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Association of Monocyte to High-Density Lipoprotein Cholesterol Ratio with Diabetic Retinopathy in Patients with Type II Diabetes Mellitus

Monosit/Yüksek Dansiteli Lipoprotein Kolesterol Oranının Diyabetik Retinopati ile İlişkisinin İncelenmesi

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ABSTRACT

Objectives: The purpose of the study was to evaluate the association of monocyte to high-density lipoprotein cholesterol ratio (MHR) with diabetic retinopathy (DR) in patients with type II diabetes mellitus (DM).

Methods: Forty-five DM patients with DR included in the study. Similarly, 45 DM patients without DR and 45 healthy subjects were determined as control groups. The data were composed based on a retrospective scan of the medical records and laboratory archives of patients.

Results: The mean MHR was significantly higher in DR patients compared to DM patients without DR and healthy subjects. There was also a statistical difference between DM patients without DR and healthy subjects. The optimal cutoff value of MHR for DR was 9.17 with 82.9% sensitivity and 59.8% specificity and an area under the receiver operating characteristics curve was 0.755.

Conclusion: The MHR recognized as a potential biomarker of inflammation was significantly higher in patients with DR compared to the DM patients without DR and healthy subjects. Our results demonstrated that the MHR has high sensitivity and low specificity for DR.

Keywords: Diabetes mellitus; diabetic retinopathy; inflammation; monocyte-to-HDL ratio; sensitivity.

ÖZET

Amaç: Bu çalışmada, tip 2 diyabet hastalarında, diyabetik retinopati ile monosit/yüksek dansiteli lipoprotein oranının (MHR) ilişkisi incelenmiştir.

Yöntem: Diyabetik retinopatisi bulunan 45 diyabet hastası çalışma grubunu oluştururken, diyabetik retinopatisi bulunmayan 45 diyabet hastası ile 45 diyabeti bulunmayan sağlıklı katılımcı kontrol grubunu oluşturdu. Hastaların retrospektif olarak medikal ve laboratuvar kayıtları tarandı.

Bulgular: Ortalama MHR, diyabetik retinopatisi bulunan hastalarda, diyabetik retinopatisi bulunmayan diyabet hastalarına ve diyabeti bulunmayan gruba göre istatistiksel olarak anlamlı yüksekti. Ayrıca MHR, diyabetik retinopatisi bulunmayan diyabet hastalarında, diyabeti bulunmayan kontrol grubuna göre anlamlı olarak daha yüksekti.

Sonuç: İnflamasyonun göstergesi olarak potansiyel bir biyobelirteç olarak kabul edilen MHR, diyabetik retinopatisi bulunan diyabet hastalarında, diyabetik retinopatisi bulunmayan diyabet hastalarına ve diyabeti bulunmayan gruba göre anlamlı olarak daha yüksek bulundu.

Anahtar sözcükler: Biyobelirteç; diyabet; diyabetik retinopati; inflamasyon; monosit/yüksek dansiteli lipoprotein oranı.

Diabetes mellitus (DM) is a systemic disease characterized by microvascular and macrovascular complications.[1] Diabetic retinopathy (DR) is the most common microvascular complication of diabetes and is an important cause of acquired blindness in working-age adults. The pathogenesis of DR is very complex, and the disease has a progressive nature. Therefore, DR is also classified as a chronic inflammatory disease that inflammatory processes play a considerable role in the pathogenesis of DR.[2] Some studies have shown that chronic inflammation caused by disorders of glucose and lipid metabolism often damages the retinal capillaries and leads to retinopathy.[2,3]

Monocytes are responsible for inflammatory reactions and take part in vascular inflammation.[4] In addition, high-density lipoprotein (HDL) cholesterol is well known for its anti-inflammatory and antioxidant effects and also defends endothelial cells against the unfavorable effects of low-density lipoprotein (LDL).[5] More recently, the monocyte/HDL ratio (MHR) was defined as a novel potential biomarker of inflammation in many systemic diseases[6-8] and also diabetic complications.[9,10] On this basis, the aim of this study was to evaluate the MHR level in patients with DR which has emerged as a new inflammatory biomarker recently in the literature.

Methods

We reviewed records of 146 patients diagnosed with type 2 DM who visited our eye clinic January 2019 through December 2020. The data were composed based on a retrospective scan of the medical records of patients who also had visits to our internal diseases clinic. The study was approved by the local Ethical Committee and adhered to the tenets of the Declaration of Helsinki.

DM patients who had mild-to-severe DR without previous history of laser and intravitreal injection treatment were enrolled in this study. DM patients without DR and healthy subjects were included in the study as control groups. We collected the following parameters from the medical records and laboratory archives; age, sex, ocular examination findings (DR condition), any chronic/systemic disease, CRP, total cholesterol (TC), triglyceride (TG), LDL cholesterol, HDL cholesterol, glycosylated hemoglobin A1c, serum creatinine (Scr), blood urea nitrogen (BUN), spot urine albumin to creatinine ratio (UACR), and estimated glomerular filtration rate (eGFR).

Patients were excluded from the study if they had type 1 DM, any acute inflammation, infection, smoking, acute or chronic renal failure, chronic liver or heart diseases, other any microvascular complications of diabetes except DR, insufficient controlled hypertension, coronary artery disease, cerebrovascular disease, connective tissue diseases, any ocular diseases except DR, macular edema, previous history of retinal laser photocoagulation and intravitreal injection, and history of any surgery within 3 months. Patients with out of normal levels of CRP, Scr, BUN, UACR, and eGFR were also excluded from the study.

All statistical analyses of this study were performed with SPSS for Windows 22.0 package program (SPSS Inc., Chicago, IL). The Kolmogorov-Smirnov test was used to test normality of distribution. Pearson's Chi-square test was performed for categorical data analyses. We compared parametric values among groups by one-way ANOVA. Bonferroni correction test was used as a post hoc test for multiple comparisons among the groups. Comparisons of non-parametric values among groups were performed by the Kruskal–Wallis test. Receiver operating characteristic (ROC) curve analysis was used to compare the prognostic powers of the MHR for DRP. $p<0.05$ was considered statistically significant.

Results

Forty-five DM patients (23 females and 22 males) who had mild-to-severe DR were eligible for the study. Similarly, 45 DM patients (24 females and 21 males) without DR and 45 healthy subjects (23 females and 22 males) determined as control groups. Patients with DR were regarded as Group 1, DM patients without DR were regarded as Group 2, and healthy subjects were regarded as Group 3. The mean age of patients was 55.9±6.9 years in DR patients, 58.2±9.5 years in DM patients without DR, and 57.8±7.8 years in healthy subjects. There were no statistical differences between the three groups in terms of age and gender ($p=0.316$ and $p=0.986$, respectively).

All laboratory parameters (monocyte counts, HDL, and MHR) are summarized in Table 1. The monocyte counts were significantly different between three groups (one-way ANOVA, $p=0.012$). While monocyte counts were significantly higher in DR patients and DM patients without DR compared to healthy subjects (Bonferroni correction test, $p=0.027$ and $p=0.025$, respectively), there was no difference between DR patients and DM patients without DR (Bonferroni correction test, $p=0.909$).

Table 1. Demographic characteristics and labarotory parameters of the groups

	Control group (without DM), n=45	DM patients without DR, n=45	DM patients with DR, n=45	p
Age	57.8±7.8	58.2±9.5	55.9±6.9	0.316†
Female/male	23/22	24/21	23/22	0.986‡
Diabet duration		10.1±5.4	10.9±6.2	0.674*
HbA1c		8.9±1.2	9.1±1.4	0.946*
HDL	51.1±10.8	50.2±11.8	42.2±8.9	<0.001†
Monocyte	402.2±82.7	469.6±96.9	456.3±101.3	0.012†
MHR	7.95±1.04	9.83±2.95	11.15±3.22	<0.001†

*: Indipendent T test, †: One-way ANOVA, ‡: Pearson's chi-square test. HbA1c: Glycated hemoglobin; HDL: High-density lipoprotein; MHR: Monocyte count to HDL ratio.

There was a statistical difference between the three groups in HDL levels (one-way ANOVA, p<0.001). While HDL levels were significantly less in DR patients compared to DM patients without DR and healthy subjects (Bonferroni correction test, p=0.001 and p<0.001, respectively), there was no difference between DM patients without DR and healthy subjects (Bonferroni correction test, p=0.989).

The mean MHR was significantly different between three groups (one-way ANOVA, p<0.001). The mean MHR was significantly higher in DR patients compared to DM patients without DR and healthy subjects (Bonferroni correction test, p=0.034 and p<0.001, respectively). There was also a statistical difference between DM patients without DR and healthy subjects (Bonferroni correction test, p=0.022). The optimal cutoff value of MHR for DR was 9.17 with 82.9% sensitivity and 59.8% specificity and an area under the ROCs curve was 0.755, as shown in Figure 1.

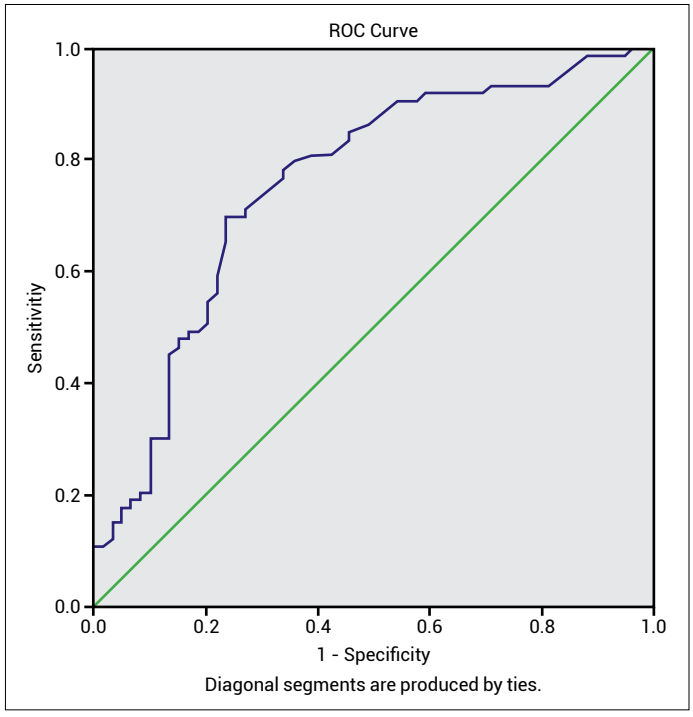

Figure 1. ROC analysis of MHR for diabetic retinopathy.

Discussion

Some studies have indicated that DM and its microvascular complications are associated with chronic inflammation[2,3,11,12] and immune responses.[12,13] In the studies investigating the relationship between inflammation and DR, C-reactive protein levels were found higher in patients who had DR.[14,15] NLR is a marker of inflammation which has been comprehensively investigated as a potential indicator of systemic inflammation; thus, recent reports confirmed that NLR is increased in DM and DR.[16,17] In addition, elevated NLR was independently related with the severity of DR.[17,18] Moreover, MHR was investigated as a new inflammation biomarker and considered as superior to subtypes of WBC in patients with cardiovascular and cerebrovascular diseases.[19-22]

Monocytes are the most important cell types in inflammatory reactions because they are responsible for secretion of pro-inflammatory and pro-oxidant cytokines.[4] On the other hand, HDL cholesterol has antioxidant and anti-inflammatory effects such as reducing macrophage accumulation, inhibiting transmigration of monocytes, increasing the expression of nitric oxide synthase in endothelial tissues, and protecting the endothelial cells.[5]

More recently, the monocyte/HDL ratio (MHR) was defined as a novel potential biomarker of inflammation in diabetes[6-8] and also its complications.[9,10] In a study conducted by Canpolat et al.,[9] MHR was higher in diabetic patients with neuropathy than without neuropathy (13 and 11, respectively). However, this difference was not statistically different. Karatas et al.[10] reported that the MHR in patients

with diabetic nephropathy was significantly higher than that of both the normoalbuminuric diabetic patients and the healthy controls (12.4, 8.2, and 8.1, respectively). Samely, Onalan et al.[23] found higher MHR levels for patients with diabetic nephropathy compared to those without diabetic nephropathy (17.1±7.9 and 10.3±3.3, respectively). In this present study, the MHR was significantly higher in DR patients than DM patients without DR. The cutoff value greater than 9.17 for MHR with a sensitivity of 82.9% and specificity of 59.8% (p=0.008 and area under the curve [AUC]=0.755) was found to be associated with DRP.

The MHR was evaluated in some ocular disorders such as branch retinal vein occlusion (BRVO), pseudoexfoliation syndrome (PEX), keratoconus, and optic norit.[24-27] The mean MHR was significantly higher in BRVO group compared to the control group (13.4±5.2 vs. 8.1±2.2) and the AUC for MHR was 0.862, and an MHR of >9.5 predicted BRVO with a sensitivity of 76% and specificity of 70.8%.[24] In another study, the mean MHR was significantly higher in patients with PEX and PEXG than the control group. The optimal cutoff value of MHR for PEX was 8.1 with 71.4% sensitivity and 67.7% specificity and an area under the ROCs curve was 0.795.[25] The mean MHR (13.7±5.0 vs. 9.1±3.7) was statistically higher in keratoconus patients compare to control group in a study conducted by Katipoglu et al.[26] Kocak et al.[27] reported that the mean MHR was significantly higher only in the arteritic anterior ischemic optic neuropathy group compared with the non-arteritic anterior ischemic optic neuropathy and control group.

There are some potential limitations of our study. The first limitation is relative small numbers of patients and the retrospective design of the study. The second limitation is the patients were not divided into groups according to DR stages. The effect of DR stages on MHR may be aims of other studies. The third limitation is the fact that monocyte count was presented as a numeric value which does not show monocyte activation. Monocyte activation might be critical in the pathogenesis of diabetic complications.

According to the outcomes of the previous studies, elevated MHR may be considered as a novel biomarker to indicate inflammatory diseases also in ophthalmic disorders. In addition, our study showed that MHR is significantly elevated in patients with DR despite some limitations. The advantages of MHR are simple, easy to calculate, and cost-effectiveness.

Disclosures

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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