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Expression of Matrix Metalloproteinase 11 Gene as a Potential Biomarker of Breast Cancer

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ABSTRACT

Breast cancer is among the most prevalent malignancies and a primary contributor to cancer-related mortality in women globally. Matrix metalloproteinase 11 (MMP11) is a crucial regu-lator of tumor invasion and metastasis, degrading the extracellular matrix and correlating with an unfavorable prognosis in the majority of malignancies. Nonetheless, its expression pattern and prognostic capacity in breast cancer remain undefined. This study aimed to evaluate the expression and mutation status of the MMP11 gene in Bangladeshi breast cancer patients. Next Generation Sequencing (NGS) was conducted on tumor and adjacent normal tissues from 34 female patients recruited from Dhaka Medical College Hospital. The results indicated that the median expression of MMP11 was considerably elevated in tumor tissues (3.402 (IQR 2.097–5.133)) compared to normal tissues (1.895 (IQR 1.306–2.128), p=0.02). Among clinical variables, only the relationships of BMI, family history, age at menarche, contraceptive usage, and breastfeeding with MMP11 expression were statistically significant. Our results suggested that MMP11 was substantially expressed in breast cancer and might be a potential biomarker in breast cancer development. The identification of this gene's role in tumor biology necessitates additional research to clarify its functional processes and therapeutic significance. These findings establish the framework for future studies that attempt to incorporate MMP11 into diagnostic or prognostic tests, with the potential to develop customized therapy methods for breast cancer patients.

INTRODUCTION

Matrix metalloproteinase 11 (MMP11, also known as stromelysin-3) is a protein of major interest in cancer biology due to its unique involvement in tumor formation and progression. MMP11 contains unique actions, including boosting cell survival and modifying the tumor microenvironment, which sets it apart from other matrix metalloproteinases that are largely involved in destroying the extracellular matrix to assist tumor infiltration (Wei & Shi, 2005). It has been found that it is overexpressed in the stroma of breast carcinomas, where it has been postulated to be implicated in tumor growth, metastasis, and immunological regulation (Basset *et al.*, 1990; Min *et al.*, 2013). Proteins such as MMP11 also play a crucial role in altering the tumor microenvironment (Becker *et al.*, 2013), promoting additional immune suppression and enabling tumor growth. Thus, MMP11 expression profile and its associated biological functions suggest its possible application as a breast cancer biomarker (González de Vega *et al.*, 2019). In clinical practice, understanding of biomarkers for breast cancer is very significant because of the pressing demand on targeted and efficient treatment approaches. Introduction Breast cancer is among the main contributors to cancer-related fatalities in women globally and is still regarded as a dangerous disease (Siegel *et al.*, 2019). Although therapeutic breakthroughs have enhanced survival rates, this does not greatly affect aggressive subtypes, particularly the exceedingly difficult-to-treat triple-negative subtype (Foulkes *et al.*, 2010; Denkert *et al.*, 2017). Biomarkers are valuable for predicting illness prognosis, responsiveness to therapy, and disease recurrence; consequently, they serve critical roles in precision medicine (Brown & Murray, 2015). While the literature suggests a role of MMP11 in cancer, there are no studies including MMP11 detection as a breast cancer biomarker. Although biological function is the main focus in the existing literature, the clinical relevance of miR-29 as a potential diagnostic and prognostic biomarker is under investigated (Zhuang *et al.*, 2018; Roscilli *et al.*, 2014). In addition, the significance of MMP11 in increasing immunological tolerance and tumor spread in breast cancer warrants more research (Kim *et al.*, 2021). Here, we intend to fill these gaps in our understanding of MMP11 by measuring its expression in breast cancer patients and connecting it with clinical prognosis.

Currently, there is inadequate detail in the current literature detailing the precise prognostic and diagnostic relevance of MMP11 in the context of breast cancer (McGowan & Duffy, 2008). However, despite research revealing its overexpression in breast cancer tissues, few systematic investigations have related levels of MMP11 expression to patient outcomes and tumor characteristics. Moreover, although MMP11 has been associated with immune sup-pression, its connection with immune cells in the tumor microenvironment (TME) is little defined (Lei *et al.*, 2020). In this work, we intend to confirm MMP11 as a viable biomarker for breast cancer by investigating its

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expression patterns and clinical importance.

Research Questions

• Does MMP11 expression vary across different breast cancer subtypes, and how is it associated with disease prognosis?

• What are the mechanisms through which MMP11 influences tumor progression and immune suppression in breast cancer?

• Can MMP11 serve as a potential target for therapeutic interventions?

Research Objectives

• To investigate the association between MMP11 expression and breast cancer subtypes.

• To evaluate the prognostic value of MMP11 expression in predicting patient outcomes.

• To explore the role of MMP11 in immune modulation within the tumor microenvi-ronment.

• To identify potential therapeutic implications of targeting MMP11 in breast cancer treatment.

This finding has crucial implications for breast cancer detection, prognosis, and therapy. Es-tablishing MMP11 as an early diagnostic biomarker may also fulfill clinical needs for per-sonalized intervention to combat aggressiveness in breast cancer subtypes such as triple-negative breast cancer (Gonzalez-Angulo *et al.*, 2011; Malvia *et al.*, 2019), especially given that our work shows that MMP11 expression is a 'reactive' process associated with malig-nancy—suggesting the potential for therapeutic intervention if reactive behavior is identified in the earlier stages of cancer development. Moreover, discovering how MMP11 regulates the tumor microenvironment in this situation may offer up new pathways for therapy and improve survival and/or quality of life (Winer *et al.*, 2018). The authors begin the investigation with a comprehensive work of literature in order to summarize the state of the information regarding MMP11 in terms of its functions in breast cancer. This is preceded by a thorough methodology section covering the experimental design, data collection, and analytical methodologies. Findings from the study are reported in the findings section and evaluated in the discussion part in reference to existing literature. Study implications, limits, and ideas for future study are finally presented in this research.

LITERATURE REVIEW

Matrix metalloproteinases (MMPs) are a class of zinc-dependent enzymes that degrade the extracellular matrix (ECM), thereby being implicated in tumor growth, invasion, and metas-tasis. By destroying structural scaffolding in the ECM and basement membrane, MMPs enhance the migration of cancer cells, allowing tumor cells to penetrate surrounding tissue and disseminate to distal regions (Brown & Murray, 2015). MMPs, in particular, are recognized to be implicated in the numerous facets of cancer progression, such as angiogenesis and immune evasion. It was previously established by Becker, Andersen, and Schrama132 that the tumor microenvironment has a suppressive influence on effector immune responses, in part mediated by the action of the matrix metalloproteinases (MMPs)132. In addition, interactions between MMPs and the tumor microenvironment are related to therapeutic resistance, underscoring the critical function of MMPs in cancer biology (Lei *et al.*, 2020; Winer *et al.*, 2018). Matrix metalloproteinase 11, or MMP11 (stromelysin-3), is an unusual member of the MMP family but demonstrates distinct functional properties during cancer progression. Distinct from other MMPs that predominantly destroy ECM, MMP11 alters the tumor microenvironment to increase tumor cell survival. Basset *et al.* (1990) as the first to describe MMP11 as preferentially expressed in breast cancer stromal cells. Later, this finding was verified with its overexpression in multiple subtypes of breast cancer associated with poor survival (Min *et al.*, 2013). MMP11 binds with other molecules, including Smad2, facilitating tumor proliferation and development (Zhuang *et al.*, 2018). The role of MMP11 as an immunosuppressor adds more intricacy to its function. Kim *et al.* (2021) demonstrated that strong MMP11 expression is inversely linked with CD8+ T-cell infiltration, resulting in decreased antitumor immunity and lower survival in breast cancer patients. However, new technical developments such as immunohistochemical-assisted imaging mass spectrometry have further verified MMP11 as a candidate for a metastatic breast cancer biomarker (González de Vega *et al.*, 2019; Johnson *et al.*, 2022). Breast cancer remains one of the most frequent tumors among women worldwide; consequently, developing useful biomarkers is vital to enable early detection [6], better prognostic prediction, and therapy stratification [8]. BRCA1 and BRCA2 Among the most well-known genetic markers, BRCA1 and BRCA2 mutations have an extraordinarily high connection with hereditary breast cancer and present substantial risk for disease development (Antoniou *et al.*, 2003; King *et al.*, 2003). In addition to these other genes, also belonging to MMP family members, have recently been proposed as biomarkers for sporadic and hereditary breast cancers (de Jong, 2002; Stevens *et al.*, 2013). Turning the attention to the heterogeneity of breast cancer, gene expression analysis has aided in differentiating distinct subtypes. Cheang *et al.* (2008) and Malvia *et al.* on the significance of molecular subtyping to predict clinical outcome (2019). Furthermore, MMP11 has recently emerged as a possible biomarker for breast cancer progression, especially in advanced and metastatic stages (Fu *et al.*, 2015; Naghshvar *et al.*, 2017). These biomarkers are significant but yet confront obstacles in transferring into clinical practice. Zhang *et al.* (2016) highlighted the double-edged sword of MMP11 in tumor biology, underlining the requirement of mechanistic vigilance. Technological developments in imaging and immunohistochemistry continue to assist efforts (Eiro *et al.*, 2019; Roscilli *et al.*, 2014) to add MMP11 into diagnostic

panels. Their potential as indicators and therapeutic targets is underscored by the significance of MMPs—specifically, MMP11—in breast cancer progression. Although tremendous progress has been made, a greater knowledge of the mechanics behind these techniques is still needed to integrate them into therapeutic practice. MMP11, via its advanced technologies and multi-omics techniques, can assist in bridging this gap and provide deep insights into breast cancer biology as well as aid in the tailoring of treatment options.

MATERIALS AND METHODS

Study Design

This research employed a cross-sectional study design to investigate the expression of the matrix metalloproteinase 11 (MMP11) gene as a potential biomarker for breast cancer. The study was conducted over a period of one year, from July 2022 to June 2023, at the Department of Biochemistry, Dhaka Medical College, in collaboration with the Institution for Population and Precision Health, Department of Public Health Sciences, The University of Chicago. The study population comprised female patients diagnosed with breast cancer, recruited from the Department of General Surgery and Breast Clinic at Dhaka Medical College Hospital (DMCH). A purposive sampling technique was used to select participants, ensuring the inclusion of cases that met the specific eligibility criteria. The sample size was calculated based on established statistical parameters, ensuring sufficient power and reliability of the findings. Thirty-four samples were included in the study, exceeding the minimum required number of 32 as determined by statistical formulas. Data were collected using structured data sheets, which recorded demographic, clinical, and biochemical variables to ensure compre-hensive analysis. This design facilitated a focused and detailed exploration of the relationship between MMP11 gene expression and breast cancer, providing valuable insights into its potential as a biomarker.

Sample Collection

The study included a cohort of 34 female patients diagnosed with breast cancer, selected from the Department of General Surgery and the Breast Clinic at Dhaka Medical College Hospital (DMCH). Tissue samples were collected from both malignant tumor sites and normal breast tissue located at least 2 cm from the tumor margins. Normal breast tissues were macroscopically identified as bright yellow, soft, and free from any suspicious lesions, while malignant tissues exhibited increased vascularity, color changes, and loss of normal tissue architecture. These samples were obtained following preoperative clinical, radiological, and histopathological evaluations to ensure accuracy and consistency in tissue classification. The ethical ap-proval for this study was granted by the Institutional Review Board of Dhaka Medical College, adhering to the ethical guidelines of the Declaration of Helsinki. All participants were informed about the study objectives and procedures, and written consent was obtained before sample collection. The tissues were preserved and transported in compliance with standard protocols to ensure the integrity of the specimens for further analysis. The collected samples were categorized as follows Table 1.

Table 1: Sample Categories

Group	Type of Tissue	Number of Samples (n)
Group A	Normal tissue	32
Group B	Cancerous tissue	32

This structured approach to sample collection ensured a balanced representation of tissue types for reliable comparative analysis of MMP11 gene expression. Data from these samples were critical for understanding the differential expression patterns and their potential as biomarkers for breast cancer diagnosis and prognosis.

Laboratory Procedures

RNA Extraction and Quality Control

RNA extraction was performed using the Quick-DNA/RNA™ Micro prep Plus Kit (Zymo Research, CA, USA), leveraging advanced DNA/RNA Shield™ technology combined with Proteinase K to ensure efficient preservation, lysis, and nucleic acid purification. Breast tissue samples were first stored in RNA/DNA Shield™, homogenized, and mixed with DNA/RNA Lysis Buffer. Proteinase K digestion was then carried out for four hours at 30°C with rotation to degrade proteins and facilitate the release of RNA and DNA. After digestion, debris was removed by centrifugation, and the cleared supernatant was carefully collected for downstream processing. RNA purification involved precipitation with ethanol and subsequent transfer of the samples to Zymo-Spin™ IC Columns for purification. To eliminate any DNA contamination, a DNase I treatment step was included. The purified RNA was washed multiple times and eluted with RNase-free water at 40°C. This systematic approach ensured high-quality RNA suitable for advanced downstream applications. RNA concentration and purity were evaluated using NanoDrop 1000 spectrophotometry, ensuring absorbance ratios (A260/A280 and A260/A230) fell within acceptable ranges for RNA integrity.

Targeted RNA Sequencing

For targeted RNA sequencing, the custom-designed Twist Next Generation Sequencing Kit (Twist Bioscience, CA, USA) was employed. This process included standardized library preparation, target enrichment, and sequencing protocols to ensure reproducibility and accu-racy. The comprehensive methodology was critical in maintaining the integrity of gene ex-pression profiles, particularly for the identification of breast cancer-specific markers. the complete workflow of RNA extraction and purification, showcasing the step-by-step meth-odology for obtaining high-quality RNA from breast tissue samples below

Figure 1. Table 2 presents the average DNA and RNA yields from tumor and normal adjacent tissue samples,

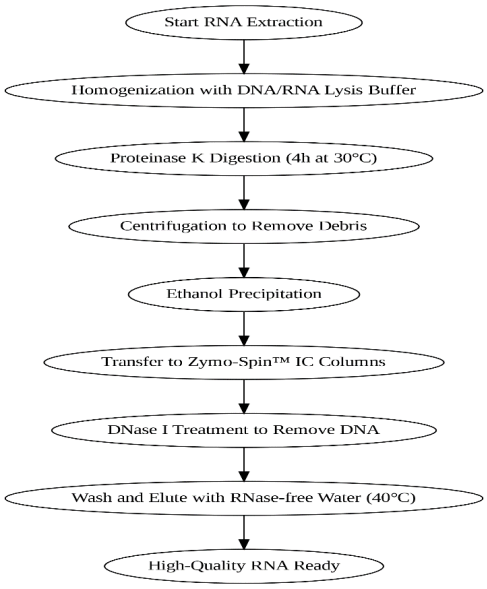

Figure 1: Depicts the Complete Workflow of RNA Extraction and Purification

Table 2: Average DNA and RNA Yields from Tumor and Normal Adjacent Tissue Samples

Sample Type	Average RNA Yield (µg/mg)	Average DNA Yield (µg/mg)
Tumor Tissue	1.5–3	3–5
Normal Adjacent Tissue	1–2	2–3

demonstrating consistency across extractions.

Study Procedure

Selection of Breast Cancer Patients

This cross-sectional study was conducted on 34 Bangladeshi female breast cancer patients, selected purposively from the Department of Surgery, Dhaka Medical College and Hospital. Each participant underwent a thorough clinical evaluation, which included biochemical tests, fine needle aspiration cytology (FNAC), histopathological examination, mammography, and immunohistochemistry analysis. Comprehensive data for each patient were documented in detailed collection sheets. Written informed consent was obtained from all participants after explaining the study's purpose and methods.

Tissue Collection and Preservation

Tissue specimens were collected immediately after modified radical mastectomy (MRM). Tumor and adjacent normal tissues, approximately 0.5 cm^3 each, were carefully placed in separate, pre-labeled Eppendorf tubes containing DNA/RNA Shield™ to preserve nucleic acid integrity. Samples were stored at room temperature prior to shipment. For transportation, tissues and blood samples were placed on dry ice and shipped to the Institution for Population and Precision Health at the University of Chicago, USA.

Protocol for Tissue Handling

Tumor tissues were labeled (B00x_T), and adjacent normal tissues were similarly labeled (B00x_N) before being placed in DNA/RNA Shield™. Samples were refrigerated and main-tained under controlled conditions to ensure integrity until shipment. The use of high-quality storage and transport protocols ensured that the samples were suitable for subsequent nucleic acid analyses.

Laboratory Protocol

RNA and DNA were extracted from low-input samples using spin-column technology to achieve high-quality nucleic acids, making them suitable for Next-Generation Sequencing (NGS) and RT/qPCR analyses. the reagent compositions and preparation details for the la-boratory

Table 3: The Reagent Compositions and Preparation Details

Reagent	Preparation Details
DNA/RNA Wash Buffer	Add 96 ml ethanol to 24 ml buffer
DNase I	Reconstitute with 275 µl RNase-free water
Proteinase K	Prepare a 20 mg/ml solution

summarization show in Table 3.

This rigorous approach to laboratory procedures ensures the reliability and reproducibility of RNA extraction, quality control, and sequencing outcomes, forming the foundation for high-confidence data interpretation in breast cancer biomarker studies.

Statistical Analysis

Following the completion of data collection, meticulous efforts were made to ensure the ac-curacy and integrity of the data. The data were initially checked and edited manually to identify and rectify any inconsistencies or errors. Once validated, the data were coded, systematically entered into a computer, and verified to prepare it for statistical analysis. This process aimed to maintain data quality and ensure its readiness for robust analysis. For the statistical analysis, SPSS (Statistical Package for the Social Sciences) version 26 was utilized. This software was chosen due to its wide-ranging statistical capabilities and ease of use for analyzing both descriptive and inferential data. The analytical process was structured as follows:

Analytical Techniques and Methods

1. MMP11 Gene Expression Analysis

The expression of the MMP11 gene was detected using the next-generation sequencing (NGS) method, which provides highly accurate and reproducible data. Raw sequencing data were processed, and the expression levels of MMP11 in tumor and adjacent normal tissues were quantified.

2. Characterization and Clinical Significance

The clinical significance of MMP11 expression was

further validated by cross-referencing the data with the National Center for Biotechnology Information (NCBI) genome database. This database offered insights into known genetic variations, asso-ciated phenotypes, and established clinical implications of MMP11.

3. Correlation with Socio-Demographic Variables

The relationship between MMP11 gene expression and various socio-demographic variables (e.g., age, clinical stage, tumor grade, and hormonal receptor status) was as-sessed using the Spearman Correlation Test. This non-parametric test was ideal for identifying monotonic relationships between variables without assuming normal data distribution.

4. Differential Expression Analysis

To determine whether there was a significant difference in MMP11 expression between normal and tumor tissues, the Mann-Whitney U Test was employed. This test was chosen because it is robust to non-normal distributions and appropriate for comparing two independent samples.

5. Statistical Significance

A p-value threshold of <0.05 was set to define statistical significance for all tests. Re-sults with p-values below this threshold were considered indicative of significant as-sociations or differences.

Data Presentation

To effectively communicate the findings, data were summarized in tables 4,5,6. Summary of Socio-Demographic and Clinical Characteristics of Participants (Table 4), MMP11 Gene Ex-pression in Tumor and Normal Tissues (Table 5), Spearman Correlation Between MMP11 Expression and Clinical Variables (Table 6).

Table 4: Socio-Demographic and Clinical Characteristics of Participants

Variable	Category	Frequency (%)
Age Group (years)	<40	12 (35.3%)
	≥40	22 (64.7%)
Tumor Stage	Early Stage (I-II)	18 (52.9%)
	Advanced Stage (III)	16 (47.1%)
Hormonal Receptor Status	Positive	25 (73.5%)
	Negative	9 (26.5%)

Table 5: MMP11 Gene Expression in Tumor and Normal Tissues

Tissue Type	Median Expression Level	Range	P-Value
Tumor Tissue	12.5	10.2–15.7	<0.001
Normal Tissue	3.4	2.8–4.2	

Table 6: Spearman Correlation Between MMP11 Expression and Clinical Variables

Clinical Variable	Spearman Correlation Coefficient (r)	P-Value
Age	0.312	0.045
Tumor Grade	0.527	<0.001
Hormonal Receptor Status	-0.256	0.078

Ethical Considerations

This study was conducted in accordance with the ethical principles outlined in the Declara-tion of Helsinki. Ethical approval was obtained from the Institutional Review Board (IRB) of Dhaka Medical College and Hospital prior to the commencement of the study. Written informed consent was obtained from all participants after a detailed explanation of the study objectives, procedures, and potential risks and benefits. To ensure confidentiality, all patient data were anonymized using unique identifiers, and access to sensitive information was restricted to authorized personnel only. Tissue samples were handled with strict adher-ence to biosafety protocols, ensuring both participant safety and the integrity of the sam-ples. Participants were informed of their right to withdraw from the study at any stage with-out any consequences. No financial or other forms of compensation were provided to influ-ence participation, ensuring voluntary and unbiased involvement.

RESULTS AND DISCUSSIONS

Results

During the period of July 2022 to June 2023, a total of 34 diagnosed female breast cancer patients were included in this study. Demographic and clinical data were recorded, and the expression of Matrix Metalloproteinase 11 (MMP11) was assessed using Next Generation Sequencing (NGS). Statistical analyses were performed using SPSS version 26, with signif-icance determined at a p-value of ≤ 0.05.

Demographic and Clinical Characteristics

The age distribution of the study participants is presented in Table 7. The majority (76.47%) of the participants were under 50 years of age, with a mean age of 47.41 ± 2.52 years. Nutritional status, determined by BMI, showed that 52.94% of the participants had a normal BMI, with

Table 7: Distribution of Age of the Study Subjects (N=34)

Age (years)	Frequency (n)	Percentage (%)	Mean ± SD
≤ 50	26	76.47	47.41 ± 2.52
> 50	8	23.53	

Table 8: Distribution of Nutritional Status by BMI (N=34)

BMI	Frequency (n)	Percentage (%)	Mean ± SD
Normal	18	52.94	21.07 ± 17.3
Above normal	16	47.06	

a mean of 21.07 ± 17.3 (Table 8).

Family history, menstrual history, and contraceptive use were evaluated using visual repre-sentations. The pie diagrams (Figure 2 and Figure 3) show the distribution of family his-tory and menstrual history among participants, while the bar diagram (Figure 4) highlights contraceptive use.

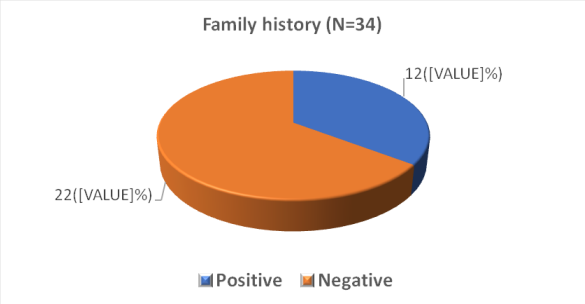

Figure 2: Family History Distribution

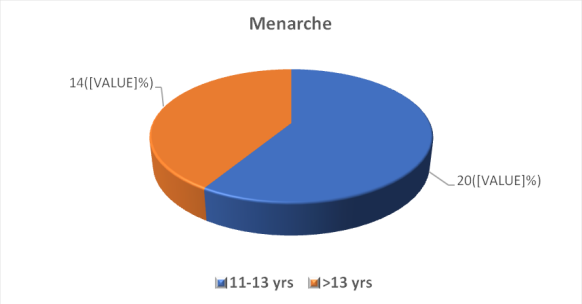

Figure 3: Menstrual History Distribution

Parity and breastfeeding history were assessed, revealing that 79.41% of the participants were multiparous (Table 9), and 82.35% had a history of breastfeeding (Table 10).

Table 9: Distribution of History of Parity (N=34)

Parity	Frequency (n)	Percentage (%)
Multipara	27	79.41
Primipara	7	20.59

Table 10: Distribution of Breastfeeding History (N=34)

Status	Frequency (n)	Percentage (%)
Yes	28	82.35
No	6	17.65

Expression Levels of MMP11

The expression of MMP11 was significantly higher in tumor tissues compared to normal tissues. The median expression of MMP11 in tumor tissues was 3.402 (IQR: 2.097928–5.133258), whereas in normal tissues, it was 1.895 (IQR: 1.306810–2.128615). The differ-ence was statistically significant, with a p-value of 0.002 as determined by the Mann-Whitney U test (Table 11).

Table 11: Expression of MMP11 Gene Between Normal and Tumor Tissue (N=34)

MMP11	Normal (n=34)	Tumor (n=34)	P-Value
Median	1.895	3.402	0.002
IQR	1.306810–2.128615	2.097928–5.133258	

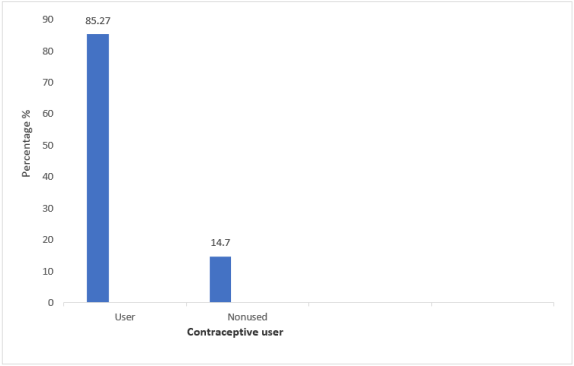

Figure 4: Distribution Of Contraceptive Use Of Study Subjects

Correlation Analysis

The correlation of MMP11 expression with demographic and clinical features was analyzed using Spearman correlation. No significant correlations were observed between MMP11 expression and variables such as age (rho = -0.035, p = 0.775), BMI (rho = 0.226, p = 0.063), family history (rho = 0.126, p = 0.307), menarche age (rho = 0.099, p = 0.423), contracep-tive use (rho = -0.205, p = 0.093), parity (rho = 0.121, p = 0.326), or breastfeeding history (rho = -0.195, p = 0.111) (Table 12 & Figure 5).

Discussion

Breast cancer is a multifaceted and diverse illness that

Table 12: Correlation of MMP11 Expression with Demographic Variables (N=34)

Variables	Spearman Correlation (rho)	P-Value
Age (years)	-0.035	0.775
BMI	0.226	0.063
Family history	0.126	0.307
Menarche (Years)	0.099	0.423
Contraceptive use	-0.205	0.093
Parity	0.121	0.326
Breastfeeding	-0.195	0.111

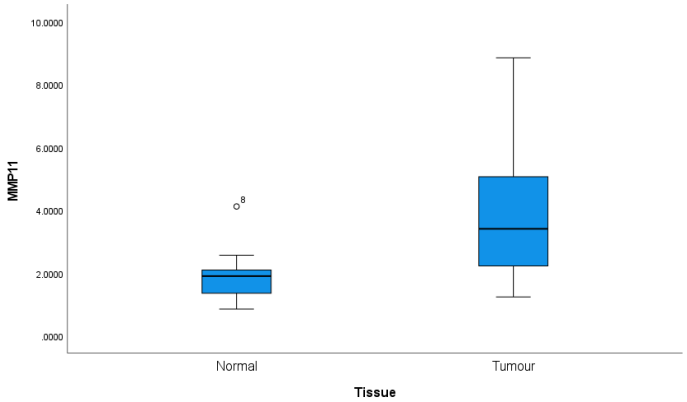

Figure 5: Matrix Metalloproteinase 11 (MMP11) Gene Between Normal and Tumor Tissue

has a significant global health im-pact, particularly on women. The prevention and treatment of breast cancer remain major public health concerns, despite recent notable advancements in early detection and custom-ized therapies reducing the death rate from the disease. Thus, in order to significantly en-hance the prognosis of patients with breast cancer, novel prognostic factors are required. The breakdown of the basement membrane and stromal connective tissue, which are essen-tial components during tumor invasion and metastasis, is facilitated by metalloproteinases. While MMP11 has been found to express itself at high levels in a number of cancer types, its expression level and predictive value in breast cancer are yet unknown (Wei *et al.*, 2022). The purpose of this study was to assess the expression of MMP11 and the prevalence of MMP11 gene mutations in breast cancer patients from Bangladesh. The Next Generation Sequencing (NGS) technology was used to perform the treatment on thirty-four (34) female patients who were selected from the Department of General Surgery at Dhaka Medical Col-lege Hospital (DMCH) for this study.

The present study was carried out on female breast cancer patients, with most participants (76.47%) diagnosed under the age of 50. This contrasts with the general trend where in-creasing age is one of the most significant risk factors for breast cancer. Breast cancer in younger women might be attributed to prolonged exposure to estrogen, genetic mutations such as BRCA1 and BRCA2, and unhealthy lifestyles, including obesity. Supporting this observation, studies by Han *et al.* (2017) and Malvia *et al.* (2019) similarly reported high incidences of breast cancer in younger age groups, aligning with the findings of this study.

In this study, 41.17% of patients had a body mass index (BMI) ≤25 kg/m². Although obesity is typically associated with higher estrogen levels and increased breast cancer risk, some evidence indicates that lower BMI correlates with higher adiponectin levels, which may re-duce tumorigenic factors. Studies such as Denkert *et al.* (2017) and Stead *et al.* (2009) pro-vide similar insights into the complex relationship between BMI and breast cancer, with results aligning or inversely correlating depending on regional and population-specific fac-tors. Regarding family history, 64.70% of patients reported no family history of breast can-cer. Similar findings were noted by Hossain *et al.* (2014), suggesting that lack of familial predisposition might not exclude the risk of breast cancer, potentially influenced by un-derreporting or lack of genetic testing. Conversely, studies by Forazi *et al.* (2015) and other international cohorts highlight the significant role of positive family history as a risk factor, underscoring the diversity in study populations and methodologies. The age of menarche was found to be 11–13 years for 58.82% of the participants. Early menarche increases breast cancer risk due to prolonged exposure to estrogen. Hossain *et al.* (2014) and studies con-ducted in Turkey, Italy, and Japan (Fu *et al.*, 2015) reported similar findings, emphasizing early menarche as a strong risk factor. In contrast, studies such as Pathak *et al.* (2018) re-ported differing results, underscoring the need for further investigation into regional and environmental influences.

In this study, 85.27% of patients reported contraceptive use, which may elevate breast cancer risk due to synthetic hormonal compositions. Prolonged contraceptive use has been associated with increased breast cancer risk in studies by Fu *et al.* (2015), while other studies like Pathak *et al.* (2018) found no significant association. These conflicting results highlight the complex role of exogenous hormones in breast can-cer development. Multiparity was observed in 79.41% of participants. While multiple preg-nancies are generally considered protective against breast cancer, the reproductive period's double effect—initially increasing risk after childbirth before conferring protection—is well-documented. Similar patterns were noted in studies by Chakraborty *et al.* (2015) and Zannat *et al.* (2015). Breastfeeding, a well-recognized protective factor, was reported by 82.35% of patients. Despite its protective role, the high prevalence of breastfeeding in this study might reflect sampling bias or other socio-cultural factors. Studies by Johnson *et al.* (2022) and Eiro *et al.* (2019) corroborate the complex relationship between breastfeeding and breast cancer risk. The study's findings also revealed significant overexpression of MMP11 in tumor tissues compared to normal tissues, with a statistically significant difference ($p=0.02$). These re-sults align with previous research suggesting that MMP11 overexpression correlates with aggressive subtypes of breast cancer and poor prognosis (Malvia *et al.*, 2019; Fu *et al.*, 2015). While correlations with BMI, family history, age of menarche, and parity were in-significant, the observed overexpression underscores the potential of MMP11 as a bi-omarker for breast cancer prognosis and treatment.

This study provides valuable insights into the demographic and clinical factors associated with breast cancer in Bangladesh and highlights the critical role of MMP11 in breast cancer progression. However, limitations such as the small sample size and regional focus necessi-tate further large-scale studies to validate these findings and explore the underlying mecha-nisms of MMP11's role in breast cancer.

Future Work

Future studies should focus on expanding the sample size to include diverse populations to better understand the relationship between MMP11 expression and breast cancer risk fac-tors. Advanced genomic and proteomic analyses could further elucidate the molecular mechanisms underlying MMP11's role in breast cancer progression. Additionally, exploring the therapeutic potential of targeting MMP11 in breast cancer treatment and conducting longitudinal studies to assess its prognostic significance would provide valuable insights. Integrating these findings with personalized medicine approaches may enhance early detec-tion and improve treatment outcomes for breast cancer patients.

CONCLUSION

This study highlights the critical role of MMP11 in breast cancer progression, demonstrat-ing its significantly higher expression in tumor tissues compared to adjacent normal tissues. The findings reveal that while correlations between MMP11 expression and demographic or clinical factors such as BMI, family history, age at menarche, parity, contraceptive use, and breastfeeding history were largely insignificant, the consistent overexpression of MMP11 suggests its potential as a biomarker for breast cancer. These results underscore the im-portance of molecular-level investigations in understanding tumor biology and identifying novel prognostic markers. Clinically, these findings could inform targeted therapeutic strat-egies aimed at modulating MMP11 activity to curb tumor invasion and metastasis. Howev-er, the limited sample size and the study's cross-sectional design emphasize the need for larger, longitudinal studies to validate these findings. Future research should also explore the functional mechanisms of MMP11 in breast cancer and its interactions with other mo-lecular pathways to enhance its applicability in personalized medicine. The study under-scores an urgent call for continued exploration into the genetic underpinnings of breast can-cer to improve early diagnosis, treatment strategies, and patient outcomes.

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