



THE CORRELATION BETWEEN THE NEUTROPHIL-LYMPHOCYTE QUOTIENT AND THE PLATELET-LYMPHOCYTE QUOTIENT AND THE OUTCOME OF STOMACH CARCINOMA.

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ABSTRACT

Background: The interconnections between environmental variables and genetics play a crucial role in the development and progression of gastric carcinoma, which is a multifactorial histological altequotientn.

Aim and objective: To determine the correlation between the neutrophil-lymphocyte quotient, the platalet-lymphocyte quotient, and the outcome of gastric carcinoma.

Methodology: Subjects with histopathologically identified stomach carcinoma were included in this prospective trial. The NLR and PLR were estimated using CBC parameters such as neutrophil, lymphocyte, monocyte, white blood cell (WBC), and platelet (Plt) count, as well as hemoglobin (Hb) level. The quotient of absolute neutrophil count to absolute lymphocyte count was defined as NLR, whereas the quotient of absolute platelet count to absolute lymphocyte count was characterized as PLR.

Results: Higher NLR values were shown to be substantially linked with patient age (p value 0.009), histological grade (p value 0.001), and disease stage (p value 0.001). (p value 0.001). The study also discovered that a greater PLR score is connected with a patient's age (p value 0.016), histological grade (p value 0.007), and disease stage (p value 0.007). (p value 0.004).

CONCLUSION: In individuals with stomach carcinoma, hematological markers such as NLR and PLR were linked to prognosis.

Keywords: WBC, Hb, NLR, PLR

Introduction

Carcinoma is often regarded as one of the world's most serious public health issues. Gastric carcinoma is a type of carcinoma that begins in the mucosa of the stomach and is one of the most common locations of visceral malignancy¹. After lung, breast, colorectum, and prostate carcinomas, gastric carcinoma is the fifth most frequent carcinoma worldwide. In comparison to global statistics, India has a low incidence and prevalence of stomach carcinoma, with just 63,000 and 45,000 cases,

respectively^{2,3}. Because to differences in social and food patterns, the incidence varies greatly across India. Because up to 80% of subjects remain asymptomatic during the early stages of stomach carcinoma, the diagnosis of gastric carcinoma is frequently delayed. In the case of stomach carcinoma, UGI endoscopy is the preferred diagnostic imaging method⁴. When paired with endoscopic biopsy, it is a highly sensitive and specific diagnostic technique. Although several biomarkers have been

developed and studied extensively, their clinical use is sometimes hampered by high costs and technical issues. In numerous carcinoma populations, laboratory markers of systemic inflammation have been studied as prognostic and predictive biomarkers^{5,6}. In clinical practice, assessing the inflammatory response to the tumor may be simpler and less expensive. CRP, Glasgow Prognostic Score (GPS), neutrophil/lymphocyte quotient (NLR), and platelet/lymphocyte quotient (PLR) are examples of these in predicting outcomes for subjects after surgical resection as well as in subjects with incurable malignancies⁷. Although the reasons of systemic inflammatory response (SIR) in carcinoma subjects are unknown, hypoxia due to tumor necrosis, changes in neuroendocrine metabolism, interleukin synthesis, and acute phase protein production have all been cited⁸. In carcinoma subjects, changes in white blood cell counts are good predictors of survival and therapeutic success. PLR and NLR associations with patient age and sex, as well as stomach carcinoma outcome, were investigated in this study⁹.

Aim and objective: To determine the correlation between the neutrophil-lymphocyte quotient, the platelet-lymphocyte quotient, and the outcome of gastric carcinoma.

Material and Methods

The current investigation was a two-year prospective study conducted in the department of surgery at a tertiary health care center. Subjects with histopathologically confirmed stomach carcinoma made up the study population.

Criteria for inclusion: 1. individuals with gastric carcinoma diagnosed histopathologically

Criteria for exclusion: 1. subjects with past or secondary carcinomas 2. 3. Subjects with inflammatory disorders 4. Subjects with hematological diseases The study was authorized by the institute's ethical council. Subjects had previously received chemotherapy.

After explaining the study to the subjects, they signed a proper written consent form. A pre-tested questionnaire was used to collect data. Data contained sociodemographic information such as age, gender, and so on. A comprehensive clinical history was collected. A comprehensive clinical examination was performed. A complete blood count (CBC) test was performed on all subjects before any therapies were administered. The NLR and PLR were estimated using CBC parameters such as neutrophil, lymphocyte, monocyte, white blood cell (WBC), and platelet (Plt) count, as well as hemoglobin (Hb) level. Subjects were followed up on for disease stage and grade, as determined by the CECT and UGI endoscopic biopsy reports, as well as intraoperative resectability and post-operative resected specimen margins. The quotient of absolute neutrophil count to absolute lymphocyte count was defined as NLR; the quotient of absolute platelet count to absolute lymphocyte count was characterized as PLR. As cut-off values, we used distribution medians. NLR was divided into two groups (2.75 and 2.75), while PLR was divided into two groups (170 and 170). n was used to represent category data (percent of cases).

Results

The bulk of the subjects in our study were under 60 years old (62%) and those over 60 years old (12%). (38 percent). The distribution of NLR levels varied significantly between those under 60 years of age and those over 60 years of age (P-value 0.009). Only 38.2 percent of subjects under the age of 60 have NLR values more than 2.75, compared to 75 percent of subjects over 60. The elderly cases have a considerably greater prevalence of high levels of NLR (P-value 0.05). (table 1) Male predominance was seen in our investigation. Males made up 55.5 percent of the total 108 subjects, while females made up 44.5 percent. According to the study, 60 percent of men and 41.6 percent of women have an NLR value greater than 2.75, which is statistically insignificant (p value 0.180). The distribution of NLR levels in the male and female cases studied

did not differ substantially (P-value>0.05). (table 2) The distribution of NLR levels in the study group varies dramatically across histological grades (P-value 0.001). According to the study, subjects with a high histological grade of stomach carcinoma have high NLR

values (about 92.3 percent in grade 3 and 100 percent in grade 4) The prevalence of high levels of NLR is considerably higher (P-value 0.05) among cases with higher histological grades.

Table1: Associations of age with Neutrophil-to-lymphocyte quotient (NLR) in gastric carcinoma subjects

Pt characteristics	no of subjects n=108	NLR		P value
		<2.75	≥2.75	
AGE years				
≥60	40(38%)	10(25%)	30(75%)	0.009
<60	68(62%)	42(61.8%)	26 (38.2%)	

Table 2: Associations of sex with Neutrophil-to-lymphocyte quotient (NLR) in gastric carcinoma subjects

Pt characteristics	no of subjects n=108	NLR		P value
		<2.75	≥2.75	
SEX				
Male		60(55.5%)	24(40%)	0.180
Female		48(44.4%)	28(58.4%)	

The distribution of NLR levels in the study group varied dramatically across different stages of carcinoma (P-value 0.001). The prevalence of high levels of NLR is substantially higher (P-value0.05) in cases with advanced stages of carcinoma. (table 3)

Table 3: Associations of stage of carcinoma with Neutrophil-to-lymphocyte quotient (NLR) in gastric carcinoma subjects

Pt characteristics	no of subjects n=108	NLR		P value
		<2.75	≥2.75	
STAGE				
1	28(25.9%)	28 (100%)	0(0%)	0.001
2	20(18.5%)	12 (60%)	8(40%)	
3	54(50%)	10 (18.5%)	44(81.5%)	
4	6 (5%)	2 (33.3%)	4(66.7%)	

The distribution of PLR levels varied significantly between those under 60 years of age and those over 60 years of age (P-value0.016). The elderly cases have a considerably higher prevalence of high levels of PLR (P-value0.05). (table 4)

Table 4: Associations of age with Platelet-to-lymphocyte quotient (PLR) in gastric carcinoma subjects

Pt characteristics	no of subjects n=108	PLR		P value
		<170	≥170	
AGE years				
≥60	40(38%)	10(25%)	30(75%)	0.016
<60	68(62%)	40(58.9%)	28(41.1%)	

According to the study, 60% of men and 41.6 percent of women had a PLR value greater than 170, which is statistically insignificant (p value 0.180). The distribution of PLR levels in the male and female cases studied did not differ substantially (P-value>0.05).

In the study group, the distribution of PLR levels varies dramatically across different histological grades (P-value 0.007). The prevalence of high levels of PLR is substantially higher (P-value 0.05) among cases with higher histological grades. (table 5)

Table 5: Associations of age with Platelet-to-lymphocyte quotient (PLR) in gastric carcinoma subjects

Pt characteristics	no of subjects n=108	PLR		P value
		<170	≥170	
HISTOLOGICAL GRADE				
1	50(46.2%)	36(72%)	14(28%)	0.007
2	26(24%)	10(38.5%)	16(61.5%)	
3	26(24%)	6(23%)	20(77%)	
4	6(5%)	0(0%)	6(100%)	

The distribution of PLR levels in the study group varies dramatically depending on the stage of carcinoma (P-value 0.004). The prevalence of high levels of PLR is considerably higher (P-value 0.05) in cases with advanced stages of carcinoma. (table 6)

Table 6: Associations of age with Platelet-to-lymphocyte quotient (PLR) in gastric carcinoma subjects

Pt characteristics	no of subjects n=108	PLR		P value
		<170	≥170	
STAGE				
1	28(25.9%)	24(85.8%)	4(14.2%)	0.004
2	20(18.5%)	10(50%)	10(50%)	
3	54(50%)	18 (33.3%)	36(66.7%)	
4	6(5%)	0(0%)	6(100%)	

Discussion

Higher NLR values were shown to be substantially linked with patient age (p value 0.009), histological grade (p value 0.001), and disease stage (p value 0.001). (p value 0.001). The study also discovered that a greater PLR score is connected with a patient's age (p value 0.016), histological grade (p value 0.007), and disease stage (p value 0.007). (p value 0.004). Both NLR and PLR have a p value of 0.180 and are unrelated to the patient's gender^{10,11}. *Helicobacter pylori* can induce chronic inflammation, which is a major risk factor for stomach carcinoma. However, the mechanisms underlying the link between increased NLR and a poor prognosis in subjects with stomach carcinoma are unknown. A high NLR indicates

that the number of lymphocytes has decreased and/or the number of neutrophils has increased. By providing a favorable milieu for carcinoma cells to proliferate, neutrophils may play a key role in carcinoma formation and progression. The bulk of circulating vascular endothelial growth factor, interleukin-18, and matrix metalloproteinase, which are assumed to be strongly connected with tumorigenesis, development, and metastasis, may be found in neutrophils. Furthermore, an increased number of neutrophils surrounding carcinoma tissues may hinder the antitumor immune responses of activated T cells and natural killer cells. As a result, a high level of circulating neutrophils could be harmful to individuals with stomach carcinoma and lead to a bad prognosis. At the same time, lymphocytes play

a critical role in carcinoma cellular adaptive immunity by attacking and eliminating tumor cells early in the tumorigenesis process. Despite the fact that NLRs were tested prior to therapy and the subjects' health was good, NLR could still be influenced by a number of confounding factors in the peripheral blood¹². As a result, controlling confounding factors in studies of the link between NLR and stomach carcinoma could be a key study topic in the future. The balance between pro-tumour inflammatory status and anti-tumour immune status is referred to as NLR. Subjects with increased NLR have relative lymphocytopenia and neutrophilic leukocytosis, indicating that the balance is thrown in favor of pro-tumour inflammatory response, which is linked to a poor oncologic outcome. Platelets, according to Bambace N M, can promote tumor growth and metastasis by producing angiogenic factors such as platelet-derived growth factor (PDGF) and vascular endothelial growth factor (VEGF). Furthermore, a high platelet count would cause relative lymphocytopenia, resulting in a hypoimmune response in the carcinoma patient, which is linked to lymphocyte-mediated antitumor action at the cellular level. Platelets can promote tumor growth by speeding up angiogenesis through the cytokine vascular endothelial factor (VEGF) pathway¹³. VEGF-A levels in carcinoma subjects' platelets were found to be significantly higher than those in a healthy control group. The strong correlation between NLR and tumor resectability and post-operative specimen margin positivity can be linked to overall survival in subjects with gastric carcinoma. However, the correlation between PLR and tumor resectability and specimen margin positivity is insignificant. In recent decades, a number of predictors for GC outcomes have been developed and implemented. CEA and Her-2 are now routinely employed in the pathological evaluation of GC. The genes Ki-67, caspase-3, and p53 have also been linked to GC survival. Furthermore, it is now well accepted that miRNAs play a critical role in carcinoma regulation. To date, a growing number of research have looked into the diagnostic and

prognostic usefulness of miRNAs in GC. MicroRNAs are expressed differently in gastric tumors, according to Ueda T, and distinct microRNAs are linked to GC progression and prognosis. However, the indicators listed above should be investigated in malignant tissues¹⁴. As a result, it's impossible to keep track of their levels as the condition progresses. NLR and PLR, on the other hand, as indicators of inflammation, can be easily measured in plasma or serum and used in the clinic. The most significant restriction in our analysis was the wide range of NLR and PLR threshold values employed in prior investigations. The wide range of cutoff values for high NLR and PLR may have influenced our findings, affecting the positive correlations between NLR, PLR, and GC prognosis. For example, cut-off scores for NLR were determined using the ROC curve, median value, or previous studies. However, subgroup analyses stratified by cut-off values revealed that the NLR's prognostic value was not significantly impacted. For more accurate results in the future, studies with a larger sample size and more carcinoma kinds will be required.

Conclusion

In individuals with stomach carcinoma, hematological markers such as NLR and PLR were linked to prognosis. Our understanding of carcinoma's inflammatory milieu has grown in recent decades, and research has focused on the link between carcinoma and inflammation. By inhibiting or activating tumor cells, inflammation plays a key role in the development and progression of numerous malignancies. As a result, many inflammatory indicators, including as NLR, platelet-to-lymphocyte quotient, and CRP, are used as diagnostic and prognostic biomarkers for malignancies.

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