ORIGINAL ARTICLE

IMPORTANCE OF NON-ALCOHOLIC FATTY STEATOSIS IN PREDICTING SEVERITY OF ACUTE PANCREATITIS

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ABSTRACT

OBJECTIVE: The purpose of this study is to establish and explore association of acute pancreatitis severity with hepatic steatosis. **METHODOLOGY:** This retrospective cross-sectional study was carried out at Shifa International Hospital, Radiology Department. Two radiologists reviewed the abdominal CT images of 129 patients (from January 2020 to December 2022) with acute pancreatitis. Diagnosis was based upon clinical presentation, elevated serum amylase / lipase levels >1000, and findings reported on CT. Fatty liver (FL) was determined by using liver- spleen index of less than or equal to 1, i.e. mean CT Hounsfield units (HU) of hepatic and splenic attenuation values. After computation, the modified CT severity index was categorized as: mild (0-2), moderate (4-6), and severe (8-10). **RESULTS:** Of 129 subjects, ages ranging from 9 to 84, 55 (42.6%) were female and 74 (57.4%) were male, 38 (29.5%) did not have fatty liver, while 91 (70%) did. 56 patients (43%) had moderate CT severity index of acute pancreatitis, 40 cases (43.9%) of these cases had fatty liver, with a significant p-value of 0.031. In particular, walled off/liquefactive necrosis and pancreatic collections occurred commonly in the FL group's post-pancreatitis sequelae. Furthermore, the frequency of extra-pancreatic complications was higher in the FL group (p-value = 0.004). **CONCLUSION:** In summary, MDCT can be used to accurately identify FL and, if it is present, can act as a prognostic factorin categorizing the severeness of acute pancreatitis, which may assist doctors in forecasting the disease's course and outcome.

Keywords: Acute pancreatitis, Nonalcoholic fatty liver disease, modified CT severity index for acute pancreatitis.

Introduction

Acute pancreatitis (AP) is a disorder involving gastro-intestinal system annually afflicting 23-49 per 100,000 individuals with notable rates of morbidity and mortality.[1] In 70% - 75% of cases, the disease course is mild and has a fatality rate of less than 1%. But in upto 30% of cases, it is moderate-to-severe, and in the latter group, mortality might exceed 50%.[2] A three-dimen-sional method is suggested by recent guidelines for predicting AP results. Scores used for clinical risk assessment (like the Bedside Index for Severity in Acute Pancreatitis (BISAP) score), host risk factors, as well as treatment response (like creatinine or chronic systemic inflammatory response) are all used for stratification of risk.[3] Using CT, Balthazar et al. first presented a radiological scoring system in 1985. Later, a 10-point CT severity index scale was crea-ted.[4,5]

Metabolic syndrome, which is metabolic status identi-fication is in actuality, a clinical diagnosis. It may augment the probability of developing cardiovascular

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diseases, including dyslipidemic syndromes, hypertension, diabetes, and obesity.[6] Nonalcoholic fatty liver disease (NAFLD) is among the metabolic syndrome phenotypes affecting the hepatic parenchyma, and is associated with all aspects of metabolic disease spectrum.[7] The most commonly encountered chronic liver disease worldwide currently is NAFLD. Global prevalence of NAFLD has increased from 25.3% in 1990-2006 ascompared to 38.0% in 2016-2019, as per a latest systematic review and meta-analysis study.[8]

It has recently been demonstrated that people with NAFLD are more prone to exhibit moderately severe acute pancreatitis (OR = 3.39, 95% CI = 1.52-7.56).[9] Nevertheless, there is still paucity of literature which highlights the significance of NAFLD in prognosticating severity of acute pancreatitis. Moreover this is the first studies to use modified CT severity index score to assess the severity of acute pancreatitis and compare the outcomes between NAFLD and non NAFLD groups.

Materials and Methods

This study was approved by the institute review board (IRB# 022-842-2020). At Radiology Department of Shifa International Hospital Islamabad, weanalysed retrospectively patients diagnosed with AP between January 2020 and December 2022. At least two of the three following factors were requisites for establishing diagnosing AP: 1) acutely occurring non resolving epigastric pain radiating to the back region; 2) values greater than thrice the upper normal limit for serum amylase and/or lipase levels; and 3) CT findings typical for AP.[10]

Exclusion criteria included: 1) Post endoscopic retrograde cholangio pancreato-graphy acute pancreatitis 2) Those patients who referred from other hospitals and did not have an initial CT study, (3) Incomplete clinical data, 4) Splenectomy patients, 5) Patients with a history of alcohol consumption. The institutional review board and ethics committee gave their approval for this study. (IRB# 022-842-2020).

The Modified CTSI (CT SEVERITY INDEX) scores were utilized to categorize AP, out of total score of 10 on the basis of the estimation of inflammation involving pancreas and necrosis.[4,5] Its components are as follows: 1) Inflammation of pancreas given as; 0: normal pancreas, 2: pancreatic parenchymal abnormalities with or without inflammatory changes in peripancreatic fat, 4: pancreatic or peripancreatic fluid collection or peripancreatic fat necrosis. 2) Necrotic changes in pancreas; 0: none, 2: 30% or less of pancreatic parenchyma, 4: more than 30% involvement of pancreatic parenchyma. 3) Associated complications; 0: none, 2: atleast one of pleural effusions, abdominopelvic ascites, vascular complications (i-e aneurysm/ thrombosis), and/or gastro-intestinal involvement. AP severity was categorized as: 0-2: mild, 4-6: moderate, 8-10: severe.[4,5] Post pancreatitis complications included; walled off necrosis, vascular complications, pseudocysts, liquefactive necrosis, fistula formation, duodenal diverticulitis, acute pancreatic collection and acute necrotic collection.

Normally on CT examination, liver has higher density than spleen. However, in fatty liver disease, there is a reversal liver-to-spleen attenuation ratio.[11,12] It was seen in the literature that the sensitivity of non-contrast CT for detecting hepatic steatosis was acceptable as proven by biopsy.[13] Taking variability of 19 HU (less than or equal to) between the CT density of liver and spleen on contrast-enhanced CT, which has a good sensitivity and a high specificity for identification of moderate to severe steatosis on portal venous phase.[14]

In our investigation, we measured the average attenuation values of the liver and spleen in Hounsfield units (HU) by placing regions of interest (ROIs) on two adjacent axial slices of CT. One slice had two ROIs in the right hepatic lobe, another one in the left lobe, and an additional ROI placedon spleen.[15] Mean liver attenuation was calculated by calculating the average of the three ROI values taken from liver. The mean HU of the liver was then divided by the HU of the spleen to obtain the liver-to-spleen attenuation ratio. FL was describedin accordance to cut off of less than 1 liver-to-spleen attenuation ratios on plain CT scans or a difference of 19HU between the liver and spleen CT densities on post IV contrast CT scans.

Quantities and proportions were used to represent categorical whereas mean ± SD or median (interquartile range) were used to represent data in continuous form. We employed descriptive statistics to explore study population’s baseline attributes. Variables between the FL and non-fatty liver (NFL) groups were compared by the means of a two-sample independent t-test (Mann-Whitney U test) for numerical variables and a Pearson chi-square test (Fisher exact test) for nominal variables.[15] To evaluate the variables associated with moderate AP severity, logistic regression analysis was applied. Linear-by-linear association method was utilized to test the patterns between the severity of AP and FL.[15] For the statistical analyses, SPSS version 25.0 was utilized. P value < 0.05, was considered statistically significant.

Results

(Tab.1) displays the patient variables and severity outcomes regarding 128 study participants. There were 55 females (42.60%) and 74 males (57.40%) in the study population having average age of 47.40 ± 17.658 years. Conforming to the Modified CT Severity Index for acute pancreatitis, 43 (33.33 %) cases were grouped as mild, 56 (43.41%) as moderate, and 30 (23.26%) of the cases as severe. 78 (60.47%) cases had no complications. Walled off necrosis, vascular complications, pseudocysts, liquefactive necrosis, fistula formation, duodenal diverticulitis, acute pancreatic collection and acute necrotic collection were seen in 19 (14.73%), 12 (9.30%), 31 (24.03%), 2 (1.55%), 1 (0.78%), 1 (0.78%), 5 (3.88%) and 2 (1.55%) cases respectively.

Extra pancreatic complications including abdomino-pelvicascites, uni/bilateral pleural effusions, vascular, pancreatic parenchymal or GIT complications, were seen in 64 (49.61%) patients. Whereas 65 (50.39%) cases showed no extra pancreatic complications. Pancreatic parenchyma was normal in 1 (0.78%) while intrinsic pancreatic abnormalities and pancreatic/peri pancreatic fluid collection were seen in 57 (44.19%) and 71 (55.04%) patients respectively. Less than 30% pancreatic parenchymal necrosis was seen in 35 (27.13%) patients, while more than 30% necrosis was seen in 8 (6.20%) patients. 86 (66.67%) had no pancreatic necrosis.

(Tab.2) compares severity parameters and attributes of AP patients having FL and those without. Out of the 129 patients, 91 (or 70.50%) had FL, whereas 38 (or 29.50%) did not. The FL group's mean liver spleen attenuation index was 0.77±0.151, while the NFL group's was 1.14±0.124 (p = 0.001). The mean age of the FL and NFL groups did not differ significantly (46.74±17.551 versus 48.97±18.050, p = 0.446). Although no discernible gender disparity was appreciated between the groups, patients with FL had female preponderance(58.24as compared to males (41.76%) (p value = 0.846). Post pancreatitis complications were frequently seen in the FL group, in particular the walled off necrosis, with a noteworthy

Patient characteristics		Frequency (%)	Mean ± SD Median (IQR)
Age (in years)		-	47.40 ± 17.658
Gender	Male	74(57.40)	-
	Female	55(42.60)	-
Fatty liver		91(70.50)	-
Non-fatty liver		38(29.50)	-
Liver spleen attenuation index		-	0.88±0.223
Post pancreatitis complications	No complications	78(60.47)	-
	Walled off necrosis	19(14.73)	-
	Vascular complications	12(9.30)	-
	Pseudocysts	31(24.03)	-
	Liquefactive necrosis	2(1.55)	-
	Fistula formation	1(0.78)	-
	Duodenal diverticulitis	1(0.78)	-
	Acute pancreatic collection	5(3.88)	-
	Acute necrotic collection	2(1.55)	-
Pancreatic inflammation	Normal	1(0.78)	-
	Intrinsic pancreatic abnormalities	57(44.19)	-
	Pancreatic or peripancreatic Fluid collection/necrosis	71(55.04)	-
Pancreatic necrosis	None	86(66.67)	-
	30% or less	35(27.13)	-
	More than 30%	8(6.20)	-
Extra pancreatic complications	No complications	65(50.39)	-
	Pleural effusion/ascities/vascular or parenchymal complications or GIT involvement	64(49.61)	-
Modified CT severity index	Mild	43(33.33)	-
	Moderate	56(43.41)	-
	Severe	30(23.26)	-

Table 1: Patient characteristics and severity outcomes of study Patients (N = 129)

among the two groups (19.78% vs. 2.63%, p=0.013). Additionally, the FL group experienced extra-pancreatic complications at a higher rate (58.24% vs. 28.94; p-value = 0.004).

Patient characteristics		Frequency (%)	Mean ± SD Median (IQR)	Frequency (%)	Mean ± SD Median (IQR)	P-value
Age (in years)		-	46.74 ± 17.551	-	48.97 ± 18.050	0.446
Gender	Male	38(41.76)	-	21(55.26)	-	0.846
	Female	53(58.24)	-	17(44.74)	-	
Liver spleen attenuation index		-	0.77 ± 0.151	-	1.14 ± 0.124	**0.001***
Post pancreatitis complications	No complications	52(57.14)	-	26(68.42)	-	0.323
	W alled off necrosis	18(19.78)	-	1(2.63)	-	**0.013***
	Vascular complications	9(9.89)	-	3(7.89)	-	1.000
	Pseudocysts	20(21.98)	-	11(28.95)	-	0.498
	Liquefactive necrosis	1(1.10)	-	1(2.63)	-	0.504
	Fistula formation	0(0.00)	-	1(2.63)	-	0.304
	Duodenal diverticulitis	1(1.10)	-	0(0.00)	-	1.000
	Acute pancreatic collection	4(4.40)	-	1(2.63)	-	1.000
	Acute necrotic collection	1(1.10)	-	1(2.63)	-	0.504
Pancreatic inflammation	Normal	1(1.10)	-	0(0.00)	-	0.229
	Intrinsic pancreatic abnormalities	36(39.56)	-	21(55.26)	-	
	Pancreatic or peripancreatic fluid collection/necrosis	54(59.34)	-	17(44.74)	-	
Pancreatic necrosis	None	58(63.74)	-	28(73.68)	-	0.419
	30% or less	26(28.57)	-	9(23.68)	-	
	More than 30%	7(7.69)	-	1(2.63)	-	
Extra pancreatic complications	No complications	38(41.76)	-	27(71.05)	-	**0.004***
	Pleural effusion/ascities/vascular or parenchymal complications or GIT involvement	53(58.24)	-	11(28.94)	-	
Modified CT severity index	Mild	25(27.47)	-	18(47.37)	-	**0.031***
	Moderate	40(43.96)	-	16(42.11)	-	
	Severe	26(28.57)	-	4(10.53)	-	

Table 2: Comparison of characteristics and severity parameters between acute pancretitis AP Patients with presence and absence of fatty liver (FL)

Vascular complications, pseudocysts, duodenal diverticulitis and acute pancreatic collection were more commonly seen in FL group, however no consequential difference was noted (all p = > 0.05). Fistula formation was observed in only one patient out of 129 and that too belonged to non-fatty liver group. Liquefactive necrosis and acute necrotic collection was almost equally seen between the two groups. Pancreatic/peripancreatic inflammatory changes and pancreatic necrosis was also commonly seen in FL group however no difference of consequence was noted (all p = > 0.05). The complication rates of acute pancreatitis with and without FL are compared in (Fig.1).

There were 25 (27.47%) mild AP cases, 40 (43.96%) of moderately AP, and 26 (28.57%) severe AP in the FL group, and 18 (47.37 %)cases of mild AP, 16 (42.11%) of moderately AP, and 4 (10.53%) of severe AP in the NFL group. Although the incidence of mild, moderate, and severe AP appeared to be more prevalent in FL group, the moderate severity of AP was statistically significant (p value = 0.031).

(Tab.3) shows factors potentially associated with moderately severe AP. Using logistic regression analysis and adjusting for confounding factors, it was seen that although moderately severe AP was

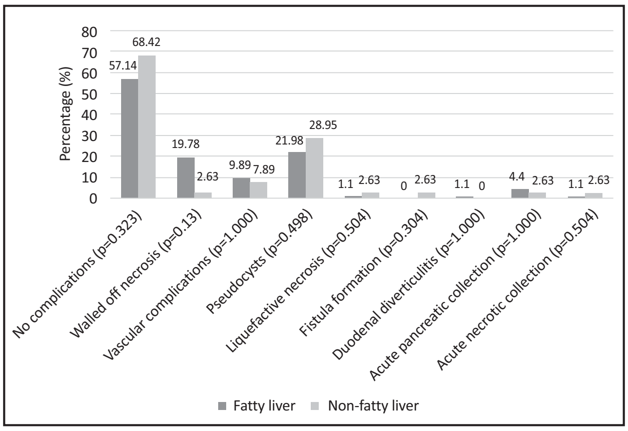

Figure 1: Comparison of complication rates of acute pancreatitis with and without fatty liver.

significantly associated with fatty liver but odds ratio was less which shows that it is not an independent risk factor.

Factor	p-value	OR	95%CI
Age (in years)	0.982	1.000	0.978 - 1.022
Gender (Male/Female)	0.753	1.132	0.524 – 2.448
Fatty liver versus non-fatty liver	**0.025**	0.405	0.183 – 0.893

CI: confidence intervals; OR: odds ratio

Table 3: Patient characteristics and severity outcomes of study Patients (N = 129)

Discussion

In current paper, we scrutinized the relationship between NAFLD, and the magnitude of severity/complications caused by acute pancreatitis. Our results showed that local as well as extra pancreatic complications of acute pancreatitis were more commonly seen NAFLD patients as compared to those without fatty liver. Using modified CT severity index for categorising acute pancreatitis, it was seen that mild, moderate, and severe acute pancreatitis were commonly seen in FL group however the prevalence of moderately severe acute pancreatitis was still significantly more common in FL patients. After regulating compounding factors of age and sex, it was observed that fatty liver is a significant risk factor for developing moderately severe grade of acute pancreatitis, nonetheless it was not proven to be independent risk factor in our study provided that the odds ratio was less than 1 in this case.

The inflammation of the pancreas caused by the gland's own enzymes digesting it is known as acute pancreatitis. The common aetiology of acute pancreatitis are gallbladder calculi, alcohol consumption and hyperlipidaemia with gallstones being the most common cause globally.[12,16] Fatty liver disease is an endemic hepatic metabolic disease and can manifest as range of clinical and morphological abnormalities from simple fatty infiltration of liver to severe cirrhotic disease. It can give rise to metabolic syndrome, diabetes and atherosclerotic changes within vessels.[17,18] FL is commonly seen in patients presenting with acute pancreatitis as both share risk factors such as high body mass index, hyperlipidaemia and alcohol consumption. More than two thirds of patients in our study had FL. The mechanism behind this association between AP and FL is explained by many theories, some of them are as follows. 1) NAFLD is an inflammatory disease whichactivates long-standing systemic inflammation,[19,20,21] which can be an etiological factor resulting inexacerbation of AP. 2) Kupfer cells represent about 70% of the total macrophages of liver and release a large amount of inflammatory factors which may induce changes of AP.[22] 3) Patients with NAFLD often have raised CPR, IL-6, leptin, and decreased adiponectin levels, which aggravates AP.[23] 4) The glycoprotein known as α-1 antitrypsin is primarily produced by the liver. By influencing a variety of inflammatory cells, it can have a major effect on reducing chronic inflammatory response. In a study it has been demonstrated that in human vs mice prototypes of acute pancreatitis, FL significantly inhibits the levels of α-1 antitrypsin,[24] another good explanation to our results.

There are certain limitations of our study; 1) we conducted a retrospective study with relatively limited sample size. 2) We routinely perform post IV contrast enhanced CT abdomen for patients with strong suspicion of acute pancreatitis and unenhanced phase is not always available to measure the attenuation of liver for fatty infiltration and a difference of 19HU on contrast enhanced CT between liver and spleen, was considered with reference to the given article.[14] 3) It was a single centred study. 4) We could not assesslong term complications in all the patients as there were some cases who lost to follow up.

Conclusion

Fatty liver can be accurately diagnosed using multidetector CT and associated increased severity and complication rate of acute pancreatitis and can be used as prognostic sign for escalated severity of clinical course of acute pancreatitis. However, this being an independent risk factor cannot be proven in our study.

CONFLICT OF INTEREST: None.

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