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Brief Report

# Nutritional profile of fibrocalculous pancreatic diabetes and primary forms of diabetes seen in Southern India

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**Summary**

Plasma levels of retinol binding protein (RBP), prealbumin, total protein, albumin, transferrin and ferritin were estimated in three groups of diabetic patients seen at a diabetes centre in S. India. The groups consisted of patients with fibrocalculous pancreatic diabetes (FCPD), non-insulin-dependent diabetes mellitus (NIDDM) and insulin-dependent diabetes mellitus (IDDM). Mean RBP levels were lower in FCPD and IDDM patients compared to controls but this did not reach statistical significance. Prealbumin levels were normal in FCPD patients, but low in IDDM compared to controls ($P < 0.005$) and NIDDM ($P < 0.05$). FCPD patients had lower transferrin levels compared to controls ($P < 0.05$). There were no differences in the levels of total protein, albumin and ferritin in any of the study groups. The study shows that biochemical evidence of undernutrition is seen in FCPD and IDDM patients while NIDDM patients are not significantly different from non-diabetic control subjects.

**Key words:** Nutritional profile in diabetes; Malnutrition diabetes; Fibrocalculous pancreatic diabetes; Tropical diabetes; Retinol binding protein; Prealbumin; Transferrin; Ferritin

## Introduction

The entity known as malnutrition related diabetes mellitus (MRDM), a unique form of tropical diabetes, was recently introduced as a distinct form of diabetes in the WHO study group classification of diabetes [1]. Under MRDM two subgroups have been proposed – protein deficient diabetes mellitus (PDDM) and fibrocalculous pancreatic diabetes (FCPD). The former is more commonly seen in northern and eastern India and the latter in southern India [2]. FCPD is characterized by clinical evidence of chronic pancreatitis – pancreatic calculi on abdominal X-rays, dilated pancreatic duct on ultrasonograms and steatorrhoea [2–4]. Protein-calorie malnutrition is believed to be one of the consistent clinical features of both varieties of MRDM [1,4]. Our earlier studies have shown that clinically apparent protein-calorie malnutrition is not necessarily

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present in all FCPD patients [5]. It is possible, however, that subtle changes of under-nutrition are present in these patients. Biochemical measurements such as plasma albumin, prealbumin, retinol binding protein and transferrin help in the assessment of protein nutrition and for documenting subclinical degrees of nutritional depletion [6]. Using these parameters, the present study compares the nutritional profile of FCPD patients with the two primary forms of diabetes namely, insulin-dependent diabetes mellitus (IDDM) and non-insulin-dependent diabetes mellitus (NIDDM) seen at a diabetes centre in southern India.

## Patients and Methods

The following groups of subjects were studied.

1. Controls ($n$ = 18). Subjects were healthy non-diabetic volunteers from the staff of the Diabetes Research Centre, Madras. All had normal glucose tolerance tests. None had a family history of diabetes or pancreatitis.
2. Non-insulin-dependent diabetes mellitus (NIDDM) ($n$ = 14). Patients were classified as NIDDM according to the WHO study group report [1]. All had an insidious onset of diabetes, were not ketotic and responded to diet and/or oral hypoglycemic agents.
3. Insulin-dependent diabetes mellitus (IDDM) ($n$ = 18). Patients classified as IDDM had an abrupt onset of diabetes, were prone to ketosis in the basal state or had established ketoacidosis in the past and needed insulin injections continuously from the time of diagnosis.
4. Fibrocalculous pancreatic diabetes (FCPD) ($n$ = 18). Patients diagnosed as FCPD were classified using previously described criteria [7]. All had a history of recurrent abdominal pain from childhood, evidence of pancreatic calculi on plain abdominal X-ray and ductal dilatation with intraductal stones on ultrasonography. None of the patients were prone to ketosis.

Consecutive diabetic patients with NIDDM, IDDM and FCPD were recruited for the study at the time of first registration at our centre. All had received treatment for diabetes from other physicians. The NIDDM patients were on treatment with sulphonylurea agents and the IDDM and FCPD patients were on insulin therapy. Antidiabetic drugs were last taken 24 h prior to the day of the test. Study groups were matched as closely as possible for sex because of the well known male preponderance in FCPD. Body mass index (BMI) was calculated using the formula: weight in kilograms divided by height in square metres. A BMI of $\leqslant 18$ kg/m$^2$ was considered as a clinical index of under-nutrition. To exclude the confounding effect of obesity, patients with obesity (i.e. body mass index $\geqslant 27$ in men and $\geqslant 25$ in women [8]) were excluded from the study but this was necessary only in the NIDDM group as none of the IDDM or FCPD patients were obese.

None of the NIDDM and IDDM patients had symptoms suggestive of pancreatic disorder e.g. abdominal pain, flatulence, chronic diarrhoea or steatorrhoea and all had normal abdominal X-rays and ultrasonograms. Two of the FCPD patients and one IDDM patient had clinical signs of protein-calorie undernutrition such as emaciation, parotid gland enlargement and skin and hair changes. None of the study subjects had evidence of any systemic infections such as tuberculosis. None of the women were on oral contraceptives. All had normal liver function tests including serum bilirubin, SGOT, SGPT and alkaline phosphatase. Total white blood counts, blood urea and serum creatinine and urinary protein excretion, measured by urinary protein/creatinine ratio were normal in all study subjects. None of the study subjects consumed alcohol. Two NIDDM patients had background diabetic retinopathy.

Blood samples were drawn at 8 a.m. after an overnight fast. Plasma was separated and stored at $-20^\circ$C till the assays were performed. Investigations included plasma glucose (glucose oxidase method, Boehringer Mannheim, F.R.G.) and glycosylated hemoglobin which was estimated by a colorimetric method [9]. Retinol binding protein

TABLE 1

Clinical details of study groups

| Study groups | Sex ratio M:F | Age (years) | Duration of diabetes (years) | BMI ($kg/m^2$) | FPG (mg/dl) | PPPG (mg/dl) | $HbA_1$ (%) |
|---|---|---|---|---|---|---|---|
| Controls ($n = 18$) | 10:8 | 29 ± 8 | – | 21.3 ± 2.5 | 91 ± 9 | 118 ± 22 | 7.1 ± 0.3 |
| NIDDM ($n = 14$) | 8:6 | 36 ± 6* | 2.1 ± 2.5 | 22.0 ± 3.2 | 206 ± 76[a] | 332 ± 98[a] | 10.7 ± 1.1[a] |
| IDDM ($n = 18$) | 11:7 | 21 ± 10**,*** | 3.7 ± 2.8 | 16.7 ± 2.9[a,b] | 190 ± 73[a] | 296 ± 77[a] | 12.7 ± 2.0[a,c] |
| FCPD ($n = 18$) | 12:6 | 31 ± 10**** | 3.6 ± 2.7 | 18.1 ± 2.1[a,b] | 206 ± 96[a] | 304 ± 92[a] | 11.5 ± 2.4[a] |

*$P < 0.05$ vs control; **$P < 0.01$ vs control; ***$P < 0.001$ vs NIDDM; ****$P < 0.01$ vs IDDM. [a]$P < 0.001$ vs control; [b]$P < 0.001$ vs NIDDM; [c]$P < 0.005$ vs NIDDM. Results are expressed as mean ± SD.

(RBP), prealbumin and transferrin were estimated using radial immunodiffusion plates (Behringwerke A.G., F.R.G.). Ferritin was estimated by the ELISA method using the reagents of Boehringer Mannheim, F.R.G. Total serum protein and serum albumin were estimated by the Biuret and the Bromocresol green dye binding methods respectively [10].

Results are expressed as mean ± SD. Statistical analysis was done on an Apricot F1 Computer using Microstats statistical programme. Analysis of variance (ANOVA) was used to test differences between groups. References to statistical significance pertain to a probability level of $\leq 5\%$.

## Results

The clinical details of the study groups are shown in Table 1. The NIDDM patients were older and the IDDM patients younger compared to the control group and FCPD patients. IDDM and FCPD patients had a lower BMI compared to controls and NIDDM patients. There were no significant differences in the fasting and postprandial plasma glucose values between the three diabetic groups. The IDDM had higher $HbA_1$ levels compared to NIDDM ($P < 0.005$) but the levels were not different from those in FCPD patients.

TABLE 2

Biochemical parameters in the study groups

| Parameters | Controls ($n = 18$) | NIDDM ($n = 14$) | IDDM ($n = 18$) | FCPD ($n = 18$) |
|---|---|---|---|---|
| Retinol binding protein (mg/dl) | 4.2 ± 1.7 | 4.6 ± 3.0 | 3.2 ± 1.7 | 3.2 ± 2.3 |
| Prealbumin (mg/dl) | 20.9 ± 5.5 | 19.2 ± 6.2 | 14.5 ± 6.2*,** | 17.8 ± 8.2 |
| Total protein (g/dl) | 7.0 ± 0.2 | 6.9 ± 0.5 | 6.7 ± 0.3 | 6.9 ± 0.2 |
| Albumin (g/dl) | 4.0 ± 0.3 | 3.9 ± 0.4 | 3.9 ± 0.3 | 3.8 ± 0.3 |
| Transferrin (mg/dl) | 362 ± 86 | 321 ± 59 | 329 ± 68 | 298 ± 93*** |
| Ferritin (ng/ml) | 51.2 ± 33.6 | 59.2 ± 36.3 | 62.9 ± 39.2 | 72.9 ± 51 |

*$P < 0.005$ vs control; **$P < 0.05$ vs NIDDM; ***$P < 0.05$ vs control. Results are expressed as mean ± SD.

The details of the biochemical parameters in the different groups are shown in Table 2. The RBP levels were lower in FCPD and IDDM patients compared to controls, but the results were not statistically significant. Prealbumin levels were normal in FCPD patients, but low in IDDM compared to controls ($P < 0.005$) and NIDDM ($P < 0.05$). There were no differences in total protein and albumin levels between any of the study groups. Transferrin levels were low in FCPD patients compared to the controls ($P < 0.05$) and normal in the other two patient groups. There were no differences in plasma ferritin levels between any of the study groups.

## Discussion

There is a paucity of data on the nutritional profile of tropical forms of diabetes. The aim of this study was to see whether the nutritional profile of FCPD patients is significantly different from other forms of diabetes seen at a diabetes centre in southern India. The nutritional profiles of three groups of diabetic patients seen in southern India, namely, FCPD, NIDDM and IDDM were studied using six accepted biochemical markers for assessment of nutrition [6]. FCPD patients had low transferrin levels compared to controls, while IDDM patients had low prealbumin levels compared to controls and NIDDM patients. The other parameters were not significantly different in any of the study groups. Our study supports the view that under-nutrition is not specific to the MRDM forms of diabetes [11,12]. It is of interest that Basu et al. [13] recently reported low levels of retinol binding protein and vitamin A in IDDM patients.

It is not possible to comment on the role of malnutrition in the aetiology of MRDM based on the findings in this study. The only conclusion that could be drawn is that at the time of presentation at our centre, patients with FCPD and IDDM had a similar nutritional status while that of the NIDDM patients resembled control subjects. This finding is of interest because we have shown in earlier studies that IDDM patients have negligible C-peptide levels while FCPD patients have partial preservation of $\beta$-cell function [14]. However, an additional factor, namely steatorrhoea, could contribute to weight loss in FCPD patients. In this context, our recent observation [15] that some FCPD patients may put on weight after adequate control of diabetes and enzyme replacement is of further interest. *In summary*, the results from this study suggest that clinical evidence of undernutrition is not a specific sign of MRDM, but may be seen in other forms of diabetes as well.

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