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GENETIC TESTING FOR BRCA MUTATION IN BREAST CANCER PATIENTS – OUR INSTITUTION EXPERIENCE

Oncology

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ABSTRACT

Breast cancer is the commonest malignancy among women globally. Genetic predisposition for familial early-onset breast cancer accounts for approximately 5–10% of all breast cancers and 7–10% of all ovarian cancers. Though genetic counseling for BRCA mutation testing is common in most of the developed countries, India still faces several challenges in mainstreaming the same .Aim of this study is to identify the proportion of patients at risk for hereditary breast cancer in our cohort and to identify BRCA gene mutation positivity rate with prevailing genetic testing practices. A retrospective analysis was done on patients who have undergone surgical treatment of carcinoma breast , either mastectomy or conservation surgery from January 2017- December 2022 in our institute. Patients who were candidates for genetic testing and counselling as per NCCN guidelines were identified and followed up with regards to genetic counselling and testing for BRCA 1 and 2 genes. Patients who underwent risk reduction surgeries were noted. 216(n) patients were included in the study. 97 patients (44%) among them were identified to have met the criteria for genetic testing as per NCCN guidelines. Of these patients , 26.8% have undergone genetic testing for BRCA 1 and 2 . 12 patients (46.1%) were tested positive for BRCA 1 or 2. 8 of those 12 patients (60%) were less than 45 years of age. Out of these 12 patients , 4 (33.3%) have undergone risk reduction surgeries, while others have opted for observation or relapsed at a later date . Overall Hereditary breast cancers comprised 5 % of the study population. Hereditary breast cancers can be managed better with effective genetic counseling and testing practices , which are still not accessible to most population in developing countries like India. Awareness regarding genetic testing and prophylactic surgeries should be included in healthcare management of breast cancer.

KEYWORDS

Breast Cancer, BRCA mutation, genetic counseling, genetic testing

INTRODUCTION

Breast cancer is the commonest malignancy among women globally[1]. It has now surpassed lung cancer as the leading cause of global cancer incidence in 2020, with an estimated 2.3 million new cases, representing 11.7% of all cancer cases[1,2] . In India, the incidence has increased significantly, almost by 50%, between 1965 and 1985. As per the GLOBOCAN data 2020, in India, Breast Cancer accounted for 13.5% (178361) of all cancer cases and 10.6% (90408) of all deaths [1] . The high mortality rate in India can be attributed mainly to early age at presentation, diagnosis at an advanced stage, delayed access to effective breast cancer screening programs, and limited access to treatment[3].

Genetic predisposition for familial early-onset breast cancer accounts for approximately 5–10% of all breast cancers and 7–10% of all ovarian cancers. BReast CAncer (BRCA) susceptibility genes *BRCA1* and *BRCA2* are mainly associated with hereditary breast and ovarian cancer (HBOC) syndrome and present an estimated 45%–65% cumulative lifetime risk of developing breast cancer and an 11%–39% risk of ovarian cancer[4,5]. In India, the prevalence of *BRCA1/2* mutation varies from 2.9% to 38% among families with genetic predisposition toward hereditary cancers[6]. BRCA mutations are the predominant genetic mutation in hereditary breast cancer patients, although few other rare mutations can be seen , which includes TP53,PTEN etc. There is ample evidence to suggest knowledge of BRCA mutation in breast cancer patients have role in specific treatment recommendations , spreading across role of prophylactic risk reduction contralateral mastectomy , bilateral salpingo oophorectomy, screening of family members at risk of harboring the mutation, use of targeted therapy like Poly (ADP-Ribose) Polymerase (PARP) inhibitors. With HBOC being linked to early-onset breast cancer and increased susceptibility to other cancers, early screening for BRCA mutations has become a pressing need. Though genetic counseling for *BRCA* mutation testing is common in most of the developed countries, India still faces several challenges in mainstreaming the same like lack of enough qualified genetic counselors , economic burden of genetic testing which ranges on an average INR 20000 – 30000 across various platforms, social stigma associated with cancer diagnosis and therapy, anxiety etc.

Aims of this study are

1) To identify the proportion of patients at risk for hereditary breast cancer in our cohort
2) To identify BRCA gene mutation positivity rate with prevailing genetic testing practices.
3) To identify the proportion of BRCA positive patients that have undergone risk reduction practices.

MATERIALS AND METHODS:

A retrospective analysis was done on patients who have undergone surgical treatment of carcinoma breast , either by mastectomy or breast conservation surgery from January 2017- December 2022 in our institute, which is a tertiary care centre in Urban Bengaluru. Through analysis of clinical records and a combination of telephonic conversation and followup at the clinic, Demographics of patient including Age at diagnosis, socioeconomic status, details of surgery and adjuvant treatments, histopathology and receptor status have been collected. Patients who were candidates for genetic counselling and testing as per National Comprehensive Cancer Network (NCCN) guidelines (Age at diagnosis less than 45 yrs, family history of breast or ovarian cancer, Triple negative breast cancer less than 60 yrs age, second primary breast cancer) were isolated. Of these, patients who underwent Genetic testing for BRCA 1 and 2 using Next generation sequencing (NGS) were identified and then followed up the BRCA positive patients that have undergone Risk reduction surgeries or kept under observation. In the patients who were eligible for genetic testing, but did not undergo testing were evaluated for the reason which may be economic burden, social stigma, lack of genetic counseling facilities, or others.

RESULTS:

216(n) patients were included in the study with age ranging from 25-83

years and mean age of 51.4 years. 75 patients (34.7%) were less than 45 yrs of age at diagnosis. Most of them belonged to lower socioeconomic class as per modified kuppuswamy classification[11]. While 107 patients(49.5%) had carcinoma of right breast, 106(49%) patients had carcinoma of left breast and 3 patients (0.5%) had bilateral carcinoma breast. 148 patients (68.5%) underwent modified radical mastectomy and 68 patients (31.5%) had breast conservation surgery. Histopathology revealed Invasive Ductal carcinoma No Special Type in 203 patients , Invasive lobular carcinoma in 2 patients and 11 patients were noted to have special types of Invasive ductal carcinoma (mucinous, colloid, metaplastic). Out of 167 patients that had IHC testing done, 81 patients (48.5%) are Luminal A and B, 21 patients (12.5%) are Her 2 positive , 23 patients (13.7%) are Triple positive and 42 patients (25.7%) are Triple negative. 35 patients (83.3%) with Triple negative Breast carcinoma are less than 60 yrs of age.

As per NCCN guidelines 97 patients (44%) among them were identified to have met the NCCN criteria for genetic testing . Of these patients , only 26 patients (26.8%) have undergone genetic testing for BRCA 1 and 2 . 12 patients (46.1%) were tested positive for BRCA 1 or 2. 8 of those 12 patients (60%) were less than 45 years of age. Out of these 12 patients , 4 (33.3%) have undergone risk reduction surgeries, while others have opted for observation 4 out of those 8 patients (50%) who opted for observation had recurrence or metastatic disease or second primary in the follow up period . 71 patients who were eligible for genetic testing , but did not undergo the same due to economic burden (20 patients) , social stigma (15 patients) and lack of information or genetic counseling facilities in 30 patients , miscellaneous reasons in 6 patients.

DISCUSSION:

Breast cancer in Indian population is noted to have early age at diagnosis and advanced presentation when compared to the western population. Mean age of our study population is 51 years, which corresponds to average age of breast cancer in Indian women. Around 34.7% of patients presented early and Heriditary breast cancers with BRCA positivity is relatively underestimated in Indian community due to various socioeconomic reasons and accessibility to genetic testing , which is evident from our study wherein only 26.8% of the eligible study population had undergone genetic testing. Overall, 5% of our study population were tested positive for BRCA 1/2 , but among patients who underwent genetic testing, 46% of them were tested positive for BRCA 1/2 , which is comparable to the prevalence of BRCA mutation in similar studies done on Indian population. In a study by Singh et al [9]., 1000 patients with breast and /or ovarian cancers were screened for mutations, 30% of the study population were mutation positive, of which 84.9 % were BRCA 1 or BRCA 2 positive. Overall prevalence of BRCA mutation in that study was 30 %. Vaidyanathan et al[6]., studied BRCA 1 and 2 mutation prevalence in 61 patients of breast cancer with positive family history and cumulative BRCA 1 and 2 detection rate was 28% in the study population.

60% of patients tested positive for BRCA in our study were less than 45 years, and 58.3% of patients had Triple negative breast cancers (TNBC) highlighting the fact that these cancers present at an early stage and are aggressive in nature. Lakhani et al.,[12] reported that 90% of BRCA1-related breast cancers were estrogen receptor-negative compared with 35% in controls. In the same study of Lakhani et al[12] 79% of BRCA1 tumors were progesterone receptor-negative, compared with only 41% in sporadic tumors. Only 26.8% of patients eligible for genetic testing , have undergone testing owing to several factors like financial constraints, fear of emotional burden on family, lack of information and genetic counseling facilities, and social stigma.

CONCLUSION:

Hereditary breast cancers can be managed better with effective genetic counseling and testing practices , which are still not accessible to most population in developing countries like India. Awareness regarding genetic testing and prophylactic surgeries should be included in healthcare management of breast cancer. It is the duty of primary physician to increase awareness and promote genetic testing in high risk individuals.

REFERENCES:

1. *Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71:209–249*
2. World Health Organization (WHO). Global Health Estimates 2020: Deaths by Cause, Age, Sex, by Country and by Region, 2000-2019. WHO; 2020. Accessed December 11, 2020. who.int/data/gho/data/themes/mortality-and-global-health-estimates/ghe-leading-causes-of-death
3. *National Cancer Registry Programme. Three Year Report of Population Based Cancer Registries 2012–2014. Bangalore: Indian Council of Medical Research (ICMR); 2016*
4. *Mehrotra R, Yadav K. Breast cancer in India: Present scenario and the challenges ahead. World J Clin Oncol. 2022 Mar 24;13(3):209-218. doi: 10.5306/wjco.v13.i3.209. PMID: 35433294; PMCID: PMC8966510.*
5. *Verma A, Nag S, Hasan Q, Selvakumar VP. Mainstreaming genetic counseling for BRCA testing into oncology clinics – Indian perspective. Indian J Cancer 2019;56, Suppl S1:38-47*
6. *Vaidyanathan, K., Lakhotia, S., Ravishankar, H. M., Tabassum, U., Mukherjee, G., & Somasundaram, K. (2009). BRCA1 and BRCA2 germline mutation analysis among Indian women from south India: identification of four novel mutations and high-frequency occurrence of 185delAG mutation. Journal of Biosciences, 34(3), 415–422. doi:10.1007/s12038-009-0048-9*
7. *Saxena, S., Szabo, C.I., Chopin, S., Barjhoux, L., Sinilnikova, O., Lenoir, G., Goldgar, D.E. and Bhatanager, D. (2002), BRCA1 and BRCA2 in Indian breast cancer patients. Hum. Mutat., 20: 473-474. https://doi.org/10.1002/humu.9082*
8. *Selvakumar VP, Garg S, Kaur J, Kadayaprath G, Rohatgi N, Walia M, et al Genetic testing for hereditary breast and ovarian cancer in Indian population: A single institutional study J Clin Oncol. 2019;37(Suppl 15):e13153*
9. *Singh J, Thota N, Singh S, Padhi S, Mohan P, Deshwal S, et al Screening of over 1000 Indian patients with breast and/or ovarian cancer with a multi-gene panel: Prevalence of BRCA1/2 and non-BRCA mutations Breast Cancer Res Treat. 2018;170:189–96*
10. *Chedda P, Pande S, Dama T, Vinarkar S, Chanekar M, Limaye S, et al Spectrum of germline BRCA mutations in hereditary breast and ovarian cancer syndrome in Indian population: A central reference laboratory experience Cancer Res Stat Treat. 2020;3:32–41*
11. Wani RT. Socioeconomic status scales-modified Kuppuswamy and Udai Pareekh's scale updated for 2019. J Family Med Prim Care. 2019 Jun;8(6):1846-1849. doi: 10.4103/jfmpc.jfmpc_288_19. PMID: 31334143; PMCID: PMC6618222.
12. Lakhani SR, Van De Vijver MJ, Jacquemier J, Anderson TJ, Osin PP, McGuffog L, Easton DF. The pathology of familial breast cancer: predictive value of immunohistochemical markers estrogen receptor, progesterone receptor, HER-2, and p53 in patients with mutations in BRCA1 and BRCA2. J Clin Oncol. 2002 May 1;20(9):2310-8. doi: 10.1200/JCO.2002.09.023. PMID: 11981002.
13. *Akram Hussain SM. Molecular-based screening and therapeutics of breast and ovarian cancer in low-and middle-income countries Cancer Res Stat Treat. 2020;3:81–4*
14. *Malvia S, Bagadi SA, Dubey US, Saxena S. Epidemiology of breast cancer in Indian women Asia Pac J Clin Oncol. 2017;13:289–95*