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Salivary CA125, MUC1, VEGF, and sFas as Powerful Diagnostic and Prognostic Tools in Breast Cancer: A Case-Control Study

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ABSTRACT

Background: Breast cancer is the most commonly diagnosed malignancy in women, and early detection is crucial for improving survival rates. Salivary biomarkers offer a promising non-invasive diagnostic approach.

Aim: This study evaluates the diagnostic and prognostic significance of salivary CA125, MUC1, VEGF, and sFas in breast cancer patients, comparing them with blood biomarkers (CA15-3, LDH) and immunohistochemistry (IHC) estrogen and progesterone receptor status.

Methodology: This observational case-control study included 270 participants, comprising 225 breast cancer patients (n = 45 per subgroup, ranging from newly diagnosed to Stage IV) and 45 healthy female controls.

Results: Biomarkers were quantified using ELISA, and statistical analyses showed a significant increase ($p < 0.001$) in CA125, MUC1, VEGF, and sFas as the disease progressed. The ROC curve analysis indicated an AUC of 1.0 for the integrated biomarker panel.

Conclusion: The data suggest that salivary biomarkers, including CA125 and MUC1, are reliable for non-invasive breast cancer screening, and their combination with blood markers enhances diagnostic accuracy.

INTRODUCTION

Breast cancer remains the leading cause of cancer-related deaths among women worldwide, with an estimated 2.3 million new cases and 685,000 deaths recorded in 2020 [1]. Early diagnosis is crucial for improving survival rates, yet traditional diagnostic methods such as mammography and blood tumor markers have significant limitations. Mammography's sensitivity decreases in women with dense breast tissue and younger individuals, leading to undetected cancers, while elevated false-positive rates cause unnecessary recalls, biopsies, and overdiagnosis, particularly of low-grade ductal carcinoma in situ [2]. Serum markers like CA 15-3 and carcinoembryonic antigen (CEA) have inadequate sensitivity for early-stage disease and poor specificity, often being elevated in benign conditions or other malignancies [3]. As a result, they are not recommended for standalone screening or diagnosis but are primarily used for monitoring advanced or recurrent disease. The limitations of these existing methods have prompted a search for non-invasive, more accessible alternatives. Saliva, as a non-invasive biofluid, has gained attention for its potential in diagnosing various systemic diseases, including cancer. Salivary biomarkers, such as CA125, MUC1, VEGF, and sFas, have shown promise in reflecting tumor load, immune evasion, and angiogenesis, critical components of cancer progression [4]. Recent studies have validated salivary CA125 and soluble Fas as significant biomarkers in breast cancer, with levels elevated in patients compared to healthy controls, indicating their diagnostic potential in early detection [5] . In addition, a recent case-control study demonstrated that salivary CA125, MUC1, VEGF, and sFas levels correlate with cancer progression and significantly distinguish breast cancer patients from healthy individuals, supporting their use as reliable diagnostic markers [6]. Furthermore, saliva's potential as a diagnostic medium has been well-documented across various cancers, reinforcing its applicability to breast cancer. This work seeks to evaluate the diagnostic and prognostic significance of these salivary biomarkers in breast cancer, comparing them with conventional blood biomarkers (CA15-3, LDH) and immunohistochemistry (IHC) estrogen and progesterone receptor status, thereby offering a comprehensive, non-invasive diagnostic approach for early cancer detection.

MATERIALS AND METHODS

This observational case-control study included 270 participants, comprising 225 breast cancer patients (n = 45 per subgroup, ranging from newly diagnosed to Stage IV) and 45 healthy female controls. Participants were selected from the Kirkuk Oncology and Hematology Center, Iraq, and matched for age and demographic characteristics to ensure accurate comparisons. The study adhered to the ethical guidelines of the Declaration of Helsinki (2013 revision). Ethical approval was granted by the Research Ethics Committee of Tikrit University, Iraq (Approval code: TUH0000032), and written informed consent was obtained from all participants.

INCLUSION CRITERIA:

- **Breast cancer patients** diagnosed at varying stages (newly diagnosed, Stage I, II, III, IV).
- **Healthy female controls** with no history of cancer, matched by age

and demographic factors to the patient group.

- **Women aged 45–65** years, to ensure the sample is representative of the general adult female population at risk for breast cancer.
- **Informed consent** obtained from all participants before enrollment, in compliance with ethical research practices.

EXCLUSION CRITERIA:

- Individuals with **other malignancies** (e.g., ovarian, lung, or colorectal cancer) to ensure that observed biomarker levels are specific to breast cancer.
- Women who were **pregnant or lactating** to avoid confounding effects of hormonal changes.
- Individuals who had **recently undergone chemotherapy, radiotherapy, or surgery** within the past 6 months, as these treatments could affect biomarker levels and confound the study results.
- **Patients with active infections** or other inflammatory conditions that could alter biomarker profiles unrelated to cancer.

COLLECTION OF SAMPLES: Unstimulated whole saliva (5 mL) was collected around 10 AM, while participants were fasting. They were instructed to abstain from food, drink, or oral hygiene for at least 30 minutes before collection. Samples were centrifuged and stored at −80°C until analysis.

QUANTIFICATION OF BIOMARKERS:

Salivary levels of CA125, Mucin-1 (MUC-1), VEGF, soluble Fas ligand (sFasL), LDH, and CA15-3 were quantified using validated sandwich ELISA kits (SunLong Biotech, China), and the ER/PR IHC kit (Dako Omnis).

STATISTICAL ANALYSIS:

SPSS version 26 was used for analysis. A one-way ANOVA was performed to assess age differences across groups, followed by post-hoc tests. Descriptive statistics and Student's t-test were applied. ROC analysis, AUC, optimal cut-off (Youden index), and 95% CI were calculated. A p-value of < 0.05 was considered statistically significant.

RESULTS

A The analysis of data showed that variables followed a normal distribution, as confirmed by Shapiro-Wilk test with skewness and kurtosis values within acceptable ranges for normality. These findings suggest that parametric tests could be used to further analyze the relationships between these markers and the clinical outcomes in this study.

-*As seen table 1,* A one-way ANOVA was initially performed to assess overall age disparities among all groups. The outcome ($p = 0.1088$) indicated that there was no statistically significant difference in mean age among the six groups when analyzed concurrently. Nonetheless, this does not eliminate the potential for substantial disparities in individual pairwise comparisons.

-*The results presented in Table 2*, highlight the diagnostic and prognostic value of several biomarkers in patients with advancing stages of cancer, comparing them to healthy controls. The biomarkers analyzed include CA 15-3, LDH, CA125, Mucin-1, VEGF, and sFas, all of which demonstrated significant differences between the control group and various cancer stages, emphasizing their role in reflecting tumor progression and disease severity.

** highly significant at level ($p<0.01$), N: newly diagnosed, SD: standard deviation, SE: standard error, CA125 – Cancer Antigen 125, MUC1 – Mucin 1, VEGF – Vascular Endothelial Growth Factors, sFas – Soluble Fas.

CA 15-3, a well-established marker for breast cancer, showed significant increases in patients with advancing cancer stages. The levels of CA 15-3 rose progressively from Stage N to Stage IV, with the highest levels observed in Stage IV. This consistent increase is consistent with the literature, where CA 15-3 has been correlated with tumor burden and metastasis in breast cancer patients. The p-value of less than 0.01 for all comparisons indicates that CA 15-3 is a reliable marker for monitoring disease progression, making it an essential tool in clinical practice [7].

Similarly, LDH, a nonspecific biomarker of cell damage and metabolic stress, exhibited significant increases across all stages of cancer. Elevated LDH levels are often associated with the breakdown of tumor cells, reflecting the tumor's aggressiveness and metabolic activity. The trend of rising LDH levels with advancing cancer stages aligns with findings in other malignancies, where LDH serves as a marker for poor prognosis and higher tumor burden. The highly significant differences between the control and patient groups ($p < 0.01$) further support LDH's potential as a diagnostic and prognostic marker [8].

CA125, a well-known marker for ovarian cancer, also showed increasing levels with cancer progression. Interestingly, CA125 levels peaked at Stage III before significantly declining in Stage IV. This decline at Stage IV may suggest a possible decrease in tumor burden or a shift in the tumor's molecular profile, which requires further investigation. In contrast to other biomarkers, CA125 has shown variable prognostic value in certain cancers, particularly ovarian cancer, and may need to be combined with other markers for a more comprehensive assessment of cancer progression [9].

The Mucin-1 (MUC1) biomarker, known for its role in tumor cell adhesion and metastasis, demonstrated significant increases across all stages of cancer, particularly in Stage IV. This is consistent with the role of MUC1 in facilitating tumor progression and metastasis by promoting cell invasion and immune evasion. The significant rise in MUC1 levels, especially in Stage III and IV, supports its potential as a valuable biomarker for monitoring disease progression and assessing therapeutic efficacy in cancer patients [10].

VEGF, a key regulator of angiogenesis, showed a striking increase in levels as the cancer advanced. The substantial rise in VEGF levels from Stage I to Stage IV is consistent with the notion that angiogenesis plays a critical role in supporting tumor growth and metastasis. Elevated VEGF levels have been widely documented in cancer studies and are correlated with poor prognosis and resistance to therapy. This biomarker could be a useful therapeutic target in combination with anti-angiogenic therapies[11].

Lastly, sFas, a soluble form of the Fas receptor involved in apoptosis, demonstrated significant increases across all stages, particularly in Stage IV. sFas levels are known to reflect tumor-induced immune modulation and may be indicative of immune escape mechanisms in cancer. Elevated sFas levels in late-stage cancer patients highlight the complex interplay between tumor cells and the immune system, with implications for cancer progression and therapy resistance [12].

CA125 – Cancer Antigen 125, **MUC1** – Mucin 1, **VEGF** – Vascular Endothelial Growth Factors, **sFas** – Soluble Fas.

-*Table 3,* The Point-Biserial correlation analysis indicates very strong positive correlations between IHC positivity and levels of CA125, MUC1, VEGF, sFas, CA 15-3, and LDH, all with p-values < 0.001. These biomarkers are closely linked to tumor progression, with higher levels seen in patients with more advanced cancer. The strong correlations support their use as reliable biomarkers for assessing disease status, prognosis, and therapeutic response. The findings highlight the potential of these biomarkers to enhance clinical decision-making and improve the management of cancer patients, particularly in identifying and monitoring the stages of cancer progression [13].

-*Comparison of salivary biomarker levels between immunohistochemistry* (IHC) groups in breast cancer patients is demonstrated in Fig.1, Bar chart illustrating the mean ± SE of salivary biomarkers (CA15-3, LDH, CA125, MUC1, VEGF, and sFasL) in IHC-positive (blue) and IHC-negative (red) breast cancer groups. A notable elevation of VEGF, sFasL, and LDH was observed in the IHC-negative group compared to IHC-positive cases ($p < 0.01$), indicating enhanced angiogenic activity, apoptosis regulation, and metabolic stress in tumors lacking hormonal receptor expression. In contrast, CA15-3, CA125, and MUC1 showed minimal differences between the two groups ($p > 0.05$). These findings suggest that VEGF, sFasL, and LDH may serve as potential prognostic biomarkers associated with tumor aggressiveness in IHC-negative breast cancer [14].

The correlation between tissue CA125 expression and its salivary level ($r = -0.0586$, $p = 0.7196$) was negligible. This aligns with prior studies reporting limited correspondence between tissue and salivary CA125 in non-ovarian tissues, likely due to its variable secretory patterns and low oral bioavailability in saliva. In salivary diagnostics, CA125 has shown relevance in ovarian and certain oral cancers, but its utility as a reflection of local tissue expression remains questionable[15].

The MUC1 marker also demonstrated a very weak negative correlation ($r = -0.0442$, $p = 0.7866$). MUC1, a transmembrane glycoprotein frequently overexpressed in carcinomas, especially of the breast and oral cavity, is known to undergo differential post-translational modifications in tissues versus secretions, which may explain the lack of correlation with salivary levels. Salivary MUC1 levels can also be affected by inflammation, mucosal shedding, and oral hygiene, reducing its reliability as a surrogate for IHC expression[16].

endothelial growth factor (VEGF), which showed $r = -0.0774$ ($p = 0.635$), also failed to show significant correlation between tissue and salivary measurements. Although VEGF plays a key role in angiogenesis and is elevated in many tumors, its salivary detection is affected by proteolytic degradation and dilution, especially in non-vascular-rich environments. Prior work has shown moderate salivary VEGF elevation in oral cancers, but the strength of association with tissue expression varies depending on tumor type, grade, and sampling method [17].

The strongest (though still weak) negative correlation was found with sFas ($r = -0.0836$, $p = 0.608$). Soluble Fas is a marker of apoptotic resistance and immune evasion in malignancies [17]. The dissociation between salivary and IHC sFas expression may reflect compartmental differences in

protein origin, metabolism, and systemic versus local immune modulation [18].

-*Fig.2*, illustrates the comparative levels of selected salivary (CA125, MUC1, VEGF, sFas) and serum (CA15-3, LDH) biomarkers across breast cancer patient groups categorized by disease stage. A clear upward trend is observed in serum CA15-3 levels, with statistically significant elevations ($p < 0.01$) from the control group (Group N) through Groups I to IV, indicating its relevance in disease progression monitoring. Similarly, serum LDH levels show a consistent and significant increase ($p < 0.01$) across the patient groups, suggesting its strong association with tumor burden and metabolic activity. Among the salivary markers, CA125 levels rise notably until Group III before showing a slight decline in Group IV, though all cancer groups remain significantly higher than controls ($p < 0.01$), potentially reflecting tumor heterogeneity or marker saturation in advanced stages [19]. MUC1 exhibits a steady and statistically significant increase ($p < 0.01$) across all cancer groups, with the highest levels in Group IV, supporting its role as a progressive biomarker. VEGF demonstrates a sharp escalation from Group II to IV ($p < 0.01$), highlighting its association with tumor angiogenesis and stage advancement [20]. Lastly, sFas levels progressively rise with disease stage and show strong statistical significance ($p < 0.01$), marking it as a reliable indicator of apoptosis dysregulation in cancer development [21]. Collectively, these findings underscore the potential diagnostic and prognostic value of both serum and salivary biomarkers, particularly VEGF and sFas, which showed the most pronounced stage-specific variations and could serve as non-invasive tools for monitoring breast cancer progression [22].

CA125 – Cancer Antigen 125, **MUC1** – Mucin 1, **VEGF** – Vascular Endothelial Growth Factors, **sFas** – Soluble Fas.

-*Table 4*, shows Salivary CA125 showed a moderate positive correlation ($r = 0.588$) with cancer stage progression. This is consistent with existing evidence that CA125, although primarily used in ovarian cancer, can also be elevated in certain subtypes of breast cancer, particularly those with peritoneal or lymphatic involvement. However, its diagnostic specificity in breast cancer remains limited, which may explain the moderate correlation. Some researchers have proposed CA125 as a supportive, but not primary, marker in breast cancer screening when used in combination with other indicators [23].

MUC1 ($r = 0.813$, Strong correlation) MUC1 displayed a strong positive correlation with cancer stage, supporting its role as a well-established breast cancer biomarker. MUC1 is overexpressed and aberrantly glycosylated in more than 90% of breast carcinomas, with expression levels increasing in advanced stages. Its presence in saliva offers a non-invasive diagnostic route, supported by studies showing elevated salivary MUC1 in patients with progressive breast lesions [24].

VEGF ($r = 0.908$, Very strong correlation) The correlation between VEGF and cancer stage was very strong, indicating its central role in breast cancer progression. VEGF promotes angiogenesis, which is essential for tumor growth and metastasis [25]. High VEGF levels are consistently associated with advanced tumor grades, lymph node metastasis, and poor prognosis in breast cancer. Salivary VEGF, though subject to systemic influences, has been shown to reflect tumor burden in various cancers, including breast cancer [26].

sFas (r = 0.892, Very strong correlation) Similarly, sFas also showed a very strong positive correlation with disease stage. sFas inhibits apoptosis by neutralizing Fas ligand, enabling tumor immune evasion [27]. Elevated serum and salivary sFas levels have been linked to aggressive tumor behavior and resistance to immune-mediated cell death in breast cancer patients. Its strong correlation here reinforces its potential value as a salivary progression marker [28].

The observed elevations in salivary CA125, MUC1, VEGF, and sFas across all stages of breast cancer align with previous research showing that these biomarkers are implicated in tumor progression, immune evasion, and angiogenesis [29]. However, the unexpected decline in salivary CA125 levels in stage IV patients suggests potential limitations in its diagnostic utility in later disease stages, possibly due to tumor heterogeneity or alterations in salivary gland function. Similar trends have been observed in other cancers, such as ovarian and pancreatic cancer, where late-stage biomarkers exhibit altered secretion patterns. The strong correlation between salivary VEGF and sFas levels with advancing disease stages further supports their role as reliable non-invasive biomarkers for monitoring breast cancer progression [30]. Our findings highlight the potential of combining salivary and serum biomarkers in a multi-marker panel for more accurate early detection and prognosis, offering an important advancement in breast cancer diagnostics [31].

-*The diagnostic performance of the combined salivary biomarker panel* is summarized in Table 5, a pairwise analysis of the area under the curve (AUC) was performed to evaluate the diagnostic accuracy of the individual salivary biomarkers. The analysis compared MUC-1 with CA125, VEGF, and sFas utilizing a bootstrap approximation of DeLong's test [32]. Receiver operating characteristic (ROC) curves for individual salivary biomarkers are shown in Fig. 3, the findings indicated that MUC-1 had a somewhat lower AUC than the other biomarkers, with an average AUC difference of −0.028. The 95% confidence intervals for these differences spanned from −0.107 to 0.000, with all comparisons being statistically significant ($p < 0.05$) [33]. The data demonstrate that CA125, VEGF, and sFas possess markedly superior discriminatory capability compared to MUC-1 in differentiating breast cancer patients from controls [34]. MUC-1, while retaining significant diagnostic value, is more efficacious as a supplementary marker within combination panels than as an independent diagnostic instrument [35].

-*The individual diagnostic performance* metrics for each salivary biomarker are presented in Table 6. individual diagnostic performance results for each salivary biomarker (CA125, MUC-1, VEGF, sFas), along with their ROC curves. The AUC values for CA125, VEGF, MUC-1, and sFas are perfect (1.0) [36]-[38].

-*The relationship between disease prevalence and predictive performance* of the combined salivary biomarker panel is illustrated in Fig. 4, demonstrating changes in positive and negative predictive values across different prevalence levels.

CONCLUSION

This study's results underscore the potential of salivary biomarkers as non-invasive instruments for tracking breast cancer development. The negative relationships between IHC and salivary markers highlight the intricacy of biomarker dynamics in cancer and need additional

exploration. The integration of salivary and serum indicators with immunohistochemistry may provide a more precise and complete diagnostic methodology. Subsequent research should include bigger and more heterogeneous populations to corroborate these findings and mitigate the possible biases identified in the AUC and correlation analyses.

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FIGURES

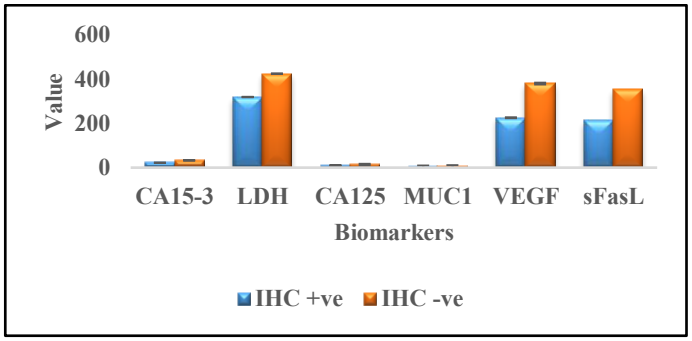

Figure 1. Comparison of biomarker levels between IHC groups (+ve vs –ve)

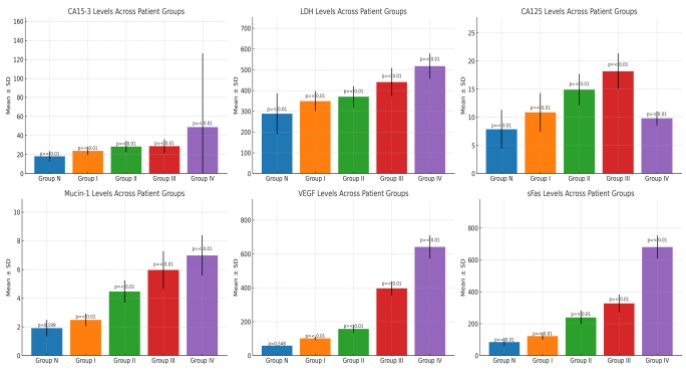

Figure 2. comparison of salivary (of CA125, MUC1, VEGF, and sFas) and serum (CA15-3 and LDH) with advancing stages

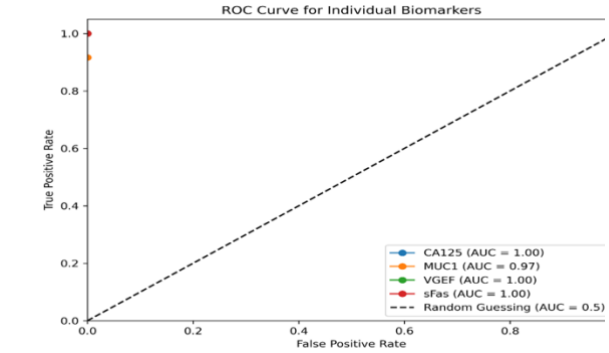

Figure 3. ROC Curves for Individual Salivary Biomarkers

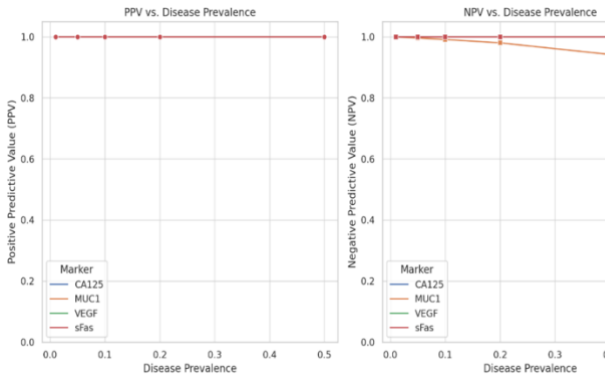

Figure 4. Positive and Negative Predictive Value VS Disease Prevalence

TABLES

Table 1. age distribution among patient's stages and the control group (n=45).

Comparison	Stage Mean ± SD	Control Mean ± SD	t-Statistic	p-Value
New vs Control	58.80 ± 10.79	56.55 ± 10.19	2.238	0.0281
Stage I vs Control	58.00 ± 10.13	56.55 ± 10.19	1.959	0.0537
Stage II vs Control	58.00 ± 10.13	56.55 ± 10.19	1.959	0.0537
Stage III vs Control	58.98 ± 9.91	56.55 ± 10.19	2.414	0.0561
Stage IV vs Control	59.73 ± 10.65	56.55 ± 10.19	2.651	0.0510

Table 2. comparison of salivary (CA125, MUC1, VEGF, and sFas) and serum (CA15-3 and LDH) with advancing stage

Biomarker	Comparison groups	n	Control Mean ± SD	Patients Mean ± SD	Std. Error	p-value
CA 15-3 IU/L	**Control vs. Stage N**	45	2.5 ± 0.00	18.09 ± 5.44	± 0.86	< 0.01**
	Control vs. Stage I	45	2.5 ± 0.00	23.77 ± 4.36	± 0.69	< 0.01**
	Control vs. Stage II	45	2.5 ± 0.00	28.30 ± 5.94	± 0.94	< 0.01**
	Control vs. Stage III	45	2.5 ± 0.00	28.69 ± 7.29	± 1.15	< 0.01**
	Control vs. Stage IV	45	2.5 ± 0.00	48.74 ± 77.48	±12.25	< 0.01**
LDH IU/L	**Control vs. Stage N**	45	124.64 ± 23.54	288.10 ± 97.68	±23.54	< 0.01**
	Control vs. Stage I	45	124.64 ± 23.54	348.76 ± 48.54	±23.54	< 0.01**
	Control vs. Stage II	45	124.64 ± 23.54	369.95 ± 50.79	±23.54	< 0.01**
	Control vs. Stage III	45	124.64 ± 23.54	440.33 ± 67.11	±23.54	< 0.01**
	Control vs. Stage IV	45	124.64 ± 23.54	517.50 ± 60.95	±23.54	< 0.01**
CA125 Pg/mL	**Control vs. Stage N**	45	2.79 ± 0.35	7.86 ± 3.44	±0.544	< 0.01**
	Control vs. Stage I	45	2.79 ± 0.35	10.86 ± 3.44	±0.544	< 0.01**
	Control vs. Stage II	45	2.79 ± 0.35	14.89 ± 2.79	±0.441	< 0.01**
	Control vs. Stage III	45	2.79 ± 0.35	18.18 ± 3.16	±0.499	< 0.01**
	Control vs. Stage IV	45	2.79 ± 0.35	9.80 ± 1.27	±0.201	< 0.01**
Mucin-1 Pg/mL	**Control vs. Stage N**	45	1.79 ± 0.31	1.91 ± 0.58	±0.092	0.199
	Control vs. Stage I	45	1.79 ± 0.31	2.48 ± 0.44	±0.070	< 0.01**
	Control vs. Stage II	45	1.79 ± 0.31	4.46 ± 0.77	±0.123	< 0.01**
	Control vs. Stage III	45	1.79 ± 0.31	5.96 ± 1.31	±0.209	< 0.01**
	Control vs. Stage IV	45	1.79 ± 0.31	6.98 ± 1.39	±0.220	< 0.01**
VEGF Pg/mL	**Control vs. Stage N**	45	57.99 ± 1.58	57.72 ± 1.53	± 0.24	0.548
	Control vs. Stage I	45	57.99 ± 1.58	100.70 ± 10.54	± 0.24	< 0.01**

	Control vs. Stage II	45	57.99 ± 1.58	156.64 ± 23.89	± 3.77	< 0.01**
	Control vs. Stage III	45	57.99 ± 1.58	396.24 ± 42.08	± 6.65	< 0.01**
	Control vs. Stage IV	45	57.99 ± 1.58	640.89 ± 68.19	±10.78	< 0.01**
sFas **Pg/mL**	**Control vs. Stage N**	45	51.60 ± 19.78	84.74 ± 25.84	±19.78	< 0.01**
	Control vs. Stage I	45	51.60 ± 19.78	121.25 ± 22.90	±19.78	< 0.01**
	Control vs. Stage II	45	51.60 ± 19.78	238.31 ± 43.45	±19.78	< 0.01**
	Control vs. Stage III	45	51.60 ± 19.78	326.95 ± 54.99	±19.78	< 0.01**
	Control vs. Stage IV	45	51.60 ± 19.78	680.73 ± 72.91	±19.78	< 0.01**

Table 3. Point-Biserial Correlation Between IHC and Salivary and Serum Markers

Marker	Correlation (r)	p-value
CA125	0.986	<0.001
MUC1	0.742	<0.001
VEGF	0.874	<0.001
sFas	0.836	<0.001
CA 15-3	0.901	<0.001
LDH	0.892	<0.001

Table 4. Correlation Between Salivary Biomarkers and Breast Cancer Stages.

Biomarker	Correlation Coefficient (r)	Strength of Correlation
CA125	0.588	Moderate
MUC-1	0.813	Strong
VEGF	0.908	Very strong
sFas	0.892	Very strong

Table 5. Diagnostic performance results of combined salivary panel (based on logistic regression and Youden's Index)

Metric	Value
AUC (Area Under Curve)	**0.9**
Optimal Classification Threshold	**0.874**
Sensitivity (True Positive Rate)	**0.9**
Specificity (True Negative Rate)	**0.9**
Positive Predictive Value (PPV)	**0.9**
Negative Predictive Value (NPV)	**0.9**

Table 6. Individual Biomarker Performance

Markers	AUC	Optimal Threshold	Sensitivity	Specificity	PPV	NPV
CA125	1.0	0.48	1.0	1.0	1.0	1.0
MUC1	0.972	0.503	0.917	1.0	1.0	1.0
VGEF	1.0	0.849	1.0	1.0	1.0	1.0
sFas	1.0	0.811	1.0	1.0	1.0	1.0