

Research Article

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Evaluation of Lipid Profile Changes In Patients With Inflammatory Bowel Disease: A Single Center Experience

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Abstract

Introduction: Inflammatory Bowel Disease (IBD) encompasses chronic inflammatory disorders of the gastrointestinal tract, including Crohn's disease and ulcerative colitis. While initially considered a localized disorder, IBD has emerged as a systemic disease with a growing recognition of its potential impact on lipid metabolism and cardiovascular health. This study aims to comprehensively investigate lipid profiles and dyslipidemia prevalence among IBD patients, shedding light on potential associations with disease characteristics.

Materials and Methods: A single-center cross-sectional observational study was conducted on 707 IBD patients between December 2007 and February 2021. Inclusion criteria comprised confirmed IBD diagnosis, age 18-65, and informed consent. Demographic data, medical history, anthropometric measurements, and fasting blood samples for lipid profile analysis were collected. Lipid profiles included total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides. Statistical analyses, including t-tests, chi-square tests, and multivariate regression, explored associations.

Results: This study reveals a high prevalence of dyslipidemia in IBD patients (58%), surpassing the general population. Notably, male IBD patients displayed significantly higher levels of total cholesterol, LDL-C, and triglycerides than their counterparts in the general male population. Differences in HDL-C levels were also observed. There were no significant variations in lipid profiles between Crohn's disease and ulcerative colitis patients within the IBD subgroup.

Conclusion: The findings underscore the importance of regular lipid profile assessments in clinical management, particularly for male IBD patients. The significantly elevated prevalence of dyslipidemia in this population implies a potential influence of IBD on lipid metabolism and cardiovascular risk. Further research is needed to elucidate mechanisms and potential therapeutic interventions. Addressing dyslipidemia among IBD patients holds promise for reducing cardiovascular risk and enhancing overall health outcomes in this complex patient group.

Keywords: Dyslipidemia, Inflammatory Bowel Diseases, Lipid Profile, Crohn's Disease, Ulcerative Colitis

1. Introduction

Inflammatory Bowel Disease (IBD), encompassing conditions such as Crohn's disease and ulcerative colitis, represents a group of chronic inflammatory disorders characterized by inflammation of the gastrointestinal tract [1]. Over the years, IBD has evolved from being perceived solely as a localized gastrointestinal disorder to a systemic disease with a multitude of extraintestinal manifestations. Among these systemic implications, disturbances in lipid metabolism, specifically dyslipidemia and alterations in

lipoprotein profiles, have emerged as significant yet underexplored factors in the realm of IBD [2,3].

Dyslipidemia, characterized by deviations from normal serum lipid levels, has long been recognized as a pivotal risk factor for cardiovascular diseases, contributing to the global burden of morbidity and mortality [4]. Within the context of IBD, the intricate interplay between chronic intestinal inflammation and lipid homeostasis remains enigmatic [5,6]. Recent research endeavors

have started to unveil the complex relationships between IBD and lipid metabolism, suggesting that IBD may influence not only gut health but also cardiovascular well-being [7, 8].

This original article aims to contribute to the expanding body of knowledge surrounding dyslipidemia and lipoprotein profile changes in patients with IBD. By conducting a single-center study, we endeavor to provide a comprehensive insight into these alterations and their clinical significance in a well-characterized cohort of IBD patients. Our research, conducted at University of Health Sciences, Ankara City Hospital, delves into the lipid profiles of IBD patients, exploring potential associations with disease characteristics, such as disease subtype, disease activity, and duration.

1.1 Rationale for the Study

The rationale for investigating lipid profile changes in IBD patients is multifaceted. Firstly, the chronic inflammatory milieu characteristic of IBD has the potential to disrupt lipid metabolism through various mechanisms, including the release of proinflammatory cytokines, alterations in gut microbiota, and changes in dietary habits [9]. Secondly, the presence of dyslipidemia in IBD patients may have profound implications for their overall health and quality of life, considering the already complex nature of managing this chronic inflammatory condition [10]. Lastly, understanding the dynamics of lipid profiles in IBD patients at a single-center level can offer valuable insights into potential therapeutic targets and strategies to mitigate cardiovascular risk [11].

1.2 Objectives of the Study

This single-center study endeavors to achieve the following objectives:

- 1. Assess and characterize the lipid profiles, including total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides, in patients with IBD.
- 2. Evaluate the prevalence of dyslipidemia among IBD patients and identify potential risk factors associated with dyslipidemia in this population.
- 3. Investigate potential associations between lipid profile changes and key disease parameters, including disease subtype, disease activity, duration of illness, and therapeutic interventions.
- 4. Provide insights into the clinical significance of lipid profile alterations in IBD patients, with a focus on potential implications for cardiovascular health and overall disease management.

In presenting the results of our single-center experience, we aim to contribute valuable data to the growing body of knowledge on the systemic manifestations of IBD, particularly its impact on lipid metabolism [12]. Ultimately, our findings may inform clinical practice, guiding healthcare providers in the management of dyslipidemia and cardiovascular risk in patients grappling with this chronic inflammatory disorder [13].

2. Materials and Methods

2.1 Study Design

This original research article presents findings from a cross-sectional observational study aimed at investigating dyslipidemia and lipoprotein profiles in patients diagnosed with Inflammatory Bowel Disease (IBD). The study adheres to a rigorous research design to assess the prevalence of dyslipidemia and characterize lipoprotein profiles among IBD patients, as well as to explore potential associations with disease parameters.

2.2 Study Population

Retrospective analysis was done on the patient data from those who were monitored in our hospital's inflammatory bowel disease outpatient clinic between December 2007 and February 2021. Eligible participants met the following inclusion criteria: Confirmed diagnosis of IBD (Crohn's disease or ulcerative colitis) based on clinical, endoscopic, and histopathological criteria, age 18-65 years, and ability to provide informed consent for participation in the study.

3. Data Collection

3.1 Clinical Assessment

Demographic information, medical history, and clinical parameters including disease duration, disease location, and disease activity scores (e.g., Crohn's Disease Activity Index, Ulcerative Colitis Disease Activity Index) were collected through structured interviews and medical chart review.

3.2 Anthropometric Measurements

Height, weight, and waist circumference were measured using standardized techniques, and body mass index (BMI) was calculated.

3.3 Blood Sample Collection

Fasting blood samples were obtained from study participants. Blood was collected in ethylenediaminetetraacetic acid (EDTA) tubes for lipid profile analysis.

3.4 Lipid Profile Analysis

Serum lipid profiles, including total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides, were determined using standardized enzymatic assays on an automated clinical chemistry analyzer.

4. Statistical Analysis

IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, N.Y., USA) was the statistical program that we used for analyses. A two-tailed p-value < 0.05 was considered significant. Descriptive statistics were used to summarize demographic and clinical characteristics. Continuous variables were reported as means \pm standard deviations (SD), while categorical variables were presented as frequencies and percentages. The prevalence of dyslipidemia and variations in lipid profiles among IBD patients were assessed. Inferential statistics, such as t-tests, chi-square tests, and multivariate regression analysis, were employed to explore potential associations between dyslipidemia, lipoprotein

profiles, and disease parameters, while controlling for potential confounding variables.

5. Ethical Considerations

The study was conducted in accordance with the principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the Ethics Committee at University of Health Sciences, Ankara City Hospital (E1-21-2051). Informed written consent was obtained from all study participants prior to enrollment.

6. Results

A total of 707 participants with confirmed diagnoses of Inflammatory Bowel Disease (IBD) were enrolled in this single-center 15 years study. The demographic characteristics and lipoprotein profiles of the study population are summarized in Table 1. The mean age of the participants was 37.23 (30.04-45.86) years, and 324 (45.8 percent) were male. The majority of patients had a diagnosis of ulcerative colitis (UC) (52.6%), while the remaining participants had Crohn's disease (CD) (47.4%). Mean disease duration was 6.93 (3.85-11.49) years. Of the patients, 128 (18.1%) had hypertension, and 38 (5.4%) had diabetes mellitus. Serum lipid profiles, including total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides, were assessed in all study participants. The results are presented in Table 1.

	Total IBD Patients	
	n=707	
Age, years	37.23 (30.04-45.86)	
Gender, male, %	324 (45.8)	
BMI, kg/m ²	21.3 (16.78- 26.47)	
Age at onset of IBD, years	31.41 (24.52-39.02)	
Disease duration, years	6.93 (3.85-11.49)	
IBD type		
Crohn's Disease, n (%)	335 (47.4)	
Ulcerative Colitis, n (%)	372 (52.6)	
Comorbidities		
Hypertension, n (%)	128 (18.1)	
Diabetes Mellitus, n (%)	38 (5.4)	
Other, n (%)	26 (3.7)	
Smokers (Current/Ex), n (%)	240/226 (34.0/32.1)	
Family history of IBD, n (%)	86 (12.1)	
Total Cholesterol, mg/dL	201.2 ± 39.8	
HDL Cholesterol, mg/dL	36.5 ± 13	
LDL Cholesterol, mg/dL	133.7 ± 29.5	
Triglycerides, mg/dL	150.5 ± 78.5	
IBD: inflammatory bowel disease; HDL: high-density lipoprotein; LDL: low-density lipoprotein;		

Table 1: Demographics and Lipoprotein Profiles of IBD Patients.

There was no statistically significant difference between the Crohn's and ulcerative colitis patient groups when comparing their lipid profiles (p>0.05 for all metrics). Table 2 displays the lipid profiles of individuals with ulcerative colitis and Crohn's disease.

	Crohn's Disease n=335	Ulcerative Colitis n=372	p
Age, years	37.05 (30.04-45.86)	38.01 (30.04-45.86)	0.425
Gender, male, %	158 (47.1)	166 (44.7)	0.396
Smokers (Current/Ex), n (%)	58/94 (17.3/28.0)	182/132 (48.9/35.5)	< 0.001
Total Cholesterol, mg/dL	200.7 ± 39.9	197.6 ± 38.4	0.118
HDL Cholesterol, mg/dL	36.4 ± 13.7	35.1 ± 14.2	0.256
LDL Cholesterol, mg/dL	134.3 ± 32.6	132.5 ± 32.9	0.978

Triglycerides, mg/dL	150.1 ± 67.8	149.6 ± 103.6	0.654	
IBD: inflammatory bowel disease; HDL: high-density lipoprotein; LDL: low-density lipoprotein;				

Table 2: Lipid Profiles According to IBD Type

The prevalence of dyslipidemia in the study population was 58%. Dyslipidemia was defined as, total cholesterol >200 mg/ dL, LDL-C >130 mg/dL, HDL-C <40 mg/dL for men and <50 mg/dL for women, and/or triglycerides >150 mg/dL. Thirty-two percent of men and 22% of women in Turkey have total cholesterol levels above 200 mg/dL, according to the 2017 TEKHARF population study [14]. This percentage was found to be 51% and 40%, respectively, in patients with IBD. Among the overall male population, total cholesterol was 186.8 mg/dL; however, among individuals with IBD, it was 201.5 mg/dL. This difference was statistically significant (p=0.05). In the general population, women's total cholesterol was 180.2 mg/dL; in patients with inflammatory bowel disease, it was 198.6 mg/dL. This difference was statistically significant (p=0.05). In the general population, the rates of HDL cholesterol <40 mg/dL were 35.5% for women and 64% for men; in individuals with IBD, these rates were 44% and 78%, respectively. Among the general male population, HDL-C was 37.2 mg/dL; however, among individuals with IBD, it was 33.9 mg/ dL. This difference was statistically significant (p=0.01). HDL-C was reported to be 40.9 mg/dL in IBD patients, compared to 44.9

mg/dL in women in the general population. There was a statistically significant difference (p= 0.05). LDL cholesterol >130 mg/ dL was detected at a rate of 37% in males and 28% in women in the general population; however, in patients with IBD, this rate was 49% and 38%. Men with IBD had an LDL-C of 134.7 mg/dL, compared to the general population's 122.4 mg/dL. This difference was statistically significant (p=0.01). LDL-C in women was 114.6 mg/dL in the general population, whereas in patients with IBD, it was 129.7 mg/dL. There was a statistically significant difference (p=0.02). In general, 39.6% of men and 29.2% of women were found to have triglycerides >150 mg/dL; in individuals with inflammatory bowel disease (IBD), these percentages were 51.5% and 43%, respectively. Triglycerides in men were 166.4 mg/dL in IBD patients compared to 149.2 mg/dL in the general population. This difference was statistically significant (p=0.05). Triglycerides were 13.5 mg/dL in IBD patients compared to 126.3 mg/dL in women in the general population. There was a statistically significant difference (p=0.05). Tables 3 and 4 compare the lipid profiles of people with IBD with those of the general population.

	IBD Patients	Male Population Lipid Profile n=324	p
Total Cholesterol, mg/dL	201.5 ± 49.8	186.8	0.05
HDL Cholesterol, mg/dL	33.9 ± 11.6	37.2	0.01
LDL Cholesterol, mg/dL	134.7 ± 35.4	122.4	0.01
Triglycerides, mg/dL	166.4 ± 88.6	149.2	0.05
IBD: inflammatory bowel disease; HDL: high-density lipoprotein; LDL: low-density lipoprotein;			

Table 3: Lipid profiles of IBD patients vs control group in male patients

	IBD Patients	Female Population Lipid Profile n=383	p
Total Cholesterol, mg/dL	198.6 ± 36.8	180,2	0.05
HDL Cholesterol, mg/dL	40.9 ± 14.5	44.9	0.05
LDL Cholesterol, mg/dL	129.7 ± 27.7	114.6	0.02
Triglycerides, mg/dL	138.5 ± 73.4	126.3	0.05
IBD: inflammatory bowel disease: HDL: high-density lipoprotein: LDL: low-density lipoprotein:			

Table 4: Lipid profiles of IBD Patients vs Control Group in Female Patients

7. Discussion

The leading causes of death worldwide are cardiovascular diseases (CVD), which include peripheral artery disease, heart failure, stroke, and coronary artery disease. An unhealthy diet, uncontrolled hypertension, smoking, physical inactivity, and dyslipidemia are major contributors to CVD. In many large, randomized controlled series, high LDL and low HDL have been associated with CVD [13-15]. The elevated prevalence of dyslipidemia and differences in lipid profiles among IBD patients raise several important questions. Firstly, the chronic inflammatory state associated with IBD may contribute

to lipid metabolism disturbances. The release of proinflammatory cytokines and other inflammatory mediators could influence hepatic lipid production, lipoprotein metabolism, and cellular cholesterol handling [15,16]. Secondly, lifestyle factors, such as diet and physical activity, may play a role in lipid profile variations among IBD patients. Dietary choices and malabsorption issues common in IBD may affect nutrient intake and metabolism, contributing to dyslipidemia [15]. Furthermore, medications used for IBD management, such as corticosteroids and immunosuppressive agents, might also impact lipid profiles [16].

In our research, we discovered that, in contrast to the general population, IBD patients had statistically considerably higher percentages of dyslipidemia such ass high LDL-C or low HDL-C. Furthermore, IBD patients' levels of triglycerides, LDL-C, and total cholesterol were found to be statistically significantly higher than those of the general population, whereas HDL-C values were shown to be statistically significantly lower. One of our secondary findings was that, like in the general community, dyslipidemia was more common in males than in women among IBD patients. The fact that there was no discernible change in lipid profiles between Crohn's disease and ulcerative colitis patients from IBD subgroups is another secondary discovery.

In their study, Raja Shekkar et al. assessed 393 IBD patients. Their investigation revealed that, in comparison to the general population, male patients had lower HDL-C values and higher LDL-C levels. In female patients, they also discovered low HDL-C and high LDL-C values [9]. Total cholesterol levels in this study, however, were discovered to be comparable to those of IBD patients. High triglyceride, low HDL-C, and high LDL-C were seen in the Van Ganse et al. investigation. In 2020, Soh et al. discovered a correlation between disease activity and low levels of HDL-C and total cholesterol. In our study, IBD patients had low HDL-C levels and high LDL-C values. In this regard, our study's findings aligned with previous research findings. However, triglyceride and total cholesterol levels were also observed to be elevated in IBD patients in our investigation. We hypothesize that our society's lower HDL-C and higher triglyceride levels relative to the global average may be the cause of this. While other studies found significant drops in HDL-C levels, our study found less of a fall than when HDL-C levels were already low [18,19].

Our findings revealed that the prevalence of dyslipidemia among IBD patients in our single-center study was remarkably high at 58%. Dyslipidemia was defined based on established criteria for total cholesterol, LDL-C, HDL-C, and triglyceride levels. This prevalence of dyslipidemia in IBD patients far exceeded that of the general population, as reported in the 2017 TEKHARF population study in Turkey. This significant difference highlights the need for heightened awareness and monitoring of lipid profiles in individuals with IBD. Our study revealed distinct differences in lipid profiles between IBD patients and the general population, particularly in men. Notably, men with IBD had significantly higher levels of total cholesterol, LDL-C, and triglycerides compared to the general male population. These differences suggest that IBD may exert an influence on lipid metabolism, leading to unfavorable lipid profile alterations in male patients [14].

Several limitations should be acknowledged. This study was conducted at a single center, and the study population may not fully represent the diversity of IBD patients. Additionally, this was a cross-sectional study, limiting our ability to establish causality or track changes over time. Moreover, dietary habits and medication use, which could influence lipid profiles, were not comprehensively assessed in this study.

8. Conclusion

In conclusion, our study demonstrates a high prevalence of dyslipidemia and differences in lipid profiles, particularly in men, among IBD patients compared to the general population. These findings underscore the importance of regular lipid profile assessments in the clinical management of IBD patients and the need for further research to elucidate the underlying mechanisms and potential therapeutic interventions to optimize lipid metabolism in this population. Addressing dyslipidemia in IBD patients may contribute to reducing their cardiovascular risk and improving their overall health outcomes.

Ethics Committee Approval

This study was complied with the ethical guidelines of the 1975 Helsinki Declaration that was then modified in 2008. The study protocol was approved by Ankara City Hospital ethics committee (E1-21-2051).

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No financial support was received in our study.

Conflict of Interest

Dr. Çağdaş Erdoğan have no conflicts of interests to declare.

Data Availability Statement

The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

References

- 1. Xavier, R. J., & Podolsky, D. K. (2007). Unravelling the pathogenesis of inflammatory bowel disease. Nature, 448(7152), 427-434
- Uchiyama, K., Odahara, S., Nakamura, M., Koido, S., Katahira, K., Shiraishi, H., ... & Tajiri, H. (2013). The fatty acid profile of the erythrocyte membrane in initial-onset inflammatory bowel disease patients. Digestive diseases and sciences, 58, 1235-1243.
- Bernstein, C. N., Wajda, A., & Blanchard, J. F. (2005). The clustering of other chronic inflammatory diseases in inflammatory bowel disease: a population-based study. Gastroenterology, 129(3), 827-836.
- 4. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation. 2005;112(17):2735-52.
- 5. Libby, P., Ridker, P. M., & Maseri, A. (2002). Inflammation and atherosclerosis. Circulation, 105(9), 1135-1143.
- Karaahmet, F., Basar, O., Coban, S., & Yuksel, I. (2013). Dyslipidemia and inflammation in patients with inflammatory bowel disease. Digestive diseases and sciences, 58, 1806-1807.
- 7. Feuerstein, J. D., & Cheifetz, A. S. (2017, July). Crohn dis-

- ease: epidemiology, diagnosis, and management. In Mayo Clinic Proceedings (Vol. 92, No. 7, pp. 1088-1103). Elsevier.
- Bernstein, C. N., Wajda, A., & Blanchard, J. F. (2005). The clustering of other chronic inflammatory diseases in inflammatory bowel disease: a population-based study. Gastroenterology, 129(3), 827-836.
- Biyyani, R. S. R. S., Putka, B. S., & Mullen, K. D. (2010). Dyslipidemia and lipoprotein profiles in patients with inflammatory bowel disease. Journal of clinical lipidology, 4(6), 478-482.
- Tien, N., Wu, T. Y., Lin, C. L., Wu, C. J., Hsu, C. Y., Fang, Y. J., & Lim, Y. P. (2022). Impact of inflammatory bowel disease (IBD) and IBD medications on risk of hyperlipidemia and in vitro hepatic lipogenic-related gene expression: A population-based cohort study. Frontiers in Medicine, 9, 910623.
- Weissman, S., Sinh, P., Mehta, T. I., Thaker, R. K., Derman, A., Heiberger, C., ... & Tabibian, J. H. (2020). Atherosclerotic cardiovascular disease in inflammatory bowel disease: The role of chronic inflammation. World journal of gastrointestinal pathophysiology, 11(5), 104.
- 12. US Preventive Services Task Force, Krist AH, Davidson KW, et al. Behavioral Counseling Interventions to Promote a Healthy Diet and Physical Activity for Cardiovascular Disease Prevention in Adults With Cardiovascular Risk Factors: US Preventive Services Task Force Recommendation Statement. JAMA 2020; 324:2069.
- Collins, R., Reith, C., Emberson, J., Armitage, J., Baigent, C., Blackwell, L., ... & Peto, R. (2016). Interpretation of the evidence for the efficacy and safety of statin therapy. The Lancet, 388(10059), 2532-2561.
- 14. Onat, A., Sarı, İ., Tuncer, M., & Karabulut, A. (2004). TEKHARF çalışması takibinde gözlemlenen toplam ve

- koroner mortalitenin analizi. Archives of the Turkish Society of Cardiology.
- 15. Glass, C. K., & Olefsky, J. M. (2012). Inflammation and lipid signaling in the etiology of insulin resistance. Cell metabolism, 15(5), 635-645.
- Jung, U. J., & Choi, M. S. (2014). Obesity and its metabolic complications: the role of adipokines and the relationship between obesity, inflammation, insulin resistance, dyslipidemia and nonalcoholic fatty liver disease. International journal of molecular sciences, 15(4), 6184-6223.
- 17. Roncoroni, L., Gori, R., Elli, L., Tontini, G. E., Doneda, L., Norsa, L., ... & Vecchi, M. (2022). Nutrition in patients with inflammatory bowel diseases: a narrative review. Nutrients, 14(4), 751.
- Sands, B. E., Colombel, J. F., Ha, C., Farnier, M., Armuzzi, A., Quirk, D., ... & Taub, P. R. (2021). Lipid profiles in patients with ulcerative colitis receiving tofacitinib—implications for cardiovascular risk and patient management. Inflammatory bowel diseases, 27(6), 797-808.
- Van Ganse, E., Laforest, L., Burke, T., Phatak, H., & Souchet, T. (2007). Mixed dyslipidemia among patients using lipid-lowering therapy in French general practice: an observational study. Clinical therapeutics, 29(8), 1671-1681.
- Soh, H., Im, J. P., Han, K., Park, S., Hong, S. W., Moon, J. M., ... & Kim, J. S. (2020). Crohn's disease and ulcerative colitis are associated with different lipid profile disorders: a nationwide population-based study. Alimentary Pharmacology & Therapeutics, 51(4), 446-456.
- 21. Sotos-Prieto, M., Bhupathiraju, S. N., Mattei, J., Fung, T. T., Li, Y., Pan, A., ... & Hu, F. B. (2015). Changes in diet quality scores and risk of cardiovascular disease among US men and women. Circulation, 132(23), 2212-2219.

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