

## Review Article

**Review on pancreatic steatosis detection by imaging modalities**Alaa Ibrahim<sup>1</sup>, Caroline Edward<sup>2</sup>, Ahlam Asiri<sup>1</sup>, H. Osman<sup>1</sup>, K. Sherrif<sup>1</sup>, Ali Yasen<sup>3</sup><sup>1</sup>Taif University College of applied medical science P O box 2425 Post code 21944, KSA Taif<sup>2</sup>Sudan University of Science and Technology College of medical radiological Science Khartoum Sudan<sup>3</sup>Taif University, Faculty of Medicine, post code 21944**\*Corresponding author**

Alaa Ibrahim

Email: [hamidssan@yahoo.com](mailto:hamidssan@yahoo.com)

**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 and aging this review study aimed to review article is to summarize the author's articles about the pancreatic steatosis. And to review the clinical significance of pancreatic steatosis by using various imaging modalities. Authors discussed and illustrated the various radiological modalities that had been used to study quantification of pancreatic fat. Such as ultrasound, computed tomography and magnetic resonance imaging. Several studies suggested that the association of fat accumulation in the pancreas with obesity, diabetes and metabolic syndrome. The study concluded that axial CT scan is considered as an appreciable radiological method for measuring the pancreas size and characterizing its structure using CT number (Hounsfield). The study also revealed that the pancreas size and CT number had significant relations with age and other body habits us.

**Keywords:** RVIEW, MDCT, MRI, pancreatic Steatosis.

**INTRODUCTION**

Pancreatic steatosis (PS) is the fatty replacement of pancreatic parenchyma, being often associated with obesity and aging. Similar to this condition in pancreas, any excessive lipidic deposition in the liver tissue are referred to as nonalcoholic fatty liver disease (NAFLD) [1].

The accumulation of fat in the pancreatic gland has been referred to different terminologies, such as pancreatic lipomatosis, fatty replacement, fatty infiltration, fatty pancreas, lipomatous pseudo hypertrophy, non-alcoholic fatty pancreatic disease and pancreatic steatosis. According to the well-quality paper of Smits et al [2].

Authors believe that pancreatic steatosis is the best description of fat accumulation in the pancreatic gland without fat replacement, and this synonyms also describes the possibility that fat accumulation is a reversible process. Accumulation of fat in the pancreas

is increasingly recognized as a cause of pancreatic dysfunction and of the death of non adiposities through lip apoptosis, ultimately leading to diabetes [3, 8].

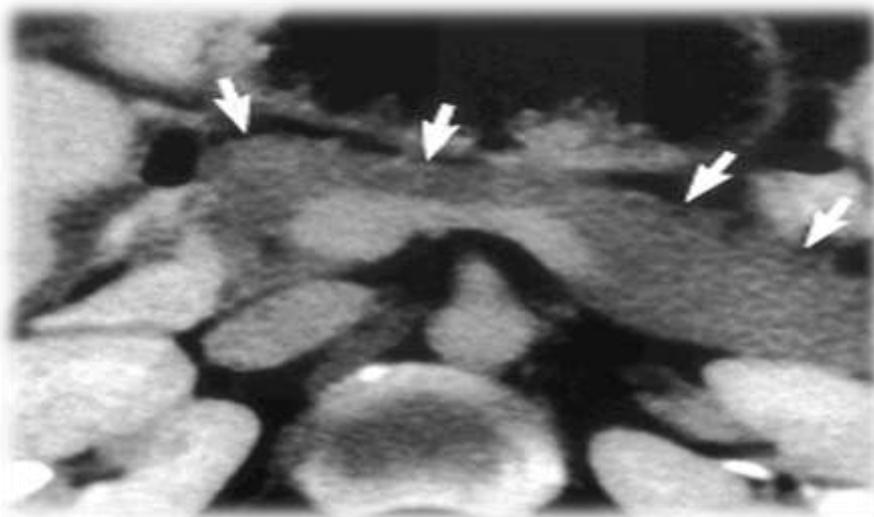
Fatty infiltration of the pancreas is generally a diffuse process; however, it may be unevenly distributed in the pancreas. Focal fatty infiltration of the pancreas is usually most prominent in the anterior aspect of the head of the pancreas and seen as a region of decreased attenuation on computed tomography and may simulate pancreatic neoplasm [9].

Focal fatty infiltration can mimic a hypoattenuating mass on CT examinations [10]. The morphology of the pancreas was qualitatively evaluated and categorized into four patterns: normal pancreas, atrophy of the pancreas without fatty replacement, partial fatty replacement of the pancreas, and subtotal or complete replacement of the pancreas by hypertrophic fatty tissue. the pattern of pancreatic fatty replacement was further visually evaluated at four pancreatic regions

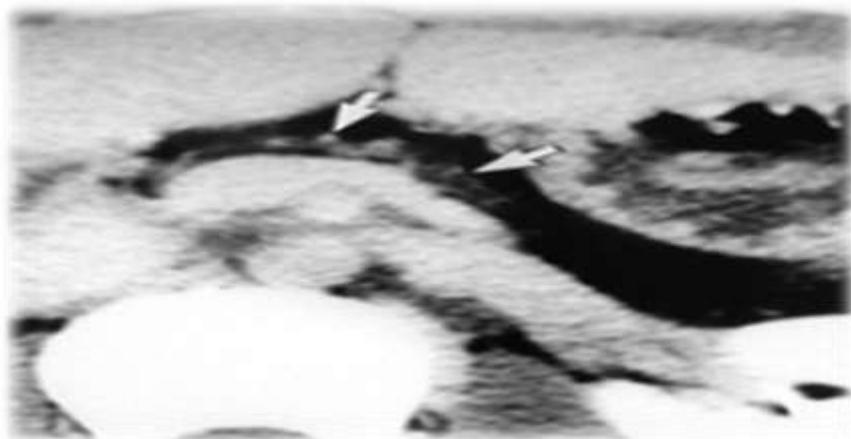
(head, neck, body, and tail) into Grade 0 corresponded to a normal appearance of a given pancreatic region, without fatty replacement (Fig1); grade 1 corresponded to fatty replacement that involved less than 25% of a given pancreatic region, grade 2 corresponded to fatty replacement that involved 25-50% of a given pancreatic region (Fig2); grade 3 corresponded to fatty replacement that involved 50-70% of a given pancreatic regions; and

grade 4 corresponded to fatty replacement that involved more than 75% of a given pancreatic region (Fig3). The degree of fatty replacement of the pancreas was correlated with the functional status of the pancreas [11].

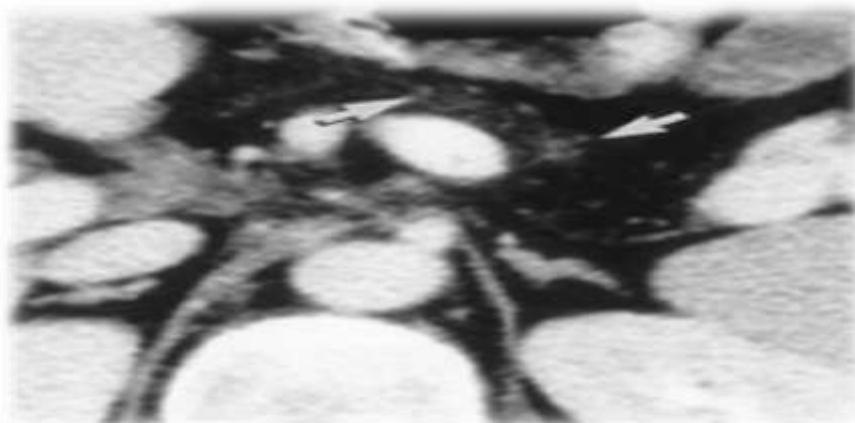
Fatty infiltration of the pancreas has been also reported in advanced cases of cystic fibrosis [11].



**Fig-1 :** a 28-year-old man. CT scan shows a normal sized pancreas without fatty replacement (Grade 0 for the four pancreatic regions) [11].



**Fig-2:** Cystic Fibrosis in a 16-year-old male adolescent. CT scan shows partial fatty replacement of the pancreas, residual glandular pancreatic tissue (arrows) is seen (grade 2 for the neck and body of the pancreas, which are seen at this level), patient had type 1 diabetes mellitus [11].



**Fig-3: Cystic Fibrosis in a 25 year-old woman .CT scan shows subtotal fatty replacement of the pancreas ,tiny areas of residual glandular pancreatic tissue (arrows)are seen (grade 4for the neck and body of the pancreas ,which are seen at this level) patient had type 1 diabetes mellitus[11].**

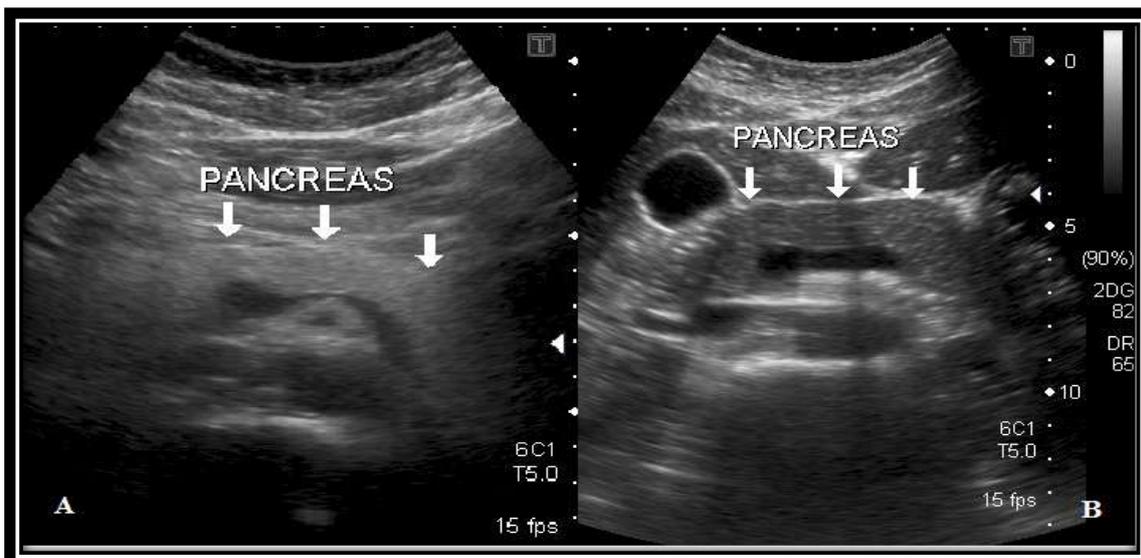
The fatty infiltration of the pancreas was first described in 1993 by Ogilvie that reported 17% pancreatic fat storage for obese cadavers as compared with 9% for lean ones. Pancreatic steatosis (PS) is the best description for fat accumulation in the pancreatic gland without fat replacement [12].The PS is a fatty replacement of pancreatic parenchyma, being often associated with obesity and aging [13].

The PS is generally a diffuse process occurring uniformly, but may be unevenly distributed in the pancreas and can be confined to region of the pancreas (focal fatty infiltration), being classified as: type 1a: preferential fatty replacement of head; type 1b: preferential fatty replacement of head, neck and body; type 2a: preferential fatty replacement of head and uncinate process; type 2b: fatty replacement of most of pancreas regions except the peribiliary region. Focal PS is a disorder without clinical significance. However, this condition may simulate a mass-like lesion [14]. Various imaging modalities including ultra sonography (US) [15, 16]. Or magnetic resonance (MR) imaging [7, 8, 17, 18] have been used to study quantification of pancreatic fat. However, US examination can be of limited value in the evaluation of the entire pancreas

due to the location of the pancreas behind the stomach or colon [19]. In addition, US do not provide reliable quantitative information [20].

Even though MR imaging (including MR spectroscopy) has the potential to allow quantification of fat content, fat quantification of the pancreas is far more challenging than that for the liver [8, 21, 18] The pancreas is prone to MR chemical shift artifacts because of its relatively small size, irregular morphology, and location in the middle of the abdomen surrounded by visceral fat [8, 15, 16] Thus, 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 [19].

In ultrasound The PS was diagnosed when there was an increase in echogenicity of the pancreas compared with the kidney. As the pancreas echogenicity could not be compared directly with the kidney in the same window, the examiner compared the difference between pancreatic echogenicity and the renal echogenicity in different window, and between hepatic and pancreatic echogenicity, to obtain an objective pancreato-renal echo contrast (Fig4)[1].



**Fig-4: A: diffuse steatosis pancreatic and B:normal pancreas using ultrasound scan[1].**

The NAFLD diagnostic criteria included characteristic echo patterns of hepato-renal echo contrast, bright liver, deep attenuation, and vascular blurring (Fig5). The Grading of NAFLD was classified as: grade I (mild): increased hepatic echogenicity with visible periportal and diaphragmatic echogenicity; grade

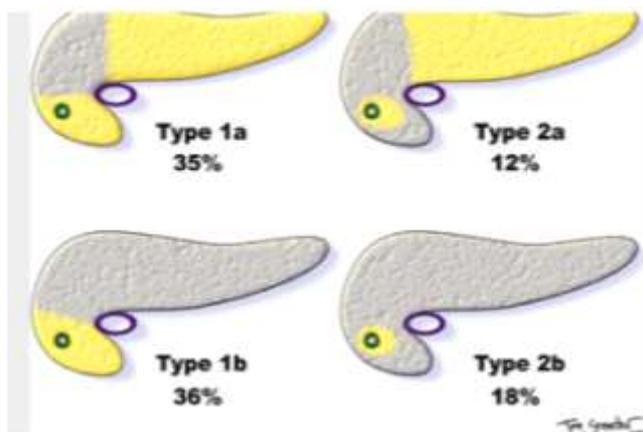
II (moderate): increased hepatic echogenicity with imperceptible periportal echogenicity, without obscuration of diaphragm; grade III (severe): increased hepatic echogenicity with imperceptible periportal echogenicity and obscuration [22].



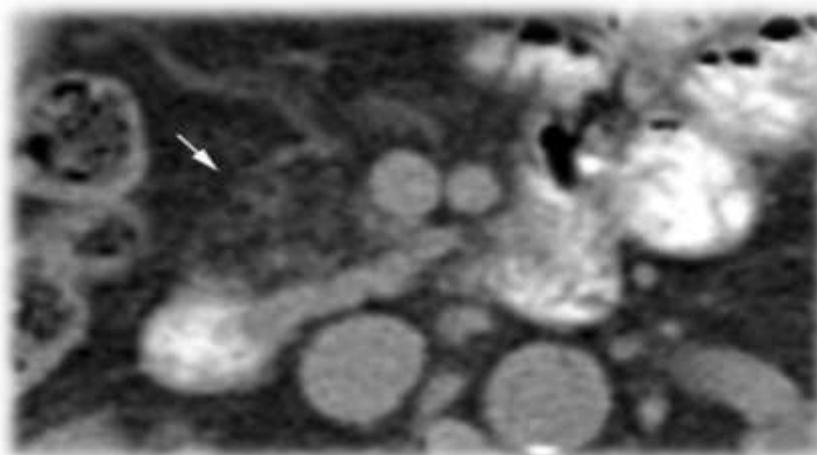
**Fig-5: A: steatosis liver and B: normal liver using ultrasound scan[1].**

Fat accumulation in pancreas is significantly correlated to NAFLD. With the following characteristics: mild PS and mild NAFLD, moderate PS and moderate and severe NAFLD (P and between severe PS and moderate and severe NAFLD [1].

The PS can be classified as diffuse or as focal fatty infiltration, this latter was classified as: type1a: preferential fatty replacement of head; type 1b: preferential fatty replacement of head, neck and body; type 2a: preferential fatty replacement of head and uncinate process; type 2b: fatty replacement of most of pancreas except peribiliary region [14].



**Fig-6: Uneven fatty replacement of the pancreas. Drawings illustrate the four different patterns of fatty replacement of the pancreas (gray areas). The percentage of cases of uneven pancreatic lipomatosis represented by each type is also indicated [14].**



**Fig-7: CT scan shows type 1a fatty replacement of the pancreatic head (arrow) [14]**

However, they subdivided the PS into mild (grade I), moderate (grade II), and severe (grade III), according with Lee et al criteria[15]. The four echogenicity grades of PS: Non-fatty pancreas, pancreatic echogenicity is equal to renal cortical echogenicity; Grade I: Mild fatty pancreas, pancreatic echogenicity is definitely lower than retroperitoneal fat; Grade II: Moderate fatty pancreas, pancreatic echogenicity is slightly lower than retroperitoneal fat; and Grade III: Severe fatty pancreas, pancreatic echogenicity is equal to retroperitoneal fat[15].

Fatty infiltration of the pancreas is relatively common condition and is often incidentally identified on abdominal computed tomographic (CT) scans [23]. Fatty infiltration is also known as adipose atrophy, fatty replacement, and lipomatosis of the pancreas [24, 25, 13]. 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 [23, 25]. However, fatty infiltration may be unevenly distributed in the pancreas and can be confined to 1 region of the pancreas (focal fatty infiltration)[26,27,10,28,29,30]. Similarly, fatty infiltration may spare regions of the pancreas (focal fatty sparing) that is analogous to focal fatty sparing in the liver [31,32]. The sonographic[26,27,29,31], CT[30,31,32],and magnetic resonance imaging (MRI) findings [10,28,31], of focal fatty infiltration and focal fatty sparing of the pancreas.

Computed tomography is accurate in detecting macroscopic fat. However, for lesions containing both fatty and non fatty tissue within a voxel, CT is less accurate in revealing microscopic fat deposits [28].

For focal nodular fatty infiltration of the liver, MRI, including a combination of in-phase and opposed-phase gradient-echo imaging, can reliably differentiate focal fatty infiltration from malignancy [33, 34]. Isserow et al reported that MRI using chemical shift technique can detect and characterize focal fatty infiltration of the pancreas and exclude a diagnosis of neoplasm [28].

On MRI, regions of focal fatty infiltration are is intense to hyper intense region relative to the surrounding pancreatic parenchyma on in-phase T1-weighted gradient-echo images, and these regions show moderate to marked signal intensity loss on opposed-phase gradient-echo images [28]. In patients with focal fatty sparing, MRI may also be helpful to exclude the presence of neoplasm by the lack of a hypo intense lesion on T1-weighted imaging with normal appearance on T2-weighted images [11, 28].

Focal fatty infiltration in the pancreas is seen as a region of decreased attenuation in the pancreas on non contrast or postcontrast CT [10]. Computed topographic attenuation within the focal fatty infiltration may be negative and show apparent fat attenuation [30]. 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 hypo attenuating mass on CT [28].

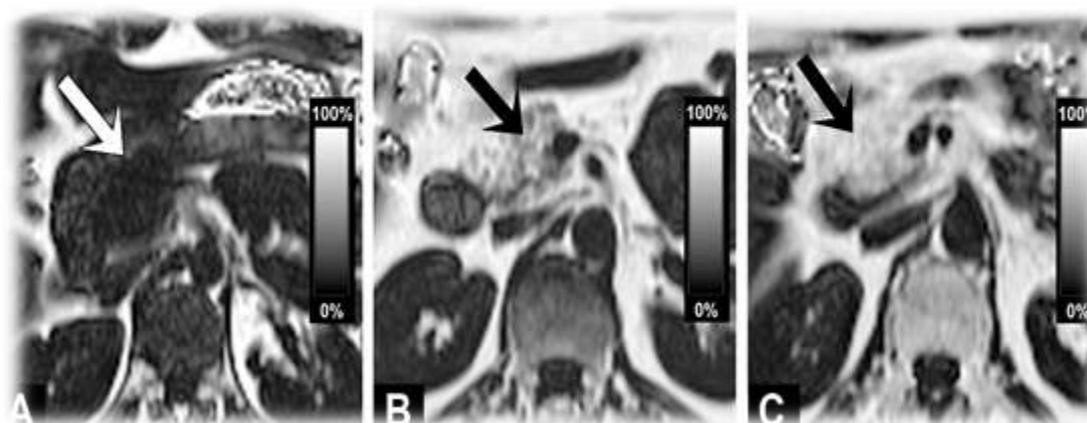
Although no single cause has been established for fatty infiltration of the pancreas, it occurs most

frequently in the elderly and obese populations [25]. It has also been associated with diabetes mellitus, chronic pancreatitis, hepatic disease, dietary deficiency, viral infection, steroid therapy, and obstruction of the pancreatic duct [13]. Fatty infiltration of the pancreas may be reversible in patients if they lose weight [35], and in patients with Cushing syndrome or steroid therapy [36].

Magnetic resonance (MR) imaging, however, allows sensitive assessment of tissue fat content [37]. One simple approach to quantifying tissue fat content is chemical shift-based technique with measurement of the proton density fat fraction (PDFF) [38, 39].

Measurement of PDFF improves the reliability of fat quantification by correcting for Confounders such as T2\* decay, T1 bias, and noise bias and for the multispectral complexity of Fat [10]. The high accuracy of the PDFF-based technique for tissue fat quantification has been shown in various organs in recent studies [37, 40, 41]. Nevertheless, only a few cohort studies have dealt with the quantification of pancreatic fat content with MR imaging [18, 42].

To the best of our knowledge, only one group of investigations has calculated the PDFF by using chemical shift imaging to assess the pancreatic fat content in a small patient group (n=43) according to Patel NS et al [43].



**Figure 8:** PDFF maps illustrate different amounts of pancreatic fat in pancreatic head (arrow) in subjects without diabetes. (a) Image shows a very small amount of fat in pancreatic head. (b) Image shows fatty replacement of pancreatic head with PDFF of 19%. (c) Image shows complete fatty replacement as a maximum variant of pancreatic steatosis [38].

Fat accumulation in the pancreas can also influence pancreatic function. Intra pancreatic fat amount has been closely associated with pancreatic-cell dysfunction [8, 44, 4]. Age, obesity, physical inactivity and dyslipidemia contribute to fat accumulation in the pancreas [45, 7], with ensuing pancreatic dysfunction. Thus, pancreatic volume and fat accumulation might together contribute to the development and progression of diabetes [46].

Authors found deficiency in literature regarding the current study of PS and little knowledge concerning this site of imaging among Practitioners in hospital and even radiologist in different departments visited by authors. So this manuscript considered attempt to enhance the role of different imaging in diagnose the PS, also it account as contribution for elevating the accurate diagnosis for these cases in hospitals.

**Objectives:**

The main Objectives of this review article is to summarize the authors articles about the pancreatic steatosis. And to review the clinical significance of pancreatic steatosis by using various imaging modalities. Other goal of this study is to discuss and illustrate the CT appearance of fatty infiltration in the pancreas that may simulate a hypo attenuating mass, and also to illustrate CT findings to help to differentiate fatty infiltration from a pancreatic neoplasm.

**Materials and Methods.**

35 articles in different peer reviewed journals were selected by authors and then analyzed and

summarized using Microsoft EXCEL 2010 version to compare between different findings. The manuscripts were selected according to the main objective of this review article , any manuscript that were not found as full-text were excluded from this review article .the article were accessed by Saudi digital library provided by Tiaf university and other were accessed by open access internet using Google search.

**Discussion**

Authors found that the CT MDCT scanning, which is the most practical method to evaluate the volume and quantity of fat in the pancreas. By using two different approaches to evaluate pancreatic fat deposit complementarily: a histogram analysis with local thresholding and the measurement of pancreatic parenchyma attenuation estimated from HU values.

So lim et al found that patients with T2D had smaller pancreatic volume and greater pancreatic fat content than normoglycemic subjects. Within patients with T2D, as duration of diabetes increased, pancreatic volume decreased and pancreatic fat content increased, resulting in an increased fat percentage in the pancreatic parenchyma. Pancreatic fat density assessed by HU values based on unenhanced MDCT images also decreased according to the duration of diabetes [46].

This means that the MDCT can be useful tools for scanning patients with high risk or development of diabetes. Represented this result by the table below.

**Table 1: The pancreatic volume and fat assessment by CT and Hounsfield unit obtained from pre enhanced CT according to glycemic status and duration of diabetes [46].**

	Normal		T2D-new		T2D<5Y		T2D≥5Y		P <sup>a</sup>
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Pancreatic volume (cm <sup>3</sup> )	66.3	13.9	58.4	9.9	54.0	13.9	49.1	16.0	<0.01
Pancreatic fat (cm <sup>3</sup> )	1.9	1.9	2.4	2.0	3.3	2.2	4.0	2.6	<0.01
Pancreatic fat %	2.9	3.4	4.3	4.0	6.6	4.9	9.3	7.7	<0.01
HU pancreas <sup>c</sup>	54.6	5.8	51.2	5.6	49.7	6.2	47.3	5.1	<0.01
HU spleen <sup>d</sup>	55.9	4.5	54.7	5.3	54.3	3.7	54.6	4.3	NS
HUp-s (HUpancreas–HUspleen)	-1.4	8.1	-3.5	7.3	-4.6	6.9	-7.3	6.7	<0.01

Kawamoto et al reported that Focal fatty infiltration of the pancreas is usually most prominent in the anterior aspect of the head of the pancreas and seen as a region of decreased attenuation on computed tomography and may mimic pancreatic neoplasm [9]

same as the study done by Matsumoto et al they reported that 57 of the 80 patients (71%) had type 1 fatty infiltration which is uneven fatty infiltration in the head of the pancreas with sparing of the posterior aspect of the head and uncinate process of the pancreas, and 23

patients (29%) had type 2 which is uneven fatty infiltration in the head and uncinata process of the pancreas with the focal area of sparing only around the common bile duct that means in the both type the head of the pancreas was involved with fatty infiltration and may affect the diameter of the pancreas head[30].

This is similar to study that done by Atri *et al* reported by ultrasound. The area of focal fatty sparing is seen as the hypo echoic zone with sharp margin with anterior aspect of the pancreatic head, and the common bile duct is often seen within this hypo echoic zone on both the transverse and sagittal views by ultrasound [26].

The area of intense fatty infiltration in the pancreatic head may gradually change to less intense fatty infiltration in the body and tail of the pancreas, and can be seen as a geographic area of hypo attenuation on axial or coronal reformations. The hypo attenuating portion of the pancreas due to focal fatty infiltration usually extends to the anterior and inferior surface of the pancreatic head, but not affect the contour of the normal the pancreas and fatty infiltration may be diffuse or focal ,it's usually more prominent in the anterior aspect of the head .

Many authors discussed the appearance of the pancreatic steatosis by using ultrasound and classified the finding depending on many part and echogenicity differences Mortelé *et al* reported that the PS was diagnosed when there was an increase in echogenicity of the pancreas compared with the kidney pancreato-renal echo contrast [14]. and Lee *et al* diagnosed the non-fatty pancreas, if the pancreatic echogenicity is equal to renal cortical echogenicity, and also diagnosed the fatty pancreas depending on the echogenicity of the retroperitoneal fat as stander and classified the presence of the fatty pancreas into Grade I: Mild fatty pancreas, pancreatic echogenicity is definitely lower than retroperitoneal fat; Grade II: Moderate fatty pancreas, pancreatic echogenicity is slightly lower than retroperitoneal fat; and Grade III: Severe fatty pancreas, pancreatic echogenicity is equal to retroperitoneal fat, and between hepatic and pancreatic echogenicity, to obtain an objective pancreato-renal echo contrast<sup>15</sup>,this attributed to thatsome researchers believe that fatty infiltration of pancreas positively correlates with fatty infiltration of liver ultrasound-determined steatosis grade as the paper done by Luis J *et al* and also showed that advanced age was positively associated with PS and NAFLD[1], compatible with the results of previous study carried by Glaser J *et al* ,due to the age-related

decrease in pancreatic parenchyma volume and increased pancreatic fat content[47].

The PS is highly associated with the metabolic syndrome the definition of metabolic syndrome remains a matter of debate, however, obesity, hyperglycemia, dyslipidemia and hypertension have been constant syndrome components and the central concept of such descriptions is the unity of the background path physiologic process and the interaction between the elements. According to

WU *et al* found that the presence of fatty pancreas and fatty liver represents a meaningful manifestation of metabolic syndrome together with obesity .the pancreatic fat replacement with acinar cell death and pancreatic fat infiltration duo to obesity contribute to PS [48].

Also another study done by Noronha M *et al* found that another important risk factor for pancreatic fat infiltration and liver fat infiltration is alcohol ingestion. Fat infiltration within pancreatic acinar cells was observed by examination in patients consuming more than 30 gr/day of ethanol. Ultra-structural changes within the cells are described on those without clinical pancreatitis, changes which are similar to those seen in the hepatocytes of alcoholics [49].

Is serow *et al* reported that MRI using chemical shift technique can detect and characterize focal fatty infiltration of the pancreas and exclude a diagnosis of neoplasm. On MRI, regions of focal fatty infiltration are iso-intense to hyper-intense region relative to the surrounding pancreatic parenchyma on in-phase T1-weighted gradient-echo images, and these regions show moderate to marked signal intensity loss on opposed-phase gradient-echo images .In patients with focal fatty sparing, MRI may also be helpful to exclude the presence of neoplasm by the lack of a hypo-intense lesion on T1-weighted imaging with normal appearance on T2-weighted images [28].

## CONCLUSION

Pancreatic steatosis is easy to be appear, measured using modern imaging techniques, such as ultra sonography, computed tomography and magnetic resonance imaging. Pancreatic steatosis is not due to the presence of diabetes mellitus but is highly associated with the metabolic syndrome.

Also the study concluded that that axial CT scan is considered as an appreciable radiological method for measuring the pancreas size and

characterizing its structure using CT number (Hounsfield). The study also revealed that the pancreas size and CT number had significant relations with age and other body habits us.

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