Research Article ISSN 2639-9334

Gastroenterology, Hepatology & Digestive Disorders

Influence of Pancreatic Steatosis on the Structural Changes of the Liver and Pancreas in Children with Overweight and Obesity

Stepanov Yu M, Zavhorodnia N Yu, Lukianenko O Yu*, Hravirovska N G, Yahmur V.B and Konenko I.S

State Institution, "Institute of Gastroenterology of National Academy of Medical Sciences of Ukraine", Dnipro, Ukraine.

***Correspondence:**
Lukianenko Olga Yu, Researcher, SI, Institute of Gastroenterology of the National Academy of Medical Sciences Ukraine, 49074, Dnipro, Ukraine, E-mail: sirenkolga@gmail.com.

Received: 23 June 2018; **Accepted:** 14 June 2018

Citation: Stepanov Yu M, Zavhorodnia N Yu, Lukianenko O Yu, et al. Influence of Pancreatic Steatosis on the Structural Changes of the Liver and Pancreas in Children with Overweight and Obesity. Gastroint Hepatol Dig Dis. 2018; 1(2): 1-4.

ABSTRACT

Introduction: *The ectopic fat accumulation in the liver, known as nonalcoholic fatty liver disease (NAFLD), is associated with insulin resistance, dyslipidemia, and high risk of diabetes and cardiovascular diseases. Nonalcoholic fatty pancreas disease (NAFPD) is defined as obesity-associated accumulation of fat in the pancreas without signs of secondary causes of steatosis. The pathophysiology of NAFPD and NAFLD is closely related. But the causal relationship between NAFLD and NAFPD has not been well established yet.*

The aim of the study is to investigate the relationship between liver and pancreatic steatosis (PS); to establish the influence of the PS on the structural changes of the liver and pancreas.

Materials and Methods: *A total of 117 children aged 6-17 years (mean 11.67 ± 2.81 years; 68 boys, 49 girls) were included. Patients were divided into 5 groups: group 1 - 37 children with combined liver and pancreatic steatosis, 2 group - 30 children with isolated steatosis of the pancreas, 3 group - 6 children with isolated liver steatosis, 4 group - 28 children with obesity / overweight without liver and pancreatic steatosis, 5 group - 16 children with normal weight. Pancreatic steatosis was established on the basis of ultrasound examination of the pancreas. Diagnosis of non-alcoholic fatty liver disease was established in the presence of signs of liver steatosis according to transient elastography with CAP function (Fibroscan 502 Touch). We also performed a quantitative estimation of the ultrasound attenuation coefficient (UAC) conducted on UltimaPAExpert apparatus ("Radmir", Ukraine). To determine the stiffness of the pancreatic parenchyma, shear wave elastography using UltimaPAExpert (Radmir, Ukraine) was performed.*

Results: *It was found that children with combined steatosis showed higher levels of UAC and CAP compared to children with normal weight ($p<0,05$). The maximum degree of liver steatosis according to the CAP was observed in the group with combined steatosis ($p<0.05$). It should be noted that children with combined liver steatosis had higher liver and pancreatic stiffness values in comparison with children having isolated pancreatic steatosis ($p<0,05$). This fact can be explained by more intensive fibrotic changes in the liver and pancreas in case of combined steatosis but also inflammatory changes in this organs can influence on stiffness parameters. In the correlation analysis, there was a positive correlation between UAC and CAP. Also we found positive correlation between pancreatic and liver stiffness according to SWE.*

Conclusion: *Our findings along with literature data show that pancreatic steatosis precedes the appearance of liver steatosis. We assume that pancreatic steatosis as well as liver steatosis is accompanied with rise of parenchyma stiffness of these organs. Patients who had signs of liver steatosis and pancreatic steatosis had the most adverse structural changes in the form of increased stiffness of the parenchyma of the liver and pancreas.*

Keywords
Liver steatosis, Pancreatic steatosis, Nonalcoholic fatty pancreas disease, Nonalcoholic fatty liver disease, Liver stiffness, Pancreatic stiffness.

Introduction
The pancreatic steatosis was first described in 1933, but this problem is given increasing attention in the last five years, which can be explained by the growing epidemic of obesity and its complications [1]. Nonalcoholic fatty pancreas disease (NAFPD) is defined as obesity-related accumulation of fat in the pancreas without signs of secondary causes of steatosis [2]. In humans, NAFPD is closely associated with increasing body mass index (BMI), visceral fat, insulin resistance and metabolic syndrome [3,4].

The type of adipose tissue distribution is an important factor in predicting obesity-related metabolic disorders [5]. The ectopic accumulation of fat in the liver, known as nonalcoholic fatty liver disease (NAFLD), is closely related with NAFPD pathophysiology. But the causal relationship between NAFLD and NAFPD has not been well established yet. Further researches are needed to study the effects of NAFPD on the course of NAFLD.

The aim is to investigate the relationship between liver and pancreatic steatosis (PS); to establish the influence of the PS on the structural changes of the liver and pancreas.

Materials and Methods
A total of 117 children aged 6-17 years (mean 11.67 ± 2.81 years; 68 boys, 49 girls) were included in the study. This study was conducted on the basis of the State Institution "Institute of Gastroenterology of the National Academy of Medical Sciences of Ukraine" during two years: 2016-2017. The inclusion criteria for the study was the presence of overweight and obesity. The exclusion criteria were: acute and chronic liver disease, acute and chronic pancreatitis, history of taking toxic drugs, type 1 diabetes and type 2 diabetes. Patients were divided into 5 groups: group 1-37 children with combined liver and pancreatic steatosis, 2 group - 30 children with isolated pancreatic steatosis, 3 group - 6 children with isolated liver steatosis, 4 group - 28 children with obesity / overweight without liver and pancreatic steatosis, 5 group - 16 children with normal weight. Groups were homogeneous in regards to age and gender.

Pancreatic steatosis was established on the basis of ultrasound examination of the pancreas using an ultrasound scanner "Toshiba Xario SSA660-A" (Japan). Diagnosis of non-alcoholic fatty liver disease was established in the presence of signs of liver steatosis according to transient elastography with CAP function (Fibroscan 502 Touch) in children with obesity/overweight in the exclusion of other secondary steatosis.

In order to diagnose pancreatic steatosis, a steatometry of the pancreas was also performed - a quantitative estimation of the ultrasound attenuation coefficient (UAC) conducted on UltimaPAExpert apparatus ("Radmir", Ukraine). To determine the stiffness of the pancreatic parenchyma, shear wave elastography using UltimaPAExpert (Radmir, Ukraine) was performed.

Methods of nonparametric statistics were used - when indicating quantitative characteristics, data were presented as median and interquartile intervals [25; 75%], for qualitative signs - in the form of relative indicators - n (%). For comparing group data, the Kruskel-Wallis criterion was used. When comparing qualitative indicators, the assessment of the differences was carried out according to Fisher's exact criterion. Correlation analysis was carried out with the calculation of the rank correlation coefficient Spearmen - R. Two-tailed $p<0.05$ indicated statistical significance. Statistical analyses were performed by using the Statistica 7.0.

Results
Among the studied 117 patients, 67 (57.3%) had signs of pancreatic steatosis, 43 patients (36.7%) – of liver steatosis. Among patients with obesity / overweight, the incidence of pancreatic steatosis was 1.5 times higher than diagnosed liver steatosis. Among patients with pancreatic steatosis in more than half of patients liver steatosis was detected, while in patients with liver steatosis more than 80% of patients were found PS.

It was found that children with combined steatosis showed higher levels of UAC and CAP compared to children with normal weight ($p<0,05$) (Table 1). The maximum degree of liver steatosis according to the CAP was observed in the group with combined steatosis ($p<0.05$) (Tab 1). It should be noted that children with combined liver steatosis had higher liver and pancreatic stiffness values in comparison with children having isolated pancreatic steatosis ($p<0,05$) (Figures 1 and 2). This fact can be explained by more intensive fibrotic changes in the liver and pancreas in case of combined steatosis but also inflammatory changes in this organs can influence on stiffness parameters.

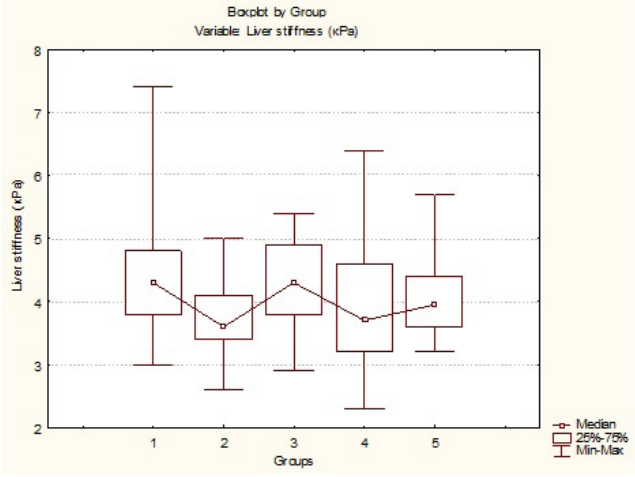

Figure 1: Liver stiffness distribution according to groups.

In the correlation analysis, there was a positive correlation between UAC and CAP (Figure 3). Also we found positive correlation between pancreatic and liver stiffness according to SWE (Figure 4).

Characteristic	1 group	2 group	3 group	4 group	5 group
UAC, dB/sm	2,50 [2,32; 2,70] #*	2,6 [2,34; 2,75] *#	2,28 [2,14; 2,95]	2,15 [1,93; 2,41]	1,87 [1,75; 2,15]
Pancreatic stiffness, кPa	3,80 [3,38; 4,27] ^	3,39 [2,90; 3,87]	3,16 [2,59; 3,53]	3,51 [3,21; 3,77]	3,56 [3,28; 3,83]
CAP, дB/m	261,0 [240,0; 282,0] *# **	206,5 [193,0; 228,0] #*	260,5 [249,0; 275,0] *#	195,0 [171,0; 209,0]	164,0 [116.5; 196.5]
Liver stiffness, кPa	4,3 [3,8; 4,8] ^	3,6 [3,4; 4,10]	4,3 [3,7; 4,7]	3,8 [3,2; 4,7]	3,95 [3,64; 4,4]

Table 1: Sonological characteristics of the patients. Note. * - p1 <0,05 compared with the 4 group; # - p1 <0,05 compared with 5 group; ^ - p <0,05 compared with group 2.

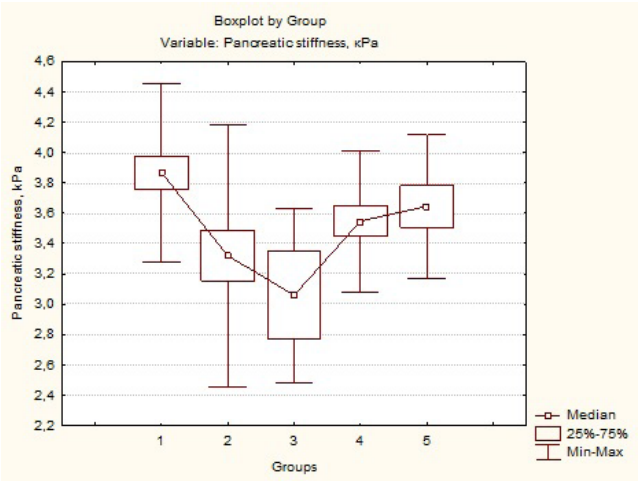

Figure 2: Pancreatic stiffness distribution according to groups.

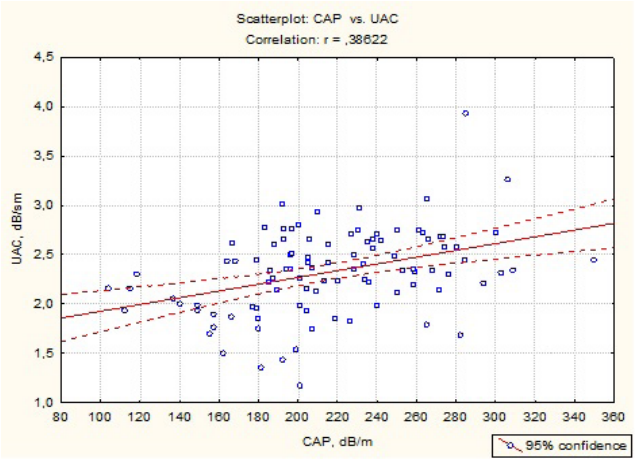

Figure 3: Correlation between CAP and UAC.

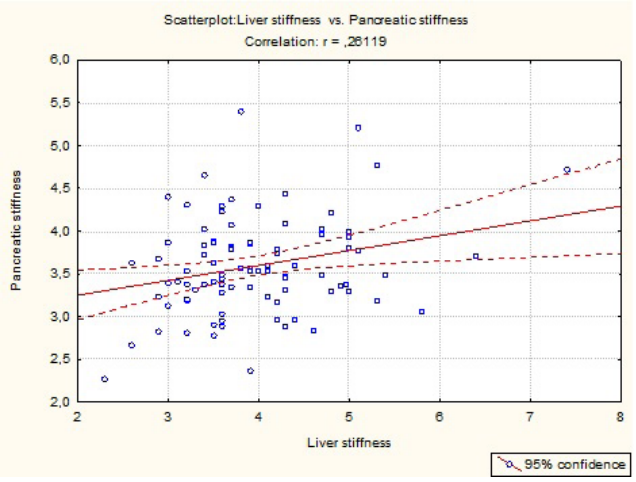

Figure 4: Correlation between liver and pancreatic stiffness.

Thus, more than half of patients with pancreatic steatosis had associated liver steatosis. Patients who had signs of liver steatosis and pancreatic steatosis had the most adverse structural changes in the form of increased liver and pancreas parenchyma stiffness. The obtained data testify to the necessity of early diagnosis of liver and pancreatic steatosis, and a differentiated approach depending on their coexistence.

Discussion

As we know, this is the first study on structural changes in the liver and pancreas, depending on the coexistence of steatosis with the determination of the attenuation of ultrasound and parenchyma stiffness.

Morphological peculiarity of pancreatic steatosis in contrast to liver steatosis characterized mainly by intracellular fatty infiltration is an increase in adipocyte content - extracellular accumulation of lipids, although intracellular accumulation may also occur [1].

Many studies show evidence of a close connection between liver and pancreatic steatosis, and fatty infiltration of the pancreas is considered as a process preceding liver steatosis. So, in the study of autopsy material, Erwin-Jan van Geenen et al. have shown that the total content of adipose tissue positively correlates with the presence of NAFLD. In 68% of cases pancreatic steatosis was accompanied by steatosis of the liver, most subjects (97%) with steatosis of the liver also had pancreatic steatosis [6]. Our study confirmed this data, so more than half of patients with NAFPD had NAFLD and 80% with NAFLD had signs of NAFPD.

According to P. Sepe et al. (2009) [7], P. E. Sijens et al. (2010) [8] the content of fatty pancreatic tissue was elevated in patients with high NAFLD activity according to the morphological study of the liver. The authors found that the total content of adipose tissue in the pancreas was reduced in patients with NAFLD with severe fibrosis of the liver, decreased degree of liver steatosis in these patients is likely to be related to the development of fibrosis.

In our study children with combined steatosis had higher level of pancreatic and liver stiffness, these parameters positively correlated between each other.

In own study E. Aleshina et al. shows that sonographic signs of pancreatic steatosis are observed in 70% of children with overweight and preceded by the discovery of signs of liver steatosis [9]. In M. Cohen et al. [10] showed that in children and adolescents, the fat content of the pancreas determined by MRI, correlated with the content of fatty tissue in the liver and visceral

fat. However, after adjusting for gender, ethnicity and puberty, the fat content of the PS was associated only with visceral fat. In contrast to this study, C. M. Toledo-Corral et al. [11] demonstrated that adolescents with pre-diabetes have a higher level of fat content in the liver and pancreas compared with control group, regardless of general and visceral obesity.

It is likely that the results of the above-mentioned works are contradictory due to the use of various methods for diagnosis of steatosis. We demonstrated that prevalence of fatty pancreas was 66.3% in obese/overweight children. Epidemiological studies showed a high incidence of fatty pancreas in population [12], but these data have rarely included population from Europe; therefore, more studies should be provided in this direction. We think that there is need for more research in obesity-related mechanisms of pancreatic and liver injury, the role of the non-alcoholic fatty pancreatic disease, and the underlying mechanisms associating obesity [13].

Conclusions

Our findings along with literature data show that pancreatic steatosis precedes the appearance of liver steatosis. Isolated liver steatosis can be explained by insufficient sensitivity of standard ultrasound study in diagnosis of pancreatic steatosis while liver steatosis was diagnosed with more sensitive method (transient electrography with CAP function). Also we suppose that genetic features of visceral fat distribution exist. We assume that pancreatic steatosis as well as liver steatosis is accompanied with rise of parenchyma stiffness of these organs.

References

1. Catanzaro R, Cuffari B, Italia A, et al. Exploring the metabolic syndrome: Nonalcoholic fatty pancreas disease. World Journal of Gastroenterology. 2016; 22: 7660-7675.
2. Hung CS, Tseng PH, Tu CH, et al. Increased Pancreatic Echogenicity with US: Relationship to Glycemic Progression and Incident Diabetes. Radiology. 2018; 170331.
3. Romana B, Chela H, Dailey F, et al. Non-alcoholic fatty pancreas disease (NAFPD): A silent spectator or the fifth component of metabolic syndrome? A literature review. Endocr Metab Immune Disord Drug Targets. 2018.
4. Pacifico L, Di Martino M, Anania C, et al. Pancreatic fat and β-cell function in overweight/obese children with nonalcoholic fatty liver disease. World Journal of Gastroenterology : WJG. 2015; 21: 4688-4695.
5. Kim JY, Cho J, Yang HR. Biochemical Predictors of Early Onset Non-Alcoholic Fatty Liver Disease in Young Children with Obesity. Journal of Korean Medical Science. 2018; 33: e122.
6. Van Geenen EJM, Smits MM, Schreuder TC, et al. Nonalcoholic fatty liver disease is related to nonalcoholic fatty pancreas disease. Pancreas. 2010; 39: 1185-1190.
7. Sepe PS, Ohri A, Sanaka S, et al. A prospective evaluation of fatty pancreas by using EUS. Gastrointestinal endoscopy. 2011; 73: 987-993.
8. Sijens PE, Edens MA, Bakker SJ, et al. MRI-determined fat content of human liver, pancreas and kidney. World journal of gastroenterology: WJG. 2010; 16: 1993.
9. Aleshina EI, Novikova VP, Gur'eva VA, et al. Hepatic steatosis and fatty pancreas--2 targets of metabolic syndrom in children. Experimental & clinical gastroenterology. 2014; 8: 16-20.
10. Cohen M, Syme C, Deforest M, et al. Ectopic fat in youth: the contribution of hepatic and pancreatic fat to metabolic disturbances. Obesity. 2014; 22: 1280-1286.
11. Toledo-Corral CM, Alderete TL, Hu HH, et al. Ectopic fat deposition in prediabetic overweight and obese minority adolescents. The Journal of Clinical Endocrinology & Metabolism. 2013; 98: 1115-1121.
12. Wang D, Yu XP, Xiao WM, et al. Prevalence and clinical characteristics of fatty pancreas in Yangzhou, China: A cross-sectional study. Pancreatology. 2018.
13. Malli A, Li F, Conwell D L, et al. The Burden of Systemic Adiposity on Pancreatic Disease: Acute Pancreatitis, Non-Alcoholic Fatty Pancreas Disease, and Pancreatic Cancer. JOP : Journal of the Pancreas. 2017; 18: 365-368.