

Comparative sonographic evaluation of the anteroposterior dimensions of the pancreas in diabetics and nondiabetics

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Abstract

Background: The pancreas is an insulin-producing gland and is prone to varying degrees of destruction and change in patients with diabetes mellitus (DM). Various morphological changes including reduction in the pancreas dimensions have been described in DM.

Objectives: To determine pancreatic anteroposterior (AP) dimensions in diabetics by sonography and compare with nondiabetics. To also evaluate the correlation of the AP dimensions with patient's anthropometry, as well as the duration of the disease in comparison with nondiabetics.

Materials and Methods: This is a comparative cross-sectional study involving 150 diabetics with 150 sex and age matched healthy normoglycemic group used as controls. Sonographic measurements of the AP dimensions of the pancreatic head, body, and tail of both study groups were performed with the use of 3.5 MHz curvilinear array transducer of a SonoAce X4 ultrasound machine. Data were analyzed using Statistical Package for Social Sciences version 17 (SPSS Inc., Chicago, IL, USA). A statistical test was considered significant at $P \leq 0.05$ and 95% confidence interval.

Results: Pancreas AP dimensions were significantly smaller in diabetics compared to those of the controls. The mean dimensions were 1.91 ± 0.26 cm, 0.95 ± 0.12 cm, and 0.91 ± 0.11 cm for the head, body, and tail, respectively, in diabetics and 2.32 ± 0.22 cm, 1.43 ± 0.19 cm, and 1.34 ± 0.20 cm in the control ($P < 0.001$ in all cases). The dimensions were also significantly smaller in the Type 1 diabetics compared to Type 2 ($P < 0.001$ in all cases). The mean duration of illness for the Types 1 and 2 diabetics were 3.09 ± 1.38 and 3.78 ± 3.12 years, respectively. Longer duration of illness was associated with smaller pancreas body and tail dimensions, while pancreas head dimension was not significantly affected by the duration of illness.

Conclusion: Diabetics have smaller pancreas AP dimensions compared to the normal population.

Key words: Diabetes mellitus, dimension, pancreas, sonography

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Introduction

The pancreas is a nonencapsulated, retroperitoneal organ that lies in the anterior pararenal space between

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the duodenal loop and splenic hilum over a length of 12.5–15 cm.^[1] Various types of morphological changes in the pancreas have been described in patients with diabetes mellitus (DM).^[2] Pathologists have demonstrated islet cell pancreatic changes in DM such as hyalinization, fibrosis, hydropic degeneration, and hyperplasia.^[3] Moreover, studies in cellular composition of the pancreas in Type 2 diabetes have demonstrated a decrease in beta cell mass.^[4]

The term DM describes a chronic metabolic disorder of multiple etiology, characterized by hyperglycemia with disturbances of carbohydrate, fat, and protein metabolism, resulting from a relative or an absolute lack of insulin.^[5] There are two types of DM; the Type 1 (juvenile onset or insulin dependent DM [IDDM]) and the Type 2 (adult onset or non-IDDM). In Type 1, there is autoimmune attack and destruction of the pancreas insulin-producing cells; whereas in Type 2, the pancreas loses its ability to appropriately produce and release insulin and the body also becomes resistant to insulin, thereby causing the blood sugar levels to rise.^[6,7]

About 171 million people had DM worldwide by the year 2000, and the total number is projected to rise to 366 million by 2030.^[7] The prevalence in a local community in Edo State (Nigeria) is 9.8%, with a male: female ratio of 1.4:1 and this increase in the incidence of DM in developing countries follow the trend of urbanization and lifestyle changes, most importantly being the Western style diet.^[7,8]

The explosive increase in number of people diagnosed with DM poses a devastating negative economic impact and human cost making this disease a new health threat in the 21st century.^[9] Understanding the etiology of the disease, ensuring early diagnosis and finding a way to prevent it is an urgent challenge for health care providers.

DM affects both the lifespan and quality of life of the affected individual. The disease places serious constraints on the patient's activities, especially when there is poor management of the condition. This makes the affected person to be partially or totally dependent: Socially, financially, and, in some cases, physically.^[10,11]

Abdominal ultrasound is used in the hospital, Radiology Department and Emergency Department, as well as in physician offices for a number of clinical applications. It has a great advantage over plain radiography in that it does not predispose tissues to the hazard of ionizing radiation. Ultrasound is also generally far better than plain radiography at distinguishing the subtle variation of soft tissue structures and can be used in different modes, such as B-mode and Doppler, for example, depending on the area of interest of the user.^[12]

The pancreatic changes in DM and the advantages of ultrasonography compared to invasive and expensive

methods, as well as its probable efficacy in predicting disease severity makes it a preferred first-line imaging modality.^[7,13,14]

Sonographic evaluation of the pancreas in previous studies shows that the size of the gland was significantly smaller in DM compared to that of the nondiabetic.^[13] In diabetes of long duration, there is a loss of pancreatic weight (size) due to atrophy of the exocrine tissue.^[15]

There is a paucity of literature on ultrasonographic assessment of the pancreas in DM in Nigeria. This study is, therefore, to determine pancreatic anteroposterior (AP) dimensions in diabetics by sonography and to evaluate the correlation with patient's anthropometry, as well as the duration of the disease in comparison with nondiabetics in Benin City.

Materials and Methods

This was a comparative cross-sectional study of ultrasound assessment of dimensions of the pancreas in diabetic subjects and a healthy control group of ages 10–60 years. The study was conducted in the Radiology Department of University of Benin Teaching Hospital (UBTH), Benin City. The Type 1 diabetic subjects were those attending the pediatric outpatient clinic while the Type 2 patients were adult diabetics attending the endocrine unit of the Medical Outpatient Department. The controls were healthy (normoglycemic, determined by fasting blood sugar) volunteers.

The control group was matched with the case group in terms of age and sex. The ratio of the subject to the control group was 1:1.

Subjects with known or possible history of pancreatic diseases such as pancreatitis, cystic fibrosis, autoimmune disorders, pancreatic tumors, and chronic alcohol consumption were excluded.

Informed consent was obtained from the subjects after adequate explanation of the objectives of the study. The recruited subjects were given assurance of the confidentiality of their health information. The relevant medical history and physical examination findings were entered into the questionnaire partly filled by the participants.

A single ultrasound machine SonoAce X4 (Medison Inc., Korea 2010) with a 3.5 MHz curved transducer was used for the study.

The scans were done with the respondents in the supine or supine oblique position when necessary. The abdomen was exposed from the xiphisternum to the lower abdomen, and acoustic gel was applied.

Each subject was scanned early in the morning after an overnight fast. Some subjects were asked to drink about 250–300 ml of water during the procedure to reduce or eliminate the “shadows” cast by “bowel gas,” thereby improving the visibility of the gland. The pancreas and its various parts were identified using the left lobe of the liver, portal vein, superior mesenteric artery, inferior vena cava, splenic vein, and abdominal aorta as landmarks.

The head of the pancreas was defined as the area anterolateral to the superior mesenteric vein; the body was identified as it runs anterior to the splenic vein. The tail was viewed by angling the transducer superolaterally from the midline toward the splenic hilum. The measurement of the various parts was done differently when the entire pancreas was not seen in a single view. When a part is in full view, on-screen calipers were used to measure the maximum AP diameter on a transverse plane from the freeze-frame ultrasound image [Figures 1-3]. All measurements were done thrice by a single sonologist, and the average values obtained to minimize intraobserver error.

Data obtained were entered into a Microsoft Excel spreadsheet and analyzed using Statistical Package for Social Sciences (SPSS) version 17 (SPSS Inc., Chicago, IL, USA).

Data comparison (statistical test of significance) was done with the Chi-square test for categorical data, *t*-test and ANOVA for continuous variables, and Pearson’s correlation coefficient where appropriate.

At 95% confidence interval, two-tailed $P \leq 0.05$ was considered statistically significant.

Ethical clearance for this study was obtained from the Ethics and Research Committee of UBTH. Written informed consent was also obtained from each subject.

Results

One hundred and fifty diabetic subjects with an equal number of age and sex-matched controls were recruited in the study. The age range of the diabetic population was 10–60 years with mean age of 49.6 ± 12.30 years. The age range of the control group was also 10–60 years with mean age of 49.5 ± 12.0 years.

Table 1 represents the anthropometric data of both the subjects (diabetics) and control groups, showing the mean and standard deviation of age, weight, height, and body mass index (BMI).

The comparison of the anthropometric data of the two groups (from unpaired *t*-test determination) showed no statistically significant difference in the age ($P = 0.921$)

and height ($P = 0.069$) of the subjects and control groups but there was statistically significant difference in the weight ($P = 0.018^*$) and BMI ($P = 0.006^*$) of both groups.

A total of 98 males participated in the study comprising of 49 diabetics (50%) and 49 controls (50%) while 202 females were recruited into the study comprising of 101 diabetics (50%) and 101 controls (50%).

Table 1: Anthropometric data of the studied population showing mean age, weight, height, and BMI (including SD) in diabetics and control

Variables	Diabetic (n=150)	Control (n=150)	P
Age (years)	49.6±12.30	49.5±12.00	0.921
Weight (kg)	69.6±14.40	66.1±11.30	0.018*
Height (m)	1.6±0.09	1.6±0.10	0.069
BMI (kg/m ²)	27.0±5.77	25.1±6.13	0.006*

*Significant. n=Number of participants; SD=Standard deviation; BMI=Body mass index



Figure 1: Transverse sonogram of the head of pancreas showing site of measurement



Figure 2: Transverse sonogram of the body of pancreas showing site of measurement

Type 1 diabetics constituted 7.3% while the remaining 92.7% were Type 2 [Figure 4].

Table 2 shows the comparison of the mean and standard deviation of the age, weight, height, and BMI of the male and female diabetics with their controls, as well as the comparison of the AP dimension of the head, body, and tail of pancreas in both groups.

The comparison showed no statistically significant difference in the age and height of the male and female diabetics compared with their respective controls; the *P* values for age in both groups were 0.905 and 0.967, respectively, while that for height were 0.278 and 0.129, respectively. There was also no statistically significant difference in the weight and BMI of the male diabetics in comparison with their controls (*P* = 0.795 and *P* = 0.193, respectively), whereas there was statistically significant difference in weight and BMI among the female diabetics in comparison with their controls (*P* = 0.003 and *P* = 0.012, respectively).

Statistically significant differences were noted in the AP dimensions of the pancreatic head, body, and tail in

both sexes (*P* < 0.001, respectively) compared with their respective controls.

Table 3 compares the pancreas dimension in the male and female diabetics, as well as their age, weight, height, and BMI data. There was no statistically significant difference in the age, weight, and height between both sexes (*P* = 0.370, *P* = 0.053, and *P* = 0.277), whereas there was a statistically significant difference in the BMI among the two groups (*P* = 0.008). There was no statistically significant difference in the pancreas dimensions among the male and female diabetics (*P* = 0.470, *P* = 0.363, and *P* = 0.349).

The comparison of the mean pancreas AP dimensions in all the diabetic groups is shown in Table 4. The mean AP diameter for the pancreas head, body, and tail in the diabetic group were 1.91 ± 0.26 cm, 0.95 ± 0.12 cm, and 0.91 ± 0.11 cm, respectively, and 2.32 ± 0.22 cm, 1.43 ± 0.19 cm, and 1.34 ± 0.20 cm, respectively, for the control group. There was statistically significant difference in the measurements for each dimension of the pancreas between the diabetics and control group (*P* < 0.001, respectively).

The mean dimensions were 1.18 ± 0.24 cm, 0.82 ± 0.13 cm, and 0.82 ± 0.12 cm for the head, body, and tail, respectively, in the Type 1 diabetics while for the Type 2 groups



Figure 3: Transverse sonogram of the tail of pancreas showing site of measurement

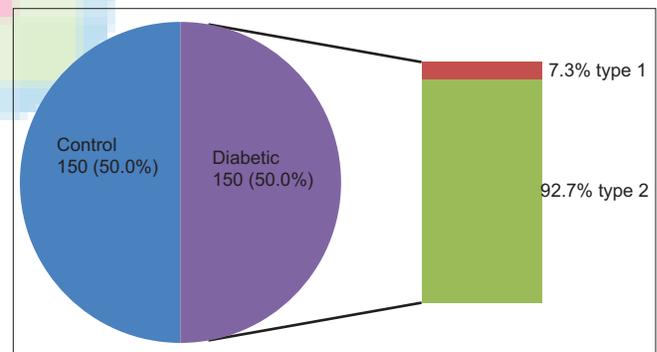


Figure 4: A bar of pie showing the percentage distribution of the study groups

Table 2: Comparison of the anthropometric indices and AP dimensions of the pancreas in the male and female diabetics with their controls

Variables	Male		P	Female		P
	Diabetic	Control		Diabetic	Control	
Age (years)	48.44 (14.94)	48.06 (14.81)	0.905	50.21 (10.68)	50.15 (10.42)	0.967
Weight (kg)	66.48 (16.18)	65.69 (13.7)	0.795	71.18 (13.16)	66.26 (9.92)	0.003*
Height (m)	1.62 (0.11)	1.64 (0.11)	0.278	1.59 (0.07)	1.62 (0.09)	0.129
BMI (kg/m ²)	25.26 (5.68)	24.03 (3.33)	0.193	27.94 (5.63)	25.66 (7.05)	0.012*
PHD (cm)	1.89 (0.35)	2.38 (0.29)	<0.001*	1.92 (0.21)	2.29 (0.18)	<0.001*
PBD (cm)	0.94 (0.13)	1.45 (0.21)	<0.001*	0.95 (0.12)	1.42 (0.18)	<0.001*
PTD (cm)	0.89 (0.11)	1.36 (0.22)	<0.001*	0.91 (0.11)	1.33 (0.19)	<0.001*

*Significant. PHD=Pancreas head diameter; PBD=Pancreas body diameter; PTD=Pancreas tail diameter; AP=Anteroposterior; BMI=Body mass index

Table 3: Comparison of anthropometric indices, as well as pancreatic AP dimensions between the male and female diabetics

Variables	Diabetic		P
	Male	Female	
Age (years)	48.29 (15.06)	50.21 (10.68)	0.370
Weight (kg)	66.33 (16.32)	71.18 (13.16)	0.053
Height (m)	1.61 (0.11)	1.59 (0.67)	0.277
BMI (kg/m ²)	25.28 (5.74)	27.94 (5.63)	0.008*
PHD (cm)	1.88 (0.34)	1.92 (0.21)	0.470
PBD (cm)	0.94 (0.12)	0.95 (0.12)	0.363
PTD (cm)	0.89 (0.11)	0.91 (0.11)	0.349

*Significant. PHD=Pancreas head diameter; PBD=Pancreas body diameter; PTD=Pancreas tail diameter; AP=Anteroposterior; BMI=Body mass index

Table 4: Comparison of the AP dimensions of the pancreas in the various study groups

	PHD	PBD	PTD
DM	1.91+0.26	0.95+0.12	0.91+0.11
Control	2.32+0.22	1.43+0.19	1.34+0.20
P	<0.001*	<0.001*	<0.001*
Type 1 DM	1.18+0.24	0.82+0.13	0.82+0.12
Type 2	1.96+0.16	0.96+0.11	0.91+0.11
P value	<0.001*	<0.001*	<0.001*
Type 1 DM	1.18+0.24	0.82+0.13	0.82+0.12
Control	2.11+0.34	1.49+0.47	1.45+0.46
P	<0.001*	<0.001*	<0.001*
Type 2 DM	1.96+0.16	0.96+0.11	0.91+0.11
Control	2.34+0.24	1.43+0.17	1.33+0.17
P	<0.001*	<0.001*	<0.001*

*Significant, PHD=Pancreas head diameter; PBD=Pancreas body diameter; PTD=Pancreas tail diameter

Table 5: Relationship of BMI of study population with pancreas AP dimensions in diabetics and controls

	BMI (mean±SD)			
	<18.5 underweight	18.5-24.9 normal	25.0-29.9 overweight	≥30 obese
PHD (cm)				
Diabetic	1.14±0.25	1.94±0.21	1.95±0.16	1.98±0.15
Control	2.43±0.22	2.29±0.26	2.34±0.17	2.26±0.15
P	<0.001*	<0.001*	<0.001*	<0.001*
PBD (cm)				
Diabetic	0.79±0.11	0.96±0.11	0.96±0.12	0.96±0.11
Control	1.67±0.32	1.39±0.19	1.45±0.15	1.39±0.16
P	<0.001*	<0.001*	<0.001*	<0.001*
PTD (cm)				
Diabetic	0.78±0.09	0.91±0.09	0.91±0.11	0.92±0.12
Control	1.58±0.35	1.31±0.18	1.34±0.19	1.28±0.17
P	<0.001*	<0.001*	<0.001*	<0.001*

*Significant. SD=Standard deviation; PHD=Pancreas head diameter; PBD=Pancreas body diameter; PTD=Pancreas tail diameter; AP=Anteroposterior; BMI=Body mass index

the values were 1.96 ± 0.16 cm, 0.96 ± 0.11 cm, and 0.91 ± 0.11 cm, respectively, with statistically significant

difference ($P < 0.001$ each for the head and body while for the tail $P = 0.004$).

Among the Type 1 diabetic group and their control, the dimension for the pancreas head, body, and tail were; 1.18 ± 0.24 cm, 0.82 ± 0.13 cm, and 0.82 ± 0.12 cm, respectively for the diabetic and 2.11 ± 0.34 cm, 1.49 ± 0.47 cm, and 1.45 ± 0.46 cm, respectively, for the control. These differences were statistically significant at $P < 0.001$ for all the measured dimensions. Similarly, for the Type 2 group and their control, the measurements were 1.96 ± 0.16 cm, 0.96 ± 0.11 cm, and 0.91 ± 0.11, respectively, for the diabetic group and 2.34 ± 0.24 cm, 1.43 ± 0.15 cm, and 1.33 ± 0.17 cm, respectively, for the control, with statistically significant $P < 0.001$ for each part of the pancreas in both subjects and controls.

There was a statistically significant relationship when the BMI was matched against the pancreas dimensions of both groups [Table 5].

The mean duration of illness for the Type 1 diabetics was 3.09 ± 1.38 years with a range of 1–6 years while for the Type 2 diabetics, the mean duration of illness was 3.78 ± 3.12 years with a range of 1–15 years.

There was positive correlation between pancreas head dimensions with age ($r = 0.634$, $P < 0.001$), weight ($r = 0.561$; $P < 0.001$), height ($r = 0.471$; $P < 0.001$), and BMI ($r = 0.402$, $P < 0.001$).

No significant correlation was demonstrated between pancreas body and tail in comparison with age, weight, height, and BMI. There was also no significant correlation between the pancreas head dimension in diabetics and duration of illness ($r = 0.075$, $P = 0.361$), whereas a negative correlation was noted between duration of illness and pancreas body and tail dimensions; $r = -0.209$; $P = 0.050$ for pancreas body and $r = -0.235$; $P = 0.004$ for pancreas tail dimensions.

Discussion

A total of 150 diabetic subjects with an equal number of healthy (normoglycemic) controls were evaluated. The lower age limit of the subjects was 10 years because the Type 1 diabetics group was mostly within the pediatric age group while the upper limit of 60 years was adopted because age-related pancreas atrophy has been reported after the age of 60.^[3]

The percentage of the Type 1 diabetic subjects among all the diabetics in this study was much smaller (7.3%) compared to the Type 2 group (92.7%) which is comparable to the distribution of both pathologies in clinical practice.^[9]

The mean pancreatic head, body, and tail AP dimensions for normal population (control) in this study were: 2.32 ± 0.22 cm, 1.43 ± 0.19 cm, and 1.34 ± 0.20 cm, respectively. The pancreatic head and body dimensions in this study were similar to the findings by Maria *et al.*^[16] Pancreatic dimensions in their study were: 2.4 ± 0.4 cm, 1.1 ± 0.3 cm, and 1.8 ± 0.4 cm for the head, body, and tail, respectively. In that study, the pancreatic tail dimension was greater than that of the body and also greater than the tail dimension in this study. In this study, however, the pancreatic body dimension was greater than that of the tail. The relative greater dimension of the pancreatic tail noted in their study may be due to the genetic peculiarity of the South American population where the study was conducted.

The mean pancreatic head AP dimensions in this study was similar to normal dimensions determined for pancreas head by Abam and Nwankwo^[17] who measured pancreas head AP dimension in 400 adult population in Port Harcourt, Nigeria. The normal dimension for the pancreas head in that study was 2.03 ± 0.33 cm and 2.33 ± 0.22 cm for this study. However, normal measurements of the pancreatic body and tail were not determined in that study.

A statistically significant difference was noted in the pancreas dimensions of the diabetics and controls in both sexes in this present study ($P < 0.001$ in all cases). Pancreas dimensions were greatest in controls and least in Type 1 diabetics. This finding was in agreement with that of Ueda^[18] who also demonstrated a significant difference in pancreas dimensions among Type 1 and Type 2 diabetics, as well as controls. In his work, he demonstrated that pancreas of the Type 1 diabetic patient was significantly smaller ($P < 0.0001$) than the pancreas of the nondiabetic subjects, whereas the pancreas of the Type 2 diabetics was less reduced in size compared to the Type 1 but smaller ($P < 0.05$) than the pancreas of the control group.

Maria *et al.*,^[16] on the other hand, noted statistically significant smaller pancreas dimensions of the head, body, and tail in the Type 1 diabetics compared to Type 2 and controls ($P < 0.004$), whereas the measurements were similar between Type 2 patients and control subjects. Type 1 patients with <2 years of disease had pancreas sizes similar to control subjects and Type 2 patients in that study. In this study, the mean duration of diabetes illness was >3 years, and it involved a larger population compared to their study. These may account for the differences between their findings and ours. In agreement with this study, Reza *et al.*^[13] also noted a smaller pancreas size in diabetes with a significant difference in the pancreas head and body dimensions in the three groups - Types 1 and 2 diabetes and controls ($P < 0.001$). Many studies have shown that smaller pancreas size in diabetes may be due to atrophy of the pancreas exocrine tissue, as well as a decrease in the beta cell mass.^[8,9,19]

Statistically significant difference was noted in the weight ($P = 0.018^*$) and BMI ($P = 0.006^*$) between diabetics and controls, this probably points to the role of obesity as a risk factor for DM.^[20] Similarly, statistically significant difference was noted in the weight ($P = 0.003^*$) and BMI ($P = 0.012^*$) among female diabetics and their controls, however, no such difference was noted among the male groups. This also may be due to the fact that most of the female diabetics were overweight (BMI = 27.94 ± 5.63) while the male diabetics were not (BMI 25.26 ± 5.68).

There was no statistically significant difference in the pancreas dimension between both sexes among the diabetic group in this study ($P = 0.470$, $P = 0.363$, and $P = 0.349$ for the head, body, and tail, respectively). There was also no statistically significant difference in both sexes among the control group ($P = 0.242$, $P = 0.495$ and $P = 0.450$ for the head, body, and tail, respectively). Probably gender does not influence the degree of pancreas size reduction in DM. There was, however, paucity of information regarding this in literature.

In this study, the pancreas body and tail dimensions did not demonstrate a significant correlation with the age, weight, height, and BMI of the diabetic subjects; whereas a significant positive correlation was demonstrated between the pancreas head AP diameter and these variables. The findings suggest that age, weight, height, and BMI do not influence pancreas dimensions significantly in adult diabetics but not so for children as a similar study by Ueda^[18] done on diabetic children showed good correlation between pancreas dimensions and age, height, weight, and body surface area.

A smaller range of duration of illness was demonstrated in the Type 1 diabetics compared to the Type 2. The mean duration of illness for the Type 1 diabetics was 3.09 ± 1.38 with a range of 1–6 years while for Type 2 diabetics, the mean duration of illness was 3.78 ± 3.12 years with a range of 1–15 years. The shorter range of duration of illness noted among the Type 1 diabetes may be a reflection of life expectancy in this group. Type 1 diabetes is an autoimmune disease seen among the younger age group.^[6,7,21] These young patients may not be able to take adequate care of themselves, ensure drug compliance, and obey the dietary restrictions like the adults.

There was no significant correlation between pancreas head dimension and duration of illness ($r = 0.075$, $P = 0.361$). However, a negative correlation existed between duration of illness and pancreatic body and tail dimensions ($r = -0.209$; $P = 0.050$ for pancreas body and $r = -0.235$; $P = 0.004$ for pancreas tail) suggesting that longer duration of illness is accompanied by a greater decrease in the pancreatic body and tail AP dimensions.

The larger parenchymal volume of the pancreas head compared to the other parts may account for the poor correlation between the pancreas head AP dimension and duration of diabetes.

The correlation result for the pancreatic body and tail in this study is in agreement with the study by Altobelli *et al.*,^[22] who demonstrated an association between longer duration of illness and a greater decrease in pancreas size. In diabetes of long duration, there is a loss of pancreatic weight (size) due to atrophy of the exocrine tissue.^[9] Ravina *et al.*,^[23] on the other hand, did not find any correlation between pancreatic size and duration of illness. The latter study, however, compared pancreatic length with duration of illness, unlike this study, where the pancreas AP dimensions and duration of illness were compared.

Conclusion

The pancreas AP dimensions of diabetics are significantly smaller than those of normal control group, with a significant difference in pancreas AP dimensions in Types 1 and 2 diabetics and even smaller dimensions in the Type 1 diabetics.

Longer duration of illness was also associated with smaller pancreas body and tail dimensions.

It is recommended, therefore, that pancreas size measurements should be included as screening parameters for suspected cases of DM while fasting blood sugar test should be requested for incidental cases of reduced pancreas dimensions noted on sonography.

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Conflicts of interest

There are no conflicts of interest.

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