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The Relationship Between Haemodialysis and Haematological Parameter Levels in Patients with End-Stage Renal Failure

Son Dönem Böbrek Yetmezliği Hastaların Hematolojik Parametre Düzeyleri ile Hemodiyaliz Arasındaki İlişkisi

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ABSTRACT

Introduction: To be able to detect proinflammatory response with cytokines such as CRP, IL-1,IL-6 in chronic renal disease patients; it is showed in some recent studies that neutrophil lmyphocyte ratio could be just as useful as other inflammatory markers.
Aim: This study purposes to show possible changes and likelyhood of inflammatory response in patients with end stage renal disesase who either follows renal replacement therapy or conservative therapy without hemodialysis within using neutrophil lmyphocyte ratio as a denovo marker.
Metods: In our study group some of these patients rejected to enter hemodialysis programme. We examined retrospectively the patients who applied during 2013-2018 to nephrology policlinics of an university hospital. It is included a to a total number of 115 patients: 59 patient who rejected RRT, so only get followed with conservative approach; 56 patient who enters hemodialysis programme. The data obtained retrospectively through patient files and and includes: levels of urea, uric acid, creatinine, GFR, MCV, parathormone, protein/creatinin ratio in spot urine test.
Results: Our Study showed no significant difference within these biochemical parameters in these two group. Although when the complete blood counts of these patients are taken into consideration, the MCVwere significantly higher in the group who followed with conservative treatment (p=0.002). When we tried to examine other possible parameters which can interfere with NLR ratio, there were no significant statistical correlation within.
Conclusion: As a final statement, it should be considered that MCV could be used to evaluate the progression of renal disease, taken account of there was significant difference between our two study groups.

Keywords: End-Stage Renal Disease, Renal Replacement Therapy, Lymphocyte Neutrophil Rate, Hemodialysis.

ÖZET

Giriş: Son Dönem Böbrek Yetmezliği olgularında böbrekte oluşan inflamatuar yanıtın belirlenmesi amacıyla son yıllarda kullanılan CRP, IL-1, IL-6 ve TNF-alfa gibi belirteçlerin yanısıra hemogramdan elde edilerek kullanılan platelet nötrofil oranı ve lenfosit nötrofil oranı gibi inflamasyonda yol gösterici olabilecek belirteçler üzerine çalışmalar yapılmaya başlanmıştır.
Amaç: Çalışmamızda RRT alan ve almayan iki grup arasında nötrofil lenfosit oranı kullanılarak inflamatuar yanıtın karşılaştırılması amaçlandı.
Yöntem: Çalışmamızda Balıkesir Üniversitesi Tıp Fakültesi, nefroloji polikliniğine başvuran hastaların 2013-2018 yılları arasındaki verileri retrospektif olarak irdelendi. RRT alan 59 olgu ile RRT almayan 56 olgu; toplamda 115 olgu çalışmaya dahil edilmiştir. Hastaların üre, ürik asit, kreatinin, glomerüler filtrasyon hızı, ortalama platelet hacmi, parathormon, spot idrarda protein/kreatinin oranı, hemogram değerleri dosyalarından retrospektif olarak elde edildi.
Bulgular: Çalışmamızda SDBY olgularında RRT alan ve almayan grupta parametrelere göre farklar incelendiğinde; biyokimyasal tetkikler açısından her iki grupta anlamlı farklılığa rastlanmadı. Hemogram parametreleri değerlendirildiğinde ise RRT alan ve almayan hastalar arasında MCV değerleri RRT almayanlarda 92,35 bulunmuş olup RRT alanlarda 88,8 saptandı anlamlı olarak daha yüksek bulundu (p:0,002). Nötrofil/lenfosit oranını etkileyebilecek diğer sayısal parametreler incelendiğinde, biyokimyasal parametreler ile nötrofil/lenfosit oranı arasında, istatiksel olarak korelasyon izlenmedi.
Sonuç: Son dönem böbrek yetmezliği olgularında MCV değerlerinin RRT alan ve almayan grupta istatiksel olarak anlamlı olarak farklı saptanması olgular için faydalı bir progresyon belirteci olabilir.

Anahtar Kelimeler: Son Dönem Böbrek Yetmezliği, Renal Replasman Tedavi, Lenfosit Nötrofil Oranı, Hemodiyaliz.

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INTRODUCTION

End-stage renal disease (ESRD) is a multisystemic disease characterized by chronic, progressive and irreversible nephron loss due to many different causes. It poses a serious threat to patient health due to its high morbidity and mortality rates and worsening quality of life, and to the health budget due to the high-cost treatments required. In meta-analyses, the prevalence of ESRD has been estimated to be between 9% and 19% worldwide, with an average prevalence of 13.4% (1). Unfortunately, the disease is mostly asymptomatic in the early stages. When ESRD patients are considered in general, many different etiologic factors and different progression rates are observed. The most common causes of the disease are diabetes mellitus and hypertension, but renal parenchymal diseases and cystic kidney disease also play a role in the etiology. ESRD is among the leading causes of homeostasis disorders such as anemia of chronic disease and fluid electrolyte disturbances. In ESRD, susceptibility to infections increases with decreased immune response. At the same time, chronic inflammation secondary to this condition is a common condition in ESRD. Chronic inflammation has a share in the formation of comorbidities such as anemia, cachexia and cardiovascular disorders in ESRD patients (2,3).

Although renal replacement therapy (RRT) plays an important role in the treatment of ESRD, renal transplantation is the permanent treatment modality. Neutrophil/lymphocyte ratio (NLR), which is accepted as one of the markers of systemic inflammation, is easily determined by the ratio of the absolute number of neutrophils to the absolute number of lymphocytes in a simple hemogram test. As a parameter associated with low-grade inflammation, NLR is recognized as an important component of ESRD and has an important role in all-cause morbidity and mortality. Since ESRD is a process characterized by chronic inflammation, it has been reported that NLR may predict progression (4,5). It is essential to identify the causes of progression of ESRD in patients with ESRD in order to prevent or slow down the progression of the disease (6-8). Recently, studies examining the link between hematologic variables and renal functions have gained importance (9).

In this study, we aimed to compare the NLR value, which may be an indicator of inflammation in ESRD patients, between patients with and without RRT and to compare the inflammatory response.

METHODS

The data of patients admitted to the nephrology clinic of a university hospital between 2013 and 2018 were retrospectively analyzed. In the study, 1500 files were reviewed. 115 patients over 18 years of age and diagnosed with ESRD were included in the study. Data of 59 patients who did not receive RRT and 56 patients who received RRT were recorded. Patients with acute infection, rheumatologic disease, malignancy and liver cirrhosis were excluded. Urea, creatinine, Glomerular Filtration Rate (GFR) Sodium (Na), potassium (K), magnesium (Mg), Calsium (Ca), phosphor (P), uric acid, parathormone (PTH), ferritin, protein/creatinine values were obtained from the patients' medical records Hematologic data White blood cell (WBC), hemoglobine (Hgb), Hemactorit (Hct), mean corpuscular volüme (MCV) Platelet (PLT), Red cell distribution width (RDW), neutrophil, lymphocyte, eosinophil values were obtained for the study. NLR values of the patients were calculated. The data in the two groups receiving and not receiving RRT were compared and analyzed.
SPSS 22.0 (Statistical Package For Social Science, SPSS Inc., Chicago, IL, USA) program was used for statistical analysis of the data. Numerical data were expressed as mean and standard deviation, categorical data as n and %. Pearson correlation test was used for correlation analysis between data. Dependent Sample t-Test was used for pairwise comparisons of data between groups, one-way ANOVA, Chi-Square and Post Hoc Tukey HSD tests were used for multiple comparisons between groups. $P< 0.05$ was accepted as a statistically significant value.

Ethics Committee Approval

Our study was approved by the Ethics Committee of Balıkesir University with the decision dated 19/08/2020 and numbered 2020/124.

RESULTS

Of the 115 patients included in our study, 73 (63.5%) were male and 42 (36.5%) were female. The mean age of the patients was 60.28 years (±14.07) and the mean age was 61.09 years (±13.82) in men and 58.88 years (±14.55) in women. While 56 (48.7%) of the patients had never received RRT, 59 (51.3%) had started RRT. The biochemical analysis results of the groups with and without RRT treatment are summarized in Table 1.

Table 1. Analysis of biochemistry parameters in groups with and without RRT

ParametrES	Did not receive (n:56)	Received RRT (n:59)	P
Üre (mg/dL)	137.82 (±53.19)	154.20 (±74.28)	0.179
Creatinin (mg/dL)	6.05 (5.05-7.46)	6.66 (5.30-7.89)	0.161
Üric Acid (mg/dL)	6.01 (±1.82)	6.50 (±1.99)	0.224
GFR (ml/dk)	8.31 (6.29-10.21)	7.38 (5.70-9.90)	0.231
Na (mmol/L)	137.00 (134.00-138.75)	136.00 (133.00-139.00)	0.410
K (mmol/L)	4.80 (4.32-5.57)	4.80 (4.20-5.30)	0.904
Mg (mg/dL)	2.40 (2.20-2.80)	2.60 (2.30-2.90)	0.231
Ca(mg/dL)	8.90 (8.20-9.55)	9.30 (8.40-9.60)	0.515
P (mg/dL)	5.10 (4.35-6.22)	5.55 (4.32-6.95)	0.215
PTH (ng/L)	258.50 (160.5-440.75)	265.00 (110.5-413.75)	0.585
Ferritin (mg/dL)	363.00 (173-703)	333 (144.25-602.25)	0.542
Protein/creatinin	2222 (1427.25-3913.25)	2788.35 (1970.5-5139	0.213

(RRT: Renal replacement therapy, GFR: Glomerular Filtration Rate, Na: Sodium, K: Potassium, Mg: Magnesium, Ca: Calsium, P: Phosphor, PTH: parathormone).

No statistically significant difference was found when we compared the biochemical values in the 2 groups that we formed as RRT and non-RRT groups. If we consider these values one by one; urea values were calculated as 154.20 mg/dL in the group receiving RRT and 137.82 mg/dL in the group not receiving RRT and no statistical difference was found. Similarly, no significant difference was found between the creatinine values of these two groups (6.66 mg/dL in the group receiving RRT; 6.05 in the group not receiving RRT; p = 0.161). When we made a comparison in terms of uric acid, no significant difference was found (non-RRT group 6.01 mg/dL; RRT group 6.5 mg/dL; p=0.224). When compared for GFR, there was no statistically significant difference (8.31 ml/min in the group not receiving RRT and 7.38 ml/min in the group receiving RRT; p=0.231). When Na was taken as a criterion, no significant difference was found (137 mmol/L in the group not receiving RRT, 136 mmol/L in the group receiving RRT, p= 0.41). When K values were considered, no difference was found (K value was 4.8 mmol/L in the group receiving RRT; 4.8 mmol/L in the group not receiving RRT, p= 0.90). On the other hand, when Mg was considered, the mean Mg value was 2.4 mg/dL in the group receiving RRT and 2.6 mg/dL in the group not receiving RRT; no statistically significant difference was found. No significant difference was observed when parathormone values were compared (265 ng/L with RRT, 258.5 ng/L without RRT p=0.58). Similarly, no significant difference was found in the ferritin values of both groups (333 mg/dL receiving RRT, 363 mg/dL not receiving RRT p=0.54). The spot urine protein creatinine ratios of both groups were 2788 in the group receiving RRT and 2222 in the group not receiving RRT and no statistically significant difference was found.

Table 2. Analysis of hemogram parameters in groups receiving and not receiving RRT

Parametres	Did not receive (n:59)	Received RRT (n:56)	p
Beyaz küre (*10³/mL)	6.88 (±1.85)	7.11 (±1.93)	0,508
Hemoglobin (g/dL)	11.34 (±1.96)	11.40 (±1.71)	0,843
Hematocrit (%)	34.39 (±6.26)	34.59 (±5.06)	0,848
MCV(fL)	88.8 (85-92.9)	92.35 (89-97.07)	0,002
Trombosit (*10³/mL)	213.35 (±58.59)	206.02 (±63.56)	0,521
RDW (%)	15.30 (14.1-16.3)	14.6 (13.32-15.9)	0,111
Nötrofil (*10³/mL)	4.30(3.4-5.4)	4.35 (3.40-5.40)	0,395
Lenfosit (*10³/mL)	1.70 (1.30-2.10)	1.60 (1.10-1.90)	0,521
Eozinofil (*10³/mL)	0.20 (0.10-0.40)	0.20 (0.10-0.30)	0,841
Neutrophils/Lymp	2.73 (1.73-3.73)	2.77 (1.89-3.77)	0,455

(RRT: Renal replacement therapy, MCV: Mean corpuscular volüme, PLT: Platelet, RDW: Red cell distribution width).

When hemogram parameters were evaluated, MCV values between patients who received and did not receive RRT were 92.35 fL in those who did not receive RRT and 88.8 fL in those who received RRT and were significantly higher (p=0.002), white blood cell values between patients who received and did not receive RRT were 6.88*10³/mL in those who received RRT; Among the patients who received and did not receive RRT, hemoglobin values were 11.34 g/dL in patients who received RRT and 11.40 g/dL in patients who did not receive RRT, which was not statistically significant, hematocrit values were 34.39% in patients who received RRT and 34.59% in patients who did not receive RRT, which was not statistically significant. Platelet values between patients with and without RRT were 213.35*10³/mL in those who received RRT and 206.02*10³/mL in those who did not receive RRT and were not statistically significant, RDW values between patients with and without RRT were 15.3% in those who received RRT and 14.6% in those who did not receive RRT and were not statistically significant, Neutrophil values between patients with and without RRT were 4.3*10³/mL in those who received RRT; 4.35*10³/mL in patients who did not receive RRT and was not statistically significant, lymphocyte values between patients who received and did not receive RRT were 1.7*10³/mL in patients who received RRT; 1.6*10³/mL in patients who did not receive RRT and was not statistically significant, eosinophil values between patients who received and did not receive RRT were 0.2*10³/mL in patients who received RRT and 0.2*10³/mL in patients who did not receive RRT.

Table 3. Correlation values between biochemical parameters and NLR

Neutrophils/Lymphocytes		
	r	**p**
Üre	0.061	0.514
Creatinin	-0.036	0.669
Üric asid	-0.015	0.889
GFR	0.042	0.659
Na	0.069	0.461
K	0.014	0.881
Mg	0.002	0.986
Ca	-0.109	0.462
P	-0.03	0.979
PTH	-0.048	0.627
Ferritin	0.094	0.339
Protein/kreatinin	0.036	0.772

(GFR: Glomerular Filtration Rate, Na: Sodium, K: Potassium, Mg: Magnesium, Ca: Calsium, P: phosphor, PTH: parathormone, NLR: Neutrophil/lymphocyte ratio).

NLR, which we wanted to use as an inflammatory marker in our study, was calculated as median 2.77 (1.89-3.77) in all patients. The median was 2.67 (2.11-3.82) in patients who did not receive RRT and 2.73 (1.73-3.73) in patients who received RRT. In the analysis, no statistically significant difference was found between patients who received and did not receive RRT (p=0.455) (Table 2). When other numerical parameters that may affect NLR were analyzed, no statistically significant correlation was observed between biochemical parameters and NLR, as correlation values of r<0.2 indicate no correlation. The analysis is summarized in Table 3.

DISCUSSION

End-Stage Renal Disease is a disease with a high prevalence worldwide and high morbidity and mortality rates. Chronic kidney disease is a multisystemic disease characterized by chronic, progressive and irreversible loss of nephrons due to many different causes. The clinical course of the disease varies according to the presence and stage of symptoms. While some patients develop serious complications in very early stages and need hemodialysis, some patients may be asymptomatic until the last stages. This situation emphasizes the importance of individual follow-up of each patient and making hemodialysis decision accordingly. In our study, there was no difference between biochemical parameters in ESRD patients with and without RRT treatment. We think that uremic complications and electrolyte disturbances were treated with the treatment administered in patients who received RRT treatment, while patients who did not receive RRT treatment achieved this with strict diet and individual close follow-up. Individual and frequent follow-up may reduce possible complications Hypertension

seems to be the most important damaging factor among these complications. It has been observed to do this both by accelerating GFR decline and by increasing the frequency of cardiovascular events. Various studies have shown that hypertension increases all-cause mortality in patients with ESRD (8). There are many publications in the literature showing that the progression of ESRD patients is slowed down and prognosis is improved with severe dietary restriction, close monitoring of daily salt intake and arterial blood pressure (9).

Anemia occurs in ESRD patients on hemodialysis due to chronic inflammation, blood loss and erythropoietin deficiency (10). In the QICKD study conducted by Dmitrieva et al. (11), the effects of anemia in ESRD patients were investigated. Among the findings of the study, the most common subtype was found to be normocytic anemia with a rate of 80.5%. In a study by Tobili et al. (12), in a group of 30 patients who could not be dialyzed, MCV values were 81.3 ± 4.1 at the beginning while anemia treatment was administered and 88.8 ± 2.9 after treatment, which was closer to normal values, and it was also shown that the frequency of cardiac events increased with ESRD. In our study, the range of MCV values was 88.8 (85-92.9) fl with normocytic anemia in those who received RRT and 92.35 (89-97.07) fl in those who did not receive RRT and normocytic anemia was also found in this group. In our study, the median NLR, which we can evaluate inflammation between patients who received and did not receive RRT, was calculated as 2.77 (1.89-3.77) in all patients. The median value was 2.67 (2.11-3.82) in patients who did not receive RRT and 2.73 (1.73-3.73) in patients who received RRT. In the analysis, no statistically significant difference was found between patients who received RRT and those who did not (p=0.455). According to the results of the analysis, the inflammation-reducing effect of hemodialysis could not be demonstrated.

When hemogram parameters were evaluated in our study, the mean feritin value was 333 mg/dL in the group receiving RRT and 363 mg/dL in the group not receiving RRT; no statistically significant difference was found. Inflammatory response may occur as a response to tissue damage in addition to foreign substances defined as antigens and pathogenic microorganisms, and may be seen in ESRD as well as in chronic diseases such as malignancy, hypertension and diabetes. Preceding acute inflammation in the kidney protects the kidney from damage and initiates healing. Subsequently, a balance between the pro-inflammatory response and anti-inflammatory response occurs. The main mediators that initiate and maintain acute inflammation are eicasonoids, cytokines, histamine, procoagulants such as the complement system and fibrinolytic molecules. In chronic inflammation, when the suppression of the acute inflammatory response process is not realized or delayed, injury occurs with the accumulation of pro-inflammatory mediators such as interleukin-1 (IL-1), interleukin-6 (IL-6), tumor necrosis factor alpha (TNF-α) in the tissue (13,14). NLR, as a parameter associated with low-grade inflammation, is recognized as an important component of ESRD and has an important role in all-cause morbidity and mortality. Uremia and metabolic acidosis are the leading causes of inflammation in ESRD. NLR, which is recognized as one of the markers of systemic inflammation, is easily detected by the ratio of the absolute number of neutrophils to the absolute number of lymphocytes in a simple hemogram test. The physiologic response of leukocytes to stress is an increase in neutrophil count and a decrease in lymphocyte count, and the ratio of these two parameters can be used as an indicator of inflammation. They can be used in renal disorders as well as in chronic diseases such as malignancies, cardiac disorders and hypertension (12). Since ESRD is a process characterized by chronic inflammation, it has been reported that NLR may predict progression (15,16).

In our study, we planned to investigate the effect of hemodialysis treatment on inflammation in patients with end-stage renal failure using the NLR. As a result of our analysis, NLR was found to be similar in patients receiving RRT and patients not receiving RRT. We think that inflammation continues in ESRD patients despite hemodialysis treatment. It is also possible that the results may be similar because our study was single-center, the number of patients was small and it was conducted retrospectively. In another retrospective study, TLO and NLR values as inflammation markers were examined in 62 patients aged 18-70 years receiving percutaneous dialysis or hemodialysis treatment and TLO was reported to be superior to NLR as an inflammation marker (17). In 2012, Turkmen K. et al. (10) examined NLR and TNF-α levels in 61 dialyzed patients and found that TNF-α levels were higher in patients with NLR 3.5 and above. As a result of this study, it was stated that NLR is an important sign of inflammation in ESRD patients. In the study conducted by Balboul et al. (18) in 2020, it was found

that a 1-unit increase in NLR caused an increase of 1.04 in risk factors, while CRP and platelet-lymphocyte ratio were found to be insignificant. In the Chines Cohort Study of Chronic Kidney Disease (C-STRIDE) study by Yuan et al. (19), 3358 cases from 39 clinical centers were included in the study and 938 cases were evaluated in terms of NLO. In the results, it was argued that NLR was a better guide for ESRD patients rather than the pre-dialysis patient group in the study. In the study, it was also determined that NLR was detected as an independent risk factor in ESRD patients. In a study conducted by Tonyalı et al. (20) on 226 patients in 2018, the relationship between NLR and GFR was examined and it was stated that NLR can be used as a predictive value in nephrectomy candidate cases. In another study conducted by Yoshitomi et al. (21) in 2019 with 83 patients with stage ESRD, they found that those with a higher NLR had a worse prognosis than those with a lower NLR. Based on this inference, it was stated that NLR may be useful in determining the prognosis in ESRD patients.

While the inclusion of only stage 5 cases in the study is statistically sufficient in terms of the number of groups, the inclusion of other stage cases in the study will be beneficial for a future study. In addition, categorizing the study into comorbidity groups such as diabetes, hypertension and malignancy, which may be the cause of chronic inflammation, will have an effect on determining the risk coefficient among the cases. Exclusion criteria in our study included smoking, use of drugs that affect chronic inflammation such as immunosuppressive drugs and anti-inflammatories. In addition, the cases were not subdivided into subgroups in terms of diseases such as cardiovascular diseases and diabetes, which are the causes of morbidity

CONCLUSION

As a result, literature review showed that the inclusion of parameters such as hemoglobin and platelet lymphocyte ratio in the evaluation of previous studies strengthens these studies. As a final statement, it should be considered that MCV could be used to evaluate the progression of renal disease, taken account of there was significant difference between our two study groups.

DESCRIPTIONS

No financial support.

No conflict of interest.

Ethical Declaration: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Ethics committee approval has been granted from our institution. Informed consent was obtained from all participants.

Data Availability: The data used to support the findings of this study are included in the article. The data supporting the findings of this study are also publicly available in the electronic health system (E-nabiz) of the patient.

Consent: The patient has given their written informed consent to publish their case (including publication of images). Approval was also obtained from the patient and his caregiver for the termination of hemodialysis treatment.

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