

Epidemiology, Clinical Presentation and Management of Advanced Breast Cancer in Nigeria

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Overview

- Breast cancer burden in Nigeria
- Epidemiology of advanced breast cancer in Nigeria
- Clinical presentation of breast cancer in Nigeria
- Management of advanced breast cancer in Nigeria

Cancer burden

- Cancer remains one of the leading causes of morbidity and mortality worldwide
- By 2020, new cases of cancer in the world will increase to >15 million, with deaths increasing to 12 million (*WHO World Cancer Report*)

Cancer burden cont.

- Much of the burden of cancer incidence, morbidity, and mortality will occur in the developing world
 - increasing life expectancy
 - part of a larger “epidemiological transition”
 - increasing risks associated with diet, tobacco, alcohol, obesity, and industrial exposures
 - already burdened by cancers some of which are attributable to infectious diseases

Cancer burden in Nigeria

- Estimated 500,000 new cases of cancer diagnosis annually (*Solanke TF, 1999*)
- Breast cancer presents a typical picture of the enormity of cancer burden on the Nigerian nation (*Adebamowo and Ajayi, 2000*)
 - increasing prevalence
 - afflicts relatively young women
 - runs an aggressive course
 - late presentation to hospital
 - bulky and scirrhous tumour

Epidemiology of advanced breast cancer in Nigeria

- peak age incidence is 42.6 years*
- mean age of 46.8 ± 11.5 years (of 1094 cases)**
- 12% of patients younger than 30 (*0.5% in Caucasian series*)
- relatively high number diagnosed during pregnancy and lactation (*12% in Ibadan in 1999, Adebamowo; 26.3% in women <50 years in Zaria, Hazzan, 1995*)

*(*Adebamowo and Ajayi 2000, **Presented at ASCO 2008)*

Epidemiology of advanced breast cancer in Nigeria cont.

- relatively high proportion of male breast cancer
 - 3.75% in Ibadan (Ihekwaba, 1994)
 - 9% in Zaria (Hazzan, 1995)
 - 3.7% in NE Nigeria (Dogo 2000)
 - 8.6% in Jos (Kidmas 2005)
 - 1.2% in Enugu (Ezeome 2008)*
 - 2.4% in Ibadan (Ogundiran 2008)*

(Yet to be published)*

Case control studies of risk factors

1. Adebamowo and Adekunle, *BJS* 1999

Compared with the control group, cancer patients:

- had a significant statistical difference in height and weight
- tended to be older at first pregnancy and at first lactation
- had a higher mean number of pregnancies
- tended to be of an early birth order, to have lactated less often, to have used contraceptives, and to have abused alcohol

2. Adebamowo, Ogundiran, Adenipekun, Oyesegun et al
(*Breast Cancer Research* 2002)

| Predictor | Odds Ratio | 95% Confidence Interval | P value |
|--|-------------------|--|----------------|
| Age | 1.07 | 1.04–1.10 | <0.01 |
| Age at menarche | 0.86 | 0.77–0.97 | 0.01 |
| Age at first full term pregnancy | 1.09 | 1.02–1.16 | 0.01 |
| Height | 1.03 | 1.00–1.07 | 0.07 |

Predictors of breast cancer among premenopausal women in Nigeria, 1998–2000

Predictors of breast cancer among postmenopausal women in Nigeria, 1998–2000

| Predictor | Odds Ratio | 95% Confidence Interval | P value |
|-----------------|------------|-------------------------------|---------|
| Age | 0.93 | 0.09–0.97 | 0.01 |
| Age at menarche | 0.89 | 0.78–1.02 | 0.08 |
| Height | 1.07 | 1.02–1.13 | 0.01 |
| Weight | 1.02 | 1.00–1.04 | 0.07 |
| Waist | 1.01 | 1.00–1.05 | 0.03 |
| Waist–hip ratio | | | |
| ≤ 0.77 | 1.00 | | |
| >0.77 to ≤ 0.85 | 1.52 | 0.67–3.42 | 0.31 |
| >0.85 | 2.79 | 1.21–6.45 | 0.02 |
| Obesity | | | |
| Yes | 2.01 | 0.99–4.09 | 0.05 |
| No | | | |

Multivariable odds ratio, 95% confidence interval and P value,
in postmenopausal women in Nigeria, 1998–2000

| Predictor | Adjusted Odds Ratio | 95% Confidence Interval | P value |
|-----------------|---------------------|-------------------------|---------|
| Waist–hip ratio | | | |
| ≤ 0.77 | 1.0 | | |
| >0.77 to ≤ 0.85 | 1.68 | 0.68–4.19 | 0.26 |
| >0.85 | 2.67 | 1.05–6.80 | 0.04 |

3. Ann Epidemiol 2003

Increasing height was positively associated with the risk of breast cancer among all women (OR 1.05, 1.01 – 1.08), pre- (1.06, 1.01–1.10) and post-menopausal women (1.07, 1.01–1.13) for each cm

4. Okobia, Uche, Anyanwu, Ezeome, et al (*Int. J. Cancer* 2006)

| Variable | Cases | Controls | OR | 95% CI | p-Value |
|--|-------------|-------------|------|--------------|---------|
| Family history breast cancer | | | | | |
| Yes | 15 (6.00) | 1 (0.40) | 8.08 | 1.003, 64.95 | 0.04 |
| No | 235 (94.00) | 249 (99.60) | 1.00 | | |
| Education (\geq high school) | | | | | |
| Yes | 136 (54.40) | 113 (45.20) | 1.35 | 1.04, 1.74 | 0.0205 |
| No | 114 (45.60) | 137 (54.80) | 1.00 | | |
| Age at first fullterm pregnancy (>20 years) | | | | | |
| Yes | 162 (77.20) | 136 (65.07) | 1.32 | 1.01, 1.71 | 0.0413 |
| No | 48 (22.8) | 73 (34.93) | 1.00 | | |
| Waist/hip ratio (>0.90) | | | | | |
| Yes | 161 (64.40) | 117 (46.80) | 1.98 | 1.27, 3.10 | 0.0026 |
| No | 89 (35.60) | 133 (53.20) | 1.00 | | |

Multiple conditional logistic regression comparing cases and controls

5. ASCO 2008

- Cases (160.0 ± 6.9 cm) were on average 1.2 cm taller than controls (158.8 ± 6.4 cm)
- OR of 1.20 (95% CI 1.11-1.30, $p < 0.001$) for each 5cm increase in height
- There was marginally significant negative correlation with body weight and BMI
- Waist circumference and waist-to-hip ratio were +vely associated with risk in both pre- and post-menopausal women

Identified genetic factors

- High penetrance low freq. genes: BRCA 1 in 4% of cohorts, 74% non truncating mutation in BRCA 2
- Low penetrance high freq genes: COMT gene, Aromatase gene (CYP19), P4501A1 gene (Okobia et al 2006, 2008)

Clinical Presentation

- In the absence of a screening program, the stage at diagnosis is a reflection of the degree of awareness of the disease in the population

Some selected features

| Author (year) | Institution | n | Peak age(mean) | Main Histological type (%) | Late Stage presentation (%) | % premenopausal |
|-------------------------|-------------|-----|----------------|----------------------------|-----------------------------|-----------------|
| Anyanwu(1987-) | Nnewi | | 35-39(44) | Invasive ductal | 64 | 69 |
| Okobia(1987-1996) | Benin | 177 | (38 median) | | 77 | |
| Hazzan(1999) | Zaria | 129 | | Invasive ductal (85) | 88 | 64 |
| Adebamowo (1992-1995) | Ibadan | 250 | (43) | Invasive ductal | 72.8 | 74 |
| Ikpat (1983-1999) | Calabar | 300 | (42.7) | Invasive ductal (80.6) | | 74.3 |
| Adesunkanmi (1996-2003) | Ife | 212 | (48) | | 80.6 | 66.7 |
| Ngadda (2001-2005) | Maiduguri | 169 | 40-49 | Invasive ductal(82.6) | | |
| Abudu (2002-3) | Sagamu | 50 | 40-49 (47.5) | Invasive ductal (94) | 72 | |
| Adebamowo(2004-5) | Ibadan | 192 | | Invasive ductal | 86.5 | |

Identified features of aggressive activity in Nigeria

- Young mean age (40-45yrs)
- 67 – 74% premenopausal
- 73% in stage III and IV
- 71 -77% grades 2 and 3 histology
- 22.8 - 25% ER positive
- Majority are basal-like in their intrinsic gene expression, suggesting distinct pathogenesis probably involving genes in the BRCA1-protein pathways

(Ikpatt et al 2002, 2004)

Immunohistochemistry in Ibadan

- Most, 65.1% of tumors were ER+, 54.7% were PR+ and 79.7% were HER2 negative
- Majority of the tumors, 77.6% were luminal type A, 2.6% were luminal type B, 15.8% were basal type and the remaining 4.0% were HER2+/ER- subtype

(Adebamowo, Famooto, Ogundiran et al. Breast Cancer Res Treat 2007)

Immunohistochemistry in Ibadan cont.

| Hormone receptor status | Composite Grade | | | Total |
|-------------------------|-----------------|-------------|-------------|-------|
| | 1 (n, %) | 2 (n, %) | 3 (n, %) | |
| ER negative | 0, 0% | 23, 18.4% | 10, 8.0% | 33 |
| ER positive | 17, 13.6% | 57, 45.6% | 18, 14.4% | 92 |
| PR negative | 1, 0.9% | 30, 25.9% | 13, 11.2% | 44 |
| PR positive | 15, 12.9% | 44, 37.9% | 13, 11.2% | 72 |
| HER2 negative | 12, 10.7% | 69, 61.6% | 25, 22.3% | 106 |
| HER2 positive | 1, 0.9% | 3, 2.7% | 2, 1.8% | 6 |

there was significant association between the grade of the tumor and the estrogen receptor status (p=0.04)

there was no association between the HER2 status and grade of tumor (p=0.54)

Common sites of metastatic disease presenting clinically

- chest
 - pleura, with effusion and respiratory distress
 - lung parenchyma
 - ribs, sternum, scapular
- bones
 - long bones, with pain, pathological fracture
 - spinal cord compression leading to paraparesis and paraplegia
 - pelvic bones
- brain
- liver

Diagnosis and staging of breast cancer in Nigeria

- Typical investigations
 - Biopsy and tissue diagnosis
 - CXR and other x-rays as necessary
 - Abdominal ultrasound scan
 - radionuclide scan
 - ER/PR test post histology (often use biopsy specimen)
 - Blood work up: FBC, E/U, ?LFT
 - (Mammography, Breast ultrasound scan)

Diagnosis and staging of breast cancer **in Nigeria**

- Use of TNM staging recommended
- Limited use of CT, mammography, flow cytometry, Frozen section histology
- Late stage at presentation makes Lymphatic basin mapping and sentinel node biopsy useless







Staging of advanced breast cancer in Nigeria

- Locally advanced: Stages IIIA, IIIB and IIIC
- Metastatic disease: Stage IV

Treatment of breast cancer in Nigeria

- Modalities include
 - surgery
 - radiation treatment
 - chemotherapy
 - hormonal manipulation
 - targeted treatment
 - Palliative/ supportive care.

Surgery for advanced breast cancer in Nigeria

- Mastectomies still predominate
 - Simple mastectomy
 - Axillary clearance may be added
 - Occasional radical mastectomy
- BCT for metastatic cases with small volume breast disease or (post neoadjuvant).
 - QUART
 - LART

Incomplete mastectomy



Breast Radiation treatment in Nigeria

- Most of our patients need RTH b/c of heavy disease load on the breast & metastasis.
- Facilities few, unevenly distributed, old.
- Co 60: UCH, EKOI, ABUTH (Gombe, RADMED)
- Linear accelerator: Abuja, (LUTH, UNTH)
- Brachytherapy: non
- Radiation in BCT: Scheduling issues and need for prior planning/discussion

Chemotherapy

- Some state of the arts drugs can be sourced
- First line drugs in the leading centers remain Doxorubicin/Epirubicin based
- The most active drugs (Taxols, herceptin) are extremely costly
- Who gets it: premenopausal patients, ER/PR negative post menopausal, ER/PR +ve post menopausal if they fail hormonal treatment.

Breast cancer chemotherapy: some commonly used regimes in Nigeria

- FAC: Day 8 of 5FU may be problem, allows lower dose of doxorubicin
- AC: easier to follow, high dosing for doxorubicin, Epirubicin more costly
- CMF: should be classical regime to be useful. Cumbersome to follow
- AT: most effective but very costly
- 1st line and 2nd line drugs

Chemotherapy for breast cancer in Nigeria: assessing and preparing patients

- Overall assessment of performance status, quality of life
- FBC, E/U
- 2D Echo (ECG).
- Counseling on cytotoxic side effects and measure to prevent/control them
- Dosages should be adequate (use BSA)

Breast Cancer in Nigeria – Hormonal Manipulation

- More of our patients are premenopausal
- Current evidence suggest that ER/PR positivity rate in Nigerians is the same as in western countries
- ER/PR test facilities are few and scattered and most use archival tissues which accounts for the hitherto low positivity rates in our populations
- Premenopausal: Tamoxifen &/or Oophrectomy, LHRH analogues
- Post menopausal : tamoxifen, anastrozole, exemesthane

Targeted therapies

- trastuzumab limited by cost and Her2 neu assay (available now at UCH)
- Biphosphonates: Zoledronic acid, pamidronate, etc

Treatment approaches in locally advanced breast cancer in Nigeria

- Neoadjuvant systemic treatment
 - Allows down staging
 - selects poor prognosis ones for post op /radiation dose intense or cross over systemic treatment

- Mastectomy with post op systemic treatments and radiation (avoid if possible)

Treatment approaches in metastatic breast cancer in Nigeria

- Principles of treatment:
 - Improve quality of life
 - Disease control for as **long as possible**
- approaches:
 - Primary systemic treatments
 - Targeted surgery and or radiation for metastatic sites/manifestations
 - Symptom palliation, supportive care

Metastatic disease treatment

- Pleural effusion
- Dyspnea from lung disease
- Bone metastasis/ pathological fracture
- Spinal cord compression
- Brain metastasis

Supportive drugs/palliative care

- Pain relief: use of opiates, NSAIDs, etc
- Antiemesis: HT₃ antagonists, high dose metoclopramide etc
- colony stimulating factors for severe neutropenia
- **Involve palliative care team from diagnosis**
- Dedicated oncology nursing: dressings etc
- Family support
- Pastoral/spiritual care

Supportive and palliative care

- Psychosocial burden of care
 - Financial burden more problematic than the adverse effect of caring on family routines
 - Most family relationships remain intact , no perceived social stigma
 - overall feeling of burden was significantly predicted by family financial distress and disruption of family routines.
 - Ohaeri et al 1999

Survival and follow up

- Historically been poor in Nigeria
- Follow up records in UNTH 2001:
 - 29.2% were followed up for 1 year, 25% mortality
 - 10.5% for 2 years and 4.12% for 3 years
- Are we helping the patients? – a need for long term survival studies in Nigeria

Thank you