RESEARCH ARTICLE

Frequency of Nonalcoholic fatty pancreatic disease in patients with carcinoma pancreas presenting for upper abdominal Endoscopic Ultrasound in a tertiary care center

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Abstract

Objective: To determine the frequency of nonalcoholic fatty pancreatic disease in patients with carcinoma pancreas presenting for upper abdominal endoscopic ultrasound.

Method: The prospective cross-sectional study was conducted in the Endoscopy Suite of Surgical Unit 4, Civil Hospital, Karachi, from October 2019 to September 2020, and comprised patients presenting for endoscopic ultrasound. Patients were divided into Group A comprising carcinoma pancreas patients, and Group B having non-carcinoma pancreas patients. Fatty pancreas was identified by hyperechogenicity on endoscopic ultrasound. Data was analysed using SPSS 19.

Result: Of the 68 patients, 44(64.7%) were male and 24(35.3%) were females. The overall mean age was 49.9±13.82 years (range: 16-80 years). There were 35(51.5%) patients in Group A and 33(48.5%) in Group B. The frequency of nonalcoholic fatty pancreatic disease was 18(26.5%) and 15(83.3%) of them were male subjects (p=0.04). Group A had 12(34.28%) subjects with nonalcoholic fatty pancreatic disease compared to 6(18%) in Group B (p=0.11).

Conclusion: Nonalcoholic fatty pancreatic disease was frequently seen in carcinoma pancreas patients undergoing endoscopic ultrasound compared to non-carcinoma pancreas patients. Most of the patients affected were males.

Keywords: Nonalcoholic fatty pancreas, NAFPD, Fatty pancreas, Steatopancreatitis, Pancreatic fibrosis. (JPMA 72: 2209; 2022)

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Introduction

Nonalcoholic fatty pancreatic disease (NAFPD) is a condition labelled as having increased fat accumulation in pancreas without patient history of alcohol consumption. One of the major players involved in the development of pancreatic adenocarcinoma is the inflammation of pancreas against the background of pancreatic steatosis.[1] The mechanism in fatty pancreas leading to carcinogenesis has not yet been fully evaluated or understood.

Ogilvie[2] first cited Pancreatic steatosis in literature. He reported pancreatic fat deposition in 17% of the obese patients, and 7% in non-obese patients. Olsen[3] in 1978 reported his examination of 394 autopsied patients in which he found increased amount of pancreatic fat deposition in a direct relationship with age. Similar results were reported by Stamm[4] as well, thereby establishing that increasing age predisposes individuals to more pancreatic fat accumulation. In 2017, Lesmana et al.[1] showed an increased prevalence of NAFPD in pancreatic adenocarcinoma patients, and established NAFPD as a significant risk factor in the development of pancreatic adenocarcinoma. Literature review of the epidemiological trials done from 2014 to 2016 showed the NAFPD prevalence ranging 16-35% in the Asian population.[5-7]

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Carcinoma of pancreas is one of the most life-threatening cancers with a dismal prognosis. Early detection of pancreatic cancer may play a role in improving the prognosis and treatment of this condition. The reason behind the advanced disease at presentation and delayed detection of pancreatic malignancy is the nondescript symptomatology and its retroperitoneal anatomical location. Moreover the biomarkers also lack accuracy when it comes to this particular cancer. Endoscopic ultrasound (EUS) is currently considered the gold standard for investigating and detecting pancreatic pathologies and for the screening and diagnosis of pancreatic cancer. However, the jury is still out regarding its cost-effectiveness. EUS, like any other ultrasound (US), is highly operator-dependent and has got a learning curve leading to few experienced individuals, thus limiting the availability of this modality of investigation.[8]

The current study was planned to determine the frequency of NAFPD in patients with carcinoma pancreas presenting for upper abdominal EUS.

Patients and Methods

The prospective cross-sectional study was conducted in the Endoscopy Suite of Surgical Unit 4, Civil Hospital, Karachi, from October 2019 to September 2020. After approval from the institutional ethics review board, the sample size was calculated while taking the frequency of NAFPD in carcinoma pancreas and non-carcinoma

pancreas cases to 64% and 30% respectively.[1] The power was kept at 80% and alpha value 0.05. The sample was raised using consecutive sampling technique from among those presenting for EUS of upper abdominal pathologies Patients with history of alcohol consumption, those with chronic pancreatitis and diabetes, those with body mass index (BMI) >30, and patients in whom EUS could not evaluate the pancreas for whatever reason were excluded.

After taking written informed consent, the patients were divided into Group A composed of carcinoma pancreas patients diagnosed on the basis of clinical findings and computed tomography (CT) scan of the abdomen, and Group B having all other patients requiring upper gastrointestinal (GI) EUS. A single experienced gastroenterologist with experience of over 500 procedures performed the EUS (Olympus UCT 180 scope). All procedures were done under conscious sedation as a day-care procedure. Fatty pancreas in both the groups was picked up on EUS as hyperechogenicity of the pancreas. Frequency of fatty pancreas was recorded in all patients undergoing EUS. A proforma was filled up for each of these patients.

Data was analysed using SPSS 19. Overall scores were compared between the groups. Chi-square was used for qualitative data, while student t-test was used for quantitative data. P<0.5 was considered statistically significant.

Results

Of the 70 patients enrolled and divided into 2 groups, 2(2.8%) had malignancy proven later with repeat EUS fine needle aspiration cytology (FNAC), and the study was completed by 68(97.1%). Of them, 44(64.7%) were male and 24(35.3%) were females. The overall mean age was 49.9±13.82 years (range: 16-80 years). The mean BMI was 21.48±3.83, and 14(20.6%) patients were overweight. There were 35(51.5%) patients in Group A and 33(48.5%) in Group B (Table 1). Pancreatic mass was the leading indication for EUS 35(51.5%) (Table 2).

The frequency of NAFPD was 18(26.5%) and 15(83.3%) of them were male subjects (p=0.04) (Table 3). Group A had 12(34.28%) subjects with NAFPD compared to 6(18%) in Group B (p=0.11) (Table 4).

Table-1: Patient characteristics in the two study groups.

	Group A (Carcinoma Pancreas)(n=35)	Group B (n=33)	*p* value
Mean Age (years)	51.09±12.45	48.82±12.25	0.130
Gender (M:F)	25:10	19:14	0.173
Overweight (Yes:No)	6:29	8:25	0.336
Height in cms	162.05±13.74	163.03±7.86	0.239
Weight in Kg	55.26±11.71	59.33±12.52	0.395
Mean BMI	20.84±3.65	22.17±3.96	0.406
NAFPD (Yes:No)	12:23	6:27	0.109

BMI: Body mass index, NAFPD: Nonalcoholic fatty pancreatic disease.

Table-2: Indications of endoscopic ultrasound EUS).

Diagnosis	n (%)
Pancreatic mass	35 (51.5)
Hepatobilliary pathology	16 (23.5)
Benign pancreatic pathology	6 (8.8)
Oesophageal cancer	4 (5.9)
Lymphoma	4 (5.9)
Stomach cancer	2 (2.9)
MEN 1 syndrome	1 (1.5)
Total	68 (100)

MEN1: Multiple endocrine neoplasia type 1.

Table-3: Patient characteristics in nonalcoholic fatty pancreatic disease (NAFPD).

	Yes	No	p-value
n (%)	18 (26.5)	50 (73.5)	
Mean Age (years)	51.61±9.53	49.40±15.11	0.56
Gender (M:F)	15:3	29:21	0.04
Overweight	5	13	0.28
BMI (mean)	22.26±3.82	21.20±3.83	0.32
Carcinoma Pancreas	12	6	0.11

BMI: Body mass index.

Table-4: Carcinoma pancreas versus non-pancreatic cancer patient characteristics in nonalcoholic fatty pancreatic disease (NAFPD).

	Carcinoma Pancreas	Non-Pancreatic	*p*-value
n (%)	12 (34)	6 (18)	0.109
Mean Age (years)	52.17±9.75	50.50±9.87	0.73
Gender (M:F)	11:1	4:2	0.245
Overweight	2	3	0.176
Mean BMI	21.10±3.51	24.57±3.57	0.06

BMI: Body mass index.

Discussion

Carcinoma pancreas is a highly lethal disease, which is usually detected late and is associated with very high morbidity and mortality. There is an absolute need to look for early diagnostic modalities and to establish risk factors that might be a precursor to this life-threatening cancer.

Diabetes and obesity have been reported as risk factors for pancreatic cancer. Several studies have found that NAFPD can be a precursor to pre-diabetes and lead to diabetes. Although these studies have not exactly identified the mechanism or pathway leading to it, the damage and fat replacement at the acinar cells leading to beta (β) cell dysfunction has been implicated. It has also been suggested that fat accumulation leads to reactive oxygen species (ROS) activation, increasing oxidative stress (OS) and resulting in more β-cell apoptosis.[9-11]

Literature review has shown that the patients who were operated upon for pancreatic adenocarcinoma and who

had increased fat in their pancreas had a significantly higher risk of postoperative complications, especially the development of pancreatic fistulas.[12-14] There are two hypotheses regarding fatty infiltrations in the pancreas. Acinar cell disruption and increase of intracellular triglycerides result in fat accumulation. The initiating factor is the high level of free fatty acid found commonly in obese patients. Increased pro-inflammatory cytokines, like tumour necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), monocyte chemotactic protein-1 (MCP-1) combined with macrophages producing IL-1b, and myeloperoxidase (MPO) are caused by OS due to the imbalance of adipokines.[1] As this cycle of progression of obesity starts, it results in excessive fat accumulation in non-adipose tissue, like the liver, pancreas, skeletal muscle and heart. Another possibility is chronic inflammation with excessive fat accumulation leading to cell injury and cancer development.[1]

Lesmana et al.[6] reported that amongst 169 patients who underwent EUS, fatty pancreas was seen in 32.7%. The frequency of fatty pancreas in the current study was 26.5% which is in correlation with other studies where the incidence cited is 16-34%6. In order to rule out the confounding effect of obesity, the current study excluded patients with obesity and diabetes, but there were 14 patients who were overweight. Of these 14 patients, 5(35.71%) had NAFPD (p=0.28). Carcinoma of pancreas was seen in 2(40%) of these patients which was much higher than 26% reported earlier.[15] The higher results in the current study could be due to a small sample of overweight patients.

Factors commonly implicated to have an association with NAFPD include male gender, age >60 years, hypertension (HTN), fasting blood glucose (FBG), triglycerides (TG), BMI, central obesity and pancreatic malignancy.[1,3-7] However, literature review has shown inconsistent results regarding the association of NAFPD with age, gender, hypertriglyceridaemia, HTN and pancreatic malignancy.[3,4,6,7] Lesmana et al.[6] reported that fatty pancreas was the only significant risk factor for pancreatic cancer.[1] The results were not statistically significant, but we did find NAFPD more in carcinoma pancreas group compared to non-pancreatic cancer group (34% vs. 18%; p=0.109). One of the reasons for the non-significant result could be the exclusion of diabetes and obesity, which could have added to the results.

Juliyanti Fu et al.[16] also revealed no association between male gender and NAFPD. Logistic regression analysis of factors, such as age, gender, diabetes and chronic pancreatitis, were not proven to be significant risk factors for pancreatic cancer.[1] Weng et al.[17] reported overall NAFPD prevalence to be 11.05%. In patients aged <55 years, NAFPD prevalence was less in females than males (p<0.05), but they found that the prevalence was similar in patient group >55 years age. In the current study, the majority of patients were males in the NAFPD group (p=0.04). Pancreatic malignancy was seen in the majority of male patients but this was not statistically significant when compared to the non-pancreatic group (p=0.24). This is supported by the previous studies evaluating fatty pancreas.[18,19]

Studies by Olsen[3] and Stamm[4] reported an increased amount of fat in the pancreas in patients with advanced age. Choi et al. reported that in patients aged 60 years and above, there was an increase in pancreatic echogenecity[20] on EUS. In the current study although there was no statistically significant difference in the mean age of patients and presence of NAFPD (p=0.56), NAFPD was seen more in the higher age group (mean age 51.61±9.53 vs. 49.40±15.11 years), thus correlating with the evidence that with increasing age there is more fat deposition. Similarly, NAFPD patients with carcinoma pancreas had a higher mean age compared to non-NAFPD patients (52.17±9.75 vs. 50.52±13.8 p=0.71) although this was not statistically significant.

Although EUS is an invasive investigation, its reliability for the evaluation of pancreas is unrefuted, though operator-dependent. A fatty pancreas would be shown as having increased pancreatic echogenicity on EUS. This increased echogenicity may, however, be due to other conditions as well, like pancreatic fibrosis.[20] There is no consensus yet on the best modality for pancreatic fat quantification except biopsy through open surgery.[19,21] The current study just looked at the fatty infiltration of pancreas in two groups by EUS performed by a single experienced endoscopist having an experience of more than 500 procedures. It did not quantify the fat deposition. Due to its invasiveness, cost and lack of technical expertise, EUS is still not a practical option as a screening tool.[22]

The limitation of the current study is that it was done at a single centre with a small sample size. Also, it did not evaluate the effect of metabolic factors, like lipid profile, obesity and diabetes, and did not quantify the fat deposition in pancreas.

Despite the limitations, the current study is the first in Pakistan looking at the frequency of NAFPD in pancreatic cancer versus non-cancer groups evaluated by EUS. Further cohort studies are needed to look at the effect and relationship between NAFPD and cancer development.

Conclusion

NAFPD was seen more in patients with pancreatic cancer compared with the non-cancer group although the difference was not statistically significant. Males and those aged >50 years were predominantly affected.

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Conflict of Interest: None.

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