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 \((WHO \ World \ Cancer \ Report)\)
• 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
  – affiliates 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**
### Predictors of breast cancer among premenopausal women in Nigeria, 1998–2000

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.07</td>
<td>1.04–1.10</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Age at menarche</td>
<td>0.86</td>
<td>0.77–0.97</td>
<td>0.01</td>
</tr>
<tr>
<td>Age at first full term pregnancy</td>
<td>1.09</td>
<td>1.02–1.16</td>
<td>0.01</td>
</tr>
<tr>
<td>Height</td>
<td>1.03</td>
<td>1.00–1.07</td>
<td>0.07</td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th>Predictor</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.93</td>
<td>0.09–0.97</td>
<td>0.01</td>
</tr>
<tr>
<td>Age at menarche</td>
<td>0.89</td>
<td>0.78–1.02</td>
<td>0.08</td>
</tr>
<tr>
<td>Height</td>
<td>1.07</td>
<td>1.02–1.13</td>
<td>0.01</td>
</tr>
<tr>
<td>Weight</td>
<td>1.02</td>
<td>1.00–1.04</td>
<td>0.07</td>
</tr>
<tr>
<td>Waist</td>
<td>1.01</td>
<td>1.00–1.05</td>
<td>0.03</td>
</tr>
<tr>
<td>Waist–hip ratio ≤ 0.77</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;0.77 to ≤ 0.85</td>
<td>0.67–3.42</td>
<td>0.31</td>
</tr>
<tr>
<td></td>
<td>&gt;0.85</td>
<td>1.21–6.45</td>
<td>0.02</td>
</tr>
<tr>
<td>Obesity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>2.01</td>
<td>0.99–4.09</td>
<td>0.05</td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Multivariable odds ratio, 95% confidence interval and P value, in postmenopausal women in Nigeria, 1998–2000

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Adjusted Odds Ratio</th>
<th>95% Confidence Interval</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waist–hip ratio</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 0.77</td>
<td>1.0</td>
<td>0.68–4.19</td>
<td>0.26</td>
</tr>
<tr>
<td>&gt;0.77 to ≤ 0.85</td>
<td>1.68</td>
<td>1.05–6.80</td>
<td>0.04</td>
</tr>
<tr>
<td>&gt;0.85</td>
<td>2.67</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

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

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

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

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Institution</th>
<th>n</th>
<th>Peak age (mean)</th>
<th>Main Histological type (%)</th>
<th>Late Stage presentation (%)</th>
<th>% premenopausal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anyanwu (1987-)</td>
<td>Nnewi</td>
<td>35-39(44)</td>
<td>Invasive ductal</td>
<td>64</td>
<td>69</td>
<td></td>
</tr>
<tr>
<td>Okobia (1987-1996)</td>
<td>Benin</td>
<td>177</td>
<td>(38 median)</td>
<td></td>
<td>77</td>
<td></td>
</tr>
<tr>
<td>Hazzan (1999)</td>
<td>Zaria</td>
<td>129</td>
<td>Invasive ductal (85)</td>
<td>88</td>
<td>64</td>
<td></td>
</tr>
<tr>
<td>Adebamowo (1992-1995)</td>
<td>Ibadan</td>
<td>250</td>
<td>Invasive ductal</td>
<td>72.8</td>
<td>74</td>
<td></td>
</tr>
<tr>
<td>Ikpat (1983-1999)</td>
<td>Calabar</td>
<td>300</td>
<td>Invasive ductal (80.6)</td>
<td>80.6</td>
<td>74.3</td>
<td></td>
</tr>
<tr>
<td>Ngadda (2001-2005)</td>
<td>Maiduguri</td>
<td>169</td>
<td>Invasive ductal(82.6)</td>
<td>80.6</td>
<td>72</td>
<td></td>
</tr>
<tr>
<td>Abudu (2002-3)</td>
<td>Sagamu</td>
<td>50</td>
<td>Invasive ductal (94)</td>
<td>80.6</td>
<td>74.3</td>
<td></td>
</tr>
<tr>
<td>Adebamowo (2004-5)</td>
<td>Ibadan</td>
<td>192</td>
<td>Invasive ductal</td>
<td>86.5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
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

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

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, EKOH, 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
• 1\textsuperscript{st} line and 2\textsuperscript{nd} 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, palmidronate, 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: HT$_3$ antagonists, high dose metclopromide 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