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Breast Cancer Awareness Month: the public health case for BRCA testing

Breast cancer is considered a public health priority because of its prevalence. Identifying, preventing, and treating hereditary cancer is crucial for public health. Hereditary cancer occurs when an individual inherits a mutation in one of the many cancer-causing genes

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Angelina Jolie's case is one of the most recognised in genomic medicine. With a strong family history of cancer, she was found to carry a mutation in the BRCA1, significantly elevating her risk for Hereditary Breast and Ovarian Cancer (HBOC). In 2013, she opted for a preventive mastectomy and in 2015 for a salpingo-oophorectomy to reduce her risk of cancer.

Early detection allows patients and at-risk family members to access preventive or early detection methods, potentially lowering their risk to that of the general population. Individuals at risk also have options like regular mammograms, chemoprevention, lifestyle changes, and contraceptive and reproductive choices, including prenatal or pre-implantation genetic diagnosis.

Hereditary cancer occurs when an individual inherits a mutation in one of the many cancer-causing genes. These germline mutations increase susceptibility to many cancers of multiple organs. Among more than 300 different inherited cancer syndromes, HBOC is one of the most studied. Most HBOC cases are due to germline mutations in the BRCA1 and the BRCA2 genes (or just BRCA), but several other genes also contribute to the risk.

Inherited mutations cause individuals to be one step closer to cancer. Unlike sporadic cancers, which are responsible for 90% of cases with an average onset age of 60 years, HBOC cancers are relatively rare (accounting for less than 10% of cancer cases) but tend to develop earlier in life. This said, with one in nine Indians at risk of developing cancer in their lifetime and a population of 1.4 billion, a large number of individuals will carry hereditary mutations that increase their predisposition to cancer. Thus, hereditary cancers are an important public health problem in India.

Importance of BRCA testing

Women with BRCA mutations face a 69-72% risk of breast cancer and a 17-44% risk of ovarian cancer by age 80, compared to the general population's lifetime risks of 12% for breast cancer and 1% for ovarian cancer. Preventive interventions such as a prophylactic mastectomy can reduce breast cancer incidence by 90-100% and breast cancer-related deaths by 81-100%. Similarly, prophylactic oophorectomy reduces ovarian cancer risk by 69-100%.

Importantly, researchers have associated germline BRCA mutations with the risk of seven types of cancer – breast, ovarian, prostate, pancreatic, biliary tract, esophageal, and gastric cancers. Their research thus indicates a broader clinical relevance for BRCA genetic testing.

In India, breast cancer incidence is on the rise. It accounts for 27% of all cancer cases, making it the most prevalent cancer among women. BRCA pathogenic variants also cause about 26% of breast cancers and 21-25% of ovarian cancers in the country. In populations with a family history of cancer, BRCA mutations are found in 55% of ovarian cancer cases and 45-65% of hereditary breast cancer cases. Thus, the greatest potential of BRCA testing lies in cancer prevention in addition to its current common use for therapy of advanced cancers.

Thus the key question for equitable breast cancer care is: why wait for cancer to develop when BRCA carriers and their at-risk family members can be identified early to prevent it?

Inequities in BRCA testing

Traditionally, BRCA testing has been offered to individuals based on their family history of cancer. This method misses about half of all actionable cases. Identifying someone with a hereditary mutation only after they develop cancer is a failure of cancer prevention. Following these traditional guidelines perpetuates health inequalities as fewer women at risk of breast cancer are identified.

With advances in next-generation DNA sequencing, genomics, and bioinformatics, large-scale population testing is now technologically feasible and has been implemented in some countries. Transitioning to population testing in India could be a complex but progressive step in preventing breast cancer, increasing BRCA testing uptake, and addressing the limitations of traditional testing models.

Two critical enablers for this approach are public education on the benefits of hereditary cancer risk and the cost of BRCA testing. The latter ranges from ₹15,000 to ₹30,000 in India. This price point may be affordable for higher-income individuals but isn't so for population-level screening. In high-income countries, population-based BRCA screening has proved useful in reducing breast and ovarian cancer incidence and is also considered cost-effective. But in India, despite the decreasing cost of DNA sequencing, the price of BRCA testing remains a barrier, which will exacerbate health inequities in breast cancer care. For any intervention to be sustainable, it must be both cost-effective and affordable.

Breast cancer is considered a public health priority because of its prevalence but also thanks to the availability of effective clinical interventions. Identifying, preventing, and treating hereditary cancer is crucial for public health. Still, the decisions following a positive BRCA result come with significant financial and emotional costs, rendering proper genetic counselling and consultation with a clinical geneticist essential.

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