CONFERENCE ABSTRACT
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Inherited mutations in \textit{BRCA1} and \textit{BRCA2} in an unselected multi-ethnic cohort of Asian breast cancer patients and healthy controls from Malaysia

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Abstract: Background: To ascertain the contribution of germline alterations in \textit{BRCA1} and \textit{BRCA2} in an unselected cohort of Asian breast cancer patients and healthy controls. Methods: Two thousand five hundred and ninety-two invasive breast cancer patients and 2,815 healthy controls were included into our study. Amplicon-based targeted sequencing of exonic and proximal splice site junction regions of 31 known and probable breast cancer susceptibility genes were performed on Fluidigm Access Array system, with sequencing conducted on Illumina HiSeq2500 platform. Variant calling was performed as per GATK recommended best practices and were validated with Sanger sequencing. Results: Comparable \textit{BRCA1} and \textit{BRCA2} carrier rates were observed among breast cancer patients with frequencies of 57 (2.2%) and 66 (2.5%), respectively. Both \textit{BRCA1} and \textit{BRCA2} conferred increased breast cancer risk with odds ratio 13.0 (95% Cl: 5.2–32.4) and 12.5 (95% Cl: 5.4–28.9), respectively. \textit{BRCA1/2} carriers were more likely to be younger, have family history of breast and/or ovarian cancer, have higher grade tumours and for \textit{BRCA1} carriers, they were more likely to have hormone receptor negative breast cancers. Notably, 45.7% of breast cancer patients fulfilled the NCCN guidelines for recommendation for genetic counselling and genetic testing, and of these, 80% of \textit{BRCA1/2} carriers fulfilled the NCCN guidelines. Conclusion: Taken together, our results show that approximately 5% of unselected Asian breast cancer patients are carriers of germline \textit{BRCA1/2} mutations. Our study could provide a framework for genetic breast cancer risk assessment and calibration, and enable risk assessment and management of Asian breast cancer patients attending clinical genetic services.

Keywords: breast cancer; germline \textit{BRCA1/2}; mutation


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