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Monocyte to Lymphocyte Ratio as a Marker to Predict Carcinoma Prostate in Prostate Biopsy

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ABSTRACT

The prevalence of prostate cancer (PCa), a prevalent tumour, is rising globally. PSA, or serum prostate-specific antigen, is frequently utilised in PCa screening. Malignancies are thought to be largely influenced by inflammation and there is a complicated connection between the local immune response and systemic inflammation. Inflammatory characteristics have been researched as a potential PCa diagnostic sign. Serum prostate-specific antigen (PSA) which is used to detect PCa does not have enough sensitivity and specificity for PCa, which leads to unnecessary biopsies, overdiagnosis and overtreatment. Therefore, there is a need for easily available and inexpensive new biomarkers that can detect clinically important PCas and prevent unnecessary biopsies. Evaluate the predictive role of the inflammatory parameter, especially MLR, on the diagnosis of Pca. A retrospective study was conducted from June 2021 to July 2022 in Vydehi institute of medical science and research centre, Bangalore. Patients who presented with obstructive LUTS were included in this study and were analyzed. In 1 year period a total of 44 patients with a PSA >4 were assessed. MLR had a Sensitivity: 87.5% and Specificity: 97.2% with a p value of 0.001 which was highly significant in detecting prostate cancer in patients subjected to biopsy Other inflammatory markers like NLR and PLR had a Sensitivity: 75%, Specificity: 50% and Sensitivity: 75%, Specificity: 81%, respectively. All inflammatory markers evaluated in our study like NLR, PLR and MLR were high in PC apatients. But only MLR value had high sensitivity and specificity in detecting prostate cancer in patients with elevated PSA.

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Key Words

Prostate cancers, monocyte to lymphocyte ratio (MLR), platelet to lymphocyte ratio (PLR), neutrophil to lymphocyte ratio (NLR)

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INTRODUCTION

A frequent malignancy, prostate cancer (PCa) is becoming more prevalent throughout the world. Notwithstanding recent developments, early PCa screening and therapy remain among the most difficult and contentious issues[1]. PCa screening frequently involves the use of serum prostate-specific antigen (PSA). It is advised to do a prostate biopsy (PBx), an invasive procedure that is presently accessible to confirm the diagnosis of PCa, if a rise in the serum PSA level is seen. Nevertheless, serum PSA is neither sensitive or specific enough for PCa, which results in pointless biopsies, overdiagnosis and overtreatment[2,3]. Hence, there is a want for widely accessible and reasonably priced novel biomarkers that can identify clinically significant PCas and save pointless biopsies.

Neoplasia, proliferation and metastasis are known to be strongly influenced by tumor-associated inflammation and the microenvironment[4,5]. PCa development has reportedly been linked to systemic inflammatory responses[6].

The absolute monocyte count divided by the absolute lymphocyte count is known as the monocyte-to-lymphocyte ratio (MLR), which has been shown to be a new haematological and inflammatory measure. Monocytes have the capacity to inhibit lymphocyte activation and accelerate tumour growth[7]. Whereas, an increased monocyte count may encourage tumorigenesis and angiogenesis by stimulating tumour neovasculogenesis and suppressing local immune function[8].

Lymphocytes play a significant part in the immune responses to cancer in the bloodstream and in the tumour microenvironment, for instance, by T-cell mediated cellular cytotoxicity[9]. A tumour may only be subject to a weak, inadequate immune response if the lymphocyte count is low[10]. It has been proposed that a high MLR, a straightforward biomarker of the host immune system, is associated with a bad prognosis in a number of malignancies[11].

In this study, we aimed to evaluate the predictive role of the inflammatory parameter, especially MLR, on the diagnosis of PCa.

Need for study: Serum prostate-specific antigen (PSA) which is used to detect PCa does not have enough sensitivity and specificity for PCa, which leads to unnecessary biopsies, overdiagnosis and overtreatment.

Therefore, there is a need for easily available and inexpensive new biomarkers that can detect clinically important PCas and prevent unnecessary biopsies.

Aims and objectives of the study: Evaluate the predictive role of the inflammatory parameter, especially MLR, on the diagnosis of Pca.

MATERIALS AND METHODS

A Retrospective study was conducted for a period of 13 months from June 2021 to July 2022 in Vydehi institute of medical science and research center Bangalore, Karnataka.

Source of data: Patients who presented with obstructive LUTS to Department of Urology, Vydehi Institute of Medical Science and Research Centre Bengaluru, Karnataka.

Inclusion criteria:

- Clinical suspicion based on high PSA
- Abnormal DRE

Exclusion criteria:

- Oncologic
- Hematologic and systemic inflammatory diseases
- Prostatic surgery
- Anti-inflammatory drug usage within 2 weeks Before trus-pbx
- Ethical clearance was obtained

Detailed history of all patients was collected with thorough clinical examination and entered into the proforma. The following data were collected and entered in the proforma.

The following data was collected:

- Age
- PSA
- Platelet count
- Neutrophil count
- Lymphocyte count
- Monocyte count
- NLR
- PLR
- MLR
- Histopathology of patients were recorded

Ethics: Ethical committee approval obtained from The Vydehi Institutional Ethical Committee with approval number-VIEC/2022/APP/003 on 23/1/2023.

Consent: Patients consent was obtained for the following study.

Statistical analysis: SPSS (Statistical Package For Social Sciences) version 20. IBM SPASS statistics [IBM corp. released 2011] was used to perform the statistical analysis:

- Data was entered in the excel spread sheet
- Descriptive statistics of the explanatory and outcome variables were calculated by mean, standard deviation for quantitative variables, frequency and proportions for qualitative variables
- Inferential statistics like:
    - Diagnostic accuracy tests like sensitivity, specificity and ROC curve was plotted for MLR, NLR and PLR to predict the prostate cancer

The level of significance is set at 5%

RESULTS

In 13 month period of study from June 2021 to July 2022, 44 patients were included. Most common age group was 61-75 year-old (70.5%) followed by 45-60 age group(22.7%) and >75 age group (6.8%).

The Mean values of T.PSA was 27.62 and the pathology results of 44 patients were as follows: BPH 34 (77.3%), adenocarcinoma 8 (18.2%) and prostatitis 2 (4.5%).

Patients with PCa were older and had higher serum PSA, PLR, NLR and MLR values compared to non PCa patients who having BPH and prostatitis histopathology.

The platelet, neutrophil monocyte and lymphocyte values were collected for all the patients and the MLR, PLR and NLR were calculated as tabulated in Table 1. The mean of MLR, PLR and NLR were calculated which were 0.332, 9.784 and 3.288, respectively.

We performed the ROC analysis for MLR and the sensitivity was 87.5% Specificity was 97.2% with cutoff value 0.404 with AUC-0.972 (p<0.001) Table 2 and Fig. 1.

We performed the ROC analysis for NLR and the sensitivity was 75% Specificity was 50% and cut off value of 3.358 with AUC-0.792 (p<0.045) Table 3 and Fig. 1.

ROC analysis for PLR was performed and the cut-off was 11.83 and the sensitivity was 75% Specificity was 81% with AUC-0.771 (p<0.018) Table 4 and Fig. 1.

MLR had a Sensitivity: 87.5% and Specificity: 97.2% with a p<0.001 which was highly significant in detecting prostate cancer in patients subjected to biopsy.

Other inflammatory markers like NLR and PLR had a Sensitivity: 75%, Specificity: 50% and Sensitivity: 75%, Specificity: 81%, respectively.

DISCUSSIONS

In previous studies, it was found that the NLR, MLR and PLR were inexpensive, non-invasive markers of a variety of inflammatory or infectious diseases. This study evaluated the diagnostic value of these markers

Table 1: Platelet, neutrophil monocyte and lymphocyte values

	N	Minimum	Maximum	Mean	Standard deviation
Platelet	44	70.000	378.000	203.136	82.1382
Neutrophil	44	39.700	87.500	64.339	11.2680
Lymphocyte	44	7.500	44.400	22.245	7.9425
Monocyte	44	1.600	12.000	6.984	2.1936
MLR	44	0.104	0.562	0.332	0.0940
PLR	44	2.789	20.594	9.784	3.8620
NLR	44	0.953	6.574	3.288	1.2390

Table 2: MLR as diagnostic marker for prostate cancer

	Area under the curve			
			Asymptotic 95% confidence interval	
Area	Standard error	p-value	Lower bound	Upper bound
0.972	0.027	0.001	0.919	1.000

a: Under the nonparametric assumption and b: Null hypothesis: True area = 0.5

Table 3: NLR as diagnostic marker for prostate cancer

	Area under the curve			
			Asymptotic 95% confidence interval	
Area	Standard error	p-value	Lower bound	Upper bound
0.792	0.111	0.045*	0.512	0.947

a: Under the nonparametric assumption and b: Null hypothesis: True area = 0.5

Table 4: PLR as diagnostic marker for prostate cancer

	Area under the curve			
			Asymptotic 95% confidence interval	
Area	Standard error	p-value	Lower bound	Upper bound
0.771	0.109	0.018*	0.557	0.984

a: Under the nonparametric assumption and b: Null hypothesis: true area = 0.5

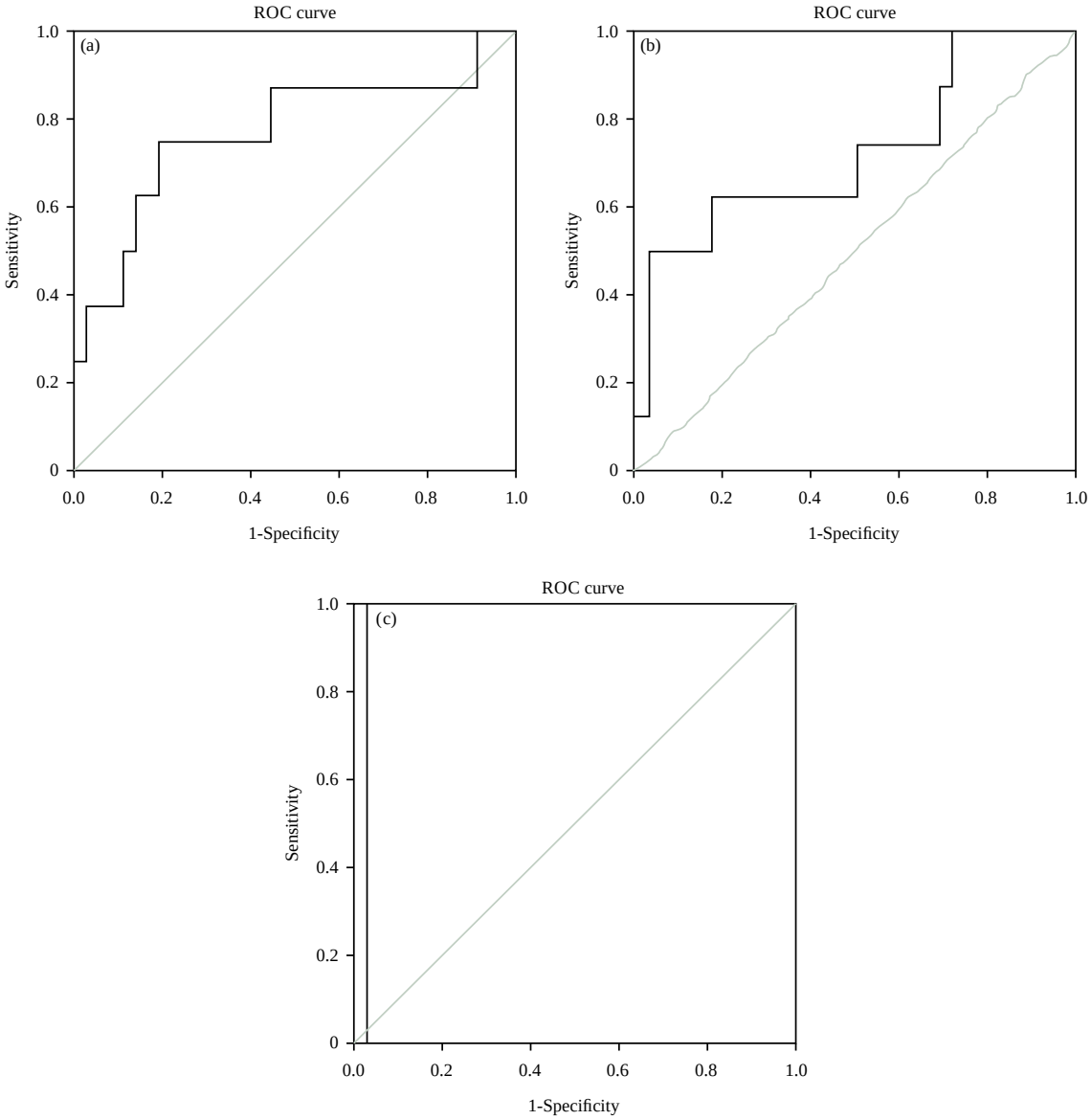

Fig. 1(a-c): ROC analysis for PLR and NLR (a) Platelet to lymphocyte ration, (b) Neutrophil to lymphocyte ration and (c) Monocyte to lymphocyte ratio

in PCa patients. Also, we contrasted PSA's predictive power with that of the NLR, MLR and PLR. It's interesting to note that NLR, MLR and PLR scores were greater in PCa patients. The diagnostic value of the MLR was greater than that of the NLR, PLR and all other measures with the exception of PSA. These results led us to the conclusion that MLR could be an effective supplemental indication for the diagnosis of PCa.

The management of PCa has advanced significantly with the advancement of molecular biology, immunology, biochemistry, ultrasound diagnostics, radiography and MRI diagnosis. Early PCa diagnosis is very important since it raises the likelihood of a full clinical recovery. Several pieces of evidence in recent years have suggested that inflammation may contribute to the development and spread of tumours[12]. Researchers have also identified a link between PCa and inflammation[13]. According to several studies, the risk of PCa increases the longer prostatitis symptoms last[14]. Men may be much more vulnerable to PCa as a result of persistent prostate inflammation and infection as well as STIs, according to several prospective studies.

Current recommendations for nonsteroidal anti-inflammatory drugs to lower the risk of PCa support the notion that inflammation and PCa are strongly associated[15,16]. Excitingly, several biomarkers

Table 5: Comparable higher sensitivity and specificity of PLR and NLR

Discussion	Present study	Demirkol *et al*.[26]	Zhanping *et al*.[27]
MLR	Sen 87.5%	Sen 60.2%	Sen 72 %
	Spec 97.2%	Spec 92.2%	Spec 87.4%
NLR	Sen 75 %	Sen 39.4%	Sen 73%
	Spec 50%	Spec 76.6%	Spec 88.3%
PLR	Sen 75%	Sen 74.2%	Sen 56%
	Spec 81%	Spec 46.6%	Spec 86.4%

associated with inflammation, like C-reactive protein and serum interleukin-7 (IL-7) levels, have been discovered to be helpful in the early identification of PCa[17,18]. None of the recently reported markers, however, can entirely replace PSA due to their unsatisfactory specificity and sensitivity.

The most crucial serum indication for PCa diagnosis nowadays is still PSA[19]. As PSA is a prostate-specific antigen rather than a PCa-specific antigen, it has drawbacks, as is well recognised. When utilising a screening technique of PSA alone, acute prostatitis and benign prostatic hyperplasia frequently boost serum PSA, which complicates the diagnosis of PCa[20,21]. Also, excessive usage of it results in a lot of needless biopsies and other problems.

In our study, the results showed that for patients with PCa, the NLR, MLR and PLR were all significantly higher than those in healthy subjects. The AUCs of these three parameters (MLR, NLR and PLR) showed the highest diagnostic value for PCa, especially the MLR, with the highest AUC among them. The NLR in peripheral blood has been shown to be a possible marker to predict PCa and other studies have suggested that the PLR can be a significant auxiliary predictor of PCa[22-23]. A few immune illness reports with diagnostic values for MLR suggested that it may indicate the degree of immunological damage and systemic inflammation[24,25]. The MLR had a better predictive value for PCa than the NLR and PLR, which is an important result from this study. There is still much to learn about the precise reason why the MLR rises in PC apatients. Our study showed that most patients with PCa had higher serum monocytes and lower serum lymphocytes.

In this study MLR has higher sensitivity and specificity than PLR and NLR comparable to studies by Demirkol *et al*.[26] and Zhanping *et al*.[27] (Table 5).

Several limitations exist in our study that should be pointed out. First, this was a retrospective single-centre study and it enrolled a relatively small cohort of patients. Second, we have not researched the pathogenesis behind the elevated NLR, MLR and PLR. Third, the peripheral MLR is a biomarker that indicates an inflammatory condition, which is not specific to PCa.

Consequently, multi-centre investigations and molecular biology studies are urgently needed in the future.

CONCLUSION

All inflammatory markers evaluated in our study like NLR, PLR and MLR were high in PCa patients. But only MLR value had high sensitivity and specificity in detecting prostate cancer in patients with elevated PSA. Men with an increased PSA and MLR should be recommended for prostate biopsy.

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