Original Article

Risk Factors for Fatty Pancreas in An Asian Population: A Prospective Study in A Tertiary Care Hospital

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ABSTRACT

Aim: To assess possible associated factors for fatty pancreas (FP) in an Asian population at a tertiary care hospital.

Methods: We prospectively collected relevant clinical data of consecutive patients who had undergone abdominal computed tomography (CT) in King Chulalongkorn Memorial Hospital, Bangkok, Thailand from August to November 2015. Criteria of CT were used for diagnosis of FP which is defined by presence lower attenuation more than 5 compare with spleen.

Results: Four-hundred-twenty-eight consecutive patients were enrolled. Sixteen (3.7%) were excluded due to pancreatic cancer (n=6), pancreatitis (n=6) and post splenectomy (n=4). The remaining 412 patients (182 M, 230 F, mean age 60.7±13.3 years) were recruited for analysis. Indications for abdominal CT were non-pancreatic cancer (n=310) and non-cancer (n=102). The prevalence of FP was 40.5%. On uni-variate analysis, significantly associated factors were impaired fasting plasma glucose (Odds Ratio (OR) 1.71, 95% CI 1.08-2.69, p=0.02) and fatty liver (OR 4.94, 95% CI 2.75-8.88, p=0.01). By using multivariate analysis, the independent associated risk factors of FP were impaired fasting blood glucose (OR 1.08, p=0.04) and fatty liver (OR 1.608, p= 0.01). Interestingly, the prevalence of FP in patients with previous exposure to systemic chemotherapy increased from 30% to 40% (mean follow-up time 6 months, p=0.01).

Conclusion: In this study, an Asian population, fatty liver and impaired fasting plasma glucose were strongly associated with FP. Systemic chemotherapy appeared to increase the prevalence of FP. Future study is required to confirm the degree of association and its clinical implication.

Key words : Fatty pancreas, Asian population

[Thai J Gastroenterol 2016; 17(3):134-138.]

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INTRODUCTION

In 2 previous studies, fatty pancreas (FP) was reported in about 16 percent of the normal population and about 60 percent in the obese population[1,2]. FP is also related to diabetes, pancreatitis and pancreatic cancer[3]. The pathophysiologic mechanism and the clinical significance of fatty pancreas (FP) are unclear. Previous studies suggested a possible association of FP with obesity, metabolic syndrome, diabetes, hyperlipidemia, drug, infection, malnourishment and biliary duct obstruction. The interpretation was limited owing to small number of studies with different study designs and different study populations[4-9].

Systemic chemotherapy as well as several medications are associated with fatty liver and pancreatic change such as pancreatitis, pancreatic atrophy but no support study about that changes.

Obesity has become an important global health problem. In Asian population, obesity increased has more than 30 percent[10,11], are 26 percent in Thailand[12]. Pancreatic steatosis, metabolic syndrome, poor diabetes control and myocardial ischemia[13] has been implicated with obesity. Triglycerides and free fatty acid induce cytokines secretion and pancreatic fibrosis[14,16,18]. Pancreatic fatty infiltration leading to fetal anomaly was reported in animal study[19]. Recent imaging multimodalities for diagnosing fatty pancreas have been described, such as ultrasonography, computed tomography, magnetic resonance imaging and endoscopic ultrasonography[15]. Computer tomography was chosen as the diagnostic tool in our study pancreas as it was readily available and easy to use.

MATERIALS AND METHODS

Patients

Adult patients undergoing abdominal computed tomography between August and November 2015 were recruited for study and informed consent was obtained. Patients with various pancreatic disease and those regular alcohol drinkers (over 40 g/day for male and over 20 g/day for female) were excluded. Medical history taking and physical examination were made. Data were collected by means of questionnaire, including, daily alcohol intake, past history, and other general characteristics. Blood collection was done. Cancer patients were scheduled for a CT-scan had before and after treatment.

Clinical and biochemical parameters

Height, body weight in light clothing, and body mass index (BMI = kg/m^2) were recorded. Waist circumference was measured horizontally between the lowest ribs and the iliac crest in an upright position. Blood samples were collected for liver functions, fasting plasma glucose, Hb_{A1c}, insulin, total cholesterol, triglyceride and high density lipoprotein after 12-hour fasting.

Computed tomography criteria

A 64-channel multiplex abdominal CT system (General Electric Medical Systems, Milwaukee, USA, system ID 0856210151, model name; Discovery CT 750 HD) was used and measurements in Hounsfield units (HU) were made at the locations of the pancreas. Five different parts of the pancreas (head, neck, body, tail, and uncinate process) and at three different parts of the spleen. The differences between the mean values of them were determined. A difference of 5 or lower was classified as fatty pancreas, and values above 5 were classified as non-fatty pancreas.

Measurements in Hounsfield units (HU) were also made at the right and the left lobes of the liver, and at three different parts of the spleen. The differences between the mean values of the liver and the splenic readings were determined. A difference of 10 or lower was classified as fatty liver, and values above 10 were classified as non-fatty liver.

Evaluation of insulin resistance

Insulin concentration was measured using a chemiluminescent immunoassay (Immulite 2000, Diagnostic Products Corp., Los Angeles, CA; CV, < 7%, normal value 6-27 μIU/mL). Measurement of insulin resistance was obtained using the HOMA-IR (Homeostasis model assessment-insulin resistance), and the calculation formula shown below: HOMA-IR: [Fasting blood sugar (mg/dL) * Fasting insulin (μU/mL)/ 405]. Serum glucose, triglyceride, and HDL-cholesterol were measured using Refloton®.

Definition of metabolic syndrome

The criteria for metabolic syndrome diagnosis followed the NCEP-Adult Treatment Panel. The visceral obesity was defined by substituting it with the standard waist circumference in the Asia-Pacific Region. Diagnostic criteria were defined as when the visceral obesity (waist circumference 90 cm for male, or waist

circumference 80 cm for female) plus two or more items of the following were met: increased triglyceride (150 mg/dL), decreased HDL (< 40 mg/dL for male, < 50 mg/dL for female), hypertension (130/85 mmHg), and fasting plasma glucose (110 mg/dL).

Statistical analysis

For statistical analysis, the SPSS for Windows (version 17.0) was used. The student's *t*-test was used for comparison between the two groups according to the existence or non-existence of fatty pancreas. The

Table 1. Indications for computed tomography.

	Indications for CT	numbers
Malignancy (n=310)	Head and neck cancer	3
	Breast cancer	35
	Lung cancer	23
	Gastrointestinal tract cancer	187
	Genitourinary tract cancer	25
	Hematologic malignancy	27
	other	10
Non malignancy (n=102)	Cancer screening	51
	Urinary tract stone	13
	other	38

Table 2. Comparison of relevant clinical parameters between patients with and without fatty pancreas.

Parameters	Fatty pancreas (n=167)	Non fatty pancreas (n=245)	*p* -value
Male (n, %)	69 (41.3%)	113 (46.1%)	0.40
Age (mean± SD)	61.3±13.25	60.3±13.25	0.71
Smoking (n, %)	8 (4.8%)	12 (4.9%)	0.97
Body weight (mean± SD)	58.1±11.11	59.5±12.00	0.85
BMI (mean± SD)	23.11±4.32	23.10±4.05	0.35
Waist circumference (mean± SD)	79.8±10.49	80.0±9.56	0.24
SBP (mean± SD)	137.8±22.13	135.9±22.87	0.66
DBP (mean± SD)	77.7±13.77	75.6±11.81	0.10
FPG (mean± SD)	105.04±36.71	97.78±27.70	0.01
HDL (mean± SD)	48.1±15.30	47.8±13.87	0.66
TG (mean± SD)	126.9±84.27	125.0±65.20	0.48
Fasting insulin (mean± SD)	9.82±15.95	8.95±10.37	0.56
HOMA-IR (mean± SD)	2.31±3.79	2.01±2.55	0.35
Metabolic syndrome (n, %)	42 (25.15%)	45 (18.37%)	0.22
Fatty liver (n, %)	47 (28.14%)	18 (7.35%)	0.01
AST (mean± SD)	34.2±30.48	34.6±30.87	0.62
ALT (mean± SD)	32.6±39.10	33.8±32.13	0.57
Ferritin (mean± SD)	367.1±484.07	331.8±487.43	0.41

BMI; body mass index, DBP; diastolic blood pressure, FPG; fasting plasma glucose, HDL; high density lipoprotein, HOMA-IR; The homeostatic model assessment-insulin resistance, HT; hypertension, TG; triglyceride, AST; Aspartate aminotransferase, ALT; alanine aminotransferase

Table 3. Odds ratio and 95% confidence interval of the parameters associated with fatty pancreas.

Parameters	Univariate analysis			Multivariate analysis
	Odds ratio	95% CI	*p*- value	*p*- value
Fatty liver	4.94	2.75-8.88	0.01	0.01
FPG	1.71	1.08-2.69	0.02	0.04

FPG; fasting plasma glucose, HDL; high density lipoprotein, HOMA-IR; The homeostatic model assessment-insulin resistance, HT; hypertension, TG; triglyceride

Table 4. Computed tomography attenuation changes after systemic chemotherapy treatment by follow up imaging (mean follow up 6 months).

Parameters	Before chemotherapy treatment	After chemotherapy treatment	*p*-value
Fatty pancreas (n, %)	82/266 (30.8%)	115/266 (43.2%)	0.01
Fatty liver (n, %)	19/266 (7.1%)	65/266 (24.4%)	0.01

χ^2 test used for relationship between fatty pancreas and multiple parameters.

RESULTS

Clinical characteristics of fatty pancreas patients and non fatty pancreas patients

The 428 patients were consecutively enrolled. Sixteen subjects (3.7%) were excluded due to pancreatic cancer (n=6), pancreatitis (n=6), and post splenectomy (n=4). One-hundred-sixty-seven of 412 subjects (40.53%) were diagnosed as fatty pancreas, of whom 69 (41.3%) were males with mean age of 61.3±13.25 years. Cancerous lesion was diagnosed in 310 (75.2%) patients. Clinical parameters of FPG 105.04±36.71 vs. 97.78±27.70 ($p < 0.01$) and number of fatty liver 47 (28.14%) vs. 18 (7.35%) ($p < 0.01$) were significant difference between both groups (Table 2). No statistical significance was noted when comparing other parameters including smoking, body weight, body mass index, waist circumference, systolic blood pressure, diastolic blood pressure, HDL-cholesterol, triglycerides, AST, ALT, ferritin, fasting insulin, HOMA-IR, and metabolic syndrome. In 266 cancerous subjects, computed tomography attenuations changes were recorded before and after systemic chemotherapy treatment (mean follow up 6 months). Fatty pancreas was noted in 82 of 266 (30.8%) patients before treatment and in 115 of 266 (43.2%) patients after treatment ($p < 0.01$). Fatty liver was present in 19 of 266 (7.1%) patients before treatment and 65 of 266 (24.4%) patients after treatment ($p < 0.01$).

DISCUSSION

Fatty pancreas is a new term, meaning pancreatic steatosis or fatty infiltration of the pancreas, a diagnosis based on pathological findings. As a retroperitoneal organ, the pancreas is difficult to biopsy. Several imaging modalities can diagnose fatty pancreas, such as ultrasonography, computed tomography, magnetic resonance imaging, endoscopic ultrasound, and elastography. We choose computed tomography because of its availability in most areas in Thailand, its relatively low cost, and ease of interpretation. Compare computed tomography findings have been like gold standard liver biopsy in previous studies.

Which showed that obesity, metabolic syndrome, drug, pancreatitis and pancreatic cancer were associated with fatty pancreas. In our study with 428 consecutive patients, significantly associated factors were impaired fasting plasma glucose (odds Ratio (OR) 1.71, 95% CI 1.08-2.69, p=0.02) and fatty liver (OR 4.94, 95% CI 2.75-8.88, p=0.01). The independent associated risk factors were also impaired fasting glucose (OR 1.08, p=0.04) and fatty liver (OR 1.608, p= 0.01). Interestingly, previous exposure to systemic chemotherapy appeared to be a new potential risk factor of

FP, as the prevalence of FP in this group of patients increased from 30% to 40 % (mean follow-up 6 months, p=0.01). Further study should be made on the impact of chemotherapy on fatty pancreas.

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