MPV and RDW İn Coeliac Disease Patients Following At Least One Year A Gluten-Free Diet

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Abstract

Celiac Disease (CD) is a chronic inflammatory disorder and requires life-long treatment and follow-up. Mean platelet volume (MPV), determinant of platelet function, is an independent risk factor for cardiovascular disease (CVD). Metabolic syndrome (MS) is a multiplex risk factor that arises from insulin resistance accompanying abnormal adipose deposition and function. It is a risk factor for coronary heart disease, as well as for diabetes, fatty liver, and several cancers.

The aim of this study was to evaluate MPV and RDW values in CD patients and the relationships between MPV, RDW, MS, impaired fasting glucose (IFG) and cardiovascular risk.

Thirty-six CD patients (mean age 29,28 ±13,35 years) and 30 healthy control individuals (mean age 31,56 ±10,54 years) were included in the study. CD patients adhered to a strict gluten-free diet and at least one year are diagnosed. The controls were matched to cases according to age, gender and BMI. A diagnosis of CD was established by positive antibodies against gliadin and/or endomysium and confirmed with histological findings of duodenum biopsy based on modified Marsh classification.

MPV and RDW levels were significantly higher in CD patients than control group (P<0,001 both). CD patients had significantly more often MS than control group (p=0,007). Patients with MS had significantly higher MPV and RDW compared to those without MS (P=0,004 vs. P=0,042 respectively).

These results suggest that CD patients are susceptible to increased platelet activation and increased MPV and RDW values that contribute to an increased risk of cardiovascular complications. The results may have clinical importance, because the parameters indicating inflammation in MS may be the early markers of developing cardiovascular events.

İntroduction

Celiac disease (CD) is an autoimmune disease which affects genetically predisposed individuals, making them susceptible to gluten. Progressive inflammation of the small intestine is the predominant underlying pathology of the disease, eventually resulting in malabsorption if gluten-containing foods are not restricted (1). A correct diagnosis is usually based on the detection of serum antibodies against endomysium and gliadin followed by histopathological confirmation by a biopsy of the small intestine, using criteria described by Marsh (intraepithelial lymphocytes, villus atrophy, and crypt hyperplasia) (1–3). Elimination of gluten from the diet is the main therapeutic approach, resulting in significant clinical and laboratory improvements in the majority of CD patients.

The MPV and RDW are easily measurable parameter, the MPV directly correlated with platelet aggregation function, proven to be increased in acute coronary syndrome, but also in the presence of cardiovascular risk factors such as the MS, dyslipidemia, DM and hypertension (4-6). Mean platelet volume (MPV) is a marker of platelet size that is easily determined on routine automated hemograms and routinely available at a relatively low cost. Subjects with a higher MPV have larger platelets that are metabolically and enzymatically more active and have greater prothrombotic potential than smaller platelets (7–11). In fact, several studies have demonstrated a significant association between higher MPV and an increased incidence of cardiovascular events and all-cause mortality (12, 13).

RDW also is a marker of cardiovascular morbidity and mortality. The variability in size of circulating red blood cells has been demonstrated to be altered in different clinical sittings as in stroke, myocardial infarction, atrial fibrillation, and heart failure (14–16).

Metabolic syndrome (MS) is a manifestation, occurring because of interaction between genetic and many environmental factors, and encompasses conditions, which predispose to the development of cardiovascular diseases (CVD) and type 2 diabetes (T2DM) (17, 18). Among the above-mentioned risk factors are glucose intolerance, insulin resistance, atherogenic lipid profile, hypertension, obesity, disorder in the process of coagulation, and increased inflammatory state (19).

The term prediabetes is used to define individuals with intermediate states of abnormal dysglicemia between normoglycemia and overt T2DM, including those with impaired fasting glucose (IFG) and those with impaired glucose tolerance (IGT) (20). Subjects with IFG or IGT are at high risk for developing T2DM. It has also been reported that IGT is associated with increased risk of CVD (21,22).

In this study, we aimed to investigate MPV, RDW levels relationship between MS, IFG and cardiovascular risk in patients with CD.

Material and Metods

Thirty-six CD patients (mean age 29,28 ±13,35 years) and 30 healthy control individuals (mean age 31,56 ±10,54 years) who came to Erzurum Region Education and Research Hospital, outpatient clinic of Endocrinology, were included in the study. All participants gave their informed consent to participate in the study, and the study was approved by local ethics institute. The controls were matched to cases according to age and BMI. CD patients adhered to a strict gluten-free diet and at least one year are diagnosed. Patients were not given any medicine affecting platelet function at least 2 weeks (e.g. acetyl salicylate, antiepileptics, heparin and so on) before the initiation of the study.

A diagnosis of CD was established by positive antibodies against gliadin and/or endomysium and confirmed with histological findings of duodenum biopsy based on modified Marsh classification (23,24). Patients with heart failure, peripheral vascular disease, acute or chronic infection, cancer, hematologic and hepatic disorders, and a history of drug use (non-steroid anti-inflammatory drugs, anticoagulant medications, and oral contraceptives) were excluded from the study.

The controls were matched to cases according to age, gender and BMI.

Body mass index (BMI) (kg/m2) were calculated using the formulas “weight (kg)/ height (m)2”. Blood Pressure was measured after at least 10-min rest in sitting position. The IDF criteria (2005) were used for diagnosis of MS, and the ADA criteria (2014) for diagnosis of IFG.

Blood glucose, total cholesterol, high-density lipoprotein cholesterol (HDLC), low-density lipoprotein cholesterol (LDL-C) and triglycerides were measured by standard laboratory methods on a biochemistry autoanalyser (Beckman Coulter AU 2700 Plus clinical chemistry autoanalyser) with the company’s original kits.

Homeostasis model assessment (HOMA-IR) was used asa measure of insulin sensitivity using the equation: Fasting insulin (mU/l) x fasting glucose (mmol/l)/22.5.

MPV and RDW were measured in a blood sample collected in EDTA. The Beckman Coulter LH 750 (impedance method) analyser was used for complete blood counts.

Statistical Analysis

All tests applied are 2-tailed, and p-value of 5 % or less is considered statistically significant.The IBM SPSS Statistics version 17 was used for statistical analysis. Student’s t-test was done to find the significance of difference between means whenever applicable. One-tailed Pearson’s correlation test was done to find the correlation between various variables. Chi-square test, and Fisher’s exact test, were done to test the association between two findings. Multiple regression analysis was used to exclude the possible confounding effect of other variables on the result of each correlation analysis. p<0.05 was considered statistically significant.

Results

The clinical and biochemical features of CD groups and controls are summarized in Table 1.

Table 1: The clinical and biochemical features of CD groups and controls

	CD patient (38)	Control group (30)	P value
Age (years)	29,2±13,3	31,5±10,5	0,44
Gender (M-F)	13-25	12-18	0,62
BMI (kg/cm^2)	22±4,8	22,4±3,2	0,76
MPV (fL)	9±1,2	7,1±1	<0,001*
RDW(%)	12,9±1,6	11,5±0,9	<0,001*
CRP (mg/dl)	0,6±0,9	2,2±3,4	0,8
Glucose (mmol/l)	100,3±47,8	88,2±10,2	0,21
Total colesterol(mg/dl)	157,1±39,9	166,5±41,3	0,44
LDL-C (mg/dl)	100,1±37,2	98,8±30,3	0,90
HDL-C (mg/dl)	46,6±13,1	53,2±11,7	0,09
Triglycerides (mg/dl)	114,8±106,8	101,7±41,2	0,56
ALT (U/L)	19,1±8,6	17,2±8,9	0,38
MCV (fL)	84,5±7,7	86,5±4,3	0,20
MCHC (g/dL)	32,7±1,3	34,3±1	<0,001*
Leukocyte (10^3/uL)	7,2±1,8	8±1,9	0,11
Hemoglobin (g/dL)	14,3±1,5	15,3±1,2	0,006*
Hematocrit (%)	43,2±4,3	44,5±3,1	0,18
Platelet (10^3/uL)	279,1±62,6	274,9±97,9	0,83
Creatinin(mg/dl)	0,5±0,1	0,7±0,1	0,001*
SBP (mmHg)	125,3±11,2	88±13	<0,001*
DBP (mmHg)	83,8±7,4	56±14,7	<0,001*
MS	11	3	0,007*
IFG	8	0	0,08

CD groups consisted of 38 patients and the control group consisted of 30 patients. There were not different in age, gender and BMİ distribution (29,2±13,3 vs. 31,5±10,5 years 22±4,8 vs 22,4±3,2 kg/cm^2 respectively, P>0,05). MPV and RDW levels were significantly higher in CD patients than control group (P<0,001 both).

CD patients had significantly more often MS than control group (p=0,007 (11 CD patients and 3 control groups). There was no significant difference in IFG between CD patients and control group (p=0,08) (8 and 0 respectively). Patients with MS had significantly higher MPV and RDW compared to those without MS (P=0,004 vs. P=0,042 respectively).

Pearson’s Correlation analysis was performed for assess the correlation between MPV and each variable. As shown in table 2, MPV had a significantly positive correlation between RDW (r=0,453 p <0,001) and uric acid (r=361 p=0,036). MPV had a significantly negative correlation between HDL-C (r=-0,349 p=0,023), totol colesterol (r=-0,301 p=0,044), MCHC (r=-0,407 p=0,001), neutrophil (r=-0,252 p=0,038), platelet (r=-319 p=0,008), leukocyte (r=-0,283 p=0,020), and monocytes (r=-0,244 p=0,045).

Table 2: Correlation assessment between MPV and other variables

Variables	Correlation Coefficient	P value
RDW (%)	0,453	<0,001
Uric acid (mg/dL)	0,361	0,036
HDL-C (mg/dL)	-0,349	0,023
Total kolesterol (mg/dL)	-0,301	0,044
MCHC (g/dL)	-0,407	0,001
Neutrophil	-0,252	0,038
Platelet (10^3/uL)	-0,319	0,008
Leukocyte (10^3/uL)	-0,283	0,020
Monocytes(10^3/uL)	-0,244	0,045

In multivariate logistic regression analysis MPV and RDW were significantly correlated with CD independently from age, MS, IFG, BMI, CRP (table 3 and table 4).

Table 3: The multiple regression analysis of MPV and other factors

	β	P value
Age	0,023	0,771
MS	17,9	0,999
IFG	0,610	0,814
BMI	0,180	0,310
CRP	0,089	0,811
MPV	3,809	0,031*

Table 4: The multiple regression analysis of RDW and other factors

	β	P value
Age	-,074	0, 221
MS	19,807	0,999
IFG	0, 232	0, 861
BMI	0, 013	0, 932
CRP	-0, 369	0, 364
RDW	1,365	0,022*

Discussion

The present study assessed MPV and RDW in CD patients, relationship between MS, IFG, cardiovascular risk for the first time. We found it MPV and RDW were significantly higher than control groups.

CD is a chronic inflammatory disorder and requires life-long treatment and follow-up. Our findings indicate that MPV and RDW were significantly higher in patients with newly diagnosed CD compared to healthy controls. Increased MPV was found to be an independent risk factor for myocardial infarction (24). It would seem that high MPV and RDW have a diagnostic and prognostic value for different inflammatory conditions and CVD.

MS consists of multiple and interrelated risk factors of metabolic origin that appear to directly promote the development of atherosclerosis. Although both of the hereditary and environmental factors contribute to the development of MS, little is known about the underlying pathogenetic mechanisms. All the components comprising MS were demonstrated to be associated with systemic inflammation (25). Consistent with the literature, the present study showed that the MPV and RDW increased in MS (26). However, associations between the new inflammatory markers (MPV, RDW) and MS have still yet to be investigated. This is the first study to evaluate the effect of high MPV and high RDW on frequency of MS in patients with CD. Those markers, are promising markers of inflammation starting to find a place in the literature, were found to be correlated with the presence MS. In our study MPV and RDW were significantly higher in CD patients independently from MS, IFG, BMI, age and CRP.

Purnak et al. (27) reported they examined the MPV, an indicator of platelet reactivity, in patients with CD. They showed that MPV values in patients with CD were significantly higher than in controls. In the dietary compliant group, introduction of a gluten-free diet resulted in a significant decrease in MPV compared to base-line. They concluded that MPV could be a useful clinical marker for monitoring of dietary compliance in CD patients. However, in our study we found that RDW and MPV were significantly higher despite gluten free diet . Although in our study it was got at least one year given a strict gluten-free diet in patients CD, MPV values were significantly higher than controls.

We found that MPV and RDW levels were significantly higher in CD patients than control group and CD patients had significantly more often MS than control group. This situation showed that CD patients are more tendencies for MS and indirectly for CVD. And we found that MPV and RDW were significantly higher in CD patients independently from age, MS, IFG, BMI, CRP.

Conclusion

It is known that systemic inflammation is involved in MS and in patients with MS, the risk for development of CVD increases. The results may have clinical importance, because the parameters indicating inflammation in MS may be the early markers of developing cardiovascular events.

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