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ORIGINAL ARTICLE

Red cell distribution width is associated with albuminuria in adults with familial Mediterranean fever



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Abstract Systematic inflammation, enhanced oxidative stress, and endothelial dysfunction are important for evolution and progression of renal damage, and they cause an increase in red cell distribution width (RDW). Familial Mediterranean fever (FMF) patients who are in the attack-free period and its relation with albuminuria and performance on assessment of microalbuminuria. One hundred and seventy-seven patients who had been diagnosed in accordance with Tel-hoshmer criteria and were in the attack-free period, and 143 age- and sex-matched healthy individuals were enrolled in our study. RDW values of FMF patients were higher compared with those of the controls (13.85 ± 1.07 and 13.15 ± 0.91 , respectively; $p < 0.0001$). RDW values of FMF patients with microalbuminuria were higher compared with those of FMF patients with normoalbuminuria and the control group ($p = 0.002$ and $p < 0.0001$, respectively). RDW values of FMF patients with normoalbuminuria were higher compared with those of the control group ($p < 0.0001$). We have showed RDW levels are positively correlated with albuminuria ($r = 0.185$, $p = 0.014$). When assessing microalbuminuria with RDW in the patients, a cutoff value of 13.85 with sensitivity of 60%, specificity of 62%, and $p = 0.002$ (area under curve: 0.651, 95% confidence interval 0.563–0.738), was observed according to receiver-operating

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characteristic curve analysis. Among the various variables associated with albuminuria in multivariate logistic regression analyses, RDW remained an independent predictor of albuminuria (95% confidence interval 0.479–0.942, $p = 0.021$). RDW may be associated with albuminuria in FMF patients and it can be a predictor of microalbuminuria.

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Introduction

Familial Mediterranean Fever (FMF) is the most common autosomal recessively inherited autoinflammatory disorder. Attacks characterized by fever, inflammation in the synovial and serosal membranes, and skin involvement are observed in most of the patients [1,2]. Attacks usually reduce within 12–72 hours, and the attack-free period may be completely asymptomatic. The pathogenesis of the disease is the mutation of Mediterranean fever gene, which encodes the pyrin/marenostrin protein in the 16th chromosome. As a result of this mutation of the gene, control of the inflammatory process fails [3,4].

Secondary amyloidosis symptoms can be observed directly in some patients without any symptoms and findings. That is prognostic and the most feared complication in the course of the disease [5]. Early stage is completely asymptomatic in this condition, during which renal involvement can be observed frequently and can be presented as microalbuminuria as well as end-stage renal impairment symptoms [5–7]. Microalbuminuria can be used as an indicator of early renal damage in the process of amyloidosis and/or renal damage development in the management of renal pathologies [8,9].

Red cell distribution width (RDW) is a simple and inexpensive marker used very often in clinical practice; it is used to assess the changes of red blood cell size in complete blood count. RDW is often used as a guide for differential diagnosis with respect to thalassemia trait in anemia [10,11]. Additionally, existence of systemic inflammation may cause an increase in RDW. There are studies related to RDW in FMF patients, and it was reported that RDW can be used as a marker of subclinical inflammation [12,13].

The goal of this study is to examine the changes in RDW, which is connected to systemic inflammation in FMF patients who are in the attack-free period, and its relation with albuminuria and performance regarding assessment of microalbuminuria.

Methods

One hundred and seventy-seven patients, who had been diagnosed in accordance with Tel-hoshmer criteria [14] and were in the attack-free period, and 143 age- and sex-matched healthy individuals were enrolled in our study. Files and archives of the patient group and healthy individuals were examined. Complete blood count, inflammatory markers, urinary albumin levels, and estimated

glomerular filtration rate of the patient group, and complete blood count and inflammatory markers of the control group were registered. Laboratory parameters of both study groups were analyzed by the same analyzer. Kidney function was estimated by glomerular filtration rate using the abbreviated formula developed and validated in the Modification of Diet in Renal Disease study. Albuminuria was calculated using the spot urine albumin/creatinine ratio.

Patients were divided into two groups according to their daily albuminuria. Patients with 0–29 mg/d albuminuria were included in the normoalbuminuria patient group and those with 30–299 mg/d albuminuria were included in the microalbuminuria patient group. Patients with anemia, B12 and folic acid deficiency, thyroid dysfunction, diabetes mellitus, hypertension, cardiovascular disease, chronic obstructive respiratory disease, acute and/or chronic infection, and a smoking history were excluded from the study. Patients with ≥ 300 mg/d albuminuria were also excluded from the study because of the small patient group.

The complete blood count was performed using the same analyzer, Mindray BC-6800 (Shenzhen Mindray Bio-Medical Electronics Co. Ltd., Shenzhen, China), which is routinely checked every month in the central laboratory of our institution. Standard tubes with a constant amount of EDTA were used.

Statistical analysis

All statistical analyses were performed with SPSS version 15.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were presented as arithmetic mean \pm standard deviation. The significance of the mean differences between groups was assessed by Student *t* test and one-way analysis of variance (ANOVA). Differences were assessed by Chi-square test for categorical variables. Relationships between variables were tested using Spearman's correlation analysis. Receiver-operating characteristic curve graphics were used in the comparison of sensitivity and specificity. Various variables associated with albuminuria in multivariate logistic regression analyses were assessed. A *p* value < 0.05 was regarded as significant.

Results

No age and sex difference were observed between FMF patients and control group (Table 1). RDW values of FMF patients were 13.85 ± 1.07 and those of the control group 13.15 ± 0.91 ; RDW values of the patients were higher

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