous carcinoma), architectural features (as in papillary carcinoma), and pattern of spread (as in inflammatory carcinoma).

1.1.2a. Invasive Ductal Carcinoma

Invasive ductal carcinomas are here divided according to two major criteria: cytoarchitecture and pattern of spread. Morphologically, invasive ductal carcinoma has numerous variants. Some of them are distinctive enough to deserve recognition as special types (25% of all cases), especially when associated with a particular behaviour. The others, which represent about 75% of all the cases, are generically designated as invasive ductal carcinomas of classic, ordinary, or not-otherwise-specified (NOS) type.

1. Classic (NOS) Invasive Ductal Carcinoma

This lesion represents the prototypic expression of breast carcinoma, and it is the tumour type usually implied when the term "breast carcinoma" is used without further qualification. The size, shape, consistency, and type of margins are highly variable; some of these factors depend on the relative amounts of tumour cells and stroma. Grossly, the typical case is firm and poorly circumscribed, cuts with a resistant gritty sensation, and shows a yellowish gray cut surface, with trabeculae radiating through the surrounding parenchyma into the fat, resulting in the notorious stellate or crab-like configuration from which the word "cancer" has originated. Sometimes these

strands are seen connecting with other tumour nodules located at some distance from the primary tumour. Areas of necrosis, haemorrhage, and cystic degeneration may be present, particularly in the larger neoplasms. The tumour may have invaded overlying skin or underlying fascia and pectoralis muscle. Tumours that are particularly hard because of the large amounts of stroma were traditionally referred to as "scirrhous carcinomas," a term no longer used. It is common for these neoplasms to exhibit "chalky streaks" on the cut surface, a feature not caused by necrosis as generally believed but by duct elastosis. The tumour may also have variants that are better delineated, softer, rounded, and lobulated. These have been variously designated as circumscribed, multinodular, or knobby carcinomas. Invasive ductal carcinoma NOS form the dominant histological type in most studies done in sub-sahara Africa; [4], Anim [5] 82.1% in Kumasi, Ghana [6] and also in Nigerian studies: accounting for 80.6% [7] and 85.2% [8] in two different works Calabar, 92.7% in jos, [9] 82.6% in Maiduguri [10] and 78.8% in Gombe. [11]. It was also highest in frequency in a study carried out on white Americans, African Americans and non-immigrant west African women.[12].

Microscopically, the tumour can grow in diffuse sheets, well-defined nests, cords, or as individual cells. There may also be well developed glandular/tubular differentiation. The tumour cells vary in size and shape, with prominent nuclei and nucleoli, and numerous mitotic figures. Areas of necrosis occur in about 60% of the cases. Foci of squamous metaplasia, apocrine metaplasia, or clear cell changes may be seen. The amount of stroma ranges from none to abundant, and its appearance from densely fibrotic to cellular ("desmoplastic"). Bulky masses of elastic tissue are present in about 90% of the cases. Calcification, either as coarse or fine granules or, rarely, as psammoma bodies can be detected in about 60% of the cases. A mononuclear inflammatory infiltrate of variable intensity is usually present at the interphase between tumour and stroma. Granulomatous inflammation can also be seen. Definite invasion of the perineurial spaces (28%), lymph vessels (33%), and blood vessels (5%) are found.

2. Special Types of Invasive Ductal Carcinoma

The other variants of invasive ductal carcinoma are regarded as special types because they have features that define their specific morphology. These are tubular, cribriform, mucinous, medullary, papillary, apocrine, juvenile(secretory), carcinoma with neuroendocrine features(including so-called carcinoid tumour), metaplastic carcinoma, sqamous cell carcinoma and related tumour and spread-related variant like inflammatory carcinoma and paget's disease.

a. Tubular Carcinoma

Tubular carcinoma is one of the special types of invasive ductal carcinonma. The average age of the patients is about 50 years. Grossly, tubular carcinomas are small with a mean diameter of about 1cm with poorly circumscribed margin and hard consistency. Microscopically, it has well-differentiated, tubular glands, absence of necrosis or mitoses, and scanty pleomorphism. The tubules are often irregular with angulated contour, open lumina with basophilic secretions. There may also be apocrine-type 'snout' in the apical cytoplasm, formation of trabecular bars with absence of the myoepithelial cells and basement membrane. The glands are even in size and haphazard arranged in a dense cellular stroma with absence of any organoid configuration. There is frequent invasion of fat at the periphery of the lesion. A high incidence of multicentricity (56%), history of bilateral breast carcinoma (38%), and family history of breast carcinoma (40%) are seen in tubular carcinomas. Metastases to axillary nodes occur in about 10% of the cases and the prognosis is excellent.

b. Cribriform Carcinoma

The tumour has a cribriform appearance similar to what is seen in in-situ ductal carcinoma but with stromal invasion. Invasive cribriform carcinoma is a rare form of breast malignancy closely related to tubular carcinoma and sharing with it an excellent prognosis. This pattern is often seen in association with tubular formations, the relative proportion of the two elements determining the term used in describing the tumour.

c. Mucinous Carcinoma

Mucinous carcinoma, also known as mucoid, colloid, or gelatinous carcinoma, usually occurs in postmenopausal women. Grossly, it is well circumscribed, crepitant to palpation, and formed by a currant jelly-like mass held together by delicate septa. Foci of haemorrhage are frequent. The frequency of this variant in works done in Calabar were 2.7% by Ikpatt et al and 2.5% by Ebughe et al. The frequency was 9.8% in Kumasi, Ghana. Microscopically, the classic and often quoted description is that of small clusters of tumour cells "floating in a sea of mucin". These clusters may be solid or exhibit acinar formations. The mucin is almost entirely extracellular, and it may be of acid or neutral type. Occasionally, mucinous carcinoma will consist almost entirely of mucin, and a thorough sampling will be necessary to detect the neoplastic epithelium. Mucinous carcinoma shows features suggestive of endocrine differentiation in 25% to 50% of cases, hence the possibility of a link with carcinoid tumour of the breast. This variation of morphologic and ultrastructural features has no influence on survival. Mucinous carcinoma is associated with a very low incidence (2% to 4%) of nodal metastases. Mucinous carcinoma carries an excellent short-term prognosis, particularly when the tumour measures less than 3 cm (or even less than 5 cm) in diameter. However, it has been shown that deaths from this tumour can occur 12 years or more after therapy, indicating the need for long-term follow-up.

d. Medullary Carcinoma

Medullary carcinoma usually appears in patients under 50 years of age and is said to be particularly common in Japanese women. Grossly, it is well circumscribed and may become large; it can be mistaken clinically and grossly for a fibroadenoma, but it lacks the trabeculation or whorling of the latter. Its cut surface is solid, homogeneous, and gray, sometimes exhibiting small foci of necrosis. Rarely, it can be partially or predominantly cystic. Microscopically, the borders are always of the "pushing" type. The pattern of growth is diffuse, with minimal or no glandular differentiation or intraductal growth and absence of mucin secretion. The tumour cells are large and pleomorphic, with large nuclei and prominent nucleoli and numerous mitoses (some of them atypical). The cell borders are indistinct, giving the tumour a syncytial or sheet-like appearance. This is accentuated by the fact that the tumour cells located at the periphery of the clusters are more elongated and have a denser, more acidophilic cytoplasm, acquiring a vague resemblance to syncytiotrophoblast. Spindle cell metaplasia, bizarre tumour giant cells, extensive necrosis, and the absence of calcification are other common features. A prominent lymphoplasmacytic infiltrate at the periphery of the tumour is a constant microscopic finding. Axillary lymph node metastases are common. The prognosis for medullary carcinoma is better than for the ordinary invasive ductal carcinoma. The prognosis is particularly good for tumours that are smaller than 3 cm.

e. Invasive Papillary Carcinoma

Invasive papillary carcinoma of the breast is not a common lesion as most are entirely or predominantly in situ lesions. The invasive component of a papillary carcinoma also may be papillary or have the features of an ordinary ductal-type carcinoma; the prognosis is substantially better for the former. This tumour occurs more frequently among whites and postmenopausal women. Part of the problem may be that although the recognition of an ordinary ductal-type carcinoma offers no difficulties, the documentation of invasion in tumours that maintain a well-differentiated pattern may not be as clear-cut. For instance, some of the cases may be erroneously reported as intracystic papillary carcinomas may be invasive papillary carcinomas with a "pushing" pattern of growth. The distinctive features of these tumours can be appreciated on fine needle aspiration (FNA) specimens.

f. Apocrine Carcinoma

Apocrine carcinoma is a very rare form of breast malignancy (ranging from 1% to 4% of all cases), at least when defined as composed entirely or predominantly of apocrine-type epithelium. The large tumour cells have an abundant acidophilic, somewhat granular cytoplasm, which may contain eosinophilic or golden brown granules that are strongly PAS positive. The nuclei are vesicular and nucleoli are prominent. Glandular differentiation is usually found, the luminal portion of the tumour having a characteristic bulbous expansion ("apocrine snout"). Some of these tumours present as mural nodules within a cyst lined by benign apocrine-type epithelium. Since apocrine changes in the breast are usually indicative of benign lesion (even when the cells exhibit prominent nucleolar enlargement), the diagnosis of apocrine carcinoma is made when the architectural features are clearly those of a malignant tumour and apocrine change is widespread.

g. Juvenile (Secretory) Carcinoma

This rare form of breast carcinoma is seen primarily in children, but it can also occur in adults. Grossly, it is well circumscribed and usually small. Microscopically, the tumour has a ‘pushing’ type margin and prominent hyalinization is present in the central portion. There is tubuloalveolar and focally papillary formations lined by cells with a vacuolated (sometimes hypernephroid) cytoplasm. The glandular lumens are filled with eosinophilic PAS-positive secretion. Nucleoli may be prominent, but mitoses are very scanty. The overall prognosis is excellent. Local recurrences and nodal metastases can develop, sometimes very late in the course of the disease.

h. Carcinoma With Neuroendocrine Features (Including Carcinoid Tumour of Breast)

The carcinoid tumour of the breast is a type of invasive ductal carcinoma exhibiting features consistent with endocrine differentiation, with none of the patient having had carcinoid syndrome. This tumour constitutes about 5% of all breast carcinomas. It is associated with multicentricity and bilaterality. The clinical presentation is the same like other breast carcinoma and there are no distinctive gross features. Microscopically, the tumour cells are small, arranged in solid nests separated by fibrous tissue. Ribbons and rosette-like formations may be formed. Mitoses are generally rare. The presence of an intraductal component and of mucin secretion has been detected in a minority of the cases. The tumour cells of carcinoid tumour of the breast are argyrophilic but not argentaffin and are found to contain dense-core secretory granules of various types ultrastructurally. Breast carcinoma of other morphologic patterns can also have endocrine differentiation examples are mucinous carcinoma, small cell (oat cell) carcinoma, classical invasive ductal-type carcinomas and some types of in situ ductal carcinoma. Carcinoid tumours of the conventional type seen in midgut derivatives are virtually non-existent in the breast.

i. Metaplastic Carcinoma

Metaplastic carcinoma of breast is a type of ductal carcinoma in which the predominant component of the neoplasm has an appearance of other tissues and cell type order than epithelial and glandular cells. Included in this metaplastic carcinoma are tumours described as sarcomatoid carcinoma (with sarcoma-like stroma) in the upper aerodigestive tract and lung; spindle cell carcinoma; carcinoma with osteoclastic giant cells and squamous cell carcinoma. Grossly the tumour tends to be well circumscribed. Microscopically the sarcoma-like component may

resemble fibrosarcoma, malignant fibrous histiocytoma, chondrosarcoma, osteosarcoma, rhabdomyosarcoma, angiosarcoma, or a combination of these various patterns. The stroma is a mixture of fibrocollagenous tissues, osseous and or cartilaginous matrix. This matiix may be intervened by spindle cell components and osteoclastic giant cells. The spindle-cell component, which may be deceptively bland, forms abundant fibrocollagenous stroma with feathered, myxoid, angioid, and storiform patterns. The behaviour of metaplastic carcinoma seems to be more aggressive than that of ordinary invasive ductal-type carcinoma. Metastases tend to be hematogenous rather than to lymph node because of the sarcomatous phenotype.

J. Squamous Cell Carcinoma and Related Tumours

Squamous cell carcinoma is an extremely rare variant of breast tumour. It can also be included as part of metaplastic carcinoma with squamous metaplasia. Grossly, it differs very little from usual breast carcinoma but sometimes with a large central keratin-filled cyst. Microscopically, histology show ductal carcinoma with squamous metaplasia. Other variants include existence of spindle –cell carcinoma, acantholytic squamous cell carcinoma (having a discohesive tumour cells resulting in pseudovascular or pseudoglandular appearance) and adenosquamous carcinoma. The behaviour of this tumour is not substantially different from that of classical ductal-type invasive carcinoma. But the acantholytic variant is associated with a very aggressive course while the low-grade adenosquamous carcinoma has a favorable prognosis.

K. Spread-Related Variants of Invasive Ductal Carcinoma

Inflammatory Carcinoma

The term inflammatory carcinoma was originally used in a clinical sense for a type of breast carcinoma in which the entire breast was reddened and warm, with widespread oedema of the skin, thus simulating the appearance of mastitis. It is thus a clinical entity and does not constitute a histological type. Pathologic studies in some of those cases revealed the lesion to be an undifferentiated carcinoma with widespread carcinomatosis of the dermal lymphatic vessels. The prognosis is very poor because of dermal lymphatic permeation by tumour cells on microscopic examination.

Paget's Diease of the Nipple

Paget disease of the nipple is a rare manifestation of breast cancer (1% to 4% of cases). Paget's disease of the nipple is an eczematoid lesion of the nipple, often associated with an invasive or non-invasive ductal carcinoma. It appears as a crusted, scaly and eczematoid lesion with palpable subareolar mass in about 50% of cases. It was originally described by Sir James Paget in 1874. The management and prognosis depend largely on the intraductal versus invasive nature of the underlying carcinoma and on the presence or absence of axillary lymph node involvement. Microscopically, large clear cells with atypical nuclei are seen within the epidermis, usually concentrated along the basal layer but also permeating the malpighian layer. The cells can be isolated or in clusters, and occasionally form small glandular structures. In rare instances they have an anaplastic appearance. A connection between the carcinoma within the duct and the Paget's disease may be demonstrated in most instances if the breast is sampled extensively. However, in some cases the underlying tumour is found 2 cm or more from the nipple.

1.1.2b. Invasive Lobular Carcinoma

1. Classical Type

Invasive lobular carcinoma comprises about 5% of all breast cancer. It is commomly bilateral and has multicentric origin in some cases. Gland formation is not a feature of classical ILC. The tumour cells are round and regular with very little pleomorphism and infrequent mitosis. The stroma which is of dense fibrous type is circumscribed schirrous mass to a poorly defined area of induration that may remain undetected by inspection as well as palpation. Microscopically, classical invasive lobular carcinoma (ILC) is characterised by the presence of small and relatively uniform tumour cells growing singly, in Indian file, and in a concentric("pagetoid") fashion around lobules involved by in-situ lobular neoplasia. The stroma is usually abundant and contains foci of periductal and perivenous elastosis in virtually every case. A lymphocytic infiltrate may be present, sometimes so intense as to obscure the neoplastic component.

2. Histiocytoid Carcinoma

Histiocytoid carcinoma is characterized by a diffuse pattern of growth by tumour cells displaying abundant granular, foamy cytoplasm. This tumour type is currently viewed as a variant of invasive lobular carcinoma exhibiting apocrine differentiation.

3. Signet Ring Carcinoma

Signet ring carcinoma is a type of breast carcinoma in which a significant number of tumour cells show intracytoplasmic mucin accumulation, resulting in the typical signet ring appearance. It can coexist with mucinous carcinoma. Most cases of signet ring carcinoma show cytoarchitectural features (such as small cell size, uniformity, and dissociation) similar to those of classic ILC and sometimes coexist with it. Most cases of signet ring carcinoma are regarded as variants of ILC.

Other variants of invasive lobular carcinoma may have closely aggregated cells, solid pattern, trabecular pattern, loose alveolar pattern and spindle-cell chains but have a relatively bland and homogenous cytologic appearance.[2]

The most distinctive forms is the alveolar pattern in which the tumour cells are arranged in sharply outlined groups separated by fibrous tissues sometimes containing osteoclast-like giant cells and the tubulolobular carcinoma in which typical areas of ILC merge with small tubules with a minute or undetectable lumen ("closed" or "almost closed" tubules). The pleomorphic variant of ILC has cells with pleomorphic nuclear features and the classical pattern of ILC is maintained.

1.1.3. Mixed Ductal and Lobular Carcinoma

Biphasic carcinomas composed in part of a component with definite features of invasive ductal carcinoma and in part of a component with definite features of invasive lobular carcinoma do occur, but they are very rare. These tumours, of course, should be distinguished from the cases in which two separate neoplasms of different microscopic appearances are present in the same breast.

1.1.4. Undetermined (unclassified) Carcinoma

This category includes all cases of invasive carcinoma in which features of ductal or lobular type are not definite enough to place it into either category. It comprises 3% to 4% of the invasive breast carcinomas.

1.2. Histological Grade

Histological grade is a prognostic factor that is also use in breast cancer classification and staging systems in this era of emerging clinical use of molecular classifiers. The Nottingham [13] modification of the Scarf-Bloom-Richardson Grading System, also known as the Nottingham Grading System (NGS), Elston and Ellis [13] is the grading system recommended by various bodies internationally (World Health Organisation,[WHO], American Joint Committee on Cancer [AJCC], European Union [EU] and Royal College of Pathologist [UK RCPath]. [14]. Histological grade can correctly predict tumour behaviour, particularly in early small tumour.[15].

In the Nottingham Grading System, three features are considered, these are: 1. Degree of tubular formation (scored 1-3); 2. Nuclear pleomorphism (scored 1-3) and 3.Mitotic counts (scored 1-3). Depending on the overall total score, breast cancer is graded into Grade 1(well differentiated) with a total score of 3-5; Grade 2(moderately differentiated) with total score of 6-7 and Grade 3(poorly differentiated) with total score of 8-9. The frequency of high grade tumour is high in sub-Sahara African countries; -in west African average from 4 different hospitals 83% was high grade tumour, Zhang, *et al.* [16] in Uganda 68% as grade 3, [17] in Eritrea Horn of Africa 90% of women had grade 3 tumour, [18] in Kumasi, Ghana grade 1(14.8%), grade 2(31.5%) and grade 3(53.7%), in Nepal Grade 1 (12.50%), grade 2 (76.79%), grade 3(10.71%) [19] and in Mexico grade 1(9.1%), grade 2(54.1%) and grade 3 (34.6%). [20]. Various studies done in Nigeria also showed that most breast cancers are of high grades: it was 100% grade 3 tumour in Abia; [21] 71-77% were grades 2 and 3 in Ibadan [22] 83% as high grade tumour [23] a Nigerian cohort study had 69.7% in grade 3 [24] and 70.6% as grade 3 in Jos.

1.3. Staging of Breast Cancer

The staging of breast cancer gives an indication of the degree of spread of the cancer to other tissues and system. The major purpose of staging is to ascertain the extent of disease severity and categorisation of cancer with similar prognosis. [25]. It also assists in making the appropriate treatment choices. Staging can be clinical or pathological. Clinical staging are information obtained prior to surgery using mammography, x-rays and CT scan; while staging at surgery and microscopy is the pathological staging and it is usually more accurate. The WHO, American Joint committee on cancer [AJCC] and the International Union Against cancer [UICC] recommends the TNM staging, which is a two-step procedure. The TNM staging first classifies cancer by several factors, T for tumour, N for nodes, M for metastasis, and then groups these TNM factors into overall stages. [26], American Joint Committee on Cancer, National Comprehensive Cancer Network (NCCN) Studies in Africa, [27] sub-Sahara Africa and developing countries of Asia [28], [29] showed that most cases of breast cancer are advanced stages. In west Africa from 4 different hospitals was 72% as advanced stages, in Uganda stages III and IV was 75%, in Kumasi, Ghana stage I(3.6%), stage II(11.2%), stage III(70.0%) and stage IV(15.2%). This is also the case in most centres in Nigeria: 73% in a study done at Ibadan were stages III and IV; 53.2% stages III and IV in calabar; 90.9% as stage II and IV in Abia , in a cohort study in Nigeria and Senegal 72% advanced stage, 58.3% as stage III and IV in Jos, 68.2% in a Nigerian cohort study and 64% were stage III and IV in Eastern Nigeria. Anyanwu [30] In the studies that pathological stage assessment of tumour size was done, T2(57.1%) and 67% but low nodal(N0) involvement in Iran [31] and N3 (involving 10 or more nodes) in Nepal study.

2. Methodology

2.1. Study Design and Material

This is a retrospective studies that aimed at describing the histopathologic characteristics of breast carcinoma diagnosed from breast samples submitted to the department of histopathology of University of Calabar Teaching Hospital (UCTH) in the period covering 1st January 2010 to 31st December 2014.

2.2. Materials and Method

The hospital and departmental record of all the breast samples submitted to the department of histopathology in a five year period starting 1st of January 2010 to 31st of December 2014. The side of tumour, location of tumour, the size of tumour, number of lymph nodes harvested were gotten from gross description and histologic type, subtype, histologic grade, number of lymph nodes infiltrated by tumour cells, presence of lymphovascular and perineural

invasion were gotten from the histology report. The variables of the breast cancer are collated and analysed. Findings are shown in tables and charts. Statistical test for significance is determined.

The histological grade was done using the Nottingham's modification of Scarfold, Blooms and Richardson (SBR). In the SBR grading, major findings like Tubules/glands formation, Nuclear Pleomorphism and Mitotic counts were scored 1-3.

For the tubules formation score (1 is >75%, 2 is 10-75%, 3 is <10%); pleomorphism (1 is mild (small, regular uniform cells, 2 is moderate (moderate increase in size and variability), 3 is severe (marked variation) and Mitotic figures (1 is <10 mitotic figure per 10 high per field, 2 is 10-19 figures per 10 high per field, 3 is >20 figures per 10 high fields).

The score is aggregated to get the final tumour grade. Grade 1 – well differentiated (3 – 5 points); Grade 2 – moderately differentiated (6- 7 points) and Grade 3 – Poorly differentiated (8 -9 points).

2.3. Sample Size

The sample size of the study was comprised of all the histological specimen that was diagnosed of breast carcinoma seen in UCTH in the period 1st January 2010 to 31st December 2014.

2.4. Data Analysis

This was done using the current version of the US Centre for Disease Control (CDC) [32] statistical software Epi-info 7 with descriptive and inferential statistics. The mean age, age range, sex distribution and histopathological characteristics like type, subtype, tumour size, tumour location, side of breast involved. Frequency tables, graphs and charts were used to display the findings.

2.5. Criteria for Selection

All breast tissue specimen diagnosed with breast carcinoma during the study period of 1st January 2010 to 31st December 2014 were included in this study.

2.6. Exclusion Criteria

All the cases that the complete gross description and histologic reports could not be gotten from the departmental records were excluded from the study.

2.7. Ethical Consideration

Ethical clearance for this study was obtained from the health research ethics committee of the University of Calabar Teaching Hospital, Calabar, Cross River state, Nigeria.

2.8. Conflict of Interest

The author has no conflict of interest.

3. Results

The total number of breast specimen submitted to the department within the study period of 1st January 2010 to 31st December 2014 is nine thousand six hundred and forty seven histology samples was received in the department of Histopathology, University of Calabar Teaching Hospital. One thousand 0ne hundred and fifty four of these samples were breast tissue and two hundred and sixty nine representing 23.3% were diagnosed as breast cancer. A total of one hundred and forty seven (147) met the inclusion criteria and was included in the study analysis.

Table-1. The age distribution of breast cancer subjects at diagnosis

Age(years)	Frequency	Percentage
20-29	12	8.16
30-39	30	20.41
40-49	47	31.97
50-59	29	19.73
60-69	23	15.65
70-79	5	3.40
80-89	1	0.68
Total	147	100%

The mean of patient age at diagnosis is 46.31 years (SD±12.75) old. The age range from 21-80 years old, modal age of 40 years and a median age of 45 years. Patients were divided into less than 40 years old 42 cases (28.57%), 40 to 55 years old 73 cases (49.66%) and greater than 55 years old 32 cases (21.77%) to facilitate comparison with breast cancer variables. The peak age group is 40-49 years and has the highest frequency of 47 cases (31.97%).

Table-2. The age group distribution of Breast cancer subjects.

Age group(years)	Frequency	Percentage
20-39	42	28.57
40-55	73	49.66
56-89	32	21.77
Total	147	100

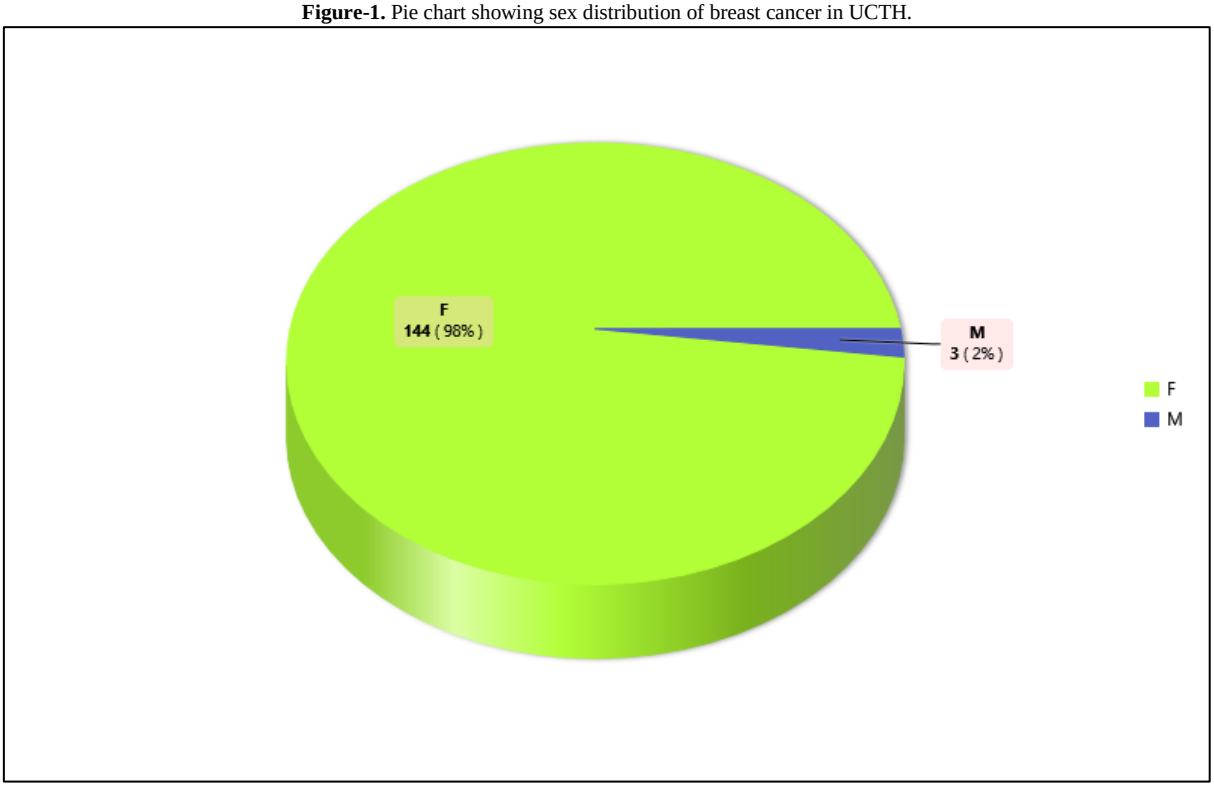
The table shows that age group 20-39 years (less than 40 years) had 42 cases (28.57%); age group 40-55 years had 73 cases (49.66%) and age group 56-89 years (greater than 60 years) had 32 cases (21.77%).

Table-3. The sex distribution of breast cancer subjects.

Sex	Frequency	Percentage
Female	144	97.96
Male	3	2.04
Total	147	100

The table shows that 144 cases (97.96%) as female and 3 cases (2.04%) as male.

Figure-1. Pie chart showing sex distribution of breast cancer in UCTH.



Key: M=Male, F=Female

Table-4. The side of breast affected by the cancer.

Side	Frequency	Percentage
Right	80	54.42
Left	67	45.58
Left and Right	0	0

The table shows that 80 cases (54.42%) has cancer in the right breast, 67 cases (45.58%) has cancer in the left breast and none have bilateral breast cancer.

Table-5. The surgery type done for breast cancer

Surgery	FREQUENCY	PERCENTAGE
Mastectomy	92	62.59
Lumpectomy	55	37.41
TOTAL	147	100

The table shows that 92 cases (62.59%) were treated surgically with mastectomy and 55 cases (37.41%) were treated surgically with lumpectomy.

Table-6. Tumour size of the breast cancer.

Tumour size(cm)	Frequency	Percentage
1.5-1.9	6	4.08
2.0-5.0	111	75.51
5.1-12.5	30	20.41
Total	147	100

The table shows that the range of tumour size to be 1.6cm to 12cm and a mean of 4.04cm with standard deviation of 1.98. The modal size of tumour is 3.2cm and the median size is 3.4cm. Six cases (4.08%) has tumour size of 1.5-1.9cm (less than 2cm); 2-5cm is 111 cases (75.51%) and 5.1-12.5cm (greater than 5cm) is 30 cases (20.41%).

Table-7. The location of the tumour in the breast on cut surface of mastectomy specimen

Location	Frequency	Percentage
Upper outer	26	28.26
Upper inner	5	5.44
Lower outer	9	9.78
Lower inner	6	6.52
Central	3	3.26
Multiple	43	46.74
Total	92	100

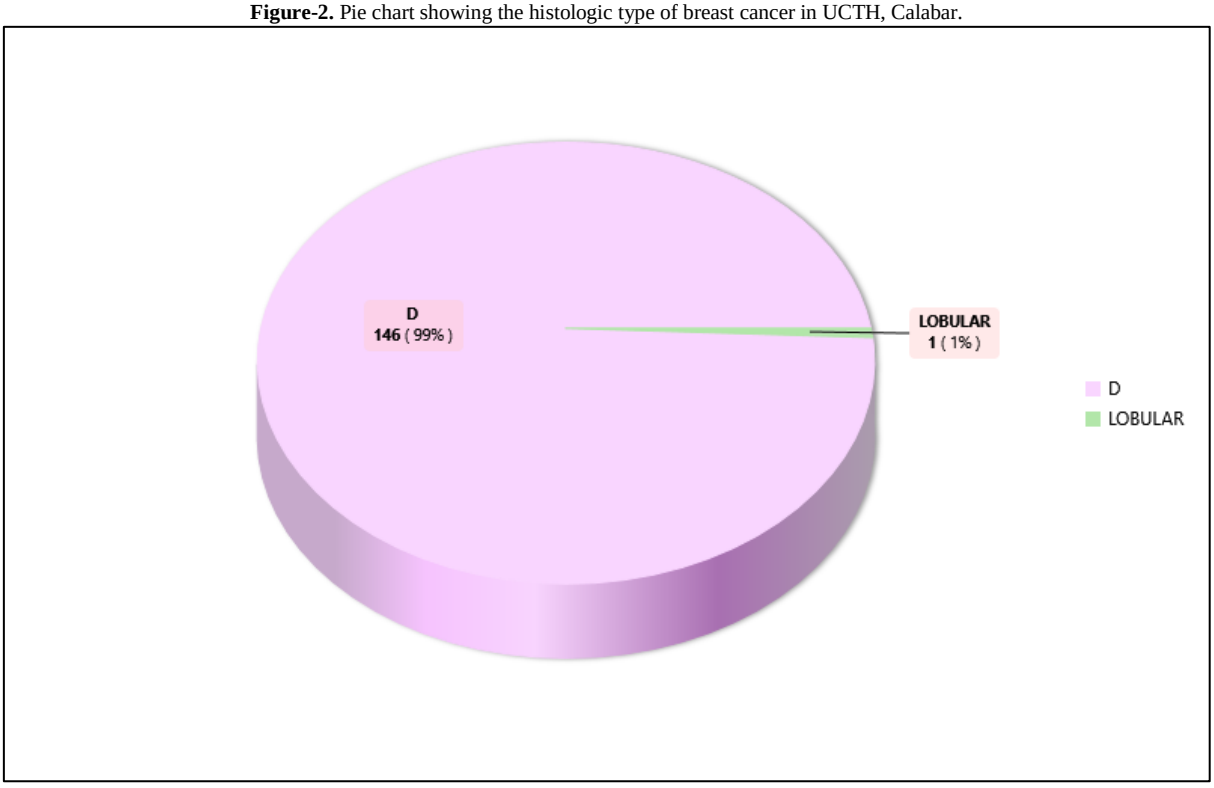
Table shows location of tumour to be upper outer quadrant in 26cases (28.26%), upper inner in 5 cases (5.44%), lower outer in 9 cases (9.78%), lower inner in 6 cases (6.52%), central in 3 cases (3.26%) and multiple in 433 cases (46.74%).

Table-8. The histologic type of breast cancer.

Histologic Type	Frequency	Percentage
Ductal	146	99.32
Lobular	1	0.68
TOTAL	147	100

The table shows that 146 cases (99.32%) as ductal type of breast cancer and 1 case (0.68%) as lobular type of breast cancer.

Figure-2. Pie chart showing the histologic type of breast cancer in UCTH, Calabar.



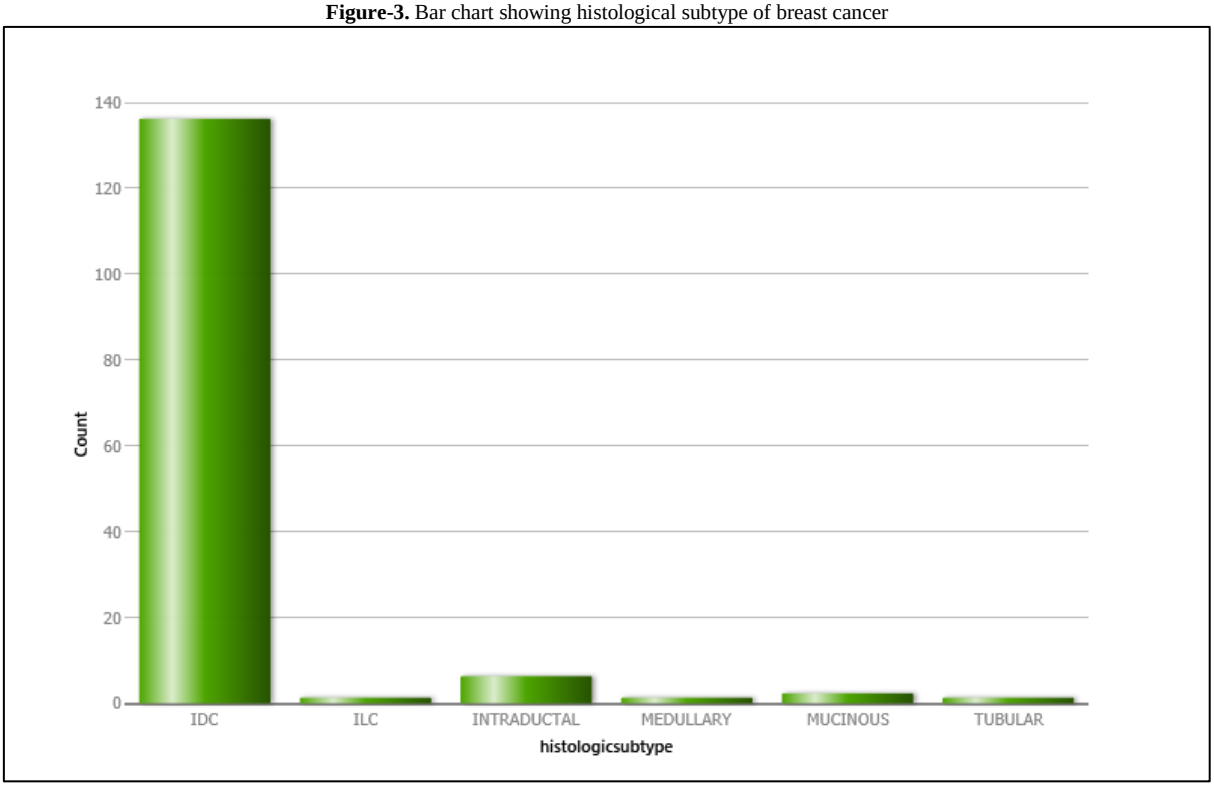
Key: D=Ductal type

Table 9: Histologic subtype of breast cancer in UCTH.

Histologic subtype	Frequency	Percentage
Invasive ductal(NOS)	136	92.52
Invasive lobular	1	0.68
Ductal carcinoma in-situ	6	4.08
Medullary	1	0.68
Mucinous	2	1.36
Tubular	1	0.68
Total	147	100

The table shows that 136 cases (92.52%) as invasive ductal carcinoma not otherwise specified; invasive lobular carcinoma as 1 case (0.68%); ductal carcinoma in-situ is 6 cases (4.08%); medullary carcinoma is 1 case (0.68%); mucinous carcinoma is 2 cases (1.36%) and Tubular carcinoma is 1 case (0.68%). The special type has a total of 5 cases (3.40%) comprising invasive lobular, medullary, mucinous and tubular carcinomas.

Figure-3. Bar chart showing histological subtype of breast cancer



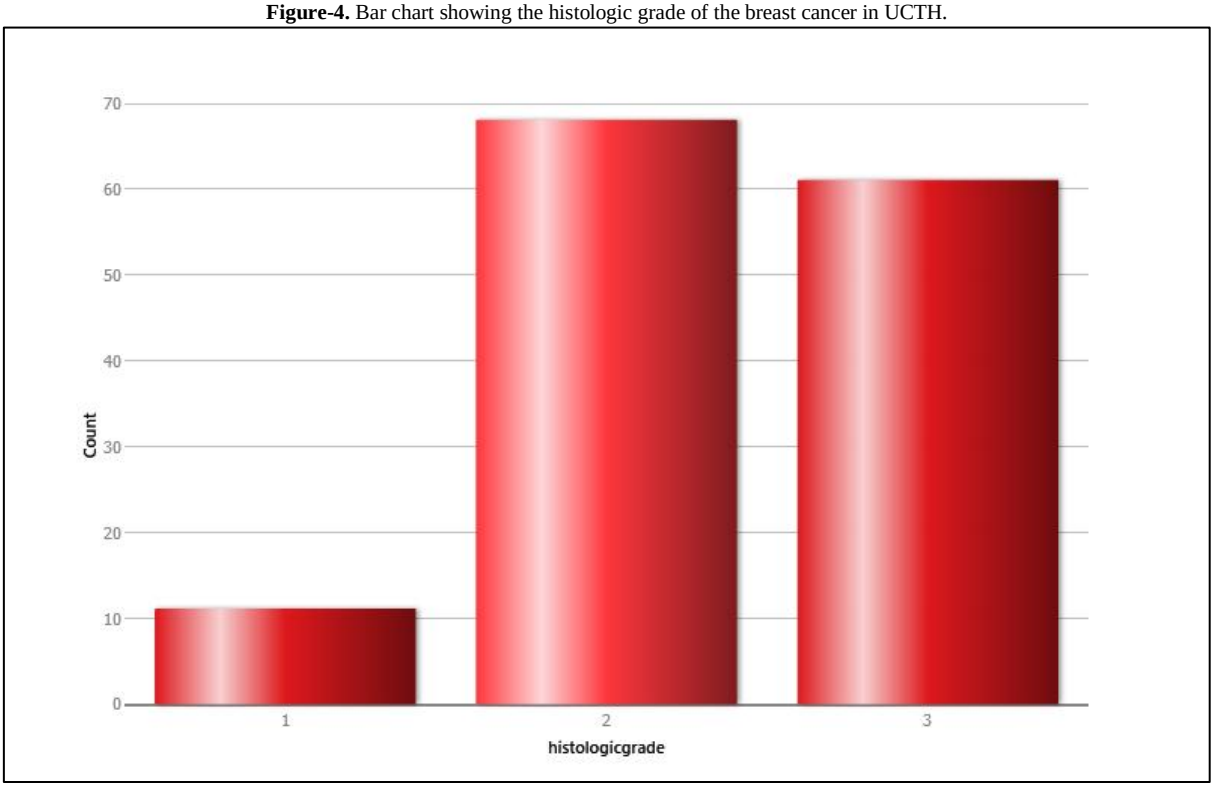
Key: IDC=invasive ductal carcinoma (NOS). ILC=invasive lobular carcinoma

Table-10. Histologic grade of breast cancer.

Histologic grade	Frequency	Percentage
1	11	7.86
2	68	48.57
3	61	43.57
Total	147	100

The table shows that grade 1 (well differentiated) is 11 cases (7.86%); grade 2 (moderately differentiated) is 68 cases (48.57%) and grade 3 (poorly differentiated) is 61 cases (43.57%).

Figure-4. Bar chart showing the histologic grade of the breast cancer in UCTH.



4. Discussion

One of the very useful prognostic factor in breast cancer is the age at diagnosis. [33] The age at diagnosis reported in many studies in Africa and Asia countries are about a decade lower than values in Europe and America, [34], Gukas, *et al.* [35]. The age range of breast cancer in the study is 21-80 years. This is in agreement with many other studies that the age also falls between the third and ninth decade of life.[36], [37], [38]. However, this is at variance with some reports that the lower limit is second decade of life [39], [40] and those that the lower limit is fourth decade.[41].

The mean age of this study is 46+/-12 years. This is in tandem with majority of works in other parts of the globe, [42] (and also in Nigeria [43], [44], [45] in which the mean age is in the fifth decade of life. The mean age for male was higher than that for female 59+/-6.08 and 46+/-12.73 respectively. This was also the finding in Nepal study, the mean age for male higher than that of female although the values are different from this study (49.29 years for female and 70.76 years for male). The median age of this study is 45 years and peak age group is 40-49 years which is similar other studies, [46], [47] but 41-50 years in Iran and Afghanistan. [48]. The mean age and peak age group both fall in the fifth decade of life. The ages are the reproductive stage of the woman's life. During this period the breast is exposed to the effects of the oestrogen and progesterone hormones that promotes its growth and development, usually any actively proliferating group of cells can be a fertile ground for cancer development. This may partly explain why breast cancer is commoner in this age group in Africans and Asians but may not explain why the age in Americans and Europeans are a decade higher. The life expectancy is lower in African and poor Asian countries (42-48 years), it means that their population in most cases will have a large number of the inhabitants being young, this may also explain while younger women will present with breast cancer as opposed to US America and European countries where the life expectancy is higher and the proportion of older women will be higher. This may partly explain the difference in peak age group between this study, other African and Asian studies and the western world. The strong association of age with breast cancer was also statistically confirmed in this study, similar to other reports associating age at presenting to an increased risk factor for breast cancer. This association remained even after correcting with other factors like tumour size and histologic grade that also affects breast cancer.

Breast cancer is one of the cancers that its incidence increases with age, this statement is however not supported by this study as majority of the patient 78.23% were in their premenopausal stage, age below 55 years old. A little above one-third of this, 28.57% are in the young (less than 40 years old). Preponderance of premenopausal age group presenting with breast cancer has been reported in works done in Africa and Nigeria. [49]. This is in contrast to studies done in America and European countries where majority of patients are in their postmenopausal age group and the proportion of young women with breast cancer is between 5 and 11%. (Centre for Disease Control (CDC) and Australian government document on breast cancer in the young [50]. The Carolina breast cancer study, in the USA however, had 53% as premenopausal and 47% as postmenopausal. [51]. This marked difference in the age group affected may be attributed to the genetic makeup of the African patients who have a higher tendency of inheriting breast cancer susceptibility genes like BRCA. In addition, changing trends in the life styles and habits of Africans predisposes the younger generation to having more cancer than the elderly.

Some of these behavioural changes that is collectively called 'westernization' includes: increase saturated fat diets, sedentary life styles, alcohol consumption, cigarette smoking added to this is changing reproductive behaviour (hormonal factors) and socioeconomic status. Some of the changing reproductive behaviours observed in the

younger age group are earlier menarche, late menopause, late marriages and consequent lower parity and less likelihood of breast feeding for up to a year because of change in socioeconomic status and the drive to imitate the westerners. These factors have contributed in explaining why the age group that presents with breast cancer in this study and other African and Nigerian studies are lower. Another major factor that may have contributed to the younger age group having more breast cancer is change in reproductive life. The women of this generation marry at an older age when compared to women of yester years. This thus exposes the breast to a longer period of oestrogenic and progesterone effects and also eradicate the protective role of early pregnancy and multi-parity, in addition, the younger generation also use various birth control method to prevent conception and reduce the number of children they ultimately give birth to while unknowingly increase their risking for developing breast cancer.

The high percentage of breast cancer patients being female seen in this study is similar to what has been documented by various researchers, it accounting for as high as 97.96% leaving the male counterpart with just 2.04%. This is at tandem with Nepal study female 97.3% and male 2.7% and Afghanistan study female 94% and male 6%. This percentage of male breast cancer is at variance with many studies done around the globe. While most are higher: 9%, [52] 2.64%, 4% and Adeniji, *et al.* [53] 8.6%; [54].others were lower <1% in Europe and America, 0.38%. The high percentage of breast cancer in the female has been linked to susceptibility of the female breast to oestrogen and progesterone during their reproductive life. This risk is further increased if there is a family history of breast cancer or if there is any added risk of a proliferative breast lesion like atypical ductal hyperplasia and atypical lobular hyperplasia.

More than half of the breast cancer was on the right side (54.42%) while the left side was (45.58%) and none had a bilateral cancer. Right and left were equal at 49% each with 2% bilateral in eastern Nigeria. Forae, et al, reported right side that was lower at 47.9%, left was 51.3% and 0.8% was bilateral. Saleh and Abdeen also reported a right side preponderance of 53.61%, left side is 42.17% and bilateral is 4.22%; [55] in Afghanistan right 47%, left was 45% and bilateral was 8%[50] and Pathak et al reported right as 49.12% and left as 50.88%.

A variation in the side of the tumour was also observed in this study and other previous work. The study showed that two main surgical procedures was offered as treatment to patient. These are mastectomy with axillary clearance which was used in 62.59% of cases and lumpectomy which was 37.41% of cases but modified radical mastectomy (48.8%). This is different from what was reported in Kuwaiti women that had similar surgeries with and without axillary clearance and quadrantectomy in addition, but the preponderance of mastectomy 63.86% and lumpectomy of 33.73% was in agreement with this study.

The range of tumour size in this study is 1.6cm to 12cm with a mean of 4.04 cm +/-1.98cmand this is at variance with Afsharfard et al that was 3.94+/-2.47cm. The modal and median sizes were 3.2cm and 3.4cm respectively. This mean is larger than report from Saudi Arabia which was 3.0cm. The study showed that 4.08% 0f the cancers had a size of less than 2cm, 75.51% had a size of 2-5cm and 20.41% were larger than 5cm. This is in tandem with study in Nepal in which the tumour size 2-5cm was also the commonest (67%) and Iran (57.1%) but is different from what was reported in Indonesian women that had most of the patient presenting with tumour size greater than 5cm (46.5%), in Nigeria study 77.4% and 59% of the tumour had size greater than 5cm. the tumour with larger size was commoner in younger patients less than 40 years which was also reported in Iran.

Majority of the tumour on cut surface was located in multiple sites (46.74%) with varying sizes. Other location quadrants of the tumour are upper outer in 28.26%, upper inner in 5.44%, lower outer in 9.78%, lower inner in 6.52% and central in 3.26%.

The two main morphologic histologic types of ductal and lobular breast carcinoma were identified in this study. The ductal type accounted for the bulk (99.32%) of the breast cancer while the lobular was just a minor fraction (0.68%). Satti reported ductal carcinoma of 90.6% which is lower than the finding of this study. This may be explained by the fact that the sample size for this study is lower than that sampled by Satti. Other studies also reported predominance of invasive ductal carcinoma: 87.1%[34] and 79% with lobular carcinoma being 7.8%.

The major histologic subtype is invasive ductal carcinoma (92.52%) not otherwise specified, this is higher than reports from most part of Nigeria: 80.6%, 85.2%. 82.6%, 78.8%, 80%, but lower than Jos 92.7%, and Lagos 95.8% and it was also the main subtype in these reports. This was also the only type in all the male patient. The proportion of this subtype is also high in other study around the globe 90%,[19] 93-96%, and 93%. [56]. The other histologic subtypes identified are ductal carcinoma in-situ, invasive lobular carcinoma, mucinous carcinoma, medullary carcinoma and tubular carcinoma. The special type (invasive lobular carcinoma, mucinous, tubular and medullary) in this study was a very minor fraction of 3.40%. This is at variance with other research work. The other variant such as metaplastic carcinoma, neuroendocrine carcinoma, pleomorphic carcinoma, clear cell were not seen in this study. The percentage of the identified special types were also different from previous studies. This disparity may not be unconnected with the fact that this study was hospital-based and the number of sample that is breast cancer may have greatly reduce the chances of getting these subtypes. Also the time period covered by the study may not have had these subtypes, and does not necessarily mean these subtypes are not in Calabar and Cross River state.

The study showed that majority of the cancers were grades 2 (48.57%) and 3 (43.57%) tumours, grade 2 was the highest and grade 1 (7.86%) was the lowest in proportion of the breast cancers. Grade 2 tumour being the commonest was also reported by Irianiwati in Indonesian women (40%),' 76.79% in Nepal in which grade I was 12.5% and grade III was 10.71% and Mexico grade II (54.1%), Grades I and III was 9.1% and 34.6% respectively. Grades I and III being at variance with this study. But the Afghanistan study is at variance with this study as it reported a predominance of grade 3 tumour (62%), grade 1 was 6% and grade 2 was 25%.

The study that nodal involvement was only in 22.6% and they were all N1 (1-3nodes) while the remaining 77.4% was No (no lymph node had any tumour cells). This is was also the finding in other studies· [57], Reddy, *et al.*

[58], Kakarala, *et al.* [59] but different from Nepal study in which N3 (involving 10 lymph nodes) with percentage of 38.4% was the highest.

Lymphovascular invasion was seen in 13.7% and perineural invasion in 8.45%. This is at variance with Nepal study that had 62.5% and 43.8% respectively.

5. Conclusion

Breast cancer is common in the premenopausal women. There. Invasive ductal carcinoma not otherwise specified is the commonest histologic subtype, the special type accounted for only a small fraction. The moderately differentiated breast cancer is the commonest. Breast cancer is commonest in female while the male breast cancer is just a fraction. The majority of the cancer has size 2-5cm and a small fraction has lymphovascular and perineural invasion.

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