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Hyperlipidemia in Acute Pancreatitis

Relationship with Etiology, Onset, and Severity of the Disease

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Summary

Serum lipid (triglycerides and cholesterol) concentrations were studied in 49 patients with acute pancreatitis (AP). The aims of the study were to investigate the prevalence of hyperlipidemia (HL) in patients with AP according to etiology and to evaluate whether HL precedes or is a consequence of AP. Moreover, we analyzed the relationship between HL and the development of pancreatic necrosis. At admission, 23 patients (47%) had HL: 9 of 19 patients with alcoholic pancreatitis, 5 of 18 patients with biliary pancreatitis, and 9 of 12 patients with AP of miscellaneous etiologies ($p < 0.05$). Severe HL (serum triglycerides > 20 mmol/L) was observed in five patients. Serum lipid levels in patients with AP and HL decreased markedly during the first 72 h of evolution, but remained slightly above the upper normal limit in most of them after 15 d. The prevalence of HL was similar in edematous and necrotizing pancreatitis. Necrotizing pancreatitis was significantly associated with the presence of hypertriglyceridemia in conjunction with hypercholesterolemia ($p < 0.05$). The observations that a) hyperlipidemia is an early event in acute pancreatitis, (b) serum lipid values decrease during the acute phase of the disease, (c) hyperlipidemia has a different prevalence in different etiologies, and (d) high serum lipid levels are not always associated to pancreatic necrosis suggest that HL is a preexistent metabolic abnormality with respect to AP. On the other hand, HL may play a role in aggravating AP.

Key Words: Acute pancreatitis; etiology; hypercholesterolemia; hypertriglyceridemia.

INTRODUCTION

Acute pancreatitis (AP) is reported to be associated with hyperlipoproteinemia (HL) in 4–46% of the cases (*1–5*). HL in AP is usually characterized

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Table 1
Etiological Factors Associated with AP

Etiological factor	Number of patients
Alcoholism	19
Biliary lithiasis	18
Hyperlipidemia	3
ERCP	1
Pancreas divisum	1
Coxsackie B infection	1
Hyperparathyroidism	1
Idiopatic	5

by high triglyceride serum concentration and normal cholesterol levels, and occasionally by the prolonged persistence of chylomicrons (*4*).

Whether HL is a preexisting metabolic disorder or a consequence of AP is still debated (*2,5*). HL is preexistent with respect to AP in patients with primary hyperlipidemic states, and also in other clinical conditions that cause secondary HL, among these alcohol abuse, diabetes mellitus, hypothyroidism, chronic renal failure, and pregnancy (*6*). Nevertheless, in some patients with AP there is no primary disorder that could explain HL. The abnormal serum lipid levels in these cases were thought to be secondary to the pancreatic inflammatory process and peripancreatic fat necrosis (*7*).

Based on epidemiological data, HL is considered to be an etiological factor of AP (*5,8*). Moreover, a role of increased serum triglycerides in precipitating AP in alcoholic patients has been postulated (*9*). However, a pathogenetic role of HL in AP is still not clarified. The toxic effect of fatty acids released within the gland from chylomicron triglycerides hydrolyzed by pancreatic lipase may be of pathogenetic relevance (*10,11*). The possible injury of pancreatic capillaries by cholesterol crystals has been also discussed (*4*).

Aims of this study were to establish the prevalence of HL in AP and its relationship with the etiological factor, to analyze the possible relationships between HL and the presence of pancreatic necrosis, and finally to evaluate whether HL precedes, or is a consequence of, AP.

PATIENTS AND METHODS

A total of 49 consecutive patients (32 male and 17 female, mean age 50 ± 15.9 yr) with AP, admitted to the Department of Internal Medicine or of Surgery of our University Hospital, have been retrospectively analyzed. Diagnosis of AP was based on a typical clinical picture, an increase of at least threefold in the upper normal value of serum specific pancreatic enzymes, and consistent morphologic findings by computed tomography and/or ultrasonography. AP episodes were associated with alcohol abuse in 19 patients, with biliary lithiasis in 18, and with other or unknown etiologies in 12 cases (Table 1). HL was considered as the etiology of AP if marked hypertriglyceridemia (more than 20 mmol/L) was evidenced in patients with no other potential etiological factor.

Table 2
Characteristics of Patients with Acute Pancreatitis and Marked Hypertriglyceridemia

Patient	Age	Sex	Associated etiological factor	Serum TG at admission, mmol/L	Serum chol. at admission, mmol/L	Pancreatic necrosis
A. A.	63	F	—	66.17	31.20	<30%
R.B.	43	M	Alcoholism	199.00	33.32	<30%
R. R.	43	M	—	23.40	13.60	<30%
I. Z.	49	M	Alcoholism	28.00	14.70	<30%
M. G.	53	F	—	226.00	126.00	>50%

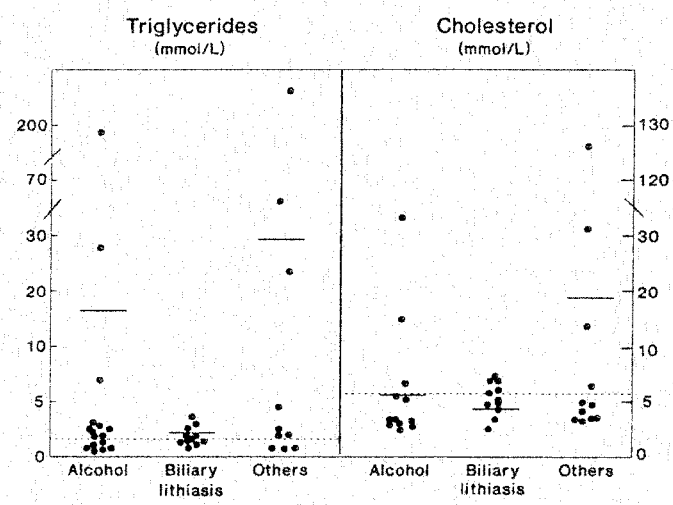

Fig. 1. Serum triglyceride and cholesterol levels at admission in patients with acute pancreatitis according to the associated etiological factor.

Existence of pancreatic necrosis was evidenced by means of contrast-enhanced computed tomography in all patients, except in nine with clearly mild episodes of AP. According to Block et al. (*12*), pancreatic necrosis was graded depending on its extension within the gland in <30%, between 30 and 50%, and >50%).

Fasting serum triglyceride and cholesterol levels at admission and evolutively till the 15th day were recorded. Upper normal limits are 1.6 mmol/L for triglycerides and 6.5 mmol/L for cholesterol.

Statistical analysis has been carried out by means of the Wilcoxon test to compare quantitative data. The chi-square test has been applied in the comparison of qualitative data, with the Yates correction in 2×2 tables.

RESULTS

At admission a total of 23 (47%) patients showed hypertriglyceridemia and five of them had triglyceride levels >20 mmol/L (Table 2). Nine patients (18%) had hypercholesterolemia, which was always associated with high triglyceride levels (Fig. 1). The frequency of HL in different etiologies of AP is

Table 3
Distribution of Patients with Acute Pancreatitis
According to Etiology and Serum Values of Triglycerides and Cholesterol

Etiology	Ntg-Nchol,[a] *n*	Htg-Nchol,[b] *n*	Htg-Hchol,[c] *n*
Alcoholism	10	6	3
Biliary lithiasis	13	2	3
Others or unknown	3	6	3

[a]Ntg: normal serum triglyceride level; Nchol: normal serum cholesterol level.
[b]Htg: high serum triglyceride level.
[c]Hchol: high serum cholesterol level.

shown in Table 3. A higher frequency of HL is observed in patients with AP from miscellaneous etiologies ($p < 0.05$). Furthermore, patients with AP secondary to miscellaneous etiologies had, at admission, higher triglyceride and cholesterol serum concentration than patients with alcoholic and biliary AP (Fig. 2). In most patients serum cholesterol levels fell rapidly, and there was no patient with abnormal serum cholesterol at the 15th d (Fig. 3). In contrast, serum levels of triglycerides, in spite of a marked decrease within the first 72 h, still were slightly elevated after 15 d in 16 patients (seven with alcoholic AP, three with biliary AP, and six with AP secondary to other etiologies (Fig. 3).

Patients with necrotizing AP (13 with necrosis $< 30\%$ and three with necrosis between 30 and 50%) had high serum triglyceride levels at admission (39.95 ± 75.491 mmol/L) compared to patients with interstitial AP (1.95 ± 1.555 mmol/L) (ns). Serum cholesterol levels were also higher in patients with necrotizing AP than in patients with interstitial AP (18.24 ± 32.667 mmol/L vs 4.55 ± 1.450 mmol/L; ns). Furthermore, in the presence of high cholesterol and triglyceride serum levels, necrotizing AP occurred more frequently ($p < 0.05$) (Table 4). In addition, all patients with serum triglyceride concentrations > 20 mmol/L developed necrotizing AP (Table 1), compared with only 11 of the remaining 44 cases ($p < 0.05$).

DISCUSSION

The prevalence of hyperlipidemia in acute pancreatitis in our series is close to 50%. Of patients with miscellaneous etiologies (including those with no abnormality other than HL), 75% had hypertriglyceridemia, compared to 47% of patients with alcoholic AP and 28% of patients with biliary AP. These data suggest the possibility that a proportion of nonalcoholic, nonbiliary episodes of AP may be caused by HL. Furthermore, the different frequency of HL in different etiologies suggests that this biochemical abnormality is rather unlikely to be secondary to AP.

It was suggested earlier that severe AP is frequent in patients with marked hypertriglyceridemia (*2*). According to our results, a close relationship seems to exist between marked HL and necrotizing AP. All patients with serum tri-

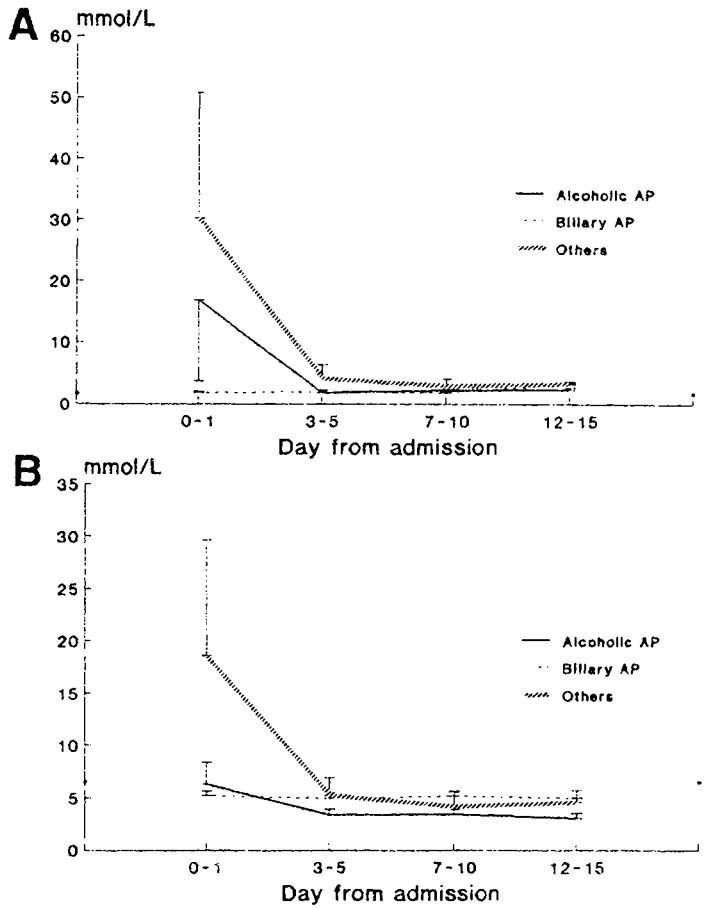

Fig. 2. Evolutive values of (**A**) serum triglyceride and (**B**) cholesterol concentrations (mean and standard error) in patients with acute pancreatitis according to etiology.

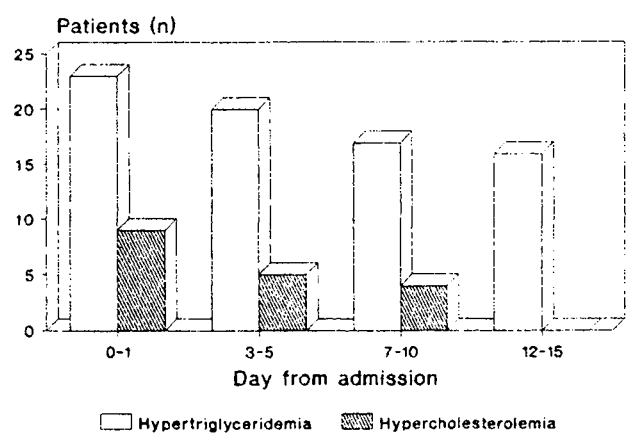

Fig. 3. Frequency of hypertriglyceridemia and hypercholesterolemia in patients with acute pancreatitis at different times after admission.

Table 4
Distribution of Patients with AP
According to Angio-CT Finding and Serum Values of Triglycerides and Cholesterol

CT finding	Ntg-Nchol,[a] *n*	Htg-Nchol,[b] *n*	Htg-Hchol,[c] *n*
AIP[d]	18	12	3
NP[e]	8	2	6

[a]Ntg: normal serum triglyceride level; Nchol: normal serum cholesterol level.
[b]Htg: high serum triglyceride level.
[c]Hchol: high serum cholesterol level.
[d]AIP: acute interstitial pancreatitis.
[e]NP: necrotizing pancreatitis.

glyceride concentration >20 mmol/L developed necrotizing AP. Also, hypercholesterolemia and pancreatic necrosis were significantly associated. The fact that 50% of patients with necrotizing AP had normal serum lipid levels almost excludes necrosis from being the cause of HL. This strengthens the above hypothesis that HL occurs prior to the onset of AP.

There remains the major question of whether HL by itself represents a potential etiological factor of AP. Alteration of the serum clearance of lipids has been described in patients with AP and HL (*13–15*). The persistent, though slight, increase in serum lipid concentration observed in most of our patients with AP and HL supports the possibility of a delayed serum clearance of lipids in these patients. Therefore, a diet of high fatty content, with or without heavy alcohol consumption, may be a risk factor in precipitating an attack of AP. Hypertriglyceridemia provides the substrate for the release of high amounts of toxic free fatty acids mediated by pancreatic lipase within the gland, and this is shown to play a pathogenetic role (*10,11*). Furthermore, high serum concentration of chylomicrons and chylomicron remnants may damage the pancreatic capillaries by the release of cholesterol crystals during lipolysis, inducing ischemic lesions (*4*).

With the necessary consideration of this being a retrospective study, these results suggest that acute pancreatitis is frequently associated to hyperlipidemia, which appears to be a preexistent abnormality to the acute event. Severe hyperlipidemia is likely to be a primary pathogenetic factor of acute pancreatitis in patients with nonalcoholic, nonbiliary episodes. Marked hyperlipidemia is usually associated with necrotizing acute pancreatitis. To further evaluate the role of lipid abnormalities in the pathophysiology and clinical course of acute pancreatitis, prospective studies are warranted.

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