

## Brief Communication

### Relationship of early hypertensive retinopathy to inflammation markers and microalbuminuria in hypertensive patients with regulated blood pressure

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Hypertensive retinopathy is the term used to describe the changes to the retinal vascular system that happen due to high blood pressure.<sup>1</sup> It is believed that retinal assessment may be a valuable tool in gathering information regarding systemic micro vascular injury.<sup>2</sup> Today, many guidelines define hypertensive retinopathy as target organ injury. Although the Joint National Committee (JNC) 7 report published in 2003 defines all retinopathy stages as target organ injury, World Health Organization (WHO) / International Society of Hypertension (ISH) 2003, British Hypertension Society (BHS) IV 2004, European Society of Hypertension (ESH)-European Society of Cardiology (ESC) 2003 guidelines suggest that only grades 3 and 4 should be accepted as target organ injury.<sup>2</sup> However, the most common grades of retinopathy are 1 and 2.<sup>3</sup> Therefore, it is important to understand the clinical significance of the retinal changes in these grades. Although certain large-scale studies conducted to understand the clinical significance of grade 1-2 retinopathy have yielded conflicting results. The aim of the present study is to investigate whether the routine inflammation markers and urinary albumin excretion are different in hypertensive patients with and without retinopathy, and also to assess whether these parameters are related to early retinopathy.

We carried out this study in Kirikkale University Medical School, between December 2004 and March 2005. A total of 118 hypertensive patients, comprising of 46 men and 72 female with ages ranging from 30-74 years were included in the study. None of them had any disease except regulated essential hypertension. All subjects were informed prior to the study and their written consent was obtained. Weight, height and waist circumference were measured and body mass index (BMI) was calculated. Blood pressure was measured 3 times following 15-minute rests and the average of these 3 measurements was taken. A blood sample was drawn in the fasting state: plasma fibrinogen C-reactive protein (CRP), hemoglobin, white blood cell, platelet, serum glucose, urea, creatinine, albumin and 24-hour urinary protein, albumin and creatin excretion were measured. Microalbuminuria was defined as urinary

albumin excretion  $\geq 30$  mg/24h and  $< 300$  mg/24h. Oral glucose tolerance test was performed on subjects whose fasting blood sugar level was above 5.5 mmol/L. The fundoscopic examination of all subjects was carried out using the ophthalmoscope. The Keith-Wagner-Baker classification was used to determine retinopathy level.<sup>1</sup> Accordingly, only those patients with retinopathy grade 1-2 were included in the study. The subjects were then divided into 2 groups based on their fundoscopic examination: subjects with retinopathy (grade 1-2 retinopathy, n=65) and subjects without retinopathy (no pathological findings in fundoscopic examination, n=53). Retinopathy was analyzed as a dichotomous variable (such as retinopathy yes or no). Means were compared by Student's t test. Analysis of categorical data was carried out with the chi-square test. Multiple logistic regression analysis was also used to assess the independent relationship between retinopathy and study variables.

There were no significant differences in age, gender, smoking, BMI, waist circumferences, systolic and diastolic blood pressure between retinopathy and non-retinopathy groups ( $p > 0.05$ ). However, white blood cell, CRP, platelet, fibrinogen and 24-hour urinary albumin excretion showed significant differences with higher values for people with retinopathy ( $p < 0.05$ ). Multivariate analysis was performed using the logistic regression with retinopathy (yes/no) as the dependent variable and with white blood cell, platelet and CRP as independent variables. Retinopathy was positively and significantly associated with white blood cell ( $\beta = 0.001$ ,  $p = 0.01$ ) and CRP ( $\beta = 0.289$ ,  $p = 0.03$ ), whereas no significant association was found with platelet. Very similar results were obtained with the use of fibrinogen instead of CRP in the model ( $\beta = 0.006$ ,  $p = 0.03$ ). Chi-square analysis showed that microalbuminuria and retinopathy were statistically significantly related ( $p < 0.01$ ). Target organ injuries, which happen during the acute or chronic stages due to high blood pressure, indicate both a failure in controlling blood pressure and increased cardiovascular risk independent of the blood pressure.<sup>3</sup> Today grades 1-2 retinopathies are the most common types whereas grades 3-4 are rare.<sup>3</sup> That is why the clinical significance of grades 1-2 is crucial to understand. Our study focuses on hypertensive patients with regulated blood pressure and no additional diseases such as diabetes mellitus. However, other studies concerning this issue generally consist of patients with no prior treatment, blood pressure regulation or careful diabetes mellitus scans, therefore, results of the present study may be more significant.<sup>3</sup> The present study also shows that grade 1-2 hypertensive retinopathy (55.1%) is more common than microalbuminuria (39%), another target organ

injury. In the literature as well, grade 1-2 hypertensive retinopathy is generally found to be more common than other target organ injuries such as microalbuminuria or left ventricular hypertrophy.<sup>3</sup> For this reason, recognition of the clinical value of grade 1-2 retinopathy may be more influential than other target organ injuries in the assessment of hypertensive patients. The present study has found a statistically significant relationship between microalbuminuria and retinopathy. As a result, it may be thought that togetherness of microalbuminuria and retinopathy develops due to systemic microvascular injury and, in relation to this; grade 1-2 retinopathy also indicates systemic microvascular injury. Another result of the present study is the relationship between grade 1-2 retinopathy findings and inflammation markers that are used frequently in clinical practice. A possible relationship between inflammation markers and retinopathy was suggested for the first time in the Atherosclerosis Risk in Communities Study study.<sup>4</sup> Additionally, in the multivariate analysis that was conducted, grade 1-2 retinopathy development was seen to be influenced by white blood cell, CRP and fibrinogen, which are important parameters of inflammation. Inflammation is one of the triggering mechanisms in various cardiovascular and cerebrovascular events.<sup>5</sup> Inflammation markers such as white blood cell, fibrinogen, CRP may be useful in identifying cardiovascular risk. Inflammation, which has a role in the development of retinopathy in hypertensive patients, may at the same time cause destruction in coronary, cerebral, renal and other similar microvascular structures and, as a result of this, grade 1-2 hypertensive retinopathy may also be exacerbating due to inflammation increase in these systems.<sup>5</sup> Therefore, grade 1-2 retinopathy may be closely related to cardiovascular risk increase. Additionally, the significant togetherness of microalbuminuria, and retinopathy also supports this view. Hypertension generally brings with itself increased cardiovascular mortality and morbidity. However, this increase is not typical in all hypertensive patients. Therefore, identifying high-risk patient groups may help decrease cardiovascular morbidity and mortality.<sup>2</sup> Displaying target organ injuries does not decrease the risk today. This makes it important to understand the clinical significance of grade 1-2 hypertensive retinopathy, which is easily and frequently identified in clinical practice.<sup>2</sup>

The conclusions of the present study support the clinical significance of hypertensive grade 1-2 retinopathy. However, the limited number of subjects and the use of ophthalmoscope for retinal assessment somewhat reduces the significance of the findings. Nevertheless, they are similar to those obtained in other studies that used the fundus photography method to make a more detailed retinal assessment.

In conclusion, retinal examination may show the existence of systemic microvascular injury. Grade 1-2 hypertensive retinopathy is frequently seen in hypertensive subject groups with regulated blood pressure. Microalbuminuria, a serious target organ injury, is related to grade 1-2 retinopathy, whose development is induced by increased inflammation. Therefore, grade 1-2 retinopathy may be important in both assessing the effectiveness of treatment and identifying cardiovascular risk increase in hypertensive patients with regulated blood pressure.

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## Diabetic scenario in Arabs

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Diabetes is a metabolic disorder characterized by resistance to the action of insulin, insufficient insulin secretion, or both. It is estimated that diabetes affects approximately 5% of the population in the industrialized nations, majority (~90%) constitute type-2 diabetes. It is expected that diabetes will be one of the most challenging public health problems of the 21<sup>st</sup> century. It is now affecting more than 150 million