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The Role of Hematological Parameters in Testicular Tumor Cases

[1]Dhiren N. Buch, [2]Kushal Kapasi, [3]Ketan D. Mehta and [4]Viraj K. Mehta

[1-3]3Department of General Surgery, Shri M P Shah Medical College, Jamnagar, Gujarat, India

[4]Department of General Surgery, Smt B K Shah Medical Institute and Research Center, Waghodia Road, Waghodia, Vadodara, Gujarat, India

ABSTRACT

Testicular cancer (TCa) is an uncommon tumor primarily affecting young men aged 18-35 years. Known risk factors include cryptorchidism, a family history of the disease and infertility. This study aimed to explore the impact of certain hematological parameters on the prognosis of testicular malignancies (TM). The study comprised 200 patients diagnosed with TM through physical examination, laboratory tests and scrotal ultrasonography, all of whom underwent radical inguinal orchiectomy. A control group of 200 age-matched subjects who had bilateral varicocelectomy via an inguinal incision was also included. Hematological and biochemical blood samples were collected the day prior to the radical orchiectomy. Parameters such as the neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR) and lymphocyte-monocyte ratio (LMR) were calculated as ratios of tstandard radical inguinal orchiectomy, tumor staging was completed based on histological findings, while clinical N and M staging were performed using imaging techniques. The average ages of patients in Groups 1 and 2 were 26.10±7.5 years and 24.9±8.2 years, respectively. Group 1 exhibited significantly elevated neutrophil counts, NLR and PLR, while Group 2 showed statistically significant increases in lymphocyte count, mean platelet volume (MPV) and LMR ($p<0.05$). Additional data on the pathological findings and follow-up results for TM patients were also analyzed and the association between hematological parameters and T stage was assessed. The NLR, due to its ease of measurement and cost-effectiveness, may serve as a valuable adjunct for clinicians. It can aid in the diagnosis of stage I testicular tumors with favorable prognoses, where early diagnosis is crucial, even if it is not the primary diagnostic tool.

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Key Words

Neutrophil/lymphocyte count, hematological parameters, platelet/lymphocyte count, testicular tumor

Corresponding Author

Viraj K. Mehta,
Department of General Surgery, Smt B K Shah Medical Institute and Research Center, Waghodia Road, Waghodia, Vadodara, Gujarat, India
drjagratigupta1701@gmail.com

Author Designation

[1]Associate Professor (Urology)
[2]Assistant Professor (Urology)
[3]Professor and Head
[4]Resident Doctor

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INTRODUCTION

Testicular Malignancy (TM) is the most prevalent solid organ cancer among males aged 15-35 years, accounting for approximately 1-1.5% of all cancer cases in men[1]. Early diagnosis significantly enhances patient outcomes, underscoring the importance of identifying and treating testicular malignancies at their initial stages. The diagnostic methods for TM include physical examinations, imaging techniques, laboratory parameter assessments and tumor marker analysis. While testicular tumors are relatively uncommon, their occurrence in younger populations makes them particularly noteworthy.

Testicular Tumors can be Categorized into Three Main Groups: germ cell tumors, sex-cord stromal tumors, and miscellaneous tumors. Germ cell tumors are further classified into seminomas and non-seminosmatous germ cell tumors. Seminomas and lymphomas are the predominant types of testicular tumors encountered in young adults and men over 60 years, respectively. Although tumor markers such as alpha-fetoprotein (AFP), human chorionic gonadotropin (hCG) and lactate dehydrogenase (LDH) play a role in the clinical management of testicular tumors-where early diagnosis can lead to prolonged survival-there is ongoing research into more affordable and effective diagnostic and monitoring methods[2].

Changes in the systemic inflammatory response can be assessed through various hematological parameters[3]. For example, elevated C-reactive protein (CRP) levels and neutrophil-lymphocyte ratios (NLR) serve as indicators of systemic inflammation in numerous cancers. Previous studies have demonstrated a correlation between high NLR values and poor prognoses in certain urological malignancies[4]. The NLR not only reflects systemic inflammatory responses but also serves as a valuable prognostic marker across various tumors[5]. Consequently, there is growing interest in utilizing easily obtainable hematological parameters, such as NLR, to predict cancer prognosis and inflammatory states[6]. NLR, lymphocyte-monocyte ratio (LMR), platelet-lymphocyte ratio (PLR) and mean platelet volume (MPV) may all function as prognostic indicators in diverse clinical scenarios.

Furthermore, platelet-related parameters, which are implicated in the inflammatory processes associated with malignancies-such as platelet count, PLR and MPV-have potential as biomarkers in various tumors[7]. However, there is limited knowledge regarding the relationship between germ cell tumors (GCT), which represent 95% of testicular tumors and the hematological parameters that are commonly assessed in other types of cancer.

In this study, we aimed to evaluate these easily measurable hematological parameters in patients diagnosed with TM, contrasting them with a control group of similar age who underwent varicocelectomy. Our goal was to investigate the impact of these hematological parameters on the prognosis of TM.

MATERIALS AND METHODS

E conducted a retrospective analysis of the cancer registry database at our institution, focusing on patients diagnosed with testicular malignancy (TM) between January 2018 and June 2023. The study comprised 200 patients diagnosed with TM through physical examination, laboratory tests and scrotal ultrasonography, all of whom underwent radical inguinal orchiectomy. A control group of 200 age-matched subjects who underwent varicocelectomy via an inguinal incision was also included. Patients were excluded from the study if they had testicular stromal tumors, infectious or inflammatory conditions, hematological disorders, other malignancies, cardiovascular disease, end-stage renal disease, cerebrovascular disease, diabetes mellitus, a history of smoking, or if they were receiving corticosteroids or ß-agonists. Additionally, patients with incomplete preoperative data (including complete blood counts and tumor markers) were excluded.

For staging, patients with TM underwent contrast-enhanced thoracoabdominal computed tomography (CT) and serum tumor marker assessments, including alpha-fetoprotein (AFP), lactate dehydrogenase (LDH) and beta-human chorionic gonadotropin (beta-HCG), after the radical inguinal orchiectomy. Clinical N and M staging was determined through imaging techniques based on final histopathological findings. Hematological and biochemical blood test results were collected one day prior to the radical orchiectomy as part of the routine preoperative evaluation. Tumor markers were assessed one week and one month after the surgery to finalize definitive staging.

Venous blood samples were drawn into ethylenediaminetetraacetic acid (EDTA) tubes for laboratory analysis. We measured neutrophil and lymphocyte counts, mean erythrocyte volume (MCV), and erythrocyte distribution width (RDW). The tumor markers AFP, beta-HCG and LDH were also analyzed. The neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR) and lymphocyte-monocyte ratio (LMR) were calculated from the respective blood cell counts.

Statistical Analysis: The compiled data were entered into a spreadsheet using Microsoft Excel 2019 and subsequently exported to SPSS version 19 (SPSS Inc., Chicago, Illinois, USA) for analysis. Quantitative variables were reported as means with standard deviations or medians with interquartile ranges, depending on their distribution. Categorical variables were expressed as counts and percentages. The

confidence level was set at 95% and the significance level was established at 5%.

RESULTS AND DISCUSSIONS

This study evaluated a total of 200 patients with TM (Group 1) and 200 controls who underwent varicocelectomy (Group 2). The mean ages of patients in Groups 1 and 2 were 26.10±7.5 years and 24.9±8.2 years, respectively. The mean body mass indexes of the patients were 23.9±6.9 kg/m² in Group 1 and 24.8±8.2 kg/m² in Group 2, with no statistically significant differences between the groups. The median values for beta-HCG, AFP and LDH in patients with TM were 26.5 mIU/ml, 32.0 IU/ml and 180 U/L, respectively. Demographic data are summarized in Table 1.

A comparison of hematological parameters revealed that neutrophil count, NLR and PLR were significantly higher in Group 1, whereas lymphocyte count, MPV, and LMR were significantly higher in Group 2 ($p<0.05$). Additionally, we compared hematological data with respect to T stages. The LMR was significantly elevated in patients with T1 stage TM, while NLR showed significantly higher levels in patients with pathologies greater than T1 ($p<0.05$). No significant differences were observed between T1 and >T1 cases regarding MPV and PLR.

Table 1: Comparison of Demographic Data Between Both Groups

Variables	Group 1 (n=200)	Group 2 (n=200)	p-value
Age (year)	26.10 ± 7.5	24.9 ± 8.2	0.22
Body mass index (kg/m2)	23.9 ±6.9	24.8 ±8.2	0.14
Tumor size (cm)	5.3 ± 2.5		
Beta-HCG+(mlU/ml)	3.8 (26.5)		
AFP+(lU/ml)	3.5 (32.0)		
LDH+(U/L)	252 (180)		

Table 2: Comparison of Hematological Data Between the Study Groups

Variable	Group 1 (n=200)	Group 2 (n=200)	p-value
Neutrophil count (x103 cells/mm3)	6.1 ±2.05	4.0 ± 1.5	0.001*
Lymphocyte count (x103 cells/mm3)	1.88 ± 0.7	2.98 ± 0.5	0.02*
Monocyte count (x103 cells /mm3)	0.65 ± 0.3	0.59 ± 0.1	0.22
Platelet count (x103 cells /mm3)	364.50 ± 75.5	249.1 ± 62.8	0.1
MPV (fL)	8.5 ± 1.4	9.2 ± 1.6	0.003*
NLR	3.79 ± 2.6	1.77 ± 0.6	0.004
LMR	3.92 ± 1.5	4.2 ± 1.6	0.01*
PLR	157.01 ±66.4	110.9 ± 32.1	0.001*

Testicular Tumors are Primarily Categorized into three Types: germ cell tumors, sex cord-stromal tumors and miscellaneous tumors[8]. Testicular germ cell tumor (TGCT) is the most prevalent subtype, accounting for over 95% of all testicular malignancies[9]. Treatment strategies depend on histopathological classification., while seminomas respond favorably to both radiotherapy and chemotherapy, non-seminomatous TGCTs respond to chemotherapy alone. In contrast, sex cord-stromal tumors resist both radiation and chemotherapy, with treatment typically involving orchiectomy and retroperitoneal lymphadenectomy.

Table 3: Pathological and Follow-up Results of Group 1

Variables	Number	Percentage (%)
	Pathology result	
Seminoma	116	58
Mixed germ cell tumor	66	33
Choriocarcinoma	4	2
Yolk sac tumor	2	1
Embryonal carcinoma	8	4
Teratoma	6	3
Tunica Vaginalis invasion	26	13
Rete testis invasion	66	33
Lymphovasculer invasion	130	65
Tunica Albuginea Invasion	78	39
	T stage	
T1	98	49
T2	92	46
T3	10	5
	Clinical stage	
1A	44	22
1B	54	27
2A	56	28
2B	12	6
3A	6	3
3B	12	6
3C	10	5
	Lymph node stage	
0	98	49
N1	56	28
N2	30	15
N3	18	9

Recent research suggests that platelets may inhibit the apoptosis of cancer cells mediated by natural killer cells and release angiogenic and tumor-promoting factors that foster tumor growth, progression and metastasis[10-12]. Numerous studies have highlighted the role and applicability of inflammatory biomarkers in urological malignancies such as prostate, bladder and kidney cancers[13-14]. However, despite the known predictive values of neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), lymphocyte-monocyte ratio (LMR) and mean platelet volume (MPV) in other cancers, their significance in testicular malignancy remains inadequately understood, potentially due to its lower prevalence. This study aims to define the potential relationship between hematological parameters based on preoperative complete blood count analysis and TM in patients undergoing radical orchiectomy, comparing them to patients who underwent varicocelectomy through a similar incision as a control group.

Research examining testicular tumors and inflammatory responses has frequently focused on the correlation between prognosis and metastasis[15]. MPV serves not only as a marker of platelet count but also as an indicator of bioactive platelets that have been activated and are involved in the inflammatory process. Previous studies have shown that reduced MPV is associated with poorer prognosis in renal cell carcinoma[16-17]. However, some researchers have suggested that MPV may not be a reliable prognostic indicator in patients with stage T1-T2-T3 TM[18].

When comparing the control group to those with TM, our findings revealed that MPV was significantly lower in patients with TM, although there was no significant difference in MPV values between stage T1 and >T1 cases. Despite the lower MPV in patients with TM, we

do not consider it a reliable prognostic factor for this malignancy. A meta-analysis comprising 100 studies and 40,559 patients identified a compelling association between elevated NLR and >20 different solid tumors. While this analysis encompasses a diverse range of malignancies, it underscores the critical role of NLR in the inflammatory and immune responses inherent to cancer biology[19]. An increased NLR indicates both systemic and local inflammation, associated with a high infiltration of tumor-associated macrophages that facilitate tumor growth, invasion and evasion. Furthermore, macrophages and neutrophils secrete tumor growth factors such as epidermal growth factor, vascular endothelial growth factor and interleukins 6 and 8, all of which significantly influence the tumor microenvironment. Additionally, these cells produce proangiogenic and matrix-degrading enzymes, including matrix metalloproteinases and elastases, that promote tumor metastasis[20]. Relative lymphocytopenia reflects a decrease in CD4+T helper lymphocytes, resulting in a suboptimal lymphocyte-mediated immune response to malignancies. Elevated NLR indicates both an increase in neutrophil-mediated inflammation and a decrease in lymphocyte-driven antitumor immunity, suggesting that higher NLR values may provide combined prognostic insights, offering stronger predictive value than each factor considered in isolation[21].

Yuksel[22] have previously compared preoperative NLR values between patients with localized testicular germ cell tumors and varicocele controls, finding significantly higher NLR values in patients with TM. Jankovich[23] reported higher NLR values in patients with pathologies greater than T1. In our study, which included patients who underwent varicocelectomy as the control group, we found that NLR values were significantly elevated in patients with TM.

There were notable differences in LMR values between patients with T1 stage tumors and those with pathologies greater than T1. These findings suggest a decline in LMR in patients with TM, particularly at higher pathological stages. The literature on the relationship between TM and LMR is limited. Notably, Herraiz-Raya[24] found that LMR values greater than 3 in TM patients were associated with smaller tumor volumes and lower cancer stages. We also observed significantly higher PLR values in the TM group compared to the healthy varicocele group, although no significant differences were found between T1 and >T1 stages regarding PLR. Therefore, we believe that increased PLR may serve as a useful parameter in TM patients, but it does not provide staging information. In their meta-analysis[25] reported lower PLR values in healthy individuals compared to patients with urological tumors, with the exception of bladder cancer.

The current study has several limitations. Firstly, it employs a retrospective design and includes a relatively small cohort of patients from a single center, which may restrict the generalizability of the findings. Additionally, the sample size is limited and there is a lack of prognostic predictive analysis.

CONCLUSION

Hematological parameters such as the neutrophil-lymphocyte ratio (NLR), due to their ease of measurement and cost-effectiveness, can serve as an adjunct tool for clinicians, offering a standard cut-off value for diagnosing stage I testicular tumors with favorable prognoses, where early detection is crucial, even if not used as the primary diagnostic method. However, larger randomized controlled studies are necessary to yield more definitive results.

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