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(Accepted 3 September 1992)

Is diabetes mellitus related to undernutrition in rural Tanzania?

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Abstract

***Objective*—To investigate the relation between undernutrition and diabetes.**

***Design*—Survey of glucose tolerance in rural Tanzania.**

***Setting*—Eight villages in three widely separated regions of Tanzania.**

***Subjects*—8581 people aged 15 and above: 3705 men and 4876 women.**

***Main outcome measures*—Oral glucose tolerance, body mass index, height, and low haemoglobin and cholesterol concentrations.**

***Results*—In the eight villages 42·7-56·9% of all men and 30·0-45·2% of all women had a body mass index below 20 kg/m^2; the lowest quintile was 18·2 kg/m^2 in men and 18·6 kg/m^2 in women. The prevalence of diabetes did not change significantly from the lowest to the highest fifths of body mass index in men (lowest 1·6% (95% confidence interval 0·8% to 2·9%) *v* highest 1·3% (0·7% to 2·5%)) or women (1·1% (0·6% to 2·1%) *v* 0·5% (0·2% to 1·2%)). In men and in women prevalence of impaired glucose tolerance was greater in the lowest fifths of height (8·2% (6·3% to 10·6%), and 11·1% (9·2% to 13·3%)) respectively and body mass index (9·6% (7·5% to 12·1%), and 8·4% (6·7% to 10·5%)) than in the highest fifths (impaired glucose tolerance 4·7% (3·4% to 6·5%); and 5·1% (3·9% to 6·7%); body mass index 5·1% (3·7% to 7·0%), and 7·7% (6·2% to 9·6%).**

***Conclusion*—Rates of diabetes were not significantly associated with low body mass index or height, but overall rates were much lower than those in well nourished Western populations. Increased impaired glucose tolerance in the most malnourished people may reflect the larger glucose load per kilogram weight. The role of undernutrition in the aetiology of diabetes must be questioned.**

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BMJ 1992;**305**:1057-62

Introduction

In 1985 the World Health Organisation expert committee on diabetes mellitus introduced malnutrition related diabetes mellitus as "a major clinical subclass, ranking with insulin dependent diabetes mellitus and non-insulin dependent diabetes mellitus."[1] Bajaj suggested that there are at least two subclasses of malnutrition related diabetes mellitus: fibrocalculous pancreatic diabetes and protein deficient pancreatic diabetes, and this classification has been adopted by the WHO.[2] Several reviews of malnutrition related diabetes have been published.[3-7] Most have favoured the view that chronic undernutrition is a key factor in the causation of malnutrition related diabetes mellitus, but direct evidence is poor and we have questioned the existence of the protein deficient form of malnutrition related diabetes mellitus.[6]

Traditionally a low body weight and energy intake were considered to decrease the risk of diabetes.[8] This view was based on observations such as the reduced incidence of diabetes mellitus in Europe during the first and second world wars[9] and the observation that the prevalence of non-insulin dependent diabetes in different countries was positively related to the "average fatness" of the population.[10] The same association has been observed in intrapopulation studies. Gupta *et al* found that, among urban Indians, rates of diabetes were 3·6% in subjects with a normal body weight and 1·5% in very lean subjects.[11] On the other hand, Rao cited the results of a large study in India in which rates of diabetes were not significantly different between urban and rural subjects as evidence pointing to an association between diabetes and undernutrition, since most rural subjects were undernourished.[4] In general, diabetes is less common in undernourished populations than in well nourished populations.[12] This does not, however, answer the question clearly whether within the same population chronic undernutrition leads to a clinically and statistically significant increase in diabetes. We attempted to answer this question by studying glucose tolerance in rural African communities with a background of malnutrition.

Patients and methods

The study was carried out in eight villages in Tanzania and forms part of a long term programme aimed at reducing morbidity and mortality with continuing care. (Treatment was offered to all those found to be ill during surveys.) Six villages were chosen at random in two contrasting regions: Kilimanjaro, one of the most prosperous, and Morogoro region, one of the more economically disadvantaged.[13] Of the remaining two villages, one in Mara region was chosen because the inhabitants had been exposed to high concentrations of dietary cyanide, and the other in Kilimanjaro region was chosen because hypertension was thought to be common. In four of the eight villages the total population aged 15 years and over was about 1000. The entire adult population in these villages was therefore invited to participate in the study. In the other villages a list of the names of the leaders of the 10 cell units (10 families) was obtained and the number of units required to provide about 1000 subjects was selected at random. Slightly more people were selected in Uswaa village. Lengthy discussions were held with village leaders before the start of the study to ensure

high rates of compliance. Table I shows that village sample sizes ranged from 899 (Mdawi) to 1430 (Uswaa) with response rates of 72·5% to 96%. Also shown are age and gender and the main staple carbohydrates consumed. Both Morogoro and Kilimanjaro regions are regions of agricultural importance, but the per capita income and meat consumption of peasant farmers in Kilimanjaro is higher than that of peasants in Morogoro. Childhood malnutrition is common in both regions despite these differences. Since information on the nutritional state of children is important when investigating a possible relation between glucose intolerance and undernutrition we attempted to document information on the nutritional state of children in the villages and districts where the surveys were carried out.

NUTRITION

The overall prevalence of protein energy malnutrition in rural Tanzania varies between 30% and 80%, with half of the under 5 year old population being undernourished in most areas.[14] If undernutrition is assessed by height for age, about 60% of children are stunted during their fourth year, and even among older children rates of stunting remain around 30%. Studies have shown that most people receive only about 60% of their daily protein requirements.[15]

The nutrition and health of children in one village in Morogoro region with similar characteristics to Msolwa (one of the villages in Morogoro in this study) have been studied extensively.[16] A high degree of stunting (35-71%) was found among children aged 1 month to 15 years and wasting in 3-20%. The infant mortality rate was 198 per 1000 births, which was much higher than the national average of 137 per 1000. A nutritional survey sponsored by UNICEF was carried out among children in Usari village, one of our study villages, in Kilimanjaro region during September-October 1987. Thirty seven per cent of the children were found to be malnourished.[17]

TABLE I—*Age and sex distribution of subjects studied in eight villages*

Village	No of subjects invited	No (%) responding	No (%) men	Mean age (years)	Staple carbohydrate
Madazini	1346	1141 (84·8)	567 (49·7)	34	Maize, rice
Mellela	1337	969 (72·5)	414 (42·7)	38	Millet
Msolwa	1027	976 (95·0)	492 (50·4)	34	Maize, rice, cassava
Mdawi	936	899 (96·0)	309 (34·4)	41	Banana
Naibili	1155	1090 (94·4)	462 (42·4)	36	Banana, maize, rice
Usari	1109	1008 (90·9)	379 (37·6)	38	Banana
Uswaa	1505	1430 (95·0)	601 (42·0)	41	Banana
Nyambori	1424	1068 (75·0)	482 (45·1)	34	Cassava

METHODS

Subjects participating in the surveys were requested to report to the village school or dispensary after an overnight fast. Venous blood samples were taken fasting and, except for known diabetic patients, two hours after a 75 g oral glucose load. A beam balance was used to measure weight without shoes or coats and height was measured in bare feet. Age and sex were recorded on a questionnaire.

Portions of the fasting and two hour blood glucose samples were drawn into fluoride tubes and analysed at the survey site with a glucose analyser (Yellow Springs Instruments, Ohio, United States) with appropriate quality control measurements as previously described.[13] An aliquot of sample was also kept frozen at −20°C for analysis of serum cholesterol by an enzymatic method[18] with the Cobas Bio centrifugal analyser (Roche, Welwyn Garden City). Serum cholesterol concentration was used to provide a crude indication of fat and animal protein intake. Haemoglobin was also used as an indicator of nutritional status and was measured with a BMS haemoglobinometer (Buffalo Medical Specialties, Buffalo, United States).

DEFINITIONS

Diabetes was defined according to the 1985 WHO criteria[1]—that is, two hour blood glucose concentration $\geq 10{\cdot}0$ mmol/l for diabetes and $\geq 6{\cdot}7$ mmol/l but < 10 mmol/l for impaired glucose tolerance. For diagnosis of diabetes at least two abnormal blood glucose values were required in an asymptomatic person but for epidemiological studies a single diagnostic value was acceptable. All the subjects with diabetes already diagnosed at the time of study had fasting blood glucose concentrations $\geq 6{\cdot}7$ mmol/l and were defined as diabetic irrespective of their current treatment. Body mass index was defined as weight (kg) divided by the square of height (m). Patients with a body mass index below 20 kg/m^2 were regarded as underweight, those with an index 20-24·9 kg/m^2 as

TABLE II—*Distribution of haemoglobin and cholesterol concentrations and body mass index in men in eight villages. Values are numbers (percentages) unless stated otherwise*

	Haemoglobin (g/l)				Cholesterol (mmol/l)			Body mass index (kg/m^2)		
Village	<110	110-129	130	Mean (SD)	<3·3*	>5·2	Mean (SD)	<20·0	>25·0	Mean (SD)
Madazini	157 (27·8)	255 (45·0)	155 (27·3)	118 (18)	258 (45·5)	35 (6·1)	3·5 (1·0)	242 (42·7)	19 (3·4)	20·4 (2·4)
Melela	92 (22·1)	208 (50·2)	114 (27·6)	118 (17)	263 (63·6)	7 (1·7)	3·0 (0·8)	191 (46·1)	7 (1·7)	20·1 (2·2)
Msolwa	165 (33·5)	227 (46·2)	100 (20·3)	115 (18)	202 (41·0)	29 (5·9)	3·6 (1·0)	248 (50·4)	8 (1·6)	19·9 (2·2)
Mdawi	12 (4·0)	107 (34·7)	190 (61·3)	132 (15)	19 (6·2)	117 (38·0)	5·0 (1·3)	176 (56·9)	13 (4·3)	19·6 (2·8)
Naibili	11 (2·4)	73 (15·8)	378 (81·8)	142 (17)	75 (16·3)	122 (26·3)	4·5 (1·3)	209 (45·3)	17 (3·6)	20·3 (2·4)
Usari	7 (1·9)	25 (6·7)	347 (91·5)	151 (19)	115 (30·3)	32 (8·4)	3·9 (1·1)	180 (47·6)	13 (3·5)	20·2 (2·3)
Uswaa	32 (5·3)	290 (48·2)	279 (46·4)	128 (14)	156 (25·9)	62 (10·3)	4·0 (1·0)	279 (46·4)	28 (4·7)	20·3 (2·4)
Nyambori	131 (27·3)	261 (54·2)	90 (18·6)	116 (14)	145 (30·0)	28 (5·8)	3·7 (0·9)	241 (49·8)	14 (2·9)	20·1 (2·5)
Total				126 (21)			3·9 (1·2)			20·1 (2·4)

*Two standard deviations below the mean for British subjects.

TABLE III—*Distribution of haemoglobin and cholesterol concentrations and body mass index in women in eight villages. Values are numbers (percentages) unless stated otherwise*

	Haemoglobin (g/l)				Cholesterol (mmol/l)			Body mass index (kg/m^2)		
Village	<110	100-119	120	Mean (SD)	<3·3*	>5·2	Mean (SD)	<20·0	>25·0	Mean (SD)
Madazini	199 (34·6)	318 (55·5)	57 (9·9)	101 (15)	200 (34·9)	40 (7·0)	3·7 (1·0)	172 (30·0)	38 (6·6)	21·6 (3·2)
Melela	122 (22·0)	296 (53·4)	137 (24·6)	107 (15)	330 (59·4)	7 (1·2)	3·2 (0·8)	251 (45·2)	37 (6·6)	20·6 (2·8)
Msolwa	112 (23·1)	246 (50·8)	126 (26·0)	108 (15)	151 (31·3)	53 (10·9)	3·9 (1·1)	200 (41·5)	24 (5·0)	20·6 (2·6)
Mdawi	20 (3·3)	177 (30·1)	393 (66·6)	122 (14)	36 (6·1)	237 (40·2)	5·0 (1·3)	248 (42·0)	45 (7·7)	20·7 (3·1)
Naibili	18 (2·8)	110 (17·6)	500 (79·6)	130 (16)	90 (14·4)	157 (25·0)	4·5 (1·3)	239 (38·0)	67 (10·6)	21·3 (3·0)
Usari	5 (0·8)	43 (6·8)	581 (92·4)	139 (16)	118 (18·8)	60 (9·6)	4·0 (0·9)	232 (36·9)	61 (9·7)	21·1 (2·9)
Uswaa	17 (2·0)	286 (34·5)	526 (63·5)	122 (12)	122 (14·7)	99 (12·0)	4·2 (0·9)	288 (34·7)	94 (11·3)	21·4 (3·1)
Nyambori	101 (17·2)	367 (62·6)	118 (20·2)	108 (13)	152 (25·9)	41 (7·0)	3·9 (0·9)	221 (37·7)	43 (7·4)	20·8 (2·6)
Total				118 (19)			4·1 (1·2)			21·0 (2·9)

*Two standard deviations below the mean for British subjects.

TABLE IV—*Crude prevalence (%) of diabetes and impaired glucose tolerance according to body mass index (divided by quintiles) and age groups*

Body mass index (kg/m²)	Diabetes				Impaired glucose tolerance			
	15-34 years	35-54 years	≥55 years	All ages (95% confidence interval)	15-34 years	35-54 years	≥55 years	All ages (95% confidence interval)
Men:								
<18·2	0·8	0·7	4·2	1·6 (0·8 to 2·9)	5·8	8·6	19·2	9·6 (7·5 to 12·1)
–19·5	0·3	0·5	3·5	1·1 (0·5 to 2·3)	5·3	6·5	15·7	9·1 (6·3 to 10·4)
–20·6	0·6	0·9	3·0	1·2 (0·5 to 2·4)	4·2	6·6	9·5	6·1 (4·5 to 8·1)
–21·8	0·5	1·3	0·8	0·8 (0·3 to 1·9)	2·5	6·1	9·2	4·8 (3·4 to 6·7)
>21·9	0·3	0·7	4·8	1·3 (0·7 to 2·5)	2·0	6·6	8·9	5·1 (3·7 to 7·0)
Total (95% confidence interval)	0·5 (0·2 to 1·0)	0·8 (0·4 to 1·6)	3·3 (2·2 to 4·9)	1·2 (0·9 to 1·6)	4·0 (3·2 to 5·1)	6·7 (5·3 to 8·4)	12·8 (10·6 to 15·4)	6·7 (5·9 to 7·6)
Women:								
<18·6	0·2	0·8	2·7	1·1 (0·6 to 2·1)	4·2	9·7	13·8	8·4 (6·7 to 10·5)
–20·1	0·0	1·3	0·5	0·5 (0·2 to 1·2)	5·8	6·6	11·9	7·2 (5·7 to 9·0)
–21·5	0·2	0·4	2·4	0·5 (0·2 to 1·3)	5·0	9·8	16·0	7·8 (6·2 to 9·7)
–23·2	0·7	0·7	3·7	1·1 (0·6 to 2·1)	4·4	6·9	10·3	5·8 (4·4 to 7·6)
>23·2	0·0	0·9	1·6	0·5 (0·2 to 1·2)	3·8	9·6	19·4	7·7 (6·2 to 9·6)
Total (95% confidence interval)	0·2 (0·1 to 0·5)	0·8 (0·4 to 1·5)	2·1 (1·3 to 3·4)	0·7 (0·5 to 1·0)	4·6 (3·8 to 5·5)	8·5 (7·1 to 10·1)	14·1 (11·8 to 16·8)	7·4 (6·7 to 8·2)

χ^2 analysis for trends non-significant for diabetes for both genders combined ($p=0·36$) and for genders separately; $\chi^2=11·51$, $p<0·0007$ for impaired glucose tolerance, genders combined.

TABLE V—*Crude prevalence (%) of diabetes and impaired glucose tolerance according to height (divided by quintiles) and age groups*

Height (m)	Diabetes				Impaired glucose tolerance			
	15-34 years	35-54 years	≥55 years	All ages (95% confidence interval)	15-34 years	35-54 years	≥55 years	All ages (95% confidence interval)
Men:								
<1·58	0·5	1·5	4·5	1·3 (0·6 to 2·6)	5·2	11·0	16·1	8·2 (6·3 to 10·6)
–1·63	0·6	1·3	2·9	1·4 (0·7 to 2·6)	3·7	8·6	18·9	9·3 (7·4 to 11·6)
–1·665	0·7	0·5	2·4	1·0 (0·4 to 2·2)	4·3	4·5	9·5	5·7 (4·1 to 7·8)
–1·71	0·6	0·0	3·9	1·1 (0·5 to 2·3)	3·3	6·3	10·5	5·8 (4·2 to 7·9)
>1·71	0·3	1·1	3·4	1·1 (0·5 to 2·2)	3·3	5·1	7·6	4·7 (3·4 to 6·5)
Total (95% confidence interval)	0·5 (0·2 to 1·0)	0·8 (0·4 to 1·6)	3·3 (2·2 to 4·9)	1·2 (0·9 to 1·6)	4·0 (3·2 to 5·1)	6·7 (5·3 to 8·4)	12·8 (10·6 to 15·4)	6·7 (5·9 to 7·6)
Women:								
<1·505	0·2	1·1	2·7	1·0 (0·5 to 1·9)	7·1	11·4	19·2	11·1 (9·2 to 13·3)
–1·545	0·4	1·0	3·1	1·0 (0·2 to 1·9)	5·0	7·5	14·8	7·5 (6·0 to 9·4)
–1·575	0·0	0·0	0·6	0·1 (0·0 to 0·7)	4·6	8·7	14·6	7·7 (6·1 to 9·7)
–1·615	0·2	0·7	2·8	0·7 (0·3 to 1·5)	3·5	8·9	8·5	5·7 (4·3 to 7·4)
>1·615	0·3	1·3	0·9	0·7 (0·3 to 1·5)	3·5	6·4	9·5	5·1 (3·9 to 6·7)
Total (95% confidence interval)	0·2 (0·1 to 0·5)	0·8 (0·4 to 1·5)	2·1 (1·3 to 3·4)	0·7 (0·5 to 1·0)	4·6 (3·8 to 5·5)	8·5 (7·1 to 10·1)	14·1 (11·8 to 16·8)	7·4 (6·7 to 8·2)

χ^2 analysis for trends non-significant for diabetes for sexes combined ($p=0·23$) or separately; $\chi^2=40·27$, $p<0·0001$ for trends for impaired glucose tolerance.

normal weight, and those with an index 25 kg/m² and over as overweight. Quintiles of body mass index and height were calculated for each sex separately.

Normal values of haemoglobin concentrations for men were 130 g/l or higher and for women 120 g/l or higher. Since, however, the haemoglobin concentrations in both sexes in rural Africa are about 10 g/l lower on average than the normal,[19] the distribution of haemoglobin in the survey populations was divided into three categories: <110, 110-129, and 130-170 g/l for men and <100, 100-119, and 120-160 g/l for women. Cholesterol values were divided into three bands: above 5·1 mmol/l (which is raised according to the European Atherosclerosis Society and the United States national cholesterol education programme[20,21]) below 3·3 mmol/l (2 SD below the mean for British subjects),[22] and 3·3-5·1 mmol/l.

ANALYSIS OF DATA

Data were analysed with the statistical package SPSS.[23] Analysis of variance (procedure, means) and χ^2 tests (procedure, cross tabulation) were used as appropriate. Multiple regression of measured variables against fasting and two hour post glucose load blood glucose concentrations was performed, as was stepwise logistic regression for determinants of diabetes and impaired glucose tolerance.

Results

Tables II and III show the distribution of body mass index, haemoglobin, and cholesterol concentrations. About half of the men and over a third of the women were underweight by the conventional criterion of body mass index <20 kg/m². Body mass index was less than 17·3 kg/m² and 17·6 kg/m² in 10% of men and women respectively, reflecting severe current undernutrition. Anaemia was common in the three villages in Morogoro region (values for both sexes together were 22·1% in Melela, 31·2% in Madizini, and 28·3% in Msolwa) and in Nyambori in Mara region (21·8%), suggesting more long term malnutrition. Mean serum cholesterol concentrations were also significantly lower in Morogoro region, reflecting the low intake of fat and animal protein in these villages. In Mdawi (Kilimanjaro region) the cholesterol concentrations were similar to those found in an Asian Muslim community in Dar es Salaam.[24]

Table IV shows the crude prevalences of diabetes and impaired glucose tolerance by age groups and fifths of body mass index. No consistent relation was found between rates of diabetes and body mass index (χ^2 analysis for trends, NS), although the prevalence of diabetes increased with age. Similarly, there was no relation between height and rate of diabetes (table V). For the lowest tenth of body mass index (<17·3 kg/m²

for men and $<17\cdot6$ kg/m^2 for women) prevalences of diabetes and impaired glucose tolerance were 1·5% (95% confidence interval 0·8% to 2·8%) and 9·0% (7·1% to 11·2%). For the highest tenth ($>23\cdot1$ kg/m^2 for men, $>24\cdot7$ kg/m^2 for women) the respective rates were 1·2% (0·6% to 2·2%) and 7·2% (5·6% to 9·2%). Impaired glucose tolerance prevalence was highest in the lowest fifths of height ($p<0\cdot05$ both sexes; $p<0\cdot05$ men only) and body mass index. However, when those overweight by conventional standards (body mass index ≥ 25 kg/m^2) were considered (n=545) the prevalence of diabetes was 1·9% and of impaired glucose tolerance 8·9%, rising to 6·0% and 20·0% respectively in the oldest age group. No correlation was seen between diabetes or impaired glucose tolerance and haemoglobin or cholesterol concentrations.

Tables VI and VII show mean blood glucose concentrations by age groups for each fifth of body mass index and height. Both fasting and two hour blood glucose concentrations were higher for the older than the younger age groups. However, no clear pattern was seen for fasting blood glucose concentrations with either body mass index or height, although two hour glucose concentrations tended to be higher in the lower than the upper fifths ($p<0\cdot05$).

Table VIII shows the determinants of the fasting and two hour blood glucose values. Not surprisingly, the two hour blood glucose was the main determinant of fasting blood glucose and vice versa. Age was the other major determinant of both glucose values. Height was strongly and negatively associated with two hour blood glucose but more weakly and positively with fasting glucose. Body mass index was, however, negatively correlated with both glucose values but this was the weakest of the associations. On stepwise logistic regression of determinants of diabetes and impaired glucose tolerance, including height, body mass index, age, and sex, only age was significantly associated with diabetes and impaired glucose tolerance.

TABLE VI—*Mean blood glucose concentrations (mmol/l) by body mass index, fifths, and age groups*

Body mass index (kg/m^2)	Fasting blood glucose				2 Hour blood glucose			
	15-34 years	35-54 years	≥55 years	All ages	15-34 years	35-54 years	≥55 years	All ages
Men:								
<18·2	4·2	4·1	4·2	4·2	4·7	4·5	5·7	4·9
-19·5	4·1	4·2	4·4	4·2	4·4	4·3	5·0	4·5
-20·6	4·1	4·2	4·4	4·2	4·3	4·3	4·8	4·4
-21·8	4·0	4·3	4·2	4·1	4·2	4·4	4·6	4·4
>21·9	4·0	4·1	4·4	4·1	4·1	4·2	4·8	4·3
Total	4·1	4·2	4·3	4·2	4·4	4·3	5·0	4·5
Women:								
<18·6	4·1	4·3	4·5	4·2	4·7	5·1	5·3	5·0
-20·1	4·0	4·2	4·3	4·1	4·7	4·8	5·1	4·8
-21·5	4·0	4·2	4·5	4·1	4·6	4·9	5·4	4·8
-23·2	4·0	4·1	4·5	4·1	4·6	4·7	5·2	4·7
>23·2	3·9	4·2	4·4	4·1	4·5	4·9	5·5	4·8
Total	4·0	4·2	4·4	4·1	4·6	4·9	5·3	4·8

TABLE VII—*Mean blood glucose concentrations (mmol/l) by height, fifths, and age groups*

Height (m)	Fasting blood glucose				2 Hour blood glucose			
	15-34 years	35-54 years	≥55 years	All ages	15-34 years	35-54 years	≥55 years	All ages
Men:								
<1·58	4·2	4·2	4·2	4·2	4·6	4·8	5·4	4·8
-1·63	4·0	4·2	4·3	4·2	4·4	4·5	5·0	4·6
-1·665	4·0	4·1	4·3	4·1	4·3	4·3	4·9	4·4
-1·71	4·1	4·1	4·5	4·2	4·3	4·1	4·9	4·4
>1·71	4·1	4·2	4·3	4·2	4·2	4·2	4·9	4·3
Total	4·1	4·2	4·3	4·2	4·4	4·3	5·0	4·5
Women:								
<1·505	4·0	4·2	4·4	4·2	4·7	5·1	5·5	5·0
-1·545	4·0	4·1	4·5	4·1	4·6	4·9	5·3	4·8
-1·575	4·0	4·2	4·4	4·1	4·6	4·9	5·1	4·8
-1·615	4·0	4·3	4·4	4·1	4·6	4·9	5·1	4·8
>1·615	4·0	4·2	4·5	4·1	4·6	4·7	5·1	4·7
Total	4·0	4·2	4·4	4·1	4·6	4·9	5·3	4·8

TABLE VIII—*Multiple stepwise regression analysis of blood glucose concentration, body mass index, height, age, and sex with fasting blood glucose and two hour blood glucose concentrations as dependent variable*

Variable	T value	Significance
Fasting blood glucose		
2 Hour blood glucose	45·09	<0·0001
Age	8·66	<0·0001
Sex	-3·03	0·0024
Height	3·70	0·0002
Body mass index	-2·52	0·0016
Constant	14·28	
Multiple R=0·478, R^2=0·228		
2 Hour blood glucose		
Fasting blood glucose	45·09	<0·0001
Height	-8·69	<0·0001
Age	8·19	<0·0001
Sex	5·73	<0·0001
Body mass index	-2·57	0·0101
Constant	9·27	
Multiple R=0·466, R^2=0·217		

Discussion

This study indicates that in Tanzania, at least, diabetes is not more common in the most undernourished members of the population, and that it is much less common than in well nourished Western populations.[25] Indeed, the Tanzanian rates of diabetes and impaired glucose tolerance may be overestimates as they were based on a single oral glucose tolerance test in a population unaccustomed to venepuncture.[26]

Rates of diabetes in the two lowest fifths of body mass index (both below 20 kg/m^2) and the lowest tenth were not significantly different from rates in the upper two fifths (1·3% and 0·8% *v* 1·0% and 0·9% respectively). There was a trend for those of lowest height, reflecting long term poor nutrition, to have higher rates of diabetes and impaired glucose tolerance. It should be emphasised that these trends reflected a tiny number of cases—2-3 per 1000 population—and the effect, even if statistically significant, is clinically trivial. Fasting blood glucose concentrations were not significantly different among fifths of body mass index and height, although two hour blood glucose values and impaired glucose tolerance rates, which are defined by two hour glucose values, were higher in the lowest fifths than in the higher fifths for both body mass index and height. This difference could either be a genuine effect or, more likely in the absence of any change in fasting blood glucose, reflect the fact that all subjects, irrespective of weight, were given 75 g glucose—that is, the lightest individuals received the highest glucose load per kilogram weight.[27] Short term malnutrition could also have contributed.[28] This also fits the observation that although there was a negative correlation between height and two hour blood glucose, a weak positive relation was seen for fasting glucose (table VIII).

IMPORTANCE OF UNDERNUTRITION

Evidence that undernutrition itself may be diabetogenic comes mainly from studies in animals,[28,29] adults,[30,31] and children[32,33] with protein energy malnutrition in whom functional abnormalities in insulin secretion and glucose tolerance have been shown. Recently, animal studies have suggested that severe maternal protein deficiency in pregnancy results in B cell damage and subsequent diabetes in the offspring[34]; others have suggested that low birth weight in humans predicts the development of impaired

glucose tolerance and non-insulin dependent diabetes mellitus in later life.[35] We have no evidence to support or refute these suggestions, although the overall low prevalence of non-insulin dependent diabetes and impaired glucose tolerance makes any important contribution unlikely. Overnutrition in later life, which increases insulin requirement, may uncover a defect in the secretory capacity of B cells, which could explain the current epidemic of non-insulin dependent diabetes mellitus in developing countries that have recently become more affluent.[36] This is a separate problem from that of malnutrition related diabetes mellitus, in which current as well as previous malnutrition is said to be a key component.

Postmortem studies in humans have also shown that severe kwashiorkor may be associated with structural changes in the pancreas.[37] It is uncertain, however, whether the functional and structural changes are sufficiently severe to lead to permanent diabetes. Our results suggest that they are not.

Undernutrition has also been suggested as a predisposing factor in tropical chronic calcific pancreatitis, possibly associated with recurrent attacks of gastroenteritis.[38] In Africa this disease has been described mainly in young adults in Uganda[38 39] and Nigeria.[40] If undernutrition were a key factor in the development of tropical chronic calcific pancreatitis it would be expected to be commoner than it is in other parts of Africa where malnutrition is more widespread.[41] Alcohol is almost certainly an important cause of chronic pancreatitis,[42] but does not account for calcific pancreatitis in the young.

ASSESSMENT OF NUTRITION

The populations we have studied could be said to be insufficiently malnourished or undernourished for an insufficient time to induce irreversible B cell failure. It is also possible that those who developed diabetes died undiagnosed. This possibility, while unlikely, cannot definitely be excluded. The assessment of undernutrition in adults is difficult. No single satisfactory measure exists, but body mass index is possibly the best available. About 40% of our population were underweight according to accepted body mass index standards. Some authorities in Africa have proposed that the lower limit of normal for body mass index in African subjects be reduced (T Johnson, personal communication). But there is no evidence on which to base this proposal, and studies have yet to be conducted which relate body mass index to mortality in Africans. We therefore believe that the low values for body mass index found in our study reflect undernourishment in a large proportion of the population. The low haemoglobin concentrations in four of the eight villages also point to poor nutritional state.

Assessment of chronic protein energy malnutrition is even more difficult. Many experts regard the ultimate height of populations as the most satisfactory index of chronic undernutrition during the period of growth and development. Genetic factors play a large part in the determination of height, but it is now widely accepted that improvement in the nutritional state of a nation's population increases the mean height of its citizens.[43 44] The mean height of the study population was significantly less than the mean height of a British population.[45] In addition, evidence of poor nutrition in children in several areas in which the studies were performed[16 17] also provided circumstantial evidence that the adults had grown up in an adverse nutritional environment. This is therefore strong evidence that both current and past undernutrition were common in the study populations. Importantly, there were also no differences between prevalence of diabetes and impaired glucose tolerance in the least advantaged and the most advantaged villages.

The proponents of malnutrition related diabetes have also suggested that while undernutrition may not lead to the development of diabetes it may increase the vulnerability of the pancreas to harmful environmental factors.[4] Cyanide from the consumption of inadequately processed bitter cassava has been proposed as a possible environmental toxin.[46] We found, however, that rates of diabetes in one village where the inhabitants were exposed to high levels of dietary cyanogenic glucosides from consumption of insufficiently processed cassava were not significantly different from rates in the seven other villages.[47]

Our studies of glucose tolerance in rural Tanzania have therefore failed to confirm the widely held hypothesis that undernutrition by itself or undernutrition and environmental toxins are a significant cause of diabetes in undernourished populations.

We thank the Ministry of Health, United Republic of Tanzania, for permission to carry out the study; the communities for their cooperation and participation; and the director general of Muhimbili Medical Centre, the British Council, and the British Diabetic Association for support. Thanks are also due to the staff of the department of biochemistry, Muhimbili Medical Centre, and department of medicine, University of Newcastle upon Tyne, for technical help.

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(Accepted 8 September 1992)

Decision to treat mild hypertension after assessment by ambulatory monitoring and World Health Organisation recommendations

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Abstrtact

***Objective*—To determine if one ambulatory blood pressure recording over 12 hours could detect those patients with mild hypertension who needed treatment according to the World Health Organisation-International Society of Hypertension (ISH) guidelines based on the casual measurement of diastolic blood pressure at successive visits to a clinic.**

***Design*—Comparison of decision to treat based on one ambulatory measurement over 12 hours and standard blood pressure measurements over six months in the same patients.**

***Setting*—Outpatient hypertension clinic.**

***Subjects*—130 men and women with diastolic blood pressure of 90-104 mm Hg at second visit to clinic.**

***Main outcome measures*—Blood pressure measurements over six months. Measurement from ambulatory monitoring. Decision to treat.**

***Results*—Of the 130 patients included, 108 were followed up over the six months. Treatment was started according to WHO-ISH criteria in 44 (13 at the third visit, 13 at the fourth, 18 at the fifth). According to the selected criteria for ambulatory blood pressure monitoring 41 patients would have been treated. Both methods agreed that the same 27 patients required treatment and the same 50 did not, but they did not agree in 31 patients. When calculated at the optimal diastolic blood pressure threshold determined by a receiver operating characteristic curve, the sensitivity, specificity, and positive predictive value of ambulatory blood pressure monitoring were 71% (95% confidence interval 57% to 84%), 82% (72% to 92%), and 66% (51% to 81%), respectively.**

***Conclusion*—If the WHO-ISH criteria are accepted as the standard for deciding to treat patients with mild hypertension the predictive value of one ambulatory blood pressure recording over 12 hours is too low to detect with confidence those patients who need treatment when managed according to these criteria.**

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BMJ 1992;**305**:1062-6

Introduction

In patients with mild hypertension the decision to treat is an important issue that has again come to the fore with the availability of several new techniques for measuring blood pressure. The rise in blood pressure induced by the act of measurement itself, referred to as the "white coat reaction," may lead to a false diagnosis of hypertension.[1] This is one reason why 40% of the patients included in large scale hypertension trials subsequently became normotensive with placebo.[2,3]

The guidelines from the World Health Organisation-International Society of Hypertension (ISH) take this into account and recommend multiple mesurements over six months before treatment is started.[4] The basis for such a policy is, firstly, that multiple measurements may be expected to give a closer estimation of the true blood pressure and, secondly, that repetition of measures over time may decrease the reaction induced by the visit to the doctor. This protocol is presently the gold standard for the decision to treat mild hypertension because epidemiological data, classification of hypertension, and evaluation of treatment efficacy are all based on clinic readings and because the white coat reaction has been shown to diminish considerably after four months.[2] This protocol, however, is tedious, risks losing patients to follow up, and the extent of its correct use by general practitioners is unknown. Consequently, it may prove to be less useful than expected when applied in reality.

Ambulatory blood pressure monitoring is a widely accepted method of measuring blood pressure, which avoids the white coat reaction[1] and becomes increasingly acceptable to patients as the equipment gets smaller. The value of a single ambulatory record in predicting the need for treatment has never been compared with that of a reference method. We assessed the predictive value of one 12 hour ambulatory blood pressure record for the decision to treat patients with mild hypertension by comparing it with the decision made during the six months' follow up in the clinic, according to the WHO-ISH protocol.[4]

Patients and methods

A total of 154 men and women who were referred to the hypertension clinic of the Broussais University Hospital for evaluation of their hypertension were screened for inclusion in the present study. The inclusion criteria were (*a*) casual diastolic blood