DOI: 10.7860/JCDR/2022/53684.17145

Original Article

Pathology Section

Histomorphological Changes in Pancreas and Liver among Chronic Alcoholics- An Autopsy Study

DANISH S SHAIKH[1], SHAILESH VARTAK[2], URMI VARTAK[3]

ABSTRACT

Introduction: The clinical and pathological association between pancreatitis and alcohol abuse is well recognised, however the concurrence of prevalence of alcoholic related pancreatitis and liver disease is less well studied.

Aim: To evaluate frequency of histomorphological changes in pancreas and liver among patients with history of alcohol abuse and observe the prevalence of coexistence between chronic pancreatitis and liver cirrhosis.

Materials and Methods: This was observational cross-sectional study conducted in Department of Pathology at Lokmanya Tilak Municipal Medical College, Mumbai, Maharashtra, India, from July 2013 to July 2018. The study included 1917 autopsies and 107 cases with a documented history of chronic alcohol abuse. Haematoxylin and Eosin (H&E) staining was done on all sections and special stain like Masson's trichrome was performed as per indication. Gross and microscopy were studied under variable defined parameters. Data was entered in Microsoft Excel sheets.

Results: Histomorphologically, 12 cases (11.21%) were diagnosed as pancreatitis; 10 cases (9.34%) were of acute pancreatitis and two cases (1.86%) were of chronic pancreatitis. Total 21 cases were diagnosed as liver cirrhosis. The most dominant pattern of fibrosis seen in pancreatitis was perilobular and interlobular periductal fibrosis. The frequency of pancreatitis (14.28%) and pancreatic fibrosis (38.09%) was found to be more in cirrhotics. Chronic pancreatitis was commonly seen in cirrhotics than in non cirrhotics. Similarly, liver cirrhosis was more commonly observed in cases of chronic pancreatitis.

Conclusion: The frequency of histomorphological changes seen in pancreas and liver was observed considerably among patients giving history of alcohol abuse. The prevalence of co-existence of chronic pancreatitis and liver cirrhosis was 50%.

Keywords: Alcoholic cirrhosis, Interlobular periductal fibrosis, Perilobular fibrosis, Stellate cells, Steatosis

INTRODUCTION

Liver disease and pancreatic changes are two conditions that commonly co-occur in chronic alcoholics. The clinical and pathological association between pancreatitis and alcohol abuse is well recognised, however the concurrence of prevalence and association of alcoholic related pancreatitis and liver disease is less well studied. Both liver and pancreatic alcoholic diseases have precursor lesions which bear association with one another.

The development of liver cirrhosis requires history of several years of chronic alcoholism [1-3]. For many years, it was considered that around 10-35% of subjects with chronic alcoholism developed alcoholic liver cirrhosis [4]. More recently, prospective studies have shown that the frequency is indeed much lower in alcoholics i.e, around 2% [1,2].

The stimulation of stellate cells as an initiating event in development of parenchymal fibrosis in chronic alcoholics, follows a similar process in both liver and pancreas [1].

The aim of the present study was to evaluate effects of chronic alcoholism on pancreas and liver in patients who gave a history of chronic alcohol abuse by examining the histological changes in pancreas and liver; and observe the prevalence of coexistence between chronic pancreatitis and liver cirrhosis as well as their precursor lesions.

MATERIALS AND METHODS

This was observational cross-sectional study conducted in Department of Pathology at Lokmanya Tilak Municipal Medical College, Mumbai, Maharashtra, India, from July 2013 to July 2018 (three years retrospective and two years prospective). The study conducted was reviewed by Institutional Ethics Committee (1/03/2017) at the Tertiary Care Hospital. The study was unanimously approved. Consent was obtained by the institute from the relatives of the patient, prior to autopsy.

Inclusion criteria: Out of the total 1917 cases in the duration of 5 years, all cases with a documented history of chronic alcohol abuse i.e 107 patients were included in the study.

Exclusion criteria: Alcoholic liver disease cases with documentation of positive antigens or antibodies against hepatitis B or C virus were excluded from the study. Liver showing findings of tuberculous necrosis, malignancies, liver abscesses and any other primary liver lesion not associated with chronic alcoholism were considered as confounding factors. Similarly, pancreatitis caused by other etiological factors like smoking, gall stones, hypertriglyceridemia and abdominal surgeries without history of chronic alcoholism were excluded from the study.

The basic data was collected from the autopsy record i.e, gender, age at death, cause of death and relevant clinical history and autopsy findings.

Procedure

The organs (liver, pancreas, heart, lungs) were dissected at the time of autopsy following appropriate protocols and obtaining consent. After dissection they were stored in formalin in the Autopsy Histopathology Department. Following adequate formalin fixation, representative tissue sections were taken from the various organs. The tissues were processed in tissue processor, and paraffin blocks were prepared. This was followed by staining with Haematoxylin and Eosin (H&E) stains and slides were prepared.

Histological parameters studied in pancreas: Fibrosis (diffuse fibrosis, perilobular fibrosis, intralobular fibrosis and interlobular periductal fibrosis), parenchymal necrosis and haemorrhage, fat necrosis and peripancreatic soft tissue necrosis, inspissated eosinophilic ductal secretions, fibrin thrombi, lobular atrophy, parenchymal calcification, fat infiltration and neutrophilic/ lymphoplasmacytic infiltration.

Histological parameters studied: Microvesicular and macrovesicular steatosis, ballooning degeneration, Mallory hyaline/Mallory Denk bodies, hepatocyte necrosis, portal tract and lobular inflammation, fibrosis in portal tract including bridging (portal to portal/central to portal) fibrosis, cholestasis and bile duct proliferation.

The special stain Masson's Trichrome was performed in all the cases where fibrosis was observed on H&E slide. Tissue from lung and uterus were used as positive control.

Staining method: Following were the reagents used in staining:

- Wiegert's Iron Haematoxylin solution: This was freshly prepared by mixing Haematoxylin stock solution and Ferric chloride stock solution (prepared fresh).
- Biebrich Scarlet-Acid fuchsin solution (1% aqueous Biebrich Scarlet 90 mL+ 1% aqueous acid fuchsin 10 mL+ glacial acetic acid 1 mL)
- Phosphomolybdic- phosphotungstic acid solution (5% phosphomolybdic acid 25 mL+5% phosphotungstic acid 25 mL).
- Aniline blue solution (aniline blue 2.5 g+ glacial acetic acid 2 mL+ distilled water 100 mL).
- 1% Acetic acid solution (glacial acetic acid 1 mL+ distilled water 99 mL) for differentiation.
- Bouin's solution (for improved staining quality).

Wiegert's Haematoxylin is resistant to decolourisation by acidic staining solutions and stains the nuclei blue. Biebrich scarlet-acid fuchsin stains all the acidic tissues like the cytoplasm, muscle, and collagen. Phosphomolybdic or phosphotungstic acid is a decolourising agent, making the scarlet-acid fuchsin diffuse out of the collagen fibres. Thus, the muscle fibres stain red. Aniline blue stains the collagen along which 1% acetic acid which is added for differentiation. The collagen fibres stain blue and the nuclei stain black, with a red background. This principle was used to detect presence, amount and distribution of fibrosis of fibrosis. Because of background staining, trichrome stains also allow easy evaluation of liver architecture.

STATISTICAL ANALYSIS

Data was entered in Microsoft Excel sheets. The prevalence or percentage was calculated from the findings of the study.

RESULTS

There were 107 patients (106 males and 1 female) who had presented with a definite history of chronic alcohol abuse. Age ranged from 20 to 80 years with a mean of 49.39 years. Of the included cases, 6 (5.6%) died of heart disease. In 22 (20.56%) cases, the cause of death was stated as due to alcoholic liver disease. Seven cases (6.54%) died due to pancreatitis. Majority of the cases died i.e., 72 cases (67.2%), were of pulmonary diseases.

Cirrhosis of micronodular type was documented in 12 cases (11.21%) and macronodular type was documented in six cases (5.60%) whereas, 89 cases (83.17%) were non cirrhotic. Grossly visible haemorrhagic pancreatitis was observed in six cases; changes of chronic pancreatitis in the form of firm and fibrotic pancreas which were slightly shrunken were documented in one case.

There were altogether 12 cases (11.21%) which were diagnosed as pancreatitis on histology, of which 10 cases (9.34%) were of acute pancreatitis and two cases (1.86%) were diagnosed as chronic pancreatitis [Table/Fig-1]. Grossly visible liver parenchymal necrosis was documented in five cases (4.67%) giving history of alcohol abuse (does not exclude tuberculosis caseous necrosis and liver abscess) and fatty change was documented in 15 cases (14.01%). The two dominant pattern of fibrosis seen in acute pancreatitis (n=10) were perilobular (n=3) and interlobular

Morphological changes in pancreas	n (%)
Diffuse fibrosis	2 (1.86%)
Perilobular fibrosis	16 (14.95%)
Intralobular fibrosis	7 (6.54%)
Interlobular periductal fibrosis	15 (14.01%)
Parenchymal necrosis and haemorrhage	6 (5.60%)
Fat necrosis within and peripancreatic area	5 (4.67%)
Inspissated secretion	4 (3.73%)
Fibrin thrombus	1 (0.93%)
Lobular atrophy	1 (0.93%)
Parenchymal calcification	0
Normal pancreas	68 (63.5%)

[Table/Fig-1]: Histopathological findings in pancreas (N=107).

periductal (n=3), which was followed by intralobular fibrosis (n=2). No evidence of diffuse fibrosis pattern was visible in cases of acute pancreatitis. Similarly, the most dominant pattern of fibrosis in chronic pancreatitis (n=2) was diffuse fibrosis which was evident in both the cases (one case of chronic pancreatitis showed more than one pattern of fibrosis). The most dominant pattern of fibrosis seen in acute pancreatitis was perilobular and that in chronic pancreatitis was diffuse fibrosis. The frequency of pancreatitis was found to be more in cirrhotics (14.28%) than in non cirrhotics (10.46%). Chronic pancreatitis was found to be more prevalent in cirrhotics (4.76%) than in non cirrhotics (1.1%). Similarly, the frequency of pancreatic fibrosis was more in cirrhotics (38.09%), than in non cirrhotics (24.4%) [Table/Fig-2-4].

Types of pancreatitis	Cirrhotic liver (n=21) (n,%)	Non cirrhotic liver (n=86) (n,%)	Total (N=107)
Acute pancreatitis	2 (9.5%)	8 (9.3%)	10
Chronic pancreatitis	1 (4.76%)	1 (1.1%)	2
Total cases of pancreatitis	3 (14.28%)	9 (10.46%)	12

[Table/Fig-2]: Prevalence of pancreatitis in cirrhotics and non cirrhotics (N=107).

Cirrhotics liver (n=21)		Non cirrhotics liver (n=86)	
With fibrosis	Without fibrosis	With fibrosis	Without fibrosis
8 (38.09%)	13 (61.9%)	21 (24.4%)	65 (75.5%)

[Table/Fig-3: Prevalence of pancreatic fibrosis in cirrhotics and non cirrhotics (N=107).

Histomorphological changes	Cirrhotic liver (n=21) (n,%)	Non cirrhotic liver (n=86) (n,%)	Total (N=107)
Diffuse fibrosis	1 (4.7%)	1 (1.1%)	2
Perilobular fibrosis	4 (19.04%)	12 (13.9%)	16
Intralobular fibrosis	3 (14.28%)	4 (4.65%)	7
Interlobular periductal fibrosis	5 (23.8%)	10 (8.6%)	15
Inspissated secretion	0	1 (1.1%)	1
Lobular atrophy	0	1 (1.1%)	1
Parenchymal calcification	-	-	0
Normal pancreas	11 (52.3%)	57 (66.2%)	68

[Table/Fig-4]: Dominant histopathological features in pancreas of cirrhotics and non cirrhotics (N=107).

Of the two cases diagnosed as chronic pancreatitis, hepatic macrovesicular steatosis was demonstrated in one case and Mallory hyaline was evident in one of the cases. Of these two cases of chronic pancreatitis, cirrhosis was seen in one case and steatosis (macrovesicular) was seen in another case. Of the total 21 cases of liver cirrhosis, 2 (9.5%) were of acute pancreatitis and one case (4.76%) was of chronic pancreatitis. Similarly, of the 29 cases of pancreatic fibrosis, liver cirrhosis was seen in eight cases (27.5%) and steatosis was seen in 16 cases (55.17%) [Table/Fig-5].

The prevalence of co-existence of chronic pancreatitis and liver cirrhosis was 50%.

Histopathology findings in liver	Cirrhotics	Non cirrhotics
Microvesicular steatosis (n=21)	7 (33.3%)	14 (66.6%)
Macrovesicular Steatosis (n=37)	10 (27.02%)	27 (72.97%)
Ballooning degeneration (n=7)	1 (14.28%)	6 (85.72%)
Mallory's hyaline (n=3)	1 (33.3%)	2 (66.6%)
Parenchymal necrosis (n=17)	2 (11.76%)	5 (88.24%)
Portal tract inflammation (n=12)	4 (33.3%)	8 (66.6%)
Bile duct proliferation	3 (60%)	2 (40%)
Bridging fibrosis	16 (64%)	9 (36%)

[Table/Fig-5]: Histopathological findings in liver in 107 cases.
*33 cases showed normal liver histology

DISCUSSION

Many investigators have explained the involved mechanisms in the co-occurrence of liver diseases and pancreatitis. Alcohol consumption has marked and specific effects on the liver and pancreas, as evidenced by the existence of disease categories. Despite the strong association between excessive alcohol consumption and development of chronic pancreatitis, alcohol alone is not sufficient to lead to the disease. Only a small proportion of chronic alcoholics (5-10%) develop chronic pancreatitis [Table/Fig-6] [5-8].

Prevalence	Agrawal P et al., [10]	Pace A et al., [13]	Griener L et al., [9]	Present study
Year of publication	2014	2009	1983	2022
Sample size	390	620	112	107
Type of study	Autopsy	Autopsy	Non autopsy	Autopsy
Chronic pancreatitis	29 (7.4%)	85 (13.7%)	65 (58.03%)	2 (1.8%)

[Table/Fig-6]: Prevalence of chronic pancreatitis in chronic alcoholics.

A retrospective study by Griener L et al., on 112 chronic alcoholics using endoscopic retrograde pancreatography and liver biopsy showed that 65 patients were diagnosed with chronic pancreatitis (58.03%) and 30.7% (20/65 cases) suffered from an additional alcoholic liver cirrhosis [9]. Thus, data shows higher susceptibility for liver disease than for pancreatic diseases in alcoholics. Cases of cirrhosis in alcoholics in the present study were more prevalent than cases of pancreatitis, thereby indicating that liver damage in alcoholics is more common than pancreatic damage [Table/Fig-7].

Variables	Present study	Agrawal P et al., [10]	Pace A et al., [13]	Renner IG et al., [21]
Sample size	107	390	620	1022
Cirrhotics	21 (19.6%)	292 (74.8%)	183 (29.5%)	786 (77%)

[Table/Fig-7]: Prevalence of liver cirrhosis in alcoholic.

A review of 1022 autopsy cases (Renner IG et al., in 1984) with alcoholic liver cirrhosis showed a prevalence of chronic pancreatitis and pancreatic fibrosis of 20% [Table/Fig-8,9] [10].

Variables	Present study	Pace A et al., [13]	Hastier P et al., [22]	Renner IG et al., [21]	Agrawal P and Vaiphei K [10]
Sample size	21	183	72	782	292
Chronic pancreatitis	1 (4.76%)	33 (18%)	14 (19%)	156 (20%)	30 (10.12%)

[Table/Fig-8]: Prevalence of chronic pancreatitis in liver cirrhosis.

In a study by Kochhar R et al., on 46 patients with alcoholic liver disease, 43.4% patients had features of chronic pancreatitis on endoscopic retrograde pancreatogram; but there was no difference in the prevalence of pancreatic changes in cirrhotic in comparison to non cirrhotic patients [11]. Caradonna P et al., (n=60), found only prevalence of 7% chronic pancreatitis in patients with alcoholic liver

Lesions	Present study (N=33)	Pace A et al., [13] (N=242)
In steatosis		
Chronic pancreatitis	1 (3.03%)	30 (12.5%)
Pancreatic fibrosis	10 (33%)	92 (38%)
In pancreatic fibrosis		
Liver cirrhosis	8 (36.3%)	92 (38%)
Steatosis	16 (72.7%)	97 (40%)

[Table/Fig-9]: Precursor Lesions.

cirrhosis [12]. The hepatic and pancreatic stellate cells play a central role in the development of fibrosis in both the liver and the pancreas, implying similar molecular mechanisms underlying the development of fibrotic changes in both liver and pancreas [13-15]. Stellate cells have been studied more in detail in the pathogenesis of fibrotic process of chronic alcohol related injuries in liver and pancreas [Table/Fig-10] [16,17].

Parameters	Present study	Pace A et al., [13]	Suda K et al., [23]	Agrawal P et al., [10]
Sample size	107	620	53	390
Type of study	Autopsy	Autopsy	Autopsy	Autopsy
Pancreatic Fibrosis	29 (27.1%)	242 (39%)	20 (37.7%)	30 (7.6%)

[Table/Fig-10]: Prevalence of Pancreatic fibrosis in chronic alcoholics.

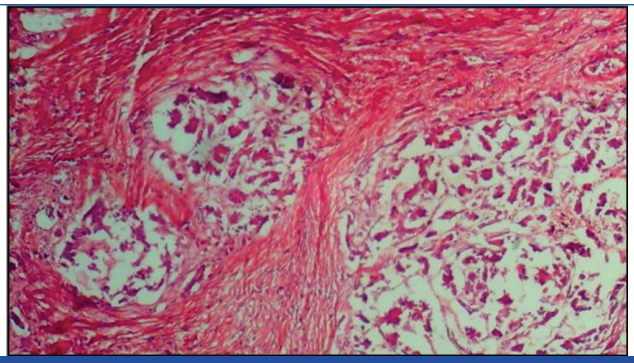
Stellate cells are believed to be activated directly by alcohol and its metabolites and also by cytokines and growth factors released during alcohol-induced pancreatic and hepatic necrosis and inflammation. This activated state of stellate cell is the main source of extracellular matrix production and collagenisation [15,16]. Gullo L et al., (1995) found an incidence of liver cirrhosis diagnosed by liver biopsy of 14% in 50 patients with chronic pancreatitis [Table/Fig-11] [18]. In a study by Pace A et al., high prevalence of pancreatic injury was also observed in association with the precursor of liver cirrhosis like severe hepatic steatosis [13]. Chronic pancreatitis and liver disease both have precursor lesions. Recent studies show that chronic pancreatitis develops through fibrosis of the pancreatic parenchyma while the precursor form of liver cirrhosis is hepatic steatosis [13,19].

Parameters	In chronic pancreatitis			
	Present study	Pace A et al., [13]	Dutta Sk et al., [24]	Gullo L et al., [18]
Sample size	2	85	50	50
Type of study	Autopsy	Autopsy	Non autopsy	Non Autopsy
Liver cirrhosis	1 (50%)	33 (39%)	9 (19%)	7 (14%)

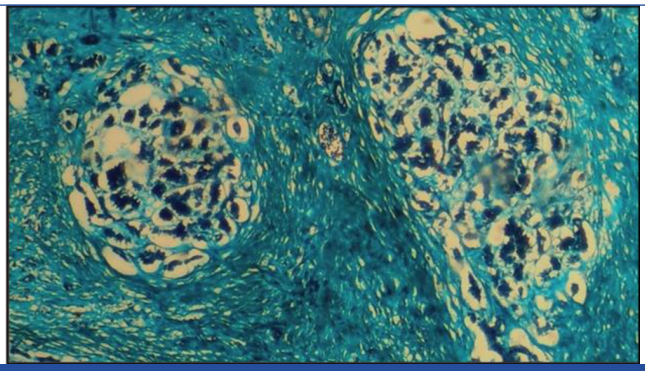
[Table/Fig-11]: Prevalence of liver cirrhosis in chronic pancreatitis.

A study by Zsori G et al., demonstrated the presence of liver fibrosis through the use of transient elastography in around one-third (33%) of alcoholic chronic pancreatitis patients [20].

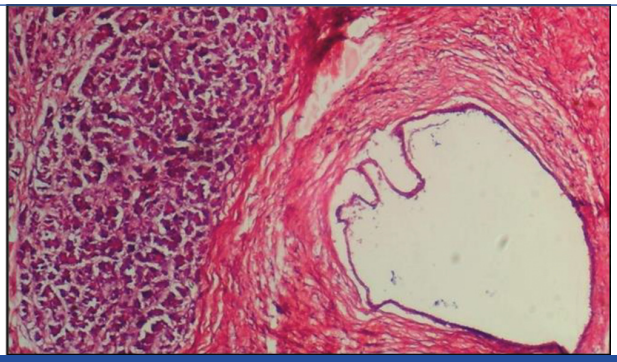
The quantity of consumed alcohol and the presence of diabetes mellitus are risk factors for the development of liver fibrosis in alcoholic chronic pancreatitis. The hepatic and pancreatic stellate cells play a central role in the development of fibrosis both in the liver and in the pancreas, implying similar molecular mechanisms underlying the development of fibrotic changes in these organs [14,15]. The two conditions were found to be closely associated. Moreover, the precursor of cirrhosis and chronic pancreatitis, steatosis and pancreatic fibrosis are commonly found in the same individual, suggesting common risk factors being predominant. The above study identified a very high prevalence of both diseases in alcoholics. The results of the current study are in contrast with several studies that have evaluated the relationship between chronic pancreatitis and liver cirrhosis. The microscopic pictures of various lesions stained with H&E and Masson's trichrome special stain are listed [Table/Fig-12-22].



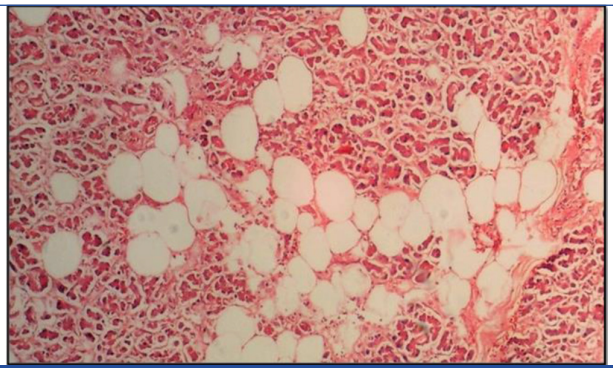
[Table/Fig-12]: Scanner view of perilobular fibrosis- pancreas. (H&E stain; 4X).



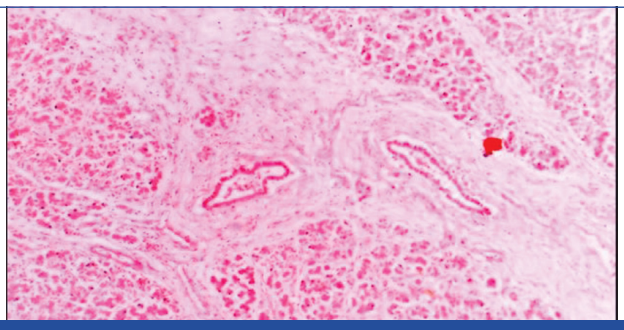
[Table/Fig-13]: Scanner view showing extensive perilobular fibrosis (Masson's Trichromestain; 4X) .



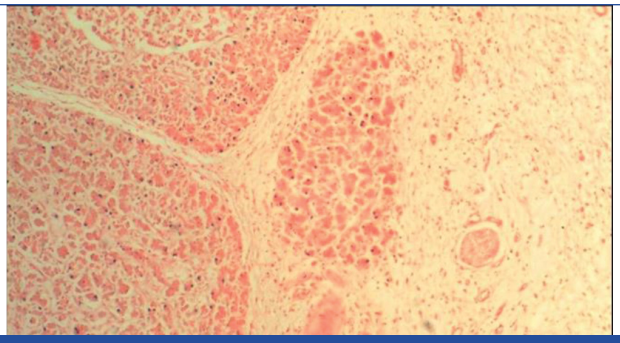
[Table/Fig-14]: Scanner view of duct dilatation with periductal fibrosis (H&E stain; 4X).



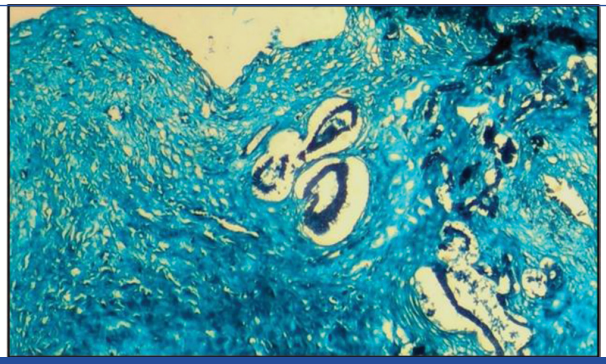
[Table/Fig-15]: Fatty infiltration of pancreatic parenchyma (H&E stain; 4X).



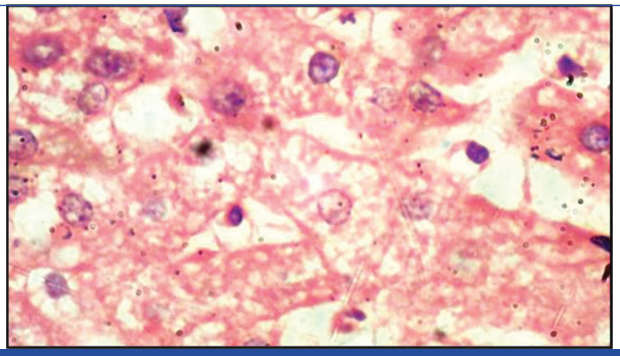
[Table/Fig-16]: Scanner view showing Interlobular periductal fibrosis. (H&E stain; 4X).



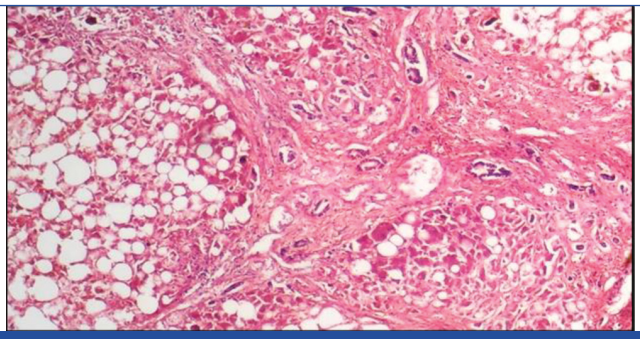
[Table/Fig-17]: Scanner view of lobular atrophy with surrounding parenchymal fibrosis (H&E stain; 4X).



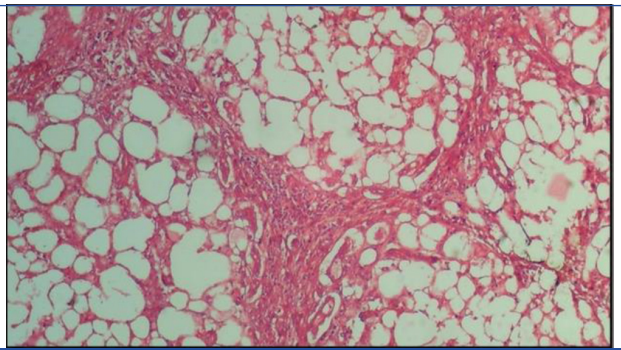
[Table/Fig-18]: Diffuse extensive parenchymal fibrosis. (Massons Trichrome stain; 4X).



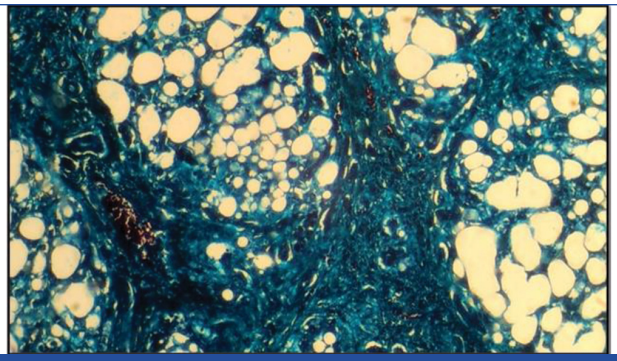
[Table/Fig-19]: Photomicrograph showing microvesicular steatosis with prominent cytoplasmic vacuoles (H&E stain,40X).



[Table/Fig-20]: High power photomicrograph showing microvesicular steatosis with prominent cytoplasmic vacuoles. (H&E stain; 40X).



[Table/Fig-21]: Bridging fibrosis with macrovesicular steatosis. (H&E stain; 100X low power view).



[Table/Fig-22]: Periportal fibrosis and portal to portal bridging fibrosis. (Masson's Trichrome stain; 10X).

Limitation(s)

One of the main limitations of the study was that there was no information about the exact quantity of daily alcohol intake, or the exact duration of drinking. History of smoking and nutritional profiles were not taken into consideration due to lack of documentation in the history sheet.

CONCLUSION(S)

In conclusion, the prevalence of chronic pancreatitis were more in cirrhotics than in non cirrhotics. The simultaneous occurrence or coexistence of chronic pancreatitis and liver cirrhosis caused by alcohol consumption in the same individual, were also closely associated. The prevalence of co-existence of chronic pancreatitis and liver cirrhosis was 50%. Moreover, the precursor lesions of chronic pancreatitis and liver cirrhosis, pancreatic fibrosis and steatosis, are frequently observed in the same individual, suggesting a predominance of common risk factors.

REFERENCES

[1] Becker U, Deis A, Sorensen T, Gronbaek M, Borch-Johnsen K, Muller CF, et al. Prediction of risk of liver disease by alcohol intake, sex, and age: A prospective population study. Hepatology. 1996;23(5):1025-29.
[2] Bellentani S, Saccocio G, Costa G, Tiribelli C, Manenti F, Sodde M, et al. Drinking habits as cofactors of risk for alcohol induced liver damage. The Dionysos Study Group. Gut. 1997;41:845-50.
[3] Grant BF, Dufour MC, Harford TC. Epidemiology of alcoholic liver disease. Semin Liver Dis. 1988;8:12-25.
[4] Lelbach WK. Cirrhosis in the alcoholic and its relation to the volume of alcohol abuse. Ann N Y Acad Sci. 1975;252(5):85-105.
[5] Worning H. The pancreas: Alcoholic chronic pancreatitis. 1st Ed. Oxford: Blackwell Science. 1998:672-82.
[6] Durbec JP, Sarles H. Multicenter survey of the aetiology of pancreatic diseases: Relationship between the relative risk of developing chronic pancreaitis and alcohol, protein and lipid consumption. Digestion.1978;18(5-6):337-50.
[7] Almela P, Aparisi L, Grau F, Sempere J, Rodrigo J. Influence of alcohol consumption on the initial development of chronic pancreatitis. Rev Esp Enferm Dig. 1997;89:741-46.
[8] Lankisch PG, Lowenfels AB, Maisonneuve P. What is the risk of alcoholic pancreatitis in heavy drinkers? Pancreas. 2002;25:411-12.
[9] Greiner L, Schubert E, Franken FH. Coincidence of chronic pancreatitis and liver cirrhosis in alcohol abuse. An x-ray and histomorphological study. Z Gastroenterol. 1983;21(9):526-32.
[10] Agrawal P, Vaiphei K. Histomorphological features of pancreas and liver in chronic alcoholics-an analytical study in 390 autopsy cases. Indian J Pathol Microbiol. 2014;57(1):02-08.
[11] Kochhar R, Sethy P, Sood A, Nagi B, Singh K. Concurrent pancreatic ductal changes in alcoholic liver disease. JGH Open. 2003;18(9):1067-70.
[12] Caradonna P, Costamagna G, Benedetti G, Gentiloni N, Gasbarrini GB. Chronic pancreatitis prevalence in liver cirrhosis. Morphological and functional study.Ital J Gastroenterol. 1996;28(2):91-94.
[13] Pace A, De Weerth A, Berna M. Hillbricht K, Tsokos M, Blaker M, et al. Pancreas and liver injury are associated in individuals with increased alcohol consumption. Clin Gastroenterol Hepatol. 2009;7(11):1241-46.
[14] Apte MV, Wilson JS. Stellate cell activation in alcoholic pancreatitis pancreas. 2003;27(4):316-20.
[15] Bachem MG, Zhou Z, Zhou S, Siech M. Role of stellate cells in pancreatic fibrogenesis associated with acute and chronic pancreatitis. J Gastroenterol Hepatol. 2006;21(3):92-96.
[16] Friedman SL. Mechanisms of hepatic fibrogenesis. Gastroenterology 2008;134(6):1655-69.
[17] Innes JT, Carey LC. Normal pancreatic dimensions in the adult human. Am J Surg. 1994;167(2):261-63.
[18] Gullo L, Casadei R, Campione O, Grigioni W, Marrano D. Alcoholic liver disease in alcoholic chronic pancreatitis: a prospective study. Ital J Gastroenterol. 1995;27(2):69-72.
[19] DonohueTM,Jr. Alcohol-induced steatosis in liver cells. World J Gastroenterol. 2007;13(7):4974-78.
[20] Zsori G, Czepan M, Illes D, Palvolgyi A, Nagy I, Czako L. Pancreatic Diabetes Mellitus and Heavy Drinking are Risk Factors for the Development of Liver Fibrosis in Alcoholic Chronic Pancreatitis. Pancreat Disord Ther. 2017;7:186.
[21] Renner IG, Savage WT, Robert L, Peters MD, Nigel H. Pancreatitis associated with alcoholic liver disease. A review of 1022 autopsy cases. Dig Dis Sci. 1984;29(7): 593-99.
[22] Hastier P, Buckley M, Francois E, Peten EP, Dumas R, Caroli-Bosc FX, et al. A prospective study of pancreatic disease in patients with alcoholic cirrhosis: comparative diagnostic value of ERCP and EUS and long-term significance of isolated parenchymal abnormalities. Gastrointest Endosc. 1999;49(6):705-09.
[23] Suda K, Shiotsu H, Nakamura T, Akai J, Nakamura T. Pancreatic fibrosis in patients with chronic alcohol abuse: correlation with alcoholic pancreatitis. Am J Gastroenterol (Springer Nature). 1994;89(11):2060-62.
[24] Dutta SK, Mobrahan S, Iber FL. Associated liver disease in alcoholic pancreatitis. Am J Dig Dis. 1978;23(7):618-22.

PARTICULARS OF CONTRIBUTORS:
1. Speciality Medical Officer, Department of Pathology, Lokmanya Tilak Municipal Medical College, Mumbai, Maharashtra, India.
2. Associate Professor, Department of Pathology, Lokmanya Tilak Municipal Medical College, Mumbai, Maharashtra, India.
3. Associate Professor, Department of Pathology, Lokmanya Tilak Municipal Medical College, Mumbai, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Shailesh Vartak,
Associate Professor, Department of Pathology,
Lokmanya Tilak Municipal Medical College, Mumbai, Maharashtra, India.
E-mail: shailvar@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Jan 12, 2022
- Manual Googling: Jan 18, 2022
- iThenticate Software: Apr 01, 2022 (21%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Jan 03, 2022**
Date of Peer Review: **Mar 02, 2022**
Date of Acceptance: **Apr 06, 2022**
Date of Publishing: **Nov 01, 2022**