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Evaluation of the Potential Antioxidant Role of High-Density Lipoprotein-Cholesterol (HDL-C) in Patients with Ulcerative Colitis

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Abstract

Background: Ulcerative colitis is a common type of inflammatory bowel disease (IBD). The aim of the present study was to examine the relationship between lipid profile, especially high-density lipoprotein (HDL), and malondialdehyde (MDA) level in patients with ulcerative colitis.

Methods: In this study, 45 patients with ulcerative colitis were selected, 25 of whom were diagnosed with active disease and 20 were in clinical remission. Moreover, 45 healthy subjects were selected as the controls. The status of serum lipid profile and MDA level were measured via precise photometric methods. The obtained data were analyzed, using independent t-test and correlation coefficient test. $P < 0.05$ was considered statistically significant.

Results: The serum level of HDL-C decreased, while the serum level of MDA significantly increased in patients with ulcerative colitis in comparison with the healthy controls ($P < 0.05$). No significant correlation was observed between the MDA level and triglyceride, cholesterol, and LDL-C levels in patients with ulcerative colitis. However, a significant inverse correlation was observed between HDL-C and MDA levels (r, -0.306; $P < 0.05$).

Conclusions: The inverse correlation between HDL-C and MDA levels can be regarded as an indicator of the protective role of HDL-C against lipid peroxidation in ulcerative colitis. In patients with ulcerative colitis, the serum level of HDL-C decreased in comparison with healthy subjects. Therefore, it is necessary to determine the HDL-C level in patients with ulcerative colitis.

Keywords: Ulcerative Colitis Disease, HDL-C Level, MDA Level, Active and Inactive Disease

1. Background

Crohn's disease and ulcerative colitis are 2 common forms of inflammatory bowel disease (IBD). However, the incidence of ulcerative colitis is higher than Crohn's disease. In general, ulcerative colitis is a chronic inflammatory disease with relapsing and remitting episodes (1). Ulcerative colitis commonly affects the rectum, but may also affect other areas of colon or the entire colon (pancolitis) (2).

Numerous studies have been conducted regarding the relationship between ulcerative colitis and other diseases. The relationship between ulcerative colitis and cardiovascular diseases is an interesting research area. In the past decade, some studies have been performed in this field, some of which have revealed a correlation between ulcerative colitis and cardiovascular disorders (3-6).

Low serum levels of high-density lipoprotein-cholesterol (HDL-C) and high serum levels of low-density lipoprotein (LDL-C) are known as significant risk factors for cardiovascular diseases. According to some studies, lipid profile may change in ulcerative colitis and Crohn's disease (7-10). Generally, HDL-C is known for its antiatherogenic properties. Besides these properties, HDL-C has multiple other features, including antioxidant potentials. In fact, some in vitro studies have revealed that HDL-C can neutralize lipid hydroperoxide (11).

According to some studies, oxidative stress occurs in ulcerative colitis, and the serum level of malondialdehyde (MDA) increases more significantly in patients with ulcerative colitis, in comparison to the healthy controls (12-15); therefore, lipid peroxidation may increase in ulcerative colitis. Furthermore, some studies on other diseases, such as cardiovascular disorders and diabetes, have revealed an inverse or direct correlation between HDL-C and MDA lev-

els (16, 17).

Moreover, HDL-C may be involved in the innate immunity system (18), and ulcerative colitis may have an immunological basis (1). According to these findings, evaluation of HDL-C status and the investigation of its correlation with serum MDA level can be useful in ulcerative colitis. Furthermore, as noted above, low HDL-C level is a risk factor for cardiovascular diseases (6); therefore, importance of HDL-C level in ulcerative colitis should be considered. With this background in mind, the current study was designed to evaluate the possible correlation between HDL-C and MDA levels in patients with ulcerative colitis. This study is an attempt to investigate the antioxidant properties of HDL-C.

2. Methods

This study was performed on patients, referring to the endoscopy department of Ayatollah Rouhani hospital, Babol, Iran. Complete clinical history was taken from all the patients, some of whom were selected in the study. The subjects had a history of ulcerative colitis and some were suspected of having inflammatory bowel disease (IBD) according to their signs and symptoms, such as rectorragia, abdominal pain, and diarrhea. All the selected patients signed the informed consent forms.

Blood samples were taken from the patients after 12 hours of fasting. The samples were taken from an arm vein and collected in specific tubes. Glass tubes were placed at room temperature for 30 minutes and were then centrifuged at 2700 rpm for 10 minutes. After centrifugation, the serum was separated and transferred into clean and labeled microtubes, using micropipettes.

The microtubes were transferred to a temperature of -80°C. A few days after collecting the blood samples, colonoscopy was performed by a gastroenterologist. According to the colonoscopy results, as well as gastroenterologist and biostatistician consultations, 45 patients with ulcerative colitis were selected. In newly diagnosed patients, biopsy samples were taken from some inflamed areas of mucosa for histopathological examination and diagnostic confirmation.

According to the Lichtiger index, patients with ulcerative colitis were divided into 2 groups (19-21). Patients with scores below 4 were considered as the remission group (22), while patients with scores above 4 were considered as the active-phase group. On the other hand, the healthy controls did not have IBD. Moreover, there was no significant difference in physical activities between patients with ulcerative colitis and healthy subjects.

2.1. Inclusion Criteria

Diagnosis of ulcerative colitis was confirmed via colonoscopy and histopathological examinations. The blood samples were collected a few days before colonoscopy. The age range of the patients was 18 years or older. All the selected patients signed the informed consent forms. The present study was confirmed by the human ethics committee of Hormozgan University of Medical Sciences.

2.2. Exclusion Criteria

Patients with the following diseases were excluded from the study: infectious colitis, colorectal cancer, colorectal polyp, history of cardiovascular and cerebrovascular diseases, diabetes, infectious diseases, liver and bile disease, renal diseases, psychological disorders, congenital diseases, history of dyslipidemia, metabolic syndrome, and smoking. Furthermore, suspicion of Crohn's disease and regular use of lipid-lowering drugs or nonsteroidal antiinflammatory drugs (NSAIDs), such as aspirin, were the other exclusion criteria.

2.3. Assessment of Disease Activity

Disease activity in patients with ulcerative colitis was evaluated, based on the clinical presentations using the Lichtiger index. This index is a rating system, used to assess the clinical activity of ulcerative colitis. It contains 7 variables, including diarrhea (number of daily bowel movements), nocturnal diarrhea, stool with visible blood (percentage of bowel movement), fecal incontinence, cramp or abdominal pain, abdominal tenderness, and need for antidiarrheal drugs (19, 20). Clinical remission in patients with ulcerative colitis is defined as a Lichtiger score below 4 (22).

2.4. Measurement of Serum Lipid Profile

Fasting blood samples were obtained from all the subjects. The serum levels of triglyceride, total cholesterol, LDL-C, and HDL-C (23) were determined, according to kit instructions (Pars Azmon, Iran), using an autoanalyzer (Hitachi, Japan).

2.5. Measurement of Serum MDA Level

The serum level of MDA was evaluated, using thiobarbituric acid reactive substance (TBARS) assay (24, 25). Briefly, MDA reacted with 2 TBA molecules, and a pink MDA-TBA complex was formed. This complex has an optical density at 532 nm, which can be measured by a spectrophotometer (Unico, USA).

2.6. Statistical Analysis

Data were collected and analyzed using SPSS version 17. The collected data showed a normal distribution, according to Kolmogorov-Smirnov test. For mean comparison of variables between the patient and control groups, as well as the active-disease and remission groups, independent sample t-test was used. Pearson's correlation coefficient was calculated to examine the relationship between variables. P value below 0.05 was considered statistically significant.

3. Results

The demographic and laboratory characteristics of patients with ulcerative colitis and healthy controls are presented in Table 1. Although the serum HDL-C level significantly decreased in patients with ulcerative colitis in comparison to the healthy controls ($P < 0.05$), there was no significant difference between the groups in terms of the serum levels of triglyceride, total cholesterol, and LDL-C (Table 1).

The serum level of MDA increased in patients with ulcerative colitis in comparison to the healthy controls ($P < 0.05$). As presented in Table 2, the serum level of MDA in patients with active ulcerative colitis increased in comparison to patients in clinical remission ($P = 0.039$). Moreover, there was no significant difference in lipid profile between these groups. Although MDA level showed no significant correlation with serum LDL-C, triglyceride, or total cholesterol, the serum HDL level was inversely correlated with the serum MDA level (r, -0.306; $P < 0.05$; Figure 1).

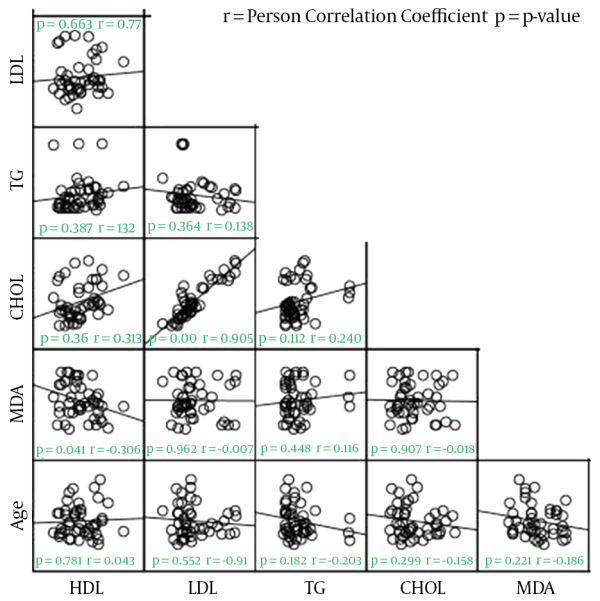

Figure 1. The Correlation Between Variables Based on Pearson's Correlation Coefficient Test

4. Discussion

In the present study, the relationship between HDL-C and MDA levels in patients with ulcerative colitis was investigated. In Western countries, the incidence of ulcerative colitis is 15 per 100,000 people per year (26). Treatments for ulcerative colitis are based on the management of inflamation, immune suppression (27), and use of 5-aminosalicylic acids and steroids.

The serum trace element levels and superoxide dismutase activity in patients with IBD changes, compared to the healthy controls (28). In addition, use of antioxidants is an important complementary treatment in cardiometabolic, neurological, and gastrointestinal disorders (29), such as ulcerative colitis. The findings of the present study demonstrated that the serum HDL-C level decreased in patients with ulcerative colitis in comparison to the healthy controls. However, there was no significant difference in the serum levels of triglyceride, total cholesterol, and LDL-C between the groups. These findings reveal that HDL-C level may decrease in patients with ulcerative colitis, which is in agreement with the findings reported by Sappati et al. (10). Nevertheless, the results were in disagreement with a study by Romanato et al. (9).

The cause of HDL-C reduction in patients with ulcerative colitis is not clear. However, it may be associated with the possible role of HDL in innate or adaptive immunity (18, 25) or HDL antioxidant characteristics (11). To obtain more reliable and precise findings, we tried to select patients precisely, as mentioned earlier. In addition, patients and healthy controls, who consumed lipid-lowering drugs, were excluded from the study. Despite a reduction in HDL-C level, MDA significantly increased in patients with ulcerative colitis in comparison to the healthy controls; these findings are in agreement with previous studies (12, 14).

The elevated serum level of MDA in patients with ulcerative colitis is an indicator of increased lipid peroxidation during persistent oxidative stress. Furthermore, we observed an inverse correlation between the serum HDL and MDA levels. These findings revealed that HDL may have antioxidant properties and inhibit lipid peroxidation in ulcerative colitis. Therefore, reduction in the serum level of HDL may be due to an increase in lipid peroxidation.

In addition, the present findings indicated that the serum level of MDA significantly increased among patients

Table 1. The Demographic and Laboratory Characteristics of Patients With Ulcerative Colitis and Healthy Controls[a]

Variables	Ulcerative Colitis	Healthy Controls	P Value
Age (years) mean ± SD	36 ± 12	36.8 ± 12	-
Sex distribution	21 females, 24 males	21 females, 24 males	-
Total cholesterol (mg/dL) mean ± SD	180.46 ± 46.15	194.37 ± 41.5	0.136
Triglyceride (mg/dL) mean ± SD	136.26 ± 82.77	133.82 ± 64.65	0.876
LDL-C (mg/dL) mean ± SD	117.32 ± 43.32	123.62 ± 37.43	0.462
HDL-C (mg/dL) mean ± SD	35.8 ± 8.2	45.22 ± 8.8	0.001
MDA (μm/L) mean ± SD	1.8 ± 0.55	1.3 ± 0.34	0.001

[a] Data are presented as mean ± SD; P value less than 0.05 was considered statistically significant.

Table 2. The Demographic and Laboratory Characteristics of Ulcerative Colitis Patients in the Active-Phase and Remission Groups[a]

Variables	Active-Phase Group	Remission Group	P Value
Age (years) mean ± SD	36 ± 8	35 ± 8	-
Sex distribution	10 females, 15 males	11 females, 9 males	-
Total cholesterol (mg/dL) mean ± SD	182.16 ± 42.43	178.35 ± 51.47	0.787
Triglyceride (mg/dL) mean ± SD	137.56 ± 89.01	134.65 ± 76.51	0.908
LDL-C (mg/dL) mean ± SD	119.31 ± 43.99	114.83 ± 43.47	0.734
HDL-C (mg/dL) mean ± SD	35.4 ± 8.3	36.5 ± 8.2	0.661
MDA (μm/L) mean ± SD	2.04 ± 0.62	1.6 ± 0.39	0.039

[a] Data are presented as mean ± SD; P value less than 0.05 was considered statistically significant.

in the active phase of ulcerative colitis in comparison to patients in clinical remission. These findings are in agreement with those reported by Achitei et al., addressing the role of lipid peroxidation in active and inactive forms of IBD (14). The reported findings substantiated the hypothesis that lipid peroxidation and oxidative stress may play significant roles in the pathogenesis of ulcerative colitis and Crohn's disease.

According to the results of the current study, serum lipid profile is not significantly different between patients with active ulcerative colitis and those in clinical remission. HDL may significantly link ulcerative colitis to cardiovascular diseases (30, 31). Also, use of some drugs such as statins (32), which increase HDL level, may have potentials in the prevention of cardiovascular disorders in patients with ulcerative colitis.

Finally, we suggest further studies with a larger sample size to clarify the role of HDL in the immunological system in ulcerative colitis and to evaluate the effects of statins on ulcerative colitis complications. Moreover, the role of lipid peroxidation in the pathogenesis of ulcerative colitis should be determined, and the possible correlation between lipid peroxidation, serum HDL level, and inflammatory and immunological agents should be examined.

4.1. Conclusion

The present results revealed that serum HDL-C and MDA levels decreased and increased, respectively in patients with ulcerative colitis in comparison to the healthy controls. Furthermore, a significant inverse correlation was observed between HDL-C and MDA levels. Therefore, HDL-C level should not be neglected in patients with ulcerative colitis.

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Footnotes

Authors' Contribution: Soheila Moein, Mostafa Vaghari Tabari, and Durdi Qujeq designed the study; Mostafa Vaghari Tabari, Mehrdad Kashifard, Javaad Shokri Shirvani, and Durdi Qujeq conducted the research; Karimollah Hajian Tilaki analyzed the data and performed statistical analyses; Mostafa Vaghari Tabari, Soheila Moein, Gholamreza Farshidfar, and Durdi Qujeq wrote the manuscript; Soheila Moein revised the final content of the manuscript.

Conflict of Interest: The authors do not have any commercial affiliations or potential conflicts of interest associated with this study.

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