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Research Article

GSTM1 GENE POLYMORPHISMS AND RISK OF BREAST CANCER IN J&K STATE

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Abstract- Homozygous deletion of *GSTM1* gene affects carcinogenic detoxification and promotes tumorogenesis in breast tissue. The present study was aimed to evaluate the frequency of GSTM1 genotypes/alleles and its association in risk of breast cancer in North Indian population of Jammu (Jammu and Kashmir). A total of 60 confirmed breast cancer patients and 90 healthy unrelated controls were enrolled in this study. Genotyping analysis was performed by Polymerase Chain Reaction (PCR) based methods and odds ratios (ORs) were calculated to know the strength of association. The frequencies of null and positive GSTM1 alleles/genotypes were 0.12/11.67% and 0.88/88.33% in patients whereas in controls it was 0.18/17.78% and 0.82/82.22% respectively. We did not found the association of *GSTM1* null genotype towards risk of breast cancer [OR=0.61, 95% CI (0.23-1.59), p=0.6]. The present study is in support of lack of association of null *GSTM1* genotype and risk of breast cancer in population of Jammu.

Keywords- *GSTM1*, null, breast cancer, Jammu.

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Introduction

The glutathione S-transferases (GSTs) are a family of enzymes which are engrossed in biotransformation phase II and detoxify a vast majority of chemicals, environmental contaminants and carcinogenic agents in human body. Functional implication of GSTs involves synthesis of less carcinogenic and more readily excreted glutathione conjugates from reactive glutathione (a tri-peptide consisting of amino acids: glycine, glutamic acid and cysteine) and electrophilic compounds by the process of conjugation [1-3]. Genetic polymorphisms in GST enzymes can modify their detoxification and anti-carcinogenic functioning and increase the risk of cancer in an individual [4-7].

GSTM1 is one of the key enzymes of GST μ class gene family which is involved in detoxification of aromatic hydrocarbon epoxides and products of oxidative stress [3,8,9]. Human *GSTM1* gene is located on chromosome 1p13.3. The homozygous deletion of both *GSTM1* alleles is responsible for complete lack of GSTM1 enzyme and it has been formulated that nearly 20%-50% of individuals carry null genotype [8,10,11]. The null *GSTM1* genotype is concerned with the formation of DNA adducts, tumorigenesis and inclination of breast cancer [12-17]. Therefore, the present study was undertaken to uncover the frequency of *GSTM1* genotypes/ alleles and their role in risk of breast cancer in North Indian population of Jammu region of the Jammu and Kashmir state.

Material and Methods

Study population: The present research was carried on 60 confirmed patients of Breast Cancer and 90 healthy unrelated females ass a control group. The subjects with benign breast disease were excluded. The patient samples were collected from Department of Pathology and Oncology, Government Medical College (GMC), Jammu. The control sampling was done from females attending OPD, GMC, Jammu with minor ailments without having any history of breast cancer and breast related complications or other chronic ailments.

Ethical authorization: The present study design was approved by Animal and Human Experimentation Ethical Committee (AHEEC), University of Jammu. Besides, an informed written consent was obtained from each study participant before enrolment in the study.

DNA extraction and Genotyping: Five millilitres of peripheral blood was collected in EDTA vacutainers from each study individual and genomic DNA was extracted using Phenol- Chloroform method with slight modifications [18]. The GST genotypes were determined using a polymerase chain reaction (PCR)-based method as described earlier

Statistical analysis: The observed Genotypes were subjected for the Hardy Weinberg Equilibrium (HWE) calculation by using chi square test. The distribution of genotype frequencies in cases and controls were compared by using 2x2 chi-square contingency tables and extent of association of *GSTM1* polymorphism with breast cancer susceptibility was determined by Odd's ratio (OR) at 95% confidence interval (CI). A p-value <0.05 is considered as statistical significant.

Results

The genotypic distribution of the *GSTM1* gene polymorphism for breast cancer patients and the control group is shown in [Fig-1]. The frequency of null *GSTM1* genotype was lower in both groups in judgement to present *GSTM1* genotype. Out of 60 patients, only 7 patients were having complete absence of *GSTM1* gene. In control group, there were 16 individuals with null genotype. No significant difference was recorded between observed and expected genotype combinations in both study groups (Chi-square=1.04, p=0.3). In cases the frequency of null

allele was 0.12 and present allele was 0.88 whereas in controls it was 0.18 and 0.82 for null and present allele respectively. Overall, frequency of null allele was 0.15 and present allele was 0.85 in the population of Jammu (data not shown in figure). The *GSTM1* genotypes were accordance with HWE. OR analysis did not reveal any significant association of null genotype towards risk of breast cancer in the study population [Table-1].

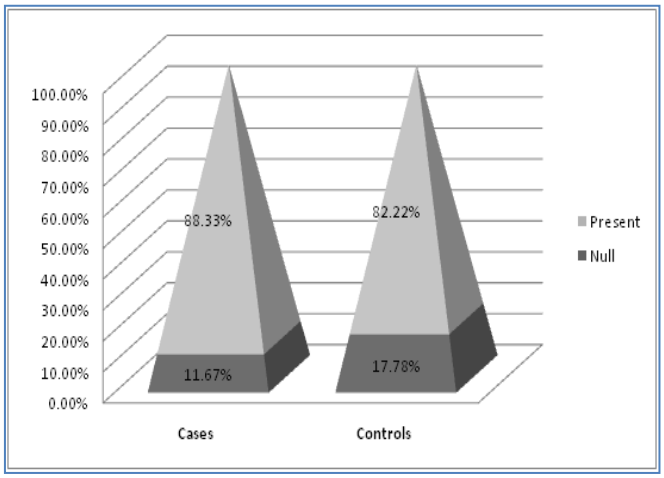

Fig-1 Graph showing frequency of GSTM1 genotypes in the study participants

Table-1 *Association of GSTM1 polymorphism with Breast Cancer*

Study Groups	GSTM1 null genotypes		GSTM1 present genotypes		OR 95% CI	p-value
	Observed	Expected	Observed	Expected		
Cases (n=60)	7	9.20	53	50.80	0.61 [0.23-1.59]	0.6
Controls (n=90)	16	13.80	74	76.20		
Chi square=1.04, df=1, p=0.3						

Discussion

The *GSTM1* locus, a member of the μ class GST gene family have been shown to be polymorphic in an ethnicity-dependent manner and confers risk for many cancers, including breast cancer [9,19-23]. The present study reported a higher frequency for present GSTM1 allele than null allele (0.85 vs 0.18) in North Indian population of Jammu region which was comparable to other Indian populations [9,24-26] and South Africans [27] but lower as reported in other populations worldwide. A comparison on the frequency of null *GSTM1* allele between present study and other geographically assorted human populations is presented in [Table-2].

Table-2 *GST M1 null allele frequency of geographically assorted human populations (Modified Source: Kasthurinaidu et al., 2015).*

Geographic area	Frequency of Null GSTM1 allele	Reference
Singapore	0.653	Lee et al., 1995
Maharashtra	**0.299**	Buch et al., 2001
Egypt	0.555	Hamdy et al., 2003
South Africa	**0.211**	Adams et al., 2003
Karnataka	**0.258**	Naveen et al., 2004
Tamil Nadu	**0.235**	Naveen et al., 2004
West Bengal	**0.270**	Sikdar et al., 2005
Pakistan	0.450	Shaikh et al., 2010
Western Europe	0.515	Kurose et al., 2012
Northern Europe	0.533	Kurose et al., 2012
Japan	0.501	Kurose et al., 2012
China	0.535	Kurose et al., 2012
Uttar Pradesh	**0.327**	Ghosh et al., 2012
Gujarat	**0.2**	Kasthurinaidu et al., 2015
Jammu	**0.18**	Present Study

*Bold value indicates comparable frequencies.

We did not find a significant association of null *GSTM1* genotype with risk of breast cancer ion our population [OR=0.61, 95% CI (0.23-1.59), p=0.6]. Linhares et al. [3] also reported no statistically significant association of the null *GSTM1* genotype and breast cancer outcome [OR=0.74, 95% CI (0.45-1.20), p=0.277]. Likewise our results, Van Emburgh and researchers [28] were too in favour of lack of considerable association of *GSTM1* null polymorphism towards risk of breast cancer in Caucasians and African-American population affinities [28]. Similarly, a previous study on South Indian population showed that *GSTM1* homozygous null genotype was not involved in breast cancer risk [14]. On contrary, another two separate reports on North Indian and Northeast Indian population respectively depicted a positive association of *GSTM1* gene deletion and susceptibility of breast cancer [29,30]. It was reported that in Mexican population there was an increased breast cancer risk associated with the *GSTM1* gene deletion polymorphism [23,31]. Recently, in a meta-analysis study it was formulated that the significant increase in risk of breast cancer for Asians was found in carriers of *GSTM1* null genotype [32]. In contrast, possible reasons for an absence of an association in the present study may be a small sample space requiring a larger sample size to reach statistical significance level. The true effects of the variant may be masked by, or present only in combination with other gene variants. The lack of statistically significant association of null genotype of *GSTM1* gene with breast cancer in our study was consistent with several other studies [2, 9, 33-35]. Conclusion: The present study depicted lack of association of null *GSTM1* genotype and risk of breast cancer in population of Jammu (J&K).

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Authors Contributions:

Ravi Sharma and Jyotdeep Kour: Blood sampling and laboratory work.
Tariq Azad: Clinical diagnosis.
Rakesh Kumar Panjaliya and Parvinder Kumar: Manuscript drafting

Abbreviations: HWE: Hardy Weinberg Equilibrium, OR= Odd's ratio, CI= Class interval

Ethical approval: The present study design was approved by Animal and Human Experimentation Ethical Committee (AHEEC), University of Jammu.

Conflict of Interest: None declared

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