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PLATELET LYMPHOCYTE AND NEUTROPHIL-LYMPHOCYTE RATIO WITH MORTALITY AND PROGNOSIS IN RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS

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ABSTRACT

Background: Rapidly progressive glomerulonephritis, or RPGN, is a clinical illness that manifests as a rapid loss of renal function and the symptoms of nephritic syndrome.

Aim: The purpose of this study was to evaluate the association between prognostic markers, platelet-to-lymphocyte ratio (PLR) and neutrophil-to-lymphocyte ratio (NLR) in individuals with RPGN (rapidly progressing glomerulonephritis) and the pathological results of renal biopsy.
Methods: The individuals in this retrospective analysis with a minimum of six months' worth of data were evaluated and had just been diagnosed with RPGN (rapidly progressive glomerulonephritis). All research participants had their eGFR (estimated glomerular filtration rate), albumin levels, CRP (C-reactive protein) levels, and CRP/albumin ratio assessed.

Results: Ferritin, CRP/albumin ratio, CRP, albumin, creatinine, neutrophils, and WBC all showed significantly higher values in primary crescentic subjects; these values were 453.56±79.52ng/ml, 28.43±6.73, 72.87±16.07 mg/dl, 2.87±±0.13 g/dl, 4.47±0.42 mg/dl, 7919.52±620.06 103/ul, and 10337.52±652.76 103/ul, respectively. For MDRD-GFR, primary and secondary crescentic subjects showed significantly lower values compared to secondary crescentic subjects; values for primary and secondary crescentic were 26.64±4.03 and 56.62±8.25, respectively.

Conclusion: The current study comes to the conclusion that systemic inflammation and NLR can be used to reliably predict death in people with RPGN (rapidly progressive glomerulonephritis). Fibrocellular crescents % showed a negative link and can be used as a proxy for glomerular inflammatory disease. In the acute phase of crescentic glomerulonephritis, PLR (platelet-to-lymphocyte ratio) can also be used as an indication to determine the severity of the disease.

Keywords: renal pathology, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, crescentic glomerulonephritis, RPGN

INTRODUCTION

One unusual clinical condition is rapidly progressive glomerulonephritis (RPGN), which affects 4%–10% of people receiving renal biopsy. Morphologically, RPGN is frequently linked to the development of the large crescent in Bowman's space. Three distinct types of crescentic glomerulonephritis are identified by histopathologic examination: type 1 is characterized by linear immunoglobulin G (IgG) deposition throughout the glomerular basement membrane (GBM; anti-GBM disease), type 2 is characterized by granular deposits (immune

complex disease), and type 3 is characterized by the absence of immunoglobulins, which is typical of pauci-immune GN seen in patients with systemic vasculitis.

The degree of crescent formation in crescentic GN subjects is related to the severity of the disease; subjects with >80% of the glomeruli exhibiting circumferential crescents show non-circumferential crescents and advanced renal failure, while subjects with <50% of the glomeruli exhibiting crescents show more indolent cruising and remission.1

The cellular crescent often appears following the creation of the fibrous and fibrocellular crescents during the active inflammatory stage. Fibrous crescent indicates a disease stage that is not susceptible to immunosuppressive medication, making this a crucial change from a therapeutic standpoint.

When left untreated, crescentic glomerulonephritis has poor clinical results, with most patients dying or developing end-stage renal disease (ESRD) in a matter of months. Therefore, as the disease progresses quickly from diagnosis to end-stage disease, the treatment approach needs to be well thought out. On the other hand, fast ESRD progression and dialysis reliance are frequently observed even following intensive therapy.2

As our understanding of the disease and the variables influencing its diagnosis has grown, doctors are better able to customize a patient's course of therapy and lower the death and morbidity rates linked to crescentic glomerulonephritis. Time since diagnosis, interstitial fibrosis, tubular atrophy, anti-GBM antibodies in GBM, fibrinoid necrosis, the crescent of >80% glomeruli, dialysis dependence at the time of admission, elevated serum creatinine at the time of admission, and the presence of anuria or oliguria are factors that are thought to be predictive for the prognosis of crescentic GN. The usual prognostic variables, however, which would forecast renal function.3 Total Leucocyte Counts, or TLCs, are readily available, reasonably priced, and provide a sensitive and approximate assessment of the inflammatory state. According to evidence from earlier studies, a small number of leucocyte-specific subtypes are more predictive of cardiovascular risk and poor prognosis in a variety of illnesses than WBC numbers. NLR denotes a bad prognosis for a number of conditions, such as cancer, chronic renal disease, and/or myocardial infarction.

MATERIALS AND METHODS

In individuals with RPGN (rapidly progressive glomerulonephritis), the purpose of the current study was to evaluate the association between prognostic variables, PLR (platelet-to-lymphocyte ratio), and NLR (neutrophil-to-lymphocyte ratio). The study was carried out at.. from. to. with approval from the relevant ethical committee.

The individuals who visited the Institute's Outpatient Department of Medicine made up the study population. The study's control group consisted of individuals of similar age and gender who attended the Institute's Medicine Department without having renal or inflammatory illness and whose blood pressure was within normal ranges.

All 289 patients whose biopsy results were verified were evaluated based on their reports of kidney biopsies. A minimum of one fibrocellular or cellular crescent was required for inclusion in the research.

The traditional methods for processing renal biopsies were immunofluorescence and microscopy. Diagnostic confirmation was aided by clinicopathologic correlation. All of the individuals' clinical data and medical records—including management, test results, clinical characteristics, demographic information, and follow-up records—were evaluated. After admission, as well as after one, three, and six months, clinical outcomes and treatment specifics, such as mortality, inflammatory markers, dialysis status, proteinuria, and renal function, were evaluated. The Modification of Diet in Renal Disease Study equation was used to calculate the estimated glomerular filtration rate, or eGFR.5. A GFR of less than 60 ml/min/1.73 m2 was considered reduced. In addition to measuring inflammation, the research participants' nutritional state was evaluated to gauge the disease activity. In addition to CRP and albumin separately, their ratio was evaluated for this. For the purpose of formulating the results, the gathered data were statistically evaluated using SPSS software version 21 (Chicago, IL, USA). Both numbers and percentages were used to express the facts. At $p<0.05$, the significance threshold was maintained.

RESULTS

In individuals with RPGN (rapidly progressive glomerulonephritis), the purpose of the current study was to evaluate the association between prognostic variables, PLR (platelet-to-lymphocyte ratio), and NLR (neutrophil-to-lymphocyte ratio). There were 42 controls and 52 participants in the research. Table 1 provides a list of the research individuals' demographic and illness characteristics. The average age of the patients and controls was seen to be 48.94±2.71 years and 49.18±2.10 years, respectively. Only the individuals had hematuria, proteinuria, and ferritin, with corresponding values of 185.74±50.69/HPF, 4327.31±682.04 mg/gun, and 375.14±64.63 ng/ml.

MDRD-GFR, albumin, hematocrit, hemoglobin, and lymphocytes were found to be significantly lower in the patients (34.37±4.07, 2.78±0.08, 30.05±0.73, 10.06±0.26, and 1401.46±91.22) compared to 103.53±4.31, 4.26±0.78, 42.11±0.94, 13.94±0.38, and 2466.82±127.94 in the controls. Table 1 displays the values of CRP/albumin ratio, CRP, creatinine, BUN, NLR, platelet, neutrophils, and WBC that were substantially higher in the participants. The respective values were 24.24±5.96, 61.99±14.37, 4.07±0.34, 50.72±3.07, 277962.94±13749.64, 7420.95±395.17, and 9720.16±587.72.

After evaluating the demographic and disease characteristics of the primary and secondary crescentic subjects, it was found that the primary crescentic subjects had significantly higher values for ferritin, CRP/albumin ratio, CRP, albumin, creatinine, neutrophils, and WBC, with respective values of 453.56±79.52ng/ml, 28.43±6.73,

72.87±16.07 mg/dl, 2.87±±0.13 g/dl, 4.47±0.42 mg/dl, 7919.52±620.06 103/ul, and 10337.52±652.76 103/ul. Table 2 illustrates the significant differences in MDRD-GFR between the primary and secondary crescentic subjects. Table 2 displays statistically non-significant changes in hematuria, proteinuria, BUN, PLR, NLR, hematocrit, hemoglobin, platelet count, and lymphocytes between the primary and secondary crescentic groups, with 39 and 13 patients, respectively.

Regarding the relationship between the research participants' histopathologic renal biopsy findings at the time of admission and dialysis dependence, mean values for fibrinoid necrosis were observed to be 19.54±6.08 for dialysis dependency and 10.47±3.56 for non-dependent. The dialysis dependency and non-dependency values for the fibrous crescent were 3.19±1.61 and 4.27±1.84, respectively, whereas the cellular crescent showed values of 39.37±6.67 and 16.72±3.34, respectively. For the fibrinoid, fibrous, and cellular crescents, these values were statistically non-significant with $p>0.05$. The values of fibrocellular crescent for dialysis dependency and non-dependency were 19.19±5.47 and 10.53±2.47, respectively, whereas the values for sclerotic glomeruli were 3.32±1.34 and 1.63±0.36, respectively. Table 3 shows a substantial connection (p-value <0.05) between dialysis reliance and fibrocellular crescent and sclerotic glomeruli.

DISCUSSION

In individuals with RPGN (rapidly progressive glomerulonephritis), the purpose of the current study was to evaluate the association between prognostic variables, PLR (platelet-to-lymphocyte ratio), and NLR (neutrophil-to-lymphocyte ratio). There were 42 controls and 52 participants in the research. The average age of the patients and controls was seen to be 48.94±2.71 years and 49.18±2.10 years, respectively. Only the individuals had hematuria, proteinuria, and ferritin, with corresponding values of 185.74±50.69/HPF, 4327.31±682.04 mg/gun, and 375.14±64.63 ng/ml. MDRD-GFR, albumin, hematocrit, hemoglobin, and lymphocytes were found to be significantly lower in the patients (34.37±4.07, 2.78±0.08, 30.05±0.73, 10.06±0.26, and 1401.46±91.22) compared to 103.53±4.31, 4.26±0.78, 42.11±0.94, 13.94±0.38, and 2466.82±127.94 in the controls.

CRP/albumin ratio, creatinine, BUN, NLR, platelet, neutrophils, and WBC all had substantially greater levels in the participants than the control group; the corresponding values were 24.24±5.96, 61.99±14.37, 4.07±0.34, 50.72±3.07, 277962.94±13749.64, 7420.95±395.17, and 9720.16±587.72. The present study's demographics and illness features were found to be similar to those examined in studies conducted by Yaprak M et al. (2016) and Maraj M et al. (2018), the authors of which evaluated patients with similar demographics.

In relation to the evaluation of the demographic and disease characteristics of the primary and secondary crescentic subjects, the primary crescentic subjects had significantly higher values for ferritin, CRP/albumin ratio, CRP, albumin, creatinine, neutrophils, and WBC, with respective values of 453.56±79.52ng/ml, 28.43±6.73, 72.87±16.07 mg/dl, 2.87±±0.13 g/dl, 4.47±0.42 mg/dl, 7919.52±620.06 103/ul, and 10337.52±652.76 103/ul. In contrast, the MDRD-GFR values for the primary and secondary crescentic subjects were significantly lower than those of the secondary crescentic subjects, with values for primary and secondary crescentic subjects being 26.64±4.03 and 56.62±8.25, respectively.

There were statistically insignificant variations in hematocrit, hemoglobin, platelet count, lymphocytes, proteinuria, BUN, PLR, NLR, hematocrit, and hemoglobin between the primary and secondary crescentic groups (n = 39 and 13, respectively). These findings were in line with those of Turkmen K et al. (2008) and Ozcicek A et al. (2017), whose authors presented the findings of the current investigation on the variations in the demographic and pathological features of the primary and secondary crescent participants.

After evaluating the relationship between the research patients' histopathologic renal biopsy findings at the time of admission and their dependence on dialysis, mean values of 19.54±6.08 and 10.47±3.56 for fibrinoid necrosis were observed for dialysis dependency and non-dependency, respectively.

Dialysis dependency and non-dependency values for fibrous crescent were 3.19±1.61 and 4.27±1.84, respectively, whereas cellular crescent had values of 39.37±6.67 and 16.72±3.34, respectively. For the fibrinoid, fibrous, and cellular crescents, these values were statistically non-significant with $p>0.05$. The values of fibrocellular crescent for dialysis dependency and non-dependency were 19.19±5.47 and 10.53±2.47, respectively, whereas the values for sclerotic glomeruli were 3.32±1.34 and 1.63±0.36, respectively. A p-value of less than 0.05 indicated a significant association between dialysis reliance and fibrocellular crescent and sclerotic glomeruli. These results corroborated those of Emiroglu N et al. (2017) and Quin G et al. (2016), who found that sclerotic glomeruli and fibrocellular crescents had a considerable dialysis reliance.

CONCLUSION

Within its limitations, the present study concludes that mortality in subjects with RPGN (Rapidly progressive glomerulonephritis) can be accurately predicted with NLR with the correlation of systemic inflammation. A negative correlation was seen with fibrocellular crescents percentage and can be considered as a measure for glomerular inflammatory condition. Also, PLR (platelet-to-lymphocyte ratio) can be taken as an indicator for assessing disease severity in the acute phase of crescentic glomerulonephritis. However, the present study had a few limitations including a smaller sample size, geographical area biases, recall bias, and single-institution nature.

Hence, more longitudinal and prospective studies with larger sample sizes, and longer monitoring periods are needed to reach a definitive conclusion.

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TABLE

Characteristics	**Subjects (n=52)**	**Controls (n=42)**
Mean age (years)	48.94±2.71	49.18±2.10
Hematuria (/HPF)	185.74±50.69	
Proteinuria (mg/gun)	4327.31±682.04	
Ferritin (ng/ml)	375.14±64.63	
MDRD-GFR	**34.37±4.07**	103.53±4.31
CRP/albumin ratio	**24.24±5.96**	0.66±0.62
CRP (mg/dl)	**61.99±14.37**	2.72±0.22
Albumin (g/dl)	**2.78±0.08**	4.26±0.78
Creatinine (mg/dl)	**4.07±0.34**	0.76±0.34
Blood urea nitrogen (mg/dl)	**50.72±3.07**	12.27±0.62
Glucose (mg/dl)	101.35±2.86	102.58±7.38
PLR	273.92±39.13	99.66±5.28
NLR	**7.04±0.88**	1.72±0.13
Hematocrit (%)	**30.05±0.73**	42.11±0.94
Hemoglobin (g/dl)	**10.06±0.26**	13.94±0.38
Platelet count (10^3/ul)	**277962.94±13749.64**	234920.02±10361.92

Lymphocytes (10^3/ul)	**1401.46±91.22**	2466.82±127.94
Neutrophils (10^3/ul)	**7420.95±395.17**	4050.85±218.16
WBC (10^3/ul)	**9720.16±587.72**	6455.62±310.17
Diastolic Blood pressure (mmHg)	79.18±1.49	77.18±1.78
Systolic Blood pressure (mmHg)	128.96±2.63	117.62±4.94

Table 1: Demographic and disease characteristics in the control and patients in the study

Characteristics	**Primary crescentic (n=39)**	**Secondary crescentic (n=13)**
Mean age (years)	52.24±2.81	36.62±5.74
Hematuria (/HPF)	165.74±68.86	157.52±32.03
Proteinuria (mg/gun)	4027.31±803.14	3912.34±1325.76
Ferritin (ng/ml)	**453.56±79.52**	131.02±31.18
MDRD-GFR	**26.64±4.03**	56.62±8.25
CRP/albumin ratio	**28.43**±6.**73**	2.26±1.67
CRP (mg/dl)	**72.87**±**16.07**	4.64±4.19
Albumin (g/dl)	**2.87**±±**0.13**	2.44±0.24
Creatinine (mg/dl)	**4.47**±**0.42**	2.95±0.74
Blood urea nitrogen (mg/dl)	**5**3.24±3.44	43.66±6.36
PLR	244.19±23.56	358.82±136.33
NLR	6.75±0.68	7.72±2.71
Hematocrit (%)	29.55±0.74	31.51±1.83
Hemoglobin (g/dl)	9.87±0.27	10.47±0.62
Platelet count (10^3/ul)	268400.02±18012.22	253857.12±11474.24
Lymphocytes (10^3/ul)	1457.52±106.03	1241.44±178.36
Neutrophils (10^3/ul)	**7919.52±620.06**	5996.44±1027.69
WBC (10^3/ul)	**10337.52**±**652.76**	7957.16±1206.66

Table 2: Comparison of demographic and disease characteristics in the primary and secondary crescentic study subjects at baseline

Histopathologic features	**Dependency on dialysis**	**Mean± S. D**
Fibrinoid Necrosis		
	Dependent	19.54±6.08
	Non-dependent	10.47±3.56
Fibrous Crescent		
	Dependent	3.19±1.61
	Non-dependent	4.27±1.84
Fibrosellular crescent		
	Dependent	19.19±5.47
	Non-dependent	10.53±2.47
Cellular crescent		
	Dependent	39.37±6.67
	Non-dependent	16.72±3.34
Sclerotic Glomeruli		
	Dependent	3.32±1.34
	Non-dependent	1.63±0.36

Table 3: Correlation between dialysis dependency and histopathologic renal biopsy findings in the study subjects at the time of admission