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Original Article

Added Value of Cross-SectionalImaging in Total Pancreatic Lipomatosis: An Institutional Experience from Northeast India

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ABSTRACT

Background:
Total fatty replacement of the pancreas results in exocrine pancreatic enzyme deficiency, which may lead to malabsorption. This study aimedto evaluate the added value of multi-detector computed tomography (MDCT) and magnetic resonance imaging (MRI) intotal pancreatic lipomatosis (TPL).

Materials and Methods:
This retrospective study covered 19 consecutive patients of TPL in a tertiary care hospital from November 2019 to June 2021 with a review of clinical and cross-sectional imaging data. MDCT was done in 10 patients, and an MRI scan in 9 patients. Pancreatic volume was measured and correlated with the patient body habitus.

Results:
19 patients (male=9, female=10) had TPL with a mean age of 39.37±14.09[SD] years.Total pancreatic parenchymal atrophy was observed in 10 patients (52.6%), followed by near-total atrophy in nine patients (47.2%). The main pancreatic duct (MPD) was gross diffuse irregularly dilated in seven patients (36.8%) and mild diffuse irregularly dilated in 11 patients (57.9%). Sixpatients (31.6 %) of TPL wereassociated with malabsorption syndrome. The mean volume of the lipomatous pancreas was 150.1±72.7 [SD] cm3. The lipomatous pancreatic volume significantly correlated with the patient's body habitus with a P value of 0.05 using an independent sample ttest.

Conclusion:
MDCT and MRI play an important role in diagnosing the degree of pancreatic lipomatosis, and they can find out the possible underlying cause of TPL and even chronic sequelae of TPL, such as malabsorption syndrome.

Keywords: Total pancreatic lipomatosis (TPL), malabsorption, computed tomography (CT), magnetic resonance imaging (MRI), chronic pancreatitis

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INTRODUCTION:

Isolated focal fatty infiltration (lipomatosis) of the pancreas has been described in association with various disorders like obesity, chronic pancreatitis, diabetes, and cystic fibrosis(1,2). However, total pancreatic lipomatosis (TPL) is an uncommonly described entity characterized by the complete replacement of the pancreas by fatty infiltration(2).Although the exact pathophysiological background of total pancreatic lipomatosis has not been well described, several factors like viral infections, metabolic syndrome, chronic and hereditary pancreatitis, hemochromatosis, type 2 diabetes mellitus,non-alcoholic fatty pancreas, pancreatic ductal obstruction, and cystic fibrosis have been implicated(2,3,4,5,6).The postulated pathophysiological mechanism has been the replacement of the pancreatic acinar cells with adipose tissue with the preservation of pancreatic ducts and islet cells(3). The commonly reported clinical presentations include abdominal pain with discomfort and features of pancreatic insufficiency. Outcomes are often poor in cases of TPL and are associated with poor quality of life(2).

There are several imaging modalities for pancreatic fat content assessment, including abdominal ultrasound (USG), computed tomography (CT), and magnetic resonance imaging (MRI). Of these, USG is an insufficient tool to quantify pancreatic fat; however, USG can evaluate the fatty changes of the pancreas, showing variable degrees and patterns of increased echogenicity of the pancreatic parenchyma, parenchymal atrophy, status of main pancreatic duct (MPD) and to identify possible causes of pancreatic lipomatosis by detecting MPD calculus, pancreatic mass etc. while MDCT and MRI are the modalities of choice for fat quantification in the pancreas, with the radiological hallmarks being complete low dense fat attenuation of the pancreason MDCT scan, bright signal intensity on T1WI and T2WI MRI images with hypo to low signal intensities on fat-suppressed MR images(7) and even pancreatic fats quantifications by using proton density fat fraction technique(6,8). This study aimed to characterize the radiological features of TPLon MDCT and MRI.

MATERIALS AND METHODS:

Study design:

After approval from the institutional ethics review committee, a hospital-based cross-sectional study was conducted in a tertiary care hospital in North Eastern India from November 2019 to June 2021 with the review of clinical and cross-sectional imaging data of 19 consecutive patients with TPL. The diagnosis of TPL was made with anMDCT scan in 10 patients and an MRI scan in nine patients.

Patient selection:We included allpatients of total and near-total pancreatic lipomatosis identified on MDCT and or MRI. Informed consent was obtained from the patients/ guardians before undergoing an MDCT or MRI scan.

Data sources and measurements: The patients' clinical and cross-sectional imaging data were obtained in 10 patients from an MDCT scan and 9 patients from an MRI scan.

MDCT Protocol:

MDCT examinations were performed using a 128-slice scanner (Philips Ingenuity 128 CT scanner, Amsterdam,Netherlands). MDCT examinations were performed with a helical scanner using the following scan parameters: voltage 120 kV; tube current of 121 mAs; slice thickness 5 mm; reconstructed slice thickness of 1 mm; collimation 64 x 0.625 mm with automatic exposure control. Post-contrast abdomen scans were acquired after intravenous injection of 1ml/kg of body weight iodinated contrast agent.

MRI protocol:

MRI scan was done using a Philips Ingenia1.5 Tesla machine (Philips Medical System, The Netherlands). Axial,coronal,and/or sagittal planes were obtained using a combination of various pulse sequences in a pancreatic MRI protocol.Various sequences of MRI sequence parameters are described below.

1.Axial T1W_TFE (turbo filed echo) images were obtained with TE:4.6-5.1ms, TR: 275-300 ms, slice thickness 5 mm, and FOV of 190-220.

2.Axial T2W images were obtained with TE: 90-105ms,TR:1000ms,slice thickness 4 mm,flip angle 900, and FOV of 190-220.

3.Coronal T2W_SPAIR images for the upper abdomen were obtained with TE: 90-105ms, TR: 1000 -2000ms, 256 x 256 matrix, 13-14, slice thickness 4 mm with 0.5 mm interslice gap, flip angle of 900 and FOV of 240-260.

4.Fat-suppressed axial T2W_SPAIR images were obtained with TE:90-100ms,TR: 1000-2500 ms, flip angle 900, slice thickness of 4 mm and FOV of 200-240.

5.Dual FFE sequences were obtained with TE 1/ TE:2.3ms/4.6ms, TR: 103 ms, slice thickness 5 mm, and FOV of 190-220 for in-phase and out-phase images.

6.Axial BTFE (balanced turbo field echo) sequence was obtained with TE: 1.86ms,TR: 3.7ms, slice thickness 4

mm, flip angle 900 and FOV of 190-220.
7.Dynamic post-contrast MR images (DCE-MRI) were obtained: 3D eTHRIVE (3D enhanced T1 high-resolution isotropic volume excitation) dynamic post-contrast MR images of the upper abdomen were obtained in an axial plane. 3D eTHRIVE sequence is a fat-suppressed 3D sequence.The arterial, portal, and venous phases of the upper abdomen were obtained after intravenous administration of 0.1mmol per kilogram of body weight gadobenatedimeglumine (Bracco Diagnostics Inc. Singen, Germany 78224) at a rate of 3-4 mL/sec followed by 20 mLnormal saline flush. The imaging parameters were TE:1.86msec,TR:3.9 msec, section thickness:2.5 mm, slice per slab: 144, flip angle 100, FOV of 240-340.

Cross-sectional image analysis:
Analysis of the MDCT image data was based on axial and reformatted images. All images were evaluated in the axial plane, followed by sagittal and coronal Maximum Intensity Projection (MIP) images. Two experienced radiologists evaluated the MDCT and MRI images with a consensus for the status of pancreatic parenchyma,the status of fatty tissue depositions, the status of MPD, the presence of MPD calculus, MPD mass, calcified MPD worm,the presence of pancreatic parenchymal calcifications, the status of the gall bladder, and bowel loops. The following findings were given close attention: location of MPD calculus, size of calculus, Hounsfield Unit (HU) value of fatty replaced pancreas, and location of excessive fatty depositions. Complete replacement of pancreatic parenchyma with fatty depositions without visualization of normal-appearing pancreatic parenchyma with only visualization of MPD either on MDCT or MRI was considered as total pancreatic lipomatosis. Excessive pancreatic fatty replacement with visualization of focal areas of normal attenuating pancreatic tissue, usually around the MPD, was considered near-total pancreatic lipomatosis.

Pancreatic volume measurement: The volume of the lipomatous pancreas was obtained using various diameters and using the volume formula(9).

Pancreas (volume) = (AP tail+AP body)/2 x L body &tail x CC body +(AP head/2)2 x 3.14 x CC head
The anterior-posterior (AP) diameters of the tail and body were measured in axial images from the splenic vein into the anterior contour of the pancreas. The AP diameter of the pancreatic head was measured at the level where SMA and SMV were demonstrated. The length of the body and tail (L body &tail) was measured as a maximum linear distance from the pancreatic neck to the tip of the pancreatic tail. The cranial-caudal diameter was measured in coronal or sagittal images. The cranial-caudal diameter of the head is measured in sagittal or coronal images just lateral to the portal vein shown in (Figure 1). Maximum latero-lateral diameter of the L1 vertebral body (LLL1) and AP diameter of midline anterior abdominal wallsubcutaneous tissue fat (APASF) are measured in the same image for assessing the patient's body habitus of patients.

Systematic review of literature: We searched a total of eight literature databases (Pubmed, CINAHL, SCOPUS, Wiley online library, Web of Science, Cochrane,Embase, and CNKI). The reference list of all identified articles was screened to find out more relevant articles. The search keywords included pancreatic lipomatosis, total pancreatic lipomatosis, malabsorption syndrome, chronic pancreatitis, and fatty pancreas.We initially screened 864 articles systematically, and after the removal of duplicates (n-451), final n- 413 articleswere analyzed, from which only 56 eligible articles were analyzed for final review.

Ethics: The institutional human ethical committee (IHEC) of the Tezpur Medical College & Hospital approved the protocol (IEC No:026/2021/TMCH)

Statistical analysis:
Descriptive data were expressed as numbers, mean with 95% confidence interval (CI).The Chi-square tests were used for proportions. Continuous variables were compared using a t test. A P value less than 0.05 was considered statistically significant. Continuous variables were compared using a ttest. Statistical analysis was performed using SPSS software version 26 (IBM Inc.).

RESULTS:

Patient clinical data:19 patients (male =9, female=10) had TPL with a mean age of 39.37±14.09[SD] years. The probable etiology for TPLwas chronic calcific pancreatitis in 10 patients (52.6%), diabetes mellitus in three patients (15.8%), indeterminate in three patients (15.8%), intrapancreatic mass, pancreatic divisum and calcified worm in MPD in each one patient (5.3%). Ten patients (52.6%) of TPL had recurrent abdominal pain, four patients (21.1%) had abdominal distension and discomfort,and another five patients (26.3%) had abdominal distension and steatorrhoea. The clinical characteristics of the patients with TPL are shown in (Table 1).

Imaging findings: MDCT was done in 10 patients and MRI in nine patients. Total pancreatic parenchymal atrophy was observed in 10 patients (52.6%) (Figure 2) and near-

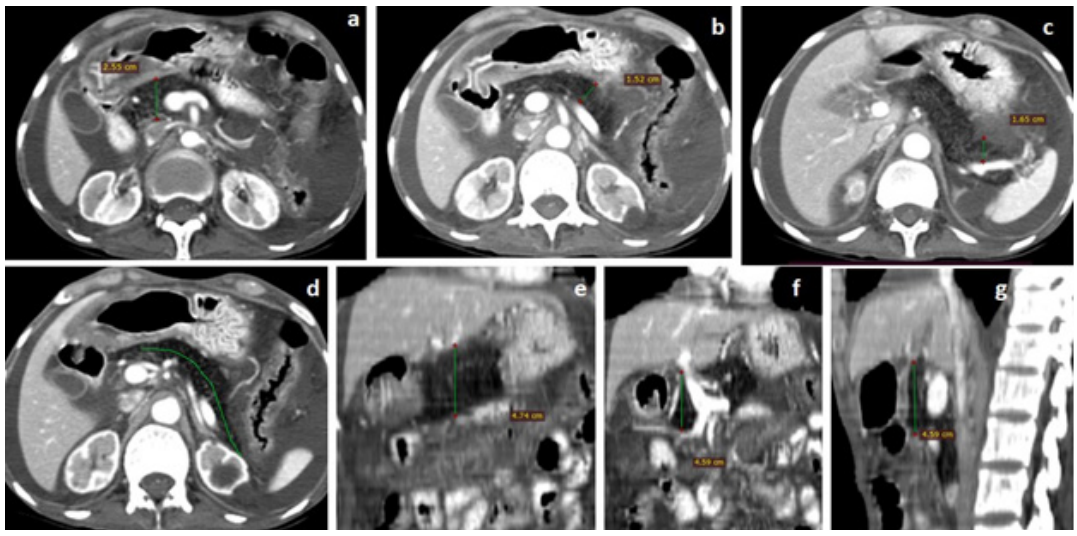

Figure 1.A 70-year-old male patient with total pancreatic lipomatosis shows various dimensions of the pancreas for pancreatic volume measurement. Axial post-contrast MDCT scan images (a,b& c) showed anterior-posterior (AP) diameter of the head, body, and tail. Axial post-contrast MDCT scan image (d) showed the length of the body and tail (L body &tail) measured as a maximum linear distance from the pancreatic neck to the tip of the pancreatic tail. Post-contrast MDCT coronal image (e) showed the cranial-caudal diameter body of the pancreas. Post-contrast MDCT sagittal images (f & g) showed the cranial-caudal diameter head of the pancreas measured just lateral to the main portal vein.

Table 1. Characteristics of 19 patients with TPL

Characteristic	**N(%)**
Male: Female (%)	1:1.1(M=52.6%,F=47.4%)
Mean age	39.37±14.09
Clinical Presentation	
Recurrent abdominal pain	10 (52.6%)
Abdominal discomfort and distension	4(21.1%)
Steatorrhea and abdominal discomfort	5(26.3%)
Presumed Etiology	
Chronic calcific pancreatitis	10 (52.6%)
Diabetes	3(15.8%)
Indeterminate	3(15.8%)
Intrapancreatic mass	1(5.3%)
Pancreatic divisum	1(5.3%)
Calcified worm in MPD	1(5.3%)
Imaging Characteristics	16.12
Pancreatic Parenchyma	
Total pancreatic parenchymal atrophy	10 (52.6)
Near-total atrophy	9 (47.2)
MPD	
Gross diffuse irregular MPD dilatation	7 (36.8)
Mild diffuse irregular MPD dilatation	11 (57.9)
Normal MPD	1 (5.3)

Table 1. Characteristics of 19 patients with TPL

Characteristic	N(%)		
Intraductal calculi	15 (78.9)		
Dilated small bowel loops	6 (31.6)		
Pancreatic divisum	1(5.3)		
Indraductal pancreatic carcinoma	1(5.3)		
Hepatocellular carcinoma	1(5.3)		
Pancreatic volume (cm3)	Combined	150.1± 72.7 [SD]	P value 0.704
	Male	157.1±79.9[SD]	
	Female	143.85±61.31[SD]	
Latero-lateral diameter of the L1 vertebral body(cm)	Combined	3.69 ±0.33 [SD]	P value 0.037
	Male	3.85±0.26[SD]	
	Female	3.54±0.32[SD]	
Midline anterior abdominal wall subcutaneous tissue fat (APASF)mm	Combined	11.49 ±7[SD]	P value 0.016
	Male	7.57±2.93[SD]	
	Female	15.01±7.87[SD]	

total atrophy in nine patients (47.4%). MPD was gross diffuse irregularly dilated in 10 patients (36.8%) (Figure 3), mild diffuse irregularly dilated in 11 (57.9%) patients, and normal in one patient (5.3%).Ten patients (52.6%) withTPL had MPD calculi (Figure3). Six patients (31.6%) withTPL were associated with malabsorption syndrome with dilated small bowel loops (Figure 2). One patient (5.3%) with TPL had associated hepatocellular carcinoma, one patient (5.3%) had pancreatic divisum, and another patient (5.3%) had intraductal pancreatic carcinoma. The cross-sectional imaging findings of the patients with TPL are shown in Table 1.

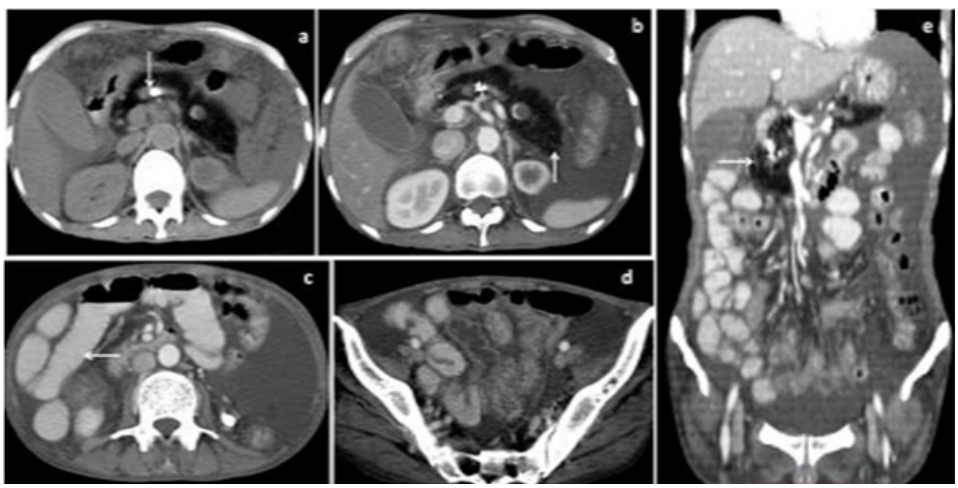

Figure 2.A 50-year-old male was a known patient with diabetes treated with oral hypoglycemic drugs who had steatorrhoea and increased frequency of stools and abdominal distension for 6 months. Axial non-contrast and post-contrast MDCT images (a & b) showed variable sizes of calculi in the main pancreatic duct with dilatation of MPD (↓arrow). Marked atrophied pancreatic parenchymal tissue was observed with excessive negative CT attenuating fatty tissue depositions in the whole extent of the pancreas (↑arrow). Axial post-contrast CT images (c & d) showed moderate ascites with fluid-filled small bowel loops and mild small bowel wall edema(←arrow). Coronal constructed CT scan image (e) showed the lipomatosis in the whole extent of the pancreas from head to tail (→arrow) with dilated small bowel loops).The findings were suggestive of TPL and malabsorption secondary to chronic pancreatitis and pancreatic ductal calculi.

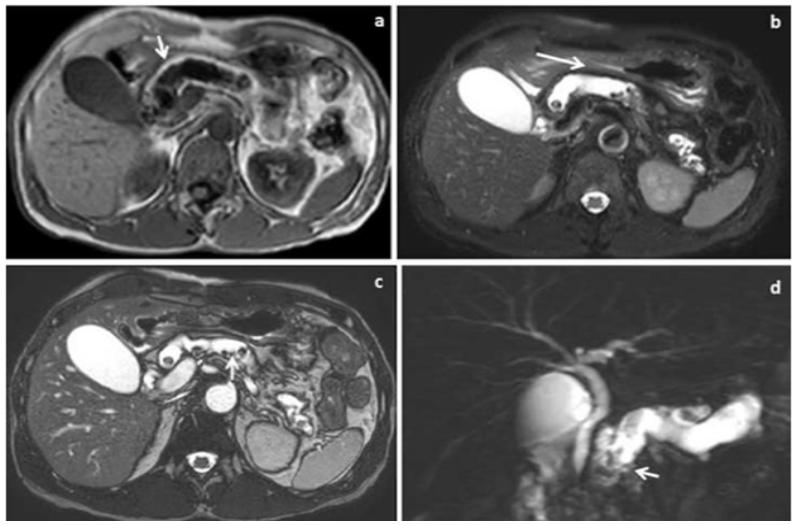

Figure 3.A 55-year-old male patient with recurrent upper abdominal pain. Axial T1W and fat-suppressed T2W images (a& b) show irregularly dilated MPD with multiple T2 hypointenseintraductal calculi and a thin rim of residual atrophied pancreatic tissue replacement with T1W hyperintense fatty tissue (↓ arrow) which get suppressed on fat-suppressed T2W image (→ arrow). Axial BTFE (balanced turbo field-echo sequence) image (c) showed the multiple hypointenseintraductal calculi (↑arrow) with irregularly dilated MPD and signal loss from the atrophied fatty replaced pancreatic parenchyma. Thick slab T2W_HASTE image (d) showed diffuse irregularly dilated MPD with narrowings (←arrow) and filling defects (↑arrow). The findings were suggestive of chronic calcific pancreatitis with TPL.

Volumetric analysis:

The mean volume of the lipomatous pancreas was 150.1±72.7 [SD]cm^3 with a minimum volume of 31.75 cm3 and a maximum of 337.45 cm^3.The mean latero-lateral diameter of the L1 vertebral body (LLL1) measured 3.69±0.33 [SD] cm. The mean AP diameter of midline anterior abdominal wall subcutaneous tissue fat (APASF) measured 11.49±7[SD] mm. The TPL significantly correlatedwith the patients' body habitus(L1 vertebral lateral diameter and APASF) with a P value of 0.05 using an independent sample ttest.Therewas no statistically significant difference (P=0.704) of TPL with pancreatic volume in accordance with the patients' sex, as shown in Table 1.

Clinical improvement:

All patients of pancreatic lipomatosis in this series were treated conservatively with the aim of treating pain, dietary deficiencies, chronic pancreatitis, and improvement of malabsorption.Oral pancreatic enzyme replacement therapy of modern pancreatin preparation (Pancreatin 10 x 200mg capsule daily) and lipase (25000-36000 IU twice daily) for 8 weeks.

Clinical improvement of the patient was assessed with the reduction of symptoms like steatorrhoea and patient weight gain. Eleven patients showed clinical improvement after enzyme replacement therapy, and eight patients did not show clinical improvement after therapy. One patient withTPL and, intraductal pancreatic neoplasia, and hepatic metastasis died after 3 months of treatment. Another patient withTPL and hepatocellular carcinoma also died after 2 months.

DISCUSSION:

TPL is an uncommon benign entity detected on imaging and typically presents with vague abdominal pain, abdominal discomfort, and steatorrhoea (3).

TPL leads to an increase in the weight and size of the pancreas. Uniform pancreatic enlargement is observed in the complete absenceof exocrine pancreatic tissues(10,11,12,13).USG sometimes fails to differentiate the echogenic lipomatous pancreas from the normal retroperitoneal fats(14).CT and MRIare reliable imaging techniques to demonstrate TPL.CT shows negative attenuating fatty components within the pancreas, while MRI scan shows hyperintense signal intensities of pancreatic lipomatosis in both T1W and T2W images and signal loss in out-phase images of chemical shift MRI imaging in comparison with in-phase images(15,16). The common differential diagnosis of total pancreatic lipomatosis is shown in Table2.

Table 2. Salient features of lesions resembling total pancreatic lipomatosis on cross-sectional imaging

	Total pancreatic lipomatosis	**Black-pigmented neuroendocrine tumor**	**Metastatic pancreatic melanoma**	**Pseudohypertrophy Lipomatosis of Pancreas**	**Pancreatic liposarcoma**	**Pancreatic teratoma**
Incidence -common in	diabetes, chronic	pancreatitis	Extremely rare Rare, 2% of	pancreatic tumor	rare condition with	an unknown etiology
Salient radiological features	-diffuse fatty replacement of pancreas -atrophied pancreatic parenchyma sparing the islets cells -sparing pancreatic ducts -evidence of chronic pancreatitis like parenchymal calcification, MPD calculi usually associated	-focal mass on CT , T1W hypo and T2W hyperintense on MRI scan -hypervascular enhancing mass -associated black pigmented Lymphnodes -close differential metastatic melanoma	-focal dark lesion on CT scan. -Hyper on T1W and hypointense on T2W on MRI -usually shows peripheral post contrast enhancement with low attenuating central area.	enlargement of pancreas due to increased fat -focal or diffuse pancreatic enlargement -not associated with diabetes, obesity or pancreatitis. -difficult to differentiate from total pancreatic lipomatosis	containing fat in pancreatic mass. -CT HU values higher than normal fat and benign lipomatosis -Larger and worst borders delimitation -Solid and internal cystic areas with thick septa, -shows heterogenous post contrast enhancement	-contains variable tissues, such as fat, fat/liquid, hair/liquid -cystic usually mature teratoma -solid common with immature teratoma - calcifications

TPL with atrophied pancreatic parenchyma has been observed in patients with chronic pancreatitis resulting from pancreatic duct obstruction by intraductal calculi or pancreatic carcinoma(17). Table 3 shows a review of available literature on TPL in the last decade.

Usually,TPL shows complete fatty replacement of

Table 3. Literature review of total pancreatic lipomatosis in last decade

Series/ year	**Number of case**	**Age / mean age(yrs)**	**Sex/ Sex ratio**	**Imaging done**	**Clinical presentation**	**Salient CT/MRI findings**	**Associated findings**	**Treatment / outcome**
Anand R et al./2011(2)	1	25	F	CT	-Steatorrhoea -decreased appetite	-Total pancreatic lipomatosis -MPD calculus -prominent small bowel loops with thickened walls	-	-
Sandhu G S etal./2017(18)	1	43	F	CT	Loose motion, loss of appetite, weight loss	-Intraductal calculi -Total pancreatic lipomatosis -Prominent small bowel loops with thickened walls	-	Treated conservatively -not improved
Naranje P. et al/2017(19)	1	31	M	CT	Chronic abdominal pain, progressive weight loss	-Multiple intraductal calculi -Dilated MPD -Total pancreatic lipomatosis	-	Conservatively with pancreatic enzyme replacement therapy

Table 3. Literature review of total pancreatic lipomatosis in last decade

Series/ year	Number of case	Age / mean age(yrs)	Sex/ Sex ratio	Imaging done	Clinical presentation	Salient CT/MRI findings	Associated findings	Treatment / outcome
Mandavdhare H S et al./2017(20)	1	18	M	CT	Recurrent cough -steatorrhoea -weight loss	-Total pancreatic lipomatosis -No MPD calculus -Bronchiectasis in both lung fields	Increased sweat chloride level (79mmol/L)	Conservatively with pancreatic enzyme replacement therapy
Kumar R et al./2017 (21)	1	60	F	CT and MRI	Recurrent cough -steatorrhoea -weight loss	-Total pancreatic lipomatosis -No MPD calculus -Bronchiectasis in both lung fields	Increased sweat chloride level (79mmol/L)	Conservatively with pancreatic enzyme replacement therapy
Nassiri S. et al/2020 (22)	1	42	M	CT	-Increased bowel frequency -Steatorrhoea	-Total pancreatic lipomatosis -No MPD calculus	Celiac disease	-Pancreatic enzyme replacement -Improved
Present study	19	39.37± 14.09[SD]	M:F= 1:1.1	CT=10 MRI=9	-10 patients had recurrent abdominal pain -Four patients had abdominal discomfort and distension - Five patients had abdominal discomfort and steatorrhoea	-Total pancreatic parenchymal atrophy in 10 patients and near total atrophy in 9 patients -Gross diffuse irregularly dilated MPD in seven patients -mild diffuse irregularly dilated in 11patients -Normal MPD in 1 patient -15patients had MPD calculi -Six patients had dilated small bowel loops with thickened walls. -mean pancreatic volume was 150.1± 72.7 [SD]cm3	-10 patients chronic calcific pancreatitis, - Three patients diabetic mellitus -Three patients indeterminate -One patient with pancreatic divisum -One patient intraductal pancreatic carcinoma -One patient hepatocellular carcinoma	-Treated conservatively with Pancreatic enzyme replacement therapy -11 showed various degree of clinical improvement. -Eight patients not showed clinical improvement -One patient with intraductal pancreatic carcinoma and hepatic metastasis died after 3 months -One patient with hepatocellular carcinoma died after 2 months

pancreatic parenchyma with only visualization of the pancreatic duct and peribiliary area. However, fatty infiltration of the pancreas usually varies from focal,diffuse pattern to near-total fatty replacement of the pancreas with more preservation of pancreatic parenchyma as compared with total pancreatic lipomatosis(6).

Limitations:Because of the small study sample in our study, a larger study sample size is needed to confirm the added value of CT and MRI findings in the diagnosis of TPL and associated complications and to detectthe possible

underlying causes of total pancreatic lipomatosis.

CONCLUSIONS:

CT or MRI can reliably diagnose and exclude pancreatic lipomatosis and may be able to find a possible cause of lipomatosis. Recognition of total pancreatic lipomatosis by cross-sectional imaging, either CT or MRI scan, is important so that the treatment of malabsorption in the form of dietary modification (low-fat diet) with modern pancreatin preparation and lipase supplementation and early diagnosis might improve the symptoms.

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CONFLICTING INTEREST :

The authors have no conflicts of interest to declare related to this work.

ETHICAL STANDARDS:

We confirm that this manuscript has not been published elsewhere and it not
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AUTHORS CONTRIBUTION:

All authors have contributed significantly and approve the content of the
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