EPIDEMIOLOGY OF DIABETES IN SINGAPORE

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SUMMARY

A country-wide diabetic survey of the population (age 15 years and above) of Singapore shows that the prevalence of diabetes mellitus in Singapore is 1.99 percent. It is commoner in males (2.36 percent) than in females (1.64 percent). The prevalence of diabetes in the age group 15-39 years is only 0.40 percent and in the age group 40 years and older it is 5.08 percent.

The prevalence of diabetes in Indians (6.07 percent) is significantly higher than that in Malays (2.43 percent) and Chinese (1.55 percent). Indian

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Prof. J S Cheah University Dept of Medicine (I) Singapore General Hospital Outram Road Singapore 0316 diabetics have an insignificantly higher incidence of positive family of diabetes (12.7 percent) than Malays (10.9 percent) and Chinese (6.5 percent). Obesity was commoner in Malay diabetics (67.4 percent) than in Chinese diabetics (41.6 percent) and Indian diabetics (35.7 percent).

The survey shows that 40.4 percent of the diabetics are known while 59.6 percent of the diabetics are newly diagnosed. The majority of the diabetics are treated with oral hypoglycaemic drugs (71.5 percent) and only 4.8 percent are receiving insulin injections.

Among the female diabetics, 63.0 percent have 4 or more pregnancies and large babies at birth are recorded in 12.3 percent. In the newly diagnosed diabetics, 64.3 percent have no symptoms.

The complications of the diabetics are hypertension (26.8 percent), n'ephropathy (9.8 percent), retinopathy (8.5 percent), coronary heart disease (6.1 percent), skin infection (4.6 percent) and neuropathy (3.3 percent).

The high prevalence of diabetes among the Indians is likely to be due to a genetic predisposition coupled with an environmental factor (obesity), although this hypothesis is not conclusively demonstrated by the present study.

INTRODUCTION

Diabetes mellitus is a common disease in the adult

population; its high prevalence rate is realised when diabetic surveys are carried out in the population. Wilkerson and Krall ¹ reported the pioneering population diabetic survey in the town of Oxford, Massachusetts, U.S.A. Following this classic survey, diabetic surveys in the population are reported from many countries; these surveys show that the prevalence of diabetes differs in various countries and ethnic groups.

In Singapore, Ho² mentioned that diabetes was commoner in Indians in a group of hospital diabetic patients. In 28,765 young men (17 years of age) we found that the prevalence of diabetes was 0.4 percent.³ Further in a survey of 5,280 Government employees, we found that the prevalence of diabetes was 0.59 percent ^{4,5} Lee and Wong⁶ surveyed 9,883 residents in a built-up area of apartment blocks and reported that the prevalence of diabetes was 1.1 percent. The above studies were not representative of the population of Singapore; a country-wide population diabetic survey was carried out in 1975-76 and the results have been reported in detail. 7 This paper reviews some of the salient data of the epidemiology of diabetes in Singapore as was found in the countrywide population diabetic survey.

SURVEY POPULATION AND METHODS

Singapore is a tropical island city-state situated just north of the Equator $(1.4^{\circ} \text{ North and } 103.8^{\circ} \text{ East})$ and has an area of 584.3 sq km with a population of 2.25 millions at the time of the survey. It is a densely populated urbanised country and its population consists of Chinese (77.6 percent), Malays (13.8 percent), Indians (7.1 percent) and other ethnic groups (1.5 percent).

The field work of the population diabetic survey was carried out from April to September 1975 and the examinations and investigations of the diabetic patients were completed in early 1976. The details of the survey population and methods have been described. ⁷

The National Statistical Commission, employing a stratified two-stage sampling technique, selected 17,679 persons as representative of the adult population (15 years and above). The survey population represented about 1/80 of the census population. Of the selected survey population (17,679), 16,808 (95.1 percent) attended the field examination and in 16,497 (93.3 percent) a post

prandial urine sample was obtained for the screening for glycosuria with Labstix (Ames).

Those with glycosuria were asked to undergo an oral glucose tolerance test using a 50g glucose load. After an overnight fast, venous blood samples were drawn at fasting and at half hourly intervals for 2 hours after the oral 50g glucose load. The blood glucose was determined using the glucose oxidase method utilising the Technicon autoanalyser. Urine samples were collected at the same time as the blood samples and glycosuria was tested for with Labstix.

The oral glucose tolerance test was defined as normal when the fasting and 2-hour blood glucose were 120 mg/100 ml or less, the peak blood glucose was 180 mg/100 ml or less and glycosuria was absent in all urine specimens. Renal glycosuria was present when the blood glucose levels were normal but glycosuria was present. The diagnosis of diabetes was made when the 2-hour blood glucose level was 140 mg/100 ml or greater. 8 Alimentary glycosuria (lag storage) was present when the fasting and 2-hour blood glucose levels were normal but the peak blood glucose exceeded 180 mg/100 ml and glycosuria was present. Those with a 2-hour blood glucose in excess of 120/100ml but below 140/100 ml were described as miscellaneous (or borderline diabetes).

In all the respondents undergoing the oral glucose tolerance test a detailed history and physical examination were recorded; investigations performed included blood urea, presence of proteinuria, chest X-Ray, electrocardiogram and fasting serum cholesterol.

Normal weight was defined as $\pm 10\%$ of the ideal weight. Hypertension was defined as resting blood pressure of 160/90 mmHg or greater. Nephropathy was defined as presence of proteinuria (more than 10 mg/100 ml) and/or an elevated blood urea (more than 40 mg/100 ml) and other causes of renal dysfunction were excluded. Coronary heart disease was defined as the presence of angina pectoris and/or myocardial infarction and/or the presence of electrocardiographic changes of myocardial ischaemia.Diabetic neuropathy was present when there was impaired sensation over the limbs and/or impaired tendon reflexes and other causes of these had been excluded and in some cases electromyographic confirmation was obtained.

Ethnic		Male			Female			All Cases	
Groups	No. screened	No. with glycosuria	% with glycosuria	No. screened	No. with glycosuria	% with glycosuria	No. screened	No. with glycosuria	% with glycosuria
Chinese	6214	214	3.44	6598	134	2.03	12812	348	2.72
Malays	1073	46	4.29	1195	31	2.59	2268	77	3.40
Indians	690	67	9.71	479	17	3.55	1169	84	7.19
Others	123	5	4.07	125	3	2.40	248	8	3.23

TABLE IV PREVALENCE OF GLYCOSURIA ACCORDING TO SEX AND ETHNIC GROUPS

that in Malays (2.43 percent; $x^2 = 29.07$, p < 0.0005) and Chinese (1.55 percent; $x^2 = 116.42$, p < 0.0005).

Of the 329 cases of diabetes, 133 (40.4 percent) were known diabetics while 196 (59.6 percent) were newly diagnosed (Table VII).

Height and weight were specified in 314 (95.0 percent) of the 329 cases of diabetes; their weight distribution is shown in Table VIII. 43.3 percent were of normal weight while 12.4 percent were underweight and 44.3 percent were overweight. Obesity is highest in the Malay diabetics (67.4 percent), followed by the Chinese diabetics (41.6 percent) and Indian diabetics (35.7 percent).

The occupational groups in the 329 cases of diabetes are shown in Table IX. Housewives form

the largest group (48.3 percent) while there were 12.3 percent in the sale services and 17.0 percent in the production and transport group.

A family (grandparents, parents, brothers, sisters or children) history of diabetes was present in 29 cases (8.8 percent) and absent in 300 cases (91.2 percent). The presence of a positive family history of diabetes among the ethnic groups is shown in Table X. Indians have a slightly higher positive family history (12.7 percent) followed by Malays (10.9 percent) and Chinese (6.5 percent) but the differences are not significant.

Of the 138 female diabetics only 13 (9.4 percent) did not conceive while 56 (40.6 percent) had more than 5 pregnancies and 87 (63.0 percent) had 4 or more pregnancies (Table XI). In 106 pregnancies, the birth weight of the babies were specified; of

			TABLE V					
PREVALENCE	OF	DIABETES	ACCORDING	то	AGE	GROUPS	AND	SEX

Age		Male			Female			Total	
Groups	No. screened	No. with Diabetes	% with Diabetes	No. screened	No. with Diabetes	% with screened	No. screened	No. with Diabetes	% with Diabetes
15-19	1556	1	0.06	1605	0	0.00	3161	1	0.03
20-24	1327	0	0.00	1388	1	0.07	2715	1	0.04
25-29	991	4	0.40	1096	1	0.09	2087	5	0.24
30-34	680	5	0.74	743	6	0.81	1423	11	0.77
35-39	731	13	1.78	747	12	1.61	1478	25	1.69
40-44	668	23	3.44	652	11	1.69	1320	34	2.58
45-49	586	41	7.00	540	24	4.44	1126	65	5.77
50-54	467	28	6.00	466	17	3.65	933	45	4.82
55-59	322	22	6.83	360	26	7.22	682	48	7.04
60 +	772	54	6.99	800	40	5.00	1572	94	5.98
Total	8100	191	2.36	8397	138	1.64	16497	329	1.99

		TEST		
Rest	alt	No.	%	
Norm	nal	65	11.2	
Abnor	mal	517	88.8	
Tot	al	582	100.0	

TABLE I RESULTS OF THE ORAL GLUCOSE TOLERANCE TEST

TABLE II THE CAUSES OF ABNORMAL GLUCOSE TOLERANCE TESTS

Diagnosis	No.	%
Diabetes Mellitus	329	63.7
Renal Glycosuria	128	24.7
Alimentary Glycosuria	49	9.5
Miscellaneous	11	2.1
All Cases	517	100.0

RESULTS

Of the 17,679 persons aged 15 years and older selected for the survey, 16,497 (93.3 percent) had their urine tested for glycosuria. 590 (3.6 percent) were found to have glycosuria with Labstix in the field examination; of these 582 cases (98.6 percent) responded for an oral glucose tolerance test while 8 cases (1.4 percent) did not respond.

The results of the oral glucose tolerance test

are shown in Tables I and II. It was normal in 65 cases (11.2 percent) and abnormal in 517 cases (88.8 percent; Table II). The causes of the abnormal glucose tolerance tests in the 517 cases are shown in Table II; diabetes mellitus was the commonest cause (63.7 percent), followed by renal glycosuria (24.7 percent) and alimentary glycosuria (9.5 percent).

Thus after the oral glucose tolerance tests, glycosuria was confirmed in 517 of the 16,497 persons surveyed; the prevalence of glycosuria was 3.1 percent. The prevalence of glycosuria according to age groups and sex is shown in Table III while Table IV shows its distribution according to sex and ethnic groups.

Diabetes was the main cause of glycosuria in the survey, there were 329 cases (63.7 percent) out of the 517 cases of glycosuria (Table II). The prevalence of diabetes in the population was 1.99 percent (Table V); it is significantly higher in males (2.36 percent) than in females (1.64 percent; $x^2 = 13.84$, p < 0.0005). The prevalence of diabetes increase with age; in the age group 15-39 years it was only 0.40 percent while in the age group 40 years and older it was 5.08 percent (Table V). The prevalence of diabetes was highest in the age group 55-59 years (7.04 percent) and lowest in the age group 15-19 years (0.03 percent; Table V).

Table VI shows the prevalence of diabetes among the ethnic groups. The prevalence of diabetes in Indians (6.07 percent) is significantly higher than

Age Groups	Male			Female			All Cases		
	No. screened	No. with glycosuria	% with glycosuria	No. screened	No. with glycosuria	% with glycosuria	No. screened	No. with _, glycosuria	% with glycosuriz
15-19	1556	8	0.51	1605	11	0.69	3161	19	0.60
20-24	1327	16	1.21	1388	5	0.36	2715	21	0.77
25-29	991	23	2.32	1096	10	0.91	2087	33	1.58
30-34	680	18	2.65	743	10	1.35	1423	28	1.97
35-39	731	23	3.15	747	15	2.01	1478	38	2.57
40-44	668	42	6.29	652	12	1.84	1320	54	4.09
45-49	586	60	10.24	540	28	5.19	1126	88	7.82
50-54	467	45	0.64	466	19	4.08	933	64	6.86
55-59	322	26	8.07	360	28	7.78	682	54	7.92
60 +	772	71	9.20	800	47	5.88	1572	118	7.51
Total	8100	332	4.10	8397	185	2.20	16497	517	3.13

TABLE III PREVALENCE OF GLYCOSURIA ACCORDING TO AGE GROUPS AND SEX.

Ethnic	Male				Female			Total		
Groups	No. screened	No. with diabetes	% with diabetes	No. screened	No. with diabetes	% with diabetes	No. screened	No. with diabetes	% with diabetes	
Chinese	6214	103	1.66	6598	95	1.44	12812	198	1.55	
Malays	1073	29	2.70	1195	26	2.18	2268	55	2.43	
Indians	690	56	8.12	479	15	3.13	1169	71	6.07	
Others	123	3	2.44	125	2	1.60	248	5	2.02	
Total	8100	191	2.36	8397	138	1.64	16497	329	1.99	

 TABLE VI

 PREVALENCE OF DIABETES IN THE VARIOUS ETHNIC GROUPS

TABLE VII NUMBER OF KNOWN AND NEWLY DIAGNOSED CASES OF DIABETES IN THE SURVEY

Туре	Males	Females	Males & Females
Known New	91 100	42 96	133 (40.4%) 196 (59.6%)
All Cases	191	138	329 (100%)

TABLE VIII WEIGHT DISTRIBUTION AMONG THE ETHNIC GROUPS IN 314 CASES OF DIABETES

Ethnic Group	Under No.	weight %	Norma No.	l Weight %	Overv No.	veight %	Total
Chinese	22	11.6	89	46.8	79	41.6	190
Indians	11	15.7	34	48.6	25	35.7	70
Malays	5	10.2	11	22.4	33	67.4	49
Others	1	20.0	2	40.0	2	40.0	5
Total	39	12.4	136	43.3	139	44.3	314

these 13 (12.3 percent) recorded birth weights of 10 lbs or greater while 107 (87.7 percent) had birth weights of less than 10 lbs.

The symptomatology in the 196 cases of newly diagnosed diabetics in the survey is shown in Table XII. 126 (64.3 percent) were symptomless while 70 (35.7 percent) had various symptoms. Polyuria, thirst and weight loss were the 3 commonest symptoms. 38 (54.3 percent) of the 70 diabetics with symptoms could not date the onset of their symptoms while 21 (45.7 percent) had symptoms of less than a year in duration (Table XIII).

In the survey there were 133 cases of known

TABLE IX OCCUPATIONAL GROUPS IN 329 CASES OF DIABETES

Occupational Groups	No.	%
Professional	9	2.7
Administrative	2	0.6
Clerical	12	3.6
Sales	41	12.3
Service	18	5.5
Agriculture	1	0.3
Production, transport	56	17.0
Housewives	159	48.3
Others	31	9.7
Total	329	100.0

TABLE X PRESENCE OF FAMILY HISTORY IN 329 CASES OF DIABETES

Ethnic Group	Positive		Nega	tive	Total
	No.	%	No.	%	
Chinese	13	6.5	185	93.4	198
Malays	6	10.9	49	89.1	55
Indians	9	12.7	62	87.3	71
Others	1	20.0	4	80.0	5
Total	29	8.8	300	91.2	329

diabetics; these were mainly treated by general practitioners (49 cases or 36.8 percent) or in Government Outpatients' Clinics (48 cases or 36.1 percent; Table XIV). 62 (46.6 percent) knew what treatment they were receiving while 71 (53.4 percent) did not know the exact nature of their medication except that they were taking oral

NUMBER OF PREGNANCIES IN THE 138 CASES OF FEMALE DIABETICS						
No. of Pregnancies	No. of Diabetics	%				
0	13	9.4				

8

10

11

21

10

56

9 138 5.8

7.2

8.0

15.2

7.2

40.6

6.6

100.0

1

2

3

4

5

5 and above

Unrecorded

All Cases

TABLE XI

TABLE XII
SYMPTOMATOLOGY IN 196 CASES OF NEWLY
DIAGNOSED DIABETES

Symptom	Nos.	%
None	126	64.3
Polyuria	35	17.9
Thirst	34	17.6
Weight loss	24	12.2
Impaired vision	12	6.1
Pruritus	8	4.1
Angina	8	4.1
Paresthesia	5	2.6
Others	2	1.0

TABLE XIII **DURATION OF SYMPTOMS IN 70 CASES OF NEWLY** DIAGNOSED DIABETICS

Duration of symptoms	Nos.	%	
Weeks	3	4.3	
One to less than 6 months	15	21.4	
6 months to less than a year	3	4.3	
One year to less than 5 years	9	12.9	
10 years or more	2	2.9	
Not known	38	54.3	
All cases	70	100.0	

tablets. The type of medication in the 62 cases who knew their exact medication is shown in Table XV. It is noteworthy that only 3 cases (4.8 percent) were receiving insulin injections while the majority (71.5 percent) were being treated with oral hypoglycaemic tablets.

The complications of the diabetics in the survey

TABLE XIV PLACE OF TREATMENT IN 133 KNOWN DIABETICS

Treatment by	Nos.	%
Self	6	4.5
General Practitioner	49	36.8
Company Doctor	4	3.0
Govt. Outpatients' Clinic	48	36.1
Hospital	3	2.3
Others	23	17.3
Total	133	100.0

TABLE XV **TYPE OF TREATMENT IN 62 KNOWN DIABETICS** WHO KNEW WHAT TREATMENT THEY WERE ON

Type of Treatment	Nos. %	
Herbs	6	9.0
Diet only	10	15.0
Tolbutamide	17	25.3
Chlorpropamide	24	35.8
Glibenclamide	6	9.0
Metformin	1	1.4
Insulin	3	4.5
Total	67*	100.0

This number is greater than 62 as some cases were on more than one type of treatment

are shown in Table XVI. Hypertension was the commonest complication and was present in 88 cases (26.8 percent); it was slightly commoner (27.0 percent) in the new diabetics than in the known diabetics (26.3 percent). Nephropathy was present in 11.3 percent of the known diabetics and in 8.7 percent of the new diabetics. Retinopathy was present in 10.5 percent of the known diabetics and in 7.1 percent of the new diabetics. Coronary heart disease was present in 6.0 percent of the known and new diabetics. Skin infection was commoner in new diabetics (5.6 percent) than in the known diabetics (3.0 percent) while peripheral neuropathy was commoner in known diabetics (5.3 percent) than in the new diabetics (2.0 percent).

In 11 cases (2.1 percent) of the 517 cases with abnormal glucose tolerance tests, the 2-hour blood glucose level was greater than 120 mg/100 ml but less than 140 mg/100 ml: these were classified as miscellaneous or borderline diabetes (Table II).

Complications	Known Diabetes		New Diabetes		All Cases	
	Number	% of 133 cases	Number	% of 196 cases	Number	% of 329 cases
Hypertension	35	26.3	53	27.0	88	26.8
Nephropathy	15	11.3	17	8.7	32	9.8
Retinopathy	14	10.5	14	7.1	28	8.5
Coronary Heart Disease	8	6.0	12	6.1	20	6.1
Skin Infection	4	3.0	11	5.6	15	4.6
Neuropathy	7	5.3	4	2.0	11	3.3
Others	3	2.3	5	2.6	8	2.4

COMPLICATION RATES IN 133 CASES OF KNOWN DIABETES AND 196 CASES OF NEWLY DISCOVERED DIABETES

DISCUSSION

In the present country-wide population survey which is statistically representative of the adult population (aged 15 years and above) of Singapore, the prevalence of glycosuria is 3.1 percent. The prevalence of glycosuria in Singapore (3.1 percent) in the present survey is comparable to other population surveys. Wilkerson and Krall¹ in their classic survey of Oxford, Massachusetts, U.S.A found that 4.7 percent of the population have glycosuria; subsequent surveys in many other countries show that the prevalence of glycosuria varies from 1.6 to 5.3 percent. 9,10,11 In the present survey, the prevalence of glycosuria is significantly higher in Indians (7.2 percent) than in Malays (3.4 percent) and Chinese (2.7 percent); this has previously been reported by us. $\overline{4,5}$

The present survey shows that the prevalence of diabetes in the adult population (aged 15 years and older) in Singapore is 1.99 percent. In an earlier survey of 5,280 Government employees we found that the prevalence of diabetes was 0.59 percent, ⁵ while in a survey of 9,883 residents in a built-up area of apartment blocks, the prevalence of diabetes was 1.10 percent; ⁶ these 2 surveys are not representative of the population. It illustrates that for a diabetic survey of the population, a statistically valid sampling of the population is vital. The prevalence of diabetes of 1.99 percent in Singapore in the present survey resembles that found in the pioneering survey of Wilkerson and Krall. ¹ Subsequent surveys have shown that the prevalence of diabetes in the population in various countries varies from 0.24 to 5.5 percent.⁸

In the present survey the highest prevalence of diabetes (7.04 percent) is found in the age group 50-54 years; in a previous study in a group of Government employees the highest prevalence (5.10 percent) is found in the age group 50-59 years. ^{4,5} These findings are in accordance with other surveys in which the highest prevalence of diabetes is found in the age group 50-70 years. ^{10,11}

Among Caucasians, diabetes is commoner in females than males.^{10,11} In the present survey diabetes is found to be commoner in males (2.36 percent) than in females (1.64 percent); this confirms earlier reports.^{2,12,5}

The present survey shows that 40.4 percent of the diabetics are known cases while 59.6 percent are newly diagnosed i.e. out of 100 known diabetics there are 147 cases in the population that are diabetic but are not aware of their disease. It is interesting to note that whatever method is used for a diabetic survey and whatever diagnostic criteria are used the proportion of newly discovered cases is about the same as the number of known cases in the population. ¹⁰

The occupational groups of the diabetics in the present survey show no distinct pattern; most of the female diabetics are housewives. It is interesting to note that 64.3 percent of the newly discovered diabetics have no symptoms; the symptomatology of those with symptoms resembles other series. ¹⁰

Of the known diabetics in the survey, only 4.8 percent are receiving insulin injections while the majority (71.5 percent) are being treated with oral hypoglycaemic drugs. This indicates the great

reluctance of our patients to receive daily insulin injections.

In the present survey, 63.0 percent of the female diabetics have 4 or more pregnancies; it appears that the fertility rate is not affected by the diabetes. Among the 106 pregnancies, 13 (12.3 percent) have babies weighing 10 lbs or greater; the tendency for diabetic mothers to give birth to large babies is well known. ^{10,11}

Hypertension is the commonest complication (26.8 percent) of the diabetics in the present survey; this compares with 31.5 percent among the Chinese diabetics in Hong Kong.¹³ In our survey, nephropathy and retinopathy are present in 9.8 percent and 8.5 percent; this compares with 6.6 percent and 13.1 percent in Hong Kong. Our diabetics have slighty commoner coronary heart disease (6.1 percent) than those in Hong Kong (5.0 percent) but less neuropathy (3.3 percent) than those in Hong Kong (13.1 percent).¹³

Singapore is an island city-state with a multiracial population comprising Chinese (77.6 percent), Malays (13.8 percent), Indians (7.1 percent) and other ethnic groups (1.5 percent). It is an ideal state for studying the prevalence of diabetes of different ethnic groups under similar geographical conditions. The present survey shows that the prevalence of diabetes is significantly higher in Indians (6.07 percent) than in Malays (2.43 percent) and Chinese (1.55 percent). This confirms earlier studies based on hospital patients ² and a group of Government employees. ^{4,5}

A positive family history of diabetes is found in 8.8 percent in the present survey; it is not significantly higher in Indian diabetics (12.7 percent) than in Malay diabetics (10.9 percent) and Chinese diabetics (6.5 percent). Among the Nauruans, with a high prevalence of diabetes (34.4 percent), a positive family history of diabetes in 72 percent of the diabetics has been found. ¹⁴

Obesity is found in 44.3 percent of the diabetics in the present survey; among Caucasians about 50 percent of the diabetics are overweight. ¹¹ In spite of the high prevalence of diabetes among the Indians (6.07 percent), obesity in the Indian diabetics (35.7 percent) is lower than that in Chinese diabetics (41.6 percent) and Malay diabetics (67.4 percent). In India, the prevalence of diabetes is 1.8 percent. ¹⁵ When Indians migrate from India and settle elswhere, the prevalence of diabetes increases sharply. ¹⁶ Thus in the present survey, the prevalence of diabetes in Indians is 6.07 percent. In neighbouring Malaysia, the prevalence of diabetes in a small group of Indians in Kuala Lumpur is 4.2 percent. ¹⁷ In South Africa, diabetes is 8 times commoner in Indians than in Africans. ¹⁸

It is likely that the Indians have a genetic predisposition to diabetes and when they settle outside India an environmental factor in the form of abundant food giving rise to obesity unmasks the genetic predisposition. ¹⁶ This has been shown to be the likely causes of the high prevalence of diabetes among the Nauruans ¹⁴ and the Pima Indians. ¹⁹ Although we have not shown this conclusively in the present study, it is a probable theory and further work remains to be done.

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