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Evaluation of Serum and Urine Dickkopf-1 Concentrations and Their Relation with Lipid Profile in Iraqi Women with Breast Carcinoma

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Abstract: Invasive ductal carcinomas account for approximately 70%–80% of all breast carcinoma (BC) cases. Dickkopf-1 (DKK-1) is a glycoprotein secreted by the tumour that functions as a negative regulator of Wnt signalling. Various clinical disorders have been linked to the misregulation of Wnt signalling. Several research groups have demonstrated that DKK-1 inhibits the Wnt signalling pathway by forming complexes on the cell surface with low-density lipoprotein receptor-related proteins 5 and 6, rather than directly interacting with Wnt or Frizzled proteins. This project aims to investigate the correlation between serum and urine concentrations of DKK-1 and their relation with lipid profiles in Iraqi women with BC. We compare these findings to those obtained for control and first-degree relative groups and assess whether urine can serve as an alternative to serum for measuring DKK-1 levels. Fasting serum and urine DKK-1 levels, as well as serum lipid profiles, were assessed in 29 patients with BC, 29 first-degree relatives, and 30 age-matched healthy controls. An enzyme-linked immunosorbent assay was employed to measure DKK-1 concentrations in both serum and urine, while the Roche Cobas c111 system was used to analyse urine creatinine and lipid profiles. The concentrations of DKK-1 in urine and serum were significantly higher in patients who BC compared to first-degree relatives and healthy controls ($p < 0.01$). Total cholesterol and low-density lipoprotein levels in the BC group were elevated compared to the control group, with the first-degree relative group falling in between. Triglyceride and very low-density lipoprotein levels did not show significant differences between the BC and control groups; however, the first-degree relative group had the highest concentrations, which were statistically different from the control group but not from the BC group. high-density lipoprotein concentrations were not significantly different among the three groups ($p = 0.093$). Receiver operating characteristic curve analysis indicated that the optimal diagnostic thresholds for serum and urine DKK-1 were 196.00 and 270 pg/mL, respectively. These findings suggest that DKK-1 serves as a valuable biomarker for diagnosis and prognosis, as well as a potential treatment option, for BC.

Keywords: *Dickkopf-1, Canonical pathway, WNT signaling, ELISA, IDC, Biomarker.*

1. Introduction

Breast carcinoma (BC), a heterogeneous disease marked by the progressive accumulation of genetic abnormalities (Mohammed *et al*., 2023), is considered a leading cause of morbidity and mortality among women globally (Testa *et al*., 2020). The risk factors of BC rise rapidly with age (Ahmad *et al*., 2022; Mahmoud *et al*., 2025). Genetic factors play a significant role in the development of hereditary BC (Afzal *et al*., 2022). In Iraq, the incidence of new cancer cases increased from 2000 to 2021. In 2021, BC emerged as the leading cause of mortality among Iraqi women and ranked among the top 10 cancers, with 7,246 cases representing 30.63% of all cancer diagnoses (Iraqi Cancer board, 2021). BC is classified into five major intrinsic or molecular subgroups based on gene upregulation patterns (Bhushan *et al*., 2021). The Wnt signalling pathway is an evolutionarily conserved signal transduction cascade that influences a wide range of processes, from embryonic development to tissue regeneration (Zhang and Wang, 2020). This pathway is further divided into canonical (β-catenin-dependent), which primarily regulates cell proliferation, and non-canonical (β-catenin-independent), which governs cell polarity and migration (Azbazdar *et al*., 2021)—both of which contribute to cancer development and dissemination, forming a network of mutual regulation (Perugorria *et al*., 2019; Liu *et al*., 2022). Various clinical disorders have been linked to the misregulation of the Wnt signalling pathway (Winter and Nusse, 2021). Multiple groups have demonstrated how Dickkopf-1 (DKK-1) blocks the Wnt signalling pathway (Castagnoli *et al*., 2020; Chu *et al*., 2021). DKK-1 is a glycoprotein with a molecular weight of 26 kDa, featuring two cysteine-rich domains and a peptide sequence of 50–55 amino acids (Shao *et al*., 2017). The human DKK-1 gene, located on chromosome 10q11.2.26, spans 1,815 kb in length (Zhu *et al*., 2021). When Wnts are activated, they bind to their receptors, which consist of frizzled proteins and low-density lipoprotein receptor-related proteins 5 and 6 (LRP5/6) (Chu *et al*., 2021). This activation triggers the cytoplasmic protein disheveled, leading to the inhibition of glycogen synthase kinase-3β (GSK-3β). Stabilised β-catenin then translocates to the nucleus, where it binds to T-cell factor/lymphoid enhancer factor transcription factors, resulting in the transcription of target genes

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(Zhu *et al*., 2021). When the Wnt signalling pathway is inactive and Wnt ligands are absent, a degradation complex that comprises β-catenin, Axin, casein kinase I, GSK-3β, and adenomatosis polyposis coli is formed. This complex phosphorylates β-catenin, leading to its subsequent ubiquitin-proteasomal degradation (Zhao *et al*., 2022). Several studies have measured sera concentrations of DKK-1 in patients with BC and healthy controls; however, the findings are also controversial. Such as a study by two studies in China discovered that sera concentration of DKK-1 in women with breast carcinoma were much greater than those in healthy individuals (Zhou *et al*., 2014; Liu *et al*., 2017). Till now, there are no studies done in Iraq on DKK-1 in sera as well as urine and no studies on DKK-1 in urine in the world.

Cancer metabolism can be categorised into two levels: cellular metabolism and metabolism associated with tumour presence. A key characteristic of cancer is the elevated production of fatty acids (Santos *et al*., 2023). Cancer cells exhibit elevated *de novo* fatty acid synthesis to support membrane biogenesis, creation of signalling molecules, and energy production (Chen *et al*., 2022).

Monoacylglycerol lipase is a key enzyme involved in cancer growth, contributing to energy supply through fatty acid oxidation. It also enhances the aggressiveness of cancer cells by promoting proliferation through the production of signalling lipids (Jaiswal and Ayyannan, 2021). In hypertrophic obesity, inadequate suppression of the Wnt classical pathway occurs due to the failure of DKK-1 gene expression in adipocyte precursor cells (Reinhold *et al*., 2020). Thus, DKK-1 inhibits the migration and invasion of BC cells through the suppression of β-catenin/MMP7 pathway, so it could be beneficial for BC therapy (Niu *et al*., 2019). Hence, this project aims to investigate the correlation between the serum and urine concentrations of DKK-1 and their relation with lipid profiles in Iraqi women with BC. We compare these findings to those obtained for control and first-degree relative groups and assess whether urine can serve as an alternative to serum for measuring DKK-1 levels.

2. Materials and Methods

Patients and Specimens

The case-control study involved 88 women divided into three groups: Group 1 involved 29 patients with BC, Group 2 consisted of 29 first-degree relatives, and Group 3 had 30 controls. All participants were treated at the Oncology Teaching Hospital in Medical City and were referred from various hospitals in Baghdad, Iraq, between November 2022 and April 2023. The Institutional Review Board (IRB) approval for this research was obtained on 14 October 2022 (approval number 20221014). The participants' ages ranged from 25 to 57 years. All patients were diagnosed according to WHO classification prior to surgery and cancer treatment, with all having invasive ductal carcinoma. Notably, 45% had a family history of tumours. All patients were estrogen receptor-positive and human epidermal growth factor receptor 2-negative; they were classified as grade II, stage I, or II.

Fasting serum and urine samples were collected from all participants. None of the examined groups had diabetes mellitus, liver disease, renal disease, heart disease, or osteoporosis. All participants were non-smokers and non-pregnant and had not taken any anti-inflammatory medications, including non-steroidal anti-inflammatory drugs.

Samples

Fasting blood samples (5 mL) and early morning mid-stream urine samples (10 mL) were collected after the participants provided consent and completed a face-to-face questionnaire. Blood was allowed to stand at room temperature for 30 min to ensure complete clotting. Urine samples were collected in disposable screw-top containers for analysing the study parameters. The specimens were then centrifuged at 4,000 revolutions per minute for 10 min. The extracted serum was used to determine the concentrations of cholesterol, triglycerides, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and very low-density lipoprotein (VLDL). Creatinine levels in the urine samples were measured immediately. The remaining serum and urine were divided into small aliquots and stored at −20℃ until the analysis of DKK-1.

Method

Calculation of Body Mass Index

Body mass index (BMI) is calculated as the weight divided by the square of the height:

$$BMI = \text{Weight (kg)}/\text{Height (m}^2\text{)}$$

Serum and Urine Marker Analysis

DKK-1 concentrations in serum and urine were measured using an ELISA assay with a commercially available kit (Catalogue No. SL2064Hu). Optical density was measured at 450 nm on a 96-well microplate reader, with DKK-1 concentrations expressed in pg/mL. Lipid profiles (total cholesterol, triglycerides, and HDL cholesterol) and urine creatinine concentrations were measured using a colorimetric assay on the Roche/Hitachi Cobas c111 system, with results expressed in mg/dL. LDL cholesterol levels were calculated as follows (Fernández et al., 2017):

[LDL cholesterol] = [total cholesterol] − [HDL cholesterol] – VLDL cholesterol

VLDL cholesterol was estimated using the formula TG/5.

To obtain a representative sample and analyse DKK-1 levels without the need for 24-h urine collection, DKK-1 concentrations in urine were normalised to the creatinine levels.

Statistical Analysis

Data analysis was conducted using SPSS software version 25. Results were reported as mean ± SD, and statistical comparisons were made using the ANOVA test, with $p < 0.05$ considered statistically significant. Pearson correlation tests were performed to examine the relations among all parameters (Norman, 2010). To evaluate the accuracy of the DKK-1 marker, the receiver operating characteristic (ROC) analysis and the area under the curve (AUC) were used.

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3. Results

The physical characteristics of the study groups are presented in Table 1. The results indicated no significant differences in age and BMI among the groups ($p > 0.05$). *Post hoc* comparisons further confirmed that all three groups were statistically similar in terms of age and BMI. Similarly, no significant difference was found in the mean ± SD values of the urine creatinine concentrations: BC (12.31 ± 5.29 mg/dL), control (13.50 ± 6.38 mg/dL), and FR (12.05 ± 5.47 mg/dL). This finding was supported by a high *p*-value (0.61) and was corroborated by *post hoc* labels indicating statistical similarity across all groups for this parameter (Table 1).

In contrast, a significant contrast was observed in the mean DKK-1 serum ± SD values across the groups, with the BC group exhibiting substantially higher levels (614.00 ± 121.63 pg/mL) compared to the control group (175.28 ± 11.98 pg/mL) and the FR group (290.91 ± 53.63 pg/mL). This notable difference was supported by a *p*-value of less than 0.001, indicating statistical significance. *Post hoc* comparisons further confirmed that all three groups were statistically distinct regarding this parameter (Table 1).

Similarly, DKK-1 concentrations in urine also varies among the study groups. The BC group showed the highest average concentration (438.31 ± 170.58 pg/mL), followed by the FR group (357.91 ± 75.86 pg/mL) and the control group (203.62 ± 31.42 pg/mL). *Post hoc* comparisons indicated that these groups were statistically different in terms of the urine concentrations (Table 1).

Table 1 also presents the ratio of DKK-1 to urine creatinine levels. There was a significant difference between the control and BC groups ($p < 0.001$). The FR group showed a significant difference compared to the control group, while the difference in the BC group was non-significant ($p < 0.05$ for the control vs. FR group and >0.05 for the BC vs. FR group).

The results for both serum and urine concentrations of DKK-1 revealed significant variations among the three groups, with the BC group consistently showing higher levels. These findings indicate that DKK-1 in serum and that in urine serve as promising biomarkers for the diagnosis or prognosis of BC. The results for serum measurements were consistent with the findings from other investigations (Zhou *et al*., 2014; Liu *et al*., 2017). However, currently, there are no studies on urine DKK-1 available worldwide. This study provides evidence that DKK-1 may be a valuable biomarker for patients with BC.

Table 1. Mean ± SD of examined parameters in serum and urine BC patients, first-degree relative group, and healthy controls.

Parameter	BC (n=29)	FR (n=29)	Control (n=30)	P^a	P^b	P^c	P^d
Age (Year)	43.62±8.36	40.35±10.51	40.96±7.01	0.365	0.964	0.471	0.334
BMI (Kg/m^2)	28.68±3.66	26.99±3.12	27.07±2.67	0.147	0.996	0.138	0.090
DKK-1 sera (pg/mL)	614.00± 121.63	290.91± 53.63	175.28± 11.98	0.000**	0.000**	0.000**	0.000**
DKK-1 urine (pg/mL)	438.31± 170.58	357.91± 75.86	203.62± 31.42	0.031*	0.000**	0.000**	0.000**
Urine Creatinine (mg/dL)	12.31± 5.29	12.05± 5.47	13.50± 6.38	0.958	0.637	0.711	0.611
DKK-1/Cr. Urine $*10^{-9}$	35.77±16.34	27.87±10.19	17.92±8.30	0.061	0.013*	0.000**	0.000**

P^a value between BC and first relative group.
P^b value between control and first relative group.
P^c value between BC and control group.
P^d value among all examined group (by ANOVA test).

Serum Lipid Profile Among the Study Groups

According to Table 2, the total cholesterol level in the BC group was significantly higher than that in the healthy control group ($p = 0.013$). The FR group fell in between, showing statistical similarity to both the BC and control groups, as indicated by the *post hoc* comparisons. In contrast, triglyceride concentrations were not statistically different between the BC and control groups ($p > 0.05$). The FR group exhibited the highest triglyceride concentrations, showing a significant difference from the control group ($p = 0.021$) but not from the BC group, as confirmed by the *post hoc* testing (Table 2).

The values of HDL, LDL, and VLDL varied across the study groups, as shown in Table 2. First, LDL concentrations in the BC group were significantly higher than those in the healthy control group ($p = 0.003$). The FR group was statistically similar to both the healthy control and BC groups, as confirmed by *post hoc* testing. Additionally, HDL concentrations among the three groups did not differ significantly ($p = 0.093$). *Post hoc* comparisons indicated that the FR group differed from the control group but not from the BC group.

In contrast, VLDL concentrations among the groups were statistically significant ($p = 0.026$). Both the BC and FR groups had higher VLDL concentrations compared to the control group, as supported by the *post hoc* test.

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Table 2. Lipid profile in all examined groups

Parameter (mg/dL)	BC (n=29)	FR (n=29)	Control (n=30)	P^a	P^b	P^c	P^d
Cholesterol	194.28± 37.81	183.70± 34.19	168.28± 30.14	0.512	0.245	0.013*	0.018*
Triglyceride	126.48± 49.44	144.96± 74.54	104.00± 34.27	0.436	0.021*	0.252	0.026*
LDL	135.93± 33.17	119.78± 27.75	108.66± 26.24	0.126	0.367	0.002**	0.003**
HDL	45.97± 9.72	42.83± 8.60	48.45± 8.82	0.436	0.075	0.554	0.093
VLDL	25.27± 9.87	28.99± 14.91	20.80± 6.85	0.430	0.020*	0.256	0.026*

P_a value between BC and first relative group.

P_b value between control and first relative group.

P_c value between BC and control group.

P_d value among all examined group (ANOVA test)

Correlations among the concentrations of the examined parameters

Correlations among the concentrations of the examined parameters in serum and urine in the BC group

The Pearson correlation matrix in Table 3 provides insights into the associations among various parameters in terms of serum from patients with BC. The results indicate a strong positive correlation between LDL and cholesterol (r = 0.863, p = 0.000) and a perfect correlation between triglycerides and VLDL (r = 1.000, p = 0.000). No strong correlations were observed among other parameters. Notably, there was a significant positive correlation between serum and urine DKK-1 levels (r = 0.370, p = 0.048), as illustrated in Figure 1.

Table 3. Correlations among the concentrations of all examined parameters in serum of BC group.

parameter		Age	BMI	Cholesterol	Triglyceride	LDL	HDL	VLDL	DKK-1
Age (Year)	r	1	0.333	-0.235	-0.199	-0.219	-0.115	-0.195	-0.063
	p		0.077	0.219	0.301	0.254	0.552	0.311	0.745
BMI (Kg/m2)	r		1	-0.060	-0.151	-0.007	0.019	-0.150	0.249
	p			0.758	0.434	0.969	0.921	0.436	0.193
Cholesterol (mg/dL)	r			1	0.230	0.863**	0.148`	0.232	0.020
	p				0.230	0.000	0.444	0.227	0.919
Triglyceride (mg/dL)	r				1	0.020	-0.358	1.000**	0.131
	p					0.919	0.057	0.000	0.497
LDL (mg/dL)	r					1	0.203	0.021	-0.044
	p						0.290	0.912	0.819
HDL (mg/dL)	r						1	-0.357	-0.057
	p							0.057	0.770
VLDL (mg/dL)	r							1	0.132
	p								0.496
DKK-1 (pg/mL)	r								1
	p								

** Correlation is highly significant at the 0.01 level (2-tailed).

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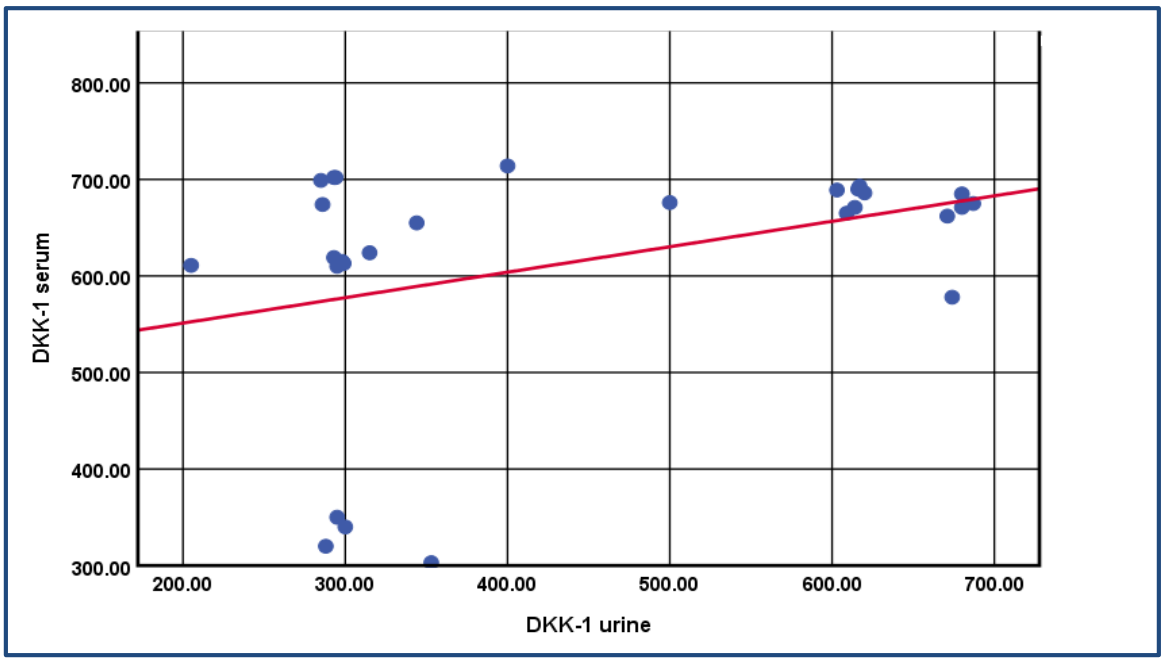

Figure 1. The correlation between serum and urine DKK-1 among BC women.

Correlations among the concentrations of the examined parameters in serum and urine in the first-degree relative group

Table 4 reveals a significant positive correlation between age and cholesterol, triglyceride, and VLDL concentrations (r = 0.543, p = 0.007; r = 0.598, p = 0.003; and r = 0.589, p = 0.003, respectively), alongside a negative correlation between age and HDL (r = −0.528, p = 0.01). Additionally, strong positive correlations were found between cholesterol and LDL concentrations, as well as between triglycerides and VLDL (r = 0.840, p = 0.000 and r = 1.000, p = 0.000, respectively), with a significant negative correlation between HDL and both triglyceride and VLDL concentrations (r = −0.501, p = 0.015). A significant negative correlation was observed between DKK-1 and both triglyceride and VLDL levels (r = −0.451, p = 0.030 and r = −0.451, p = 0.031, respectively), as shown in Figures 2 and 3. In contrast, no significant correlation was found between serum DKK-1 and urine DKK-1 (r = −0.188, p = 0.390).

Table 4. Correlations among the concentrations of all examined parameters in serum of first relative group.

parameter		Age	BMI	Cholesterol	Triglyceride	LDL	HDL	VLDL	DKK-1
Age (Year)	r	1	0.194	0.543**	0.598**	0.336	-0.528**	0.598**	0.101
	p		0.374	0.007	0.003	0.117	0.01	0.003	0.647
BMI (Kg/m^2)	r		1	-0.127	0.111	-0.408	-0.282	0.111	0.050
	p			0.563	0.615	0.053	0.193	0.615	0.821
Cholesterol	r			1	0.235	0.840**	0.170	0.235	0.246
(mg/dL)	p				0.281	0.000	0.438	0.281	0.223
Triglyceride	r				1	-0.031	-0.501*	1.000**	-0.451*
(mg/dL)	p					0.887	0.015	0.000	0.030
LDL (mg/dL)	r					1	0.154	-0.031	0.216
	p						0.482	0.887	0.322
HDL (mg/dL)	r						1	-0.501*	0.241
	p							0.015	0.268
VLDL	r							1	-0.451*
(mg/dL)	p								0.031
DKK-1	r								1
(pg/mL)	p								

** Correlation is highly significant at the 0.01 level (2-tailed)

* Correlation is significant at the 0.05 level (2-tailed)

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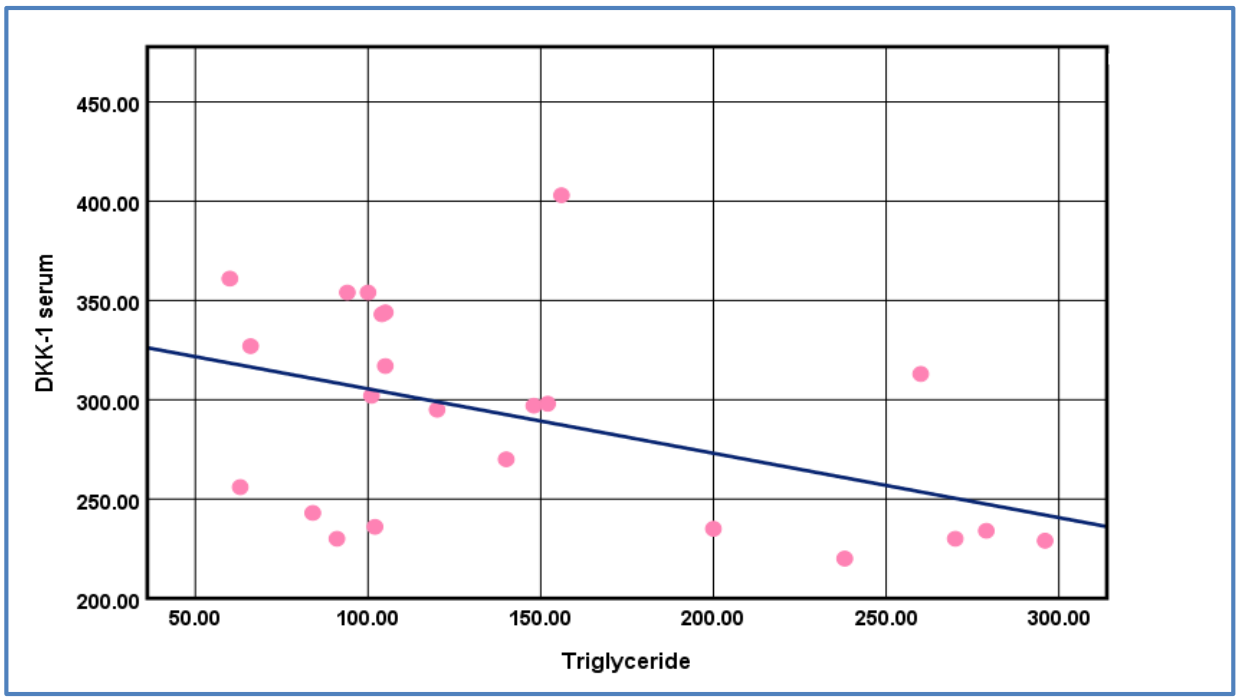

Figure 2. The correlation between DKK-1 and Triglyceride concentrations in serum of first relative group.

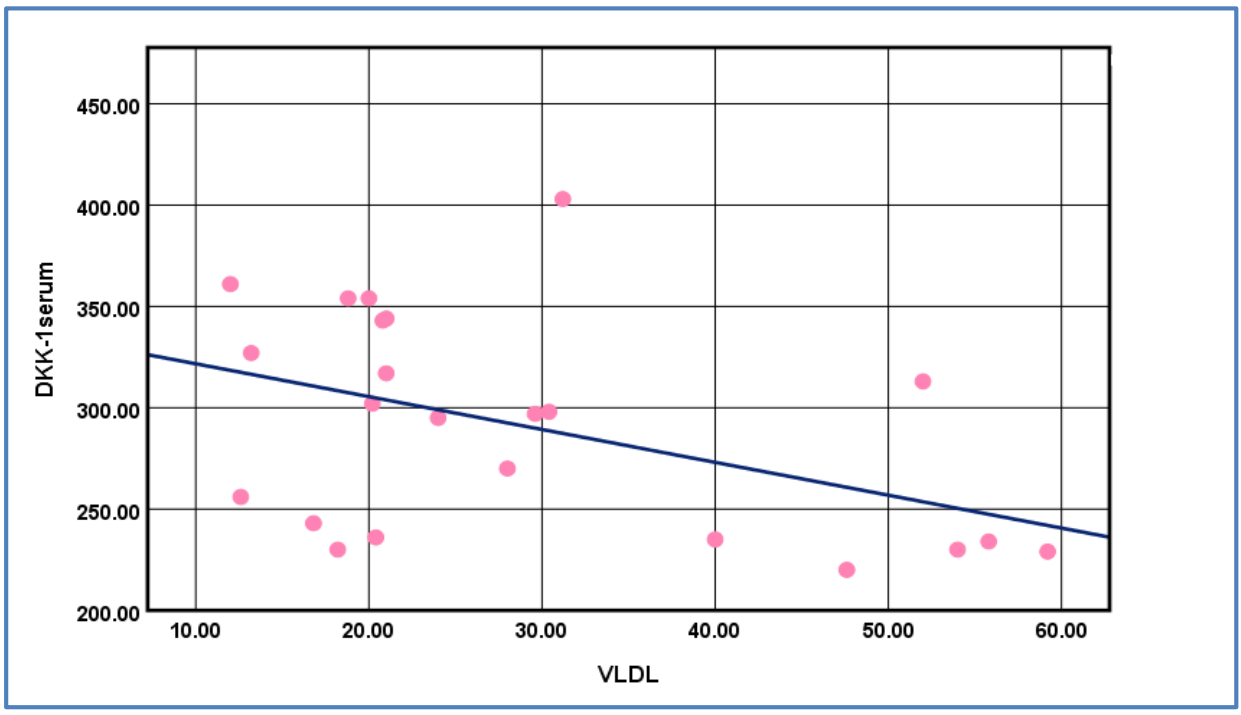

Figure 3. The correlation between DKK-1 and VLDL concentrations in serum of first relative group.

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Correlations among the concentrations of the examined parameters in serum in the control group

Table 5 shows a highly significant positive correlation between age and BMI, as well as triglyceride and VLDL concentrations (r = 0.676, p = 0.000; r = 0.526, p = 0.003; and r = 0.526, p = 0.003, respectively). Additionally, there were significant positive correlations between age and cholesterol and LDL concentrations (r = 0.454, p = 0.013 and r = 0.394, p = 0.035). BMI also demonstrated strong positive correlations with cholesterol, triglyceride, LDL, and VLDL (r = 0.574, p = 0.001 for all). Cholesterol was strongly and positively correlated with triglyceride, LDL, and VLDL (r = 0.634, p = 0.000; r = 0.858, p = 0.000; and r = 0.634, p = 0.000). Triglycerides were positively correlated with both LDL and VLDL (r = 0.572, p = 0.001 and r = 1.000, p = 0.000). However, there were no significant correlations between DKK-1 and other parameters in this group (p > 0.05), nor between serum and urine DKK-1 (p > 0.05).

Table 5. Correlations among the concentrations of all examined parameters in serum of control group.

parameter		Age	BMI	Cholesterol	Triglyceride	LDL	HDL	VLDL	DKK-1
Age (Year)	r	1	0.676**	0.454*	0.526**	0.394*	-0.329	0.526**	0.070
	p		0.000	0.013	0.003	0.035	0.081	0.003	0.719
BMI (Kg/m^2)	r		1	0.543**	0.574**	0.531**	-0.244	0.574**	-0.002
	p			0.002	0.001	0.003	0.202	0.001	0.993
Cholesterol (mg/dL)	r			1	0.634**	0.858**	-0.343	0.634**	0.286
	p				0.000	0.000	0.068	0.000	0.132
Triglyceride (mg/dL)	r				1	0.572**	-0.356	1.000**	0.000
	p					0.001	0.058	0.000	1.000
LDL (mg/dL)	r					1	-0.333	0.572**	0.298
	p						0.078	0.001	0.116
HDL (mg/dL)	r						1	-0.356	0.164
	p							0.058	0.394
VLDL (mg/dL)	r							1	0.000
	p								1.000
DKK-1 (pg/mL)	r								1
	p								

** Correlation is significant at the 0.01 level (2-tailed)

* Correlation is significant at the 0.05 level (2-tailed)

ROC analysis for DKK-1 in serum and urine in patients with BC compared to control subjects

Table 6 highlights the diagnostic performance of DKK-1 in differentiating between various groups. Both serum and urine DKK-1 showed remarkable diagnostic accuracy, evidenced by high sensitivity, specificity, and AUC values. According to the ROC curve analyses, the serum and urine DKK-1 concentrations exhibited high sensitivity and specificity, with a high AUC across all groups. These findings indicate that this marker is highly effective in distinguishing BC and FR from controls, suggesting its potential as a reliable screening marker for predicting BC in FR cases.

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Table 6. ROC curve results for DKK-1 in urine and serum among all groups.

Between BC and control				
Parameters	Cutoff	Sensitivity	Specificity	AUC
Sera DKK-1	>196.00	1.00	1.00	1.00
Urine DKK-1	>270.00	0.97	1.00	0.99
Between BC and FR				
Parameters	Cutoff	Sensitivity	Specificity	AUC
Sera DKK-1	490.5	86	100	0.96
Urine DKK-1	490.0	41	100	0.59
Between FR and control				
Parameters	Cutoff	Sensitivity	Specificity	AUC
Sera DKK-1	208	100	100	1.00
Urine DKK-1	272	96	100	0.99

4. Discussion

The average age of the patients in this study was 40.62 ± 12.36 years. The risk of developing BC increases with age, as follows: 1.5% risk at age 40, 3% at age 50, and more than 4% at age 70 (Zhu et al., 2023). Women who have had long-term oestrogen circulation in their bodies are more susceptible to BC (Bieuville et al., 2023). An increased number of menstrual cycles increases the risk of BC. Women who menarche early and menopause later are more likely to develop BC (Das et al., 2024). BMI classifications are as follows: underweight (<18 kg/m2) and normal weight (18.5–24.9 kg/m2). While overweight (BMI between 25.0 and 29.9 kg/m2), Class I obesity (BMI of 30.0–34.9 kg/m2), Class II obesity (BMI of 35.0–39.9 kg/m2), and Class III or severe obesity (BMI of 40 kg/m2) are all examples of obesity, the medical risk increases gradually as the degree of obesity increases (Jan and Weir, 2021; Al-Shimmery et al., 2023). As summarised in Table 1, the BMI of all studied groups was more than 25 Kg/m2, indicating that all three study groups were overweight. Epidemiological data indicate that obesity increases the risk of developing BC (Andò et al., 2019). According to Fontvieille et al. (2023), women over 50 who have a higher BMI are more likely to develop BC compared to those with a lower BMI. Additionally, the authors linked higher BMI to more aggressive biological characteristics of the tumour, such as larger size and higher percentage of lymph node metastasis. According to a meta-analysis by Smith et al. (2021), there is a low positive correlation between BC risk and BMI, with an increase of approximately 5 kg/m2 in BMI leading to an increase of approximately 2% in BC risk. In contrast, among premenopausal women, a higher BMI reduces the risk of BC. Obesity and overweight are thought to provide protection against premenopausal BC, with the exception of women having a family history of the cancer. Therefore, as compared to BMI or body weight, body fat may be a better measure of BC risk in postmenopausal women. Body fat distribution may also influence BC risk (Tran et al., 2024). According to observational data, women with or without a family history of BC may have a similar link between their BMI and risk of developing the disease (Cao et al., 2024).

DKK-1 is a secreted protein that inhibits the canonical Wnt signalling pathway, playing a significant role in cancer development (Zhu et al., 2021). The role and expression of DKK-1 vary based on the location of the malignancy. As an autocrine regulator, the DKK-1 gene and protein are transiently activated and released during the development of human progenitor cells (Longo et al., 2019). DKK-1 may serve as a promising target for original treatment approaches (Mazon et al., 2016), as it has been identified as a predictive marker across a wide range of malignancies (Liu et al., 2014).

Lipids play a crucial role in the body's physiological systems and the functional equilibrium of biological membranes. They are also essential for cellular signalling, functioning as second messengers and hormones (Pandeya et al., 2018; Ali and Szabó 2023). Cholesterol is a significant risk factor for BC (Nouri et al., 2022; Santos et al., 2023). Moreover, the combination of statins with anticancer therapy has been shown to have a protective effect against BC recurrence (Kolb and Weizhou, 2020; Jung et al., 2020).

In the current study, total and LDL cholesterol concentrations were significantly higher in patients with BC compared to age- and sex-matched healthy controls (Table 2). These findings are consistent with those of Nelson et al. (2014), Abd et al. (2019), Kumie et al. (2020), and Chowdhury et al. (2021), who demonstrated that cholesterol has clear pathogenic effects on breast tumour progression. Meanwhile, Arif et al. (2020) and Olabumuyi et al. (2021) expressed that there are no differences between healthy controls and patients with BC. The first relative group expressed no significant differences with healthy controls and patients with BC. The proposed interpretation of elevated cholesterol levels in BC aligns with the theory that it acts as a risk factor in tumour initiation. Dyslipidemia, characterised by higher cholesterol levels in cell membranes, alters membrane fluidity and associated signalling, potentially promoting tumour angiogenesis.

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In patients with BC, elevated serum LDL levels are more susceptible to oxidation, which can lead to increased lipid peroxidation. This process may induce oxidative stress, resulting in cellular and molecular damage that contributes to malignant transformations and cell proliferation. These findings indicate that LDL follows a similar pattern to total cholesterol.

The triglyceride concentrations in patients with BC did not show a significant increase compared to the control group, as indicated by the p-value greater than 0.05. This finding contrasts with those of previous studies (Nelson et al., 2014; Abd et al., 2019; Kumie et al., 2020; Arif et al., 2020; Chowdhury et al., 2021), which reported a highly significant increase between BC and control groups. The FR group showed the highest concentrations, which were statistically different from the control group (p = 0.021) but not from the BC group, as confirmed by post hoc testing (Table 2). Additionally, the same table indicates no differences in HDL levels among all examined groups. Meanwhile, VLDL levels exhibited a pattern similar to that of triglycerides, showing significant elevations only in the FR group compared to both the BC and control groups.

In the BC group, DKK-1 levels showed a significant positive correlation between serum and urine (r = 0.370, p = 0.048), suggesting that urine could be used as an alternative to serum for this measurement.

Concerning Ethics

This study project was authorised by the scientific committee in the Department of Chemistry and Biochemistry/College of Medicine on 10th September 2022. The approval of the IRB at the College of Medicine was obtained on 1st October 2022.

5. Conclusions

Patients with BC exhibited higher DKK-1 concentrations compared to the control and first relative degree groups. The ROC results suggested that DKK-1 could function as a detection and prediction biomarker. Additionally, the correlation between serum and urine D

6. References

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