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RESEARCH ARTICLE

ASSOCIATION ANALYSIS OF MULTIDRUG RESISTANCE GENE ABCB1 IN BREAST CANCER PATIENTS OF PUNJAB

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Abstract

Aims: This study aims to determine the frequency distribution of genetic polymorphisms of ABCB1 (rs1128503 and rs1045642) gene in breast cancer patients and the healthy controls and the association of these genotypes, if any, with susceptibility to breast cancer.

Methods: The present case control study was conducted on the population of Punjab (North India). The cases included 300 breast cancer confirmed patients and the control group included (n=300) healthy female volunteers from general public after taking clearance from Institutional Ethical Committee (IEC) of Punjabi University, Patiala. Genomic DNA was isolated from whole blood collected in EDTA coated tubes by employing the standard inorganic (Salting Out) extraction method (Miller et al, 1988). PCR-RFLP technique was used for the amplification of the target region of the gene by using a single pair of primers. Genotyping of the PCR products and digested fragments obtained after RFLP was done by agarose gel electrophoresis. For PCR products, 1% gel was made and for the restriction digestion products, 3.5% gel was made. After separation, the bands representing products/ fragments were visualized under UV light for genotyping.

Results: The frequency distribution of CC, CT, and TT genotypes of rs1045642 (C3435T) among breast cancer patients were 34%, 46.67% and 19.33% and among controls were 38.67%, 45.67% and 15.67% respectively. The frequencies of genotypes CC, CT and TT of rs1128503 (C1236T) among cases were 28%, 45.67% and 26.33% and among controls were 28.33%, 42% and 29.67%, respectively. The frequency of the wild allele (C) and mutant allele (T) of rs1045642 among cases was 57.33% and 42.67% and among controls, 61.5% and 38.5% respectively. The frequencies of the wild allele (CC) and mutant allele (T) of rs1128503 among cases were 50.83% and 49.17% and among controls were 49.33% and 50.67%, respectively.For association analysis, the contingent chi square test did not show any statistically significant differences between cases and controls for rs1045642 and rs1128503 gene polymorphisms neither at genotypic level and nor at allelic level.

Conclusion: We found no evidence that reveals any statistically significant association of C3435T and C1236T polymorphisms with susceptibility to breast cancer in Punjab, India.

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Introduction:-

Breast cancer develops when breast cells grow uncontrollably, often resulting in a tumor. This tumor can sometimes be detected through an x-ray or as a palpable lump. If the tumor's cells spread to nearby tissues or distant parts of the body, it is classified as malignant. Although breast cancer predominantly affects women, men are also susceptible to the disease (American Cancer Society, 2017).Breast cancer is the most common female cancer worldwide representing nearly a quarter (25%) of all cancers with an estimated 1.7 million new cases (25% of all cancers in women) and 0.5 million cancer deaths (15% of all cancer deaths in women) in 2012. According to Globocan (WHO), for the year 2012, India recorded 70,218 deaths due to breast cancer, more than any other country in the world. Incidence of breast cancer is predicted to increase to 85 per 100,000 women by 2021 (Akram et al., 2017). There are five main intrinsic molecular subtypes of breast cancer: Luminal A, Luminal B, HER2-positive (also known as ERBB2-positive), basal-like, and normal-like. Both Luminal A and Luminal B cancers are estrogen receptor (ER) positive, though Luminal B has a worse prognosis. Basal-like breast cancer is particularly aggressive, as it includes tumors that do not express ER, progesterone receptor (PR), or HER2, earning it the term "triple-negative."Treatment strategies for breast cancer depend predominantly on these molecular subtypes with respect to the hormone receptor status. Chemotherapy is considered the most effective approach for treating metastatic tumors. However, a major challenge in its success is the development of multidrug resistance (MDR), a phenomenon where cancer cells become resistant to multiple drugs simultaneously. This resistance extends to various drugs that differ in both structure and function, posing a significant barrier to effective treatment. It enables a cell to withstand the effects of toxic molecules that vary in size, structure and site of action in the cell. Clinical multidrug resistance is caused by a group of integral membrane proteins called as ATP binding cassette (ABC) transporters. ABC transporters represent one of the largest families of transporter proteins. In human alone, there are 48 ABC transporters and they are exclusively exporters. They are predominantly involved in the efflux of endogenous materials such as metabolic products, vitamins, lipids and sterols, as well as exogenous drugs and toxins from cytoplasm into extracellular space or intracellular compartments such as endoplasmic reticulum and peroxisomes. Therefore, human ABC transporters play essential roles in a majority of physiological, pathological, and pharmacological processes including detoxification (ABCB1/MDR1, ABCC1/MRP1), absorption and secretion processes (MDRs, MRPs), lipid metabolism (ABCA1, MDR3, ABCGs), antigen presentation (ABCB2/TAP1 and ABCB3/TAP2), and to protect susceptible organs and tissues such as the brain, testis, fetus, and inner ear from toxic xenobiotics and oxidative stress (ABCCs/MRPs) (Mamo et al., 2017). ABC transporters are highly expressed in the gut, liver and kidneys where they restrict the bioavailability of administered drugs. Even though most of the human ABC transporters play a role in the export of physiological substrates and xenobiotics (amino acids, peptides, lipids, inorganic ions…), one of them play critical clinical roles in chemotherapeutic drug resistance. This is P-glycoprotein (ABCB1/Pgp) and is a full transporter. Typically, full transporters, such as ABCB1, comprise two homologous halves and are characterized by two membrane-spanning domains (MSDs) and two nucleotide binding domains (NBDs) with an arrangement of MSD1-NBD1MSD2-NBD2 as given in figure 1.

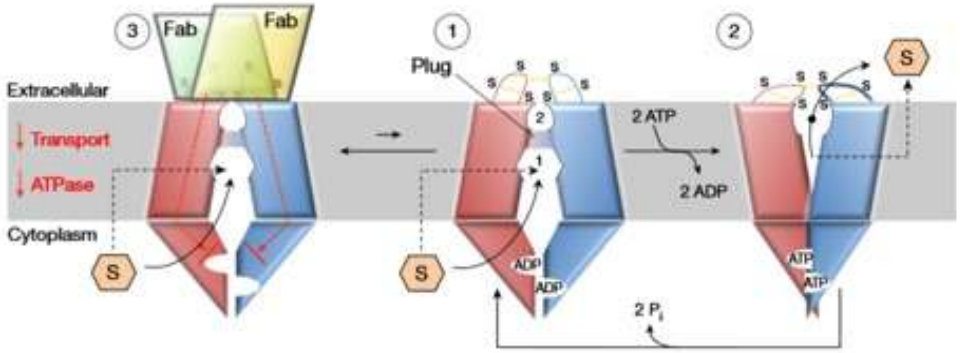

Figure 1:- Mechanism of drugs efflux proposed for ABCB1 and ABCG2 genes (Taylor et al., 2017).

When highly expressed in the plasma membrane of tumor cells, these transporters can lead to chemotherapy failure by shielding cancer cells from cytotoxic drugs. The ABCB1 gene, located on chromosome 7q21.12, spans a genomic region of 209.6 kb and consists of 28 exons and 28 introns. It produces a 4,872 bp-long mRNA, which encodes P-glycoprotein (P-gp), a polypeptide chain composed of 1,280 amino acids with a molecular weight of 170 kDa, spanning approximately 100 kb. Also referred to as the multidrug resistance gene (MDR1) or cluster of

differentiation 243 (CD243), ABCB1 has been linked in breast cancer research to both expression levels and genetic variations that influence therapeutic outcomes. Numerous studies have investigated the association of ABCB1 polymorphisms with chemotherapy-induced toxicity and overall survival (OS) in breast cancer patients.(Tulsyan et al., 2016). But to date, no study has been conducted in Punjab examining this topic. Therefore, the proposed research aims to investigate the association between breast cancer risk and polymorphisms in ABCB1 (rs1045642 and rs1128503).

Material and Methods:-

A case-control study comprising of 300 breast cancer patients and 300 controls were conducted after taking clearance from Institutional Ethical Committee (IEC) of Punjabi University, Patiala. A complete history of the breast cancer patients including demographic profile, clinical and pathological characteristics were recorded from hospital records. **Inclusion criteria:** a) Women diagnosed with breast cancer were included as cases. b) Age-matched healthy women without a family history of breast cancer were recruited as controls. **Exclusion criteria:** Men were excluded from the study due to the rarity of breast cancer in males. Genomic DNA was isolated from blood samples using the salting-out technique described by Miller et al. (1998). The quality and quantity of the DNA were evaluated by measuring absorbance at 260 nm and 280 nm with a spectrophotometer. Genotyping of the selected ABCB1 SNPs was performed using the PCR-RFLP method.

Table 1:- Primer sequences and genotyping methods employed for the analysis of ABCB1 polymorphisms.

SNPs & Method of Genotyping	Primer sequences 5'…..3'	Amplicon size (bp)& Restriction Enzyme	Thermocycler conditions	Genotypes
ABCB1 rs1045642 C3435T (PCR-RFLP)	Forward Primer: TGTTTTCAGCTGCTTGATGG Reverse Primer: AAGGCATGTATGTTGGCCTC	**197** **Sau3AI**	Initial Denaturation: 94 °C for 2 minutes Denaturation (30 cycles): 94 °C for 30 seconds Annealing (30 cycles): 60 °C for 30 seconds Extension (30 cycles): 72 °C for 30 seconds Final Extension: 72 °C for 7 minutes	CC– 158, 39 CT – 197, 158, 39 TT – 197
ABCB1 rs1128503 C1236T (PCR-RFLP)	Forward Primer: TATCCTGTGTCTGTGAATTGCC Reverse Primer: CCTGACTCACCACACCAATG	**370** **HaeIII**	Initial Denaturation: 94 °C for 2 minutes Denaturation (30 cycles): 94 °C for 30 seconds Annealing (30 cycles): 60 °C for 30 seconds Extension (30 cycles): 72 °C for 30 seconds Final Extension: 72 °C for 7 minutes	CC – 273, 62, 35 CT – 273, 97, 62, 35 TT –273, 97

The PCR reaction mixture consisted of 10 µl of Hot Start Taq 2X master mix, 1 µl of each primer for PCR, 2 µl of DNA sample, and distilled water (TDW) to bring the total volume to 20 µl.The thermocycling conditions for each SNP are provided in Table 1. Restriction enzyme digestion was performed following the instructions provided by the manufacturer.Agarose gel electrophoresis was used to separate the digested products, which were then directly observed under UV light. Statistical analysis was conducted using the MedCalc and SNPStat software for Windows. The relationship between exposure (risk factors) and breast cancer was evaluated by calculating the odds ratio (OR) as outlined by Andrade (2015). A 95% confidence interval (CI) was used to assess the precision of the OR, and statistical significance was determined at a p-value < 0.05. Haplotype frequencies were estimated using the SNPStats software accessible at https://www.snpstats.net/start.html.

Results and Discussion:-

Study Population Distribution:

The study comprised 300 women with clinically confirmed breast cancer and an equal number of healthy female controls matched for age and gender.According to our earlier findings (Kaur et al., 2024), district Ludhiana had the highest incidence (32%) of breast cancer cases, while district Mansa and Amritsar reported the lowest (0.7%).

Evaluation of genetic data:

The detailed genotypic and allelic frequencies of both the SNPs of ABCB1gene (rs1128503, and rs1045642)along with a comparison between breast cancer cases and healthy subjectsare provided in Table 2, 3 and 4.

Table 2:- Distribution of Genotype and Allele Frequencies of rs1128503 and rs1045642of ABCB1 gene polymorphisms.

SNP	Genotype	Genotype Frequency		P-Value	Allele Frequency		P-Value
		Cases (N=300) n (%)	Controls (N=300) n (%)		Cases n (%)	Controls n (%)	
ABCB1 (rs1128503)	CC	84 (28)	85 (28.33)	0.589 (1.06)	C-305 (50.83)	C-296 (49.33)	0.60 (0.27)
	CT	137 (45.67)	126 (42)				
	TT	79 (26.33)	89 (29.67)		T-295 (49.17)	T-304 (50.67)	
ABCB1 (rs1045642)	CC	102 (34)	116 (38.67)	0.35 (2.08)	C-344 (57.33)	C-369 (61.5)	0.14 (2.16)
	CT	140 (46.67)	137 (45.67)				
	TT	58 (19.33)	47 (15.67)		T-256 (42.67)	T-231 (38.5)	

The distribution of the genotype and allele frequencies of the rs1045642 and rs1128503 did not show any significant difference.

Further, to assess the relationship between the chosen SNPs and breast cancer, a genetic model-based analysis was performed.

Table 3:- Comparison of ABCB1 gene polymorphism frequency between breast cancer cases and controls across various genetic models.

Models	Genotype	Cases N=300 n (%)	Controls N=300 n (%)	OR (95%CI)	P-value
rs1128503					
Co-dominant	CC	84 (28)	85 (28.33)	Referent	
	CT	137 (45.67)	126 (42)	1.10 (0.74-1.61)	0.63
	TT	79 (26.33)	89 (29.67)	0.90 (0.59-1.38)	0.62
Allele	C	305 (50.83)	296 (49.33)	0.94 (0.75-1.18)	0.60

	T	295 (49.17)	304 (50.67)		
Dominant	CC	84 (28)	85 (28.3)	1.02 (0.71-1.45)	0.93
	CT+TT	216 (72)	215 (71.67)		
Recessive	TT	79 (26.33)	89 (29.67)	0.85 (0.59-1.21)	0.36
	CC+CT	221 (73.67)	211 (70.33)		
rs1045642					
Co-dominant	CC	102 (34)	116 (38.67)	Referent	
	CT	140 (46.67)	137 (45.67)	1.16 (0.81-1.66)	0.41
	TT	58 (19.33)	47 (15.67)	1.40 (0.88-2.24)	0.16
Allele	C	344 (57.33)	369 (61.5)	1.19 (0.94-1.50)	0.14
	T	256 (42.67)	231 (38.5)		
Dominant	CC	102 (34)	116 (38.67)	1.22 (0.88-1.71)	0.23
	CT+TT	198 (66)	184 (61.33)		
Recessive	TT	58 (19.33)	47 (15.67)	1.29 (0.85-1.97)	0.24
	CT+CC	242 (80.67)	253 (84.33)		

The genetic model analysis of rs1045642 did not find any significant association between the rs1045642 variant of the ABCB1 gene and risk of breast cancer, which is consistent with the findings reported by Gupta et al., 2017, Tazzite et al., 2016 and Chaturvedi et al., 2013.Similarly, the analysis of different genetic models in this study did not show a significant link between the rs1128503 variant and breast cancer risk.

The studied SNPs were then analyzed to investigate their possible associations with several clinical factors, including cancer stage, tumor status, lymph node involvement, metastasis, tumor grade, and CA 15.3 levels.

Table 4:- Analysis of the relationship between SNPs in the ACB1 genes and clinico-pathological characteristics.

Clinical Variables / Genotypes	Stage		Tumor Status		Lymph Node Status		Metastasis		Grade		CA 15.3 U/ml	
	I,IIA, IIB	IIIA, IIIB, IIIC,IV	**T_1**	**T_2 – T_4**	**N_O**	N1 – N3	**M_O**	**M_1**	**Low (1)**	**High (2,3,4)**	**<30**	**≥30**
rs1045642												
CT+TT	132	66	29	169	76	122	183	15	16	182	155	12
CC	74	28	11	91	46	56	94	8	6	96	90	43
OR (95% CI)	1.32 (0.78-2.24)		0.70 (0.34-1.48)		1.32 (0.81-2.14)		0.96 (0.39-2.35)		0.71 (0.27-188)		0.16 (0.08-0.32)	
P-value	0.30		0.35		0.26		0.93		0.50		< **0.0001***	
rs1128503												
CT+TT	145	70	31	184	85	130	196	19	16	199	175	40
CC	61	24	9	76	37	48	81	4	6	79	70	15
OR (95% CI)	1.23 (0.71-2.13)		0.70 (0.32-1.55)		1.18 (0.71-1.96)		1.96 (0.65-5.95)		0.95 (0.36-2.50)		1.07 (0.55-2.05)	
P-value	0.47		0.38		0.53		0.23		0.91		0.85	

***p-value <0.05 (statistically significant)**

The findings for rs1045642 indicated a notable association between CA15.3 levels greater than 30 and both genotypes. In contrast, rs1128503 showed no significant association with the clinical variables assessed.

To further explore the association between ABCB1 gene genotypes and breast cancer subtypes, we classified the breast cancer cases into distinct subtypes and analyzed the frequency distribution of the mentioned SNPs across these groups. The resulting data are presented in the tables below (5-14):

Table 5:- Distribution of genotype and allele frequency ofpolymorphisms of ABCB1 gene among Ductal carcinoma in situ (DCIS) patients and controls.

SNP	Genotype	Genotype frequency		P-Value	Allele frequencies		P-Value
		Cases (N=22) n (%)	Controls (N=22) n (%)		Cases n (%)	Controls n (%)	
ABCB1 (rs1045642)	CC	08 (36)	05 (23)	0.43 (1.69)	C=27 (61) T=17 (39)	C=21 (48) T=23 (52)	0.20 (1.63)
	CT	11 (50)	11 (50)				
	TT	03 (14)	06 (27)				
ABCB1 (rs1128503)	CC	08 (36)	10 (45)	0.83 (0.38)	C=23 (52) T=21 (48)	C=26 (59) T=18 (41)	0.52 (0.41)
	CT	07 (32)	06 (27)				
	TT	07 (32)	06 (27)				

Table 6:- Distribution of genotype and allele frequencies of polymorphisms of ABCB1 gene among Invasive Ductal Carcinoma (IDC) patients and controls.

SNP	Genotype	Genotype frequency		P-Value	Allele frequencies		P-Value
		Cases (N=250) n (%)	Controls (N=250) n (%)		Cases n (%)	Controls n (%)	
ABCB1 (rs1045642)	CC	84 (34)	100 (40)	0.18 (3.41)	C=285 (57) T=215 (43)	C=314 (63) T=186 (37)	0.06 (3.49)
	CT	117 (47)	114 (46)				
	TT	49 (20)	36 (14)				
ABCB1 (rs1128503)	CC	68 (27)	69 (28)	0.59 (1.03)	C=252 (50) T=248 (50)	C=244 (49) T=256 (51)	0.61 (0.26)
	CT	116 (46)	106 (42)				
	TT	66 (26)	75 (30)				

Table 7:- Distribution of genotype and allele frequencies of polymorphism of ABCB1 gene among Invasive Lobular Carcinoma (ILC) patients and controls.

SNP	Genotype	Genotype frequency		P-Value	Allele frequencies		P-Value
		Cases (N=17) n (%)	Controls (N=17) n (%)		Cases n (%)	Controls n (%)	
ABCB1 (rs1045642)	CC	04 (24)	07 (41)	0.08 (5.11)	C=13 (38) T=21 (62)	C=22 (65) T=12 (35)	**0.03* (4.69)**
	CT	05 (29)	08 (47)				
	TT	08 (47)	02 (12)				
ABCB1 (rs1128503)	CC	05 (29)	01 (6)	0.19 (3.25)	C=18 (53) T=16 (47)	C=13 (38) T=21 (62)	0.22 (1.46)
	CT	08 (47)	11 (65)				
	TT	04 (24)	05 (29)				

Table 8:- Distribution of genotype and allele frequencies of polymorphismsof ABCB1 gene among Lobular carcinoma in situ (LCIS) patients and controls.

SNP	Genotype	Genotype frequency	P-Value	Allele frequencies	P-Value

		Cases (N=11) n (%)	Controls (N=11) n (%)		Cases n (%)	Controls n (%)	
ABCB1 (rs1045642)	CC	06 (55)	04 (36)	0.17 (3.51)	C=17 (77) T=5 (23)	C=12 (55) T=10 (45)	0.12 (2.47)
	CT	05 (45)	04 (36)				
	TT	00	03 (27)				
ABCB1 (rs1128503)	CC	04 (36)	5 (45)	0.34 (2.11)	C=14 (64) T=8 (36)	C=13 (59) T=9 (41)	0.76 (0.09)
	CT	06 (55)	03 (27)				
	TT	01 (9)	03 (27)				

Table 9:- Distribution of genotype and allelefrequencies of polymorphismsof ABCB1 gene among Familial breast cancer patients and controls.

SNP	Genotype	Genotype frequency		P-Value	Allele frequencies		P-Value
		Cases (N=19) n (%)	Controls (N=19) n (%)		Cases n (%)	Controls n (%)	
ABCB1 (rs1045642)	CC	10 (53)	10 (53)	0.88 (0.23)	C=26 (68) T=12 (32)	C=25 (66) T=13 (34)	0.81 (0.05)
	CT	06 (32)	05 (26)				
	TT	03 (16)	04 (21)				
ABCB1 (rs1128503)	CC	05 (26)	07 (37)	0.75 (0.55)	C=20 (53) T=18 (47)	C=22 (58) T=16 (42)	0.65 (0.21)
	CT	10 (53)	08 (42)				
	TT	04 (21)	04 (21)				

Table 10:- Distribution of genotypes and alleles of polymorphismsof ABCB1 gene among Sporadic Breast Cancer patients and controls.

SNP	Genotype	Genotype frequency		P-Value	Allele frequencies		P-Value
		Cases (N=281) n (%)	Controls (N=281) n (%)		Cases n (%)	Controls n (%)	
ABCB1 (rs1045642)	CC	92 (33)	106 (38)	0.23 (2.95)	C=316 (56) T=246 (44)	C=344 (61) T=218 (39)	0.09 (2.87)
	CT	132 (47)	132 (47)				
	TT	57 (20)	43 (15)				
ABCB1 (rs1128503)	CC	80 (28)	78 (28)	0.57 (1.12)	C=287 (51) T=275 (49)	C=274 (49) T=288 (51)	0.44 (0.60)
	CT	127 (45)	118 (42)				
	TT	74 (26)	85 (30)				

Table 11:- Distribution of genotype and allele frequencies of polymorphismsof ABCB1 gene among Luminal A breast cancer patients and controls.

SNP	Genotype	Genotype frequency		P-Value	Allele frequencies		P-Value
		Cases (N=73) n (%)	Controls (N=73) n (%)		Cases n (%)	Controls n (%)	
ABCB1 (rs1045642)	CC	29 (40)	29 (40)	0.36 (2.06)	C=87 (60) T=59 (40)	C=93 (67) T=53 (36)	0.47 (0.51)
	CT	29 (40)	35 (48)				
	TT	15 (21)	09 (12)				
ABCB1 (rs1128503)	CC	16 (22)	25 (34)	0.24 (2.80)	C=63 (43) T=83 (57)	C=75 (51) T=71 (49)	0.16 (1.97)
	CT	31 (42)	25 (34)				
	TT	26 (36)	23 (32)				

Table 12:- Distribution of genotype and allele frequencies of polymorphismsof ABCB1 gene among Luminal B breast cancer patients and controls.

SNP	Genotype	Genotype frequency		P-Value	Allele frequencies		P-Value
		Cases (N=113) n (%)	Controls (N=113) n (%)		Cases n (%)	Controls n (%)	
ABCB1 (rs1045642)	CC	45 (40)	45 (40)	0.93 (0.14)	C=137 (61) T=89 (39)	C=139 (62) T=87 (38)	0.84 (0.03)
	CT	47 (42)	49 (43)				
	TT	21 (19)	19 (17)				
ABCB1 (rs1128503)	CC	30 (27)	31 (27)	0.57 (1.12)	C=119 (53) T=107 (47)	C=114 (50) T=112 (50)	0.64 (0.22)
	CT	59 (52)	52 (46)				
	TT	24 (21)	30 (27)				

Table 13:- Distribution of genotype and allele frequencies of polymorphismsof ABCB1 gene among Her2neu + breast cancer patients and controls.

SNP	Genotype	Genotype frequency		P-Value	Allele frequencies		P-Value
		Cases (N=48) n (%)	Controls (N=48) n (%)		Cases n (%)	Controls n (%)	
ABCB1 (rs1045642)	CC	10 (21)	18 (38)	0.19 (3.27)	C=45 (47) T=51 (53)	C=55 (57) T=41 (43)	0.15 (2.07)
	CT	25 (52)	19 (40)				
	TT	13 (27)	11 (23)				
ABCB1 (rs1128503)	CC	14 (29)	11 (23)	0.69 (0.72)	C=51 (53) T=45 (47)	C=45 (47) T=51 (53)	0.39 (0.75)
	CT	23 (48)	23 (48)				
	TT	11 (23)	14 (29)				

Table 14:- Distribution of genotype and allele frequencies of polymorphismsof ABCB1 gene among Triple Negative Breast Cancer (TNBC) patients and controls.

SNP	Genotype	Genotype frequency		P-Value	Allele frequencies		P-Value
		Cases (N=66) n (%)	Controls (N=66) n (%)		Cases n (%)	Controls n (%)	
ABCB1 (rs1045642)	CC	18 (27)	24 (36)	0.48 (1.45)	C=73 (55) T=59 (45)	C=82 (62) T=50 (38)	0.26 (1.26)
	CT	37 (56)	34 (52)				
	TT	11 (17)	08 (12)				
ABCB1 (rs1128503)	CC	25 (38)	18 (27)	0.39 (1.86)	C=74 (56) T=58 (44)	C=62 (47) T=70 (53)	0.14 (2.17)
	CT	24 (36)	26 (39)				
	TT	17 (26)	22 (33)				

Among all the subtypes, statistically significant differences were observed only at the allelic level for rs1045642 exclusively in patients and controls with Invasive Lobular Carcinoma (ILC). For the remaining subtypes, neither of the two SNPs showed any statistically significant differences.

Conclusions:-

The genotype frequency distribution analysis of the studied SNPs did not reveal any significant differences between cases and controls for the ABCB1 gene. The SNPs rs1045642 of the ABCB1 gene exhibited a significant association with CA15.3 level (OR = 2.67, 95% CI: 1.42–5.03, P = 0.002), whereas no statistically significant associations were observed with other clinico-pathological variables.Among all the subtypes, statistically significant differences were observed only at the allelic level for rs1045642 exclusively in patients and controls with Invasive Lobular

Carcinoma (ILC). For the remaining subtypes, neither of the two SNPs showed any statistically significant differences.In conclusion, this study did not identify any significant associations between the SNPs of ABCB1 gene (rs1045642 and rs1128503) and breast cancer subtypes. These findings suggest that the role of these SNPs in breast cancer risk may be limited or influenced by other genetic, environmental, or epigenetic factors. Further research involving larger, more diverse cohorts and comprehensive analyses is needed to better understand the genetic contributions to breast cancer and identify more reliable biomarkers.

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