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Original Research Article

A possible association between certain cases of pancreatitis and central hypothyroidism

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ABSTRACT

Introduction: Hypothyroidism can occur due to decreased thyroid gland stimulation by pituitary or hypothalamus. Serum triglyceride and also cholesterol can increase in secondary hypothyroidism. Since hypertriglyceridemia is a well known risk factor for pancreatitis, there is a chance of association of central hypothyroidism with pancreatitis. Serum lipase and amylase are established markers of pancreatitis; so, these enzymes might be elevated in serum in central hypothyroidism. But there was no study on serum amylase or lipase levels in hypothyroidism. The aim of our study was to evaluate whether there was alteration in serum amylase or lipase levels in central hypothyroidism, and if so, whether the alteration was significant.

Methods: Serum levels of amylase, lipase and lipid profile were estimated in 14 central hypothyroidism patients (group 1) and 17 controls (group 2). Statistical analysis of the data was performed and inferences were drawn.

Observations and Results : Serum lipase and triglycerides were highly significantly increased in group 1 compared to group 2. Serum amylase was significantly increased in group 1 compared to group 2.

Conclusion: Serum levels of lipase, amylase and triglyceride, all were increased in central hypothyroidism. The present findings might indicate central hypothyroidism to be a predisposing or risk factor for pancreatitis.

Keywords: Central hypothyroidism, pancreatitis.

Introduction

Hypothyroidism results when thyroid gland fails to produce sufficient amounts of thyroid hormones for our body metabolism. Hypothyroidism can occur due to primary thyroid gland failure or decreased thyroid gland stimulation by pituitary or hypothalamus. Hypothyroidism is one of the most common endocrine disorders, with a greater burden of disease in women and the elderly.[1] Hypothyroidism was found to be a common form of thyroid dysfunction affecting 10.9% of Indian urban population.[2] Central hypothyroidism apparently accounts for about one of 1,000 hypothyroid patients because its prevalence was estimated to range from 1:20,000 to 1:80,000 in the general population.[3]

Hypothyroidism produces a variety of signs and symptoms involving multiple tissues. The disease affects every major organ system and metabolic process. The diagnosis of primary hypothyroidism can be perplexing to the clinician because of its insidious onset and wide array of nonspecific manifestations. Complaints of fatigue, muscle weakness, lethargy, and weight gain are often at first attributed to emotional or other health problems. Additionally,

patients may not seek medical care because they are unaware that they are ill. Clinicians need to be familiar with the signs and symptoms of hypothyroidism so that a timely diagnosis and treatment can be initiated.[4]

Laboratory findings in hypothyroidism may include hyponatraemia, hypercapnia, hypoxia, normocytic anaemia, elevated creatine kinase, hyperprolactinaemia, and hyperlipidaemia.[5] Type IIb hyperlipidemia, where serum triglyceride and also cholesterol increases, was the most common lipid abnormality in patients with secondary hypothyroidism.[6] Since hypertriglyceridemia is a well known risk factor for pancreatitis, there is a chance of association of central hypothyroidism with pancreatitis.[7] Serum lipase and amylase are established markers of pancreatitis; so, these enzymes might be elevated in serum in central hypothyroidism. But, in spite of the above mentioned facts, even after extensive search of literature, there was no study on serum amylase or lipase levels in hypothyroidism in India or abroad. Also there was dearth of research or data regarding incidence of pancreatitis in hypothyroidism.

Aims and objectives

The aim of our study was to evaluate whether there was alteration in serum amylase or lipase levels in central hypothyroidism, and if so, whether the alteration was significant.

Materials and Methods

The study was carried out in a tertiary care hospital for two years and seven months. Before starting the study, approval was obtained from the ethics committee for human studies, and informed consent for inclusion in the study and for invasive modalities had been obtained prior to performance from all study participants. 15 cases and 20 age and sex matched controls were included in the study. Only females were included so as to exclude variations due to sex. Central hypothyroid patients attending the outpatient department served as cases. All hypothyroid patients were ambulatory and in good general health. Normal women, mainly staff members, their relatives and friends, were included as controls. After overnight fasting, all women underwent full medical assessment, which included history and clinical and laboratory examinations (including hematology and blood chemistry and urine analysis) to exclude nonthyroidal illness. Among the exclusion criteria were:

1. primary hypothyroidism
2. elevated serum amylase secondary to causes other than pancreatitis such as parotitis, cholecystitis, peptic ulcer and other causes
3. elevated serum lipase secondary to causes other than pancreatitis such as acute cholecystitis, appendicitis, intestinal obstruction, malignancy, etc
4. pancreatitis secondary to gallstones, autoimmune, infective, neoplastic or other causes
5. Smoking, alcoholism, gallstones and other risk factors for pancreatitis.

Venous blood sample collected from each case and control was coded and assayed for amylase, lipase and lipid profile in a blind fashion by an investigator who was unaware of the subjects' clinical status. Assay of serum amylase was carried out by the method of Ceska et al.[8] Assay of serum lipase was performed by the method of Ziegenhornet et al.[9] Serum triglyceride was assayed by the method described by Fossati P et al.[10] Serum cholesterol was assayed by the method of Allain et al.[11] Serum HDL-cholesterol was assayed by the method of Harris et al.[12]

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Data were coded and checked for completeness and consistency. Then, the data were entered and analyzed. For statistics, results were expressed in terms of mean ± standard deviation and presented, using tables according to the types of tool used. $p < 0.05$ was considered to be significant and $p<0.001$ was considered highly significant.

Observations and results

Out of the initial subjects, 1 case and 3 controls dropped out. Statistical calculation was done for the resultant 14 cases and 17 controls. The age range of the subjects was 28 to 53 years.

Mean serum lipase levels in patients and controls were 47.1 U/L and 42.3 U/L respectively and the difference was found to be highly significant ($p < 0.001$) (Table 1).

Table 1. Serum lipase levels (in U/L) in patients and controls (SD= Standard deviation, SEM=Standard error of the mean, N= Number of subjects)

Group	Group 1	Group 2
Mean	47.1	42.3
SD	3.9	3.2
SEM	1.042	0.776
N	14	17

t test results are as follows:

p value and statistical significance: The two-tailed p value equals 0.0008. By conventional criteria, this difference is considered to be statistically highly significant.

Confidence interval: The mean of Group 1 minus Group 2 equals 4.800. 95%. Confidence interval of this difference is from 2.194 to 7.406.

Intermediate values used in calculations are: t = 3.7666, df = 29, standard error of difference = 1.274.

Mean serum amylase levels in patients and controls were 84.1 U/L and 79.5 U/L respectively and the difference was found to be significant ($p < 0.05$) (Table 2).

Table 2. Serum amylase levels (in U/L) in patients and controls (SD= Standard deviation, SEM=Standard error of the mean, N= Number of subjects)

Group	Group 1	Group 2
Mean	84.1	79.5
SD	6.8	4.3
SEM	1.817	1.043
N	14	17

t test results are as follows:

p value and statistical significance: The two-tailed p value equals 0.0294. By conventional criteria, this difference is considered to be statistically significant.

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Confidence interval: The mean of Group 1 minus Group 2 equals 4.6. 95%. Confidence interval of this difference is from 0.495 to 8.705.

Intermediate values used in calculations: t = 2.2918, df = 29, standard error of difference = 2.007.

Mean serum triglyceride levels in patients and controls were 164.0 mg/dl and 127.2 mg/dl respectively and the difference was found to be highly significant ($p < 0.001$) (Table 3).

Table 3. Serum triglyceride levels (in mg/l) in patients and controls (SD= Standard deviation, SEM=Standard error of the mean, N= Number of subjects).

Group	Group 1	Group 2
Mean	164.0	127.2
SD	12.9	9.8
SEM	3.448	2.377
N	14	17

t test results are as follows:

p value and statistical significance: The two-tailed p value is less than 0.0001. By conventional criteria, this difference is considered to be extremely statistically significant.

Confidence interval: The mean of Group 1 minus Group 2 equals 36.8. 95% Confidence interval of this difference is from 28.463 to 45.137.

Intermediate values used in calculations: t = 9.0272, df = 29, standard error of difference = 4.077.

Table 4. Serum cholseterol levels (in mg/l) in patients and controls (SD= Standard deviation, SEM=Standard error of the mean, N= Number of subjects).

Group	Group 1	Group 2
Mean	201.2	186.1
SD	17.3	15.8
SEM	4.624	3.832
N	14	17

t test results are as follows:

p value and statistical significance: The two-tailed p value is 0.0168. By conventional criteria, this difference is considered to be statistically significant.

Confidence interval: The mean of Group 1 minus Group 2 equals 15.1. 95% Confidence interval of this difference is from 2.929 to 27.271 .

Intermediate values used in calculations: t = 2.5374, df = 29, standard error of difference = 5.951.

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Discussion

Serum lipase is produced mainly from pancreatic acinar cells. More than 99% of the stored lipase gets excreted from the apical poles of the acinar cells into the ductal system of the pancreas.[13] During acute pancreatitis, serum lipase increases within 4 to 8 hours, peaks at 24 hours, and remains elevated for 1 to 2 weeks, with a half life between 7 and 14 hours.[14] Amylase is produced in the pancreas and also in salivary gland. When the pancreas is diseased or inflamed, amylase is released into the blood.[15] Levels of amylase often start to increase by 6-24 h after the onset of acute pancreatitis, usually peak at 48 hours and typically over the period of next 5-7 days, tend to normalize.[16] In the present study, serum lipase levels were highly significantly raised and serum amylase levels were significantly increased in the cases (group 1) in comparison to the respective levels in the controls (group 2) (tables 1 and 2).

On the other hand, serum triglyceride levels are increased in about 35% hypothyroid patients.[6] This is in accordance with our study where approximately one third patients (cases) had high serum triglyceride levels, and the mean serum triglyceride levels were highly significantly raised in the cases (group 1) in comparison to the respective levels in the controls (group 2) (table 3). Also and the mean serum cholesterol levels were significantly raised in the cases (group 1) in comparison to the respective levels in the controls (group 2) (table 4). As mentioned earlier, high serum triglycerides predispose to pancreatitis. Hydrolysis of triglycerides by pancreatic lipase and formation of free fatty acids that induce inflammatory changes are postulated to account for the development of pancreatitis induced by high triglyceride levels.[17] In the present study, high triglycerides might have caused subclinical pancreatitis, which was reflected by high serum amylase and lipase levels. Although hyperlipidemia can be associated with acute pancreatitis as an epiphenomenon, hypertriglyceridemia or chylomicronemia is the underlying cause in up to 7% of all cases of pancreatitis. Hypertriglyceridemia is the most common cause of acute pancreatitis not due to gallstones or alcohol.[18-21] Hypertriglyceridemia-induced pancreatitis rarely occurs unless triglyceride levels exceed approximately 180 mg/dl.[20,22] Therefore, lower levels of triglyceride are less prone to cause frank pancreatitis.

Autoimmune pancreatitis is associated with hypothyroidism.[23,24] But apart from autoimmune pancreatitis, we found no other correlation of pancreatitis with hypothyroidism after rigorous search of literature.

Our study has several weaknesses: firstly, it was done in urban India, and the prevalence of hypothyroidism in rural India remains unknown. Secondly, we cannot rule out that we would have found more significant differences between the case and the control group had we included more subjects and parameters. However, to include 15 subjects with central hypothyroidism, we had to screen almost 10000 subjects, and a larger group would be hard to find. In addition, we excluded a considerable number of subjects because of concomitant diseases, and our results do therefore mostly apply to a less diseased population.

Conclusion

To conclude, serum levels of lipase, amylase and triglyceride, all were increased in central hypothyroidism. The present findings might indicate central hypothyroidism to be a predisposing or risk factor for pancreatitis. But still, we feel there is need of further detailed research to substantiate our observation, and to establish serum lipase and amylase as reliable indicators, so that appropriate measures can be initiated early, to prevent pancreatitis and its complications.

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