

## ULTRASONOGRAPHIC EVALUATION OF THE PANCREAS IN TROPICAL PANCREATIC DIABETES

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Tropical pancreatic diabetes (TPD) is a type of diabetes peculiar to the tropics<sup>18</sup>. Individuals with TPD exhibit distinct clinical features such as emaciation, protein malnutrition, abdominal pain from childhood, evidence of pancreatic calcification in the plain x-ray of the abdomen and/or steatorrhea<sup>4,19</sup>. While these clinical features are seen in most cases, very often they may be absent. A recent study has stressed the heterogeneity in the clinical and biochemical profile of TPD<sup>11</sup>.

In the natural history of TPD, calcification occurs rather late and is seen in only 30-50% of patients even in advanced stages of the disease<sup>20</sup>. Extensive fibrosis and shrinkage of the pancreas, which is often reduced to the size of a little finger, is however a characteristic feature of the disease<sup>15</sup>.

Until recently, it was not possible to study the macroscopic appearance of the pancreas without laparotomy or other invasive procedures. With the advent of ultrasonography and computerized tomography it became possible to assess the size, shape and appearance of the pancreas by these non-invasive procedures<sup>1,6</sup>.

This paper deals with an ultrasonographic study of the pancreas of patients with TPD. This is the first study of the morphological appearance of the pancreas in this type of diabetes by a non-invasive technique.

### PATIENTS AND METHODS

The population studied consisted of diabetic subjects attending the Diabetes Research Centre, Madras and M.V. Hospital for Diabetes at Madras, India, a large referral centre for diabetes.

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The following terms were used to describe the type of diabetics studied:

- (a) Maturity onset diabetes of young (MODY) defined according to the criteria of TATTERSALL and FAJANS<sup>16</sup>.
- (b) Insulin dependent diabetes mellitus (IDDM): Non-obese diabetics who are insulin dependent and exhibit ketosis if insulin injections are withdrawn.
- (c) Tropical pancreatic diabetes (TPD): Non-obese diabetics with the following criteria laid down by MOHAN et al.<sup>13</sup>.
  1. Onset of diabetes between 15 and 35 years of age.
  2. Insulin requiring but ketosis resistant.
  3. History of abdominal pain and steatorrhea.
  4. Pancreatic calcification in plain X-ray of the abdomen.
- (d) Control subjects: Non-obese, healthy subjects with no family history of diabetes.

The diagnosis of diabetes was based on fasting plasma glucose or oral glucose tolerance test using the criteria of the National Diabetes Data Group<sup>14</sup>. Plasma glucose was estimated by the O-toluidine method and HbA<sub>1c</sub> by a colorimetric method<sup>2</sup>. The body mass index was calculated using the formula: weight in kg/square of the height in meters.

*Ultrasonography* - Real time B mode ultrasonography was performed at the Dr. Henschke Memorial Research Foundation, using a 3 MHz transducer. A low residue diet was given on the day prior to the investigation. Antiflatulents and mild laxatives were given to dispel abdominal gas. The investigation was performed at 09<sup>00</sup> after an overnight fast of 12h. Scans were done with the patient initially in the supine position. The patient was also scanned in the prone position whenever supine scanning failed to visualize the tail of the pancreas. Ingestion of a large amount of water was also tried in some cases where there was an overlying area of gas. In 6 patients the scanning was not satisfactory despite all these measures and they had to be excluded from the study. In 20 subjects in each group the ultrasonograms were satisfactory.

The pancreas was identified after locating the vascular landmarks and neighbouring organs. The antero-posterior diameters of the head, body and tail were measured by standard techniques<sup>9,10</sup>. To measure the length of the pancreas, several transverse-oblique sections were taken and the maximum length measured from the extreme right lateral margin of the head to the extreme left lateral margin of the tail. The pancreatic duct was visualized by standard techniques<sup>20</sup> and the diameter measured in the body region. The duct was considered dilated if it measured more than 3 mm in antero-posterior diameter. Student's *t*-test was used for statistical analysis.

## RESULTS

Table 1 summarizes the clinical details of the patients. All four groups were matched for age and sex and all diabetics were matched for duration of diabetes which was not more than 10 years in any patient in this study.

Table 2 shows the ultrasonographic A-P measurements of the length, head, body and tail of the pancreas in the four groups studied. There were no significant differences in the measurements of the pancreas in MODY. In IDDM

patients all measurements were smaller compared to controls but the differences were not statistically significant. In TPD patients, the length of the pancreas appeared to be reduced ( $p < 0.001$ ). Measurements of the head, body and tail were also significantly reduced ( $p < 0.001$ ).

Table 3 lists the various ultrasonographic abnormalities seen in patients with TPD. Reduction in size of the gland was a consistent finding. Calcification was also confirmed in all patients. The site of calcification in the pancreas could be localized by ultrasound. Pancreatic calcifications were recognized sonographically as small reflective particles which gave the gland a stippled appearance. Stones lying free in a dilated pancreatic duct were distinguishable from peripheral calculi. Acoustic shadowing behind stones was sometimes present. In all patients with TPD, the gland as a whole appeared to have an increased echogenicity even in non-calculous areas, probably due to fibrosis. The margins of the gland could be identified and were found to be irregular in 90% of TPD patients. There were no significant abnormalities in the morphology of the pancreas in MODY or IDDM patients.

The pancreatic duct was found to be dilated in 8 TPD patients and in three of these pancreatic calculi were found within this dilated duct. The diameter

group	sex		body mass index	age mean and range (years)	age at onset of diabetes (years)	duration of diabetes (years)	plasma sugar (mM/l)	HbA <sub>1c</sub> (%)
	M	F						
controls (n = 20)	12	8	21.3 ± 1.0	23 ± 1.2 (18-35)	—	—	7.4 ± 0.72	7.2 ± 0.5
MODY (n = 20)	11	9	22.5 ± 1.5	26 ± 1.5 (16-32)	20 ± 1.4	6.4 ± 2.3	10.3 ± 0.72	8.5 ± 0.9
IDDM (n = 20)	11	9	20.3 ± 1.2	24 ± 2.5 (14-34)	19 ± 2.0	7.2 ± 2.0	13.3 ± 0.67	10.4 ± 1.5
TPD (n = 20)	12	8	19.6 ± 0.9	25 ± 2.3 (17-35)	22 ± 1.8	5.4 ± 3.0	12.4 ± 0.56	9.6 ± 1.2

all values are means ± SD

Tab. 1 - Clinical details of various groups of diabetics.

groups	length	head	body	tail
controls	8.68 ± 1.29	2.85 ± 0.37	2.04 ± 0.21	1.88 ± 0.16
MODY	7.13 ± 0.94	2.52 ± 0.50	1.83 ± 0.32	1.62 ± 0.32
IDDM	6.84 ± 1.19	2.11 ± 0.53	1.67 ± 0.39	1.52 ± 0.38
TPD	5.72 ± 0.97*	1.66 ± 0.32*	1.27 ± 0.40*	1.10 ± 0.29*

\*  $p < 0.001$  in comparison with controls

Tab. 2 - Ultrasonographic measurements of pancreas in different groups; antero-posterior measurement of pancreas (in cm).

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feature	n	%
fibrosis	20	100
calculi	20	100
in whole gland	7	35
in head	7	35
in body	3	15
in tail	3	15
irregular margins	18	90
dilatation of pancreatic duct	8	40
ductal calculi	3	15

Tab. 3 - Ultrasonographic features of pancreas in TPD patients.

of the ducts varied from 4 to 15 mm in these patients. The pancreatic duct was normal in size in MODY and IDDM patients.

Routine ultrasound study of the upper abdominal organs was done which showed evidence of cirrhosis of the liver in 3 TPD patients. Two patients with MODY had silent gallstones that were detected by ultrasonography.

#### DISCUSSION

This study presents the results of ultrasonographic evaluation of the pancreas in patients with tropical pancreatic diabetes. This is a condition in which there is gross pathology of the pancreas with characteristic macroscopic and microscopic features<sup>15</sup>. While the histopathology of the pancreas is fairly typical, this paper describes a simple non-invasive method by which fibrosis and alterations in shape and size of the gland could be ascertained in patients with TPD.

In the diagnosis of TPD the clinical features such as young age at onset, emaciation, abdominal pain and/or steatorrhea are helpful clues, but these may often be absent<sup>11</sup>. The presence of calcification in a plain x-ray of the abdomen in a young diabetic in tropical countries is a fairly reliable sign of TPD, once other causes of calcification such as alcoholism, gallstones and hyperparathyroidism have been excluded. However, when the calcification is small and solitary, it is sometimes difficult to be sure that it arises from the pancreas. Differential diagnosis would include gallstones, kidney stones and calcified tuberculous or other lymph nodes. While other radiological investigations can help to solve this problem, ultrasonography offers a simple non-invasive method of directly localizing the calculi in the pancreas<sup>20</sup>.

Since ultrasonography provides information on fibrosis and other morphological changes, the diagnosis of TPD is made easier. Of the two non-invasive imaging techniques, ultrasonography and computed tomography (CT), ultrasound is best suited for patients with little or no fat layers whereas for CT examination the more developed the fat layers, the better the visualization of the pancreas<sup>7</sup>. Since patients with TPD are usually malnourished, ultrasonography would appear to be the method of choice in this group of patients.

GILINSKY et al.<sup>5</sup> have recently reported that ultrasonography has a 93% sensitivity in detecting chronic pancreatitis.

A diagnosis of TPD is not merely of academic interest. Since exocrine dysfunction is invariably present in TPD<sup>21</sup>, the management of this condition would include replacement therapy with pancreatic enzymes and other supplemental therapy.

Ultrasonography helped to diagnose dilatation of the pancreatic duct in five patients in this study. Identification of a dilated duct might suggest papillary stenosis which can then be corrected by endoscopic surgical papillotomy<sup>22</sup>. It might also provide information as to which patients require further investigation to identify possible candidates for various drainage and other surgical procedures that are frequently done in patients with this condition<sup>17</sup>.

The detection of cirrhosis of the liver in three TPD patients is interesting because cirrhosis is not uncommon in patients with this type of diabetes<sup>3</sup>. The detection of silent gallstones in the MODY patients suggests that ultrasonography might prove useful in other types of diabetes as well.

Some degree of fibrosis occasionally occurs in IDDM patients and rarely in non-insulin dependent diabetic patients. However, this is only seen in patients with long duration of diabetes and especially in the older age groups<sup>8</sup>.

In the tropics, other types of diabetes of the young, such as MODY, are also common<sup>12</sup>. Hence, for the differential diagnosis of diabetes in young subjects in the tropics ultrasonography is found to be a useful procedure.

#### SUMMARY

Ultrasonography was performed in three groups of young diabetics in the tropics, namely MODY, IDDM and tropical pancreatic diabetes (TPD). Several morphological abnormalities of the pancreas such as fibrosis and shrinkage of the gland, increased echogenicity and ductal dilatation were found in patients with TPD. It also helped to localize the site of calculi in the pancreas. MODY and IDDM patients did not show any significant changes except a slight reduction in size of the gland. Ultrasonography is a useful tool in differential diagnosis of young diabetics in tropical countries.

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