

Average Values of Neutrophil Lymphocyte Ratio among a Representative Sample of Adult Population in a Tertiary Care Teaching Hospital

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ABSTRACT

Introduction: Several studies have been conducted over the years for a simple, reliable, cost effective investigation to know the intensity of systemic inflammation in patients suffering from shock, major surgery, sepsis, cancers, thromboembolic disorders (stroke, cardiovascular diseases, peripheral vascular diseases). Significance of granulocytes especially the critical role played by neutrophils in pathophysiology of various infections, inflammatory diseases and cancers has recently begun to emerge. Increased number of neutrophils in the peripheral blood and tumour microenvironment is seen in different type of cancers. Neutrophilia with lymphocytopenia is the feature of various infections. Neutrophil Lymphocyte Ratio (NLR) has been proposed as a simple, reliable and cost effective test. The NLR can be calculated easily from data that are routinely available. NLR could be an important predictor of outcome of critically ill patients.

Aim: To explore the average values of NLR in adult, both outpatient and inpatient undergoing diagnostic investigation in a tertiary care, teaching hospital, Bengaluru, India.

Materials and Methods: Prospective study was conducted for a period of 3 months from February to April 2015. Subjects <18 years and who were prescribed steroids, chemotherapy, immunomodulators and antibiotics or surgery were excluded.

Results: Overall 549 subjects are included in this study. The average value of absolute neutrophils is 5600 cells/mL, Absolute lymphocytes 2300 cells/mL and the average NLR is 2.8 ± 2.2 . Subjects who reported inflammatory diseases had higher NLR compared to diabetes, hypertension. Smokers had significantly higher NLR than subjects who did not. Differences in male and female NLR was seen. Significant difference in NLR was seen with different religion.

Conclusion: The present study is an attempt in providing preliminary data on disparities in NLR as a marker of inflammation, which is seen to be associated with outcome of many chronic illnesses. This calls for setting of various cut off points for these conditions. In our study, mean NLR is 2.8 ± 2.2 . High mean NLR is seen in male subjects, smoker, obese individuals and those suffering from inflammatory diseases.

Keywords: Inflammatory response, Lymphocyte count, Neutrophil count

INTRODUCTION

Monocytes, lymphocytes and neutrophils play a crucial role in the systemic inflammatory response to the severe infection, injury, polytrauma and shock. Fever, leukocytosis, and increased serum levels of acute phase proteins are characteristic features of systemic inflammation [1].

Lymphocytopenia and neutrophilia, a physiological response of innate immune system to the systemic inflammation, injury and stress. The process of neoplasia is complex, which may arise from the sites of infection, chronic inflammation and irritation. Inflammatory cells play major role in promoting, proliferation, survival and migration, which is proved by presence of inflammatory cells around the tumour micro environment. Growth factors such as platelet derived growth factor, platelet factor 4, and thrombospondin are released by platelets. Over the past 150 years extensive investigations

have been done to know the relationship of inflammation and cancerous growth. Neutrophilia is commonly associated with malignancies.

Several studies have been conducted over the years for a simple, reliable, cost effective investigation to know the intensity of systemic inflammation in patients suffering from shock, major surgery, sepsis, cancers, thromboembolic disorders (stroke, cardiovascular diseases, peripheral vascular diseases) [2]. Significance of granulocytes especially the critical role played by neutrophils in pathophysiology of various infections, inflammatory diseases and cancers has recently begun to emerge. Increased number of neutrophils in the peripheral blood and tumour micro environment is seen in different type of cancers. Neutrophilia with lymphocytopenia is the feature of various infections. NLR has been proposed as a simple, reliable and cost effective test.

NLR may also be used as a biomarker to differentiate neoplastic and non neoplastic although histopathology is gold standard investigation [3,4]. In clinical ICU practice, NLR can be used on routine basis to know the prognosis of critically ill patients.

The NLR can be calculated easily from data that are routinely available. NLR could be an important measure of systemic inflammation as it is cost effective and readily available.

MATERIALS AND METHODS

To establish the average values of absolute neutrophil count, absolute lymphocyte count and NLR, with the approval of local Ethical Committee, a descriptive cross-sectional study was carried out on a representative population in a tertiary care teaching hospital at Attibelle Bengaluru, India, in central laboratory Department of Pathology. The study was prospectively conducted for a period of 3 months from February to April 2015. The sample population consists of all subjects coming to various outpatient departments with different morbidities like diabetes, hypertension, peripheral vascular diseases, appendicitis, arthritis, gastritis, rhinitis etc., and routine health check up aged more than 18 years only. Individuals less than 18 years and who were prescribed with steroids, antibiotics, chemotherapy, immunomodulators or surgery were excluded.

Data Collection and Laboratory Analysis

Data collected regarding demographic information (age, religion, education), current medication use, diagnosis of medical conditions (both previous and current), and lifestyle behaviors (smoking and alcohol use) were collected by self prepared questionnaire provided to all the patients above 18 years coming to central laboratory sample collection center with their informed consent.

Body Mass Index (BMI) (kg/m^2) was measured by taking weight (kg) and height (meters).

Laboratory tests were performed on aseptically collected blood specimens in EDTA vacutainers with an informed consent from the subjects to provide information on neutrophil count (1,000 cells/mL) and lymphocyte count (1,000 cells/mL). NLR was calculated as the ratio of neutrophil cell count to lymphocyte cell count. The Coulter's method was used to determine neutrophil and lymphocyte counts (Sysmex Xp-100) within six hours of sample collection.

STATISTICAL ANALYSIS

Continuous variables are expressed as mean \pm standard deviation. Categorical variables are expressed as percentages. To compare parametric continuous variables, the independent sample t-test or the Mann-Whitney U-test was used. One-way analysis of variance or the Kruskal-Wallis test was used to compare the three groups. Statistical significance is determined at p-value of 0.05. Statistical analyses are done using SPSS version 16.0.

RESULTS

Total 549 subjects were enrolled in the study with their informed consent, aged between 18 to 92 years. Mean age of 39 years was noted, composed of 322 (58.7%) between 18 to 40 years and 227 (41.3%) between 40 to 92 years. High NLR value was noted in older age group (NLR-3.0). Mean absolute neutrophil count of 5.6 k/mL, mean absolute lymphocyte count of 2.3 k/mL and mean NLR of 2.4 was noted.

Male subjects were 232 (42.3%) and female subjects were 317 (57.7%). Male subjects showed high NLR compared to female subjects. Total 230 vegetarian were noted with mean NLR of 3.0, which is higher compared to 319 non vegetarians who had mean NLR of 2.7.

Smokers 69 (12.6%) and non smokers 480 (87.4%) showed mean NLR value of 3.3 and 2.8 respectively. Alcoholics 63 (11.5%) and non alcoholics 486 (88.5%) had mean NLR value of 3.1 and 2.8 respectively [Table/Fig-1].

In our study, statistical significant difference was seen between the religious groups (p-value=0.05). No significant difference noted in terms of age, gender, education, diet, smoking, alcoholism and BMI (p-value > 0.05).

[Table/Fig-2] shows division of the participants based on BMI, NLR value showed significant increasing trend with increase in BMI. High NLR observed in obese individuals.

In our study frame work subjects diagnosed with inflammatory conditions (like appendicitis, bronchitis, gastritis, pneumonia,

Parameters	Sub groups	Total count (n)	Percentage (%)	NLR (mean \pm SD)	p-value
Gender	Male	232	42.3%	2.9 \pm 2.3	0.195
	Female	217	57.7%	2.8 \pm 2.1	
Age	18-40 years	322	58.7%	2.7 \pm 1.8	0.087
	40-92 years	227	41.3%	3.0 \pm 2.5	
Education	< High school	278	50.6%	2.8 \pm 2.3	0.628
	> High school	271	49.4%	2.8 \pm 1.9	
Religion	Muslim	87	15.8%	2.4 \pm 1.7	0.050
	Hindu	452	82.4%	2.9 \pm 2.2	
	Christian	10	1.8%	1.7 \pm 0.5	
Diet	Non-vegetarian	319	58.2%	2.7 \pm 1.9	0.105
	Vegetarian	230	41.8%	3.0 \pm 2.3	
Smoking	Yes	69	12.6%	3.3 \pm 2.1	0.092
	No	480	87.4%	2.8 \pm 2.2	
Alcohol	Yes	63	11.5%	3.1 \pm 2.1	0.278
	No	486	88.5%	2.8 \pm 2.1	

[Table/Fig-1]: Display of average values of NLR based on demographic information and life style (Total sample size= 549).

sepsis, hepatitis, rhinitis) had higher NLR (3.2) compared to diabetes, hypertension and those who came for routine health checkup. However, no statistical significant difference is noted between these groups (p -value 0.241) [Table/Fig-3].

BMI	Total count (n)	Percentage (%)	NLR (mean±SD)	p-value
Under-weight	101	18.4%	2.5±1.8	0.254
Normal	275	50.1%	2.8±2.0	
Over-weight	147	26.7%	2.9±2.4	
Obese	26	4.8%	3.3±3.1	

[Table/Fig-2]: Display of average NLR related to Body Mass Index, tested by one way ANOVA between groups and within groups (Total sample size= 549).

Morbidity	Total (n)	Percentage (%)	NLR (mean±SD)	p-value
Diabetic	78	14.2%	2.6±1.8	0.241
Hypertension	16	2.9%	3.1±2.0	
Routine check up	281	51.9%	2.8±2.0	
Inflammatory Conditions	174	31.6%	3.2±1.3	

[Table/Fig-3]: Display of Average NLR values related to Disease conditions, Tested by oneway ANOVA between groups and within groups (Total sample size= 549).

DISCUSSION

Inflammation underlies the pathologies of various local and systemic disease conditions. NLR is potent marker of inflammation. Literature shows value of NLR is higher in inflammatory as compared to non inflammatory diseases [5-7]. In clinical practice, NLR can be used on routine basis to know the prognosis of critically ill patients. Our study also shows high NLR value for inflammatory diseases.

The major finding in our study showed mean absolute neutrophil count of 5.6k cells/mL, absolute lymphocyte count of 2.3 kcells/mL and mean NLR of 2.4 in our locality. Our NLR value is lower compared to study conducted in North Central Nigeria [8] (2.8) but higher than the value reported in non Hispanic blacks (2.24) and whites (1.76) in a study conducted in United States [2].

Additionally, Many studies show increased NLR is associated with Type 2 diabetes mellitus [9], severe coronary artery stenosis [10,11], S-T segment elevated myocardial infarction [12], various cancers like esophageal cancer [13], idiopathic sudden sensorineural hearing loss [14]. Different studies have shown different derived NLR values [Table/Fig-4].

Our study showed high NLR value for age groups between 40-92 years (3.0±2.5) and lower value for age groups between 18 to 40 (2.7±1.8) which was almost similar to a study conducted by Alexander NI with NLR values of 3.1 (50-85 years) and 2.7 (18-85years) [8]. Another study by Mohamed MM et al., [19] showed NLR value of 1.2±0.5 for age group <40 years and 1.1±0.4 for >40 years.

	Studies	Cut-off NLR values
1.	Our study	2.8±2.2
2.	Patric Forget et al., [15].	1.65±1.96
3.	Gonul Gurol et al., [16].	1.8±1.5
4.	Hafez Ahmed et al., [17].	
	-Group A	3.27±0.66
	-Group B	2.75±0.38
5.	Park CH et al., [18].	3.18
6.	Marwa M Mohamed [19].	1.2±0.45

[Table/Fig-4]: comparison of cut-off NLR values of our study with different studies. Thus, indicating that there is no standard cut-off values of NLR which could be universally accepted. NLR values show disparities with different races.

[Table/Fig-5] shows comparison of mean NLR values related to gender, education and BMI of our study with the study conducted in US [2]. Here our mean values are higher compared to Azab B et al., study [2]. In both studies, value of NLR shows increasing trend with increase in BMI and males have high NLR. But study by Mohamed MM et al., did not show much difference with gender related NLR values (males=1.1±0.3, females=1.2±0.5) [19].

Parameters		Our study	Azab B et al[2].
Gender	Male	2.9	2.19
	Female	2.8	2.11
Education	< high school	2.8	2.16
	>high school	2.8	2.13
BMI	Underweight	2.5	2.06
	Normal	2.8	2.11
	Overweight	2.4	2.13
	Obese	3.3	2.21

[Table/Fig-5]: comparison of Mean NLR values of our study with the study conducted at United States.

Shiny A et al., [20] and Khandare SK et al., [21] in their study showed subjects with high glycemic index had higher NLR values (2.2±1.12 and 2.83±0.85 respectively) compared to subjects with normal glycemic index (1.5±0.41 and 1.94±0.65 respectively), in our study we have derived mean NLR value of 2.6±1.8 in diabetic subjects. Hypertensive subjects showed higher NLR value (3.1±2.0) compared to those who came for routine check up (2.8±2.0).

LIMITATION

As the present study is from a single institution with observation involving small sample population, it is subject to many unaccounted confounders in the study. Additionally, the diagnostic value is not very significant, both in sensitivity and specificity. Therefore, these findings must be confirmed with a study involving a larger number of patients for longer duration.

CONCLUSION

The present study is an attempt in providing preliminary data on disparities in NLR as a marker of inflammation, which is seen to be associated with outcome of many chronic illnesses. This calls for setting of various cut-off points for these conditions. In our study mean NLR is 2.8 ± 2.2 . High average NLR is seen in male subjects, smokers, obese individuals and those suffering from inflammatory diseases. Considering the limitations of the present study, further research with large sample size and standard investigations should be conducted.

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