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Association of Serum Lipid Profile with Severity of Acute Pancreatitis

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Abstract

*Background***:** Acute pancreatitis, characterized by local and systemic inflammation, is a common cause of acute abdominal conditions. Revision of the 1992 Atlanta Classification provides a newer classification to describe clinical behavior and imaging characteristics of acute pancreatitis. This study aims at assessing changes in serum lipid profile in acute pancreatitis and to correlate level of serum lipid profile with severity of acute pancreatitis and outcome of the patient. *Methods***:** The study group included 70 cases of acute pancreatitis and control group included 70 cases of non traumatic acute abdominal conditions other than acute pancreatitis. The data for this study include the lipid profile of the patients. *Results***:** This study demonstrated significant lowering of HDL in cases of severe acute pancreatitis when compared to mild and moderate acute pancreatitis and showed that duration of hospital stay of a patient was more in cases of patients with significantly lower levels of HDL. Also there was lowering of all three lipid profile values of HDL, LDL and total cholesterol in cases of acute pancreatitis when compared to control group. *Conclusion***:** Serum lipid levels can be used as one of the components for assessing the severity of acute pancreatitis and as a prognostic indicator to predict outcome of patients with severe acute pancreatitis.

Keywords: Acute Pancreatitis; Severity of Acute Pancreatitis; Serum Lipid Profile Levels.

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Introduction[1]

Acute pancreatitis is characterized by local and systemic inflammation, which is observed clinically from no systemic sign through the local and systemic inflammatory response, organ failure, persistent organ failure, pancreatic necrosis and death. Although most patients experience minor episodes characterized by mild parenchymal edema without organ dysfunction, they respond to conservative management, and even recover completely. More severe episodes may progress to pancreatic necrosis, systemic inflammatory response syndrome (SIRS), multiorgan failure, clinical deterioration, and even death[2]

Recent years have seen advances in the classification and management of acute pancreatitis including evidence-based guidelines and a notable shift toward nonoperative management of even the most severe cases of infected pancreatic necrosis. Revision of the 1992 Atlanta Classification of acute pancreatitis to provide a newer classification to more precisely describe the clinical behavior and imaging characteristics of acute pancreatitis[3] has allowed more uniform categorization of the disease in recent years.

Lipid profile in acute pancreatitis

It has been reported that metabolic capacity of pancreatic cells in removing free radicals is very low and free radicals increase in acute pancreatitis

cases and play an important role in the severity of the disease. Furthermore, it has been shown that high-density lipoprotein (HDL) has antioxidant and anti-inflammatory properties. Low serum HDL levels and decreased paraoxonase 1 activity, which is responsible for HDL's antioxidant activity, have been demonstrated in an experimental study of pancreatitis. Thus, a decrease in antioxidant and anti-inflammatory activity might be expected in cases with acute pancreatitis due to low serum HDL levels, which may be associated with an increase in severity of the disease.[4]

The underlying pathophysiology through which local pancreatic injury drives the systemic inflammatory response has not been fully elucidated, but cumulative data suggest that immune systems play pivotal roles. Impaired lipid metabolism plays a pivotal role in the pathogenesis of numerous diseases conditions, including cardiovascular conditions, infectious diseases diabetes and carcinoma.[5]

Compared with other lipoproteins, high density lipoprotein cholesterol (HDL-C) is carried within lipoprotein particles that are particularly heterogeneous, varying in size, composition, metabolism and function. Decreased plasma concentrations of HDL-C is frequently observed in a series of acute phase conditions associated with immune activation. It is accepted that HDL may become dysfunctional in some disease conditions, and the concept that the anti-inflammatory status of HDL may be associated with the risk of cardiovascular and other disorders. In addition to playing a central role in reverse cholesterol transport in vascular protection, HDL and its mimetics have several other functions including antioxidant, antithrombotic and anti-apoptotic functions.[5]

Alcohol use is known to induce changes in lipid metabolism in many ways although acute and chronic effects differ. Heavy alcohol use might be associated with poor nutrition which in turn might change the serum fatty acid profile.[6]

Plasma triglyceride concentration may increase, remain unchanged, or decrease in different types of acute conditions. Hepatic triglyceride production, however, is always increased and results from an increased availability of free fatty acids released by stimulated lipolysis in peripheral (and visceral) adipose stores (under the action of catecholamines and `cachectic' cytokines, tumor necrosis factor alpha (TNF-a), interleukin-1, and interferon-a, b, and g), as well as from de-novo fatty acid synthesis in the liver (as a response to TNF-a and b, interleukin-1, interleukin-6 and interferon-a).[7]

In fact, acute conditions induce no decrease but an increase in cholesterol production in man. Thus, cholesterol lowering results either from an increased catabolism of cholesterol-rich lipoproteins, or their margination outside the plasma compartment.[7]

HDL plays a central role in FFA clearance and reverse cholesterol transport. Besides, HDL and its mimetics also show anti-oxidant, anti-thrombotic and anti-apoptotic functions.[8] Several researchers figured out that a low amount of HDL-C, which has anti-inflammatory properties, can in turn lead to a more severe systemic inflammatory response.[9] Other laboratories found that HDL can repress inflammatory gene expression in cytokine activated endothelial cells and other cell types.[10,11]

Apart from the basic function of lipid transference, human LDL is also shown to be involved in organismal protein transfer and delivering pro-inflammatory and pro-thrombotic protein mediators from synthetic place to the site of inflammatory organ systems.[12] In response to inflammatory conditions, native LDL is chemically modified, forming LDL-containing circulating immune complexes, which leads to local accumulation and activation of macrophages, releasing pro-inflammatory cytokines and mediators.[13] Modified LDL, especially oxidized LDL, is a key molecule in the early progression of endothelial dysfunction. Studies have demonstrated that oxidized LDL plays a central role in the induction of both pro-inflammatory mediators and anti-inflammatory cytokines such as tumor necrosis factor-a (TNF-a), interleukin-6 (IL-6) and interleukin-1 1(IL-1) in human peripheral blood mononuclear cells.[14,15]

The possible mechanisms causing decreased values of serum lipid cholesterol (including HDL-C and LDL-C) in acute pancreatitis are as follows: the reduction of lipoprotein synthesis in the liver, a lower rate of general catabolic metabolism, and the activation of immune system during the acute phase response. In contrast, the production of triglycerides in the liver increases during the acute inflammatory response.[6]

In this study, we sought to ascertain changes in the serum lipid profile in patients with acute pancreatitis of varying etiology soon after admission and whether these changes were associated with the development of complications, the severity of pancreatitis or mortality.

Normal Lipid Levels considered for this study are: HDL is 35-75 mg/dl, LDL is 70-120 mg/dl and Total Cholesterol is 140-250 mg/dl.

Methodology

The study was a prospective study done on patients admitted with Acute Pancreatitis in Department of General Surgery in Karnataka Institute of Medical Sciences, Hubli. The data for this study include the lipid profile of the patients. The inclusion criteria were patients clinically diagnosed to have Acute Pancreatitis proven by biochemical and radiological parameters and exclusion criteria for both cases and controls were chronic pancreatitis, cirrhosis of liver, hyperlipidemias, patients on hypolipidaemic drugs and metabolic disorders like diabetes mellitus. The Study Group consisted of cases being all the cases of acute pancreatitis and controls being cases of non traumatic acute abdominal conditions other than acute pancreatitis.

Results

Patients were divided into two groups, cases and controls where cases are patients with Acute Pancreatitis and controls were patients with non traumatic Acute Abdominal conditions. Among the cases, male patients were the most in number and most common etiology was alcohol.

In cases, patients were divided into three groups on the basis of severity of Acute Pancreatitis: Mild, Moderate and Severe Acute Pancreatitis.

Patients with severe acute pancreatitis had either a longer length of hospital and ICU stay or much higher mortality. All the patients who died during hospitalization were in the severe group.

A total of 70 cases and 70 controls were considered for the study, of which in cases 66 were males and 4 were females: in controls 42 were males and 28 were females. Out of 70 cases of acute pancreatitis, the most common etiology was found to be alcoholic with 60 cases, 2 being gallstones and 8 were idiopathic. The severity grading of acute pancreatitis was done based on Revised Atlanta Classification 2012. In a total of 70 cases, 37 cases were of mild acute pancreatitis, 25 were moderate acute pancreatitis and 8 cases were of severe acute pancreatitis. When outcome of the patients were noted, 61 cases were discharged after conservative management and symptomatic improvement, 5 had gone against medical advice and there were 4 deaths, all of which were in the severe acute pancreatitis category.

When mean HDL values of cases (21.91 mg/dl) and controls (36.24 mg/dl) were compared, there was a significant decrease in HDL values of cases ($p = 0.0001$). A similar observation was seen among LDL and total cholesterol values of cases (53.44 mg/dl and 103.14 mg/dl respectively) and controls (122.71 mg/dl and 181.69 mg/dl respectively) with a significant decrease seen of both in the cases ($p = 0.0001$).

The mean HDL, LDL and total cholesterol values among the cases of mild, moderate and severe acute pancreatitis were compared and the following tables show the statistical results. It was seen that HDL values in severe acute pancreatitis were significantly reduced when compared to mild (P=0.0007) and moderate (P=0.0032) acute pancreatitis. No such observation was seen in LDL and total cholesterol values.

When serum lipid levels and duration of hospital say was analyzed, it was found that there was an inverse relation between HDL levels and duration of hospital stay that is lesser the HDL levels more was the duration of hospital stay (p=0.0449) and also related to severity of the disease. No such observation was found with regard to LDL and total cholesterol levels.

Table 1: Comparison of Atlanta classifications in cases with HDL scores.

Atlanta classifications	Mean	SD
Mild AP	23.32	5.47
Moderate AP	22.44	8.01
Severe AP	13.75	1.39
Total	21.91	6.86
P-value	0.0009*	
Pair wise comparisons of classifications		
Mild vs moderate	P=0.8493	
Mild vs severe	P=0.0007*	
Moderate vs severe	P=0.0032*	

Table 2: Comparison of Atlanta classifications in cases with LDL scores.

Atlanta classifications	Mean	SD
Mild AP	51.86	22.74
Moderate AP	56.60	23.01
Severe AP	50.75	13.08
Total	53.45	21.83
P-value	0.6656	
Pair wise comparisons of classifications		
Mild vs moderate	P=0.6880	
Mild vs severe	P=0.9909	
Moderate vs severe	P=0.7909	

Table 3: Comparison of Atlanta classifications in cases with total cholesterol scores.

Atlanta classifications	Mean	SD
Mild AP	100.68	37.49
Moderate AP	103.72	31.28
Severe AP	112.75	88.59
Total	103.14	43.41
P-value	0.7777	
Pair wise comparisons of classifications		
Mild vs moderate	P=0.9613	
Mild vs severe	P=0.7611	
Moderate vs severe	P=0.8685	

Table 4: Correlation between hospital stay with HDL, LDL, total cholesterol and triglycerides scores in cases.

Variables	Correlation between hospital stay of cases with p value
HDL	0.0449*
LDL	0.2965
Total cholesterol	0.6757

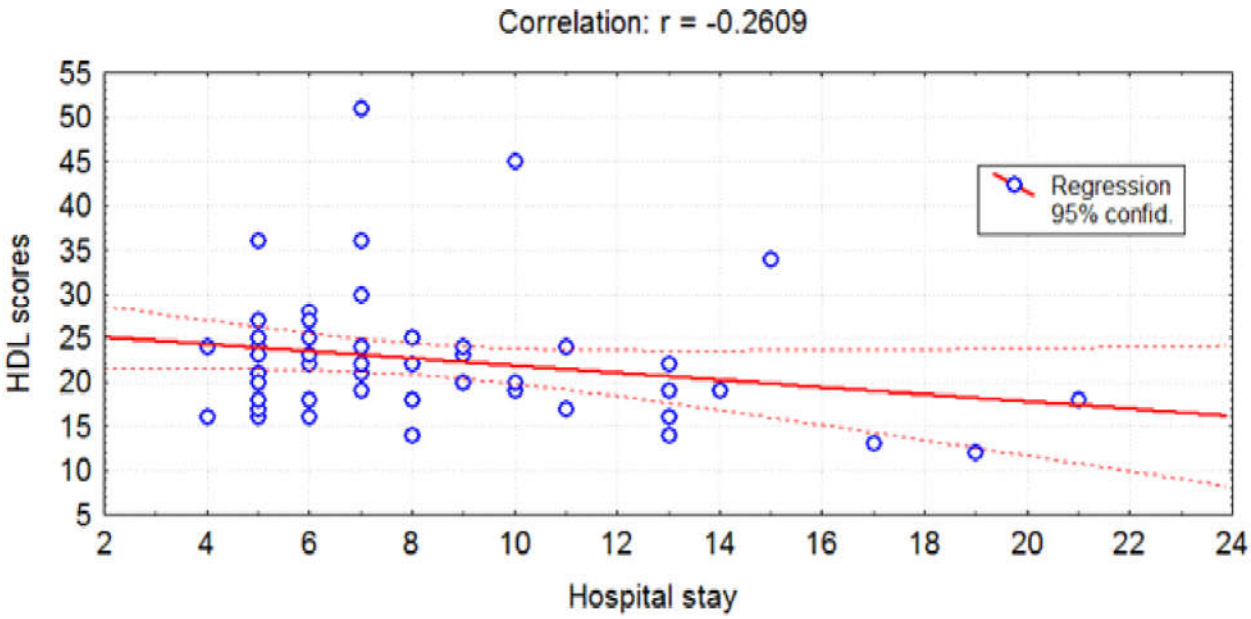

Fig. 1: Graph showing relation between HDL levels and duration of hospital stay.

Discussion

We conducted a prospective study to identify the changes in serum lipid profile in acute pancreatitis and to co-relate the level of serum lipid profile with the severity of acute pancreatitis. An analysis was also done to assess whether the predictive outcome of acute pancreatitis based on serum lipid profile could be done.

A few studies have evaluated the role of serum lipid profile in a case of acute pancreatitis and its helpfulness in assessing the severity of the disease.

It is a known fact that hypertriglyceridemia is a causative agent in acute pancreatitis hence the triglyceride component has not been assessed in this study.

Jahangir Khan et. al. in a study demonstrated that there were profound changes in the serum lipid concentrations during acute pancreatitis.[16]

Serum total cholesterol, high-density lipoprotein (HDL) cholesterol and low-density lipoprotein (LDL) cholesterol concentrations measured within 2 days of admission were significantly lower in patients who developed severe pancreatitis ($p = 0.001; < 0.000; < 0.000$, respectively).

Low serum total cholesterol, HDL cholesterol and LDL cholesterol concentrations were moreover associated with in-hospital mortalities and longer hospitalization ($p < 0.05$).

Mehmet Sait Bugdaci et. al. in their study demonstrated that the low levels of HDL in acute pancreatitis cases during acute attack are associated with severity of the disease and found a significant relation between HDL level and duration of hospitalization ($r = -0.615$, $P < 0.001$).[4]

Yushun Zhang et. al. concluded in a study that HDL level can independently predict persistent organ failure, pancreatic necrosis and mortality in patients with acute pancreatitis in an Asian-Chinese population.[5]

Yun-Shing Peng et. al. in a study demonstrated that the concentrations of HDL and APO A-I are inversely related to disease severity in patients with predicted severe acute pancreatitis admitted to ICU and serum levels of HDL and APO A-I at admission to ICU can predict persistent organ failure.[17]

Jahangir Khan et. al. in a study reported profound changes in the serum lipid levels in patients with acute alcohol induced pancreatitis.[7] The levels of serum total cholesterol, LDL-cholesterol and HDL cholesterol were significantly lower in acute pancreatitis patients than in controls during the acute disease but not after follow-up.

This study demonstrated a significantly lower levels of HDL in cases of severe acute pancreatitis when compared to mild ($p=0.0007$) and moderate ($p=0.0032$) acute pancreatitis and also showed that the duration of hospital stay of a patient was more in cases of patients with significantly lower levels of HDL ($p=0.049$).

This study demonstrated a significant lowering of all three lipid profile values of HDL (0.0001), LDL (0.0001) and total cholesterol (0.0001) when compared to lipid profile values of the control group which were patients with non traumatic acute abdominal conditions other than acute pancreatitis.

This study did not demonstrate a significant lowering of LDL ($p=0.66$) and total cholesterol (0.77) levels in cases of severe acute pancreatitis when compared to mild and moderate acute pancreatitis and also did not show any significant association with the lowering of LDL and total cholesterol levels and duration of hospital stay ($p=0.29,0.65$ respectively).

Conclusion

In this study, it was found that there was a significant decrease in the serum lipid levels that is HDL, LDL and total cholesterol values in cases of acute pancreatitis and more severe the disease, more significant was the lowering of lipid profile values, especially HDL levels.

With respect to HDL values, it was found that the outcome of the patient was inversely related to decrease in the HDL values where the duration of hospital stay of the patients were more in patients with significantly low HDL values were.

Serum lipid levels, hence, can be used as one of the components for assessing the severity of acute pancreatitis and can be used as a prognostic indicator to predict the outcome of patients with severe acute pancreatitis. Among the serum lipid levels, HDL is the most reliable indicator to assess severity and prognosis of the patient.

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