Original Research

Prevalence of Pancreatic Steatosis in Inflammatory Bowel Disease Patients

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Abstract

Objectives: Inflammatory bowel diseases (IBD) are chronic, immune-mediated disorders of the gastrointestinal system. Pancreas can be affected in IBD patients with a wide array of clinical conditions including acu-te pancreatitis, abnormalities of pancreatic duct and pancreatic insufficiency. Pancreatic steatosis (PS) is an important but often overlooked pathology of pancreas. In this study, we aimed to investigate the prevalence of PS in IBD patients to reveal the possible association in between in a patient group already prone to pancreatic disease involvement.

Methods: This retrospective study included 153 IBD patients who had a computed tomography scan in the last five years to evaluate the presence of PS. PS was defined as a pancreas/spleen attenuation ratio of below 0.70 in accordance with previous studies available in the literature. Demographic data, IBD subtype and treatment modality used for IBD were recorded and analyzed.

Results: 78 patients had Crohn's disease and 75 patients had ulcerative colitis. Presence of PS in IBD patients was 23.5%. Age and treatment modality were found to be related to PS presence. Logistic regression analysis revealed a statistically significant relationship between PS and advanced age (p=0.000) but not with treatment modality (p=0.290).

Conclusion: PS is an important pathology of the pancreas with serious complications. In an already burdensome disease like IBD, PS can add more challenges to patient management. Although a direct correlation between PS and IBD prognosis is not established in current literature, evaluation of IBD patients for PS will help in prevention and management of PS-related conditions which will improve the overall well-being of IBD patients.

Keywords: Crohn's disease, fatty pancreas, inflammatory bowel disease, pancreatic steatosis, ulcerative colitis

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Inflammatory bowel diseases (IBD), namely Crohn's disease (CD) and ulcerative colitis (UC), are chronic, immune-mediated disorders of the gastrointestinal system.[1] Although mainly diseases of gastrointestinal tract, both CD and UC are multi-organ disorders which can present with varying clinical pictures including arthritis, skin involvement and ocular manifestations.[2,3] Pancreas can also be affec-ted in both disease entities with a wide array of clinical conditions including acute pancreatitis, abnor-malities of pancreatic duct and pancreatic insufficiency.[4]

Pancreatic steatosis (PS), also known as fatty pancreas and non-alcoholic fatty pancreas disease, is an important but

often overlooked pathology of pancreas. While the current literature is lacking study data on the relationship between PS and IBD in terms of IBD symptoms, treatment success or prognosis, conditions related to PS can increase the disease burden in IBD patients. PS has been associated with pancreatitis, metabolic syndrome, diabetes mellitus and cardiovascular diseases.[5] PS has also been linked to exocrine pancreatic insufficiency.[6] Addition of these clinical conditions to the IBD picture will surely negatively affect the overall being of patients with IBD.

In this study, we aimed to investigate the association of PS with IBD, to define and underline the im-portance of PS in this particular patient group, who are already at risk for pancreatic disorders due to multi-organ affecting nature of IBD.

Methods

Patients

This retrospective study was carried out at Antalya Training and Research Hospital. IBD patients at-tending Antalya Training and Research Hospital in terms of treatment and regular outpatient clinic fol-low-ups were selected from outpatient clinic and hospital registry system records. Hospital radiological registry system was scanned retrospectively for five consecutive years back to 2019. IBD patients with unenhanced (non-contrast enhanced) computed tomography (CT) scans including pancreatic images in the last five years, along with outpatient clinic records including treatment modality used at the time of CT scan were designated as the study group. Patients without required radiological or treatment data were excluded from the study, as well as patients below 18 years of age. Patients with an existing panc-reatic disorder or malignancy of pancreas or periampullary region detected in the CT scan were exclu-ded from the study. None of the patients included in the study had preexisting systemic disorder affec-ting spleen. Overall, 153 IBD patients were included in the study.

Patients were split into two groups in terms of the treatment they were on at the time of CT scan: con-ventional therapy group, which consisted of azathioprine, 5-amino-salicylic acid and budesonide and biological therapy group which consisted of biologic agents and small-molecule therapy.

Evaluation of PS

Adipose tissue is characterized by negative attenuation on unenhanced CT and measured by Hounsfield Units (HU). HU values between -150 and -30 is typical for adipose tissue. Evaluation of PS by unenhanced CT through direct calculation of HU value of pancreas is not possible. Most commonly used calculation to evaluate PS by unenhanced CT is pancreas to spleen ratio (P/S) of attenuation in terms of HU and a P/S ratio of <0.70 is considered as the presence of PS.[7-9]

One radiologist with over 15 years of experience evaluated all CT studies, blindly, on Sectra Picture Archiving and Communication System (PACS). Pancreas attenuation was calculated from three circular region of interests (ROIs) with 1 centimeter diameter, with one each ROI in head, body and tail of pancreas. Attenuation of spleen was also calculated from three different ROIs with 1 cm diameter each, from three different points of spleen.

Statistical Analysis

Categorical variables were presented as the frequency and percentage and continuous variables were presented as the mean (±SD). Kolmogorov-Smirnov and Shapiro-Wilk tests were used to test normal distribution. Normal distributed variables between two groups were compared with Mann-Whitney U test. Rank correlation between two non-normal distributed variables were analyzed with Pearson corre-lation coefficient. Chi-square test, Yates's correction and Fisher's exact test were used to analyze cate-gorical variables. Logistic regression analysis was performed to analyze the relationship of independent variables with PS. Level of significance was $p<0.05$. All statistical analysis was performed using SPSS version 20.0 for Windows (SPSS Inc., Chicago, IL, USA).

Ethics committee approval was obtained from the Antalya Training and Research Hospital Ethics Committee (Date: 07.03.2024, No: 2/8, 2024-023). Since this is a retrospective study, no informed consent was required. This study was carried out in accordance with Declaration of Helsinki.

Results

The study population consisted of 153 patients. Mean age of the study population was 48.28 (±17.18) years. 56 patients (36.6%) were female and 97 patients (63.4%) were male. There were 78 CD patients (51%) and 75 UC patients (49%) in the study group. 98 patients (64.1%) were on conventional therapy and 55 patients (35.9%) were on biological therapy at the time of CT scan. 36 patients (23.5%) were found to have PS according to study criteria (P/S <0.70). Mean attenuation value of retroperitoneal fat was -94.25 (±19.0) HU in the study population. Baseline characteristics of patient population are given in Table 1.

Relationship of PS with study parameters were evaluated. Increased age was found to be correlated to PS presence. Mean age of patients with PS was 59.33±14.78 compared to 44.88±16.47 in patients wit-hout PS and this difference

Table 1. Baseline characteristics of patient population

	Number of patients (n=153)	Percentage (%)
Age (years, mean±SD)	48.28±17.18	
Sex		
Female	56	36.6
Male	97	63.4
IBD subtype		
CD	78	51
UC	75	49
Treatment modality		
Conventional therapy	98	64.1
Biological therapy	55	35.9
Presence of PS	36	23.5
Retroperitoneal fat attenuation value (HU, mean±SD)	-94.25±19.0	

SD: Standart Deviation; IBD: Inflammatory Bowel Disease; CD: Crohn's Disease; UC: Ulcerative Coli-tis; PS: Pancreatic Steatosis; HU: Hounsfield Units.

was statistically significant (p=0.000). Treatment modality the patient was on at the time of CT was also found to be correlated to PS presence. 29 out of 98 patients on conventi-onal therapy had PS compared to 7 out of 55 patients on biological therapy and this difference between two groups was statistically significant (p=0.018). There were no relationship found between presence of PS and sex of patients. Retroperitoneal fat attenuation was not related to PS. Relationship of PS with study parameters are given in Table 2.

Logistic regression analysis was performed to analyze the relationship of age and treatment modality with PS. Analysis revealed a statistically significant relationship between PS and advanced age (p=0.000) but not with treatment modality (p=0.290).

Discussion

With this study, we aimed to investigate the presence and characteristics of PS in patients with IBD. Advanced age was found to be correlated to PS, whereas biological therapy was associated with a lower rate of PS presence in patients with IBD, although the latter association was not found in logistic reg-ression analysis.

Pancreatic fat was first described by Ogilvie in 1933[10], who showed that obese cadavers had greater adiposity in pancreas compared to controls. A larger study by Olsen in 1978[11] backs the findings of Ogilvie, revealing the relationship between obesity and age with pancreatic fat. Since then, pancreatic fat has been an intriguing but an under-investigated topic in medicine, gaining importance and more focus in the recent decades. PS has been linked to a wide array of aetiological factors. These include metabo-lic causes (diabetes, malnutrition, obesity), drugs (antiretrovi-rals, gemcitabine), infections (hepatitis B, human immuno-deficiency virus, coronavirus disease 2019) and pancreatic disorders such as pancrea-titis and pancreatic ductal obstruction.[12,13] Aside from these aetiological relationships, PS has been shown to be a risk factor for both exocrine pancreatic insufficiency and pancreatic cancer.[6,14] Transabdominal ultrasonography should be the first choice of diagnostic modality in evaluating the both the presence and grading of PS.[15] In situations where transabdominal ultrasonography is not applicable, whether due to operator-dependent restrictions or patient-related conditions like morbid obesity, com-puted tomography or magnetic resonance imaging can be utilized.[16,17]

Our first finding was the relationship between age and PS. PS was found to be positively correlated with increased age. This finding was in line with previous studies demonstrat-

Table 2. Relationship of pancreatic steatosis with study parameters

	PS present (n=36)	PS not present (n=117)	p
Age (years, mean±SD)	59.33±14.78	44.88±16.47	0.000
Sex			0.474
Female (n=56)	15	41	
Male (n=97)	21	76	
IBD subtype			0.894
CD (n=78)	18	60	
UC (n=75)	18	57	
Treatment modality			0.018
Conventional therapy (n=98)	29	69	
Biological therapy (n=55)	7	48	
Retroperitoneal fat attenuation value (HU, mean±SD)	-95.74 ±19.42	-93.79±18.93	0.591

PS: Pancreatic Steatosis; SD: Standart Deviation; IBD: Inflammatory Bowel Disease; CD: Crohn's Dise-ase; UC: Ulcerative Colitis; HU: Hounsfield Units.

ing the relationship between advanced age and increased prevalence of PS.[11,16,18,19] Considering the comorbidities PS is linked with like metabolic syndrome, diabetes mellitus, pancreatitis and pancreatic cancer; PS should be kept in mind in daily practice and patients especially in older age groups should be evaluted for the presence of PS.

Second important finding of our study is the relatively low prevalence of PS among patients with IBD. 36 patients in the study group were found to have PS (23.5%). This percentage is in line with some of the study data available in the literature in which the prevalence of PS was found to vary between 16 and 35%.[20,21] Contrarily, in a nation-wide study carried out in Türkiye by Sezgin and colleagues, prevalence of PS was found to be 68.9%.[5] This wide variance between prevalence data emphasizes the need for further investigation of PS both in general population and specific patient groups to define at-risk populations and importance and impact of PS on different clinical scenarios.

Another finding of our study is the relationship between treatment modality and PS. Treatment modali-ties for inflammatory bowel diseases include aminosalicylate therapy, immunomodulatory drugs, biologics and small-molecule inhibitors.[22,23] Biologics, which target different steps in inflammatory cascades, provide a more potent suppression of inflammation compared to conventional therapies, aminosalicylates and immunomodulatory drugs. In our study, patients on biological therapy were found to have a lower ratio of PS but this relationship was not present in logistic regression analysis. Patients on conventional therapy or biological therapy were statistically significantly different in terms of age distribution with older patients being more common in conventional therapy group. This difference created a bias towards younger patients with having lower prevalence of PS, who are more likely to be on biological therapy compared to older patients. That being said, although regression analysis did not reveal a significant difference between treatment modality groups, we hypothesize that the higher antiinflammatory potency of biologics may be protective against development of PS in IBD patients on biological therapy. Prospective studies on this topic will reveal more about the relationship between treatment modality used in inflammatory bowel disorders and development of PS.

The main limitation of our study is the retrospective nature, which limited us in gathering more data on possible causes of PS. Clinical conditions proposed to be linked to PS such as metabolic syndrome could not be evaluated. A prospective study evaluating every possible causative agent of PS, as well as comparing long-term treatment modalities and their relationship with PS within themselves would re-veal valuable data on this intriguing topic. Another limitation of the study is the lack of body-mass index (BMI) data. BMI values were planned to be included in the study data as a high BMI value can be linked to PS as it is to hepatosteatosis, but due to the retrospective nature of the study, BMI data was missing for a majority of patients hence it could not be included in study parameters.

Conclusion

In conclusion, this study investigating IBD and PS relationship is a pioneer study and will lay the bed-rock for future studies on the significance of cooccurrence of these important disease entities.

References

1. Törüner M, Ünal NG. Epigenetics of inflammatory bowel diseases. Turk J Gastroenterol 2023;34:437–48. [CrossRef]
2. Momayez Sanat Z, Vahedi H, Malekzadeh R, Fanni Z. A systematic review and meta-analysis of extra-intestinal manifestation of inflammatory bowel disease in the Eastern Mediterranean Region (EMRO) countries. Ann Med Surg (Lond) 2024;86:2892–9. [CrossRef]
3. Kavcar Z, Civan HA, Taskin DG, Hatipoglu SS. extraintestinal manifestations in children diag-nosed with inflammatory bowel disease. Sisli Etfal Hastan Tip Bul 2023;57:73–8. [CrossRef]
4. Fousekis FS, Theopistos VI, Katsanos KH, Christodoulou DK. Pancreatic involvement in inf-lammatory bowel disease: a review. J Clin Med Res 2018;10:743–51. [CrossRef]
5. Sezgin O, Yaraş S, Cindoruk M, Kasap E, Ünal H, Şeref Köksal A, et al. prevalence of pancrea-tic steatosis and its associated factors in Turkey: a nation-wide multicenter study. Turk J Gastroenterol 2024;35:239–54. [CrossRef]
6. Tahtacı M, Algın O, Karakan T, Yürekli ÖT, Alışık M, Köseoğlu H, et al. Can pancreatic steato-sis affect exocrine functions of pancre-as? Turk J Gastroenterol 2018;29:588–94. [CrossRef]

7. Fukuda Y, Yamada D, Eguchi H, Hata T, Iwagami Y, Noda T, et al. CT density in the pancreas is a promising imaging predictor for pancreatic ductal adenocarcinoma. Ann Surg Oncol 2017;24:2762–9. [CrossRef]

8. Kim SY, Kim H, Cho JY, Lim S, Cha K, Lee KH, et al. Quantitative assessment of pancreatic fat by using unenhanced CT: pathologic correlation and clinical implications. Radiology 2014;271:104–12. [CrossRef]

9. Hoogenboom SA, Bolan CW, Chuprin A, Raimondo MT, van Hooft JE, Wallace MB, et al. Pancreatic steatosis on computed tomography is an early imaging feature of pre-diagnostic pancreatic cancer: a preliminary study in overweight patients. Pancreatology 2021;21:428–33. [CrossRef]

10. Ogilvie R. The island of Langerhans in 19 cases of obesity. J Pathol 1933;37:473–81. [CrossRef]

11. Olsen TS. Lipomatosis of the pancreas in autopsy material and its relation to age and overwe-ight. Acta Pathol Microbiol Scand A 1978;86A:367–73. [CrossRef]

12. Öz A, Akçalar S. Increased incidence of pancreatic steatosis detected using computed tomog-raphy at initial diagnosis of coronavirus disease 2019. Turk J Gastroenterol 2023;34:270–7. [CrossRef]

13. Nuransoy Cengiz A, Bilgiç Y, Karatoprak S, Gökçe A, Evren B, Akbulut S, et al. Evaluation of development of nonalcoholic fatty pancreas disease after post-endoscopic retrograde cholangiopancre-atography pancreatitis in liver transplant patients: computerized tomography versus ultrasound. Turk J Gastroenterol 2023;34:1180–5. [CrossRef]

14. Lipp M, Tarján D, Lee J, Zolcsák Á, Szalai E, Teutsch B, et al. Fatty pancreas is a risk factor for pancreatic cancer: a systematic review and meta-analysis of 2956 patients. Cancers (Basel) 2023;15:4876. [CrossRef]

15. Sezgin O, Yaraş S, Özdoğan O. Pancreatic steatosis is associated with both metabolic syndrome and pancreatic stiffness detected by ultrasound elastography. Dig Dis Sci 2022;67:293–304. [CrossRef]

16. Koç U, Taydaş O. Evaluation of pancreatic steatosis prevalence and anthropometric measure-ments using non-contrast computed tomography. Turk J Gastroenterol 2020;31:640–8. [CrossRef]

17. Abbasoğlu A, Karçaaltıncaba M, Karaosmanoğlu AD, Özmen MN, Akata D, İdilman İS. Asso-ciations between hepatic and pancreatic steatosis with lumbar spinal bone marrow fat: a single-center magnetic resonance imaging study. Turk J Gastroenterol 2023;34:618–25. [CrossRef]

18. Stamm BH. Incidence and diagnostic significance of minor pathologic changes in the adult pancreas at autopsy: a systematic study of 112 autopsies in patients without known pancreatic disease. Hum Pathol 1984;15:677–83. [CrossRef]

19. Aktürk Y, Özbal Güneş S. Computed tomography assessment of pancreatic steatosis in associa-tion with anthropometric measurements: a retrospective cohort study. Arch Clin Exp Med 2018;3:63–6. [CrossRef]

20. Ramkissoon R, Gardner TB. Pancreatic steatosis: an emerging clinical entity. Am J Gastroente-rol 2019;114:1726–34. [CrossRef]

21. Zhou J, Li ML, Zhang DD, Lin HY, Dai XH, Sun XL, et al. The correlation between pancreatic steatosis and metabolic syndrome in a Chinese population. Pancreatology 2016;16:578–83. [CrossRef]

22. Rahman S, Patel RK, Boden E, Tsikitis VL. Medical management of inflammatory bowel disea-se. Surg Clin North Am 2024;104:657–71. [CrossRef]

23. Erdoğan Ç, Yeşil B, Bacaksız F, Arı D, Gökbulut V, Yüksel M, et al. Use of vedolizumab in inflammatory bowel disease: a single-center experience. Turk J Gastroenterol 2022;33:831–7. [CrossRef]