Breast Cancer In Nigeria: A Review

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ABSTRACT

Breast cancer is the most common cancer in Nigeria. It afflicts mostly young women with a peak age incidence in 40 – 45 years group. Risk factors identified among Nigerian patients include - early age of onset of periods, age at first full term pregnancy greater than 20 years, early maternal birth order, oral contraceptive use, positive family history of breast cancer in first and second degree relatives, and waist/hip ratio more than 0.9. Breast cancers among Nigerians are very aggressive, presents mostly at advanced stage (73% in stage II & IV), are mostly premenopausal, with poor histological grade, and low expressed estrogen/progesterone receptor status (22.8 - 25%). BRCA 1 and 2 protein truncating mutations occur in a smaller proportion compared to similar groups in western countries but non-truncating variants in BRCA2 are very high.

Preventive strategies are yet to be adopted in the fight against breast cancer in Nigeria. Mastectomy is the most common surgery but breast conservation is increasingly being adopted. Doxorubicin based combinations are the first line chemotherapy in most centers in the country. While ER/PR assay is not done for most patients outside of the leading centers, the low receptor status of Nigerian tumours suggests that most of them do not respond to hormonal manipulation. Supporting drugs like high potency antiemetics and colony stimulating factors are available mostly in the leading centers. Palliative care is in its infancy.

Breast cancer treatment in Nigeria is fragmented. There is an urgent need for more specialists in the field especially medical oncologists. A body of clinical oncologists to set the standards and drive the development of the field in the country is needed.

INTRODUCTION/EPIDEMIOLOGY

Breast cancer is the second most common cancer worldwide (1.15 million new cases) and the fifth leading cause of cancer deaths in the world.[1] It is by far the number one cancer of women (23% of all cancers). The incidence rates are low in most of Africa (30 per 100,000) with the exception of South Africa. The lowest incidence is in the Central African region (16.5 per 100,000). While survival is very good in affluent countries, the same cannot be said of poor countries including most of Africa. The estimated age adjusted 5yrs survival rate in sub-Saharan Africa is 32% in contrast to 81% in the U.S. The incidence rates are increasing in most countries with the changes greatest where rates were previously low.[1]

Breast cancer is the most common cancer in Nigeria and the prevalence is increasing.[2] General population studies do not exist but estimates from hospital based studies put the incidence at 33.6 cases per 100 thousand of the population.[3] Breast cancer incidence as recorded in the National Cancer Registry has increased over the last four decades to displace cervical cancer as the most common cancer in Nigeria.[2] The reasons for the increased incidence are debatable but may be from a combination of several factors - more patients are presenting since there is increased awareness it can be treated; life expectancy in Nigeria is increasing and therefore more of our ladies survive into the higher incidence age group; the age of the population of Nigeria is rising so that there are more elderly people in the population than before and we should expect more diseases of old age including cancers. Also our life style is changing towards western patterns and therefore we are acquiring the risk factors that predispose to breast cancer.[4]

Breast cancer is a disease of the female population with male breast cancer accounting for less than 1% in most western series. In Nigeria, the prevalence of male breast cancer (3 9%) is slightly higher than the developed world.[5,6] There are significant differences in breast cancer epidemiology in individuals of African ancestry compared to caucasians.[7,8] In the U.S., breast cancer is commoner among Caucasians but premenopausal breast cancer is more among African Americans. The peak age incidence among Caucasians is in 65 70years age group in contrast to 55 -60 years among African Americans. Nigerian breast cancer patients are much younger with the peak age incidence in the 40 45 years age group.[4,7]

AETIOLOGY OF BREAST CANCER

Genetic damage is the fundamental cause of every cancer. Genetic damages accumulate with increasing age as a result of environmental influences (both social and biological) and life style choices. Reproductive factors revolving around the female sex hormone, estrogen play a big role in the development of breast cancer. Prolonged exposure to unopposed estrogen action as occurs in early menarche (before 12year of age), late menopause (after 50 years of age), use of oral contraceptive pills and hormone replacement therapy are associated with higher risk of breast cancer. Pregnancy is associated with prolonged high estrogen action. In the short term, it increases breast cancer risk but its long term overall effect is a reduction in risk of breast cancer due to maturation and stabilization of breast tissues. Nulliparity is therefore associated with increased risk. Young age at first full term pregnancy (before 24 years of age) and lactation gives some protective effect while late first time pregnancy (after 35years) and not breastfeeding increases risk. Case controlled studies among Nigerians have identified the following risk factors to significantly increase risk of breast cancer- late age at first pregnancy and first lactation, increased parity, early maternal birth order, oral contraceptive use and alcohol abuse,[9] positive family history of breast cancer in first and second degree relatives, education to high school level and above, age at first full term pregnancy greater than 20 years, and waist/hip ratio more than 0.9.[10,11] Other significant risk factors are increasing age, increasing height, irregular periods, and early age of onset of periods.[10,11]

A past history of breast cancer or benign breast disease especially with a histology that demonstrates high proliferative index and atypical hyperplasia increases the risk of breast cancer. Atypical hyperplasia in the breast is now regarded as the earliest form of premalignant breast cancer lesion. Increased risk also results from family history of breast cancer in first degree relatives and family history of other cancers like ovarian or colon cancer. Life style choices that increase risk of breast cancer include lack of physical activity, high fat intake and alcohol intake while high intake of fresh vegetables and vitamin C reduces risk. Radiation exposure increases risk of breast cancer especially in individuals with ATM gene.

BREAST CANCER GENETICS

Cancer is a genetic disease. While few of the genetic damages that lead to cancer are inherited (hereditary cancer), most of the damage are acquired and accumulate during an individual's life time. The predictive factors for hereditary breast cancer include multiple cancers in the family members, early onset breast cancer, bilateral primary breast cancer and cluster of other cancers in the family. Hereditary breast cancers account for only about 5 -

10% of all breast cancers. Two broad categories of genes play some role in breast cancer development- high penetrance low prevalence genes like BRCA 1and 2 genes and low penetrance high prevalence genes like the estrogen polymorphism genes.[12] The genes in the earlier group are very important not only because they play a big role in the development of hereditary breast cancer but also because much of our understanding of the genetics of breast cancer come from their study. The latter group is of interest mostly in genetic epidemiology of cancer and public health. Six high penetrance gene defects are now identified in hereditary breast cancer: BRCA1 gene, BRCA2 gene, P53 gene (Li-Fraumeni syndrome), PTEN gene (MMAC1), ATM gene, STK11 gene and CHECK 2 gene.[12] BRCA 1 and 2 genes are tumour suppressor genes. Their mutations have been most studied of all breast cancer associated genes. BRCA1 mutation accounts for 50% of all familial early onset female breast cancer while BRCA 2 mutation account for 35% of such cancers. The prevalence of BRCA mutations in all breast cancer patients has been put at 3%. Among individuals of African ancestry, there is a diverse spectrum of *BRCA1* and *BRCA2* mutations and sequence variations that are unique to Blacks of African descent.[13] BRCA 1 and 2 protein truncating mutations have been found in 4% of a cohort of young breast cancer patients in Nigeria.[14] This is lower than previously reported figures among clinic or population-based cohorts of young white women with breast cancer. In another study, 74% of Nigerian breast cancer cohorts were shown to carry non-truncating variants in BRCA2 consistent with reports of an exceptionally high level of overall genetic diversity in people of African ancestry.[15] African cohorts generally show a much greater frequency of variability in BRCA2 than BRCA1.[15]

PATHOLOGY

Non specific ductal carcinoma (80%) is the predominant histological type of breast carcinoma all over the world. In Nigeria, non specific ductal carcinoma is most common (76 - 93%) but medullary carcinoma is disproportionately high.[7,16,17] The intrinsic biologic behaviour of breast cancer is very variable hence, prognostication based on the tumour biology differs from patient to patient. Prognosis is assessed using several parameters like tumour type, tumour size, cytological and histological characteristics, DNA policy, estrogen and progesterone receptor expression, proliferative index (Ki67), Her-2/née oncogene amplification, tumour suppressor gene mutation, expression of epidermal growth factor receptors and presence of lymph node metastasis.[18] The Bloom Richardson scale and the Nottingham scale which assesses tubule formation (glandular differentiation), nuclear pleomorphism and mitotic counting are commonly used by

pathologists to measure biologic behaviour[19] Other biologic prognostic parameters include lymphatic permeation, insitu component, vascular permeation and TNM stage. Table 1 shows good and bad prognostic indicators.

Several studies have shown that breast cancer in Africans and Nigerians in particular tend to be more aggressive and has a poor prognosis compared to tumours in patients from developed countries.[7,20,21] Nigerian tumors tend to be less differentiated with a paradoxically high degree of apoptosis.[21] Ikpatt et al noted significant differences in standardized mitotic index (SMI), mean nuclear area (MNA) and fraction of field with tubular differentiation (FTD) between Nigerian, African American and Caucasian Breast cancer even after adjusting for other confounding variables like age and stage.[22] These differences are likely genetically programmed with the African American features masked by genetic admixture. Other biological markers of aggressive activity seen in Nigerian patients include a young mean age at presentation (40-45yrs),[8,21] predominance of premenopausal tumours (67   74%),[8,21] advanced stage at presentation (73% in stage II and IV),[4,9] poor histological grade (71 -77% grades 2 and 3),[7,16] and low expressed estrogen receptor status (22.8 - 25%).[16,23] Hormone receptor negativity and aggressive histological features which resembles *BRCA1*-associated cancers are hallmarks of breast cancer in women of African ancestry.[24] Majority of breast cancer from Nigeria are basal-like in their intrinsic gene expression, suggesting distinct pathogenesis probably involving genes in the BRCA1-protein pathways.[24] The low ER/PR expression in Nigerian breast cancers implies that hormonal manipulation for breast cancer treatment in Nigeria will be ineffective in the majority of cases. These data have implications for the treatment since these ladies are often placed on tamoxifen or have oophrectomy without knowledge of their ER/PR status.

STAGING

Breast cancer staging involves both clinical and pathological staging. The clinical staging uses all the information, including pre-op imaging studies and biopsy results to assign a TNM stage to the patient's disease. While the clinical staging guides the initial treatment, including surgery; the ultimate treatment depends on the pathological staging which will incorporate the findings at surgery and the pathological examination of the surgical specimen. A full pathologic anatomy staging of breast cancer will include the following information: nodal involvement, extent of local tumour spread, distant spread as well as histological and cytological features. It also includes information on biological markers like hormone receptor status, proliferative index, tumour cell ploidy, oncogene and suppressor gene amplification and cathepsin

D expression. Full staging is limited in Nigeria by absence or cost of such investigative tools like mammography, CT scan, scintigraphy, flow cytometry and immunohistochemistry

SENTINEL NODE BIOPSY

This investigation is now a standard of care for early stage breast cancer especially for non palpable lesions detected through screening. It allows surgeons to avoid the morbidity of full axillary dissection in early breast cancer by selecting only the axilla with metastasis for treatment. Lymphatic basin mapping using technetium 99 lymphocyntigraphy in conjunction with isosulphan blue or patent blue violet is used to outline the sentinel node of the involved area of the breast. One or two of these nodes are then removed for histology. Frozen sections of the sentinel nodes guide decision to either proceed with axillary dissection or to leave the axilla alone. The advanced presentation in Nigeria does not encourage the development of this technique locally.

TNM STAGING

The UICC/AJCC TNM system of staging is the current standard staging system for breast cancer. The latest version of the staging can be accessed freely at http://caonline.amcancersoc.org/cgi/content/full/56/1/37. While older staging systems are still used in some institutions in Nigeria, TNM staging is now accepted as the basis for all treatment and outcome comparisons. The staging is useful for planning of treatment, reporting of results, prognosticating, and comparison of outcomes. Refinement in the TNM staging is the force behind individualized care that is increasingly adopted in the management of breast cancer and indeed most cancers all over the world. Survival is also closely linked with the TNM stage.

PREVENTION OF BREAST CANCER

Breast cancer is a disease of public health importance. The presence of modifiable risk factors makes it amenable to prevention. Both primary and secondary prevention are feasible. Primary prevention aims to modify the risk factors so as to reduce the chances of the cancer developing. Secondary prevention focuses on early detection of the cancer and treatment so as to reduce its morbidity and mortality. Drug treatment, surgery and life style modifications are used for primary prevention. Prophylactic mastectomy is recommended for people with hereditary breast cancer due to the major genes like BRCA 1 and 2 genes. It gives only 90% protection since it is difficult to extirpate all breast tissue with surgery. Accurate and objective risk assessment is therefore needed as well as genetic counseling before this approach is adopted.
Randomized trials in high risk individuals have shown that tamoxifen reduces the incidence of new primary breast

cancer by 49%.[25] Included as high risk individuals are patients that have survived an initial breast cancer, patients more than 60 years of age, those with carcinoma in situ, patients with atypical hyperplasia on histology of breast biopsy, patients with strong family history of early onset breast cancer and those with 5 year aggregate risk up to 1.67%.[25] Each woman's exact risk level can now be calculated using one of the risk assessment models like the Gail model. This approach however has not caught up in Nigeria because of the marked differences between the Nigerian and the Western models of breast cancer epidemiology. Local studies are yet to look at the risk level calculation models to see how they predict the risk of breast cancer among Nigerians. Also there is no population study of breast cancer in Nigeria on which to base the risk assessment. Clinicians in the local environment can however confidently recommend tamoxifen as prophylaxis against a second primary for any lady that has survived a previous breast cancer. While there has been no evidence based confirmation that diet and exercise makes a difference, it is generally recommended that balanced diet with high content of fresh food and vitamin C is a good general health measure. There are some studies mostly from European countries suggesting that olive oil and mono unsaturated fats may have some protective effect on breast cancer.[26]

The greatest impact on breast cancer prevention has come from secondary prevention through mass screening programs. The advantages of screening and early detection are to optimize chances for cure, improve survival, avoid mutilating surgeries, and engender healthy life style measures in patients. The sustained downward trend in the mortality of breast cancer in the US has been attributed largely to wide spread screening with mammography.[27] Screening programs however consume a lot of resources and Nigeria is not in a position to mount such a program. While there are mammography machines in different centers in the country, there is no public screening program. Many centers in Nigeria use nonstandard or outdated machines for their mammography and these do not give reliable findings. Screening also has a special problem in a country like Nigeria where the peak incidence of breast cancer is in premenopausal ladies. The recommended age for annual screening in Nigeria will be much earlier than the recommended age of 50yrs in developed countries or the actual practice in most countries to commence screening at 40 years. Many authorities in breast cancer in Nigeria recommend screening to start by 30 - 35years of age. The problem with this is that mammography has a lot of false positive findings in young breasts because of their dense breast tissues. Augmentation of such a program with Magnetic Resonance imaging (MRI) of the breast may help in defining suspicious lesions. Screening as part of individual personal checkups take place in many clinics in

Nigeria but most of the mammography centers do not have facilities for pre-symptomatic lesion biopsy like stereotactic biopsy needle or X-reidy needle. Such screenings are therefore useless in non palpable lesions.

Monthly breast self examination and annual physical exam by a clinician have not been shown to make any difference in the mortality. However, since most of our patients present late with stage III and IV disease, these measures are recommended to encourage stage migration at presentation toward the earlier stages. Breast self examination should be done by every lady from 20 years of age, at about a week after onset of menstruation when the breast tissues are at rest and the breast is least likely to be tender.

CLINICAL MANIFESTATIONS

Breast cancer can present with symptoms of local or systemic disease. Local changes in the breast include palpable lump, breast thickening and breast pain. Painless breast mass is the commonest presentation. Breast pain is often a late presentation of breast cancer and its absence at initial stages contributes to delays in seeking treatment. Nipple changes include nipple discharge, nipple retraction or itchy nipple. Most breast nipple discharges are not malignant. Discharges from malignant lesions are often unilateral, spontaneous, bloody and may have associated breast changes like a mass or thickening of the breast. Nipple retraction when unilateral and of resent onset or associate with a lump should always be investigated for malignancy. Breast skin changes like edema or erythema occur late in locally advanced disease. Regional axillary node involvement shows as palpable axillary mass, axillary thickening and axillary pain. Infraclavicular, supraclavicular and lower cervical node involvement presents as discrete or matted lumps. Skin metastasis can lead to subcutaneous skin nodules, intra cutaneous nodules or patchy hyper or hypo pigmented skin infiltration. Satellite intracutaneous metastasis on the skin of the chest wall and breast will lead to cancer encurasse. Blood borne metastases go to the lungs, presenting as cough and difficulty with breathing; to the pleura where pleural effusion commonly results. Bone is the commonest site for metastasis especially to the ribs, spine, and heads of the long bones. Rib metastasis shows are pleuritic chest pain and local chest wall tenderness. Spinal metastasis may result in back pain, paresthesia and or paresis/paralysis. Pathological fracture of the long bones can occur when they are involved. Metastases reach the liver through the lymphatics and blood to cause right upper quadrant pain from enlargement and stretching of its capsule. Ascitis may occur while kidney metastasis can lead to anuria. Involvement of the brain may lead to persistent or recurrent headaches, blurring of vision,

stroke and death due to raised intracranial pressure. Typically metastasis to the brain and the liver are very poor prognostic features with survival less than 6 months in most cases. Lung and pleural metastasis and discrete bone metastasis are associated with good response to chemotherapy and hormonal manipulation. Bone marrow involvement is another poor prognosis feature characterized by progressive anaemia in the absence of actual blood loss.

DIAGNOSIS

Tissue diagnosis is a basic requirement. This can be obtained through core needle biopsy or fine needle biopsy. Core needle biopsy is commonly used as an office procedure when there is a palpable mass. Stereotactic or X-reidy needle localized biopsies are done for non palpable image detected lesions. Fine needle aspiration biopsy is now used for a number of the tissue diagnosis but it depends on the availability of an experienced cythopathologists for a reliable result. Treatment with fine needle cytology is justified in clinically obvious lesions but for early lesions, most clinical oncologists will not base mutilating treatments on cytology alone. In such situations, fine needle cytology becomes an initial diagnostic tool enabling the counseling of the patients for the definitive treatment as histology is awaited.

Preoperative imaging studies include beast ultrasound scan which is used to augment mammography. Ultrasound scan is also very useful in detecting liver metastasis, pleura effusion and ascitis. Mammography is the anchor tool in screening programmes but in clinically palpable lesions, mammography is important for evaluation of the contralateral breast and also for the involved breast where breast conserving surgery is contemplated. Plain x-rays are symptom directed as the yield of a blind skeletal survey is not rewarding. Other imaging modalities used routinely are CT scan of the brain, chest and abdomen and bone scan with technetium 99 which is the standard of care for detecting bone metastasis.

TREATMENT

The therapeutic options for breast cancer include surgery, radiation treatment, chemotherapy, hormonal manipulation; monoclonal antibody targeted treatment as well as supportive care.

The surgical treatment options include breast conserving treatment by local excision of the tumour (wide local excision or quadrantectomy) combined with axillary clearance or a simple mastectomy with axillary clearance. Modified radical mastectomies and radical mastectomies are now only used where the local disease force such a

procedure. The axillary disease is usually treated with axillary clearance in combination with the local excision or the mastectomy. Level II or occasionally level III axillary clearance is done. Radiation can also be used to treat the axillary disease where the load of axillary disease is not much. Mastectomy may be followed by immediate or delayed breast reconstruction either as a cosmetic replacement of the breast or to achieve skin cover where tissue defect exists after the mastectomy. The most commonly used flaps for reconstruction are latissimus dorsi flap and the transverse rectus abdominus muscle (TRAM) flap.

Surgeons played the dominant role in the early years of breast cancer treatment but now treatment is a multidisciplinary affair. In developed countries, less mutilating surgeries are the order of the day with mastectomies reserved as salvage procedures. In Nigeria however, mastectomies still remain the predominant surgery but many centers are now doing breast conserving surgery. The limitations for breast conservation in Nigeria include the late presentation of diseases, the cost of breast conserving treatment and the close monitor and follow up that breast conservation entails. Radiation therapy is a compulsory part of the local treatment for breast conservation and the paucity and cost of the facility has limited a more widespread adoption of breast conserving treatment. It is hoped that in the coming 5 10 years results of breast conserving treatment from local centers will be available.

Chemotherapy for breast cancer has come a long way. In the developed western countries, first line agents now include a taxol and doxorubicin or epirubicin with or without cyclophosphomide. The use of chemotherapy in Nigeria has kept a reasonable pace with developments in the best of places in the rest of the world. The first line combinations used in leading centers in Nigeria include doxorubicin and cyclophosphomide with or without fluorouracil. Prednisolone may be added to any of the combinations to improve tolerance for the chemotherapy. Second and third line combinations include CMF (Cyclophosphomide, Methotrexate and Fluorouracil), MMM (Mitoxanthrone, Mitomycin C and Methotrexate), MMC (Mitomycin C, Methotrexate and cyclophosphomide) and Taxols (Docetaxel or Paclitaxel). Cost has limited a more widespread use of taxols which are currently the most active agents for breast cancer.

Treatment of patients with chemotherapy in Nigeria has suffered from the all comers affair in the management of cancer patients. There are no medical oncologists in the country. Many general surgeons who are often the first contact of these patients with specialist care are not experienced with chemotherapy and give these patients less than optimum dosages and combinations. Many still use non classical regimes of CMF which have been known

not to make a difference in outcome. Many physicians do not take the pain of calculating dosages with body surface area so that patients end up getting sensitizing doses of the drugs thereby inducing resistance. Adjuvant drugs are not commonly available outside the major centers or the treating surgeons may not be conversant with them so that many patients are under medicated for emesis and pain thereby limiting the dose of chemotherapy these patients are able to tolerate.

Radiation treatment has been the most limiting aspect of breast cancer treatment in Nigeria. Radiation facilities are grossly inadequate. Until now, coverage across the nation has been very sparse and uneven. There is no radiation facility in the eastern parts of the country. Currently there is only one privately owned center at EKOH hospital Lagos while the Federal government has 4 centers at LUTH, UCH Ibadan, National hospital Abuja and ABU Zaria. A fifth center is about to come on stream at UNTH Enugu by the middle of this year. While the older centers are struggling to have their equipments updated and running, even with all the centers on board, many patients will still have to wait for months to get their radiation.

Most radiation treatment for breast cancer use external beam radiotherapy with either cobalt 60 or the more modern linear accelerator machines. When breast conserving therapy is used for the local disease, radiation of the breast becomes a compulsory part of the treatment but if mastectomy is done, radiation to the breast is done selectively depending on the local disease burden and the type of surgery done. Radiation is also very useful for localized metastasis and some oncologic emergencies. External beam radiation is given over a course of 4-6 weeks using up to 70Gy to the whole breast with a booster dose of 500 centi Grays (5Gy) to the tumour bed. Interstitial radiation with intra-operative placement of catheter applicators at the tumour bed is now preferred in some centers since it gives a more precisely placed radiation over a shorter length of time (4 6 days).

Knowledge of estrogen and progesterone receptor expression is critical in deciding when to use hormonal manipulation for the patient since they predict which patients will respond to hormonal treatment. Up till recently, most breast cancer patients in Nigeria were placed on tamoxifen after diagnosis or following surgery and chemotherapy because of the absence of facilities for ER/PR receptor assay in the country. This was based on studies in western populations that showed that at least a third of all breast cancer will respond to hormone treatment. More than 65% of breast cancers in Nigeria do not express ER and PR receptors.[16,23] The implication is that most Nigerian breast cancer patients were being subjected to the side effects of these drugs at a monetary cost without the benefit of the drug. This has now influenced the drive in the leading centers in the country to do routine hormone assay in all breast cancer patients and selectively use hormone manipulation guided by the assay.

Table 2 shows the hormonal options available for breast cancer treatment. In postmenopausal patients, the first line treatment for ER/PR positive tumours is anastrozole. Tamoxifen is used as second line when anastrozole fails or is not available. In premenopausal women, the first option is tamoxifen or oophrectomy. While the effect of tamoxifen may be reversible (some ladies may still desire children), oophrectomy is a simple procedure, cheaper in the long run and avoids need for long term ingestion of drugs. Radiation oophrectomy will obviate the need for surgery but the effect takes time to set in and may not be guaranteed until castrate hormone level is obtained. Surgical oophrectomy is now done as laparoscopic procedure or by mini laparotomy as a day procedure under minimal anaesthesia. Its effect on the hormone level is more predictable.

The most recent event in the management of breast cancer is the inclusion of targeted therapies among the standard of care. Monoclonal antibodies are now tagged with agents against particular protein products of the tumour gene. These are used to kill the tumour cells. Tratuzumab (Herceptin) is used for tumours that over express the Her2-neu gene product and it has made a difference in the survival of these poor prognosis tumours. Her2-neu assay is not yet widely available in Nigeria. Other drugs in the same class are being investigated. Biphosphonates have been in clinical use for a long time even though it is yet to be widely used among cancer patients in Nigeria. Its principal use is to treat hypercalcaemia and bone pain from metastasis and to prevent bone metastasis.

The integration of all the difference modalities in the management of breast cancer is an art that is based on science and increasingly requires sub specialization in different areas of clinical oncology. This has become necessary as we move into the era of personalized cancer care where individualized treatment plans are made based on each patient's unique characteristics and tumour biology. With the absence of medical oncologists in the field in Nigeria, the job of clinical oncology has fallen on surgical oncologists and radiation oncologists to plan the treatment of each patient in a way to maximize the benefit for the patient.

 Each of the treatment modalities can be given as primary treatment, adjuvant treatment or as palliative treatment. Generally, patients with early stage cancer are said to be curable (surgically curable). Surgery for this group becomes the primary mode of treatment with chemotherapy, radiotherapy and hormonal manipulation added as adjuvants. If the patient had breast conserving surgery, the primary treatment comprise the local surgery with the radiotherapy while the chemotherapy and the hormonal

treatment are given as adjuvants. Stages III and VI tumours are regarded as incurable and the aim of treatment at these stages is not to cure the patient but to increase the quantity and or the quality of life.

Systemic treatments with chemotherapy, hormonal treatment and targeted agents become the primary treatment modalities while surgery and or radiotherapy may be needed as an adjunct or to palliate some symptoms. In some locally advanced stage III tumours, a preoperative chemotherapy or hormonal manipulation is done to down stage the tumour as a neo-adjuvant treatment, followed by surgical treatment and then post operative radiation, chemotherapy and hormonal treatment. Chemotherapy and hormonal treatment are generally given sequentially because reaction to chemotherapy is more when they are given concurrently. Part of the action of chemotherapy in premenopausal ladies is the chemical castration it induces.

Hormonal manipulation is better tolerated than chemotherapy in elderly ladies and response to it is better in post menopausal ladies. For these reasons, hormonal manipulation is used as the first line of systemic therapy in post menopausal ladies while in premenopausal ladies, chemotherapy is always given first before the hormonal manipulation.

SUPPORTIVE TREATMENT AND PERSONNEL

Breast cancer management like most oncology services demands a multidisciplinary approach. Apart from radiation oncologists who trained primarily for radiation therapy, the field in Nigeria is populated by surgeons. The best of the hands have gained experience and international recognitions through dedicated practice in the field and short exchange programs in aspects of clinical oncology. Medical oncologists have been conspicuously absent and there is no specific fellowship or post residency programme to train subspecialists in the field. Most breast cancer patients in Nigeria get their initial treatments from surgeons with no expertise in oncology leading to suboptimal treatment in many cases. The same scenario obtains in the nursing field where dedicated oncology nurses in the major centers gained expertise and recognition through experience and exchange programmes. There is therefore a need for sub specialty training for both physicians and nurses in the field of oncology in Nigeria. Hopefully, this will be one of the gaps that the new Society for clinical oncology and research in Nigeria (SCOCRON) will fill.

Most breast cancer patients will need supportive treatment in one form or another. Palliative care services are under developed in Nigeria. Palliative care services are currently rendered by different oncology units with no dedicated personnel in the field. The scarcity of strong opiates makes pain palliation grossly inadequate. Units outside of the

major centers lack access to and are not conversant with use of adjuvant drugs like biphosphonates, colony stimulating factors (e.g. erythropoietin, granulocyte macrophage colony stimulating factors) and more potent newer generation antiemetics. No center currently uses central venous access for dose intense chemotherapy and nutritional support. Nutritional support beyond supplemental intravenous fluid and modified enteral feeds are not in use. All these are areas of development which hopefully will become generally available all over the country in the near future as more and more specialists and centers enter the field.

CONCLUSION

Breast cancer is common in Nigeria. Its epidemiology and tumour biology are in some ways different from the disease in western countries. Some of these unique characteristics like early onset, aggressive behavior, unique genetic characteristics and absent hormonal receptor expression are now being studied in detail among our patients. These findings are informing modifications in local treatment strategies. Most breast cancer patients in Nigeria still present at late stages. Mastectomy is the main form of surgery but patients are now getting better chemotherapy and hormonal treatment. Outside of the major centers, treatment is uncoordinated and done by physicians not experienced in the subspecialty. There is an urgent need for subspecialty training and a coordinated effort to establish a local standard of care.

Table 1: Good and Bad prognostic indicators

Good prognostic indicators	Poor prognostic factors
older age at onset of disease,	patients under 40 years
Tumours < 1cm in diameter	Large tumours > 5cm
Axillary node not involved	Axillary node involved
No local tumour extension	Presence of local tumour extension
Histology well differentiated	Anaplastic tumour
Tumour with little atypia	Severe nuclear atypia
Hormone receptors expressed (ER+ and PR+)	Hormone receptor negative (ER-ve and PR –ve)
Her2/neu not expresses	Her-2/neu protein over expressed

Table 2: Hormonal manipulation options

SERMs	Tamoxifen, Toremifene and Raloxifene
Oophretomy	Surgical or Radiation
Progestogens	Megesterol acetate, Medroxyprogesterone acetate
Aromatase inhibitors	Anastrozole, Letrozole, Fadrozole, Exemestane
LH-RH analogs	Goserelin, Buserelin
Estrogens	DES, Estradiol
Androgens	Fluoxymestrone

1.　Parkin DM, Bray F, Ferlay J and Pisani P. Global Cancer Statistics, 2002. CA Cancer J Clin 2005; 55: 74-108
2.　National cancer Registry Ibadan
3.　Ihekwaba FN. Breast cancer in Nigerian women. Br J Surg 1992; 79: 771-5.
4.　Adebamowo CA, Ajayi OO. Breast cancer in Nigeria. West Afr Med J
5.　Dogo D, Gali BM and Ngadda HA. Male breast cancer in North Eastern Nigeria. Niger J Clin Pract 2006; 9:139 141
6.　Kidmas AT, Ugwu BT, Manasseh AN, Iya D and Opaluwa AS. Male breast malignancy in Jos University Teaching Hospital. W Afr J Med 2005; 24: 36 40
7.　Ikpatt OF, Kuopio T, Ndoma-Egba R, Collan Y. Breast cancer in Nigeria and Finland: epidemiological, clinical and histological comparison. Anticancer Res. 2002; 22: 3005-12.
8.　Fregene A and Newman LA. Breast Cancer in Sub-Saharan Africa: How Does It Relate to Breast Cancer in African-American Women? Cancer 2005; 103: 154050.
9.　Adebamowo CA, Adekunle OO. Case controlled study of the epidemiological risk factors of breast cancer in Nigeria. BJS 1999; 86: 665 668
10.　Okobia M, Bunker C, Zmuda J, Kammerer C, Vogel V, et al. Case controlled study of risk factors for breast cancer in Nigeria women. Int J Cancer 2006; 119: 2179 2185
11.　Okobia MN, Bunker CH, Zmuda JM, Osime U, Ezeome ER, et al. Anthropometry and Breast Cancer Risk in Nigerian Women. The Breast Journal 2006; Volume 12: 462466
12.　Nathanson KL, Wooster R and Weber BL Breast cancer genetics: What we know and what we need. Nature Medicine 2001; 7: 552 558
13.　Wagner TM, Hirtenlehner K, Shen P, Moeslinger R, Muhr D, et al. Global sequence diversity of BRCA2: analysis of 71 breast cancer families and 95 control individuals of worldwide populations. Hum Mol Genet 1999; 8: 41323.
14.　Gao Q, Adebamowo CA and Fackenthal J et al. protein truncating BRCA1 and BRCA 2 mutations in African women with premenopausal breast cancer. Human Genetics 2000; 107: 192 194
15.　. Fackenthal JD, Sveen L, Gao Q. Complete allelic analysis of BRCA1 and BRCA2 variants in young Nigerian breast cancer patients. J Med Genet 2005; 42: 276 281
16.　Gukas ID, Jennings BA, Mandung BM et al. Clinicopathological features and molecular markers of breast cancer in Jos, Nigeria. West Afr J Med 2005; 24: 209 213
17.　Ekanem VJ and Aligbe JU. Histopathological types of breast cancer in Nigerian women: a 12-year review (1993-2004). Afr J Reprod Health 2006; 10: 71 75
18.　Elledge RM, Clark GM, Chamness GC and Osborne CK. Tumor biologic factors and breast cancer prognosis among whites, Hispanic and Black women in the United States. J Nat Cancer Institute 1994; 86: 705 712
19.　C W Elston CW & Ellis IO. Pathological prognostic factors in breast cancer. I. The value of histological grade in breast cancer: experience from a large study with long-term follow-up. Histopathology 1991; 19: 403410
20.　Ikpatt OF, Kuopio T and Collan Y. Proliferation in African Breast Cancer: Biology and Prognostication in Nigerian Breast Cancer Material. Mod Pathol 2002; 15: 783789
21.　Ikpatt F, Kuopio T, Erekul A and Collan Y. Apoptosis in breast cancer: Nigerian vs. Finnish material. Anal Quant Cytol Histol. 2002; 24: 73-80.
22.　Ikpatt FO, Dignam JJ, Khramtsov A, Grushko T, Fackenthal J, et al. Breast tumor morphometry in relation to race reveals significant differences among Nigerians, African-Americans and Caucasian Americans. [Abstract]. In ASCO 2004. Journal of Clinical Oncology 2004; 22, (14S): 9567
23.　Ikpatt OF, Ndoma-Egba R. Oestrogen and progesterone receptors in Nigerian breast cancer: relationship to tumour histopathology and survival of patients. Cent Afr J Med. 2003; 49: 122-6.
24.　Ikpatt OF, Xu J, Kramtsov A, Ndoma-Egba R, Perou C and Olopade O. Hormone receptor negative and basal-like subtypes are overrepresented in invasive breast carcinoma from women of African ancestry.[Abstract]. In Proc Amer Assoc Cancer Res, Volume 46, 2005. Abstract no 2550
25.　Bernard Fisher, Joseph P. Costantino, D. Lawrence Wickerham, Carol K. Redmond, Maureen Kavanah, Walter M. Cronin, Victor Vogel, André´ Robidoux, Nikolay Dimitrov, James Atkins, Mary Daly, Samuel Wieand, Elizabeth Tan-Chiu, Leslie Ford, Norman Wolmark, and other National Surgical Adjuvant Breast and Bowel Project Investigators. Tamoxifen for Prevention of Breast Cancer: Report of the National Surgical Adjuvant Breast and Bowel Project P-1 Study. J Natl Cancer Inst 1998; 90: 13711388
26.　Vecchia CL, Negri E, Franceschi S, Decarli A, Giacosa A and Lipworth L Olive oil, other dietary fats, and the risk of breast cancer (Italy). Cancer causes and control 1995; 6: 545 550
27.　Jemal A, Murray T, Ward E, Samuels A, Tiwari RC et al. Cancer Statistics, 2005. CA Cancer J Clin 2005; 55: 10-30