ORIGINAL ARTICLE

ASSOCIATION OF NON-ALCOHOLIC FATTY PANCREATIC DISEASE IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE

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ABSTRACT

Objective: To study the association of nonalcoholic fatty pancreatic disease (NAFPD) with nonalcoholic fatty liver disease (NAFLD).

Method: This cross-sectional study was done from 1st Jan to 30th September 2024 in the department of medicine and radiology at Pakistan Railways Hospital. Hundred patients were divided in two groups with fifty participants in each. Group 1 included patients with NAFLD proven on ultrasound and group 2 included healthy subjects. The patients' demographics, abdominal ultrasound, biochemical and metabolic data were recorded and analyzed using SPSS version 21.0.

Results: NAFPD was strongly associated with NAFLD. It was present in 46% patients with NAFLD while 14% in healthy subjects. Statistically significant association of fatty pancreas was seen compared to healthy group with body mass index (30.39 versus 27.31), type 2 diabetes (76% versus 6.97%), hypertension (30% versus 8%), and metabolic syndrome (78% versus 16.27%).

Conclusion: Our study showed that NAFPD is strongly associated with NAFLD and other metabolic risk factors.

Key words: Non-Alcoholic Fatty Pancreas Disease, Non-Alcoholic Fatty Liver Disease, Ultrasonography, Metabolic Syndrome

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INTRODUCTION

NAFPD is the accumulation of fat in the pancreas in the absence of alcohol, toxins, or infection. Initially the fat accumulation is reversible but if prolonged and continuous it leads to chronic inflammation, fibrosis, and finally pancreatic adenocarcinoma. It affects all ages, and it is important risk factor for type 2 diabetes mellitus.[1] In the last few decades, quantity, and type of food consumption along with sedentary lifestyle has led to increased prevalence of obesity and metabolic syndrome. Over nutrition leads to hyperinsulinemia that promotes lipogenesis.[2] Hyperinsulinemia also promotes insulin resistance that result in accumulation of excess fat in viscera leading to fatty liver and fatty pancreas.[3]

NAFLD is the most common type of liver disease prevalent throughout the globe. It is linked with metabolic dysfunction and is recognized as hepatic part of metabolic syndrome. It also increases the risk of diabetes by two-fold and promotes fat accumulation in pancreas which eventually leads to the development of frank diabetes mellitus.[3] Each percentage increase in pancreatic fat increases the risk of diabetes by 7%. Evidence has shown that removal of this visceral fat by low caloric diet / and bariatric surgery induces

biochemical remission by reducing insulin back to normal thus improving glucose tolerance.[4]

Globally prevalence of NAFPD is 16% to35%.[5] In Pakistan diabetes prevalence is 26.3% and the prevalence of NAFLD is 30%[6] indicating poor metabolic health. A study from Pakistan reported frequency of fatty pancreas is 26.5%.[7] Finding of fatty pancreas should not be regarded as benign entity but a marker of future pancreatic endocrine and exocrine dysfunction. Obese, overweight people should be screened for metabolic health. Early detection and management can help prevent and cure metabolic dysfunction, the root cause of non-communicable diseases. It is needed to take real life practical steps to create awareness among patients and health care professionals. Motivation to implement healthy diet and exercise is dire need of time.

We aim to study the association of NAFPD with NAFLD in our population and study its effect on metabolic parameters.

METHODS

This cross-sectional study was done on one hundred patients in department of medicine and radiology of Pakistan Railway Hospital from 1st Jan till 30th September 2024. Study was started after approval from hospital's ethical review committee. Written informed consent was taken. Patients were divided in two groups. First group included 50 patients with NAFLD proven on ultrasound. Second group included of 50 healthy subjects without fatty liver on abdominal ultrasound. History and clinical examination were done along with calculation of body mass index (BMI). Blood samples were taken for serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma glutamyl transferase (ϒ-GT), total cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL), triglyceride, fasting blood sugar and serum uric acid. We used cut off uric acid level for men < 5 mg/dl and for females 2-4 mg/dl as this is optimal level for good metabolic health.[8] Similarly for the same reason we used lower cut off level for serum ALT 25u/l for males and 17u/l for females.[9] All ultrasounds were done by the more than five-year experienced radiologists by using Mindray ultrasound machine with 2-7 MHZ frequency probe to diagnose fatty liver and fatty pancreas.

NAFPD was diagnosed in four grades.[10]

Grade 0: pancreas and kidney had same echogenicity.

Grade1: pancreas was slightly more echogenic than kidney.

Grade2: pancreas was more echogenic but less compared to retroperitoneal fat.

Grade3: Pancreas was same or more echogenic than retroperitoneal fat.

NAFLD was diagnosed in three grades[11].

Grade1: increased liver echogenicity but with appreciable periportal and diaphragmatic echogenicity.

Grade2: increased echogenicity with unclear periportal echogenicity but preserved echogenicity of diaphragm.

Grade3: diffusely increased echogenicity with vague periportal and diaphragmatic echogenicity.

The data collected on structured proforma. Continuous variables like age were expressed as mean ± standard deviation and categorical variables like gender, fatty pancreas, fatty liver, BMI, triglycerides etc. were expressed in the form of frequencies and percentages. P value of <0.05 was taken as significant. Data was analyzed using SPSS version 21.0.

RESULTS

Out of 100 patients, 32 were males and 68 were females in this study. The age range in both groups was 18 -85 years. Significant higher mean age in group 1 compared with group 2. Fatty pancreas was seen in 46% patients with NAFLD (group1) while 14% patients in the healthy group. Overall NAFPD was seen 60%. There was significant difference about the severity of fatty pancreas. Grade III fatty pancreas was not seen in healthy group. Majority of patients in NAFLD group were overweight and obese and their BMI was significantly higher than group 2 participants. About 78% had metabolic syndrome and higher frequency of metabolic syndrome parameters (hypertension, fasting blood sugar, triglycerides, HDL, waist circumference) compared with group 2. Grades of NAFPD were shown in Table 1. Higher triglyceride/HDLC ratio was seen in 66% in group 1 (Table 2). There was also higher ALT and uric acid level in group 1 patients. In NAFLD group 61.71% had hyperuricemia and 60% patients had higher ALT levels. Comparison of biochemical profile of NAFLD versus healthy controls is shown in Table 3

Table 1. Grades of non-alcoholic fatty Pancreas in patients with non-alcoholic fatty liver disease versus healthy controls

Non-lcoholic Fatty pancreas	Group 1 (NAFLD) (n=50)	Group 2 (Controls) (n=50)	P value (<0.005)
Grade1	7	4	
Grade II	13	3	
Grade III	3	0	
Total	23 (46%)	7 (14%)	<0.005

Table 2. Comparison of demographic and clinical characteristics of the study population

Variables	Group 1 NAFLD (50)	Group 2 Controls (50)	P value <0.005
Age (years)	48± 16	35± 15	<0.005
Sex M/F	12/38	20/30	
Mean BMI Kg/m²	30.39	27.31	<0.005
Type 2 diabetes	38 (76%)	3 (6.97%)	<0.005
Hypertension	30 (60%)	4 (8%)	<0.005

Metabolic syndrome	39 (78%)	7(16.27%)	<0.005

Table 3. Comparison of biochemical profile of NAFLD patients versus healthy controls

Variables	Group1 NAFLD	Group 2 Healthy controls	P value
Uric acid mg/dl	3.29 ± 2.31	3.20 ± 1.08	<0.005
ALT U/L	23.12 ± 6.1	21.17 ± 5.25	<0.005
AST U/L	20.81 ± 8.0	21.47 ±7.8	0.12
ϒ-GT U/L	15±5	15±3	0.01
Triglycerides mg/dl	157.76 ± 55.63	92 ± 29.82	<0.005
LDL-C mg/dl	114.8 ± 7.4	88.6 ± 16.3	0.02
HDL-C mg/dl	35 ± 7.01	38 ±7.12	<0.005
TG/HDL-C ratio > 4	66%	18%	<0.005
Fasting blood sugar mg/dl	90 (93.5-153.76)	79 (81.5-96.76)	<0.005

DISCUSSION

Results of our study showed that almost 46 % with NAFLD has NAFPD while 14%of healthy subjects had NAFPD. A study from Egypt has shown that 76% of patients with fatty liver had NAFPD.[12] While 50.7%, 65.8% concurrence has been reported by others.[13, 14]

Fatty liver and fatty pancreas both are correlated possibly due to same endodermal embryonic origin. Fat accumulation in both organs is explained by twin cycle hypothesis[15]. Chronic hyperglycemia causes hyperinsulinemia which promotes de novo lipogenesis in the liver resulting in NAFLD. Excess triglycerides in liver are also transported as VLDL to pancreas causing NAFPD. Fat accumulation in pancreas damages beta cell and increasing insulin resistance enhance fatty liver. [16] Both organs go into self-perpetuating cycle of fat accumulation suggesting bidirectional relationship. Fatty pancreas is associated with more severe inflammation and fibrosis grading of liver. [17,18] About 54% NAFLD had no steatosis in pancreas while Celal et al reported similar discordance of around 55.1% suggesting the need for further exploration of confounding factors.[13]

In our study grade I fatty pancreas was seen 26%, while 14%, 6% have grade II and grade III pancreatic steatosis in group1 NAFLD patients suggesting it a statistically significant risk factor. Similarly, Reda et al. reported grade I fatty pancreas in 16% and grade II in 8% and grade 3 in 52% patients with NAFLD.[12]

We found that the mean age of patients with NAFPD alone and with NAFLD was higher than healthy individuals. Similar trend has been shown in other studies that fatty pancreas prevalence increases with age may be due to prolonged deregulated metabolism.[1,12] Our study disagreed with higher prevalence in male patients as reported in earlier studies we found higher prevalence in females.

Majority of patients in NAFLD group were obese or overweight. Our results are in accordance with previous studies as obesity is significant risk factor for fatty pancreas.[1,12,13] In Asian population overall higher prevalence of NAFPD up to 61.4% is seen in obese patients.[1, 2]

Our study found fatty pancreas to be associated with components of metabolic syndrome. Diabetes, hypertension, and hypertriglyceridemia were present in higher frequency in group 1. Patients had higher level Triglycerides, LDL cholesterol, while lower HDL level when compared with healthy individuals. While study from Egypt found higher level of triglycerides, LDL, total cholesterol but normal level of HDL.[12] While, others found lower HDL level in NAFPD patients.[19,20] When we calculated TG/HDL-C ratio as a marker of insulin resistance, a higher ratio was observed in patients with NAFPD.

High uric acid increases insulin resistance by oxidative stress. As regard to uric acid level patient with fatty pancreas showed higher uric acid level. About 60 % patients with NAFLD had hyperuricemia. Progressive rise in its level over time heightens the risk of NAFLD and NAFPD.[8,19] We noted higher ALT level in patients with fatty pancreas and our result matched with result of earlier studies. But no significant change was seen for other liver enzymes.[13]

As NAFPD is a significant predictor of prediabetes and type 2 diabetes and we are facing increasing prevalence of diabetes. By understanding its pathophysiology, we can bring paradigm shift in the management of type 2 diabetes targeting to reduce hyperinsulinemia and insulin resistance.[21] Implementing healthy lifestyle, fasting and low caloric diet in its treatment will remove visceral fat and reverse diabetes. We will be able to reduce morbidity and mortality due to these chronic metabolic diseases as well as total health care cost.

CONCLUSION

NAFPD is strongly linked with fatty liver and has unfavorable effect on systemic metabolism.

Limitation of study is that of cross-sectional design. Longitudinal study will explore the relation deeply with substantial number of participants.

ETHICAL APPROVAL

Ethical approval was granted by the Institutional Review Committee of Islamic International Medical College, Rawalpindi vide reference No Riphah/IRC/23/3100 dated: 27/09/2023

CONFLICT OF INTEREST:

Authors declare no conflict of interest.

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AUTHOR'S CONTRIBUTIONS

SK: Drafting of article and manuscript writing
FF, AF: Data collection and statistical analysis
KF: Concept, design and manuscript writing
SF: Critical analysis and revision of manuscript
FZS: statistical analysis and manuscript writing
ALL AUTHORS: Approval of the final version of the manuscript to be published

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