

High Prevalence of Triple-Negative Breast Cancer and Poor Survival Outcome in Nigeria: A Call for Further Molecular Subtyping of Triple-Negative Breast Cancer

Triple-negative breast cancer (TNBC) is an aggressive heterogeneous type of tumor that accounts for 15%–20% of all female breast cancers worldwide. They are negative for estrogen and progesterone receptors and lack human epidermal growth factor receptor 2 amplification.^[1] Sung *et al.* stated that the risk of having TNBC varies with birthplace, especially among black women.^[1] The tumor subtype is less frequently identified in women of European ancestry than in Nigerian women,^[2,3] especially those that are 60 years and below.^[1,4] Interestingly, a preponderance of TNBC has been reported in Southern Nigeria than in Northern Nigeria: Kano (North-West; 46.6%),^[5] Maiduguri (North-East; 76.9%),^[6] Jos (North-Central; 41.3%),^[7] Uyo (South-South; 62.3%),^[8] Aba (South-East; 64.7%),^[9] and Lagos (South-West; 87%).^[10] According to Zheng *et al.*, Nigerian women with TNBC are 23.4 and 10.3 times more likely to have BRCA1 and BRCA2 mutations, respectively.^[4] They also opined that BRCA mutations greatly influence the invasiveness of breast cancer than any other gene mutations. This suggests that patients aged 60 years or less should be tested for the mutations.^[11] This information is vital for early cancer detection and treatment.

Few patients with TNBC respond to primary treatment options such as surgery, anthracycline- and taxane-based chemotherapy, and radiation therapy. This is because of the high rate of progression, reoccurrence, and relapse that leads to death in less than a year following the treatment. The survival rate in high-resource countries is greatly improved owing to the fact that TNBCs are further subtyped to inform improved new molecular targeted therapies. Identifying patients with tumor-infiltrating lymphocytes (TILs; CD8+ TILs or a high CD8+/FOXP3+ ratio) and those expressing programmed death-ligand 1 (immune evasion molecules) in tumor microenvironment inform prognosis and molecular-based therapeutic targets.^[2] Furthermore, a recent case study reveals that a combination of durvalumab (anti-PDL-1 antibody) and paclitaxel (a chemotherapeutic agent) completely treats TNBC.^[12] Unfortunately, most Nigerian patients cannot afford the already subsidized fee for the hormonal-based subtyping, let alone paying for the current molecular technique for subtyping TNBCs. The different subtypes of TNBC include: (1) basal-like subtype (BL1 and BL2) – it accounts for 50%–75% of all TNBCs. BL1 is associated with an elevated DNA damage response, p53 and BRCA1 mutations, retinoblastoma gene inactivation, high Ki67 expression, and downregulation

of B-cell, T-cell, and natural killer cells. (2) The luminal androgen receptor (LAR) subtype – it has a 10-fold expression of androgen receptor (AR) than the other subtypes. (3) Mesenchymal and mesenchymal stem-like subtypes – they possess high motility and cell differentiation while interfering with Epidermal growth factor receptor (EGFR), calcium signaling, and G-protein receptors. (4) Immunomodulatory subtype – it is another type of BL subtype with high STAT genes and activated immune (TILs) cells. Specific therapies for BL1, BL2, immunomodulatory subtype (IM), mesenchymal subtype (M), mesenchymal stem cell-like subtype, and LAR include cisplatin and Poly-ADP-ribose polymerase (PARP) inhibitors, mTOR and growth factor inhibitors, cisplatin and PARP inhibitors, NVP-BE235 (a PI3K/mTOR and growth Src factor inhibitor), dasatinib (an Abl/Src inhibitor), and bicalutamide (AR antagonist), respectively.^[11] Further molecular testing of all TNBCs will reduce the wastage of time and resources and improve the survival outcome of patients.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Jude Ogechukwu Okoye

Department of Medical Laboratory Science, Faculty of Health Sciences and Technology, Nnamdi Azikiwe University, Awka, Anambra State, Nigeria

Address for correspondence: Dr. Jude Ogechukwu Okoye, Department of Medical Laboratory Science, Faculty of Health Sciences and Technology, Nnewi Campus, Nnamdi Azikiwe University, Awka, Anambra State, Nigeria.
E-mail: jog.okoye@unizik.edu.ng

REFERENCES

1. Sung H, DeSantis CE, Fedewa SA, Kantelhardt EJ, Jemal A. Breast cancer subtypes among Eastern-African-born black women and other black women in the United States. *Cancer* 2019;125:3401-11.
2. Marra A, Viale G, Curigliano G. Recent advances in triple negative breast cancer: The immunotherapy era. *BMC Med* 2019;17:90.
3. Galukande M, Wabinga H, Mirembe F, Karamagi C, Asea A. Molecular breast cancer subtypes prevalence in an indigenous Sub Saharan African population. *Pan Afr Med J* 2014;17:249.
4. Zheng Y, Walsh T, Gulsuner S, Casadei S, Lee MK, Ogundiran TO, *et al.* Inherited breast cancer in Nigerian women. *J Clin Oncol* 2018;36:2820-5.
5. Usman A, Iliyasu Y, Atanda AT. Molecular subtyping of carcinoma of the female breast in a tertiary teaching hospital in Northern Nigeria. *Ann*

- Trop Pathol 2019;10:20-6.
6. Imam BA, Okechi OO, Abdullahi K, Abubakar U, Musa AB, Okorie N. Immunohistochemical pattern of breast cancer in Maiduguri, Borno state. *J Cancer Tumor Int* 2017;5:1-10.
 7. Mandong BM, Emmanuel I, Vandi KB, Yakubu D. Triple negative breast cancer at the Jos Univeisty teaching hospital. *Ann Trop Pathol* 2017;8:20-4.
 8. Tanimowo MC, Abudu EM, Udo IU, Abdulareem FB. Histopathological and immunohistochemical characteristics of breast carcinomas in Uyo subtropical region of Africa. *Med J Zambia* 2019;46:100-8.
 9. Adisa CA, Eleweke N, Alfred AA, Campbell MJ, Sharma R, Nseyo O, *et al.* Biology of breast cancer in Nigerian women: A pilot study. *Ann Afr Med* 2012;11:169-75.
 10. Makanjuola SBL, Ayodele S, Javid FA, Obafunwa JO, Oludara MA, Popoola AO. Breast cancer receptor status assessment and clinicopathological association in Nigerian women: A retrospective analysis. *J Cancer Res Ther* 2014;2:122-7.
 11. Abramson VG, Lehmann BD, Ballinger TJ, Pietenpol JA. Subtyping of triple-negative breast cancer: Implications for therapy. *Cancer* 2015;121:8-16.
 12. Al Sayed AD, Elshenawy MA, Tulbah A, Al-Tweigeri T, Ghebeh H. Complete response of chemo-refractory metastatic metaplastic breast cancer to paclitaxel-immunotherapy combination. *Am J Case Rep* 2019;20:1630-5.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

Received on: 16-10-19 **Review completed on:** 20-11-19

Accepted on: 09-12-19 **Published on:** 08-08-20

Access this article online

Quick Response Code:



Website:

www.atpjournal.org

DOI:

10.4103/atp.atp_36_19

How to cite this article: Okoye JO. High prevalence of triple-negative breast cancer and poor survival outcome in Nigeria: A call for further molecular subtyping of triple-negative breast cancer. *Ann Trop Pathol* 2020;11:98-9.