Assessing the Prevalence and Impact of HER1-rs11543848 Polymorphism in Breast Cancer Development Among Bangladeshi Women: A Case-Control Study

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A thesis submitted to the School of Pharmacy in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy (Hons.)

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Declaration

It is hereby declared that

1. The thesis submitted is my/our own original work while completing degree at Brac University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. I/We have acknowledged all main sources of help.

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Approval

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Ethics Statement

This study was carried out with thorough compliance to ethical standards, prioritizing the safety, rights, and well-being of all participants involved. In that, they agree with established ethical standards, the Institutional Review Board (IRB) of BRAC University (IRB No BRACUIRB120220005) was approached and subsequently granted approval. The Institutional Review Board undertook a comprehensive evaluation of the research proposal to ensure its adherence to all relevant ethical standards and regulatory restrictions.
All participants provided informed consent before engaging in the study. Participants were provided with an extensive array of information regarding the aims, methods, potential risks, and benefits of the study. The participants were informed that their involvement was entirely voluntary and that they retained the right to withdraw from the study at any moment without facing any consequences for doing so.

This inquiry diligently conformed to the standards and protocols established by the Institutional Review Board (IRB). Methodology and procedures were carried out in a systematic manner. This comprised the careful handling of biological specimens, the secure preservation of data to maintain participant anonymity, and the strict compliance with protocols aimed at minimizing any possible harm to the participants. The research meticulously ensured that all collected data was anonymized to preserve privacy and was utilized solely for the objectives of this study.

Dedication

This work is dedicated to my mother, whose love, sacrifices, and prayers have strengthened me and have shaped me for my existence. To my father, whose passion, advices, and faith in me have always kept me focused. I am truly grateful to my dear sisters and Surjo, whose love and laughter have been my constant support throughout this journey. I could not have reached this milestone without your unwavering support and encouragement. To everyone whose love and belief in me made this journey possible, I offer my deepest gratitude. I dedicate this to you with heartfelt appreciation and love.

- Abdullah Al Abid (21146010)

The dedication of this work is split seven ways: To my mother who is the superstar of my life and to whom I owe everything. To my father who has been my Pole star in navigating the waves of life and my biggest source of inspiration. To my friends who have stuck with me through thick and thin and made life bearable. To my grandparents who have hearts as big as oceans and taught me the power of kindness. To my favourite superhero Spiderman who has taught me there's a hero inside us all. I am forever indebted to you all.

- Rana Tabassum (21146029)

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Abstract

Breast cancer is a leading cause of fatality among women all over the world, with its incidence steadily increasing, particularly in developing countries including Bangladesh. Here, we report the results of a case-control study designed to assess the influence of the HER1-rs11543848 (R497K) polymorphism in the HER1 receptor gene on breast cancer susceptibility in a Bangladeshi female population. Dysregulation of HER1 receptor, one of the epidermal growth factor receptors (EGFR) family that is also a key regulator of cell proliferation, survival, migration, and invasion, has been related to the development of breast cancer. Genomic DNA was isolated from whole blood samples of 112 breast cancer patients and 124 age- and gender-matched healthy controls. Tetra-Primer Amplification Refractory Mutation System Polymerase Chain Reaction (T-ARMS-PCR) was employed for the genotyping identification of the HER1-rs11543848 polymorphism. The heterozygous GA genotype was significantly associated with the increased risk of breast cancer (OR = 1, p = 0.0001), while the homozygous AA genotype was of no statistically meaningful association. The HER1-rs11543848 polymorphism may be quite a risk factor for breast cancer in Bangladeshi women and needs further studies for its functional relevance. Overall, the adoption of genetic knowledge in screening and treatment can improve early detection and individual-based intervention at the personal level, ultimately easing in anticipating consequences for breast cancer development.

Keywords: Breast Cancer, HER1, Polymorphism, T-ARMS-PCR, Bangladeshi Women

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List of Acronyms

EGF	Epidermal Growth Factor
EGFR	Epidermal Growth Factor Receptor
HER1	Human Epidermal Growth Factor Receptor 1
HER2	Human Epidermal Growth Factor Receptor 2
HER3	Human Epidermal Growth Factor Receptor 3
HER4	Human Epidermal Growth Factor Receptor 4
IARC	International Agency for Research on Cancer
IBC	Inflammatory Breast Cancer
T-ARMS-PCR	Tetra-Primer Amplification Refractory Mutation System Polymerase Chain Reaction
TGF-alpha	Transforming Growth Factor Alpha
TNBC	Triple-Negative Breast Cancer

Chapter 1

Introduction

Breast cancer is one of the most prevalent and deadliest diseases that is taking the lives of women all across the globe. Breast cancer has become one of the most common cancers with an estimated 2.3 million new cases reported in the year 2020 alone and a staggering total of 685,000 deaths (Arnold et al., 2022). As per the International Agency for Research on Cancer (IARC), the number of novel breast cancer cases is anticipated to exceed 3 million annually by 2040, with over 1 million fatalities per year (Sedeta et al., 2023). In Bangladesh alone, the breast cancer incidence rate is quite about 22.5 per 100,000 women, with a higher prevalence of 19.3 per 100,000 among women aged 15-44 years (Begum et al., 2019). Furthermore, breast cancer accounts for 69% of all cancer-related deaths among women in Bangladesh, indicating a significant public health issue and a substantial burden on domestic healthcare (Francies et al., 2020). Although the incidence of breast cancer in Bangladesh is lower than that observed globally but shows a troubling upward trend. The latest data from the National Institute of Cancer Research and Hospital in Dhaka shows that the rate of developing breast cancer went up from 26.4% in 2008 to 30.1% in 2017. This is in line with a global trend of rising breast cancer rates, especially in developing countries (Islam, 2021).

Breast cancer is an amalgamation of malignancies that takes root in the mammary glands. The majority of breast cancers are composed of carcinomas while sarcomas and angiosarcomas are rarely seen (Feng et al., 2018). According to Łukasiewicz et al. (2021), the risk of breast cancer can be increased by lifestyle factors, environmental variables, and genetic predisposition, much like any other cancer. However, genetic and epigenetic changes are some of the core factors for developing breast cancer, leading to dysregulation of multiple signaling pathways in the

epithelial cells of the mammary glands (Howard & Ashworth, 2006). Additionally, the activation of chemokines and growth factors further enhances breast cancer progression by altering the tumor microenvironment through interactions with various receptor families (Nagarsheth et al., 2017). Among them, the epidermal growth factor receptor (EGFR) family, characterized by a tyrosine kinase domain is crucial to the development of breast cancer, as it directs cell growth, proliferation, differentiation, and survival (Masuda et al., 2012). The human EGFR family comprises four closely related receptors: HER1 (erbB1 or EGFR), HER2 (erbB2), HER3 (erbB3), and HER4 (erbB4) (Hsu & Hung, 2016). In accordance with Hsu and Hung (2016), the four receptors are dynamic transmembrane glycoproteins that possess an external ligand-binding domain that is responsible for the capture of signals and an internal receptor tyrosine kinase domain that is responsible for the driving of cellular responses. Increased aggressiveness of breast cancer and decreased overall and disease-free survival rates are closely associated with the activation of the EGFR family (Hortobagyi et al., 2006). Additionally, the EGFR overexpression leads to hormone receptor negativity, increased tumor size, poor clinical result coupled with a histopathological grade (Lee et al., 2014).

The HER1 receptor belonging to the EGFR family is a transmembrane protein that plays a crucial role in cell signaling pathways that control cell division, differentiation, adhesion, migration and survival (Wee & Wang, 2017). As a result, the dysregulation of its signaling pathways brings about malignant diseases (Wee & Wang, 2017). The HER1 receptor consist of 1210 amino acids along with three domain structure: extracellular domain which is approximately 621 amino acids long, transmembrane domain of about 23 amino acids spanning through the cell membrane, cytoplasmic domain that includes a tyrosine kinase domain which is approximately 542 amino acids long (Wee & Wang, 2017). The HER1 gene comprises of 28 exons and 27 introns where the extron structure can be further divided into three parts: the

extracellular domain consists of 1-14 exons, the transmembrane domain contains exon 15 and finally the intracellular domain contains exon 16-28 (Uribe et al., 2021). There are various ligands that can bind to the HER1 receptor and activate it (Purba et al., 2017). Upon binding of established ligands like EGF or TGF-alpha to the extracellular domain, dimerization occurs, which can lead to either homo- or heterodimerization with other members of the EGFR family, resulting in the autophosphorylation of the tyrosine kinase that activates downstream signaling pathways (Purba et al., 2017). The HER1 receptor overexpression is observed in approximately 7-43% of breast cancers, with an elevated incidence in aggressive subtypes such as inflammatory breast cancer (IBC) and triple-negative breast cancer (TNBC) (Masuda et al., 2012). Through downstream signaling pathways like PI3K/AKT and MAPK/ERK, overexpressed EGFR enhances cell proliferation, survival, migration, and invasion, enhancing tumor growth. There are two underlying mechanisms of EGFR overexpression that lead to breast cancer: amplification of the EGFR gene and activation of mutations of EGFR (Masuda et al., 2012). The amplification of the EGFR gene has been noticed in 25% of cases of metaplastic breast cancer, a distinct phenotype of triple-negative breast cancer (TNBC), as well as in various other malignancies, including oligodendroglioma, glioblastoma, and lung cancer (Hortobagyi et al., 2004). On the contrary, EGFR mutation activation is quite unusual in breast cancer, it has been observed in tumors of the central nervous system and lung cancer (Kim et al., 2017). However, it is crucial to mention that a majority of missense mutations occurred in the tyrosine kinase domain of the EGFR exon 20, and that this mutation was more common in hereditary breast cancer than in sporadic breast cancer (Masuda et al., 2012).

Through encouraging cell division, survival, migration, and invasion, the HER1 receptor contributes significantly to the advancement of breast cancer (Hynes & Lane, 2005). It has been seen that nearly half of the recorded breast cancers in women who have a previous family

record of the disease can be accounted for by a known genetic component (Brewer et al., 2017). Therefore, genetic variations are undoubtedly the most important aspect in the development of cancer and must be investigated thoroughly. Single nucleotide polymorphism (SNP) represents a prevalent form of human genetic variation that plays a significant role in increasing susceptibility to cancerous transformation and is observable across numerous genes (Talseth-Palmer & Scott, 2011). In the HER1 gene itself, a single nucleotide variation called the R497K polymorphism (rs11543848) occurs at 497 codon situated in the extracellular domain where Arginine (R) is substituted to Lysinine (K) which has been identified in breast cancer along with gliomas, lung and colorectal cancer (AbdRaboh et al., 2013). For example, in research undertaken regarding colorectal carcinoma patients, the R497k (rs11543848) polymorphism reduced the activation of its target genes and it was hypothesized that it could be a potential determinant for reduced tumour recurrence in stage 2, or stage 3 colorectal cancer patients undergoing surgery to remove all malignant tissue (Wang et al., 2007). Moreover, several studies have been conducted to ascertain an association between the HER1-rs11543848 polymorphism and breast cancer risk; nevertheless, definitive results remain elusive (Baderi et al., 2022). Hence, the HER1-rs11543848 polymorphism must be scrutinised in order to better understand the underlying mechanisms and to evaluate whether there is a possibility that the HER1-rs11543848 polymorphism in the HER1 receptor gene contributes to the risk of developing breast cancer.

Therefore, the primary objective of this study is to examine the relationship between the HER1-rs11543848 gene polymorphism in the HER1 receptor and the appearance of breast cancer among women in Bangladesh. This investigation aims to evaluate the degree of resemblance between individuals diagnosed with breast cancer and a control group of healthy volunteers in Bangladesh concerning the HER1-rs11543848 gene polymorphism within the human

epidermal receptor (HER1) gene. Genetic analysis in this study will be done by utilizing the Tetra-Primer Amplification Refractory Mutation System Polymerase Chain Reaction (T-ARMS-PCR). By investigating this genetic variation, this research strives to gain a thorough understanding of the potential impact that it may have on the susceptibility of Bangladeshi women in developing breast cancer.

This study aspires to provide a comprehensive genetic assessment that will further shed light on the etiological impact that the HER1-rs11543848 polymorphism plays in breast cancer. The objective of this study is to enhance awareness of the genetic risk factors that are linked to the development of breast cancer, with the objective of fostering early detection and prevention initiatives. The project focuses on developing personalized screening strategies and preventive measures specifically tailored to the Bangladeshi population. This will be achieved by identifying key genetic markers, such as the HER1-rs11543848 polymorphism. By offering valuable insights that can improve risk assessment, facilitate early intervention, and support targeted treatments, the ultimate objective is to enhance and improve health outcomes for women all over Bangladesh.

Chapter 2

Methodology

2.1 Approach Participants and Ethical Considerations

This case-control study involved 236 Bangladeshi women, comprising 112 breast cancer patients and 124 healthy controls matched by age and gender. Participants were selected from the National Cancer Research Institute Hospital, located in Mohakhali, Dhaka, Bangladesh. The study focused solely on patients diagnosed with breast cancer, excluding those with other complications. This study, was conducted as a part of final year thesis project in B. Pharm. (Hons.), received ethical approval from the BRAC University Institutional Review Board (IRB No BRACUIRB120220005). Following the clarification and explanation of the study's aims and methods, all participants provided their written informed consent.

2.2 Collection of Sample

Approximately 5 mL of whole blood was collected from each participant in EDTA tubes by venipuncture. Whole blood samples were stored at -20°C before genomic DNA was extracted.

2.3 Documentation of Data

A standardized questionnaire was used to ensure the collection of comprehensive and accurate data pertaining to medical history, demographic and lifestyle factors.

Demographic and Medical Data

- Family History of Cancer: Documentation of any breast cancer or other familial cases types of cancer.
- Past Medical History: Information on previous medical conditions including hormonal disorders as well as benign breast diseases.
- Reproductive History: Things to be aware of are the age of onset of menstruation begins, in the year of the first full-term pregnancy, the number of pregnancies someone has breastfed, the age they reached menopause, and whether they have taken hormonal replacement therapy or contraception.
- Surgical history: details of any surgery previously carried out on the chest or genitalia.
- Age, Ethnicity, Education Level, Occupation, and Residence: Age up to 10 years, ethnicity, education level, occupation, and residence, along with ethnicity, highest level of education completed, current occupation and employment status, and urban or rural residence.

Psychological and Lifestyle Factors

- Dietary Patterns: The regular food patterns, specific to fruits, veggies, red meat, processed foods, and alcohol.
- Exercise: The number, duration and type of exercise programs the participant does regularly.
- Smoking & use of Alcohol: Frequency & volume of Alcohol and cigarette and consumption and current smoking behaviours.
- Body Mass Index (BMI) and Sleep Patterns: Average sleep duration, quality, and as well as the height and weight measurements that are used to derive BMI.

- Socioeconomic Status: Type and availability of health insurance and household income per month or per year.
- Stress, Social Support, and Mental Health: Details about any diagnosed mental health conditions, perceived stress levels, and the presence of social support networks.

2.4 Confidentiality and Data Management

The collected data was carefully recorded and stored in a secure database up to January 2025. To protect personal information, we used data anonymization procedures to ensure that participants remained anonymous at all times. Data was only accessible to authorized personnel ensuring compliance with all data protection and ethical standards. Overall, this approach to documenting the data varied and accumulated high quality data that laid a strong foundation for analysis and interpretation of the study results.

2.5 Procedures Carried out in Laboratory

Genomic DNA was extracted using the spin-column extraction method, as per the previously established laboratory protocol, which is as follows: 5 ml Peripheral blood samples were obtained with venipuncture and transferred to a 15 ml sterile tubes with ethylenediaminetetraacetic acid (EDTA)-Na_2 as an anticoagulant. The FavorPrep™ Blood Genomic DNA Extraction Kit (Favorgen BiotechCorporation, Taiwan) was used per manufacturer instructions to isolate DNA from the blood samples (the genomic DNA). The extracted DNA were also kept at -20°C for further procedures.

Genotyping of the HER1-rs11543848 polymorphism was conducted with the Tetra-primer amplification refractory mutation system polymerase chain reaction (T-ARMS-PCR) method, as previously optimized in the laboratory. The collection of outer and inner primer sequences (forward and reverse) was done from the publication by Sombal et al. (2024) to identify homozygous and heterozygous alleles.

The PCR reaction mixture (10 µL) was prepared with the following:

- 5 µL master mix (2X)
- 1 µL forward primer (1µM)
- 1 µL reverse primer (1µM)
- 2 µL ddH2O
- 1 µL of template DNA

The primers employed for amplifying the HER1-rs11543848 polymorphism were:

- Forward outer: 5'-TTGTCCTTCCAGTCACGGTCG-3'
- Reverse outer: 5'-TCAAACAGAATGCCTGTAAAGCT-3'
- Forward inner: 5'-GGGGCCCGGAGCCCAA-3'
- Reverse inner: 5'-GGCAAGAGACGCAGTCCC-3'

PCR amplification was performed under the following conditions:

- The process starts with a 5-minute initial denaturation stage that is conducted at 98°C.
- After that, there are 40 cycles of denaturation for 40 seconds at the same temperature, annealing for 30 seconds at 55°C, and extension for 60 seconds at 72°C.
- The final extension phase was performed at 72°C for 5 minutes.

Two types of bands can be found in the gel after electrophoresis of the T-ARMS PCR product:

- G or Wild Type shows a band at 268 bp
- A or Mutant type shows a band at 171 bp

And based on the following band patterns the HER1-rs11543848 polymorphism was identified:

- GA Heterozygote shows band for G and A at 268 bp and 171 bp
- GG Common homozygote shows only one band for G at 268 bp
- AA Rare homozygote shows only one band for A at 171 bp

The genotypes for both breast cancer patients and controls were scored by inspection of the digestion banding pattern on the agarose gel.

The amplicons were confirmed by amplification products on a 2% agarose gel by electrophoresed with a 100 bp DNA ladder.

2.6 Quantitative Analysis of Data

Statistical analysis was performed by using the Statistical Package for Social Sciences (SPSS) version 25.0 (SPSS Inc., Chicago, IL). In contrast, the distribution of HER1-rs11543848.

The Chi-squared test had been used to examine the deviations in the distribution of SNPs (single nucleotide polymorphisms) between healthy individuals and those diagnosed with breast cancer. Odds ratios (ORs) and their corresponding 95% confidence intervals (CIs) were evaluated to assess the relationship between the two groups.

Chapter 3

Result

In this study, we investigated and examined whether HER1–rs11543848 polymorphism affected breast cancer risk levels in our research area. The genotyping process included 112 breast cancer patients together with 124 demographically matched healthy controls. The research data showed reliable results because both groups met the criteria of Hardy-Weinberg equilibrium ($p > 0.05$).

Allele	**Cases (n = 112)**	**HWE**		**Controls (n = 124)**	**HWE**		**Genetic models**	**OR**	**95% CI**	***P*-value**
		X^2	***P***		**X^2**	***P***				
GG Common homozygote	18.75%	0.274	0.600	18.75%	0.274	0.600	Additive model 1 (GA vs. AA)	1	0.167 - 5.984	0.0001
							Additive model 2 (AA vs. GG)	1	0.041 - 24.549	0.8806
GA Heterozygote	75%			75%			Dominant model (GA+AA vs. GG)	1	0.169 - 5.903	0.0001
AA Rare homozygote	6.25%			6.25%			Recessive model (AA vs. GA+GG)	1	0.057 - 17.510	0.9597
							Overdominant model (GA vs. GG+AA)	1	0.202 - 4.955	0.0001
p>0.05 obeyed Hardy-Weinberg equilibrium										

Table 1: Association between Breast Cancer with HER1 (rs11543848) Polymorphism

In table 1, the heterozygous genotype GA was found to create a statistically strong link between increased breast cancer risk levels (OR = 1, 95% CI = 0.1694–5.9027, p = 0.0001). Data indicated that individuals bearing the heterozygous GA genotype displayed a higher vulnerability to breast cancer based on the overdominant model (OR = 1, 95% CI = 0.202–4.955, p = 0.0001). Information about homozygous AA genotype showed no meaningful statistical association with breast cancer (OR = 1, 95% CI = 0.057–17.510, p = 0.9597) regardless of possession of two A alleles. The additive model evaluation between AA and GG frequencies (OR = 1, 95% CI = 0.041–24.549, p = 0.8805) demonstrated no statistically relevant significance thus supporting the hypothesis that homozygous AA lacks substantial independent risk for breast cancer. The observed GA heterozygous genotype suggests that it could be responsible for breast cancer susceptibility by potentially offering advantage in disease risk partnership. Further research about this SNP's functional effects becomes essential because of the significant results obtained in dominant and overdominant genetic models. Additional extensive studies that include various ethnic groups need to analyze breast cancer genetic relationships and discover the biological processes that drive this connection.

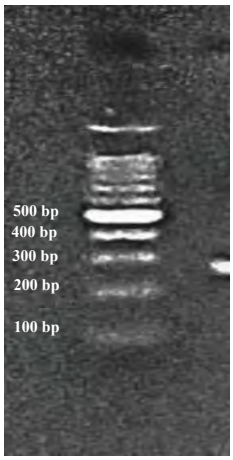

Fig 1: 100 bp DNA ladder after electrophoresis of 2% agarose gel

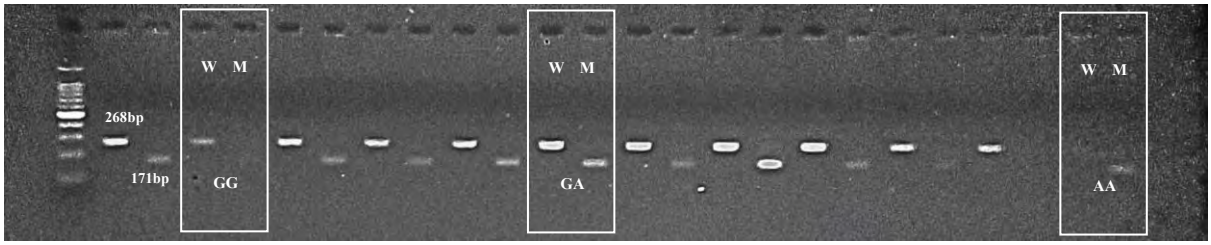

Fig 2: Representative image of gel electrophoresis of HER1-rs11543848 gene polymorphism detected in Breast Cancer (Case) group

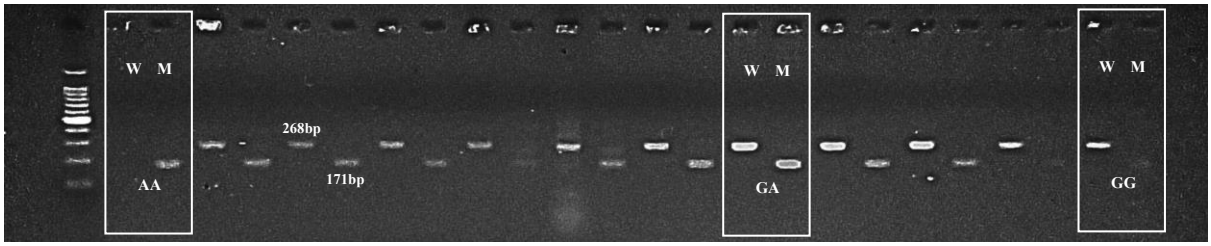

Fig 3: Representative image of gel electrophoresis of HER1-rs11543848 gene polymorphism detected in Healthy Volunteer (Control) group

Chapter 4

Discussion

4.1 Key Findings Summary

The objective was to investigate the association of the HER1-rs11543848 polymorphism with the risk of developing breast cancer in a Bangladeshi setting. Key highlights included:

The genotypic distribution in the controls complied to Hardy-Weinberg equilibrium (HWE), suggesting that this group was representative.

We observed in the study, that the risk of breast cancer was significantly associated with the GA genotype (OR = 1, 95% CI = 0.169–5.903, p = 0.0001).

The AA genotype was not as significant as the GA genotype, but it was associated with breast cancer development risk according to our study (OR = 1, 95% CI = 0.057–17.510, p = 0.9596).

4.2 Comparison with Existing Literature

Conflicting findings were reported in earlier publications regarding the association between the HER1-rs11543848 polymorphism and breast cancer risk. Our results are concordant with those of Sombal et al. (2024), strongly linked breast cancer susceptibility to the GA genotype. But studies in other populations have shown differing levels of association, likely due to genetic and environmental differences. Further studies are needed to confirm the role of HER1-rs11543848 in breast cancer across diverse populations. Differences in genetic backgrounds, environmental exposures, and study designs may explain conflicting findings. Functional analyses could provide insights into its biological impact and potential therapeutic relevance.

4.3 Consequences of Results

- Clinical Relevance: Our study suggests that HER1-rs11543848 GA genotyping might serve as a potential biomarker for breast cancer susceptibility in Bangladeshi women.
- Genetic Counseling and Risk Assessment: There should be a thorough genetic counseling with multiple genetic and environmental factors.

4.4 Limitations

- Sample Size: A larger study population is required to validate our findings and improve statistical power.
- Ethnicity Specificity: Results could be specific to the Bangladeshi population and may not be generalizable to other ethnicities.

4.5 Prospective Research Areas

- Larger Population Studies: Future studies like this one should encompass larger groups of more diverse populations to increase statistical reliability.
- Functional Studies: By understanding the fundamentals of the molecular mechanisms underlying HER1-rs11543848 polymorphism's role in breast cancer is crucial.
- Breast Cancer Risk Genetics: Genome-wide association studies (GWAS) will help identify additional genetic markers associated with breast cancer risk, leading to more personalized prevention strategies.

Chapter 5

Conclusion

The objective of this investigation was to clarify the relationship between the HER1-rs11543848 polymorphism and breast cancer risk in Bangladeshi women, a topic that has not been previously explored. The case-control study involving 112 breast cancer patients and 124 healthy control individuals provides valuable insights into the genetic susceptibility for breast cancer within the same population. The genotyping results indicated a statistically significant association between the GA genotype with heterozygosity and the risk of breast cancer, as demonstrated under the overdominant model (OR = 1, 95% CI = 0.2018–4.9547, p = 0.0001) (Table 1). On the other hand, the homozygous AA genotype did not show a significant association with breast cancer risk.

The HER1-rs11543848 polymorphism, especially GA genotype, could be a potent risk factor in inducing breast cancer development in Bangladeshi women. As, there was no significant association for the AA genotype which indicates that there can be interaction of other genetic and environmental factors in breast cancer susceptibility. Additionally, our study reinforces the potential utility of genetics in the field of cancer risk, paving the way for larger, multi-institutional studies to evaluate the same hypotheses on a larger scale and to clarify these findings.

Therefore, identification of HER1-rs11543848 as a high-risk marker will help develop early screening strategies as well targeted intervention approaches for breast cancer. The finding has important clinical implications. Further studies are needed to understand the functional consequences of this polymorphism on HER1 signaling pathways as well as its role in tumor progression. Moreover, merging genetic discoveries with environmental and lifestyle data will

facilitate crafting personalized preventive and therapeutic strategies for breast cancer in Bangladesh.

Ultimately, our findings provide strong support for a possible genetic basis associated with the HER1-rs11543848 polymorphism, but still require confirmation and further exploration of genetic risk factors of breast cancer. Strengthening genetic research in Bangladesh would ultimately help to better diagnostic tools and early detection and personalized therapeutic strategies and would reduce the burden of breast cancer in the area.

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