Biochemical analysis of serum pancreatic amylase and lipase enzymes in patients with type 1 and type 2 diabetes mellitus

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ABSTRACT

Objectives: To examine the pancreatic exocrine insufficiency in patient with diabetes mellitus by estimating serum pancreatic amylase and lipase enzymes in healthy subjects and in type 1 and type 2 diabetic patients.

Methods: The study was conducted on 20 normal healthy volunteers and 39 diabetic patients referred to Al-Isra Medical Laboratory, Amman, Jordan during the period from April - November 2003 after recording their age and gender. The age of onset of diabetes and the type of treatment were determined and the patients were categorized into type 1 and type 2 diabetics. Blood samples were collected and analyzed for fasting blood sugar (FBS), glycosylated hemoglobin (HbA1C), serum insulin, and serum pancreatic amylase and lipase enzymes. All biochemical tests were carried out in the medical laboratories of Islamic Hospital, Amman, Jordan. All estimates were presented as means ± SD, and statistical treatment of data were performed using student t-test.

Results: The FBS and HbA1C estimates were consistently higher in type 1 and type 2 diabetic patients, while no significant changes were observed in the estimates of serum insulin between the normal and diabetic patients. The reduction in serum pancreatic amylase was recorded in both types of diabetes, which amounted to 71% for type 1 diabetics and 49% for type 2 diabetics. On the other hand, reduction in serum lipase was only detected in type 1 diabetics amounting to 31%. Correlation of the reduction in serum amylase and lipase levels with the duration of disease revealed a remarkable decrease in both enzymes in patients with long-standing disease (76% and 39%) in type 1 diabetic patients. Whereas, patients with very low serum insulin estimates the reduction in serum amylase was 77% while serum lipase level was reduced by 42%. Similarly, the reduction in serum amylase in type 2 diabetes was higher in patients with longer duration of illness (59%) and in patients with low serum insulin value (79%), while reduction in serum lipase was only detected in patients with very low serum insulin (34%). No differences in all measured parameters between males and females were recorded in type 1 and type 2 diabetics.

Conclusion: Although most of diabetic research has been focused on dyslipidemia as a major risk factor for cardiac, cerebral and renal complications, the present study clearly illustrates an impairment of pancreatic exocrine function in type 1 and type 2 diabetes. We suggest that analysis of serum pancreatic enzymes could be an additional informative parameter for the assessment of chronicity and progress of the illness as well as the response to therapy.

Saudi Med J 2005; Vol. 26 (1): 73-77

The pancreas of human, as in other higher vertebrates, has a complex cellular organization in which clusters of different endocrine cells are dispersed among the exocrine acinar tissue.[1,2] The proximity of endocrine cells to enzyme secreting acinar cells has postulated that islet hormones can

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Received 13th June 2004. Accepted for publication in final form 6th September 2004.

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modulate pancreatic exocrine activity.[3,4] A large number of morphological, biochemical and immunohistochemical studies on streptozotocin-induced diabetes in the experimental animals have demonstrated a reduction in pancreatic enzymes activity.[5-7] The findings were attributed to the insulin depletion caused by beta cell damage, which was reversible upon insulin administration.

In the human diabetic research, very little concern on pancreatic exocrine insufficiency has been paid, and the majority of studies are focused on metabolic derangement induced by persistent hyperglycemia due to lower insulin levels. Diabetic dyslipidemia manifested by elevated levels of a very low density lipoproteins, low density lipoproteins, and decreased levels of high density lipoproteins being the major risk factor leading to life-threatening complications in type 1 and type 2 diabetes.[8-10] Diabetic complications due to dyslipidemia result from the microangiopathies leading to retinopathy, nephropathy, peripheral and visceral neuropathy, and from the macroangiopathies causing cardiovascular, cerebrovascular and peripheral vascular diseases.[11] Reviewing the literature, it seems that very few studies on pancreatic exocrine function in human diabetes have been conducted, therefore the aim of the present work was to evaluate the changes in serum pancreatic amylase and lipase enzymes in patient with type 1 and type 2 diabetes compared with normal healthy individuals.

Methods. The survey was conducted on 20 normal healthy volunteers (8 males, 12 females with average age of 30 ± 11.3 years), 25 type 2 diabetic patients (10 males, 15 females with average age of 57 ± 10.8 year), and 14 type 1 diabetic patients (6 males, 8 females with average age of 34 ± 14.2 year). All cases included in the study were referred to Al-Isra Medical Laboratory, Amman, Jordan, during the period from April - November 2003 after obtaining the informed consent. The duration of diabetes and type of treatment were recorded, and all selected patients have no history of gastrointestinal cancer, surgery, or inflammation. Fasting blood samples were collected into plain tubes, and tubes containing ethylene diamine tetraacetic acid (EDTA). Serum samples from plain tubes were immediately prepared and analyzed for fasting blood sugar (FBS), insulin, and pancreatic amylase and lipase, while samples for glycosylated hemoglobin (HbA1C) measurements were assayed from EDTA-containing tubes. All biochemical tests were conducted in the Medical Laboratories of Al-Islamic Hospital, Amman, Jordan. The FBS was determined using glucose oxidase method, while HbA1C was assayed by turbidimetric inhibition immunoassay method (Roche Diagnostic, Mannheim, Germany). Serum pancreatic amylase and lipase were determined by the enzyme-colorimetric method using Automated Hitachi Analyzer, and serum insulin was measured using Immulite Automated Immunoassay Analyzer (Diagnostic Product Corporation, Los Angeles, California, United States of America). Data of FBS, HbA1C, insulin and serum pancreatic amylase and lipase were presented as means ± standard deviation (SD), and statistical treatment of data were performed using student t test.

Results. **Table 1** illustrates the mean data of FBS, HbA1C, serum insulin and serum pancreatic amylase and lipase in the normal individuals and

Table 1 - The mean estimates ± SD of FBS, HbA1C, serum insulin and serum pancreatic amylase and lipase in normal controls and in type 1 and type 2 diabetic patients.

Parameters	Normal	Type 1 diabetes	Type 2 Diabetes
Number	20 (M=8, F=12)	14 (M=6, F=8)	25 (M= 10, F=15)
Age (years)	30 ± 11.3	34 ± 14.2	57 ± 10.8
FBS (mg/dL)	92 ± 13[a,b]	273.3 ± 52[a]	210.4 ± 62.8[b]
HbA1C (%)	4.7 ± 0.3[c,d]	8.9 ± 2[c]	7.3 ± 1.2[d]
Serum Insulin (µU/ml)	10 ± 3.8	9.8 ± 6.2	11.3 ± 5.4
Amylase (U/L)	69.7 ± 13[e,f]	20.4 ± 8.8[e]	35.3 ± 17.8[f]
Lipase (U/L)	28.8 ± 3.5[g]	19.8 ± 5.6[g]	26.5 ± 7.8

SD - standard deviation, FBS - fasting blood sugar, HbA1C - glycosylated hemoglobin, M - male, F - female), a,b,c,d,e,f,g - statistically significant at $p<0.001$.

Table 2 - Correlation of serum levels of pancreatic amylase and lipase ± SD with duration in type 1 diabetes.

Parameters	Controls (n=20)	Type 1 diabetic patients		
		1-4 years (n=4)	5-9 years (n=4)	10-20 years (n=6)
Amylase (U/L)	69.7 ± 13[a,b,c]	22.7 ± 10.3[a]	21.3 ± 11.7[b]	16.7 ± 5.6[c]
Lipase (U/L)	28.8 ± 3.5[d,e,f]	22.6 ± 4.8[d]	19.8 ± 4.8[e]	17.5 ± 6.3[f]

SD - standard deviation, n - number, a,b,c - statistically significant at $p<0.001$, d - statistically significant at $p<0.025$, e,f - statistically significant at $p<0.005$.

Table 3 - Correlation of serum pancreatic amylase and lipase estimates with serum insulin levels ± SD in type 1 diabetes.

Parameters	Controls (n=20)	Type 1 diabetic patients		
		1-4 µU/ml (n=4)	5-9 µU/ml (n=4)	10-20 µU/ml (n=6)
Amylase (U/L)	69.7 ± 13[a,b,c]	16.1 ± 4.3[a]	18 ± 5.4[b]	24.8 ± 11.4[c]
Lipase (U/L)	28.8 ± 3.5[d,e,f]	16.8 ± 6.1[d]	19.9 ± 3.3[e]	24 ± 4.7[f]

SD - standard deviation, n - number, a,b,c,d,e - statistically significant at $p<0.001$, f - statistically significant at $p<0.1$.

Table 4 - Correlation of serum levels of pancreatic amylase and lipase ± SD with duration in type 2 diabetes.

Parameters	Controls (n=20)	Type 2 diabetic patients		
		1-4 years (n=7)	5-9 years (n=9)	10-20 years (n=9)
Amylase (U/L)	69.7 ± 13[a,b,c]	46.9 ± 17.2[a]	33 ± 20.6[b]	28.5 ± 11.7[c]
Lipase (U/L)	28.8 ± 3.5[d,e,f]	25.1 ± 10.3[d]	28.7 ± 8.3[e]	25.6 ± 5.3[f]

SD - standard deviation, n - number, a - statistically significant at $p< 0.005$, b, c - statistically significant at $p<0.001$.

type 1 and type 2 diabetic patients. The FBS values were significantly higher in type 1 and type 2 diabetic patients compared with that in normal cases ($p<0.001$) **Table 1** Similarly, the HbA1C estimates were remarkably higher in both types of diabetic patients ($p<0.001$). No significant changes in the serum insulin levels between normal individuals and diabetic patients were detected (**Table 1**). Reduction in serum pancreatic amylase was noticed in patients of type 1 and type 2 diabetes, and being more remarkable in type 1 diabetics. The reduction of amylase in type 1 diabetics was 71% compared with normal values ($p<0.001$), while the reduction in type 2 diabetics amounted to 49% ($p<0.001$). On the other hand, the reduction in serum pancreatic lipase was only detected in patients with type 1 diabetes (**Table 1**), which amounted to 31% compared with that of normal value ($p<0.001$).

Tables 2 & 3 records the changes in serum pancreatic amylase and lipase in relation to the duration of illness and to the serum insulin levels in type 1 diabetes. The reduction in both enzymes was proportional to the duration of illness, and being maximal in patients who had diabetes for more than 10 years (**Table 2).** The reduction in amylase amounted to 76% ($p<0.001$), while for lipase amounted to 39% ($p<0.005$). Similarly, the reduction in amylase and lipase was proportional to the serum insulin values, and was higher in patients with insulin estimate of <4 µU/ml (**Table 3**). For amylase it was estimated at 77% ($p<0.001$), while for lipase at 42% ($p<0.001$). **Tables 4 & 5** illustrates the correlation of serum pancreatic amylase and lipase estimates with the duration of disease and with serum insulin levels in type 2 diabetics. The reduction in amylase was also proportional to the duration of illness and to serum insulin levels, and it was reduced by 59% in those having diabetes for 10-20 years (28.5 ± 11.7 U/L versus 69.7 ± 13 U/L, $p<0.001$), and by 79% in patients with serum insulin level of <4 µU/ml (14.6 ± 3.8 U/L versus 69.7 ± 13 U/L, $p<0.001$). On the other hand, no significant reduction in lipase was recorded in relation to the duration of type 2 diabetes, but a 31% reduction in

Table 5 - Correlation of serum pancreatic amylase and lipase estimates with serum insulin levels ± SD in type 2 diabetes.

Parameters	Controls (n=20)	Type 2 diabetic patients		
		1-4 µU/ml (n=4)	5-9 µU/ml (n=9)	10-20 µU/ml (n=12)
Amylase (U/L)	69.7 ± 13[a,b,c]	14.6 ± 3.8[a]	42.4 ± 16.2[b]	36.8 ± 17.5[c]
Lipase (U/L)	28.8 ± 3.5[d]	19.1 ± 6.7[d]	29.1 ± 5.4	27 ± 8.6

SD - standard deviation, n - number, a,b,c - statistically significant at $p<0.001$, d - statistically significant at $p<0.025$.

Table 6 - Mean data ± SD of FBS, HbA1C, serum insulin and serum pancreatic amylase and lipase in the males and females of controls and type 1 and type 2 diabetic patients.

Parameters	Controls		Type 1 diabetic patients		Type 2 diabetic patients	
	Male (n=8)	Female (n=12)	Male (n=6)	Female (n=8)	Male (n=10)	Female (n=15)
FBS (mg/dL)	92 ± 12.8	91.8 ± 13.2	268 ± 53	276 ± 51	206 ± 50.4	213 ± 75
HbA1C (%)	4.8 ± 0.3	4.6 ± 0.25	8.5 ± 2.4	9 ± 1.6	6.8 ± 1.4	7.7 ± 1
Insulin (µU/ml)	9 ± 2.7	11 ± 4.4	9.5 ± 7.6	10 ± 4.8	10.9 ± 6.4	11.6 ± 4.5
Amylase (U/L)	68.8 ± 16	70.5 ± 11.7	19.4 ± 10	21.4 ± 7.8	33.2 ± 17.2	37.4 ± 17
Lipase (U/L)	27.8 ± 3.6	29.7 ± 3.3	20.7 ± 4.5	18.8 ± 6.6	25.6 ± 7.1	27.3 ± 8.5

SD - standard deviation, FBS - fasting blood sugar, HbA1C - glycoslated hemoglobin

lipase was detected in patients with serum insulin value of <4 µU/ml (19.1 ± 6.7 U/L versus 28.8 ± 3.5 U/L, $p<0.025$). Analysis of the mean data of FBS, HbA1C, serum insulin and serum pancreatic amylase and lipase between male and female patients revealed no significant difference in both type 1 and type 2 diabetes (**Table 6**).

Discussion. Diabetes mellitus is one of the most common chronic diseases, which endangers the life of millions of population all over the world. It is manifested by hyperglycemia and lowered serum insulin value, and has been classified into type 1 (IDDM) and type 2 (NIDDM) according to the age onset of the disease and the need for insulin therapy. Dyslipidemia is a major risk factor in diabetic complications and has been widely and thoroughly investigated.[12-14] It is the main cause of nephropathy, retinopathy, neuropathy, cardiovascular, cerebrovascular and peripheral vascular complications due to micro and macroangiopathies.[11] The majority of diabetic research has been focused on normalization of hyperglycemia and abnormal lipid profile to minimize serious consequences of the disease. On the other hand, very little concern on pancreatic exocrine function in diabetes has been paid. The present study, investigated the changes in serum pancreatic amylase and lipase enzymes in type 1 and type 2 diabetic patients compared with normal healthy individuals. It clearly illustrates an impairment of pancreatic enzyme activity in both types of diabetes, and amylase being most remarkably affected. Reduction in amylase activity was detected in both type 1 and type 2 diabetics, and was more severely affected in long-standing illness and with a very low serum insulin level. The reduction in lipase activity in type 1 diabetes was lower than that recorded for amylase, but it well corresponded with the duration of illness and serum insulin level. In type 2 diabetes, the reduction in lipase was only detected in patients with very low serum insulin level.

Corresponding with these findings, our previous study on streptozotocin-diabetic rats illustrated a reduction of 66% in amylase and 43% in lipase in pancreatic tissue homogenates.[7] The amylase and lipase activity were returned nearly to control values after in-vivo insulin administration. The study of Semakula et al[15] on insulin dependent diabetic

patients revealed a lowered serum lipase and isoamylase levels. The finding thought to be due to reduced acinar cell function in the vicinity of insulin-depleted islets. Similar reduction in the pancreatic amylase, lipase, trypsin and elastase have been recorded by Lorini et al,[16] Yajnik et al[17] and Kim et al.[18] Analysis of pure pancreatic juice aspirated directly from the pancreatic duct showed a significant decrease in amylase activity with little changes in lipase and bicarbonate concentrations in diabetic patients with uncontrolled hyperglycemia.[19] Strict glycemic control resulted in an increase of pancreatic juice amylase activity. Goda et al[20] studied the relationship of the volume of the pancreas using helical computed tomography with the serum level of immunoreactive trypsin in type 1 and type 2 diabetic patients. There was a strong correlation between the reductions of pancreatic volume with the impairment of trypsin activity in type 1 diabetics. Recent studies from several diabetic centers working on the measurement of fecal elastase 1 concentrations as a screening tool for exocrine pancreatic activity have indicated a high prevalence of exocrine dysfunction in diabetic population.[21-25]

In conclusion, the present study demonstrates an impairment of pancreatic amylase and lipase activity in type 1 and type 2 diabetic patients, a finding being more significant in type 1 diabetes. It is suggested that analysis of pancreatic enzymes in diabetic patients could be a useful parameters in assessing the progress of illness.

Acknowledgment. The study was supported by a research grant from the Deanship of Scientific Research, Al-Zaytoonah University, Amman, Jordan.

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