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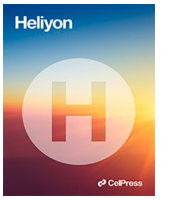

Research article

Assessing the use of the triglyceride-glycemic index (TyG), neutrophil-lymphocyte Ratio (NLR), and platelet-lymphocyte Ratio (PLR) in distinguishing benign and malignant tumors among patients with complaints of breast mass

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ABSTRACT

Introduction: Breast cancer is a prevalent global health concern characterized by uncontrolled cell growth in breast tissue. In 2020, approximately 2.3 million cases were reported worldwide, with 162,468 new cases and 87,090 fatalities documented in India in 2018. Early diagnosis is crucial for reducing mortality. Our study focused on the use of markers such as the triglyceride-glycemic index and hematological markers to distinguish between benign and malignant breast masses.
Methods: A prospective cross-sectional study included female patients with breast mass complaints. The target sample size was 200. Data collection included medical history, clinical breast examination, mammography, cytological assessment via fine-needle aspiration cytology (FNAC), and blood sample collection. The analyzed parameters included neutrophil-to-lymphocyte Ratio (NLR), platelet-to-lymphocyte Ratio (PLR), and triglyceride-glycemic index (TyG). Histopathological examination confirmed the FNAC results. Statistical analysis including propensity score matching, Kolmogorov–Smirnov tests, Mann–Whitney U tests, receiver's operator curve (ROC) analysis, and logistic regression models was conducted using SPSS and R Software. Additional validation was performed on 25 participants.
Results: This study included 200 participants. 109 had benign tumors and 91 had malignant tumors. Propensity score matching balanced covariates. NLR did not significantly differ between the groups, while PLR and TyG index differed significantly. NLR correlated strongly with the breast cancer stage, but not with the BI-RADS score. PLR and TyG index showed moderate positive correlations with the BI-RADS score. ROC analysis was used to determine the optimal cutoff values for PLR and TyG index. Logistic regression models combining PLR and TyG index significantly improved malignancy prediction.
Conclusions: TyG index and PLR show potential as adjunctive markers for distinguishing breast masses. NLR correlated with cancer stage but not lesion type. Combining TyG and PLR improves

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prediction, aiding clinical decisions, but large-scale multicenter trials and long-term validation are required for clinical implementation.

1. Introduction

According to the American Cancer Society (ACS), breast cancer is defined as a malignant growth originating from uncontrolled cell proliferation in breast tissue [1]. It ranks as the most frequently diagnosed cancer in women, with approximately 2.3 million global cases reported in 2020 [2]. In 2018, an Indian breast cancer statistics report documented 162,468 newly registered cases and 87,090 reported fatalities [3]. As one of the most prevalent cancers globally, early diagnosis plays a vital role in reducing mortality and morbidity.

The emergence of any breast tumor typically begins with the presence of a mass in the breast. Benign masses include fibroadenomas, phyllodes, and intraductal papillomas, which remain localized to their site of origin and are generally amenable to surgical removal [4]. On the other hand, malignant masses, such as invasive ductal carcinoma, invasive lobular carcinoma, and inflammatory breast cancer, infiltrate and damage nearby structures, and tend to spread to distant locations by metastasis [5].

The characteristics of benign breast masses include having a clearly outlined border and a smooth or round shape. They are typically painless, can move around within the breast, and tend to maintain a consistent size. On the other hand, malignant breast masses display irregular borders, come in various shapes, and are less mobile. They may cause discomfort or pain and often grow larger over time [6].

The diagnosis of breast cancer depends on a multimodal approach that combines self-breast examination, clinical evaluation, imaging studies, blood investigations, tissue sampling, genetic testing, and molecular profiling [7].

Physicians perform physical examinations to detect any palpable breast lumps, skin changes (peau d'orange appearance), nipple discharge or retraction, or axillary swelling. Mammography which involves capturing X-ray images of the breast to detect microcalcifications or masses is used as a screening tool. Digital mammography and 3D tomosynthesis are recent advances that provide higher-resolution images [8]. Ultrasound uses high-frequency sound waves to create images of breast tissue and distinguishes solid masses from fluid-filled cysts. Magnetic resonance imaging (MRI) and computed tomography (CT) scans are useful for assessing the extent of the disease [9].

Blood investigations include the measurement of tumor markers such as CA 15-3 or CA 27–29, which are used to monitor the tumor load and the response to treatment [10,11]. Tissue sampling followed by histopathological or cytological examination is the definitive diagnostic test for breast cancer. Histopathological examination (HPE) refers to a surgical biopsy of the tumor, which is stained and examined under a microscope. Cytological examination refers to fine needle aspiration, a minimally invasive procedure for aspirating cells and subjecting them to examination [12].

Malignant cells exhibit metabolic abnormalities and undergo changes in their metabolic processes, impacting the pathways responsible for glucose, glutamine, and fatty acid metabolism. These modifications lead to the production of ATP and metabolic compounds that support the continued growth and proliferation of cancer cells. The Warburg phenomenon is one such alteration in which malignant cells switch to aerobic glycolysis [13].

Our study aimed to assess the role of biochemical markers such as the triglyceride-glycemic index (TyG) and hematological markers such as NLR and PLR in distinguishing between the benign and malignant breast masses. The rationale behind our choice of these markers is their association with metabolic dysfunction in malignant tumors and their roles in the tumor microenvironment, where inflammation is a hallmark of cancer. Considering these factors, we identified the TyG index, NLR, and PLR as potential biomarkers relevant to breast cancer diagnosis.

Our preference for these markers over existing ones is driven by their cost-effectiveness, simplicity, and feasibility for measurement in peripheral healthcare settings. Recognizing the challenges faced in resource-limited environments, we aimed for these biomarkers to serve as supplementary tools for decision-making in referral services.

2. Patients and methods

2.1. Study participants

We conducted a prospective, cross-sectional study that included female patients who reported to the outpatient department (OPD) of the Department of General Surgery at the Government Medical College, Omandurar, Chennai, from April 2023 to September 2023, with complaints of breast masses. We included patients with breast masses diagnosed as either benign or malignant breast tumors, by cytological and HPE analyses of biopsy specimens. We excluded individuals who had chronic infections or inflammatory disorders, diabetes mellitus, who were younger than 18 years of age, who were taking hypolipidemic drugs, and who had a family history of hypercholesterolemia or hypertriglyceridemia.

The target sample size for this study, calculated using the prevalence formula with a desired 95 % confidence interval and a margin of error of 6.5 %, was determined to be 200. After obtaining the cutoff, 25 individuals were additionally recruited for validation.

2.2. Data collection methods

After the study protocol was explained to the patients and written informed consent, was obtained, a thorough medical history was obtained, and a clinical breast examination was conducted. The patients underwent radiological imaging (mammography), and the Breast Imaging Reporting and Data System (BI-RADS) score was obtained for these patients. Subsequently, the breast mass was characterized as benign or malignant based on cytological assessment using fine-needle aspiration cytology (FNAC).

Before initiating treatment, we collected 2 mL of venous blood in a fasting state using CB PLUS® Gray Vacutainers (containing potassium oxalate and sodium fluoride), CB PLUS® Purple Vacutainers (containing K2EDTA), and BIOPRO® Red Vacutainers (containing clot activator).

Serum fasting glucose and serum triglycerides were estimated using the ERBA MANNHEIM® XL640 Automated Biochemical Analyzer through automated photoelectric colorimetry, employing the glucose oxidase-peroxidase (GOD-POD) method for glucose and the glycerol phosphate oxidase (GPO) method for triglycerides. A complete blood count with differential (CBC with differential) was performed using the SYSMEX® XN-350 automated hematology analyzer.

Subsequently, we calculated the NLR and PLR from the CBC results. TyG was calculated using the formula: $ln((Serum\ Triglycerides * Serum\ Fasting\ Glucose)/2)$ where ln represents the natural logarithm.

The FNAC results were confirmed by subjecting the breast mass to HPE with hematoxylin and eosin (H&E) staining of the specimen obtained via biopsy. The lesions were further classified according to the criteria established by the World Health Organization (WHO).

2.3. Ethical approval and informed consent

This study was approved by the Institutional Ethics Committee of Government Medical College, Omandurar, Government Estate (Registration Number – ECR/1492/Inst/TN/2021) with approval number 40/IEC/GOMC/2023.

All procedures performed in studies involving human patients were in accordance with the ethical standards of the 1964 Helsinki Declaration and its later amendments. Written informed consent was obtained from all individual participants included in the study. This article does not contain any studies with animals performed by any of the authors.

2.4. Statistical analysis

All the data were collected in Microsoft Excel 2020 and later imported into IBM SPSS 26.0 (Statistical Package for the Social Sciences) and R software to carry out the statistical analysis. Age, BMI, serum glucose, triglycerides, neutrophil count, platelet count, lymphocyte count, NLR, PLR, and TyG were entered as continuous variables, while the type of breast lesion, BI-RADS score, and stage of malignant breast tumor were entered as categorical variables. Continuous variables are expressed as mean $\pm$ standard deviation (SD) or median with 25–75 percent interquartile range (IQR), while categorical variables are expressed as percentages with a 95 % confidence interval. The Kolmogorov–Smirnov (KS) test and Anderson–Darling (AD) test were used to assess the normality of distribution of the data. To obtain an overall view of the data collected, descriptive analysis was performed. Summary statistics such as the mean, median, standard deviation, and interquartile range were computed to explore the dataset.

To address potential confounding effects and balance covariates between benign and malignant breast lesions, propensity score matching was performed using the MatchIt package in R. A binary outcome variable was created, denoted 0 and 1 for benign and malignant breast tumors, respectively. A logistic regression propensity score model was constructed with the outcome variable and covariates. The nearest neighbor matching method was used to match individuals with similar propensity scores across the benign and malignant groups. This resulted in a matched dataset where each observation in the malignant group was paired with a comparable observation in the benign group based on their propensity scores. The balance of covariates between the matched groups was assessed using summary statistics and standardized mean differences. Subsequently, the matched dataset was extracted for further analysis.

The Mann–Whitney *U* test was used to assess the presence of statistically significant differences between the NLR, PLR, and TyG index among the benign and malignant breast lesion groups. Spearman correlation analysis was conducted to explore the relationships between the NLR, PLR, and TyG index, and malignant breast tumor stage and the BI-RADS score. Subsequently, receiver operating characteristic (ROC) curves were constructed for the NLR, PLR, and TyG. The optimal cutoff point was determined based on the maximization of Youden's index (YI).

To validate the cutoff points, two 2x2 tables were constructed for an additional 25 participants, with the rows and columns representing the benign or malignant classification according to the cutoff using TyG and PLR respectively, and the HPE results. Chi-square tests were conducted to evaluate the associations between biomarker classifications and HPE results.

Logistic regression models were used to assess the associations between benign or malignant breast tumors and the TyG Index and PLR. A combined model incorporating both predictors was also developed. ANOVA was used to compare the individual and combined models to determine whether combining the TyG Index and PLR significantly enhanced the prediction of benign and malignant breast lesions.

3. Results

We enrolled 200 out of the 265 patients who were initially identified with breast lesions after applying the exclusion criteria. Among the 200 patients, 109 patients were diagnosed with benign breast lesions, and 91 patients had malignant lesions. In the malignant lesion group: 27 individuals were classified as Stage 1, 21 individuals as Stage 2, 21 individuals as Stage 3, and 22 individuals as

Stage 4. The average weight of the patients was 63.1 kg, with a standard deviation of 8.63 kg. Out of these study participants, 133 had undergone radiological imaging (mammography), and BI-RADS scores were obtained, with 31 having a score of 2, 64 having a score of 3, 31 having a score of 4, and 7 having a score of 5.

KS and AD tests revealed that the data did not follow a normal distribution. The mean values, standard deviations, medians, and interquartile ranges (IQRs) for age, BMI, blood counts and biochemical parameters for both benign and malignant breast lesions are tabulated in Supplementary Table 1. Figs. 1–10 in the supplementary material contain representative pathological diagnostic images depicting both cytological and HPE views of benign and malignant breast nodules. Table 1 tabulates descriptive statistics by age group (20–40 years, 40–60 years, and 60–80 years), while Table 2 tabulates descriptive statistics by BMI group (less than 23.5, 23.5–25.5, and more than 25.5), for the NLR, PLR, and TyG index.

Propensity score matching was performed using age and BMI to match patients with benign and malignant breast masses. Table 3 presents the balance assessment conducted before and after matching to evaluate the effectiveness of the matching procedure. This balanced the covariates between patients with benign and malignant breast masses, enhancing the comparability of the two groups for subsequent analyses.

According to Spearman's rank correlation, the NLR demonstrated a strong positive correlation with breast cancer stage (rho = 0.935, $p < 00.001$), indicating that the NLR increased with increasing disease stage. Similarly, the PLR exhibited a moderate positive correlation with breast cancer stage (rho = 0.350, $p < 00.001$), suggesting that the PLR is more strongly correlated with breast cancer stage. However, the TyG index showed no correlation with disease stage. In contrast, the NLR demonstrated no correlation with the BI-RADS score (rho = −0.043, $p = 0.625$), indicating that there was no association between the NLR and mammography findings. Conversely, the PLR and TyG index exhibited a moderate positive correlation with the BI-RADS score (rho = −0.457, $p < 00.001$ and rho = 0.470, $p < 00.001$, respectively), suggesting that a lower PLR and higher TyG index were associated with more suspicious mammography findings.

Receiver operating characteristic (ROC) curve analysis was performed to determine the cutoff values for the NLR, PLR, and TyG index for distinguishing between benign and malignant breast tumors. Fig. 1 shows the ROC curves for the NLR, PLR, and TyG index. The order of the NLR and PLR was malignant > benign, while for the TyG index, it was malignant < benign.

The area under the curve (AUC) for the NLR was 0.512, with an optimal cutoff value of 1.83 (YI - 0.0924). In contrast, the PLR exhibited an AUC of 0.871, with an optimal cutoff value of 94 (YI - 0.582, sensitivity – 72.48 %, specificity – 85.71 %), and TyG index displayed an AUC of 0.835 with an optimal cutoff value of 8.95 (YI - 0.606, sensitivity – 65.93 %, specificity – 93.58 %). The classification outcomes of patients with benign or malignant breast lesions, specifically based on the designated cutoff values for TyG and PLR, are tabulated in Table 4.

To assess the validity of the cutoff points, two 2x2 contingency tables were constructed, delineating the benign or malignant classifications based on the TyG and PLR cutoffs, as well as the HPE results, from an additional 25 recruited patients. These tables are presented in Tables 5 and 6. Chi-square tests yielded statistically significant results, of 6 and 6.25, with p-values of 0.014 and 0.012, respectively.

Logistic regression models were fitted to investigate the associations between the TyG index or PLR, and the likelihood of breast tumor malignancy. Separate models were constructed for the TyG index (Model 1) and PLR (Model 2), as well as a combined model incorporating both predictors (Model 3). ANOVA revealed a significant improvement in model fit when both the TyG index and PLR were included compared to the individual models (Residual Deviance: Model 1 = 174.92, Model 2 = 160.85, Model 3 = 115.51; $\chi^2 = 45.347$, $p < 0.001$).

4. Discussion

Two hundred patients with breast lesions were recruited, 109 of whom were diagnosed with benign breast tumors and 91 with malignant tumors. Propensity score matching using age and BMI balanced the covariates between the two groups. Significant differences were observed in the PLR and TyG index between benign and malignant lesions, indicating their potential as diagnostic markers. The NLR did not significantly differ between the groups. The NLR exhibited a strong positive correlation with breast cancer stage, while the PLR showed a moderate positive correlation. The TyG index demonstrated no correlation with disease stage. In contrast to its association with breast cancer staging, the NLR showed no correlation with the BI-RADS score, whereas the PLR and TyG index exhibited a moderate positive correlation with the BI-RADS score. ROC curve analysis revealed the optimal cutoff values for the

Table 1
Descriptive statistics by age group.

Age Group	Variable	Mean	Median	SD	IQR (25–75)
20–40 Years n = 59	NLR	2.20	1.82	1.064	1.48–2.71
	PLR	142.34	136.07	62.611	90.51–178.21
	TyG Index	8.79	8.75	0.132	8.70–8.90
40–60 Years n = 109	NLR	2.25	1.96	1.027	1.50–2.75
	PLR	101.82	80.53	57.922	59.41–138.70
	TyG Index	8.91	8.83	0.224	8.73–9.10
60–80 Years n = 32	NLR	2.40	2.01	1.206	1.63–2.51
	PLR	65.83	63.66	24.841	46.68–83.15
	TyG Index	9.01	9.09	0.213	8.81–9.17

Table 2
Descriptive statistics by BMI group.

BMI Group	Variable	Mean	Median	SD	IQR (25–75)
Less than 23.5 n = 76	NLR	2.36	1.99	1.215	1.48–3.11
	PLR	114.42	90.82	64.374	69.07–140.58
	TyG Index	8.91	8.84	0.213	8.75–9.10
23.5–25.5 n = 49	NLR	2.05	2.00	0.651	1.52–2.44
	PLR	111.69	96.00	59.808	75.53–150.00
	TyG Index	8.84	8.76	0.205	8.69–8.96
More than 25.5 n = 75	NLR	2.30	1.93	1.111	1.53–2.78
	PLR	99.13	77.78	57.808	52.83–148.38
	TyG Index	8.90	8.85	0.215	8.73–9.09

Table 3
Balance assessment of age and BMI before and after matching for malignant and benign breast tumors.

Variable	Means (Malignant)	Means (Benign)	Standard Mean Difference	Variance Ratio	eCDF Mean	eCDF Max
Before Matching						
Age	54.84	28.82	2.32	1.99	0.44	0.85
BMI	25.19	25.11	0.03	0.85	0.05	0.13
After Matching						
Age	54.84	30.75	2.15	2.39	0.41	0.82
BMI	25.19	24.65	0.19	0.97	0.07	0.20

The Mann–Whitney test revealed no significant difference in the NLR between benign and malignant breast lesions ($W = 4204.5$, $p = 0.8582$). However, significant differences were observed in the PLR ($W = 7262.5$, $p < 0.001$) and TyG index ($W = 1339.5$, $p < 0.001$) between the two groups, indicating their potential as diagnostic markers for distinguishing benign from malignant breast masses.

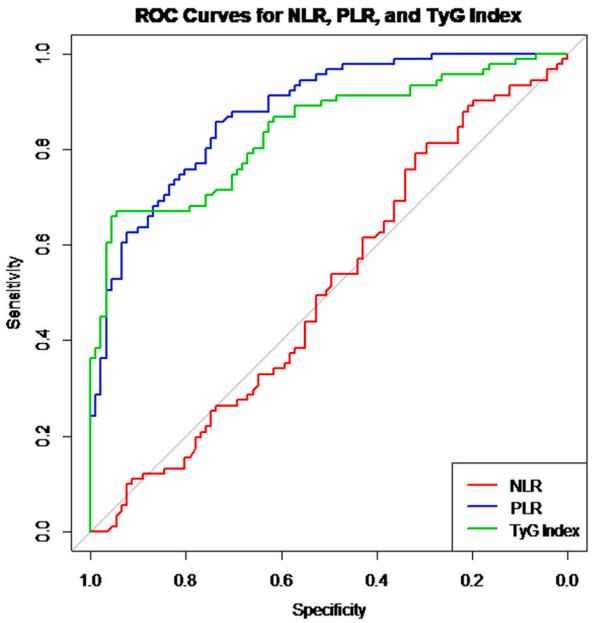

Fig. 1. ROC curves for NLR, PLR, and TyG index.

Table 4
Classification outcomes based on cut-off values for TyG and PLR in patients with breast lesions.

Biomarker	Benign	Malignant
Histopathology	109	91
TyG Index	131	69
PLR	92	108

Table 5
Contingency table for mass type by pathology and mass type by TyG.

Mass Type by HPE	Mass Type by TyG		Total
	Benign	Malignant	
Benign	13	2	15
Malignant	4	6	10
Total	17	8	25

Table 6
Contingency table for mass type by pathology and mass type by PLR.

Mass Type by HPE	Mass Type by PLR		Total
	Benign	Malignant	
Benign	12	3	15
Malignant	3	7	10
Total	15	10	25

NLR, PLR, and TyG index for distinguishing between benign and malignant breast tumors. Contingency tables constructed for an additional 25 patients showed significant results, supporting the validity of the cutoff points for the TyG and PLR. Logistic regression models revealed that including both the TyG index and the PLR significantly improved the model fit for predicting breast tumor malignancy compared to that of the individual models.

The current diagnostic guidelines for diagnosing malignant breast cancer begin with a clinical examination of the breast to check for any abnormal palpable mass. Imaging such as diagnostic mammography and ultrasound, are subsequently performed to confirm the findings of the examination. Tissue sampling by FNAC or biopsy is performed to confirm the diagnosis and also helps in classifying and grading the tumor, guiding the treatment modality [14].

Our study aimed to identify simple blood biomarkers that can be used as an add-on tool for diagnostic mammography to distinguish between benign and malignant breast lesions. Additionally, these biomarkers have the potential to supplement suspicious mammography findings. The TyG index and PLR are readily available through routine blood tests, making them a cost-effective and easily accessible markers. If validated in larger cohorts and prospective studies, these markers could be integrated into clinical practice to aid in the initial assessment of patients with breast masses. The gold-standard confirmatory diagnosis by HPE or FNAC is subsequently carried out.

The Warburg hypothesis proposes that malignant cells undergo metabolic changes characterized by elevated glucose consumption through glycolysis, even when oxygen is available (referred to as aerobic glycolysis). This metabolic shift results in heightened glucose uptake and the production of lactate, which is essential for meeting the energy and biosynthetic requirements of rapidly dividing malignant cells. Consequently, this altered metabolism can lead to decreased serum glucose levels in patients with malignancies [15].

Malignant cells exhibit metabolic reprogramming in which there is a reduction in the number or dysfunction of mitochondria, which are the cellular powerhouses responsible for energy production [16]. This can disrupt the normal cellular energy balance. Consequently, cancer cells exhibit reduced beta-oxidation, which occurs within mitochondria due to the breakdown of fatty acids to generate energy. This metabolic shift may lead to inefficient utilization of fatty acids, causing an increase in serum triglyceride levels [17,18].

These metabolic shifts could be responsible for elevated TyG levels in patients with malignant breast lesions. Another theory proposed by Alkurt E. G. et al. [19] revolves around insulin resistance, which may contribute to cancer pathogenesis. Higher TyG values are an indirect indicator of insulin resistance, which leads to compensatory hyperinsulinemia. Elevated insulin promotes cell proliferation, inhibits apoptosis, and enhances tumor angiogenesis, potentially creating a microenvironment conducive to tumorigenesis and metastasis.

The findings of our study are consistent with the research conducted by Shi, Haimeng et al. [20], who concluded that a higher TyG index is significantly linked to a greater incidence of gynecologic and breast cancers. Another study by Panigoro, Sonar Soni et al. [21] concluded that a TyG >8.87 is associated with an increased risk of breast cancer.

Inflammation is considered a hallmark of cancer progression. The NLR, calculated from complete blood counts, has emerged as a marker of systemic inflammation [22]. It reflects the balance between neutrophils (proinflammatory response) and lymphocytes (antitumoral immune response). A high NLR suggests a shift towards a proinflammatory state, potentially contributing to cancer progression. Neutrophils also play a role to in the formation of NETs (neutrophil extracellular traps) in the tumor microenvironment around the breast [23]. Our study findings are consistent with those of Elyasinia, Fezzeh et al. [24], who reported an increase in the NLR with increasing stage of breast cancer. This finding has important clinical implications, as a higher NLR in patients with malignant breast tumors is associated with a worse prognosis.

However, our findings did not reveal a significant difference in the NLR between these two groups, which was unexpected since malignant tumors are usually associated with a heightened inflammatory response. These findings conflict with those reported by Fang, Qiong et al. [25], Gago-Dominguez, Manuela et al. [26], and Corbeau, Iléana et al. [27], all of whom reported elevated NLR levels in patients with breast malignancies. Fang, Qiong et al. [25] included individuals with hyperglycemia and hyperlipidemia,

contrasting with our study, which excluded patients with these conditions.

The non-significance of the NLR in distinguishing breast tumors could be attributed to several factors. This may be due to the geographical origin of the patients and differences in the age distribution of patients with malignant and benign breast tumors. Malignant breast tumors are more commonly observed in elderly, postmenopausal women, whereas benign tumors are frequently diagnosed in younger, premenopausal women. Since menopausal status is associated with significant hormonal changes, it is plausible that these hormonal fluctuations may impact the immune system and inflammatory response differently in premenopausal and postmenopausal women. While our study suggests these possible explanations, further research is needed to understand the specific mechanisms driving these associations.

Platelets play a multifaceted role in cancer progression. They have the ability to form a protective barrier around tumor cells, shielding them from the immune attack of lymphocytes [28]. They also release proangiogenic factors such as vascular endothelial growth factor (VEGF) and platelet-derived growth factor (PDGF), which contribute to angiogenesis within the tumor [29]. Platelets contribute to the proinflammatory microenvironment within tumors by releasing inflammatory mediators that support cancer cell survival and proliferation [30]. This leads to the consumption of platelets in patients with malignant tumors. Our study revealed a significant difference in the PLR between patients with benign and malignant breast tumors, with the PLR being elevated in the former. This contradicts the findings of Alizamir, Aida et al. [31], whose study concluded that a higher NLR, PLR, and CRP predict the risk of breast malignancy.

Our study has several limitations. First, the study population is limited, and a larger multicentric study is needed to further investigate the use of these parameters in distinguishing between breast masses. Second, the patients were not followed up to assess their NLR, PLR, and TyG values after surgical removal of the breast mass. Finally, our study was conducted at a single institution, which limits the generalizability of our findings to broader populations.

5. Conclusion

In conclusion, our study highlights the potential utility of the TyG index and PLR as adjunctive markers for distinguishing between benign and malignant breast masses, as well as for supplementing suspicious mammography findings. While the NLR was correlated with breast cancer stage, its ability to distinguish between benign and malignant lesions was not significant. The combination of the TyG index and PLR demonstrated enhanced predictive power compared to that of the individual markers. These markers are readily available through routine blood tests and could serve as cost-effective and easily accessible tools in clinical practice. This method may be useful in clinical decision-making after larger multicentric studies are conducted.

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Data availability statement

The data utilized in this research will be accessible upon request from the first author but will not be publicly accessible to safeguard the confidentiality and privacy of the patients who participated. Requests for data access must specify the purpose for which the data will be utilized. In cases of data reuse, a proposal outlining the purpose, the intended usage of the data, and a letter from the department head or the institution's leadership will be mandatory. Additionally, any subsequent data generation should be communicated to the primary author.

CRediT authorship contribution statement

Hamrish Kumar Rajakumar: Writing – original draft, Validation, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Varsha Coimbatore Sathyabal:** Writing – original draft, Methodology, Investigation, Conceptualization. **Thilaga Thamilarasan:** Writing – review & editing, Supervision, Project administration, Methodology, Conceptualization. **Pushpa Balamurugesan:** Writing – review & editing, Validation, Supervision, Resources, Methodology, Conceptualization. **Gayathri Ganesan:** Writing – review & editing, Validation, Supervision, Methodology, Investigation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e30321.

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