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ROLE OF FABP1 AS A DIAGNOSTIC BIOMARKER FOR NON-ALCOHOLIC FATTY PANCREATIC DISEASE

By

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ABSTRACT

Background: Fatty pancreas or nonalcoholic fatty pancreatic disease (NAFPD) is an excessive fat infiltration of the pancreas due to obesity. The need of laboratory marker that can be used as simple non-invasive biomarker to aid in diagnosis is crucial to be adding to the investigations, especially when used the abdominal ultrasound. Fatty acid binding protein 1 (FABP1) is a tissue specific marker that can be used to diagnose NAFPD as per Nature.

Objective: To determine the incidence of NAFPD among obese and non-obese Egyptian people with or without DM, evaluate for possible association with DM or obesity, correlate between pancreatic steatosis (NAFPD) and non-alcoholic liver disease, and evaluate the diagnostic role of FABP1 in Egyptian patient with or without DM in relation to obesity.

Patients and methods: A prospective cohort study included 80 patients aged from 18-70 years, attended the outpatient clinic of the Liver and Digestive System and Infectious Diseases Department at Al-Azhar University Hospital (Cairo) from January 2020 to December 2020. Patients were a divided into 4 equal groups: Group 1: Apparently healthy individuals with normal BMI and non-diabetic, Group 2: Patients with normal BMI, diabetics or impaired fasting blood glucose, Group 3: Patients with BMI over 25 non-diabetics, and Group 4: Patients with BMI over 25, diabetics or impaired fasting blood glucose level.

Results: There was a significant statistically difference between groups as regard to FABP1. The results of this study showed that the level of FABP1 was significantly higher in grade I, II and III more than grade 0 of pancreatic echogenicity. On the other hand, the level of FABP1 showed a significant increase in grade III liver echogenicity more than grade I and II. Also, grade I, II and III showed a significant increase in FABP 1 more than grade I liver echogenicity. By using FABP 1 as a predictor to pancreatic echogenicity, it was found that at cut off value 32.0, the sensitivity of FABP1 to diagnose pancreatic echogenicity was 86.0%, specificity was 80.0%, and total accuracy was 84.0%. By using FABP1 as a diagnostic marker in liver echogenicity at cut off value 31.0, the sensitivity was 81.0%, specificity was 76.0% and total accuracy was 78.0%.

Conclusion: FABP1 can be used a diagnostic biomarker for non-alcoholic fatty pancreatic disease.

Keywords: FABP1, Non-Alcoholic Fatty Pancreatic Disease

INTRODUCTION

Fatty pancreas or nonalcoholic fatty pancreatic disease (NAFPD) is an excessive fat infiltration of the pancreas due to obesity in the absence of significant alcohol intake *(Pacifico et al., 2015)*. High energy intake in human (Obesity) may lead to excessive fat which could be accumulated in visceral organs that are unusual for adipose tissue storage, the so-called ectopic fat *(Heber et al., 2017)*. Fatty pancreas is a common ultrasound finding which has increased echogenicity when compared to the normal pancreas *(Mathur et al., 2017)*.

Fatty liver disease (NAFLD), the potential systemic and local consequences excessive fat accumulation in the pancreas have not been well established. Fatty infiltration in the pancreas has been showed to correlate with the metabolic risk factors and may represent a meaningful manifestation of metabolic syndrome. Epidemiology study also suggests that obesity is a risk factor for pancreatic cancer *(Lesmana et al., 2018)*.

Based on a recent study, fatty infiltration in the pancreas may increase the risk of pancreatic ductal adenocarcinoma beyond the effect of obesity alone *(Tariq et al., 2016)*. It is usually an incidental finding during transabdominal ultrasound examination and its clinical significance is still poorly understood. Prevalence of NAFPD has been reported in Asia as well as in Western countries. In Taiwan, Wang et al. reported that 16% of Chinese population had fatty pancreas *(Wang et al., 2014)*.

In addition, available data suggest that decreased pancreatic volume and increased pancreatic fat content are more frequently observed in subjects suffering from impaired glucose metabolism, and pancreatic fat content was reported to correlate with insulin secretion in subjects at increased risk for metabolic diseases. One explanation of these heterogeneous findings may be the different imaging modalities used for the assessment of pancreatic fat content, including ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI) *(Lesmana et al., 2018)*.

Given its nonionizing nature and high soft tissue contrast, MRI may be particularly suited to gain insights into the role of pancreatic fat content. Update imaging modalities to study pancreas is not available among most hospitals. NAFPD may allegedly develop into chronic pancreatitis and further leads to pancreatic cancer, and facilitates its dissemination. Patients with type 2 DM have a 2-fold increase in the risk of pancreatic cancer. T2DM patients with NAFPD should be considered for pancreatic cancer screening and surveillance. Factors which are known to be associated with NAFPD in general population include male, age over 60 years hypertension, fasting blood glucose, triglycerides, body mass index, central obesity and nonalcoholic fatty liver disease (NAFLD) *(Tariq et al., 2016)*.

The need of laboratory marker that can be used as a simple non-invasive biomarker to aid in diagnosis is crucial to be adding to the investigations, especially when used the abdominal ultrasound. Fatty Acid Binding protein 1 (FABP1) is a tissue specific marker that can be used to diagnose NAFPD as per Nature *(Furuhashi and Hotamisligil, 2018)*.

The aim of the present study was to determine the incidence of NAFPD among obese and non-obese Egyptian people with or without DM, evaluate for possible association with DM or obesity, correlate between pancreatic steatosis (NAFPD) and non-alcoholic liver disease, and evaluate the diagnostic role of FABP1 in Egyptian patient with or without DM in Relation to obesity.

PATIENTS AND METHODS

This was a prospective cohort study including 80 patients aged from 18-70 years, attended the outpatient clinic of the Liver and Digestive System and Infectious Diseases Department at Al-Azhar University Hospital (Cairo) from January 2020 to December 2020. They were divided into 4 equal groups: Group 1: Apparently healthy individual with normal BMI and non-diabetic, Group 2: Patients with normal BMI, diabetics or impaired fasting blood glucose, Group 3: Patients with BMI over 25, non-diabetics, and Group 4: Patients with BMI over 25, diabetics or impaired fasting blood glucose level.

Inclusions Criteria: All subjects aged from 18-70 years old.

Exclusions Criteria: Drugs induced pancreatitis (Amiodarone, cortisone, Valproate, methotrexate). Alcohol intake >20gm /day. Advanced co-morbidities

The patients had been evaluated clinically and examined as follow:

- Blood pressure, body mass index (BMI) = weigh (Kg)/ height (meter) 2>30 kg/m2
- Complete blood count (CBC, ESR).
- Fasting blood sugar.
- HbA1c%.
- HCV antibody and HBVs antigen.
- Liver function tests including alanine amino transferase, aspartate aminotransferase, gamma glutamyl transpeptidase, alkaline phosphatase (ALT, AST, GGT, ALP) serum bilirubin, and serum albumin.
- Lipid profile including cholesterol, triglycerides, HDL, and LDL.
- Fatty Acid Binding protein1 (FABP1) which had been evaluated by the enzyme-linked immunosorbent assay (ELISA), and the deviation from the normal had been correlated with other investigations and clinical manifestations of the subjects.
- Abdominal Ultrasound grading of fatty liver and pancreas by radiologist or gastroenterologist.

Fatty liver had been diagnosed as follows *(Ahn et al., 2016)*:

Level 0	Normal liver echogenicity.
Level 1	A slight increase in liver echogenicity with no attenuation in the far field.
Level 2	A moderate increase in liver echogenicity with light attenuation in the far field and the diaphragm and vessels clearly visible.
Level 3	A substantial increase in liver echogenicity with poor visualization of the diaphragm and the vessels.

NAFLD was diagnosed when the liver appeared as level 1 to 3.

The pancreas echogenicity was also classified into 4 grades *(Lee et al., 2010)*:

Level 0	The pancreas echogenicity was similar to renal parenchyma.
Level 1	The pancreas was slightly high than in kidney when the operator can see both in the same view in the transverse epigastric scan with slight move to the right. if kidney and pancreas couldn't be displayed in the same screen, the radiologist compared the kidney with the liver and then compared the liver with the pancreas
Level 2	A substantial increase in pancreas echogenicity but lower than retroperitoneal fat echogenicity.
Level 3	The pancreas echogenicity is similar to or higher than rectoperineal fat.

NAFPD had been diagnosed when the pancreas appeared as level 1

Statistical analysis:

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for the Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Wilk test. Qualitative data were represented as frequencies and relative percentages. Chi square test ($\chi 2$) to calculate difference between two or more groups of qualitative variables. ROC curve used to detect a cutoff of certain outcome. Quantitative data were expressed as mean ± SD (Standard deviation). Independent samples t-test was used to compare between two independent groups of normally distributed variables (parametric data). P value < 0.05 was considered significant.

RESULTS

There was a significant statistically difference between groups regarding to BMI. There was no significant statistically difference between groups regarding to age and sex **(Table 1)**.

Table (1): Comparison between different studied groups regarding basic demographic and clinical data

Groups / Parameters	Group (1) (n=20)	Group (2) (n=20)	Group (3) (n=20)	Group (4) (n=20)	P value
Age (years)					
Range	35.00-47.00	34.00-58.00	36.00-55.00	36.00-55.00	>0.05
mean ±SD	41.20±6.46	43.15±11.86	45.95±5.28	44.35±5.17	
Gender					
Male	10 (50.0%)	12 (60.0%)	9 (45.0%)	6 (30.0%)	>0.05
Female	10 (50.0%)	8 (40.0%)	11(55.0%)	14 (70%)	
BMI (kg/m2)					
Range	21.00-24.50	21.00-24.50	26.30-34.00	26.30-36.30	<0.001
mean ±SD	23.16±0.96	23.16±0.92	29.73±2.18	32.31±2.67	
P1		>0.05	0.0036*	0.001*	
P2			0.0029*	0.001*	
P3				>0.05	
Current smoking	4 (40.0%)	6 (30.0%)	6 (30.0%)	5 (25.0%)	>0.05
Systolic blood pressure (mmH)					
Range	25.0-135.0	25.0-138.0	25.0-135.0	25.0-138.0	>0.05
mean ±SD	121.75±23.36	125.05±23.99	121.60±23.34	124.90±23.94	
Diastolic blood pressure (mmHg)					
Range	65.00-85.00	60.00-85.00	60.00-85.00	65.00-85.00	>0.05
mean ±SD	77.00±5.71	68.50±7.96	68.30±6.91	77.50±5.74	
Hepatomegaly	1 (5%)	2 (10%)	1 (5%)	3 (15%)	>0.05

P1 comparison between group 1 and other groups,
P2 comparison between group 2 and other groups,
P3 comparison between group 3 and 4.

There was significant statistically difference between groups as regard to hematological parameters **(Table 2)**.

Table (2): Comparison between groups as regard to haematological parameters

Groups / Parameters	Group (1) (n=20) mean ±SD	Group (2) (n=20) mean ±SD	Group (3) (n=20) mean ±SD	Group (4) (n=20) mean ±SD	P *value*
Hemoglobin (g/dL)					
Range	13.00-14.70	11.00-13.40	11.00-13.40	11.00-14.70	< 0.001
mean +SD	13.64±0.45	12.32±0.61	12.33±0.57	12.09±0.47	
P1		<0.001	<0.001	<0.001	
P2			0.958	0.190	
P3				0.155	
MCV (fL)					
Range	82.00-89.00	70.00-89.00	53.00-89.00	82.00-89.00	0.004
mean +SD	85.75±2.36	80.35±6.04	83.95±7.73	85.80±2.35	
P1		0.001	0.326	0.947	
P2			0.109	0.001	
P3				0.312	
RDW (%)					
Range	13.0-14.80	12.00-14.80	12.0-14.80	11.90-15.00	0.002
mean +SD	14.36±0.30	13.50±0.92	13.64±0.82	13.80±0.69	
P1		<0.001	0.001	0.002	
P2			0.614	0.251	
P3				0.508	
MPV (fL)					
Range	7.30-7.90	6.00-7.80	6.00-7.90	7.40-8.60	<0.001
mean +SD	7.58±0.19	6.97±0.59	7.04±0.65	7.99±0.36	
P1		<0.001	0.001	<0.001	
P2			0.723	<0.001	
P3				<0.001	
Leukocyte (10^9/L)					
Range	6.20-6.80	6.30-8.70	6.20-6.80	6.30-8.70	<0.001
mean +SD	6.51±0.20	7.40±0.83	6.49±0.21	7.60±0.80	
P1		<0.001	0.759	<0.001	
P2			<0.001	0.443	
P3				<0.001	
Platelet (10^9/L)					
Range	244.00-265.00	213.00-239.00	220.00-265.00	220.00-265.00	<0.001
mean +SD	254.15±5.79	225.15±7.67	248.95±11.03	248.55±10.71	
P1		<0.001	0.070	0.047	
P2			<0.001	<0.001	
P3				0.908	
ESR					
Range	13.00-16.50	12.00-16.00	15.00-20.00	13.00-16.50	<0.001
mean +SD	15.16±0.79	14.17±1.01	17.78±2.05	15.18±0.80	
P1		0.001	<0.001	0.937	
P2			<0.001	0.001	
P3				<0.001	

P1 comparison between group 1 and other groups, P2 comparison between group 2 and other groups, P3 comparison between group 3 and 4.

There was a significant statistically difference between groups as regard to ALT, AST and GGT (0.001, 0.002 and 0.001). There was a significant statistically difference between groups as regard to triglycerides (p value < 0.001) **(Table 3)**.

Table (3): Comparison between groups a regard to hepatic laboratory investigation

Groups / Parameters	Group (1) (n=20)	Group (2) (n=20)	Group (3) (n=20)	Group (4) (n=20)	P value
ALT (U/L)					
Range	16.00-21.00	23.00-37.00	45.00-58.00	65.00-78.00	<0.001
Mean ±SD	18.15±1.63	29.15±4.26	53.35±3.44	71.35±4.04	
P1		0.008	0.001	0.001	
P2			0.021	0.003	
P3				0.008	
AST (U/L)					
Range	20.00-38.00	21.00-33.00	44.00-55.00	58.00-71.00	<0.001
Mean ±SD	26.65±5.25	27.60±3.76	49.40±3.41	64.10±3.93	
GGT (U/L)					
Range	22.00-35.00	22.00-35.00	44.00-59.00	61.00-72.00	<0.001
Mean ±SD	27.30±3.97	26.30±4.61	52.60±4.17	66.20±3.47	
P1		0.211	0.005	0.001	
P2			0.007	0.001	
P3				0.082	
Triglycerides (mg/dL)					
Range	115.00-134.00	133.00-150.00	190.00-211.00	217.00-234.00	<0.001
mean ±SD	123.20±5.41	141.35±5.0	202.80±5.93	223.35±5.20	
P1		0.053	0.002	0.001	
P2			0.031	0.001	
P3				0.107	

P1 comparison between group 1 and other groups,
P2 comparison between group 2 and other groups,
P3 comparison between group 3 and 4.

The level of FABP1 was significantly higher in grade I, II and III more than grade 0 of pancreatic echogenicity. On the other hand, the level of FABP1 showed a significant increase in grade III liver echogenicity more than grade I and II. Also, grade I, II and III showed a significant increase in FABP 1 more than grade I liver echogenicity **(Table 4)**.

Table (4): Comparison between groups a regard to FABP 1, pancreatic echogenicity and liver echogenicity

Groups / Parameters	Group (1) (n=20)	Group (2) (n=20)	Group (3) (n=20)	Group (4) (n=20)	P value
FABP 1 (ng/mL)					
Range	19.00-28.00	24.00-39.00	25.00-39.00	30.00-48.00	**<0.001**
Mean ±SD	23.25±3.02	30.25±4.23	32.70±4.11	40.75±4.87	
P1		0.036	0.035	0.011	
P2			0.126	0.022	
P3				0.047	
Pancreatic echogenicity					
Grade 0	20 (100%)	13 (65%)	9 (45%)	6 (30%)	0.001
Grade 1	0 (0%)	7 (35%)	8 (40%)	11 (55%)	
Grade 2	0 (0%)	0 (0%)	3 (15%)	2 (10%)	
Grade 3	0 (0%)	0 (0%)	0 (0%)	1 (5%)	
P1		>0.05	0.011	0.003	
P2			>0.05	0.001	
P3				0.042	
Liver echogenicity					
Grade 0	20 (100%)	14 (70%)	10 (50%)	6 (30%)	0.002
Grade 1	0 (0%)	6 (30%)	7 (35%)	11 (55%)	
Grade 2	0 (0%)	0 (0%)	3 (15%)	2 (10%)	
Grade 3	0 (0%)	0 (0%)	0 (0%)	1 (5%)	
P1		0.046	0.002	0.001	
P2			0.061	0.001	
P3				0.014	

P1 comparison between group 1 and other groups,
P2 comparison between group 2 and other groups,
P3 comparison between group 3 and 4.

The present study showed that there were significant statistically differences a between groups as regard to FABP 1. There were significant statistically differences between groups as regard to pancreatic echogenicity, and liver echogenicity **(Table 5)**.

Table (5): Relation between FABP1 level and pancreatic echogenicity, liver echogenicity, pancreatic echogenicity grade and liver echogenicity grade

FABP 1	**No**		**Yes**	
Pancreatic echogenicity:				
Range	19.0-48.0		24.0-47.0	
Mean±S.D.	29.56±7.43		35.00±6.33	
P	<0.001			
Liver echogenicity:				
Range	19.0-47.0		24.0-48.0	
Mean±S.D.	29.61±7.25		35.09±6.61	
P	<0.001			
	Grade 0	**Grade I**	**Grade II**	**Grade III**
Pancreatic echogenicity grade:				
Range	19.0-40.0	24.0-37.0	25.0-37.0	35.0-47.0
Mean±S.D.	27.56±7.43	35.57±6.64	32.0±4.69	35.9±0.0
P	0.009			
P1		0.002	0.016	0.003
P2			0.211	0.365
P3				0.211
	Grade 0	**Grade I**	**Grade II**	**Grade III**
Liver echogenicity grade:				
Range	19.0-42.0	24.0-48.0	30.0-39.0	37.0-37.0
Mean±S.D.	28.61±7.25	35.16±7.16	34.40±4.27	37.00±0.0
P	0.013			
P1		0.001	0.001	0.001
P2			0.652	0.452
P3				0.107

P1 comparison between group 1 and other groups,
P2 comparison between group 2 and other groups,
P3 comparison between group 3 and 4.

By using FABP 1 as a predictor to pancreatic echogenicity, it was found that at cut off value 32.0 the sensitivity of FABP1 to diagnose pancreatic echogenicity was 86.0%, specificity was 80.0% and total accuracy was 84.0%. By using FABP1 as a diagnostic marker in liver echogenicity at cut off value 31.0, the sensitivity was 81.0%, specificity was 76.0% and total accuracy was 78.0% **(Table 6)**.

Table (6): Sensitivity, specificity and accuracy of FABP 1 in prediction the pancreatic echogenicity and liver echogenicity

Area	Cut off value	P value	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
Pancreatic echogenicity				
0.821	32.0	0.001	0.610	0.832
Sensitivity	86.0			
Specificity	80.0			
Accuracy	84.0			
Liver echogenicity				
0.795	31.0	0.001	0.604	0.829

DISCUSSION

There were significant statistically differences between groups regarding to BMI, and no significant statistically differences between groups regarding to age and sex.

In agreement with our results, *Shi et al. (2012)* found that there were no significant differences in age and gender between obese and normal-weight subjects. *Tirkes et al. (2019)* found that distribution of patient's sex was similar in patients with and without CP and T2DM. Patients in the CP (Chronic Pancreatitis) group were older (age, 60 years; range, 22–75 years) than those in the no CP group (age, 50 years; range, 19–78 years). Patients with and without T2DM had similar age (57 vs 55 years, respectively).

The present study showed that there was no significant statistically difference between groups as regard to hematological parameters. There were a significant statistically differences between groups as regard to blood glucose level, there was a significant increase in both fasting glucose and HbA1c in both group 2 and 4 more than other two groups.

In agreement with our results, study of *Nakamura et al. (2017)* reported that HbA1c was significantly higher in the T2DM group compared with the non-DM group.

Furthermore, *Wu and Wang (2013)* revealed that as compared to the normal pancreas group, the fatty pancreas group was characterized by significantly higher FBG, PBG (postprandial blood glucose), HbA1c and by a significantly higher platelet count.

In addition, *Della Corte et al. (2015)* found obese children with NAFLD complicated with NAFPD had a higher insulin resistance and circulating levels of tumor necrosis factor-α and interleukin-1β than those without NAFPD. Similarly, a community cohort study held by *Wong et al. (2014)* also proved that adults with both NAFPD and NAFLD had a higher homeostasis model assessment of insulin

resistance (HOMA-IR) than those with either condition alone. Pancreatic fat content was associated with HOMA-IR, even after adjusting for hepatic fat content and BMI. A study conducted by *van der Zijl et al. (2011)*, involving patients with impaired fasting glucose and/or impaired glucose tolerance that used hyperglycemic clamp to assess insulin sensitivity, showed an inverse correlation between pancreatic fat content and insulin sensitivity.

The current study showed that there was significant statistically difference between groups as regard to ALT, AST and GGT. There was significant statistically difference between groups as regard to triglycerides.

Our results were supported by study of *Shi et al. (2012)* as they reported that compared with normal-weight subjects, obese subjects had higher BMI, waist circumference (WC), blood pressure, ALT, AST, TG, TC, LDL-c and fasting glucose.

Furthermore, *Nakamura et al. (2017)* revealed that between the two groups, mean AST, ALT, TG and low-density lipoprotein (LDL)-cholesterol were significantly higher in the T2DM group compared with the non-DM group.

However, *Wu and Wang (2013)* revealed that as compared to the normal pancreas group, the fatty pancreas group was characterized by significantly higher mean total cholesterol, TG, and LDL-C values. No statistically significant differences between the two groups were observed for liver function tests involving aspartate aminotransferase, alanine aminotransferase, and γ-glutamyl transpeptidase measurements or for tumor markers including carcinoembryonic antigen and carbohydrate antigen.

In the past, the diagnosis of pancreatic steatosis was made on in vivo autopsy specimens. With the advent of more advanced and sophisticated imaging modalities, pancreatic steatosis is most often found using these imaging techniques. Ultrasonography is the most widely and commonly used imaging technique *(Tariq et al., 2016)*.

In the study in our hands, there was significant statistically difference between groups as regard to pancreatic echogenicity. There were significant statistically difference between groups as regard to liver echogenicity.

Lee et al. (2010) diagnosed an increased echogenicity of pancreatic body over the kidney echogenicity during ultrasonography as fatty pancreas. They found that insulin resistance, visceral fat, triglyceride, and alanine aminotransferase (ALT) tended to increase with the degree of fat deposition in the pancreas. They found the presence of fatty pancreas along with fatty liver concurrently in many cases. They suggested that fatty pancreas might be the initial indicator of “ectopic fat deposition” and as an early marker of insulin resistance, which is a key element of fatty liver and/or metabolic syndrome.

Another study done by *Al-Haddad et al. (2018)* who used endoscopic ultrasound, also found hepatic steatosis, alcohol use, and increased BMI as predictors of pancreatic steatosis, with hepatic steatosis being the strongest predictor with an odds ratio of nearly 14-fold. Ultrasonography has some limitations considering that pancreas may not be well visualized in obese patients

and pancreatic fibrosis also appears hyperechogenic. To avoid the later problem, kidneys or liver can be used as a reference point; a higher pancreatic echogenicity as compared to liver or kidney indicates pancreatic steatosis, while an echogenicity similar to retroperitoneal fat suggests highest amount of pancreatic fat deposition *(Smits and van Geenen, 2011)*.

The present study showed that there was significant statistically difference between groups as regard to FABP 1. Positive significant correlation between FABP 1 and age and BMI, while there is non-significant correlation between FABP 1 and female sex, systolic blood pressure (mmHg), diastolic blood pressure (mmHg), currently smoking, total cholesterol, triglycerides, HDL, LDL, GGT, AST, ALT, HbA1c and Leukocyte.

However, previous studies provided inconsistent results regarding the association of NAFPD with age, sex, hypertension, hypertriglyceridemia, and NAFLD. These inconsistent results may be due to difference in diagnostic methods, small sample size in some studies and its retrospective design. Also, the need of laboratory marker that can be used as simple non-invasive biomarker to aid in diagnosis is crucial to be adding to the investigations, especially when used the abdominal ultrasound. Fatty Acid Binding protein 1 (FABP1) is tissue specific marker that can be used to diagnose NAFPD as per Nature *(Furuhashi and Hotamisligil, 2018)*.

In the study of *Nakamura et al. (2019)*, in T2DM, FABP4 had no significant correlation between FABP4 and BMI.

Lu et al. (2020) reported that in multiple logistic regression analysis after adjustments for age and sex, a high FABP1 level was associated with overt NAFLD. In addition, SBP, DBP, BMI, waist circumference, total cholesterol, TGs, HDL-cholesterol, LDL-cholesterol, GGT, AST, ALT, HOMA-IR, HbA1c, eGFR, and WBC count were significantly associated with the presence of overt NAFLD.

In the study of *Wellen and Hotamisligil (2015)*, they revealed that adipocyte/ macrophage fatty acid binding proteins, aP2 and mal1, act at the interface of metabolic and inflammatory pathways. These fatty acid binding proteins are involved in the formation of atherosclerosis predominantly through the direct modification of macrophage cholesterol trafficking and inflammatory responses. In addition to atherosclerosis, these fatty acid binding proteins also exert a dramatic impact on obesity, insulin resistance; type 2 diabetes and fatty liver disease. The creation of pharmacological agents to modify fatty acid binding protein function will provide tissue or cell-type-specific control of these lipid signaling pathways, inflammatory responses, atherosclerosis, and the other components of the metabolic syndrome, therefore offering a new class of multi-indication therapeutic agents.

In our study, the level of FABP1 was significantly higher in grade I, II and III more than grade 0 of pancreatic echogenicity. On the other hand, the level of FABP1 showed a significant increase in grade III liver echogenicity more than grade I and II. Also, grade I, II and III

showed significant increases in FABP 1 more than grade I liver echogenicity.

By using FABP 1 as a predictor to pancreatic echogenicity, it was found that at cut off value 32.0 the sensitivity of FABP1 to diagnose pancreatic echogenicity was 86.0%, specificity was 80.0% and total accuracy was 84.0%. By using FABP1 as a diagnostic marker in liver echogenicity at cut off value 31.0, the sensitivity was 81.0%, specificity was 76.0% and total accuracy was 78.0%.

In agreement with our results, *Lu et al. (2020),* found that the patients with overt NAFLD (grade 2 or 3) had a significantly higher serum FABP1 level than those with grade 1 NAFLD and normal subjects. In addition, the patients with overt NAFLD had higher rates of hypertension, hyperlipidemia, CKD, angiotensin converting enzyme inhibitor and angiotensin II receptor blocker treatment, and stages 3 and 4 of CKD classes.

Serum FABP-1 levels were shown to decrease after remission period although the differences were not statistically significant. Fatty-acid trafficking in cells is a complex and dynamic process affecting many aspects of cellular function. Fatty acids function both as an energy source and signals for metabolic regulation, acting through enzymatic and transcriptional networks to modulate gene expression, growth and survival pathways, and inflammatory and metabolic responses. FABP-1 is known to bind polyunsaturated fatty acids and long-chain fatty acid peroxidation products *(EK et al., 2010).*

Sztefko and Panek (2010) have suggested that high serum free fatty acid concentration may be involved in the development of complications in acute pancreatitis by binding polyunsaturated fatty acids; FABP-1 modulates the availability of these fatty acids to intracellular oxidative pathways. In addition to these well-known functions, studies have shown that FABP-1 plays a protective role in kidney injury. From a theoretical point, it was suggested that high levels of FABP-1 could protect against oxidative stress and inflammation in the pancreatic tissue *(Kanaguchi et al., 2011).*

CONCLUSION

FABP1 can be used a diagnostic biomarker for non-alcoholic fatty pancreatic disease. There was significant statistically difference between groups as regard to FABP 1, and positive significant correlation between FABP 1 and age & BMI while there is non-significant correlation between FABP 1 and female sex, systolic blood pressure (mmHg), diastolic blood pressure (mmHg), currently smoking, total cholesterol, triglycerides, HDL, LDL, GGT, AST, ALT, HbA1c and Leukocytes.

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دور البروتين المرتبط بالحمض الدهني 1 كمؤشر بيولوجي تشخيصي لمرض البنكرياس الدهني غير الكحولي

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خلفيـــة البحـــث: البنكريـــاس الـــدهني أو مـــرض البنكريـــاس الـــدهني غيـــر الكحـــولي هـــو تسـلل مفـرط للـدهون فـي البنكريـاس بسـبب السـمنة فـي حالـة عـدم تنـاول الكحـول بشـكل كبيـر البنكريـاس الـدهني, وهـو اكتشـاف شـائع بالموجـات فـوق الصـوتية, ويزيـد مـن صـدى القلـب بالمقارنـة مـع البنكريـاس الطبيعـي. أيضًـا، وهنـاك حاجـة إلـى علامـة معمليـة يمكـن اسـتخدامها كمؤشـر حيـوي بسـيط غيـر جراحـي للمسـاعدة فـي التشـخيص أمـرًا ضـروريًا لإضـافتها إلـى التحقيقـات، خاصـة عنـد اسـتخدام الموجـات فـوق الصـوتية علـى الـبطن. وبـروتين ربـط الأحمـاض الدهنيـة 1 هـو علامـة خاصـة بالأنسـجة يمكـن اسـتخدامها لتشـخيص مـرض البنكريـاس الـدهني غيـر الكحـولي حسب الطبيعة.

الهـدف مـن البحـث: تحديـد نسـبة حـدوث مـرض البنكريـاس الـدهني غيـر الكحـولي بـين المصـريين البـدناء وغيـر المصـابين بـداء السـكري أو بدونـه، وتقيـيم الارتبـاط المحتمـل مـع مـرض السـكري أو السـمنة، والـربط بـين تـنكس البنكريـاس الـدهني ومـرض الكبـد غيـر الكحـولي وتقيـيم التشـخيص. ودور بـروتين ربـط الأحمـاض الدهنية 1 في المريض المصري المصاب بالسكري أو بدونه فيما يتعلق بالسمنة.

المرضـي وطـرق البحـث: تضـمنت دراسـة جماعيـة مسـتقبلية 80 مريضًـا تتـراوح أعمـارهم بـين 18-70 عامًـا, حضـروا إلـي العيـادة الخارجيـة لقسـم الكبـد والجهـاز الهضـمي والأمـراض المعديـة بمستشـفى جامعـة الأزهـر (القـاهرة) مـن ينـاير 2020 إلـى ديسـمبر 2020. وتـم تقسـيم إلـى 4 مجموعـات متسـايين: المجموعـة 1: أفـرد يتمتعـون بصـحة جيـدة علـى مـا يبـدو مـع مؤشـر كتلـة جسـم طبيعـي وغيـر مصـاب

بالسكري, والمجموعة الثانية: مرضي بمؤشر كتلة جسم طبيعي، ومرضى السكر أو يعانون من ضعف جلوكوز الدم أثناء الصيام, والمجموعة 3: مرضي بمؤشر كتلة الجسم فوق 25، غير مصابين بالسكري, والمجموعة 4: مرضي بمؤشر كتلة الجسم فوق 25، ومرضى السكر أو ضعف مستوى الجلوكوز في الدم أثناء الصيام.

نتائج البحث: توجد فروق ذات دلالة إحصائية بين المجموعات فيما يتعلق ببروتين ربط الأحماض الدهنية 1. وأظهرت نتائج هذه الدراسة أن مستوى بروتين ربط الأحماض الدهنية 1 كان أعلى بكثير في الصف الأول والثاني والثالث من الصف 0 من صدى البنكرياس، من ناحية أخرى، أظهر مستوى بروتين ربط الأحماض الدهنية 1 زيادة ملحوظة في صدى الكبد من الدرجة الثالثة أكثر من الدرجة الأولى. والثاني، ويظهر كلا من الصف الأول والثاني والثالث زيادة ملحوظة في بروتين ربط الأحماض الدهنية 1 أكثر من صدى الكبد من الدرجة الأولى. باستخدام بروتين ربط الأحماض الدهنية 1 كمؤشر لتولد الصدى في البنكرياس، وقد وجد أنه عند القيمة المقطوعة 32.0، كانت حساسية بروتين ربط الأحماض الدهنية 1 لتشخيص صدى البنكرياس 86.0٪، وكانت النوعية 80.0٪ والدقة الكلية 84.0٪. باستخدام بروتين ربط الأحماض الدهنية 1 كعلامة تشخيصية في صدى الكبد عند القيمة المقطوعة 31.0، وكانت الحساسية 81.0٪ والنوعية 76.0٪ والدقة الكلية 78.0٪.

الاستنتاج: يمكن إستخدام بروتين ربط الأحماض الدهنية 1 كمؤشر بيولوجي تشخيصي لمرض البنكرياس الدهني غير الكحولي.

الكلمات الدالة: بروتين ربط الأحماض الدهنية 1، مرض البنكرياس الدهني غير الكحولي.