The role of neutrophil to lymphocyte ratio as a predictor of testicular torsion

El papel de la proporción de neutrófilos a linfocitos como predictor de torsión testicular

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Abstract

Introduction: The diagnosis of testicular torsion (TT) is an enigma in clinical settings. The challenges depicted by the lack of differential diagnosis with other scrotal pathologies due to similarity in clinical presentation leading to confusion in diagnosis. Urgent diagnosis could potentiate emergency treatment to prevent testicular loss, especially in the first 6 hours. We sought to clarify, if WBCs could have a diagnostic role especially the neutrophil-to-lymphocyte ratio (NLR). **Methods**: In this prospective study, a total of 51 medical patients (aged 12 to 33 years, 32 patients diagnosed with TT who presented to the Duhok governorate emergency hospital with acute scrotal pain, and 19 age-matched non-TT). Age, medical, and surgical history of patients recorded. Blood samples were collected and hematological analysis was performed to calculate NLR. Results: NLR has been significantly (<0.0001) elevated in TT compared to non-TT patients. High sensitivity and specificity for TT versus non-TT implies that NLR could be used as a diagnostic tool for differentiating TT from other scrotal pathologies. **Conclusion**: NLR has been shown elevation in TT patients compared to non-TT, henceforth, could be utilized as an adjuvant diagnostic tool for additional differential diagnosis for the scrotal pathologies, alongside being used for predicting testicular viability following TT.

Keywords: Lymphocyte, Neutrophil, Testicular torsion, Orchiectomy, Doppler ultrasonography.

Resumen

Introducción: El diagnóstico de torsión testicular (TT) es un enigma en el ámbito clínico. Los desafíos representados por la falta de diagnóstico diferencial con otras patologías escrotales debido a la similitud en la presentación clínica que lleva a confusión en el diagnóstico. El diagnóstico urgente podría potenciar el tratamiento de urgencia para prevenir la pérdida testicular, especialmente en las primeras 6 horas. Intentamos aclarar si los glóbulos blancos podrían tener una función diagnóstica, especialmente la proporción de neutrófilos a linfocitos (NLR). **Métodos**: En este estudio prospectivo, se incluyó a un total de 51 pacientes médicos (de 12 a 33 años, 32 pacientes diagnosticados con TT que acudieron al hospital de emergencia de la gobernación de Duhok con dolor escrotal agudo y 19 sin TT de la misma edad). Edad, antecedentes médicos y quirúrgicos de los pacientes registrados. Se recogieron muestras de sangre y se realizaron análisis hematológicos para calcular el NLR. Resultados: El NLR se ha elevado significativamente (<0,0001) en los pacientes con TT en comparación con los pacientes sin TT. La alta sensibilidad y especificidad para TT versus no TT implica que la NLR podría usarse como una herramienta de diagnóstico para diferenciar la TT de otras patologías escrotales. **Conclusión**: Se ha demostrado que la NLR está elevada en pacientes con TT en comparación con los que no tienen TT; de ahora en adelante, podría utilizarse como una herramienta de diagnóstico adyuvante para el diagnóstico diferencial adicional de las patologías escrotales, además de usarse para predecir la viabilidad testicular después de la TT.

Palabras clave: Linfocitos, Neutrófilos, Torsión testicular, Orquiectomía, Ultrasonografía Doppler.

Introduction

Twisting of the spermatic cord is known as "testicular torsion", which is a serious medical condition associated with blocked blood supply to the testicles, which needs immediate surgical intervention with an annual prevalence of 3.8 in 100,000 males under the age of 18 years, 1 in 4,000 male under the age of 25; with an annual prevalence of 10-15% of acute scrotal disorders in children[1]. It's more serious in children when occurs, since 42% of operated scrotal torsion; is ultimately ended by orchiectomy[2]. Therefore, early diagnosis is crucial to avoid the risk of infarction and infertility, however, diagnosis remains challenging in clinical settings[3]. Unfortunately, differential diagnosis is hindered by overlapping clinical and physical examination, even though ultrasonography is used[4–7], the sensitivity and specificity are not highly effective, hence forth searching for alternative diagnostic tools is plausible.

Complete blood count (CBC) is a routine cheap and fast test in current medical laboratory blood testing. Testicular torsion is associated with inflammatory reactions and haematological abnormalities[8,9]. The association of hematologic parameters with inflammation suggest adding the changes in haematological parameters alongside other diagnostic tools to differentiate between TT and other testicular diseases with similar symptoms[10]. We sought to investigate the role of the neutrophil-lymphocyte ratio as a predictor of testicular torsion to provide a clear differential diagnosis.

Materials and methods

This study prospectively examined the medical records of 51 patients aged 12 to 33 years who presented to the Duhok Governorate Emergency Hospital with acute scrotal pain between November 2022 and October 2023. Patients who had undergone orchiectomy or surgical distortion due to testicular torsion diagnosed by scrotal power Doppler and intraoperatively confirmed testicular torsion were included in the study. Patients with epididymal-orchitis and patients with appendicular testicular torsion were excluded. The control group consisted of healthy men who had presented to the urology clinic for any reason and had not been diagnosed with epididymal-orchitis, testicular trauma, liver, kidney or hematologic disease, or previous scrotal surgery. Patient demographics and complete blood count (CBC) on admission were recorded. For the CBC, 3 mL of peripheral venous blood was drawn. A CBC analysis was performed. Neutrophil to lymphocyte ratio (NLR), groups were compared for age, hematologic parameters and NLR.

Ethical approval: The study was conducted by the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with patients' verbal and written approval before the sample was taken. The study protocol the subject information and the consent form were reviewed and approved by a local ethics committee according to document number 56 on 14/2/2022. Written and verbal informed consent was also obtained from all subjects in the control group.

After obtaining approval from the ethics committee. In the surgical field, the decision of orchiectomy or orchiopexy was made by the primary surgeon after assessing the viability of the testes after relieving the twisted spermatic cord structure by applying warm saline for at least 5 minutes. When patients visited our emergency department, they or their caregivers were asked about symptom duration and responses were recorded. Symptom duration was defined as the time between the onset of symptoms (acute scrotal pain) and arrival at our emergency department. After the history was taken, venous blood was drawn to determine the white blood cell (WBC) count the neutrophil-to-lymphocyte differential and the neutrophil-to-lymphocyte ratio (NLR). The time between the visit to the emergency room and the start of anaesthesia in the operating room was also taken from the medical record.

Statistical analyses: The general, medical, and lab characteristics of the patients of both TT and Non-TT groups were presented in mean and standard deviation or number and percentage. The comparisons of general, medical and lab characteristics between testicular torsion (TT) and Non-TT groups were examined in an independent t-test, Pearson chi-squared test, or Fishers' exact test as appropriate. AUC values, cut-off point, optimum, sensitivity and specificity for TT intraoperative diagnosis were determined using a Roc Curve analysis. The statistical calculations were performed using Statistical Package for Social Sciences version 25 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.)

The patient's characteristics of the disease are tabulated below in Table 1. Past medical and surgical history have shown a non-significant difference between TT and non-TT groups. The onset of TT was significantly (p=0.02) higher in night compared to non-TT, however, non-significant (p=0.1) differences existed between the two groups regarding the duration of torsion. More cases of TT undergone Orchiopexy than orchiectomy, these both operations were non applicable for non-TT. Non-significant (p=0.14) differences have been reported according to laterality. Younger (p=0.004) age groups represented with TT than non-TT (Table 1).

Table 1. Comparisons of general and medical characteristics between testicular torsion (TT) and Non-TT groups

Characteristics (n=51)	Study groups		P (two-sided)
	Non-TT (n=19)	TT (n=32)	
PMH			
Negative	16 (84.21)	26 (81.25)	1.0000[a]
Positive	3 (15.79)	6 (18.75)	
PSH			
Negative	19 (100)	26 (81.25)	0.0725[a]
Positive	0 (0.00)	6 (18.75)	
Onset of testicular torsion			
Morning	14 (73.68)	12 (37.50)	0.0201[a]
Night	5 (26.32)	20 (62.50)	
Duration of torsion			
< 6 hrs.	11 (57.89)	11 (34.38)	0.1011[b]
> 6 hrs.	8 (42.11)	21 (65.63)	
Orchiopexy			
No	Not applicable	14 (43.75)	Not applicable
Yes	Not applicable	18 (56.25)	
Orchiectomy			
No	Not applicable	18 (56.25)	Not applicable
Yes	Not applicable	14 (43.75)	
Affected side			
Left	14 (73.68)	16 (50.00)	0.1426[a]
Right	5 (26.32)	16 (50.00)	
Age (12-33 years)	20.89 (6.77)	16.8 (2.41)	0.0039[c]

PMH: Past medical history; **PSH**: Past surgical history
[a] Fisher's exact test, [b] Chi-squared test, and [c] independent t-test were performed for statistical analyses.

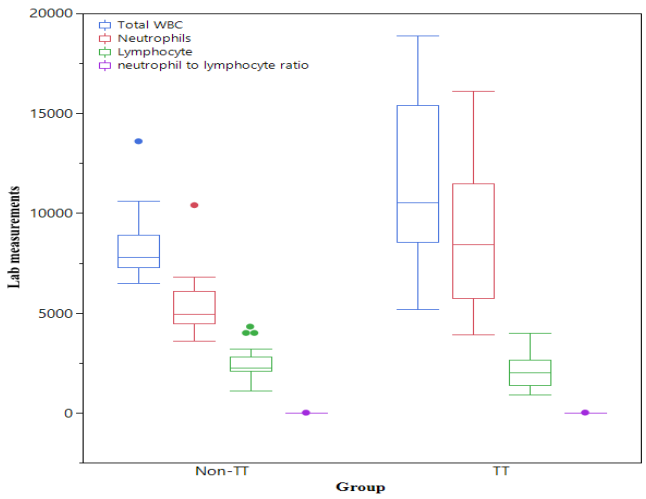
Following a diagnosis of TT, the haematological parameters of the studied group were compared between TT and non-TT and the findings revealed that TT is associated with significantly (p<0.05) higher WBC count, Neutrophils, and Neutrophil/Lymphocyte ratio compared to non-TT, with non-significant differences in lymphocyte between the TT and non-TT (Table 4 and Figure 1). Boxplots revealed that the interquartile ranges for total WBC and neutrophil have a wide variation and range in TT compared to non-TT while the boxplot of lymphocyte and Neutrophil/Lymphocyte ratio have nearly similar interquartile values, further confirming that the Neutrophil/Lymphocyte ratio is more reliable than other tests (Figure 1).

Table 2. Comparisons of laboratory findings between testicular torsion (TT) and Non-TT groups

Characteristics (n=51)	Study groups		P (two-sided)
	Non-TT (n=19)	TT (n=32)	
Total WBC	7911.11 (1133.91)	11700 (3802.12)	0.0002
Neutrophils	5056.67 (892.17)	8864.06 (3491.91)	<0.0001
Lymphocyte	2200.63 (558.21)	2054.69 (792.13)	0.5137
Neutrophil/Lymphocyte ratio	2.10 (0.70)	4.49 (1.98)	<0.0001
Range	0.98-5.55	0.98-10.85	
Torsion degree (Range: 180-1080)	Not applicable	464.06 (291.96)	Not applicable

An independent t-test was performed for statistical analyses.

Figure 1. Lab measurement soft TT and Non-TT groups.



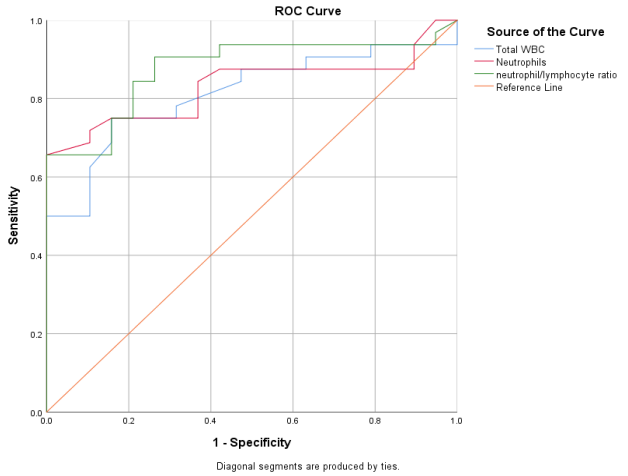
ROC curve analysis indicated that the Neutrophil/lymphocyte ratio has shown to be the best of these parameters reaching up to 84% sensitivity and a higher AUC of 0.88 (Table 3 and Figure 2).

Table 3. AUC values, cut-off point, optimum, sensitivity and specificity for TT intraoperative diagnosis

	AUC	Optimum point	Cut-off points	Sensitivity	Specificity	P value
Total WBC	0.81	9400	8200-9550	71.9	84.2	<0.0001
Neutrophils	0.83	6250	5810-6650	75	84.2	<0.0001
Neutrophil/lymphocyte ratio	0.88	3.07	2.55-3.29	84.4	78.9	<0.0001

Roc-curve analysis was performed for statistical analyses.

Figure 2. ROC curve for diagnosis of intraoperative testicular torsion.



Discussion

The TT is the only scrotal diseases that require urgent surgical intervention, whereas other scrotal diseases need only medical care and no surgery required. Unfortunately, great similarities exist between symptoms of TT and non-TT scrotal conditions, hindering differential diagnosis, therefore, proper investigation is important to avoid false negative cases prone to surgery. Improper diagnosis is possible in light of the similarity of clinical findings (scrotal swelling, redness, and testicular sensitivity) coupled with faulty decision resulting in scrotal misdiagnosis. Henceforth, searching for alternative or adjuvant diagnostic tools is crucial for clinicians to avoid this error. Inflammation is involved in TT, then this could be used as a unique or additional tool for diagnosis, therefore, WBCs could be the target for diagnosis of TT, in particular, neutrophils[7,10–12].

In this study, no clear differences existed between TT and non-TT regarding past-family history or past-surgical history. Similarly, a case series study has revealed no correlation between TT and family history in recurrent TT[13]. However, in alternative study conducted on three generation of first degree relatives and the study concluded that the TT is up to 10% positively related to family history[14]. Despite being weakly related, it helps physician for taking final decision to ascertain surgical operation. In line with that, a case study presented with familial testicular torsion in siblings of different age groups acute scrotum pain were diagnosed as TT with a confirmative decision by family history of siblings[15].

In the present study, significantly ($p<0.05$) more cases of TT started at night while non-TT started at morning, the duration of pain has shown non-significant clear-cut frontline between TT or non-TT. No consent exist regarding onset time and literatures confirming that is lacking[16,17]. However, TT-associated pain has been responsible about sleep disturbances and frequent awakening in other studies[18–21]. These studies have proposed several mechanism for night onset of TT and yet confirmation is obscure. The duration of TT presentation has been reported in several studies with consent lacking, some of these studies reported TT presentation of few to several hours[20-23] while other recorded presentation as few to several days[19].

The laterality in the present study has shown non-significant ($p>0.05$) differences between TT or non-TT, however, more non-TT cases were started at left and less at right. In contrast, earlier studies more left side TT-cases were reported than right side[2,19,22–24].

Affected age in TT group were younger than non-TT. Similarly, a previous studies conducted have reported that the TT affected age were younger than non-TT despite that the mean age in the present study was younger than other comparative studies[1,25-29].

Neutrophils play a crucial role in the inflammatory processes, more specifically, the neutrophils-lymphocyte ratio is a better diagnostic tool for inflammatory diseases. In TT, NLR has been slightly relied on as a diagnostic tool for the evaluation of testicular viability after TT[1,6,9,30–36]. The present study has included non-TT as a control group for comparison. There were non-significant ($p>0.5$) differences between both groups regarding past medical or surgical history.

We uncovered a considerable links between NLR and the diagnosis of TT. NLR was found to be related to the duration of symptoms in patients with TT. Thus, in terms of outcomes, NLR seems to be a helpful parameter for TT prognosis. These results suggest that NLR is an accessible, cost-effective, predictive parameter for testicular vitality in the context of TT.

Most patients (>50%) in the present study undergo orchiopexy than orchiectomy**,** however, still the percentage of orchiectomy is relatively high, therefore, searching for additional diagnostic tool could be helpful for earlier rescue. The duration of torsion seems to be related to the increased number or orchiectomy i.e. increase in duration increases the number of orchiectomy while decreased duration increases the number of orchiopexy, these has been reported in previous studies[1,2].

Moreover, Güneş et al. (2015) stated considerable links between scrotal diseases and NLR(2). In harmony with that Bitkin et al. (2018) confirmed that NRL identified TT with an AUC of 0.744 and a sensitivity and specificity of 70.1% and 76.9%, respectively[37]. These values are close to sensitivity (84.4%) and specificity (78.9%) of the present study.

One of the limitations of the present study was the relatively small sample size. NLR interfere with the results

positively when other systemic inflammatory disease present and the present study has not measured any markers to exclude these inflammatory disease, for example, C-reactive protein levels and erythrocyte sedimentation rate is also a limitation of the study.

Conclusions

The limitation in full differential diagnosis between TT and other scrotal pathologies despite in presence of diagnostic tools, has led to searching for additional adjuvant tools, hereby the study has proved that NLR could give clear clue about the type of scrotal pathology being reciprocally related to the severity of TT, thereby saving the false-negative patient from being undergone surgery.

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