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Original Article

Prognostic Significance of COL10A1 Overexpression in Breast Cancer Patients from Different Sociodemographic Backgrounds

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Abstract

Background: Breast cancer is the most common cancer among women worldwide and shows wide variation in how it behaves and how patients respond to treatment. Identifying dependable molecular biomarkers that are linked to prognosis and sociodemographic factors is important for improving personalized care. Collagen type X alpha 1 chain (COL10A1) has recently gained attention as a possible biomarker because of its role in tumor progression and remodeling of the extracellular matrix.

Objective: To assess the prognostic value of COL10A1 overexpression in breast cancer patients and to examine its relationship with selected sociodemographic and clinicopathological characteristics.

Materials and Methods: This cross-sectional study was conducted in the department of Biochemistry, Dhaka medical college, Dhaka in collaboration with Institute for Population and Precision Health, Department of Public Health Science, the University of Chicago, USA from July 2022 to June 2023 after receiving approval from Research Review Committee and Ethical Review Committee. Thirty-four female patients with histopathologically confirmed breast cancer were recruited from the Department of General Surgery and the Breast Clinic of Dhaka Medical College Hospital (DMCH). Sociodemographic and clinical information was collected using a structured questionnaire, and COL10A1 gene expression was measured from tumor tissue samples using standard molecular techniques. Statistical analyses were performed to explore associations between COL10A1 expression, sociodemographic factors, and prognostic indicators.

Results: A considerable number of patients showed overexpression of COL10A1. Higher expression levels were significantly associated with advanced tumor stage, lymph node involvement, and other poor prognostic features. Differences in COL10A1 expression were also noted among various age groups and socioeconomic categories, suggesting a possible link between molecular expression patterns and sociodemographic background.

Conclusion: COL10A1 overexpression appears to be a promising prognostic biomarker in breast cancer. Its strong association with adverse clinicopathological characteristics indicates that it may be useful for risk assessment and personalized treatment planning, particularly in settings with limited resources.

Keywords: Breast cancer, COL10A1, Prognostic biomarker, Gene expression, Sociodemographic factors.

Introduction

Breast cancer is the most frequently diagnosed malignancy and one of the leading causes of cancer-related mortality among women worldwide. Global cancer statistics indicate that breast cancer constitutes a significant proportion of female cancer incidence and deaths, with a rising burden particularly evident in low- and middle-income countries.[1] In Bangladesh, breast cancer represents a significant public health challenge, with many patients presenting at advanced stages due to delayed diagnosis, low screening uptake, and limited access to specialized oncology services; these factors contribute to poor outcomes and underscore the need for improved awareness, early detection programs, and strengthened cancer care infrastructure.[2] These challenges often result in late-stage presentation and unfavorable

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clinical outcomes. Breast cancer is a biologically heterogeneous disease comprising multiple molecular subtypes that exhibit diverse clinical behaviors, prognoses, and responses to therapy. Traditional prognostic factors—such as tumor size, histological grade, lymph node status, and hormone receptor expression—remain fundamental to clinical management; however, they are insufficient to accurately predict disease progression and patient outcomes in all cases.[3] As a result, increasing attention has been directed toward identifying novel molecular biomarkers that more precisely reflect tumor biology and enhance prognostic stratification. The tumor microenvironment, particularly the extracellular matrix (ECM), plays a pivotal role in breast cancer initiation, invasion, and metastasis. Alterations in ECM components can promote tumor progression by stimulating angiogenesis, facilitating epithelial–mesenchymal transition, and enabling metastatic spread.[4,5] Among ECM-associated molecules, members of the collagen family have attracted considerable interest due to their involvement in tumor progression and stromal remodeling. Collagen type X alpha 1 chain (COL10A1) is a short-chain collagen that is primarily expressed during endochondral ossification and skeletal development, with negligible expression in most normal adult tissues. Accumulating evidence suggests aberrant re-expression of COL10A1 in various solid malignancies, including breast, colorectal, lung, and gastric cancers.[6,7] In breast cancer, COL10A1 expression is predominantly localized to the tumor stroma and neovasculature, indicating a potential role in tumor–stromal interactions.[8] Recent transcriptomic and immunohistochemical analyses have shown that elevated COL10A1 expression is associated with aggressive tumor characteristics, advanced disease stage, lymph node metastasis, and poorer survival outcomes in breast cancer patients.[9-11] Mechanistically, COL10A1 is thought to contribute to ECM remodeling, increased tissue stiffness, and activation of pro-tumorigenic signaling pathways, thereby promoting invasion and metastasis [12].

Despite these observations, the majority of existing studies have been conducted in Western or East Asian populations. There remains a significant lack of data regarding the prognostic significance of COL10A1 in South Asian populations, where genetic heterogeneity, environmental factors, and sociodemographic conditions may influence tumor behavior. Elucidating the expression patterns and clinical relevance of COL10A1 in this setting is therefore crucial for the development of population-specific prognostic markers. Accordingly, the present study aimed to assess the prognostic significance of COL10A1 overexpression in breast cancer patients from diverse sociodemographic backgrounds in Bangladesh and to examine its association with clinicopathological features.

Materials and Methods

Study Design and Setting: This cross-sectional study was conducted at the Department of Biochemistry, Dhaka Medical College, Dhaka, in collaboration with the Institution for Population and Precision Health, Department of Public Health Sciences, The University of Chicago Biological Sciences, USA after receiving approval from Research Review Committee and Ethical Review Committee. A total of 34 female patients with histopathologically confirmed breast cancer were enrolled. The study was carried out between July 2022 to June 2023 from the Department of General Surgery and the Breast Clinic of Dhaka Medical College Hospital (DMCH).

Inclusion Criteria: Female patients with a confirmed histopathological diagnosis of breast cancer were eligible for inclusion. Participants were required to provide informed written consent and to have sufficient tumor tissue available for molecular analysis.

Exclusion Criteria: Patients who had undergone neoadjuvant chemotherapy or radiotherapy prior to tumor tissue collection were excluded to minimize treatment-related effects on molecular expression. Patients with recurrent disease or evidence of distant metastasis at initial presentation were also excluded.

Data Collection: Sociodemographic information, including age, place of residence, educational level, and socioeconomic status, along with clinicopathological data such as tumor size, histological grade, lymph node involvement, and disease stage, were collected through structured questionnaires and review of medical records.

Laboratory Analysis: Tumor tissue samples were processed according to standard laboratory protocols. COL10A1 gene expression was quantified using appropriate molecular methods, including quantitative real-time polymerase chain reaction (qRT-PCR). Expression levels were classified as overexpressed or low/normal based on predefined cutoff values.

Statistical Analysis: Statistical analyses were performed using SPSS version 26.0. Descriptive statistics were applied to summarize the study variables. Associations between COL10A1 expression and sociodemographic as well as clinicopathological parameters were assessed using suitable statistical tests, with a p-value of less than 0.05 considered statistically significant.

Results

A total of 34 histopathologically confirmed female breast cancer patients were included in the final analysis. The results are presented across ten tables summarizing sociodemographic characteristics, clinicopathological features, and their association with COL10A1 expression.

Table I. Sociodemographic Characteristics of the Study Population (n=34)

Variable	Category	Frequency (n)	Percentage (%)
Age (years)	<40	8	23.5
	≥40	26	76.5
Residence	Urban	20	58.8
	Rural	14	41.2
Education	≤Secondary	19	55.9
	>Secondary	15	44.1
Socioeconomic status	Low–Middle	21	61.8
	Upper	13	38.2

Table I shows that most participants (26/34, 76.5%) were aged ≥40 years, while 8 (23.5%) were under 40. Urban residents were slightly higher (20/34, 58.8%) compared to rural (14/34, 41.2%). Regarding education, 19 (55.9%) had up to secondary level, and 15 (44.1%) had higher education. Most patients belonged to low- to middle-income groups (21/34, 61.8%), while 13 (38.2%) were from upper-income groups.

Table II. Clinicopathological Characteristics of Breast Cancer Patients

Variable	Category	Frequency (n)	Percentage (%)
Tumor size	≤2 cm	10	29.4
	>2 cm	24	70.6
Histological grade	Grade I–II	18	52.9
	Grade III	16	47.1
Lymph node status	Negative	13	38.2
	Positive	21	61.8

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Table II shows the majority of tumors were larger than 2 cm (24/34, 70.6%), while 10 (29.4%) were ≤2 cm. Histological grading revealed 18 (52.9%) had Grade I–II tumors and 16 (47.1%) had Grade III. Lymph node involvement was observed in 21 patients (61.8%), whereas 13 (38.2%) were node-negative, indicating a high rate of regional disease at diagnosis.

Table III. Distribution of Clinical Stage at Diagnosis

Stage	Frequency (n)	Percentage (%)
Stage I	5	14.7
Stage II	16	47.1
Stage III	13	38.2

Table III indicates that Stage II was the most common at diagnosis (16/34, 47.1%), followed by Stage III (13/34, 38.2%), and Stage I (5/34, 14.7%). This shows that most patients were diagnosed at intermediate to advanced stages, highlighting the need for earlier detection and screening strategies.

Pattern of COL10A1 Gene Expression

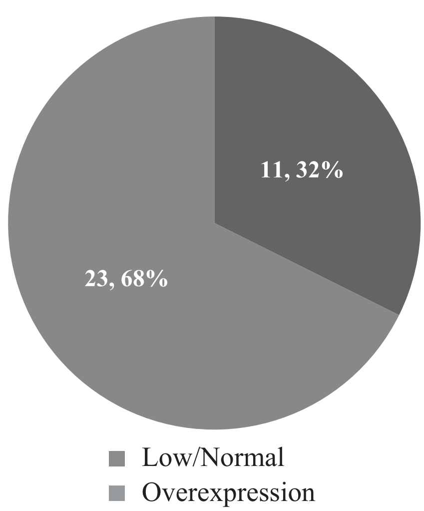

Fig 1. Pattern of COL10A1 Gene Expression

Figure 1 illustrates the distribution of COL10A1 gene expression among the study participants using a pie chart. The chart shows that a majority of patients (23 cases, 68%) exhibited COL10A1 overexpression, while a smaller proportion (11 cases, 32%) demonstrated low or normal expression levels.

Table IV. Association Between COL10A1 Expression and Age Group

Age Group	Low/Normal	Overexpression	p-value
<40 years	4	4	0.041
≥40 years	7	19	

Table IV shows that among patients <40 years, COL10A1 overexpression was observed in 4 out of 8 patients, while the other 4 had low/normal expression. In patients ≥40 years, 19 out of 26 showed overexpression, and 7 had low/normal levels. The association between age and COL10A1 expression was statistically significant (p=0.041), indicating higher expression in older patients.

Table V. Association Between COL10A1 Expression and Socioeconomic Status

Socioeconomic Status	Low/Normal	Overexpression	p-value
Low–Middle	5	16	0.038
Upper	6	7	

Table V demonstrates that 16 out of 21 patients from low–middle socioeconomic groups had COL10A1 overexpression, compared to 7 out of 13 patients from upper socioeconomic groups. Low/normal expression was observed in 5 and 6 patients from low–middle and upper groups, respectively. The association was significant (p=0.038), suggesting higher expression in lower socioeconomic patients.

Table VI Association Between COL10A1 Expression and Tumor Size

Tumor Size	Low/Normal	Overexpression	p-value
≤2 cm	6	4	0.009
>2 cm	5	19	

Table VI indicates that in tumors ≤2 cm, 6 patients had low/normal expression and 4 had overexpression. For tumors >2 cm, 19 patients showed overexpression, while 5 had low/normal levels. The difference was statistically significant (p=0.009), showing that COL10A1 overexpression is more frequent in larger tumors.

Table VII. Association Between COL10A1 Expression and Histological Grade

Grade	Low/Normal	Overexpression	p-value
Grade I–II	9	9	0.012
Grade III	2	14	

Table VII shows that COL10A1 overexpression was observed in 14 out of 16 Grade III tumors, compared to 9 out of 18 Grade I–II tumors. Low/normal expression was higher in Grade I–II (9 patients) than in Grade III (2 patients). The association was statistically significant (p=0.012), indicating higher expression in high-grade tumors.

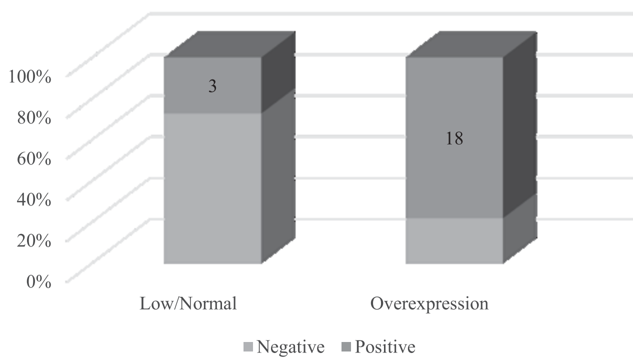

Fig 2. Association Between COL10A1 Expression and Lymph Node Status

Figure 2 shows the association between COL10A1 expression and lymph node status. In the Low/Normal group, most cases were lymph node negative (3 vs 1 positive), while in the Overexpression group, most were positive (18 vs 6 negative), indicating that COL10A1 overexpression is linked to higher lymph node involvement.

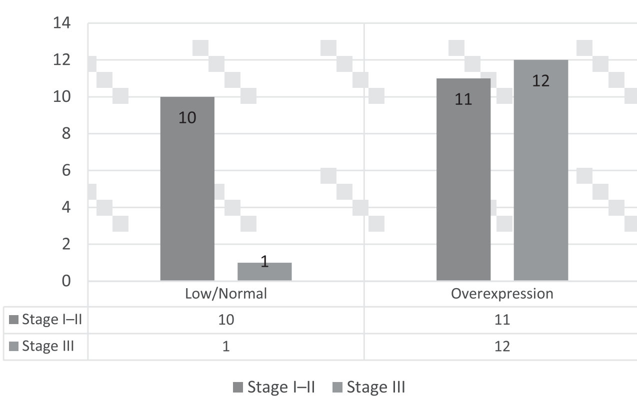

Fig 3. Association Between COL10A1 Expression and Clinical Stage

Figure 3 shows that low/normal COL10A1 expression is more common in Stage I–II (n=10) than Stage III (n=1), whereas COL10A1 overexpression is predominantly observed in Stage III (n=12) compared to Stage I–II (n=11). This indicates an association between COL10A1 overexpression and advanced clinical stage.

Discussion

The present study evaluated the prognostic significance of COL10A1 overexpression in breast cancer patients from Bangladesh and identified a strong association between elevated COL10A1 expression and unfavorable clinicopathological features. These findings contribute to the expanding evidence highlighting extracellular matrix–related genes as key regulators of tumor aggressiveness and disease progression. In the current cohort, COL10A1 overexpression was detected in nearly two-thirds of patients, aligning with prior transcriptomic and immunohistochemical studies that have reported higher COL10A1 expression in malignant breast tissues compared with normal controls.[13,14] The higher frequency of overexpression among patients aged ≥40 years may be indicative of age-associated alterations in tumor biology and stromal remodeling, consistent with earlier studies linking ECM dysregulation to tumor progression in older individuals.[15] A significant relationship was also observed between COL10A1 overexpression and lower socioeconomic status. Although the precise biological mechanisms underlying this association remain unclear, factors such as delayed diagnosis, reduced access to early screening, and prolonged tumor–stromal interactions in socioeconomically disadvantaged populations may contribute to increased ECM remodeling and gene overexpression.[16] This finding underscores the potential interplay between sociodemographic factors and molecular tumor characteristics in low- and middle-income countries. Notably, COL10A1 (collagen type X alpha-1) has been reported to be overexpressed in breast cancer and associated with

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tumor progression, including enhanced proliferation, migration, invasion, and poorer survival outcomes. Bioinformatics analysis and clinical studies indicate that elevated COL10A1 expression correlates with advanced clinical stage, unfavorable prognosis, and aggressive tumor behavior in breast cancer, supporting its role as a potential prognostic biomarker across diverse populations.[17–19] These observations support the hypothesis that COL10A1 facilitates tumor progression through extracellular matrix modification, increased tissue rigidity, and promotion of epithelial–mesenchymal transition and metastatic spread.[20] The strong association between COL10A1 overexpression and lymph node metastasis observed in this study suggests a potential role for COL10A1 in enhancing tumor invasiveness. These findings support the biological plausibility of COL10A1 contributing to metastatic dissemination through modulation of the tumor microenvironment.[21] A poor prognosis, haematogenous dissemination, and lymph node metastases are all associated with the abnormal overexpression of COL10A1 in the tumour stroma of solid tumor and cancer cell migration, thereby facilitating regional and distant metastasis. COL10A1 has a role in ECM remodelling and can interact with proteins including integrin subunit beta 1 and prolyl 4-hydroxylase subunit beta to promote tumour cell growth and metastasis.[22] Moreover, COL10A1 has been implicated in the activation of pro-tumorigenic signaling pathways, including TGF-β and PI3K/AKT, both of which are known to drive breast cancer progression.[23] Despite the limited sample size, this study offers important insights into the prognostic relevance of COL10A1 in a South Asian population, where molecular data on breast cancer are relatively scarce. The concordance of these results with findings from international studies enhances the biological plausibility of COL10A1 as a prognostic biomarker. Future large-scale, multicenter investigations incorporating survival analyses and functional studies are necessary to validate its clinical utility and to assess its potential as a therapeutic target in breast cancer management.

Conclusion

This study shows that overexpression of COL10A1 is closely linked to poor clinicopathological features in breast cancer patients, such as larger tumor size, higher tumor grade, lymph node involvement, and advanced disease stage. These findings suggest that COL10A1 may have an important role in driving tumor aggressiveness and disease progression. The fact that these associations were seen across different sociodemographic groups highlights the potential value of COL10A1 as a prognostic marker for breast cancer patients in Bangladesh. Including COL10A1 expression analysis in routine molecular testing could help improve risk assessment and guide more individualized treatment decisions, especially in settings with limited resources.

Recommendations

Future studies should include larger patient populations from multiple centers to confirm the prognostic role of COL10A1 in breast cancer. Long-term, prospective studies are needed to examine its relationship with survival and treatment response. Combining COL10A1 with other molecular and immunohistochemical markers may provide a more complete and accurate prognostic model. Further research into the biological mechanisms of COL10A1 in tumor progression could also support the development of targeted therapies. Finally, integrating molecular research with sociodemographic and public health perspectives may help promote more equitable and effective precision oncology in Bangladesh.

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