Diabetes and Ischemic Heart Disease among Yemenite Immigrants in Israel

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Abstract

Background: The pattern of diabetes and ischemic heart disease among emigrants from pre-industrialized societies to more developed countries may be explained by both genetic and environmental factors.

Objectives: To describe and interpret the pattern of diabetes and ischemic heart disease among Yemenite immigrants in Israel and their second-generation offspring.

Methods: Medical record charts of adult Yemenites were surveyed in a primary care health center, and the data were compared with prevalence rates derived from a non-Yemenite population.

Results: There was a marked excess of non-insulin dependent diabetes mellitus among Yemenite immigrants over 45 years of age, but not of hypertension or ischemic heart disease. Yemenites with diabetes were far less likely to develop ischemic heart disease than non-Yemenites with diabetes (odds ratio for non-Yemenites compared with Yemenites, 3.5; confidence interval $1.54 < OR < 7.77$).

Conclusions: There was less of an association between diabetes and ischemic heart disease among Yemenites. This finding requires further investigation of the relative roles of genetic and environmental factors.

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The Yemenite Jews in Israel are an example of the phenomenon of an immigrant group that initially has very low rates of diabetes mellitus but quickly develops the disease at rates even higher than the indigenous population [1]. Other examples include Native Americans (Indians) [2], and South Asians in Britain [3]. In contrast, ischemic heart disease among Yemenites did not seem to follow the same pattern, leading to speculation that there was a genetic cardioprotective factor involved [4,5].

Type II diabetes is an expression of an insulin resistance syndrome associated with central obesity and IHD in most

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OR = odds ratio

IHD = ischemic heart disease

groups, immigrants and indigenous, but not in all, notably the Afro-Caribbeans in Britain [6]. The literature is divided as to the question of whether Yemenite diabetes is associated with IHD. Brunner's group [7] has maintained consistently over many years that there is a relative absence of vascular disease in Yemenites with diabetes, whereas Cohen's studies suggest the opposite [8].

Both genetic [4] and environmental factors [9,10] have been proposed to explain the high rates of diabetes among immigrants, but whereas a "thrifty gene" hypothesis predicts low rates of IHD, environmental factors alone would predict high rates of IHD [11]. In order to elucidate this issue, we report here on a controlled community-based study of the prevalence of IHD among Yemenites who have already developed diabetes mellitus.

Materials and Methods

The Yemenite Jewish community migrated to Israel en bloc between 1949 and 1951. The largest single concentration of these immigrants settled in Rosh Ha'ayin, where 15,000 of them and their descendents live to this day. The local primary care health center serves 90% of the Yemenite population of the town, and Yemenite patients account for 90% of the clinic's patient population. A full description of this population has been provided in detail elsewhere [12].

We reviewed the medical charts for the presence of IHD and hypertension and for serum cholesterol levels among patients with and without diabetes mellitus. Yemenite origin of the patients whose charts were reviewed was confirmed by the characteristic names used by this ethnic group and by reference to the family tree in the charts.

A formal random stratified procedure was used to provide a 1 in 10 sample out of a total clinic population of about 10,000 over age 20. Because a lower prevalence of diabetes was expected in the younger age groups, 500 charts of patients aged 20–44 years were included in the sample, and 250 each for the age groups 45–64 and over 64 years. Because no diabetes was found in the 20–24 years age group ($n = 59$), they were omitted from the analysis.

A parallel chart review was performed at a clinic in a neighboring suburb with a population of mainly European

Table 1. Age and gender structure of the population samples: Yemenite/Ashkenazi

	25–34 yr	35–44 yr	45–54 yr	55–64 yr	65–74 yr	75 + yr	Total
Male	99/65	120/88	67/184	52/108	58/78	52/57	448/580
Female	105/105	117/137	65/221	64/109	70/108	72/87	493/767
Total	204/170	237/225	132/405	116/217	128/186	124/144	941/1347

Table 2. Prevalence rates (%) for diabetes mellitus, hypertension, and ischemic heart disease in Yemenites (Y) and non-Yemenites (NY), by age group and gender

Age	25–34		35–44		45–54		55–64		65–74		75 +	
	Y	NY	Y	NY	Y	NY	Y	NY	Y	NY	Y	NY
Diabetes												
Male	2.0	0	0.8	1.1	6.0	2.7	19.2	9.3*	36.2	15.4**	25	8.8***
Female	1.9	0	0.9	0.7	10.8	1.8**	17.2	6.4*	30	6.5***	20.8	11.5*
Hypertension												
Male	1.0	0	4.2	2.2	14.9	12.0	23.1	18.5	32.8	28.2	23.1	28.1
Female	1.0	0	0	2.2	3.1	6.3	14.1	21.1	31.4	35.2	27.8	40.2
Ischemic heart disease												
Male	0	0	0.8	0	1.5	1.6	15.4	8.3	13.8	16.7	21.2	12.3
Female	0	0	0	0	0	0	3.1	2.8	5.7	16.7*	16.7	18.4

* $P<0.05$, difference between Yemenites and non-Yemenites by chi-square
** $P<0.01$
*** $P<0.0001$

(Ashkenazi) extraction. In this clinic, with an Ashkenazi population of 1,869 patients (1,347 over the age of 25), all charts of patients under surveillance for diabetes, hypertension and IHD are filed separately, so that we had access to complete data [Table 1].

We could not compare cholesterol levels between the two populations because the non-Yemenite clinic charts and laboratory data records were not adequately detailed in this respect. Neither could we analyze body mass index in either population because weight and especially height were not fully recorded or kept up to date [13].

Diabetes was defined by documentation of the diagnosis with two measurements of fasting blood glucose above 140 mg/dl (7.8 mmol/L) or 2 hour postprandial blood glucose above 200 mg/dl (11.1 mmol/L). Diabetic patients with a juvenile age at onset were designated as insulin dependent, while patients with late-onset diabetes were designated non-insulin dependent even if they were controlled on insulin. Hypertension was defined by three blood pressure recordings above 140/90, or by documentation of the diagnosis and the regular prescription of anti-hypertensive medication. IHD was defined by documentation of angina pectoris, myocardial infarction, coronary angioplasty, or by diagnostic findings on ergometry, scintigraphy or cardiac catheterization.

Data collection and analysis
All the charts were examined by a physician specially trained in the methodology of the study. Data were recorded of age, gender, diagnoses, and the most recent serum cholesterol level. Patients on lipid-lowering drugs were excluded. Prevalence rates by gender and age groups for diabetes, IHD and hypertension in Rosh Ha'ayin are compared with the rates derived from the non-Yemenite

clinic. Logistic regression analysis was used to correct for the possible confounding effects of gender, age and hypertension on the relation between diabetes and IHD in the two populations.

Results
There was a marked excess of diabetes among the Yemenites, the prevalence rising from 2% in the 25–44 year age group to 14% in the 45–64 group, and 30.2% in those over 65. The ratio of IDDM to NIDDM among Yemenites was 1:10.4, and the male to female ratio was 1:1. Detailed comparison with the non-Yemenite population shows an excess prevalence among the Yemenites in the immigrant generations, but not in the Israeli-born generation. The prevalence of hypertension and IHD were similar in the Yemenite and non-Yemenite populations.

Yemenites with diabetes were 3.5 times less likely to have IHD than non-Yemenites with diabetes (95% confidence interval $1.54<OR<7.77$), after taking into account age, gender and co-existing hypertension. The overall model fit for the logistic regression analysis was significant ($P=0.0004$), indicating that the model provided an adequate fit to the data. The lack of fit test was not significant ($P=0.203$), indicating that we were probably not missing any other important predictors in the model. Yemenite women with diabetes were more likely to develop IHD than Yemenite men with diabetes ($OR=2.5$, $P=0.0257$) [Table 3].

Yemenite men aged ≥45 with diabetes did not have significantly higher cholesterol levels than Yemenite men without diabetes (222±52 mg/dl, n=36 vs. 219±44 mg/dl, n=116) but among women the difference was significant:

IDDM = insulin-dependent diabetes mellitus
NIDDM = non-insulin-dependent diabetes mellitus

with diabetes, mean cholesterol 253±47.9 mg/dl (n=48), without diabetes 228±45.9 (n=156); P=0.001. In the younger age group, below 45 years of age, there were too few eligible patients with diabetes to allow statistical analysis of differences in cholesterol levels between subjects with and without diabetes, but the group mean cholesterol levels were 201±42 mg/dl for men (n=45) and 186±43 mg/dl for women (n=72).

IHD in Yemenites was not significantly associated with hypertension in men or women, nor were cholesterol levels significantly raised in IHD.

Discussion

Our results show a remarkably high rate of diabetes among Yemenite Jewish immigrants in Israel, but with less hypertension and IHD. Estimates of the prevalence of diabetes among Yemenite Jews in Israel have been made at intervals during the 45 years since the Yemenite mass immigration. These show that diabetes was nearly non-existent during the first 10 years after immigration, with a prevalence of 0.25% in those aged over 30 years, rising to 2.9% 30 years after immigration, and to 4.6% 40 years after immigration1 [1]. Another study at the 30 year stage found 7.1% among male civil servants [13]. At first it was the men who were affected, with the women following, reaching equity by the 1990s. Diabetes in Yemenite women has been found to be associated with overweight and obesity and an atherogenic lipoprotein pattern, but not in men [8]. Although we do not have data on body weight in our subjects, we can confirm that mean cholesterol was higher for women than men in the older age group, and a male–female equivalence in diabetes prevalence. The process of increasing rates of diabetes has thus reached unprecedented heights. We sampled twice as many of the younger group, realizing that the prevalence rates would be lower than in the older groups. Time will tell whether the second generation will develop high rates of diabetes as they grow older.

There are very little systematic and reliable data on diabetes morbidity for the general Israeli population. The best available evidence suggests prevalence rates in the range of 3% to 6.7% in those over the age of 20 [15]. One regional study gives a figure of 6.2% over the age of 30 among European Israelis in 1989, 5.4% among Middle-Eastern Israelis, and up to 7.5% among North African Israelis [16]. These Israeli rates are slightly higher than rates in other western countries; for example, 4% among British whites [17] and 4.6% in Central America [18]. However, certain ethnic groups show very high rates, such as the migrant Asians (19%) and Afro-Caribbeans (14.6%) in Britain [17], and the Native Americans [2] and immigrant Mexicans [19] in North America.

The absence of an excess of IHD among diabetic Yemenite immigrants, as confirmed by our findings, suggests that in this group, as in the Afro-Caribbeans, there may be special mechanisms involved, presumably genetically determined, but their nature is as yet obscure. We can,

Table 3. Ischemic heart disease among Yemenites and non-Yemenites with diabetes, and logistic regression analysis to correct for age, gender and hypertension

	Yemenites	Non-Yemenites	Total
No IHD	101	42	143
IHD	16	21	37
Total	117	63	180

Two-tailed Fisher's exact test P=0.0033

Logistic regression:

Variable	P chi-square	Odds ratio	95% C.I.
DM/IHD	0.0016		
Ethnicity	0.0027	3.453 (non-Yemenite: Yemenite)	1.54–7.77
Hypertension	0.3076	1.511	
Age	0.0084	0.949 (per year)	
Gender	0.0257	0.399 (M:F)	

however, confirm the known relatively increased susceptibility of women with diabetes to develop IHD as compared with men (M:F odds ratio 0.4, P<0.03), and we note that women, but not men, with diabetes had higher cholesterol levels than those without diabetes. Others have noted the propensity to obesity among Yemenite women, but not men, with diabetes [1]. These changes may be related to the more domesticated lifestyle of Yemenite women as compared to men in Israel, with differences in physical activity and diet.

Are our observations consistent with a genetic or an environmental hypothesis? Whereas both hypotheses predict high rates of diabetes, they differ in their predictions of the prevalence of IHD, with the genetic hypothesis predicting low rates and the environmental hypothesis predicting high rates. Our data, then, seem to fit a genetic explanation better, since Yemenites with diabetes retain their resistance to IHD. The second generation should inherit the same susceptibilities as the first generation. If this is the case, those under 45 years might also be expected to develop high rates of diabetes over the next 10–20 years even though they were born and bred in Israel. Our efforts are now directed towards identifying the molecular basis of the susceptibility to diabetes and the resistance to IHD among Yemenites [20].

Limitations of the study

The data are derived from a chart audit at a primary medical care facility in the community. Morbidity data collected in primary care are known to be reliable and valid at the level of major diagnoses [21]; however, there may be under-diagnosis of diabetes and hypertension, which are asymptomatic conditions at first, so that the figures derived for these conditions should be regarded as conservative estimates. IHD, as defined in this study, refers to a clinically symptomatic and significant syndrome that is unlikely to go unrecorded. Similarly, there is a limit to which clinical records may be relied upon for risk factor analysis, since such items as smoking, body weight and height, and

cholesterol levels are recorded irregularly and are more likely to be recorded when there is a clinical indication, rather than as a routine.

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