

## Study of Pancreatic Steatosis in Diabetics Patients Using Multi detectors Computed Tomography

Alaa Ibrahim<sup>1</sup>, Caroline Edward<sup>2</sup>, Ahlam Asiri<sup>1</sup>, Hamid Osman<sup>1</sup>, K. Sherrif<sup>1</sup>, Yassen<sup>1</sup>

<sup>1</sup>Taif University College of applied medical science, Taif, P O box 2425 Post code-2194, KSA

<sup>2</sup>Sudan University of Science and Technology College of medical radiological Science, Khartoum, Sudan.

### \*Corresponding author

*Alaa Ibrahim*

### Article History

*Received: 10.09.2017*

*Accepted: 16.09.2017*

*Published: 30.09.2017*



**Abstract:** The accumulation of fat in the pancreas has been referred to as fatty infiltration, fatty pancreas, fat non-alcoholic pancreatic disease and pancreatic steatosis. Pancreatic steatosis is the best description of fat accumulation in the pancreatic gland without fat replacement, and this term also describes the possibility that the fat accumulation is a reversible process. Pancreatic steatosis is an increasing problem due to the increasing incidence of obesity, aging, diabetes and metabolic syndrome. We aim to evaluate the diagnostic capacity of abdominal computed tomography in the assessment of pancreatic steatosis in diabetic patients. High-resolution MDCT scans of 44 patients (26 diabetic patients) that underwent CT examinations of the abdomen CT was performed with conventional sequences of unenhanced examination. Attenuation in CT of the pancreas and spleen were measured in Hounsfield units and scored by two blinded radiologist. The study shows the age group distribution in the diabetic patients with significant different in the age group between (60 years and more) with p value (.054). The percentage between the male and female were no significant differences in respect to gender in the presence of diabetes. the main findings of this study for the diabetic patients images comparing to the control group were found that, highly significant CT number ( $p=0.000$ ) and hypodense signal compared to spleen with significant value ( $p=.054$ ) distribution of the pancreas head CT number with highest percentage in the diabetic patient in (25 HU) compared to highest percentage of non-diabetic patient in (35 HU). and no significant different in the other part of the pancreas. Pancreatic steatosis is a common, benign pancreatic condition observed in clinical practice. The study concluded that axial CT scan is considered as an appreciable radiological method for characterizing the pancreas structure using CT number (Hounsfield). Pancreatic steatosis is not due to the presence of diabetes but is highly associated with the metabolic syndrome.

**Keywords:** MDCT, diabetes, obesity, pancreatic Steatosis

## INTRODUCTION

Pancreatic steatosis referred to the accumulation of fat in the pancreatic gland has been referred to using various synonyms, such as pancreatic lipomatosis, fatty replacement, fatty infiltration, fatty pancreas, lipomatous pseudohypertrophy, non-alcoholic fatty and pancreatic disease [1]. Pancreatic steatosis and fat replacement of the pancreas are the most frequent benign pathologic conditions of the adult pancreas [2-4]. Classically, the phenomenon causes an increasing hypodensity of the pancreas on CT and a typical hyperechogenicity on ultrasound (US) examination.

Accumulation of fat in the pancreas is increasingly recognized as a cause of pancreatic dysfunction and of the death of nonadipocytes through

lipoapoptosis, ultimately leading to diabetes [5-10]. Fatty infiltration of an organ, which occurs in patients with nonalcoholic fatty liver disease, is known to trigger inflammatory cascades [11,12].

Fatty infiltration of the pancreas is generally a diffuse process occurring uniformly throughout the gland and occurs most frequently in the elderly and obese populations [13,14]. However, fatty infiltration may be unevenly distributed in the pancreas and can be confined to 1 region of the pancreas (focal fatty infiltration) [15-20]. Similarly, fatty infiltration may spare regions of the pancreas (focal fatty sparing) that is analogous to focal fatty sparing in the liver [21,22].

Focal fatty infiltration can mimic a hypoattenuating mass on CT examinations [17], and

fatty sparing of the pancreatic head can appear as a "pseudomass [22]. These are both normal variants and should not be confused with a neoplasm or other pathological processes. Alternatively, hypoattenuating neoplasms in the pancreatic head should not be mistaken as focal fatty infiltration. Computed tomography (CT) may be a more practical, noninvasive imaging modality for the pancreas because it is widely available and is performed with a short acquisition time [23].

CT shows fatty infiltration in an organ as a decrease in attenuation. However, because the CT attenuation can be affected by other components such as manganese [24], an abundance of manganese in the pancreas could mask a change in CT attenuation caused by fatty infiltration [25]. Similar concerns were raised for the quantification of hepatic fat because iron deposition may prevent an accurate assessment of the fat content [26].

Focal fatty infiltration is often most prominent in the anterior aspect of the head of the pancreas, whereas the posterior aspect of the head of the pancreas and the area around the common bile duct tend to be spare [15,20,21]. Focal fatty infiltration is often stable on follow-up CT examination [15]; however, the extent of involvement may progress on serial scans [21]. Focal fatty infiltration in the pancreas is seen as a region of decreased attenuation in the pancreas on noncontrast or postcontrast CT [17].

Computed tomographic attenuation within the focal fatty infiltration may be negative and show apparent fat attenuation [20]. In these cases, diagnosis of focal fatty infiltration can be supported by measuring CT attenuation. However, when focal fatty infiltration is mild, the region may not show apparent fat attenuation and may simulate a hypoattenuating mass on CT [18]. In such cases, differentiation of tumor and focal fatty infiltration can be difficult.

#### **Ct findings to help differentiate focal fatty infiltration from pancreatic neoplasm**

On CT, the area of hypoattenuation by focal fatty infiltration preserves the normal pancreatic contour and lobular appearance of the parenchyma [20]. There are no associated features of malignancy; for example, the pancreatic and bile ducts are not dilated, the adjacent vessels are not displaced or invaded, and there is no associated adenopathy in patients with focal fatty infiltration [17, 18, 21]. The sharp interface from the embryological ventral pancreas that extends in the craniocaudal direction, well visualized on sagittal-reformatted CT images, also helps to distinguish focal fatty infiltration from a pathological process [15].

The uncinata process maintains its normal configuration in patients with focal fatty sparing. However, in some cases, it is difficult or impossible to differentiate focal fatty infiltration from a non-border-deforming neoplasm of the pancreas on CT [21]. Comparison of fatty pancreas by sonography and abdominal CT.

To determine correlations between metabolic parameters and fatty pancreas appearing on CT finding pancreas and those found by sonography, the difference between the averages Hounsfield Units (HU) from mean pancreas HU to mean spleen HU was calculated. If the difference was  $\leq -5$  or lower the subjects were classified into the fatty pancreas group on CT finding, and others were classified into the non-fatty pancreas group. A comparison of metabolic syndrome factors and body measurement factors found no difference in visceral fat, lipid profile, and liver chemistry between the two groups, based on CT findings [27]. Pancreatic fat density assessed by HU values based on unenhanced MDCT images also decreased according to the duration of diabetes [28].

The pancreatic HU values were significantly different between groups: They were lowest in the  $T2D \geq 5Y$  group, intermediate in the  $T2D < 5Y$ , and  $T2D$ -new groups and highest in the Normal group, indicating greater fat accumulation in patients with a longer duration of T2D compared with those with a shorter duration of T2D or with the Normal group [28]. There was significant difference of  $HUP-s$  between the Normal and the  $T2D < 5Y$  or  $T2D \geq 5Y$  groups. When the pancreatic-to-splenic HU ratio ( $HUP-s$ ) was used, similar difference was found between the groups [28].

More than 90% of population would have less than 5% of fat infiltration in pancreas [29]. The etiology of pancreatic steatosis varies from congenital related to acquired conditions. However, it can be classified into 4 groups: obesity and metabolic syndrome; there are some clinical studies [30-34] regarded the patients who were diagnosed as fatty pancreas from endoscopic ultrasound, MRI or CT scan which demonstrated that high body mass index (BMI) and metabolic syndrome were associated with fatty pancreas (Odd Ratio (OR) 1.05-3.13 while nonalcoholic fatty liver showed a 14-fold correlation with pancreatic steatosis [35]. congenital syndromes such as cystic fibrosis, Shwachman-Diamond syndrome (which was a rare autosomal recessive disorders characterized by association of pancreatic exocrine insufficiency, due to fat infiltration and atrophy, bone marrow dysfunction and skeleton abnormalities) [36-40], and Johanson-Blizzard syndrome (a rare genetic disorder characterized by short stature, mental retardation, pancreatic insufficiency, sensorineural hearing loss, hypoplastic nasal alae, scalp defect and dental abnormalities) [41,42].

toxic agents and medications such as steroid therapy and gemcitabine chemotherapy which all of these medication related cases were reported case only [43,45,4] other rare causes such as reoviral infection [46], human immunodeficiency virus infection that could cause pancreatic steatosis through a combination of malnutrition-related and viral-related effects, and chronic hepatitis B infection[47].

Clinical Impact of Fatty Pancreas the prevalence of NAFLP was reported to be around 16% in Hong Kong Chinese population [32]. There was a statistically significant correlation between NAFLP and non-alcoholic fatty liver disease (NAFLD) (odds ratio [OR]=2.22; 95% confidence interval [CI], 1.88–2.57; P<0.001), central obesity (OR = 2.16; 95% CI, 1.85–2.52; P<0.001), age (OR = 1.05; 95% CI, 1.04–1.05; P<0.001), hypertriglyceridemia (OR = 1.32; 95% CI, 1.13–1.55; P=0.01), aspartate aminotransferase and alanine transaminase level elevation.

(OR = 1.29; 95% CI, 1.13–1.70; P=0.02), and diabetes mellitus (DM) (OR = 1.59; 95% CI, 1.30–1.95; P<0.001).Data suggest that fat accumulation in the pancreas may lead to similar processes as in non-alcoholic steatohepatitis (NASH). Patel *et al.* demonstrated in 2013 [48] that higher pancreatic fat content correlated with a higher grade of hepatic steatosis in patients with biopsy-proven NAFLD, but did not correlate with body mass index (BMI) or DM. This study also demonstrated no difference in the distribution of fatty content among the pancreatic portions (head, body, and tail). Although pancreatic steatosis was reported as a clinical manifestation of metabolic syndrome, other research indicates that this condition might lead to beta-cell dysfunction, causing DM.

#### Importance of study

This study is important to have a reliable, noninvasive method for quantification of pancreatic fat by using unenhanced multidetectors computed tomography for abdomen.

#### The objectives

The objectives of this manuscript were to evaluate the diagnostic capacity of abdominal computed tomography in the assessment of pancreatic steatosis in diabetic patients.

### MATERIALS AND METHODS

#### Samples

This study included 44 patients (26 diabetic Pt) that underwent CT examinations of the abdomen CT was performed with conventional sequences of unenhanced examination.

#### CT Positioning

All the patients lie supine on the examination couch. The body is adjusted so that the midsagittal line is perpendicular to the couch and the horizontal alignment light passes through the xiphoid. Straps and foam pads are used for immobilization.

#### CT Protocols and Techniques

CT was performed by using a (General electric GE Medical system, 128 detectors row scanner). The scanning and reconstruction parameters included tube voltage, 120 kVp; effective tube current-time product, 200 mAs; collimation, 16 × 1.5 mm; rotation speed, 0.5 second; pitch, 1.25; section thickness, 5 mm; and reconstruction interval, 4 mm. The conventional CT abdomen Protocols are selected to produce the scout images in the two planes ( Lateral , AP “anterior-posterior”) Transverse images of the abdomen were obtained during the unenhanced phase and no oral or intravenous contrast was used .

A Spiral Scan Mode are used to avoid the Motion Artifacts from the involuntary movement of the abdominal organs The scan is performed with breath hold ( suspended expiration ) and cover the abdominal region ( from bases of lungs to iliac crest ).

#### METHOD OF EVALUATION

The data were collected from CT images using PACS (Picture archiving and communication system) from radiology measured the CT number of the pancreas and spleen.

#### CT analysis

All CT imaging was evaluated in the non-contrast phase by two blinded radiologists. Fatty infiltration (i.e. steatosis) of the pancreas, and spleen was assessed by attenuation, which was measured in Hounsfield units (HU). Pancreatic attenuation was measured in three ROIs with areas of 1.0 cm<sup>2</sup> in three different sections head, body and tail of the pancreas; CT attenuation in the spleen was measured The data were collected on the check lists analyzed using the crosstabs frequency tables of statistical computer program ( SPSS ).

CT images were acquired from normal and diabetic patient with standard clinical abdominal CT protocols utilizing a multi slice ct scanner. For diagnosis of the steatosis pancreas , it will appear hypodense compared with the spleen on CT scan ( less than normal in CT number ) .The difference between pancreatic and splenic attenuation and the pancreas-to-spleen attenuation ratio were calculated Samples are evaluated according to the age group and the percentage of the diabetes in the male and female .

### RESULTS

**Table-1: Distribution of Age groups by diabetic patient Status**

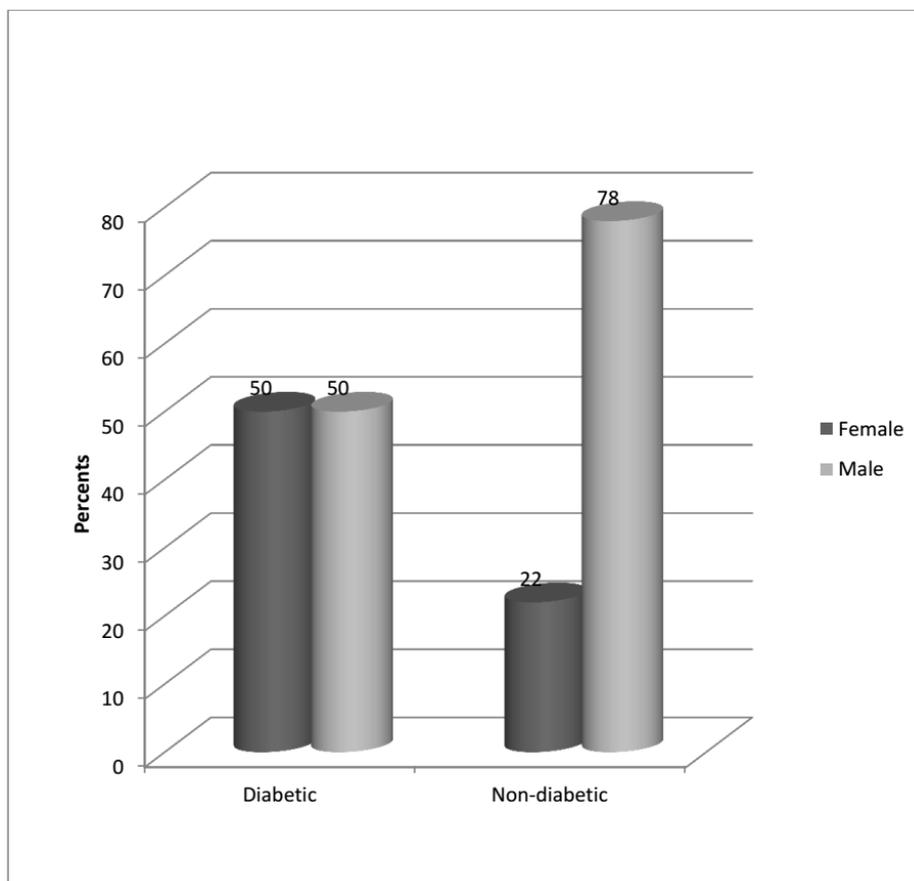
		Patient status		Total	p
		Diabetic NO. %	non diabetic NO. %		
Age groups	< 50 years	6 23.1%	10 55.6%	16 36.4%	.054
	50 - <60 years	8 30.8%	5 27.8%	13 29.5%	
	60 years and more	12 46.2%	3 16.7%	15 34.1%	
Total		26 100.0%	18 100.0%	44 100.0%	

Table 1: shows the age group distribution in the diabetic patients with significant different in the age group between (60 years and more) compared to non-

diabetic patients with significant different in the age group between (<50 years).

**Table-2: Distribution of gender by diabetic patient status**

		patient state		Total	p
		Diabetic NO. %	non diabetic NO. %		
sex	female	13 50.0%	4 22.2%	17 38.6%	.063
	Male	13 50.0%	14 77.8%	27 61.4%	
Total		26 100.0%	18 100.0%	44 100.0%	



**Fig-2: shows the distribution of gender in the diabetic patients**

Table 2 and Fig.2 shows the distribution of gender in the diabetic patients compared to non-diabetic patients

and there is no significant different between the male and female.

**Table-3: Distribution of pancreas head CT number by measurement the density (HU) for diabetic patient status**

		patient state		p
		Diabetic NO. %	non diabetic NO. %	
pancreas head CT number	25 HU	12 46.2%	1 5.6%	0.000
	30 HU	3 11.5%	5 27.8%	0.000
	35 HU	11 42.3%	12 66.7%	0.000
Total		26 100.0%	18 100.0%	.

Table3: shows the distribution of the pancreas head CT number with highest percentage in the diabetic

patient in (25 HU) compared to highest percentage of non-diabetic patient in (35 HU).

**Table-4: Distribution of pancreas body CT number by measurement the density (HU) for diabetic patient status**

		patient state		p
		Diabetic NO. %	non diabetic NO. %	
pancreas body CT number	30 HU	11 42.3%	7 38.9%	.476
	33 HU	9 34.6%	9 50.0%	.466
	35 HU	6 23.1%	2 11.1%	.707
Total		26 100.0%	18 100.0%	

Table 4: shows the distribution of the pancreas body CT number (density) with no significant different in the diabetic patients and non-diabetic patients.

**Table-5: Distribution of pancreas tail CT number by measurement the density (HU) for diabetic patient status**

		patient state		p
		Diabetic NO. %	non diabetic NO. %	
pancreas tail CT number	30 HU	10 38.5%	7 38.9%	.998
	33 HU	10 38.5%	7 38.9%	.998
	35 HU	6 23.1%	2 11.1%	.957
Total		26 100.0%	18 100.0%	

Table 5: shows the distribution of the pancreas tail ct number (density) with no significant

different in the diabetic patients and non-diabetic patients.

**Table-6: Distribution of spleen CT number by measurement the density (HU) for diabetic patient status**

		patient status		p
		Diabetic Count %	non diabetic Count %	
spleen CT number	40 HU	1 3.8%	3 16.7%	.346
	45 HU	8 30.8%	5 27.8%	.347
	50 HU	17 65.4%	10 55.6%	.266
Total		26 100.0%	18 100.0%	

Table 6: and Fig3 show the distribution of the spleen CT number by measurement the density and

there is no significant different between the diabetic patients and non-diabetic patients.

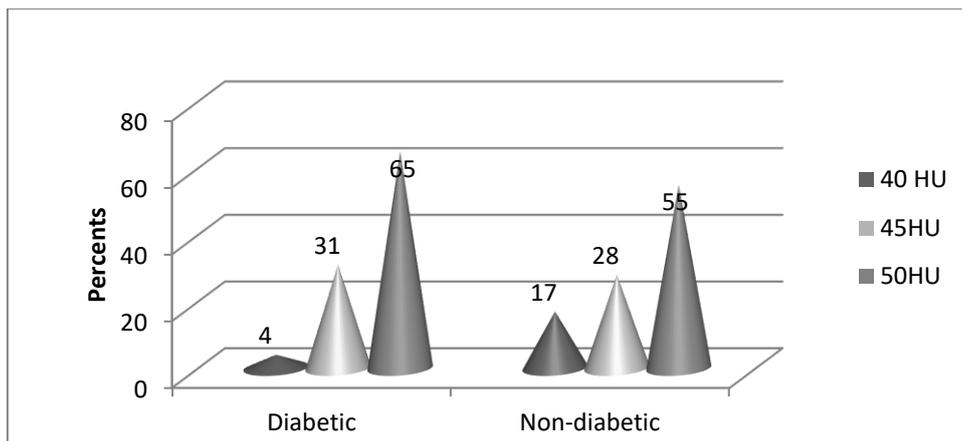


Fig-6: Distribution of spleen CT number by measurement the density (HU) for diabetic patient status

Table-7: Relation between pancreas head CT number (density) and spleen CT number (density) in the diabetic patients

		Spleen CT number				p	
		40 HU		45 HU			50 HU
		Count	%	Count	%	Count	%
Pancreas head CT number	25 HU	1	100.0%	00.0%		2	11.8%
	30 HU	00.0%		5	62.5%	7	41.2%
	35 HU	00.0%		3	37.5%	8	47.1%
Total		1	100.0%	8	100.0%	17	100.0%

Table 7: shows the relation between the pancreas head ct number and spleen CT number with significant different among the diabetic patients

Table-8: Relation between pancreas body CT number and spleen CT number in the diabetic patients

		Spleen CT number				P	
		40 HU		45 HU			50 HU
		Count	%	Count	%	Count	%
Pancreas body CT number	30 HU	0	0.0%	4	50.0%	7	41.2%
	33 HU	0	0.0%	2	25.0%	7	41.2%
	35 HU	1	100.0%	2	25.0%	3	17.6%
Total		1	100.0%	8	100.0%	17	100.0%

Table 8: shows the relation between the pancreas body ct number and spleen CT number with non-significant different among the diabetic patients.

Table-9: Relation between pancreas tail CT number and spleen CT number in the diabetic

		Spleen CT number			Total	P	
		40 HU	45 HU	50 HU			
		Count	%	Count	%	Count	%
Pancreas tail CT number	30 HU	00.0%		337.5%		741.2%	
	33 HU	1100.0%		337.5%		635.3%	
	35 HU	00.0%		225.0%		423.5%	
Total		1100.0%		8100.0%		17100.0%	

Table 9: shows the relation between the pancreas tail ct number and spleen CT number with non-significant different among the diabetic patients.

## CONCLUSION

Pancreatic steatosis is a common, benign pancreatic condition observed in clinical practice. Clinical knowledge of this condition is essential for gastroenterologists to be able to care for their patients. The study concluded that axial CT scan is considered as an appreciable radiological method for characterizing the pancreas structure using CT number (Hounsfield). Pancreatic steatosis is not due to the presence of diabetes but is highly associated with the metabolic syndrome.

## REFERENCES

- Smits MM, van Geenen EJ. The clinical significance of pancreatic steatosis. *Nat Rev Gastroenterol Hepatol.* 2011;8:169–177.
- Ozbulbul NI, Yurdakul M, Tola M. Does the visceral fat tissue show better correlation with the fatty replacement of the pancreas than with BMI. *The Eurasian journal of medicine.* 2010 Apr;42(1):24.
- Kim HJ, Byun JH, Park SH, Shin YM, Kim PN, Ha HK, Lee MG. Focal fatty replacement of the pancreas: usefulness of chemical shift MRI. *American Journal of Roentgenology.* 2007 Feb;188(2):429-32.
- Altinel D, Basturk O, Sarmiento JM, Martin D, Jacobs MJ, Kooby DA, Adsay NV. Lipomatous pseudohypertrophy of the pancreas: a clinicopathologically distinct entity. *Pancreas.* 2010 Apr;39(3):392.
- Unger RH, Zhou YT. Lipotoxicity of beta-cells in obesity and in other causes of fatty acid spillover. *Diabetes* 2001;50(Suppl 1):S118–S121.
- Pinnick KE, Collins SC, Londos C, Gauguier D, Clark A, Fielding BA. Pancreatic ectopic fat is characterized by adipocyte infiltration and altered lipid composition. *Obesity (Silver Spring)* 2008;16(3):522–530.
- Shimabukuro M, Higa M, Zhou YT, Wang MY, Newgard CB, Unger RH. Lipoapoptosis in beta-cells of obese prediabetic fa/fa rats. Role of serine palmitoyltransferase overexpression. *J Biol Chem* 1998;273(49):32487–32490.
- Shimabukuro M, Wang MY, Zhou YT, Newgard CB, Unger RH. Protection against lipoapoptosis of beta cells through leptin-dependent maintenance of Bcl-2 expression. *Proc Natl Acad Sci U S A* 1998;95(16):9558–9561
- Heni M, Machann J, Staiger H, Schwenzer NF, Peter A, Schick F, Claussen CD, Stefan N, Häring HU, Fritsche A. Pancreatic fat is negatively associated with insulin secretion in individuals with impaired fasting glucose and/or impaired glucose tolerance: a nuclear magnetic resonance study. *Diabetes/metabolism research and reviews.* 2010 Mar 1;26(3):200-5.
- Tushuizen ME, Bunck MC, Pouwels PJ, Bontemps S, Van Waesberghe JH, Schindhelm RK, Mari A, Heine RJ, Diamant M. Pancreatic fat content and  $\beta$ -cell function in men with and without type 2 diabetes. *Diabetes care.* 2007 Nov 1;30(11):2916-21.
- Farrell GC, Larter CZ. Nonalcoholic fatty liver disease: from steatosis to cirrhosis. *Hepatology* 2006;43(2 Suppl 1):S99–S112.
- McCullough AJ. Pathophysiology of nonalcoholic steatohepatitis. *J Clin Gastroenterol* 2006;40(Suppl 1):S17–S29
- Katz DS, Hines J, Math KR, Nardi PM, Mindelzun RE, Lane MJ. Using CT to reveal fat-containing abnormalities of the pancreas. *AJR. American journal of roentgenology.* 1999 Feb;172(2):393-6.
- Olsen TS. Lipomatosis of the pancreas in autopsy material and its relation to age and overweight. *APMIS.* 1978 Jul 1;86(1-6):367-73.
- Atri M, Nazarnia S, Mehio A, Reinhold C, Bret PM. Hypoechoic embryologic ventral aspect of the head and uncinat process of the pancreas: in vitro correlation of US with histopathologic findings. *Radiology.* 1994 Feb;190(2):441-4.
- Donald JJ, Shorvon PJ, Lees WR. A hypochoic area within the head of the pancreas—a normal variant. *Clin Radiol.* 1990;41:337-338.
- Hague J, Amin Z. Focal pancreatic lesion: can a neoplasm be confidently excluded? *Br J Radiol.* 2006;79:627-629.
- Isserow JA, Siegelman ES, Mammone J. Focal fatty infiltration of the pancreas: MR characterization with chemical shift imaging. *AJR Am J Roentgenol.* 1999;173:1263-1265.
- Marchal G, Verbeken E, Van Steenberghe W, Baert A, Lauweryns J. Uneven lipomatosis: a pitfall in pancreatic sonography. *Abdominal Imaging.* 1989 Dec 1;14(1):233-7.
- Matsumoto S, Mori H, Miyake H, Takaki H, Maeda T, Yamada Y, Oga M. Uneven fatty replacement of the pancreas: evaluation with CT. *Radiology.* 1995 Feb;194(2):453-8.
- Jacobs JE, Coleman BG, Arger PH, Langer JE. Pancreatic sparing of focal fatty infiltration. *Radiology.* 1994 Feb;190(2):437-9.
- Silverman PM, McVay L, Zeman RK, Garra BS, Grant EG, Jaffe MH. Pancreatic pseudotumor in pancreas divisum: CT characteristics. *Journal of computer assisted tomography.* 1989;13(1):140-1.
- Hoff FL, Gore RM. Pancreas: normal anatomy and examination techniques. *Textbook of*

- gastrointestinal radiology. Philadelphia, Pa: WB Saunders. 2000:1728-45.
24. Zinreich SJ, Kennedy DW, Malat J, Curtin HD, Epstein JI, Huff LC, Kumar AJ, Johns ME, Rosenbaum AE. Fungal sinusitis: diagnosis with CT and MR imaging. *Radiology*. 1988 Nov;169(2):439-44.
  25. Ly JN, Miller FH. MR imaging of the pancreas: a practical approach. *Radiol Clin North Am* 2002;40(6):1289-1306.
  26. Siegelman ES, Rosen MA. Imaging of hepatic steatosis. *Semin Liver Dis* 2001;21(1):71-80.
  27. Lee JS, Kim SH, Jun DW, Han JH, Jang EC, Park JY, Son BK, Kim SH, Jo YJ, Park YS, Kim YS. Clinical implications of fatty pancreas: correlations between fatty pancreas and metabolic syndrome. *World journal of gastroenterology: WJG*. 2009 Apr 21;15(15):1869.
  28. Lim S, Bae JH, Chun EJ, Kim H, Kim SY, Kim KM, Choi SH, Park KS, Florez JC, Jang HC. Differences in pancreatic volume, fat content, and fat density measured by multidetector-row computed tomography according to the duration of diabetes. *Acta diabetologica*. 2014 Oct 1;51(5):739-48.
  29. Lingvay I, Esser V, Legendre JL, Price AL, Wertz KM, Adams-Huet B, Zhang S, Unger RH, Szczepaniak LS. Noninvasive quantification of pancreatic fat in humans. *J Clin Endocrinol Metab* 2009; 94: 4070-6.
  30. Choi CW, Kim GH, Kang DH, Kim HW, Kim DU, Heo J, Am Song G, Park DY, Kim S. Associated factors for a hyperechogenic pancreas on endoscopic ultrasound. *World journal of gastroenterology: WJG*. 2010 Sep 14;16(34):4329.
  31. Sepe PS, Ohri A, Sanaka S, Berzin TM, Sekhon S, Bennett G, Mehta G, Chuttani R, Kane R, Pleskow D, Sawhney MS. A prospective evaluation of fatty pancreas by using EUS. *Gastrointestinal endoscopy*. 2011 May 31;73(5):987-93.
  32. Wong VW, Wong GL, Yeung DK, Abrigo JM, Kong AP, Chan RS, Chim AM, Shen J, Ho CS, Woo J, Chu WC. Fatty pancreas, insulin resistance, and [beta]-cell function: a population study using fat-water magnetic resonance imaging. *The American journal of gastroenterology*. 2014 Apr 1;109(4):589.
  33. Hu HH, Kim HW, Nayak KS, Goran MI. Comparison of fat-water MRI and single-voxel MRS in the assessment of hepatic and pancreatic fat fractions in humans. *Obesity (Silver Spring)* 2010; 18: 841-7.
  34. Lee JS, Kim SH, Jun DW, Han JH, Jang EC, Park JY, Son BK, Kim SH, Jo YJ, Park YS, Kim YS. Clinical implications of fatty pancreas: correlations between fatty pancreas and metabolic syndrome. *World journal of gastroenterology: WJG*. 2009 Apr 21;15(15):1869.
  35. Al-Haddad M, Khashab M, Zyromski N, Pungpapong S, Wallace MB, Scolapio J, Woodward T, Noh K, Raimondo M. Risk factors for hyperechogenic pancreas on endoscopic ultrasound: a case-control study. *Pancreas*. 2009 Aug 1;38(6):672-5.
  36. Feigelson J, Pécau Y, Poquet M, Terdjman P, Carrère J, Chazalotte JP, Ferec C. Imaging changes in the pancreas in cystic fibrosis: a retrospective evaluation of 55 cases seen over a period of 9 years. *J Pediatr Gastroenterol Nutr* 2000; 30: 145-51.
  37. Ruggiero A, Molinari F, Coccia P, Attinà G, Maurizi P, Riccardi R, Bonomo L. MRI findings in Shwachman diamond syndrome. *Pediatr Blood Cancer* 2008; 50: 352-4.
  38. Gana S, Sainati L, Frau MR, Monciotti C, Poli F, Cannioto Z, Comelli M, Danesino C, Minelli A. Shwachman-Diamond syndrome and type 1 diabetes mellitus: more than a chance association? *Exp Clin Endocrinol Diabetes* 2011; 119: 610-2.
  39. Sanklecha M, Balani K. Chronic pancreatic insufficiency-think of Shwachmann Diamond Syndrome. *Indian Pediatr*. 2012; 49: 417-8.
  40. Nakaya T, Kurata A, Hashimoto H, Nishimata S, Kashiwagi Y, Fujita K, Kawashima H, Kuroda M. Young-age-onset pancreatoduodenal carcinoma in Shwachman-Diamond syndrome. *Pathol Int* 2014; 64: 75-80.
  41. Hoffman WH, Lee JR, Kovacs K, Chen H, Yaghmai F. Johanson-Blizzard syndrome: autopsy findings with special emphasis on hypopituitarism and review of the literature. *Pediatr Dev Pathol* 2007; 10: 55-60.
  42. Godbole K, Maja S, Leena H, Martin Z. Johanson-blizzard syndrome. *Indian Pediatr*. 2013; 50: 510-2.
  43. Makay O, Kazimi M, Aydin U, Nart D, Yilmaz F, Zeytinlu M, Goker E, Coker A. Fat replacement of the malignant pancreatic tissue after neoadjuvant therapy. *Int J Clin Oncol* 2010; 15: 88-92.
  44. Lin WC, Chen JH, Lin CH, Shen WC. Rapidly progressive pancreatic lipomatosis in a young adult patient with transfusion-dependent myelodysplastic syndrome. *J Formos Med Assoc* 2007; 106: 676-9.
  45. Oliveira NM, Ferreira FA, Yonamine RY, Chehter EZ. Antiretroviral drugs and acute pancreatitis in HIV/AIDS patients: is there any association? A literature review. *Einstein (Sao Paulo)*. 2014 Mar;12(1):112-9.

46. Walters MI, Leak PJ, Joske RA, Stanley NF, Perret DH. Murine infection with reovirus: III. Pathology of infection with types 1 and 2. *British journal of experimental pathology*. 1965 Apr;46(2):200.
47. Sasaki M, Nakanuma Y, Ando H. Lipomatous pseudohypertrophy of the pancreas in a patient with cirrhosis due to chronic hepatitis B. *Pathology international*. 1998 Jul 1;48(7):566-8.