The clinical and hormonal (C-peptide and glucagon) profile and liability to ketoacidosis during nutritional rehabilitation in Ethiopian patients with malnutrition-related diabetes mellitus

J. Abdulkadir[1], B. Mengesha[1], Z. Welde Gebriel[2], H. Keen[3], Y. Worku[1], P. Gebre[2], A. Bekele[2], K. Urga[2] and A.-S. Taddesse[2]

[1] Departments of Internal Medicine and Biochemistry, Faculty of Medicine, Addis Ababa University,
[2] Ethiopian Nutrition Institute, Addis Ababa, Ethiopia, and
[3] Unit for Metabolic Medicine, Division of Medicine, Guy's Hospital, London, UK

Summary. Cases of malnutrition-related diabetes mellitus conforming to the description of the protein deficient pancreatic diabetes type in Ethiopian patients were compared with Type 1 (insulin-dependent) and Type 2 (non-insulin-dependent) diabetic. Fourteen of 39 malnutriton-related diabetes mellitus patients had fat malabsorption compared with only two of ten Type 1 diabetic patients and one of nine control subjects. Xylose absorption was normal favouring a pancreatic cause for the malabsorption. Plasma C-peptide during oral glucose tolerance test was significantly lower than that in Type 2 diabetic patients and normal control subjects ($p < 0.01$ to 0.001) and was also consistently but not significantly higher than in Type 1 diabetic patients. Glucagon secretion patterns were similar in malnutriton-related and Type 1 diabetic patients. Of 23 new malnutrition-related diabetic patients treated with glibenclamide after nutritional rehabilitation and insulin treatment, only three responded, 14 were unresponsive but remained ketosis free for over eight days while another six developed ketoacidosis or sig-

nificant ketonuria within two to six days during the trial. Sixteen unselected Type 1 diabetic patients who discontinued their insulin therapy all developed frank ketoacidosis after a mean of 5.5 days. The similarity of the malnutrition-related and Type 1 diabetes mellitus in age of onset, insulin requirement for diabetic control and appearance of ketosis-proneness in some cases, together with the similarity of C-peptide and glucagon secretion patterns suggest that the protein deficient pancreatic diabetes variant of malnutrition-related diabetes mellitus may be Type 1 diabetes mellitus modified by the background of malnutrition rather than an aetiologically separate entity. Community based studies are required to ascertain frequency and types of diabetes mellitus in malnourished populations and the role of genetics and environment in their aetiology.

Key words: Ethiopian malnutrition-related diabetes mellitus, nutritional rehabilitation, ketosis-resistance, fat malabsorption, C-peptide, glucagon.

A preliminary study of diabetes mellitus associated with malnutrition in Ethiopian patients [1] had shown that the majority were young adults from a poor socioeconomic background susbsisting on a diet inadequate in animal protein and vitamins (ascorbic acid in particular) and persistently or seasonally in food energy as well [2, 3]. Patients presented with classic symptoms of thirst, polyuria and wasting often of several months' or a few years' duration but had little or no ketoacidosis. Attempts to control their hyperglycaemia with oral agents, on admission to hospital or after initial treatment with insulin therapy, were unsuccessful in the majority of cases. However, these patients did not develop ketoacidosis after withdrawal of

insulin therapy. They thus demonstrated the need for insulin and ketosis-resistance, well-known characteristics of malnutrition-related diabetes mellitus (MRDM). Of the two main variants of MRDM, i. e. the fibrocalcific pancreatic diabetes (FCPD) and the protein deficient pancreatic diabetes (PDPD also known as the Jamaica or J-type) [4] the Ethiopian cases were closer to the latter type. However, in contrast to the Jamaican and Indian patients who required 80 IU or more of insulin (at least initially) [5, 6] most of our patients responded to modest doses (50 IU or less) from the start of treatment.

The objectives of this study were to relate the clinical and hormonal (C-peptide and glucagon) responses to glu-

cose to the liability of Ethiopian MRDM patients to ke-
toacidosis during a period of nutritional rehabilitation.
These patients would then be compared with Type 1 (in-
sulin-dependent) and Type 2 (non-insulin-dependent)
diabetic patients. An additional objective was to re-exa-
mine the possibility of treating malnutrition-related dia-
betic patients with oral agents after nutritional rehabilita-
tion and some recovery of their endogenous insulin
secretion.

Patients and methods

The study was conducted at the Ethiopian Nutrition Institute in
Addis Ababa over a period of 22 months from June 1986. The pur-
pose of the study was explained and agreement was obtained from
each patient and normal control subject (and parents or guardians in
the case of minors; minors were not included in the normal control
group) participating in the study including their freedom to with-
draw from the study at any stage without jeopardy to their care if
they did so, in accordance with the Helsinki Declaration. Patients in
each category of diabetes (see below) were included in the order in
which they were seen (by J.A. and B.M.). Application of various
tests, some of which were introduced during the study, was deter-
mined by their availability. All information was recorded on a proto-
col prepared for the purpose. In the case of the MRDM patients, the
first objective of treatment was to improve their nutritional status
over a period of six to eight weeks.

Classification of patients and management

MRDM. A poor socioeconomic background with any three of
the following four additional characteristics: (1) Presentation with
the classic symptoms of diabetes mellitus of at least three months'
duration. (2) Undernourished or cachectic when first seen with a
body mass index (BMI) of $< = 18$ kg/m^2. (3) Without significant
ketonuria (less than $+ +$ with Ketostix). (4) Requiring insulin for
diabetic control (i.e. failure to respond adequately to oral agents).

Type 1 diabetes. (1) A history of ketoacidosis on presentation.
(2) Rapid development of ketoacidosis after insulin withdrawal or in
the face of acute stress such as infection, trauma or surgery.

Type 2 diabetes. (1) No socioeconomic or clinical evidence of malnu-
trition. (2) A diagnosis of diabetes mellitus based on fasting hyper-
glycaemia of > 7.8 mmol/l whole blood on more than one occasion
with symptoms of diabetes mellitus or whole blood glucose values of
> 10 mmol/l at 2 h and at one other time during standard oral glu-
cose tolerance test (OGTT) in asymptomatic cases. (3) Response to
diet and oral agents.

Unclassified. Patients put in this category were those requiring in-
sulin but without ketosis-proneness or malnutrition in their history
or clinical findings and, provisionally, MRDM type patients with age
of onset of diabetes above 40 years because they are not included in
most MRDM studies.
Patients with hypertension or kidney disease, or those who were
breast feeding were excluded.

Normal control subjects. The subjects chosen were adults, unrelated
to the patients, with a BMI of 19–25 kg/m^2 with normal fasting blood
glucose and with no family history of diabetes.
There were 55 MRDM patients, 19 with Type 1 diabetes, 18 with
Type 2 diabetes and 16 normal control subjects in various compo-
nents of the study.

Management during the study

All MRDM patients, and uncontrolled and new Type 1 patients
were admitted to the metabolic ward of the Ethiopian Nutrition In-
stitute for treatment. Their diet contained 113 to 120 g of protein
allowing at least 1 g/kg body weight of animal protein, 96 to 116 g of
fat and total energy 10,000–12,600 kJ (2,700–3,000 kcal) per day.
Well-controlled Type 1 and all Type 2 diabetic patients came from
their homes on the morning of the test.
Insulin treatment was initiated for MRDM patients on admission
to the study. After improvement in their nutritional state (three to
four weeks after admission) insulin was withdrawn for trial with
glibenclamide (Daonil, Hoechst, Frankfurt, FRG). Insulin was re-
started if ketoacidosis or persistent ketonuria ($+ +$ or more on re-
peated testing with ketostix (Ames (Miles Ltd.), Slough, England))
occurred, or if there were recurrence and progression of the classic
symptoms of diabetes despite glibenclamide treatment.

Biochemical procedures and methods

OGTT was performed within two to three weeks of admission ac-
cording to the standard procedure (75 g glucose in 300 ml of water
after withholding insulin from 18.00 hours the day before the test)
after relief of the acute symptoms with insulin treatment. Venous
blood was sampled every 30 min through an indwelling needle kept
patent with heparinized 154 mmol/l NaCl. Aprotinin (Midran, Novo
Industri S/C, Copenhagen, Denmark) was added to the samples for
glucagon determination and all the specimens were stored at $-20\,^\circ$C
pending hormone assay.
C-peptide and glucagon were measured by RIA in duplicate
samples using reagents supplied by Novo Industri following their
directions.
Stool was collected for fat determination (after appropriate treat-
ment in those harbouring intestinal parasites), early in the study for
24 h and later for 72 h at the time of admission and repeated once or
twice after nutritional improvement[7]. Normal control subjects (free
of intestinal parasites) were put on the same diet as the patients for six
days and stool was collected for fat determination from day 4 to day 6.
D-xylose absorption was determined using the same method [8]
as in our previous study. Blood was sampled at 30 min and 60 min for
serum xylose determination (normal values being > 150 mg/l at
30 min and > 250 mg/l at 60 min).

Statistical methods

The Student's *t* test was used for statistical analysis.

Results

Of a total of 63 patients, 56 males and seven females, in-
cluded in the category of MRDM initially, two patients
were later put in the unclassified category because their
history indicated an adequate nutritional background and
six others because of onset of symptoms after the age of
40 years. These patients were excluded from the hor-
monal studies. The age pattern is shown in Table 1.

Clinical and biochemical findings

As shown in Table 2, MRDM patients had many of the
physical characteristics associated with malnutrition
which were not seen in Type 1 patients although a BMI of

Table 1. Age at onset in malnutrition-related diabetes (MRDM), Type 1 (insulin-dependent) diabetes and Type 2 (non-insulin-dependent) diabetes

Age	MRDM		Type 1 diabetes		Type 2 diabetes	
	M	F	M	F	M	F
10–19	19	3	7	3	0	0
20–29	18	2	6	1	0	0
30–39	13	2	1	0	1	0
40–49	4	0	0	0	8	2
50 +	2	0	0	0	5	3
Total	56	7	14	4	14	5

Table 2. Clinical and biochemical findings in 55 (+ 6 patients aged 40 years and above) new malnutrition related diabetes mellitus patients

	Present
Parotid enlargement	35 + 2 [a]
Scalp hair changes	11 + 2
Oedema with skin changes	9 + 1
Without skin changes	2 + 1
Scabies	7 + 2
Intestinal parasites	13 + 3
Amoebic liver abscess	1
Elevated transaminases (44)	17 + 1
Elevated alkaline phos (44)	7 + 2
Haemoglobin (49) < 120 g/l	11 + 2

( ) = total number tested when less than 55. Numbers after plus sign apply to the 6 patients aged 40 years and above.
[a] Unrecorded in 5 cases; all other cases normal or above the given value as applicable

Table 3. D-xylose absorption in relation to stool fat in malnutrition related diabetes (MRDM) [a], Type 1 (insulin-dependent) diabetes and normal control subjects

Stool fat	MRDM	Type 1	Normal control subjects
Normal	9 (16 + 3)	(9)	(9)
Abnormal [b]	6 (14)	(2)	(1)
Abnormal [c]	6 (9 + 3)	(0)	(0)
	21 (39 + 6)	(11)	(10)

[a] Including three patients of six over 40 years of age; [b] Without intestinal parasites; [c] With intestinal parasites. Numbers in parentheses indicate the total number of subjects in each group in relation to stool fat; numbers before the parentheses indicate the number who had the D-xylose test Numbers after the plus signs indicate patients aged 40 years and above

< 18 kg/m² was also found in some of these patients. Most of the MRDM patients described significant weight loss occurring after the onset of diabetic symptoms. The mean initial BMI of 24 new MRDM patients was 15.60 ± 1.45 kg/m². There were no MRDM patients with clinical evidence of liver disease at the time of admission to the study but 17 of 47 patients had mild elevation of transaminases, seven (aged 18 years and above) had isolated elevation of alkaline phosphatase and two patients showed elevation of both. Of 10 Type 1 patients tested none showed these abnormalities. Haemoglobin was 120 g/l or less in 12 of 49 MRDM patients. Fat malabsorption (Table 3) was found in 23 of 39 (plus three pa-

tients over 40 years old) unselected MRDM patients 14 of them without intestinal parasites. This abnormality was found in only two of 10 Type 1 patients and one of nine control subjects tested. D-xylose absorption was normal in all 12 MRDM patients with excess faecal fat who were tested. Two previously well-nourished but subsequently cachectic Type 2 patients also showed fat malabsorption.

C-peptide and glucagon patterns during OGTT (Tables 4 a and b)

The mean C-peptide values of MRDM patients were higher than those of Type 1 patients, although the difference was not significant; they were, however, significantly lower than those in Type 2 patients and normal control subjects ($p < 0.01$ to 0.001 at various times during OGTT in each case). The values were highest in the mild MRDM cases (who responded to the oral agent) approximating those of Type 2 diabetic patients, lowest in the severe group (those who showed ketosis-proneness) being indistinguishable from Type 1 diabetic patients, and intermediate in the intermediate group (those who required insulin but were ketosis-resistant on insulin interruption). The glucagon secretion patterns were similar in MRDM and Type 1 diabetes. The values for the ratio of C-peptide to glucose concentration showed a reversal of the relation of C-peptide levels between Type 2 and normal control subjects.

Response to treatment

Weight gain in MRDM patients was from 1.1 to 5.4 kg/m² on insulin and diet in those who stayed at the Ethiopian Nutrition Institute for four weeks or more except in three patients whose desire for food was reduced by painful neuropathy. The clinical manifestations of malnutrition resolved including reduction in size or disappearance of the parotid enlargement. In three patients who had soft offensive stools the physical characteristics of the stool returned to normal and the fat content also diminished. Abnormal liver function also resolved or improved and there was improvement in haemoglobin levels.

Trial on oral agent (Table 5)

The mean BMI of 24 MRDM patients at the start of oral agent therapy was 18.67 ± 1.55 kg/m² vs 15.6 ± 1.45 kg/m² at the time of admission ($p < 0.001$). The mean duration of the trial was 8.9 days. Only three patients responded and only one had an initial BMI of < 18 kg/m². Manifestations of ketoacidosis appeared in two patients and persistent moderate ketonuria in one other within two to four days of starting the oral agent. Another three developed ketonuria without progression to ketoacidosis from day six of treatment while 17 did not show any evidence of ketosis for the duration of their trial as shown in Table 5 but had fasting blood glucose values persistently

Table 4a. C-peptide values (nmol/l) during oral glucose tolerance test in all three types of diabetes mellitus

Time hours	Malnutrition-related diabetes mellitus	Type 1 (insulin-dependent)	Type 2 (non-insulin-dependent)	Normal control subjects
0	0.21 ± 0.15 (22)	0.15 ± 0.09 (11)	0.57 ± 0.38 (8)	0.41 ± 0.11 (8)
0.5	0.23 ± 0.15 (22)	0.17 ± 0.09 (11)	0.60 ± 0.44 (8)	0.55 ± 0.11 (8)
1.0	0.25 ± 0.14 (22)	0.19 ± 0.12 (11)	0.69 ± 0.47 (8)	0.57 ± 0.15 (8)
1.5	0.29 ± 0.16 (22)	0.20 ± 0.14 (11)	0.68 ± 0.43 (8)	0.55 ± 0.14 (8)
2.0	0.30 ± 0.19 (22)	0.23 ± 0.13 (10)	0.71 ± 0.45 (8)	0.52 ± 0.12 (8)
2.5	0.29 ± 0.19 (16)	0.20 ± 0.09 (8)	0.79 ± 0.45 (6)	0.53 ± 0.15 (7)
3.0	0.31 ± 0.20 (15)	0.24 ± 0.14 (8)	0.81 ± 0.45 (6)	0.52 ± 0.15 (7)

Numbers in parentheses indicate number of individuals tested

Table 4b. Glucagon values (nmol/l) during oral glucose tolerance test in the three types of diabetes

Time hours	Malnutrition-related diabetes mellitus	Type 1 (insulin-dependent)	Type 2 (non-insulin-dependent)	Normal control subjects
0	52.3 ± 15.3 (14)	48.3 ± 7.3 (5)	73.2 ± 24.0 (5)	53.5 ± 41.6 (5)
0.5	52.4 ± 17.7 (14)	48.0 ± 13.2 (5)	63.8 ± 3.8 (5)	42.4 ± 24.5 (5)
1.0	54.3 ± 20.0 (14)	50.6 ± 11.3 (5)	62.5 ± 10.9 (5)	45.7 ± 14.4 (5)
1.5	52.2 ± 20.5 (14)	49.0 ± 6.0 (5)	65.0 ± 14.0 (5)	40.5 ± 36.4 (5)
2.0	52.3 ± 16.5 (14)	49.6 ± 7.5 (5)	62.0 ± 14.6 (5)	33.3 ± 28.2 (5)
2.5	44.2 ± 10.3 (12)	56.9 ± 13.4 (4)	64.5 ± 17.2 (3)	20.7 ± 14.5 (4)
3.0	46.3 ± 8.1 (12)	43.1 ± 6.8 (4)	56.7 ± 12.0 (3)	26.5 ± 10.7 (4)

Numbers in parentheses indicate number of individuals tested

Table 5. Duration of insulin withdrawal

Days off insulin	No. of cases	No. showing ketosis [a]
– 4	24 [b]	3
5– 9	20	3
10–14	17	0
15 +	3	0

[a] Includes ketoacidosis and persistent ketonuria of + + or more;
[b] 1 patient withdrew from the trial after the 3rd day

> 11.1 mmol/l, recurrence of polyuria and polydipsia and decline of body weight. The mean age of onset of diabetes of the six patients who developed ketoacidosis or persistent ketonuria during the trial with glibenclamide was 19.7 years, BMI at the time of the trial was 19.2 kg/m^2 (increase in BMI 1.0–5.4 kg/m^2) while the mean age of onset of the 17 who remained ketosis-free during the trial was 23.0 years, the mean BMI was 18.5 kg/m^2 (increase in BMI 1.0–4.8 kg/m^2). There was no significant difference between patients in either age of onset of diabetes ($t = 1.052, p > 0.3$) or BMI at the time of the trial with oral agent ($t = 0.914, p > 0.3$). In 17 recorded episodes of frank ketoacidosis in 16 Type 1 patients who interrupted their insulin treatment for a variety of reasons, the median interval between interruption of injections and appearance of ketoacidosis was three days and the mean was 5.5 days, the difference between median and mean being due to one patient in whom the interval was recorded as 30 days.

Discussion

We have no ready explanation for the great preponderance of male subjects with MRDM seen in our present and previous studies although other studies have also shown a preponderance of male patients [9]. Most of the MRDM patients were from rural areas and this may mean that debilitated female patients are more reluctant to undertake the long journey to hospital or there may be a true preponderance of males with this type of diabetes. In agreement with our earlier findings [1], the diabetic patients from a poor socioeconomic environment not only had a low BMI but the other well-known indicators of malnutrition such as parotid enlargement, hair and skin changes, pitting oedema, anaemia (aggravated in some cases by parasitic infestation) and also abnormal liver function tests. These findings are similar to those described by Zuidema from Indonesia [10] with the difference being that among his cases a significant number had pancreatic calcification while, so far, this feature is lacking in Ethiopian MRDM. In our patients the abnormalities improved or resolved during treatment but the severity of the diabetes did not improve in the majority with respect to insulin need for diabetic control.

Excess stool fat, not attributable to intestinal parasites, was found in 14 of 39 MRDM patients. This confirms our previous finding of malabsorption in association with MRDM [1]. D-xylose absorption was normal in all 21 patients who had the test. This does not by itself rule out intestinal abnormality but favours pancreatic pathology in conjunction with the postmortem findings in two previous MRDM cases both showing marked reduction in pancreatic size with fibrosis and in one case with areas of polymorphnuclear, lymphocytic and plasma cell infiltration in the acini and islet tissues.

However, exocrine pancreatic pathology (though not pancreatic calcification) also occurs in the Type 1 and Type 2 diabetes [11–13]. On the other hand, malabsorption was more common in the MRDM than in Type 1 diabetic patients in this study suggesting an interaction between malnutrition, which is common in Ethiopia [2, 3]

and the diabetes in causing the pancreatic damage and producing a condition which, in its most severe form, is akin to kwashiorkor. This hypothesis is strengthened because regression of the parotid enlargement and reduction of the stool fat in some of the patients during treatment suggest that the pancreatic abnormality is partially reversible.

On the other hand, ketoacidosis is not restricted to Type 1 diabetes since it can occur in diabetes developing after near-total pancreatectomy [14] and in the FCPD variant of MRDM [15]. Therefore, based on clinical characteristics alone, even ketoacidosis cannot provide conclusive evidence of the aetiological category of the diabetes [16].

Concerning ketosis-resistance in MRDM, this study has confirmed our earlier findings and those of others [1, 2, 15] that the majority of patients exhibit this characteristic on insulin withdrawal in comparison to Type 1 diabetic patients, even after a significant gain in body weight, for a longer period than the average Type 1 patient although our patients were not withdrawn from insulin for as long as those in the study by Ahuja et al. [17]. Furthermore, the serum carnitine level of Ethiopian diabetic patients was not found to be significantly lower than that of normal control subjects although the nutritional state of the patients tested is not obvious in the report [18].

Weight gain during nutritional rehabilitation in the six MRDM patients who developed ketoacidosis or significant ketonuria and the 17 who did not was similar and glucagon secretion patterns in MRDM and Type 1 diabetes were also similar. On the other hand, the C-peptide in the MRDM group was consistently (though not significantly) higher than that in the Type 1 group. Furthermore, in the MRDM group it was highest in the oral agent responsive group and lowest in the ketosis-prone group. These findings are in favour of residual insulin secretion as the main factor for ketosis-resistance in MRDM. But aggravation of carnitine and body fat depletion in the course of the diabetes could be contributory factors. However, levels indistinguishable from those with Type 1 diabetes as well as wide variations in basal and stimulated levels similar to those found in this study have been reported in MRDM [19, 20]. These differences may be partly due to differences in the nutritional and metabolic status of the patients when the test is done. In addition, the possibility, also applying to our study, that ketosis-prone patients from rural areas are less likely to reach medical care because of rapid progression to ketoacidosis, thus contributing an inherent bias in the clinical identification of MRDM.

The geography of diabetes [21, 22] shows that MRDM is confined to tropical countries where malnutrition is common and in most of these countries it is peculiar to the poorer segment of the population but such an association does not necessarily indicate a cause-effect relationship. Therefore, the aetiology of MRDM remains unresolved [23].

On the basis of several characteristics including onset in youth, insulin treatment required and ketosis-proneness, developing in some cases during the natural history or after nutritional rehabilitation and the glucagon and C-peptide levels, the PDPD variant of MRDM could be considered a mild form or variant of Type 1 diabetes peculiar to malnourished populations rather than an aetiologically separate entity. In addition, a limited study of the HLA pattern in MRDM patients has shown a significantly higher frequency of HLA-DR3 than in non-diabetic control subjects and similar to that in Type 1 diabetes in the same population [24]. However, a definitive answer to its identity requires more extensive community-based studies to ascertain frequency and type of diabetes in malnourished populations and the role of genetics and environment in their aetiology.

References

1. Abdulkadir J, Mengesha B, Wolde Gebriel Z, Gebre P, Beastall G, Thomson JA (1987) Insulin-dependent ketosis-resistant diabetes in Ethiopia. Trans Roy Soc Trop Med Hyg 81: 539–543
2. Selenius R, Awalom G, Gobezie A (1971 a) Dietary studies in Ethiopia II: dietary pattern in two rural communities in North Ethiopia. Acta Soc Med Upsal 76: 17–38
3. Selenius R, Gobezie A, Knutsson E, Valquist R (1971 b) Dietary studies in Ethiopia. Dietary pattern among the Rift Valley Arsi Galla. Am J Clin Nutr 24: 365–377
4. World Health Organization (1985) Diabetes mellitus. Tech Rep Ser 727 pp 20–24
5. Hugh-Jones P (1955) Diabetes in Jamaica. Lancet II: 891–899
6. Tripathy BB, Kar BC (1965) Observations on clinical patterns of diabetes mellitus in India. Diabetes 14: 404–412
7. Natelson S (1971) Techniques of clinical chemistry, 3rd ed. Charles C. Thomas, Springfield, pp 325–477
8. Meeuwisse G, Dano G (1965) The xylose absorption test in infancy. Acta Paed Scand 54: 33–42
9. Lester FT, Abdulkadir J, Larson D, Quana'a P (1976) Diabetes mellitus Clinical features in 404 Ethiopians. Ethiop Med J 14: 185–198
10. Zuidema PJ (1959) Cirrhosis and disseminated calcification of the pancreas in patients with malnutrition. Trop Geog Med 11: 70–74
11. Lohr M, Kloppel G (1987) Residual insulin positivity and pancreatic atrophy in relation to duration of chronic Type 1 (insulin-dependent) diabetes mellitus and microagiopathy. Diabetologia 30: 757–762
12. Editorial (1987) Pancreatic abnormalities in Type 2 diabetes mellitus. Lancet II: 1497–1498

13. Fonseca V, Berger LA, Beckett AG, Dandona P (1985) Size of pancreas in diabetes mellitus: a study based on ultrasound. Br Med J 291: 1240–1241
14. Morrow CE, Cohen JI, Sutherland DER, Najarian JS (1984) Chronic pancreatitis: Long term surgical results of pancreatic duct drainage, pancreatic resection, and near-total pancreatectomy and islet autotransplantation. Surgery 96: 608–616
15. Mohan V, Mohan R, Susheela L, Snehalata C, Bharani G, Mahajan VK, Ramachandran A, Viswanahan M, Kohner EM (1985) Tropical pancreatic diabetes in South India: heterogeneity in clinical and biochemical profile. Diabetologia 28: 229–232
16. Lester F (1984) A search for malnutrition diabetes in an Ethiopian diabetic clinic. IDF Bulletin 29: 14–16
17. Peters W-H, Seim H, Loster H, Strack E, Lubs H, Kohnert K-D (1987) Ketosis, serum carnitine and its precursor aminoacids in normal and diabetic Ethiopians. Exp Clin Endocrinol 90: 83–92
18. Ahuja MMS, Talwar GP, Varma VM, Kumar A (1965) Diabetes mellitus in young Indians. Ind Jour Med Res 53: 1138–1147
19. Rao RH, Vigg BL, Rao KSJ (1983) Suppressible glucagon secretion in young, ketosis-resistant, Type "J" diabetic patients in India. Diabetes 32: 1168–1171
20. Ahuja MMS, Sharma GP (1985) Serum C-peptide content in nutritional diabetes. Horm Metabol Res 17: 267–268
21. Keen H, Ekoe JM (1984) The geography of diabetes mellitus. Br Med Bull 40: 359–365
22. Rao RH (1988) Diabetes mellitus in the undernourished: coincidence or consequence? Endocr Rev 9: 67–87
23. Abu-Bakare A, Gill GV, Taylor R, Alberti KGMM (1987) Tropical or malnutrition-related diabetes: a real syndrome? Lancet I: 1138–1153
24. Abdulkadir J, Worku Y, Schreuder GMT, D'Amaro J, de Vries RR, Ottenhoff TMH (1989) HLA-DR and -DQ antigens in malnutrition-related diabetes mellitus in Ethiopians: a clue to its aetiology? Tissue Antigens 34: 284–289

Dr. J. Abdulkadir
Faculty of Medicine,
Addis Ababa University
P. O. Box 1176
Addis Ababa
Ethiopia