Correlation of N-telopeptide of type 1 collagen and C-telopeptide of type 1 collagen in Iraqi women with breast cancer

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Abstract

Breast cancer is one of the most common cancers worldwide. It is a varied sickness that is the leading cause of cancer-related mortality in women. Prognostic biomarkers, N-telopeptide of type 1 collagen (NTX-1) and C-telopeptide of type 1 collagen (CTX-1), are undergoing increasing amounts of research; nevertheless, additional studies are required to enhance specificity and ascertain the true therapeutic utility of specific indications. The ELISA method was utilized to measure the levels of both (CTX-1 and NTX-1). These markers were examined at the Oncology Teaching Hospital in the Medical City of Baghdad, in the serum of ninety women, fourty of whom were healthy and fifty of whom had the disease. The women's ages ranged from 40 to 60 years old. The statistical research showed that NTX-1 levels were significantly increased in the subjects with the disease, while CTX-1 did not reveal any discernible variation in comparison with healthy subject's, with p-values (P≤0.0001). The best marker for breast cancer diagnosis, according to a Receiver Operating Characteristic curve analysis, is NTX-1. Our results indicate that serum NTX-1 has potential applications as a prognostic biomarker for bone metastases of several cancers, including breast cancer in Iraqi women.

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Key words: N-telopeptide of type 1 collagen; C-telopeptide of type 1 collagen; serum blood; breast cancer.

Contributions: ZAS carried out the Biochemistry studies and the immunoassays (ELISA), participated in the design of the study; RAA participated in the study design and coordination and participated in the sequence alignment and drafted the manuscript; HKM performed the statistical analysis. All authors read and approved the final manuscript.

Conflict of interest: authors do not have any conflict of interests to declare.

Ethics approval: this study was approved by the Research Ethics Committee of the College of Dentistry, University of Baghdad, Baghdad, Iraq. Committee number 930 dated July 24, 2024. A signed written consent was obtained from each individual participating in the study.

Received: 17 June 2024.
Accepted: 11 January 2025.
Early view: 11 April 2025.

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Journal of Biological Research 2025; 98:12728
doi:10.4081/jbr.2025.12728

Introduction

After heart disease and stroke, cancer ranks third in terms of the primary causes of mortality worldwide.[1,2] Cancer was the cause of 10 million deaths worldwide in 2020.[3] With 2,088,849 cases reported worldwide in 2018, breast cancer accounted for 11.6% of all new cancer cases.[4] A better prognosis and rate of survival for breast cancer patients have been made possible by advances in screening and treatment.[5,6]

The majority of people with initial breast cancer die as a result of metastases. A number of prognostic pathologic indicators are employed in clinical practice to pinpoint the individuals who are most at risk of passing away due to metastatic spread. Additionally, evaluating biomarkers that could possibly be involved in tumor pathology allows physicians to select people with breast cancer for certain chemotherapies.[7] Matricellular proteins operate as mediators for a variety of cellular processes, such as cell adhesion and migration, Extra Cellular Materials (ECM) deposition, cell proliferation, and cell survival.[8,9] When bone metastasis begins, the morphological alterations appear much later than the changes in biochemical markers of bone metabolism[10]. The traditional biochemical markers of bone metabolism, however, have a low specificity and a limited range of applications in clinical practice due to their susceptibility to many variables. A number of biochemical markers of bone metabolism, sensitive indicators of bone resorption, such as Carbon Terminal Peptide (CTX), type1 collagen cross-linked Carboxy Terminal Peptide (ICTP), and N-Telopeptide of type1 collagen (NTX), were discovered recently.[10] These markers are now used in the clinical estimation of metabolic bone diseases.[10] According to Zhang *et al.*, they can also be helpful markers for treating and diagnosing metastatic bone cancers.[11] Wang *et al.*[12] demonstrated the growth of both osteoclastic and osteoblastic bone metastases. While not much is known regarding the function of osteoblasts, activating osteoclasts is a key aspect of breast bone disease brought on by cancer.[13]

Materials and Methods

Fifty women with breast cancer (phase II) and forty healthy women serving as case-controls were enrolled in the study. The Oncology Teaching Hospital in the Medical City in Baghdad between January and February 2024 has selected every patient with breast cancer. The samples were divided into two groups: group 1: 50 women with breast cancer, while group 2: 40 healthy women. Under standard conditions, blood samples were taken from all participants. A venous blood specimen (5 mL) was collected in a gel tube; the serum was removed after centrifugation at 3,000 rpm, for 10 minutes and stored at -20°C until analysis. Serum NTX-1 and CTX-1 in the samples were measured using the enzyme-linked immune-sorbent assay (ELISA) method by double antibody sandwich.

Inclusion criteria

Age: 40-60 years old also with breast cancer disease from phase II without any chemotherapy trials.

Exclusion criteria

Other malignancies such as stomach cancer, lung cancer, or diseases such as Inflammatory Bowel Disease (IBD), diabetes, kidney illness, and rheumatoid arthritis.

Statistical analysis

The study variables were analysed using SPSS by using Receiver Operating Characteristic (ROC) curve analysis and were expressed as mean ± Standard Deviation (SD). A P value ≤0.0001 was considered as significant.

Results

While the levels of NTX-1 in breast cancer patients were found to be substantially lower than those of healthy controls, the levels of CTX-1 in the blood were not statistically dissimilar between the two groups. Table 1 shows the mean and SD for NTX-1 and CTX-1, while Table 2 shows significant differences between healthy women and women with breast cancer, as it was found that NTX-1 marker was 0.278 ng/mL, which is higher in breast cancer patients than in the control. In contrast, CTX-1 showed non-significant difference between control and the breast cancer women patient's group.

The values of NTX-1 (0.810 ng/mL) and CTX-1 (0.729 ng/mL) were higher in patients compared to healthy group as can be showed in Table 3 and Figure 1, which were found to be significant (P≤0.0001); the ROC curve analysis was used for predicting the response to treatment in breast cancer patients and the evaluation of the diagnostic value of CTX-1 and NTX-1. This curve confirmed that the current results showed an excellent prediction of Area Under the Curve (AUC).

Discussion

In this study, serum CTX-1 and NTX-1 were measured in individuals with and without breast cancer. The difference of means between the groups was calculated. According to a number of studies, high NTX levels have been linked to a bad prognosis for cancer patients.[14,15] other researchers, however, asserted that NTX and cancer prognosis were unrelated.[16,17] Furthermore, Li *et al.* discovered that NTX had a high sensitivity (98.3%) for diagnosing bone metastasis.[18] However, Ulrich *et al.* study found that NTX had a comparatively low sensitivity (44%) for diagnosing cancer Bone Metastases (BM).[19] Regretfully, no relevant meta-analysis was available to assess the impact of NTX level on early detection and prognosis prediction for human cancer with BM. NTX and CTX may serve as sensitive indicators of BM associated with breast cancer. For example, NTX levels were considerably greater in a small unit of 19 patients with BM compared to individuals with other bone illnesses (n = 22) or BM with breast cancer absence (n = 65).[20] Furthermore, NTX may be employed as a marker to track how well BM patients with breast cancer are responding to treatment. According to Chung *et al.*,[21] NTX levels sharply decreased in individuals with breast cancer BM who responded to anticancer therapy, while they elevated in non-responsive. Another study by Li *et al.* showed that AUC for Asian individuals was 0.86 (0.83 ± 0.89)%. The pooled Hazard Ratio (HR) was 2.12 (1.74 ± 2.58) for high versus low NTX-1 level in the prognosis of human

Table 1. Comparison of C-telopeptide of type 1 collagen (CTX-1) and N-telopeptide of type 1 collagen (NTX-1) values between patients and control groups.

Group	Mean±SD CTX-1 (ng/mL)	Mean±SD NTX-1 (ng/mL)
Patients	0.275 ±0.007	0.358 ±0.009
Control	0.291 ±0.006	0.291 ±0.006
P-value	0.0918 NS	0.0001****

NS, non-significant, **** (P≤0.0001).

Table 2. Correlation between N-telopeptide of type 1 collagen (NTX-1) and C-telopeptide of type 1 collagen (CTX-1).

		NTX-1 (ng/mL)
CTX-1 (ng/mL)	Pearson Correlation	0.278
	Sig. (2-tailed)	0.082
	Number	40

Table 3. Receiver Operating Characteristic (ROC) curve analysis of N-telopeptide of type 1 collagen (NTX-1) and C-telopeptide of type 1 collagen (CTX-1).

Markers	AUC %	Standard error	AUC P value	Confidence interval	
				Lower limit	Upper limit
NTX-1 (ng/mL)	0.810	0.047	P≤0.0001	0.717	0.903
CTX-1 (ng/mL)	0.729	0.056	P≤0.0001	0.619	0.838

AUC, Area under the curve.

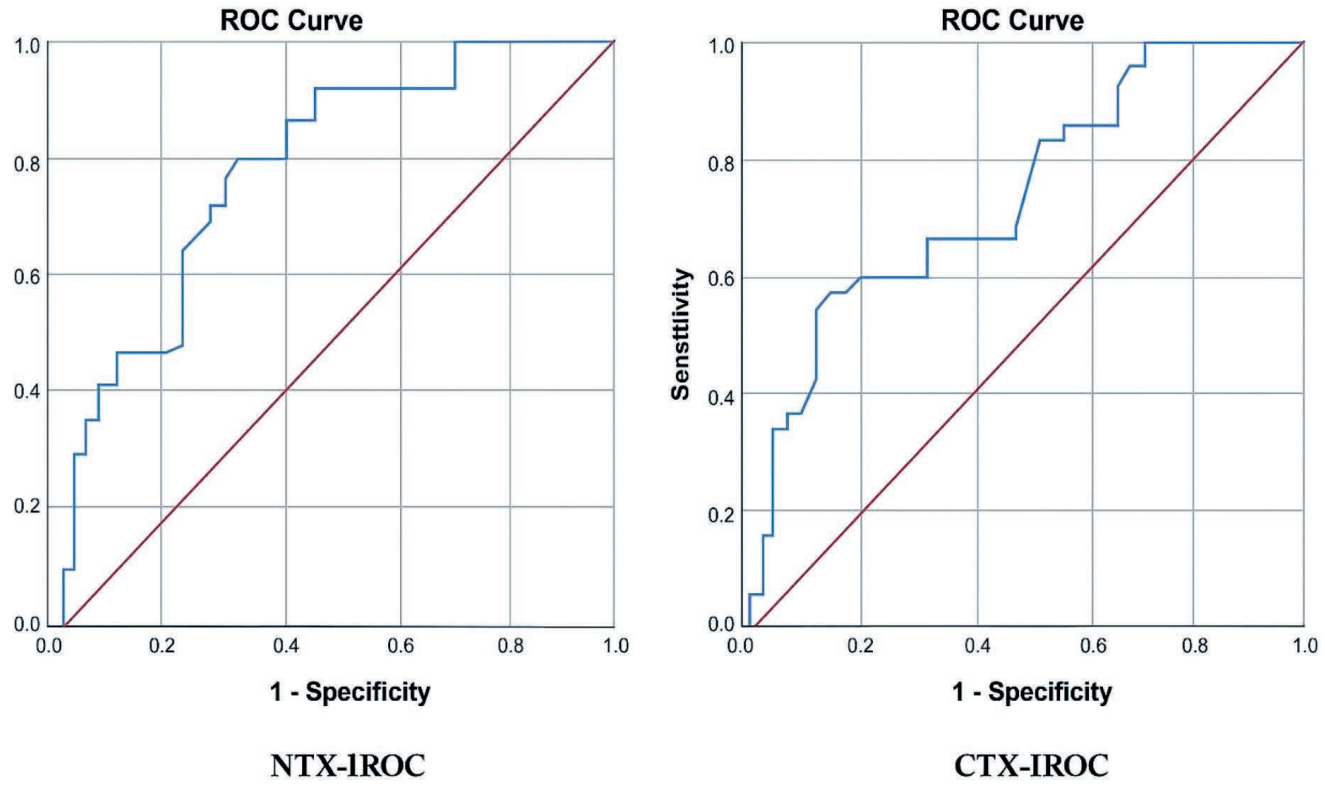

Figure 1. ROC curve of N-telopeptide of type 1 collagen (NTX-1) and C-telopeptide of type 1 collagen (CTX-1) in breast cancer.

malignancies with bone metastases, suggesting that a high NTX level would raise the probability of a poor overall survival.[10] Furthermore, it was shown that CTX could both expect and facilitate the identification of breast cancer BM.[10] When breast cancer patients without BM (n = 28) and those with BM (n = 50) had their serum CTX levels examined, Zulauf *et al.*[22] discovered that the CTX level in patients with BM was considerably greater compared to those of individuals without BM. They hypothesised that CTX values might be employed as a method to identify and rule out BM.[22] The AZURE experiment was a large phase III clinical research in which Brown *et al.*[23] evaluated the levels of CTX in 872 individuals who had breast cancer at the initial stages. They discovered that the elevated CTX level was predictive of BM recurrence. Finally, while the response to adjuvant therapy with zoledronate was not shown to be predicted by CTX and NTX levels, these parameters are anticipated to be predictive of treatment efficacy for BM.[15,23] We came to the conclusion that NTX would be a useful diagnostic and prognostic biomarker for human cancers, despite the contradictory findings from several studies about the relevance of NTX in cancer diagnosis and prognostic prediction.[24,25]

Conclusions

Recent studies have improved our knowledge of tumor characteristics, which has increased our knowledge of breast cancer biomarkers. Our results demonstrate the potential of serum NTX-1 as a biomarker for BM of a variety of cancers, including breast cancer in Iraqi women, and as a prognostic indicator for these biomarkers. Breast cancer is becoming more prevalent and lethal in people in Iraq, where it is still mostly a disease of the elderly. To account for these serious changes, health policy involving breast cancer, as well as public awareness, screening, and management techniques, must be reconsidered.

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