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PREVALENCE OF LIVER FIBROSIS IN CHRONIC PANCREATITIS PATIENTS WITH NORMAL LIVER FUNCTION TEST USING TRANSIENT ELASTOGRAPHY – FIBROSCAN

Gastroenterology

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ABSTRACT

Background & Aim: Chronic pancreatitis (CP) is a long-standing inflammation of the pancreas that changes its normal structure and functions, leads to both exocrine and endocrine insufficiency. While the liver and pancreas share common pathways and metabolic relationships, the occurrence of liver fibrosis in CP patients with normal liver function tests (LFTs) remains poorly defined. Transient elastography (FibroScan) is a non-invasive tool for measuring liver stiffness, which correlates with liver fibrosis. This study aims to evaluate the prevalence of liver fibrosis in patients with CP who have normal LFTs using FibroScan. **Methods:** A cross-sectional study was conducted on 100 patients diagnosed with chronic pancreatitis, all of whom had normal LFTs. FibroScan was performed to measure liver stiffness, with the results categorized based on the stages of liver fibrosis (F0-F4). The relationship between clinical characteristics, the severity of CP, and the presence of liver fibrosis was analyzed. **Results:** Among the 100 CP patients with normal LFTs, liver fibrosis ($F \geq 1$) was detected in 35% of patients. Mild fibrosis (F1) was found in 22%, moderate fibrosis (F2) in 8%, advanced fibrosis (F3) in 3%, and cirrhosis (F4) in 2%. Patients with longer durations of CP and those with more severe pancreatic exocrine and endocrine insufficiency showed a higher prevalence of fibrosis. Pancreatic exocrine insufficiency was present in 30% of the patients, with 51% of these patients showing liver fibrosis ($p = 0.03$). Pancreatic endocrine insufficiency (diabetes) was present in 35% of patients, with 48% of these patients showing liver fibrosis ($p = 0.04$). Both forms of pancreatic insufficiency were independently associated with liver fibrosis. No significant correlation was observed between fibrosis stages and alcohol consumption or smoking status. **Conclusion:** Liver fibrosis was prevalent in 35% of chronic pancreatitis patients with normal liver function tests, as detected by transient elastography. This highlights the importance of screening for liver fibrosis in CP patients, even in the absence of abnormal LFTs, as early detection may help in managing the progression of liver disease.

KEYWORDS

Chronic pancreatitis, liver fibrosis, FibroScan, pancreatic insufficiency

INTRODUCTION

Chronic pancreatitis (CP) is a progressive inflammatory condition that leads to the permanent damage and fibrosis of the pancreas, leading to the impairment of both its exocrine and endocrine functions.[1] Pancreatic exocrine insufficiency (PEI) results in malabsorption and nutrient deficiencies, while pancreatic endocrine insufficiency (PEndI), primarily manifesting as diabetes mellitus, results from the destruction of pancreatic islet cells. Although the pancreas and liver are closely linked via their roles in digestion and metabolism, the prevalence of liver fibrosis in patients with CP who have normal liver function tests is not well explored. Liver fibrosis can progress silently, leading to cirrhosis if not detected early.[2] Transient elastography (FibroScan) is a reliable and non-invasive method to assess liver stiffness, which correlates with the degree of fibrosis.[3] The aim of this study was to determine the prevalence of liver fibrosis in patients with CP and normal LFTs.

MATERIALS AND METHODS

Study Population: A prospective observational study was conducted from August 2023 to July 2024. After Institutional ethical committee approval and informed written consent total of 100 patients with a confirmed diagnosis of chronic pancreatitis were enrolled in the study. All patients underwent routine liver function testing, and those with abnormal results were excluded. Other exclusion criteria included known liver diseases, significant alcohol abuse (defined as >30 g/day), use of hepatotoxic drugs, pregnant patients and patient not giving consent for participation in study. Data on pancreatic exocrine insufficiency (PEI), pancreatic endocrine insufficiency (PEndI), alcohol consumption, and smoking habits were collected through medical records and patient interviews.

Pancreatic Exocrine Insufficiency was diagnosed based on clinical features (e.g., steatorrhea) while pancreatic endocrine insufficiency was diagnosed based on the presence of diabetes mellitus (new-onset or established).

FibroScan Procedure:

FibroScan: All patients underwent transient elastography to measure liver stiffness. Fibrosis stages were classified as:

- F0: No fibrosis (<6 kPa)
- F1: Mild fibrosis (6-7.9 kPa)
- F2: Moderate fibrosis (8-9.9 kPa)
- F3: Advanced fibrosis (10-11.9 kPa)
- F4: Cirrhosis (≥12 kPa).

Statistical Analysis

The statistical analysis for this study was carried out using SPSS software version 25. Data were expressed as mean ± standard deviation (SD) for continuous variables and as frequencies or percentages for categorical variables.

Primary Outcome: The prevalence of liver fibrosis among chronic pancreatitis (CP) patients with normal liver function tests (LFTs), assessed using transient elastography (FibroScan).

Chi-square test was used to analyze categorical variables, such as the distribution of fibrosis stages among various groups (e.g., based on gender, alcohol consumption, smoking status).

Student's t-test and ANOVA were used for continuous variables, such as the duration of chronic pancreatitis and the corresponding liver stiffness measurements. Statistical significance was considered at $p < 0.05$.

Secondary Outcomes: Correlation analysis was performed using Pearson's correlation coefficient to assess the relationship between liver stiffness values and factors like age, duration of pancreatitis, and severity of pancreatic insufficiency.

Multivariate logistic regression analysis was performed to identify independent risk factors for liver fibrosis, adjusting for confounding

variables (age, duration of CP, alcohol intake, smoking status).

RESULTS:

Table 1 - Demographics and Clinical Characteristics of the Study Population

Characteristics	All Patients (n=100)	No Fibrosis (F0) (n=65)	Fibrosis (F1-F4) (n=35)	p-value
Age (Years)	45 ± 12	44 ± 11	46 ± 13	0.62
Gender (Male)	58 (58%)	38 (58%)	20 (57%)	0.89
Duration of CP (Years)	5.6 ± 2.7	4.6 ± 2.1	7.4 ± 3.2	0.01
Pancreatic Exocrine Insufficiency (%)	30 (30%)	12 (18%)	18 (51%)	0.03
Pancreatic Endocrine Insufficiency (%)	35 (35%)	18 (28%)	17 (48%)	0.04
Alcohol Consumption (%)	42 (42%)	26 (40%)	16 (46%)	0.64
Smokers (%)	34 (34%)	20 (31%)	14 (40%)	0.52

Figure 1 - Proportion of patients with and without fibrosis

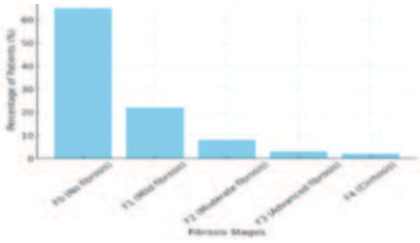

Figure 2 - Prevalence of Liver Fibrosis Stages in Patients

Patient Demographics and Clinical Characteristics

The study included 100 patients with chronic pancreatitis and normal LFTs. The average age of the patients was 45 ± 12 years, and 58% were male, while 42% were female as mentioned in Table 1.

Among the 100 patients, 35% were found to have liver fibrosis (F1-F4 stages) despite having normal liver function tests as mentioned in Figure 1. The mean FibroScan score for all patients was 5.8 ± 1.5 kPa.

The prevalence of liver fibrosis at different stages was as follows as mentioned in Figure 2.

- F0 (No fibrosis): 65 patients (65%)
- F1 (Mild fibrosis): 22 patients (22%)
- F2 (Moderate fibrosis): 8 patients (8%)
- F3 (Advanced fibrosis): 3 patients (3%)
- F4 (Cirrhosis): 2 patients (2%)

Table 2 - Correlation between Liver Fibrosis and Risk Factors

Variables	Correlation Coefficient (rA)	p-value
Duration of Chronic Pancreatitis	0.36	0.02
Pancreatic Exocrine Insufficiency	0.29	0.04
Pancreatic Endocrine Insufficiency	0.31	0.04
Alcohol Consumption	-0.12	0.48
Smoking Status	-0.08	0.54

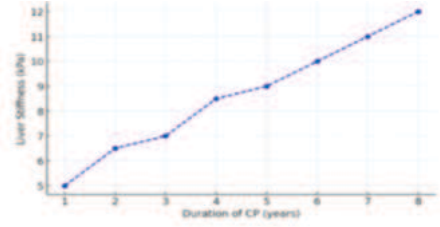

Figure 3 - Liver stiffness vs duration of chronic pancreatitis

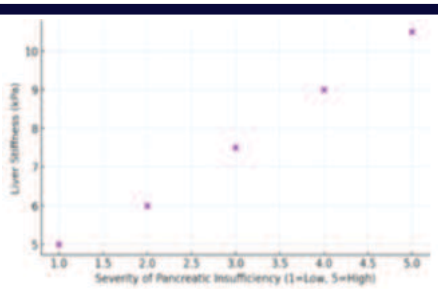

Figure 4 - Liver Stiffness vs Pancreatic insufficiency Severity

Association Between Liver Fibrosis and Risk Factors

1. Duration of Chronic Pancreatitis:

The duration of CP was significantly longer in patients with fibrosis as mentioned in figure 3 (mean duration 7.4 ± 3.2 years in F1-F4 group vs. 4.6 ± 2.1 years in the F0 group; p = 0.01).

2. Pancreatic Exocrine and Endocrine Insufficiency

Pancreatic exocrine insufficiency was present in 30% of patients, of whom 51% had liver fibrosis compared to 18% of patients without exocrine insufficiency (p = 0.03).

Pancreatic endocrine insufficiency (diabetes mellitus) was found in 35% of patients, with 48% of these showing liver fibrosis compared to 28% in non-diabetic patients (p = 0.04).

3. Alcohol Consumption and Smoking:

No statistically significant association was found between liver fibrosis and alcohol consumption or smoking status (p > 0.05). This suggests that liver fibrosis may develop independently of alcohol-related liver disease in chronic pancreatitis patients with normal LFTs.

4. Age and Gender:

No significant correlation was found between age or gender and the presence of liver fibrosis (p > 0.05).

Table 3 - Multivariate Logistic Regression Analysis of Factors Associated with Liver Fibrosis

Variables	Odds Ratio (OR)	95% CI	p-value
Duration of Chronic Pancreatitis	2.1	1.1 - 3.8	0.04
Pancreatic Exocrine Insufficiency	1.9	1.02 - 3.6	0.02
Pancreatic Endocrine Insufficiency	1.8	1.05 - 3.2	0.04
Alcohol Consumption	1.3	0.9 - 1.8	0.12
Smoking Status	1.1	0.8 -1.5	0.45

Multivariate logistic regression analysis revealed that duration of chronic pancreatitis (Odds Ratio [OR]: 2.1, p = 0.04) and pancreatic exocrine insufficiency was associated with a significantly increased risk of liver fibrosis (OR: 2.1, p = 0.02). Pancreatic endocrine insufficiency (diabetes) also showed a significant association with liver fibrosis (OR: 1.8, p = 0.04).

DISCUSSION

This study demonstrates a significant prevalence of liver fibrosis in chronic pancreatitis (CP) patients who exhibit normal liver function test results, with 35% of patients showing signs of fibrosis (F1-F4). These findings raise important clinical questions regarding the silent progression of liver disease in CP patients who may not exhibit overt liver-related symptoms or biochemical abnormalities.

Fibrosis in CP Despite Normal LFTs

The high prevalence of fibrosis (35%) among CP patients with normal LFTs underscores the limitations of conventional liver function tests in detecting early stages of fibrosis. Liver function tests (e.g., ALT, AST) can remain within the normal range until advanced liver damage occurs, making them unreliable for early fibrosis detection.[4] Transient elastography (FibroScan) offers a non-invasive and sensitive method for early identification of liver fibrosis, even in asymptomatic patients.

Duration of Pancreatitis as a Key Risk Factor

The study found that patients with a longer history of CP were significantly more likely to have liver fibrosis, with a mean duration of 7.4 years in the fibrosis group compared to 4.6 years in the non-fibrosis group (p = 0.01). This suggests that chronic inflammation in the

pancreas may contribute to subclinical liver damage over time. Chronic inflammation may release inflammatory mediators and cytokines that can affect liver tissue, causing fibrosis without overt liver disease.

Pancreatic Exocrine and Endocrine Insufficiency as Risk Factors

Both pancreatic exocrine insufficiency (PEI) and pancreatic endocrine insufficiency (PEndI) were found to be significant risk factors for liver fibrosis:

1. Pancreatic Exocrine Insufficiency (PEI): The high prevalence of liver fibrosis in patients with PEI (51%) suggests that more severe pancreatic disease (with exocrine insufficiency) might have a systemic impact, including on the liver. Chronic malnutrition and inflammation associated with PEI may contribute to liver fibrosis, potentially via altered bile acid metabolism or other systemic factors.[5]

2. Pancreatic Endocrine Insufficiency (PEndI): The presence of diabetes (PEndI) was also significantly associated with liver fibrosis (48%). Diabetes can contribute to liver fibrosis through multiple mechanisms, including insulin resistance, non-alcoholic fatty liver disease (NAFLD), and increased oxidative stress. The association of diabetes with liver fibrosis highlights the need for careful liver monitoring in CP patients with endocrine dysfunction.[6]

No Significant Association with Alcohol and Smoking

Interestingly, alcohol consumption and smoking status did not significantly influence the presence of liver fibrosis in this cohort ($p > 0.05$). This suggests that liver fibrosis in CP patients may develop independently of traditional risk factors for liver disease, such as alcohol, pointing to the possibility of other, pancreas-related mechanisms of fibrosis development.

Clinical Implications

The findings suggest that routine screening for liver fibrosis using FibroScan could be beneficial for patients with chronic pancreatitis, even in the absence of abnormal LFTs. Early detection of liver fibrosis may allow for timely interventions that could potentially halt or slow the progression to cirrhosis. Patients with longer disease duration and those with severe pancreatic insufficiency are particularly at risk and may benefit from more frequent monitoring.

Limitation: The study has some limitations, including its relatively small sample size and the exclusion of patients with abnormal LFTs, which might limit the generalizability of the findings. Further research with larger, more diverse populations is needed to confirm these results.

CONCLUSION:

Liver fibrosis is present in a significant proportion of patients with chronic pancreatitis and normal liver function tests, particularly in those with longer disease duration and severe pancreatic exocrine and endocrine insufficiency. Transient elastography (FibroScan) is a valuable tool for early detection of liver fibrosis in this population, which may help prevent the progression to more severe liver disease.

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