Review of: "Effect of Ethnic Differences on Breast Cancer Presentation and Prognosis in Singapore"

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Potential competing interests: No potential competing interests to declare.

Thank you for providing me with the opportunity to review this paper. It provided interesting insights into populations that I am unfamiliar with.

The focus of the publication:

The focus of the manuscript centers around specific features of breast cancer presentation and prognosis compared among women representing three different ethnic groups in Singapore. The study was based on data gathered from anonymized breast tumors collected by the Singapore Cancer Registry and the Joint Breast Cancer Registry. Various interesting conclusions were drawn, notably the most important being that Malay women present at a younger age and exhibit poorer survival rates despite lower incidence rates. The author also explored the prevalence of TNBC across these groups, identifying variations in incidence and prognosis, with factors such as lifestyle, obesity, breastfeeding practices, socioeconomic status, and genetic predispositions considered as potential contributing factors. Due to the aggressiveness of TNBC, the findings highlight the need for population-specific interventions to increase awareness and earlier detection. Once these factors have been addressed, it will contribute to better outcomes for these women.

When considering the following questions:

*** Is this paper useful and relevant to the practice of clinical oncology?**

Yes. The information discussed in this publication is not only relevant to the healthcare system of Singapore but is also applicable to multiple other countries (such as South Africa, which has the second highest number of Indians in the world apart from mainland India), as the difficulties encountered in the diagnosis and follow-up of patients due to ethnic differences are a universal problem. We are all attempting to increase access to healthcare and genetic testing for deserving or appropriate patients while simultaneously increasing awareness of the benefits of being tested and knowing your risks.

* **Does the manuscript add to the available literature?**

Yes. The data highlights the differences in the perceptions of women representing each of these groups regarding their risk, preventative measures, detection methods, treatment options, and future prognosis once diagnosed.

*** Can parts of this paper be shortened?**

No. I recommend expanding on some of the lifestyle factors included. The author's findings can be substantiated a lot more by discussing and referencing more topic-specific literature, as the article covers a comprehensive number of important lifestyle factors involved in susceptibility.

Requested changes:

Entire document:

- The terminology used is no longer correct for genomic sequencing/screening. The word "mutation" needs to be changed to "pathogenic variant" according to Jarvik and Evans 2017 recommendations (DOI: 10.1038/gim.2016.139). The only term to include the word "mutation" should be "*BRCA1/2* mutation carrier".
- Replace the word "breast cancer" with the acronym BC throughout the text.
- Please write the gene names such as BRCA in *italics*.
- In various places, the word "ref" is indicated in brackets. I assume that previous reviewers have recommended an additional reference to substantiate the statements made; however, it has not been inserted yet. Example: bottom of page 2, first paragraph under Breast Cancer Incidence and Patient profile.
- The abbreviation SGH is used in the Methods section, without indicating what it stands for. Please correct.
- Numerical values under 10 should be written out, such as "3 – page 1", "2 – page 8", and "6".
- The referencing style needs some attention as in some cases the reference is missing ("ref"), with others written out (Ng et al., 2020), and others indicated by both round and square brackets (27) and [31].

Methods and Results sections:

The specific sample numbers for the various objectives investigated have not been clearly indicated/discussed. I found it confusing to determine which cohort the author was referring to when discussing his observations, as initially, a total number of 28,692 (collected from 1960 to 2019) patients was mentioned, followed by 289 patients with TNBC. In the case of the data representing the older patients, molecular subgrouping was either unavailable at that stage or non-specific. To compare heterogeneous breast cancer characteristics between these three groups, the actual classification needs to be accurate and trustworthy for the conclusions to be trusted. It would, therefore, be beneficial to mention the size of each cohort investigated for that specific parameter. Even in the absence of gene expression profiling, the immunohistochemistry panel of markers used for distinguishing between the five basic molecular subtypes should be included, as it is needed to determine the prognosis and type of treatment. The panel might not have included all the markers currently used (such as ER, PR, HER2, Ki-67, epidermal growth factor receptor (EGFR), and basal cytokeratins such as CK14 and CK5/6 etc.).

Please remove the "italics" in the following sentence on page 2:.. "Reasons for these ethnic differences in the incidence of breast cancer and, specifically, TNBC *are multifactorial and are caused due to a combination of biological and* non-biological factors. Overall……"