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Original Article

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Role of Neutrophil to lymphocyte (NTL) ratio as a prognostic indicator in patients of diabetic foot syndrome (DFS)

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ABSTRACT

BACKGROUND & OBJECTIVE: Neutrophil to lymphocyte ratio has an important role to predict the outcome of diabetic foot syndrome. The aim is to evaluate NTL ratio as a prognostic factor in diabetic foot syndrome and its importance in diabetic wounds.

METHODOLOGY: Descriptive cross-sectional study was to evaluate NTL ratio for prognosis of DFS. All cases were assessed for smoking, body mass index, presence of wound, glycated hemoglobin level, peripheral limb ischemia and infection. Patients were examined for a period of 12 months to assess wound if it resulted in minor amputation (below the level of ankle), major amputations (below/above knee amputation), chronic wound or completely healed wound. Chi-Square test was applied for categorical data.

RESULTS: Total 100 patients were included and 61% were smokers. Average BMI was 31.7 and 34.5 in males and females. Complete wound healing found in 18% cases after debridement and chronic wounds in 15% patients. Subjects had to undergo major (above ankle) 16% and minor (below ankle) 51% amputations. Mean NTL count was 3.5 in fully healed wounds, 4.3 in chronic wounds, 6.9 in major amputations, and 5.2 in minor amputations. As the p-value indicates, there is a significant relationship between healed wounds, minor amputations, Chronic wounds and major amputations and the NTL ratio.

CONCLUSION: Results revealed NTL ratio has independent prognosis in DFS for anticipating wound upshot. NTL ratio has a significant link with healed wounds, minor amputations, and major amputations, as indicated by p-value.

KEYWORDS: Neutrophil to lymphocyte ratio, Diabetic foot syndrome, Below knee amputation, Above knee amputation.

INTRODUCTION

Diabetes mellitus is a systemic illness that is prevailed all over the world and it is 4th most common, non-communicable disease. It is silent killer all over the globe. The incidence of Diabetes mellitus has increased to 9% in men and 7.9% in women all over the world until 2019 [1]. The national Diabetes Survey of Pakistan concluded it has prevalence of 26.3% in Pakistan in 2016-17[2]. It has multitude of presentations and diabetic foot syndrome is one of them. It is multifactorial which include peripheral limb ischemia, peripheral neuropathy, infections and uncontrolled diabetes mellitus. One important principle is, if it is diagnosed in time and treated appropriately, a limb can be saved. On the other hand, just a minor ulcer on the foot can result in fatal complication like amputation, increasing the morbidity of patient. To diagnose it timely, it is important that patient is self-aware of the disease. Other parameters that help

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are ankle brachial pressure index (ABPI), foot X-ray and evaluation of limb for neuropathy. Diabetic foot syndrome (DFS) has incidence of 13.9% in Pakistan and it is becoming a crucial health problem which is a cause of discomfort and agony [3,4].

Recently, the interest in inflammatory markers eg. C reactive protein, TNF-alfa and IL-6 is increasing. Studies have established their role in distinguishing the subclinical inflammation, dysfunction of endothelium and their predictive value [5]. Neutrophil to lymphocyte ratio (NTL) is one of the important inflammatory markers. Its part is being evaluated to identify inflammation in different autoimmune, malignant and cardiac diseases. NTL ratio is superior to just WBC count in its diagnostic, predictive and differentiating abilities [6-10]. It costs low, it is available widely and it is easy to reproduce. All these factors make it advantageous over other inflammatory markers. Unfortunately, Pakistan being a developing country does not relish an immense health care system that is available to every common man.

That is why there is a need to introduce a heath care structure that is low priced but efficacious. Studies that were conducted in Pakistan have shown that if NTL ratio is increasing, it predicts increasing sugar levels and that it is useful in follow up of disease as well [11].It has advantages like it is easily done, not influenced by level of physical activity, hydration status of patient or by handling of samples that put limitations in cases of other investigations.

The purpose to conduct the present work is to find out the significance of NTL ratio to anticipate and avoid amputations as a consequence of DFS. It will also help the surgeons and physicians to make a decision and patients will not face the deadly complications of disease such as amputations.

METHODOLOGY

It was a cross sectional descriptive study that included 100 successive patients of DFS who presented in surgical out patient department or admitted in surgical ward of Aziz Fatimah Hospital Faisalabad through emergency from January 1st 2018 till December 31st 2018. Certificate from ethical panel was procured (DME/572-19). All the patients were assessed for history of smoking, body mass index (BMI), presence of wound, glycated hemoglobin levels, peripheral limb ischemia and infection. The patients were examined over a period of 12 months to assess the wound if it resulted in minor amputation (beneath the level of ankle), major amputation (high up the level of ankle), chronic wound or the wound that healed completely. Those wounds that did not heal completely in a period of six months were labeled as chronic wounds. The wounds that healed completely after debridement and didn't need any amputation were labelled completely healed wounds. Their blood samples were sent to the laboratory for complete blood count along with differentiated count and NTL ratio. Glycated Haemoglobin levels were also obtained and documented. The evaluation of patients and lab tests was mainly done by the main author of the study and subsequently reviewed by other authors of the study. Mean±SD of variables such as age was calculated. The Chi Square test is applied for categorical data. Frequency and percentages of qualitative data like gender, wound infection, amputations (minor or major) and healing outcomes were obtained.

RESULTS

The total no. of patients included in the study were 100. In table-I, Features of patients are shown and table-II shows patient's information.

Table-I: General characteristics of patients.

Features of patients		n(%)
Males		64 (64)
Females		36 (36)
Age (Mean ± SD)		56.49 ± 7.39
Smokers		61(61)
Average BMI	Men (Mean ± SD)	31.7±3.11
	Women (Mean ± SD)	34.5±3.36

Table-II: Patient's disease outcome and their relationship with laboratory parameters.

Sequel of patients	n(%)
Healed wounds	18(18)
Major amputations	16(16)
Minor amputations	51(51)
Chronic wounds	15(15)
Glycated Hemoglobin higher than 7.0	n(%)
Major amputations	34(34)
Minor amputations	12(12)
Chronic wounds	45(45)
Complete healing	9(9)
Indications for major amputations	n(%)
Osteomyelitis	39(39)
Septic wound	28(28)
Gangrene	14(14)
unhealed ulcers	19(19)
Mean NTL ratio in all four groups	Mean ± SD
Completely healed wounds	3.5±0.38
Major amputations	6.9±0.49
Minor amputation	5.2±0.46
Chronic wounds	4.3±0.88

In table-III, the Chi Square test is applied to check the association among the NTL ratio and DFS. The result is considered to be significant if the p-value less than 0.05. As the results shown in table-III all the p-value shows significant result.

Table-III: Association table among the NTL ratio and DFS by applying Chi Square test.

Variable	Category	NTL ratio N (%)				p-value
		2 to 2.99	3.0 to 3.99	4.0 to 4.99	> 5	
Healed wounds	Yes	7(38.9)	10(55.6)	1(5.6)	0	<0.001
	No	6(7.3)	20(24.4)	48(58.5)	8(9.8)	
Chronic wounds	Yes	1(20.0)	1(20.0)	1(20.0)	2(40.0)	0.046
	No	12(12.6)	29(30.5)	48(50.5)	6(6.3)	
Minor amputations	Yes	5(8.2)	18(29.5)	37(60.7)	1(1.6)	0.002
	No	8(20.5)	12(30.8)	12(30.8)	7(17.9)	
Major amputations	Yes	0	1(6.3)	10(62.5)	5(31.3)	<0.001
	No	13(15.5)	29(34.5)	39(46.4)	3(3.6)	

*NTL Neutrophil to lymphocyte.
*DFS Diabetic foot syndrome.

DISCUSSION

The NTL ratio has been studied in different diseases. Chronic inflammation results in different types of cancer and that is the reason that different inflammatory markers such as NTL ratio is being studied in head and neck malignancies [12], gastrointestinal carcinoma [13], hepatocellular carcinoma [14] etc. NTL ratio has also been studied in different cardio vascular diseases like acute myocardial infarction to assess the mortality associated with the disease [15].

Its role has also been established as helpful prognostic indicator for the use of Infliximab in the treatment of moderate to severe inflammatory bowel diseases like ulcerative colitis [16] and independent risk factor for increased morbidity and mortality in patients of acute pancreatitis in a study over a duration of 6 years [17, 18].Recently, trend is seen to establish the role of NTL ratio in prognosis of diabetic foot syndrome and its healing outcome. Still there is no established cut off value of NTL and it is being investigated. Mostly cut off value is taken as 5 as calculated by ROC curve. Another study concluded it to be 3.0-4.5 [19].Although it is still debatable. In one study it was concluded that the patients who had osteomyelitis of underlying bone or who needed major amputations due to diabetes mellitus had considerably increased NTL ratio than their comparative group [20].

Different studies are being done to see effect of diabetic drug on diabetes complications [21]. It would be interesting to see the effect of NTL ratio & its association with therapeutic modalities of DM.

Our work showed NTL ratio was 4.8 in patients who had osteomyelitis of underlying bone and hence resulted in amputations. Peripheral limb ischemia is also a contributory factor of diabetic foot syndrome, and this risk factor has been separately studied by Han Luo et all, with relation to NTL ratio and it was recognized as an independent risk factor. Other causative factors of diabetic foot syndrome such as peripheral limb ischemia and peripheral neuropathy showed the same results, thus favoring the importance of NTL ratio as a helpful tool for surgeons and physicians [22,23,24]. Neutrophils are essential cells seen immediately after the inflammatory process and lymhocytes are their modulators,

If NTL ratio is high, it indicates damage to endothelium and its dysfunction. Different studies in Pakistan have shown that high NTL ratio has a direct relationship with higher HbA1c levels and thus responsible for poor healing of wounds and bad outcome [11].Our study showed that HbA1 c>7 predicts, poor outcome of the wounds.

A 72% of the patients who had HbA1c levels more than 7 had to undergo major amputations. At the same time, 83% of patients with chronic wounds had elevated HbA1c levels. These results suggest the significance of NTL ratio in estimating inflammatory process and thus predicting the outcome in diabetic foot syndrome.

CONCLUSION

The patients who have higher NTL ratio are actually having a more severe diabetic foot infection. They are at more risk of undergoing amputations, resulting in a prolonged hospital stay. Such patients need more aggressive management. So, NTL is an important prognostic factor in assessment of diabetic foot syndrome. There is significant association among the healed wounds, minor amputations and major amputations among the NTL ratio as the p-value shows significant result.

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Khurram Saqib: Final editing of the manuscript.
Humaira Ahmad: References and final compilation.
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