MEDICAL SCIENCE MONITOR

CLINICAL RESEARCH

e-ISSN 1643-3750
© Med Sci Monit, 2016; 22: 1534-1539
DOI: 10.12659/MSM.896116

Received: 2015.09.28
Accepted: 2015.11.06
Published: 2016.05.06

Inflammatory and Lipid-Associated Markers of Cardiovascular Diseases in Children with First Exacerbation of Inflammatory Bowel Disease

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEFG Elżbieta Pac-Kożuchowska
ABCDEF Paulina Krawiec
ABCDEF Agnieszka Mroczkowska-Juchkiewicz
ABCDF Agnieszka Pawłowska-Kamieniak
ABCDF Katarzyna Kominek

Department of Pediatrics, Medical University of Lublin, Lublin, Poland

Corresponding Author: Elżbieta Pac-Kożuchowska, e-mail: elzbietapackozuchowska@umlub.pl
Source of support: The study was funded by the Medical University of Lublin (scientific grant No. DS406 to EPK)

Background: Adult patients with inflammatory bowel disease (IBD) are at increased risk of early atherosclerosis and atherosclerosis-driven cardiovascular diseases. However, data on the development of early, subclinical atherosclerosis in children with IBD are scarce. The aim of this study was to assess selected biomarkers of atherosclerosis in children with IBD.

Material/Methods: The study group comprised 30 children with first exacerbation of IBD. Twenty healthy children were enrolled into the control group. Total cholesterol, triglycerides, low-density lipoproteins (LDL), high-density lipoproteins (HDL), lipoprotein (a) (Lp(a)), interleukin 6 (Il-6), high sensitivity C-reactive protein (hs-CRP), and oxidized LDL (ox LDL) were determined.

Results: There were no significant differences in lipids profiles in IBD children and controls. Mean IL-6 level (8.996 pg/ml) was significantly higher in the IBD group compared to controls (3.502 pg/ml). Mean hs-CRP concentration was significantly higher in IBD children than in controls (7.648 and 1.290 µg/ml, respectively). In the IBD group, mean ox-LDL concentration (144.837 ng/ml) was lower than in controls (162.352 ng/ml), but the difference was non-significant (P=0.4). Mean Lp(a) serum level was higher in patients with IBD (19.418 mg/dl) than in controls (10.970 mg/dl), but it was also non-significant.

Conclusions: No significant differences were found in biomarkers of atherosclerosis in children with IBD compared to controls. Elevated IL-6 and hs-CRP level are well-established inflammatory markers. Further studies are needed to fully determine cardiovascular risk factors in IBD children.

MeSH Keywords: Atherosclerosis • Colitis, Ulcerative • Crohn Disease • Inflammatory Bowel Diseases

Full-text PDF: http://www.medscimonit.com/abstract/index/idArt/896116

2135 2 — 31

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

Background

Atherosclerosis is a chronic, progressive disease characterized by the accumulation of lipids and fibrous elements in the medium and large arteries. It is initiated by endothelial denuding injury leading to the proliferation of smooth muscle cells in the arterial intima and increased production of extracellular macromolecules [1].

There is abundant scientific evidence indicating the pivotal role of inflammation in every stage of atherosclerosis, including initiation, evolution, and thrombotic complications. Moreover, patients with chronic inflammatory diseases, such as rheumatoid arthritis, psoriasis, or systemic lupus erythematosus, are at increased risk of accelerated atherosclerosis and cardiovascular disorders [2–4]. There is ongoing debate concerning the association between other chronic immune-mediated inflammatory disorders, such as inflammatory bowel disease (IBD), and atherosclerosis.

Inflammatory bowel disease is a chronic, relapsing-remitting, immune-mediated disorder of the gastrointestinal tract, which includes Crohn's disease, ulcerative colitis, and IBD-unclassified. Although the etiology of IBD remains unclear, several pathogenic factors have been proposed, including aberrations in multiple susceptibility genes, variations in the luminal microflora, environmental triggers, and aberrant immunoregulation [5]. Moreover, mesenteric microvascular thrombosis was identified in altered perfusion, inflammation, and tissue injury in IBD [6]. Thus, it has been described as another plausible pathogenic factor in IBD. A recent experimental study revealed another potential pathogenetic factor of IBD; Kim et al. found that *in vitro,* the administration of 4-nonylphenol up-regulates proinflammatory genes and decreases the expression of the anti-inflammatory genes in human cells lines, promoting gastrointestinal tract inflammation [7].

Increased risk of deep venous thrombosis and pulmonary embolism has been shown in IBD patients [8]. Clinical studies have revealed that the incidence of systemic thromboembolic complications in adults with IBD ranges between 1% and 7.7% [9]. Although the link between venous thromboembolic events and IBD is well-established, the risk of arterial thromboembolic events, such as ischemic heart disease or cerebrovascular events, in IBD patients is controversial. While some reports indicate that patients with IBD are at increased risk of early atherosclerosis and atherosclerosis-driven cardiovascular diseases [9–12], several studies do not support these findings [13–15].

In addition, most relevant studies have been carried out in adults, but atherogenesis originates in early stages of life and may remain asymptomatic for decades. Thus, studies on the identification of early, subclinical atherosclerosis in children with IBD are required.

Several groups of atherosclerosis biomarkers have been proposed for diagnostic use: inflammatory markers (e.g., high-sensitivity C-reactive protein, interleukin 6, and CD40L); lipid-associated markers (e.g., low-density lipoproteins, high-density lipoproteins, oxidized low-density lipoproteins, triglycerides, and lipoprotein (a)); markers of endothelial dysfunction (e.g., nitric oxide, asymmetric dimethylarginine, soluble vascular adhesion molecules, von Willebrand factor, and endothelial progenitor cells); oxidative stress (e.g., neutrophil myeloperoxidase); markers of neovascularization (e.g., placental growth factor and stroma-derived factor 1); and genetic markers (e.g., polymorphism within low-density lipoprotein receptor gene, apolipoprotein B gene, CYP7A1 gene, and transforming growth factor beta 1 gene) [16].

The aim of our study was to assess selected biomarkers of atherosclerosis in children with IBD.

Material and Methods

A total of 30 children hospitalized at the Department of Pediatrics, Medical University of Lublin, Poland, with their first exacerbation of IBD, were recruited to the study. The diagnosis of IBD was based on clinical presentation, endoscopy, and histology according to the Porto criteria [17].Twenty healthy children were enrolled into the control group.

Blood samples were collected after overnight fasting for the laboratory tests. The following parameters were determined: total cholesterol (T-Chol), triglycerides (TG), low-density lipoproteins (LDL), high-density lipoproteins (HDL), lipoprotein (a) (Lp(a)), interleukin 6 (Il-6), high-sensitivity CRP (hs-CRP), and oxidized LDL (ox-LDL). Plasma lipid levels were determined by the colorimetric enzymatic method (Cormay). The measurement of hs-CRP (Immundiagnostic AG), Il-6 (GennProbe Diaclone SAS), Lp (a) (IBL International GMBH), and ox-LDL (Immundiagnostic AG) were performed using commercially available ELISA kits.

Statistical analysis was carried out using Statistica 10 software. Results are presented as mean ± standard deviation. Comparison between groups was performed by using a Mann-Whitney *U*-rank test for quantitative variables without normal distribution and Student's t-test for quantitative variables with normal distribution. Results were considered statistically significant at $P<0.05$.

Written informed consent was provided by parents and also by the patient in the case of a child aged ≥16 years. The study was approved by the Bioethics Committee at the Medical University of Lublin (KE-0254/25/2013).

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

Table 1. Comparison of the laboratory parameters of inflammatory bowel disease children and healthy controls.

	IBD children n=30 M±SD	Healthy controls n=20 M±SD	*P*
T- Chol, mg/dl	131.41±25.60	123.65±28.04	0.3
HDL, mg/dl	45.06±13.63	40.94±9.1	0.4
LDL, mg/dl	76.77±20.53	75.65±23.81	0.9
TG, mg/dl	86.10±32.65	71.40±26.48	0.1
hs-CRP, µg/ml	7.648±6.84	1.29±1.44	0.0
Il-6, pg/ml	8.996±11.83	3.502±9.28	0.0
Lp (a), mg/ml	19.418±19.52	10.97±9.92	0.4
ox-LDL, ng/ml	144.837±140.79	162.35±160.96	0.4

Data are presented as mean ± standard deviation. A *P* value of <0.05 is considered statistically significant. HDL – high density lipoprotein; hs-CRP – high sensitivity C-reactive protein; IBD – inflammatory bowel disease; Il-6 – interleukin 6; Lp (a) – lipoprotein a; LDL – low density lipoprotein; M – mean; ox-LDL – oxidized low density lipoprotein; SD – standard deviation T-Chol – total cholesterol; TG – triglyceride.

Results

The study group comprised 30 children with IBD, including 16 (53%) with ulcerative colitis and 14 (47%) with Crohn's disease. All subjects were experiencing their first exacerbation of the IBD and were treatment-naive. There were 16 (53%) boys and 14 (47%) girls. The mean age of patients was 13±2.7 years and ranged from 5.5 to 17.5 years. The mean Cole's index was 95.6±18.2%. According to Cole's index, 16 (53.3%) children had normal nutritional status, 4 (13.3%) were undernourished, 5 (16.7%) were cachectic, and 5 (16.7%) were overnourished.

Among the children with ulcerative colitis, there were 11 (69%) girls and 5 (31%) boys, with mean age 12.8±3 years. The mean Cole's index was 101.3±18.3%. The majority of patients (12; 75%) presented with pancolitis, 2 (12.5%) with proctitis, and 2 (12.5%) with left-sided colitis. The mean severity index according to Truelove and Witts modified by Ryżko and Woynarowski was 5.2±2.6 points.

Among the children with Crohn's disease, there were 11 (79%) boys and 3 (21%) girls, with mean age 13±2.3 years. The mean Cole's index was 90±16.9%. Crohn's disease affected the terminal ileum and colon in 4 (28.5%); the ileocecal region in 3 (21.5%); the upper gastrointestinal tract, terminal ileum, and colon in 3 (21.5%); only the colon in 3 (21.5%); and the upper gastrointestinal tract and ileocecal region in 1 (7%) child. The mean Pediatric Crohn's Disease Activity Index was 33.5±16 points.

There were no statistically significant differences in age and Cole's index between children with ulcerative colitis and those with Crohn's disease.

Twenty healthy children aged between 5 and 18 (mean 12.5±3.6) years, including 11 (55%) girls and 9 (45%) boys, were in the control group.

Table 1 presents a comparison of laboratory parameters of IBD patients and healthy controls. High-sensitivity C-reactive protein and interleukin 6 levels were significantly higher in children with IBD compared to those of controls. No statistically significant differences were found in the lipids profile, lipoprotein a, or oxidized LDL between the study group and healthy controls.

Data regarding the comparison of Crohn's disease patients and ulcerative colitis patients are shown in Table 2. In children with Crohn's disease, the levels of high-sensitivity C-reactive protein and interleukin 6 were significantly higher compared with ulcerative colitis children. Serum lipid levels, lipoprotein a, and oxidized LDL were similar in patients with Crohn's disease and those with ulcerative colitis. Interleukin 6 was significantly higher in children with Crohn's disease and ulcerative colitis than in controls. High-sensitivity C-reactive protein was significantly higher in children with Crohn's disease, but not in those with ulcerative colitis, compared with controls.

Discussion

The traditional view regarded atherosclerosis as a localized lipid storage disease leading to flow-limiting arterial stenosis [18]. However, the understanding of atherosclerosis has undergone a remarkable evolution. Atherosclerosis is now considered a chronic inflammatory process of the arterial

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

Table 2. Comparison of the laboratory parameters of children with Crohn's disease, ulcerative colitis and healthy controls.

	CD patients n=16 M±SD	UC patients n=14 M±SD	Healthy controls n=20 M±SD	P-values		
				CD *vs.* UC	CD *vs.* controls	UC *vs.* controls
T-Chol, mg/dl	127.69±25.36	134.43±26.21	123.65±28.04	0.4	0.7	0.4
HDL, mg/dl	42.83±14.99	47.25±12.68	40.94±9.1	0.3	0.9	0.2
LDL, mg/dl	73.86±21.58	79.76±20.11	75.65±23.81	0.5	0.9	0.6
TG, mg/dl	95±42.36	78.88±20.75	71.40±26.48	0.5	0.2	0.4
hs-CRP, µg/ml	11.60±5.98	4.19±5.66	1.29±1.44	0.0	0.0	0.1
Il-6, pg/ml	14.86±15.00	3.87±3.88	3.502±9.28	0.0	0.0	0.0
Lp (a), mg/ml	20.08±19.54	18.83±20.14	10.97±9.92	0.7	0.3	0.5
ox-LDL, ng/ml	157.20±155.51	134.02±130.75	162.35±160.96	0.9	0.8	0.3

Data are presented as mean ± standard deviation. A *P* value of <0.05 is considered statistically significant. HDL – high density lipoprotein; hs-CRP – high sensitivity C-reactive protein; IBD – inflammatory bowel disease; Il-6 – interleukin 6; Lp (a) – lipoprotein a; LDL – low density lipoprotein; M – mean; ox-LDL – oxidized low density lipoprotein; SD – standard deviation T-Chol – total cholesterol; TG – triglyceride.

wall with an autoimmune component resulting from the interplay of lipid metabolism imbalance, maladaptive immune response, and genetic alterations [18–20]. As the fundamental role of inflammation in all stages of atherogenesis has been established, markers of inflammation and endothelial activation may become useful indices of early atherosclerosis and predictors of outcomes, in addition to those provided by traditional risk factors [21].

It is well-established that the initial step in atherogenesis is endothelial injury. The term "endothelial dysfunction" refers to decreased production or availability of the key endothelium-derived relaxing factor – nitric oxide – and increase of contracting factors, including endothelin-1, angiotensin, and oxidants, leading to vasoconstriction [21].

Traditional atherosclerotic risk factors, including hypercholesterolemia, hypertension, and diabetes, promotes inflammatory cascade and endothelial damage. Hypercholesterolemia induces adhesion of blood leucocytes to the endothelium [22]. Increased C-reactive protein reduces production and bioavailability of nitric oxide, which in turn inhibits angiogenesis [23]. Oxidized low-density lipoprotein promotes vasoconstriction by decreasing biological activity of endothelium-derived nitric oxide, enhances the expression of pro-inflammatory genes, and triggers activation of inflammatory signalling pathway CD40/CD40L [21,24]. Angiotensin II is a vasoconstrictor that also promotes production of reactive oxygen species and expression of proinflammatory cytokines, such as interleukin 6, monocyte chemoattractant protein-1, and vascular cell adhesion molecule-1, on the epithelium [21].

Dyslipidemia is one of the most important risk factors of atherosclerosis. Pro-atherogenic lipid profile is defined as elevation in total plasma cholesterol, low-density lipoprotein and triglycerides, and a decrease in high-density lipoprotein [25]. Recent studies indicate that patients with IBD, particularly those with Crohn's disease, exhibit lower levels of total plasma cholesterol and low-density lipoprotein compared to healthy controls [26,27]. No significant alterations have been found in IBD patients in triglycerides and high-density lipoprotein level in a study performed by Agouridis et al. [26]. However, Levy et al. found significantly higher levels of triglycerides in children with Crohn's disease compared to controls [27]. The pathophysiology of hypocholesterolemia in IBD patients is not clear; it may be linked to systemic inflammation, malabsorption, or malnutrition. Several inflammatory mediators may alter lipid metabolism in IBD. Interleukin-6 and C-reactive protein inhibit adipocyte lipoprotein lipase activity. Tumor necrosis factor-α stimulates lipolysis and hepatic triglyceride synthesis, and decreases adipocyte lipoprotein lipase activity [28]. In patients with IBD, especially Crohn's disease, the distal ileum, which is responsible for bile acid absorption, is involved in the inflammatory process. Thus, the intestinal malabsorption leading to the loss of bile acids and cholesterol in the stool may be also responsible for alterations in lipid levels in patients with IBD [25].Contrary to expectations, our study did not reveal any significant differences in lipid levels between children with IBD and healthy controls. These results are consistent with those of Aloi et al., who also found no significant differences in lipid levels between children with IBD and a control group [10]. Relatively short disease duration, mild and moderate activity of inflammation, and normal nutritional status in most of the

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

patients may explain the lack of significant alterations in lipid profile in our study population.

Oxidatively modified low-density lipoprotein plays a critical role in several stages of atherogenesis, including endothelial injury, activation and dysfunction of endothelial cells, formation of foam cells, and proliferation and migration of smooth muscle cells [24,29]. Grip et al. showed increased plasma level of oxidized low-density lipoprotein in a small group of adults with IBD, reflecting the increased oxidative stress and higher risk of atherosclerosis [29]. In our study, no differences in ox-LDL were observed between IBD children and controls. However, these data must be interpreted with caution. We presume that the lack of a significant increase in ox-LDL results from the young age of the studied patients and the short disease duration.

Lipoprotein (a) is a well-established independent risk factor for atherosclerosis and thrombosis in adults. Koutroubakis et al. found increased levels of lipoprotein (a) in patients with Crohn's disease, but not in ulcerative colitis patients, compared to healthy controls. Moreover, lipoprotein (a) was significantly higher in active Crohn's disease compared to non-active Crohn's disease patients [30]. We did not observe alterations in lipoprotein (a) in IBD children compared to healthy children.

Increased inflammatory markers, such as high-sensitivity CRP and Il-6 in healthy adults, are predictors of the risk of cardiovascular events [22]. On the other hand, CRP and Il-6 are clinical markers of inflammation in IBD. Thus, in patients with chronic inflammatory conditions such as IBD, it is not possible to establish whether the elevation of inflammatory markers is connected with atherogenesis and increased risk of cardiovascular events. In the present study, the level of Il-6 was significantly increased in both Crohn's disease and ulcerative colitis patients compared to controls, while hs-CRP was significantly elevated solely in Crohn's disease patients. Il-6 and hs-CRP were significantly higher in children with Crohn's disease than in children with ulcerative colitis.

A recent meta-analysis showed that IBD is associated with a modest increase of the risk of cerebrovascular accidents and ischemic heart disease, particularly in women and patients younger than 40–50 years [31]. In children with IBD, Aloi et al. evaluated carotid intima media thickness and brachial flow-mediated dilation, and found subclinical structural and functional endothelial dysfunction, suggesting that premature atherosclerosis can occur in children with IBD. Moreover, traditional risk factors of atherosclerosis, except for passive smoking, have no serious effects on children with IBD [10].

Conclusions

Our study found no significant differences in lipid profile and lipoproteins composition in children experiencing the first exacerbation of IBD compared to controls. However, due to the small sample size and relatively short disease duration, our results must be interpreted with caution, as the findings cannot be extrapolated to the whole population of children with IBD. Further long-term prospective studies are needed to monitor lipid and lipoprotein profiles with ultrasonographic markers for subclinical atherosclerosis in children with IBD.

References:

1. Libby P, Ridker PM, Hansson GK: Inflammation in atherosclerosis: From pathophysiology to practice. J Am Coll Cardiol, 2009; 54: 2129–38
2. Avina-Zubieta JA, Thomas J, Sadatsafavi M et al: Risk of incident cardiovascular events in patients with rheumatoid arthritis: a meta-analysis of observational studies. Ann Rheum Dis, 2012; 71: 1524–29
3. Patel RV, Shelling ML, Prodanovich S et al: Psoriasis and vascular disease-risk factors and outcomes: a systematic review of the literature. J Gen Intern Med, 2011; 26: 1036–49
4. Cervera R, Khamashta MA, Font J et al: Morbidity and mortality in systemic lupus erythematosus during a 10-year period: a comparison of early and late manifestations in a cohort of 1,000 patients. Medicine (Baltimore), 2003; 82: 299–308
5. Principi M, Mastrolonardo M, Scicchitano P et al: Endothelial function and cardiovascular risk in active inflammatory bowel diseases. J Crohns Colitis, 2013; 7: e427–33
6. Hatoum OA, Spinelli KS, Abu-Hajir M et al: esenteric venous thrombosis in inflammatory bowel disease. J Clin Gastroenterol, 2005; 39: 27–31
7. Kim A, Jung BH, Cadet P: A novel pathway by which the environmental toxin 4-Nonylphenol may promote an inflammatory response in inflammatory bowel disease. Med Sci Monit Basic Res, 2014; 20: 47–54
8. Bernstein CN, Blanchard JF, Houston DS et al: The incidence of deep venous thrombosis and pulmonary embolism among patients with inflammatory bowel disease: a population-based cohort study. Thromb Haemost, 2001; 85: 430–34
9. Papa A, Danese S, Urgesi R et al: Early atherosclerosis in patients with inflammatory bowel disease. Eur Rev Med Pharmacol Sci, 2006; 10: 7–11
10. Aloi M, Tromba L, Di Nardo G et al: Premature subclinical atherosclerosis in pediatric inflammatory bowel disease. J Pediatr, 2012; 161: 589–94
11. Yarur AJ, Deshpande AR, Pechman DM et al: Inflammatory bowel disease is associated with an increased incidence of cardiovascular events. Am J Gastroenterol, 2011; 106: 741–47
12. Dagli N, Poyrazoglu OK, Dagli AF et al: Is inflammatory bowel disease a risk factor for early atherosclerosis? Angiology, 2010; 61: 198–204
13. Broide E, Schopan A, Zaretsky M et al: Intima-media thickness of the common carotid artery is not significantly higher in Crohn's disease patients compared to healthy population. Dig Dis Sci, 2011; 56: 197–202
14. Dorn SD, Sandler RS: Inflammatory bowel disease is not a risk factor for cardiovascular disease mortality: results from a systematic review and meta-analysis. Am J Gastroenterol, 2007; 102: 662–67
15. Maharshak N, Arbel Y, Bornstein NM et al: Inflammatory bowel disease is not associated with increased intimal media thickening. Am J Gastroenterol, 2007; 102: 1050–55
16. Spagnoli LG, Bonanno E, Sangiorgi G et al: Role of inflammation in atherosclerosis. J Nucl Med, 2007; 48: 1800–15
17. Inflammatory Bowel Disease in Children and Adolescents: Recommendations for Diagnosis-The Porto Criteria IBD Working Group of the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN). J Pediatr Gastroenterol Nutr, 2005; 41: 1–7

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

18. Libby P, Theroux P: Pathophysiology of coronary artery disease. Circulation, 2005; 111: 3481–88
19. Weber C, Noels H: Atherosclerosis: current pathogenesis and therapeutic options. Nat Med, 2011; 17: 1410–22
20. Singh RB, Mengi SA, Xu YJ et al: Pathogenesis of atherosclerosis: A multifactorial process. Exp Clin Cardiol, 2002; 7: 40–53
21. Szmitko PE, Wang CH, Weisel RD et al: New markers of inflammation and endothelial cell activation: Part I. Circulation, 2003; 21: 1917–23
22. Libby P, Ridker PM, Maseri A: Inflammation and atherosclerosis. Circulation, 2002; 105: 1135–43
23. Verma S, Wang CH, Li SH et al: A self-fulfilling prophecy: C-reactive protein attenuates nitric oxide production and inhibits angiogenesis. Circulation, 2002; 106: 913–19
24. Dayuan L, Mehta JL: Oxidized LDL, a critical factor in atherogenesis. Cardiovasc Res, 2005; 68: 353–54
25. Sappati Biyyani RS, Putka BS, Mullen KD: Dyslipidemia and lipoprotein profiles in patients with inflammatory bowel disease. J Clin Lipidol, 2010; 4: 478–82
26. Agouridis AP, Elisaf M, Milionis HJ: An overview of lipid abnormalities in patients with inflammatory bowel disease. Ann Gastroenterol, 2011; 24: 181–87
27. Levy E, Rizwan Y, Thibault L et al: Altered lipid profile, lipoprotein composition, and oxidant and antioxidant status in pediatric Crohn disease. Am J Clin Nutr, 2000; 71: 807–15
28. Romanato G, Scarpa M, Angriman I et al: Plasma lipids and inflammation in active inflammatory bowel diseases. Aliment Pharmacol Ther, 2009; 29: 298–307
29. Grip O, Janciauskiene S, Lindgren S: Circulating monocytes and plasma inflammatory biomarkers in active Crohn's disease: elevated oxidized low-density lipoprotein and the anti-inflammatory effect of atorvastatin. Inflamm Bowel Dis, 2004; 10: 193–200
30. Koutroubakis IE, Malliaraki N, Vardas E et al: Increased levels of lipoprotein (a) in Crohn's disease: a relation to thrombosis? Eur J Gastroenterol Hepatol, 2001; 13: 1415–19
31. Singh S, Singh H, Loftus EV Jr et al: Risk of cerebrovascular accidents and ischemic heart disease in patients with inflammatory bowel disease: a systematic review and meta-analysis. Clin Gastroenterol Hepatol, 2014; 12: 382–93

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]