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Are There Differences in the Management of Acute Pancreatitis Cases Due to Severe Hypertriglyceridemia in Pregnant Women?

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Data Collection B
Statistical Analysis C
Data Interpretation D
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Background: The aim of this study was to determine the prognosis of severe disease and treatment approaches of both normal and pregnant, especially in patients with severe pancreatitis due to hypertriglyceridemia.

Material/Methods: We included 30 patients (20 females and 10 males) in this study whose follow-ups and treatments were performed after a diagnosis of hypertriglyceridemia-induced acute pancreatitis between January 2011 and May 2017. Patient personal information, such as age, sex, pre-treatment and post-treatment triglyceride levels, receipt of anti-hyperlipidemic treatments or plasmapheresis, and family history, were collected from hospital records and patient files. Patients with severe pancreatitis history, score, and prognosis were included to increase the value of our study. Mild and moderate cases were excluded.

Results: The mean age of the patients was 35±6 years. Twenty-four patients (80%) received an anti-hyperlipidemic treatment before their pancreatitis attacks. Plasmapheresis was performed on 8 patients before their pancreatitis attacks. Eighteen patients (60%) had a family history suggesting familial hypertriglyceridemia. Twelve patients (40%) were pregnant.

Conclusions: The treatment of hypertriglyceridemia-induced acute pancreatitis was mostly confined to supportive, palliative treatments. However, plasmapheresis is a possible treatment option and should be used in the early stages of this disease. The response to medical treatment and support treatment was better in pregnant patients than in the other patient group, and pregnant patients did not require plasmapheresis.

MeSH Keywords: Hypertriglyceridemia • Pancreatitis • Pregnant Women

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Background

Acute pancreatitis develops as a result of the premature activation of pancreatic enzymes and manifests as abdominal pain and elevated pancreatic enzymes. The causes of acute pancreatitis are most frequently gallstones and alcohol, but another cause can be hypertriglyceridemia [1]. Pregnant women often experience acute pancreatitis as a result of hypertriglyceridemia. Hypertriglyceridemia is responsible for approximately 1–4% of acute pancreatitis cases; serum triglyceride levels over 1000 mg/dL may trigger an attack of acute pancreatitis. Acute pancreatitis may develop when triglyceride levels reach 500–1000 mg/dL [1–3].

The probable mechanism of acute pancreatitis in cases of hypertriglyceridemia is the release of excessive local free fatty acids and lysolecithin from the lipoprotein substrates in pancreatic cells, which damages the acinar cells and the microvascular membranes when albumin exceeds the carrying capacity of the pancreas [4–6].

Currently there is no standard of care in cases of hypertriglyceridemia-induced acute pancreatitis. However, some treatment modalities consist of a combination of insulin and heparin, which are both based on an increase in lipoprotein lipase activity. Furthermore, plasmapheresis has been performed successfully in resistant cases [7–9].

In this study, we present demographic characteristics, treatment response rates, treatment methods, family histories, and follow-up status of patients, including pregnant women, diagnosed with hypertriglyceridemia-induced acute pancreatitis.

Material and Methods

Participants

We retrospectively evaluated the records of 30 patients diagnosed with hypertriglyceridemia-induced acute pancreatitis who were followed at the Department of Endocrinology and Gastroenterology, Dicle University School of Medicine and Firat University School of Medicine, between January 2011 and May 2017. We recorded patient demographic characteristics (age, sex, and family history) as well as clinical and laboratory histories. We also recorded data on patient medical therapies. The study protocol was approved by the ethics committee of Firat University, Faculty of Medicine, Elazig, Turkey.

Clinical examination

Changes in pre-pancreatitis and post-pancreatitis triglyceride levels and their correlations were evaluated. If any anti-hyperlipidemic drugs were taken before the development of pancreatitis, this was noted. When plasmapheresis was performed, resistant cases were those that did not respond to supportive or medical treatments (such as insulin or low-molecular-weight heparin); these cases were evaluated separately.

Biochemical measurements

Ranson criteria and Atlanta criteria were considered in terms of pancreatitis severity and prognosis. Patients with Ranson criteria level 4 and greater and according to Atlanta criteria (1993) with severe acute pancreatitis were included to our study. We used both Ranson and Atlanta criteria (most important for organ failure than laboratory findings) so as not to affect the result of the tests if a patient's serum level indicated extremely lipemic condition which can negatively affect real values. Our patients stayed in intensive care unit more than 48 hours with organ dysfunction (shock, pulmonary insufficiency, renal failure).

Diagnosis and exclusion criteria

The etiology of acute pancreatitis; choledocholithiasis, alcoholism, drug use (salicylates, estrogens, oral contraceptives, azathioprine, thiazide diuretics, beta-blockers, retinoids, antipsychotics, etc.), metabolic disease (diabetes mellitus, hypothyroidism, hypercalcemia, gut disease, malignancy, renal insufficiency, liver failure, etc.), trauma (surgery, endoscopic retrograde cholangiopancreatography, accidental), vascular factors (hypotension, chronic heart failure, embolism, vasculitis, hypercoagulability), and infection (cytomegalovirus, coxsackie virus, mumps virus, human immunodeficiency virus (HIV), tuberculosis, parasites, etc.) were excluded. After the clinical conditions of the patients were corrected, they were evaluated by the endocrinologists in the control process.

Statistical analysis

Variables were expressed as means ± standard deviations (SDs), and categorical variables were expressed as counts and percentages. All calculations were analyzed using SPSS 21 (IBM Corp., Armonk, NY, USA).

Results

The mean age of the patients (20 females and 10 males) was 35±6 years. The mean age of males was 39±6 years, and the mean age of females was 34±7 years. Twelve female patients were pregnant. Triglyceride levels in all pregnant patients were extremely high (mean: 4185±616 mg/dL). Twenty-four patients (80%) received anti-hyperlipidemic treatments before the onset of pancreatitis. Eight of the 24 patients received a combination

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Table 1. Pregnant patients.

Mean age	32
Pretreatment amylase, mean (U/L)	665.5
Pretreatment triglyceride, mean (mg/dL)	4185
Posttreatment triglyceride, mean (mg/dL)	677
Number of patients who received anti-hyperlipidaemic treatment before pancreatitis	9 (75%)
Number of patients who received plasmapheresis during pancreatitis	0
Number of patients who received plasmapheresis before pancreatitis	0
Number of patients with a family history	6 (50%)

Table 2. Nonpregnant female and male patients.

Pretreatment amylase, mean (U/L)	453.1
Pretreatment triglyceride, mean (mg/dL)	2385.5
Posttreatment triglyceride, mean (mg/dL)	406.6
Number of patients who received anti-hyperlipidaemic treatment before pancreatitis	15 (83.3%)
Number of patients who received plasmapheresis during pancreatitis	8 (26.6%)
Number of patients who received plasmapheresis before pancreatitis	6 (20%)
Number of patients with a family history	12 (66.6%)
Sex	10 M, 20 F

of fenofibrate (250 mg once per day) and gemfibrozil (600 mg once per day), whereas the other 16 received only fenofibrate (250 mg once per day). Eighteen patients (60%) had a family history of hyperlipidemia. Low-molecular-weight heparin, insulin, and conservative treatments were able to moderate the symptoms of 21 patients (70%). Low-molecular-weight heparin was given at a dose of 0.1 unit/kg twice a day; 5–8 units of insulin +5% dextrose was given twice a day in the form of 1 unit of insulin for 5 g glucose. The disease was not managed effectively in 27% of patients who were given standard medical treatments, whose clinical symptoms were more severe and whose triglyceride levels were high. For these patients, plasmapheresis was deemed the best option. After plasmapheresis, triglyceride levels decreased below 500 mg/dL in all patients (Table 1). It was observed during follow-up that all of these patients had recovered from their clinical symptoms. The pre-treatment triglyceride levels of patients who underwent plasmapheresis were higher than those of other patients (plasmapheresis-receiving group mean: 2965±422 mg/dL, plasmapheresis non-receiving group mean: 2186±122 mg/dL). Twelve patients (40%) were pregnant; their triglyceride levels and their pancreatitis were brought under control via insulin, low-molecular-weight heparin, and conservative treatments. Plasmapheresis was not used on pregnant patients with pancreatitis. These patients were only given conservative medical treatments (Table 2).

Discussion

Hyperlipidemia is a significant problem that needs to be considered in the differential diagnosis of acute nonbiliary pancreatitis. Hyperlipidemia is an etiological factor of acute pancreatitis [10]. This study found that acute pancreatitis induced hypertriglyceridemia in 30 patients and that recovery occurred when patients reached post-treatment as determined by the pancreatitis table.

The incidence of acute pancreatitis is 5–30/100 000 with hypertriglyceridemia-induced pancreatitis estimated to occur in 1–4% [11–13]. When the inclusion/exclusion criteria were applied in our study (mild and moderate cases, elderly patients, and chronic illnesses were excluded from our study), the average rate was reduced to the equivalent of 2–5 person per million. Thus, reducing the number of the patients of our study. In this study, we aimed to determine the proportion of both normal and pregnant patients, the prognosis of severe disease, and the treatment approaches, especially in patients with severe pancreatitis due to hypertriglyceridemia.

Patients received 1, 2 or all 3 treatments: insulin, low-molecular-weight heparin, plasmapheresis. Treatments were administered to the 30 patients based on clinical, radiological, biochemical, and familial findings, and clinical profiles of all of the patients were recovered.

Hypertriglyceridemia is responsible for approximately 1–4% of acute pancreatitis cases. Serum triglyceride levels over 1000 mg/dL may trigger attacks of acute pancreatitis. Studies suggest that acute pancreatitis may develop at triglyceride levels between 500 and 1000 mg/dL [1,2,14]. In our study, triglyceride levels were between 500 and 1000 mg/dL in 6 out of the 30 patients. Triglyceride levels were greater than 1000 mg/dL in the other 24 patients.

Both primary (genetic) and secondary disorders of lipoprotein metabolism may lead to hypertriglyceridemia-induced acute pancreatitis. Congenital types I, II, and V are usually diagnosed in childhood. Because of an increase in hyperchylomicronemia and VLDL (very-low-density lipoprotein) levels, the fasting serums of patients become cloudy and milk-like. This trend is particularly present in children with lipid metabolism disorders and severe hypertriglyceridemia and who develop pancreatitis at an early age. These children also experience

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homozygote lipoprotein lipase or APO-C2 deficiency. Reducing serum triglyceride levels below 400 mg/dL prevents pancreatic attacks under these conditions [4,15,16]. In our study, 66% of the cases were detected in childhood, and there was an established family history.

It is important to note that measurement of serum pancreatic enzymes in hyperlipidemic plasma may give false low results and that enzymes may be at normal levels during a pancreatic attack. Because amylase activity is inhibited by rich lipoproteins, hyperlipidemic samples should be diluted for measurement [1,17]. However, the average amylase level in this study was 528.95 U/L (range: 254–954) at the onset of pancreatitis (although levels were high during acute pancreatitis episodes). In pregnant patients, this average was 665.5 U/L (range: 393–954).

Teamwork is particularly important for treating acute pancreatitis, particularly for managing severe pancreatitis and its complications. Radiologists determine the severity of pancreatitis according to a computed tomography severity index. If necessary, a gastroenterologist carries out an endoscopic retrograde cholangiopancreatography and sphincterotomy. Surgeons carry out a neurectomy of the infected necrotic tissue. An infectious disease specialist chooses suitable antibiotics to treat the pancreatic infections. While these procedures are carried out, hemodynamic monitoring, fluid treatment, as well as management of cardiovascular, pulmonary, and renal failure should be performed by an intensive care specialist. Almost all patients with acute pancreatitis, particularly patients experiencing their first attack and pregnant patients, should be hospitalized to determine the cause, given supportive treatment, and assisted in their disease management. Acute mild inflammations of chronic pancreatitis are rarely treatable at home. Patients with organ failure should be supervised in intensive care units. The patients in this study received treatment and follow-up from doctors in gastroenterology, endocrinology, general surgery, and radiology [7,8].

There are no published articles in the literature on pregnant patients. More case-based studies have been reported [18]. Our article will be one of the first studies reported in this area.

When treating pancreatitis, the main objective is to decrease serum triglyceride levels and to suppress systemic inflammatory response. Heparin and insulin stimulate lipoprotein lipase activity and accelerate chylomicron degradation. Furthermore, microcirculation recovers, and neutrophil activation is prevented. Plasmapheresis is used as a lipid-reducing method, and studies suggest that complete recovery is observed in 75% of patients [7,8]. However, equipment problems and the need for a high volume of plasma are among the disadvantages of this treatment option. Short-term veno-venous hemofiltration is effective for treating acute pancreatitis secondary to hyperlipidemia and decreases circulating tumor necrosis factor (TNF) levels while increasing interleukin (IL)-10 levels [9]. In our study, 73.33% of patients were effectively treated with heparin, insulin, and conservative treatments. Plasmapheresis was performed in 26.67% of cases, for patients who had more severe clinical symptoms and whose triglyceride levels were very high. After the procedure, we determined patient recovery by analyzing patient profiles.

No guideline has been defined for the management of hypertriglyceridemia in acute pancreatitis that develops during pregnancy. Case reports and series were published, including treatment methods, such as intravenous insulin and glucose, heparin and apheresis, together with restriction of feeding [19–21]. Twelve patients (40%) in our study were pregnant, and triglyceride levels and pancreatitis of these patients were managed through the use of insulin, low-molecular-weight heparin, and conservative treatments. Plasmapheresis was not needed.

Conclusions

The preexistence of hypertriglyceridemia needs to be examined when determining treatment options for patients. Treatments for acute pancreatitis are mostly supportive and palliative. However, plasmapheresis is a potential option for severe cases when clinical recovery is not obtained despite the use of conservative treatments. Plasmapheresis should therefore be performed at an early stage. In our study, the response rate for medical and support treatments was better in pregnant patients than in the other patient group. Pregnant patients did not require plasmapheresis.

Conflict of interest

None.

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