Prevalence, incidence, predictors and outcome of type 2 diabetes in Turkey

Türkiye'de tip 2 diyabetin prevalansı, insidansı, öngördürücüleri ve akıbeti

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ABSTRACT

Objectives: To investigate prospectively the incidence, certain predictors and outcomes of type 2 diabetes (DM), as well as to determine its prevalence cross-sectionally, in a representative sample of Turkish men and women.

Methods: Prospective evaluation of 3401 male and female participants (aged 48.2 ±12 years). Follow-up constituted 19,050 person-years. Individuals with DM were diagnosed with criteria of the American Diabetes Association. Fatal and nonfatal coronary heart disease (CHD) was identified by clinical findings and Minnesota coding of resting electrocardiograms. Cut-points of ≥95 cm in males and ≥91 cm in females were selected for abdominal obesity. For prospective evaluations, cases with DM or CHD were excluded.

Results: Prevalence of DM in Turkish adults was estimated as 2.89 million (11.0% of the population aged ≥35 years). Over a mean follow-up of 5.9 years, incident DM developed in 223 subjects, yielding an incidence per 1000 person-years of 11.0 in women and 12.4 in men. This corresponded to a 300,000 annual incidence. Following risk parameter levels but not HDL-cholesterol were significantly elevated at baseline in subjects developing DM compared to those without: age (5 years), waist girth (7 cm), blood pressure (12/6 mmHg), apolipoprotein B (7 mg/dl), total cholesterol (14 mg/dl), and fasting triglycerides (only in women, 52 mg/dl). Abdominal obesity (RR 2.61 [95%CI 1.87; 3.63]) and age in both genders, hypertension (RR 1.81 [95%CI 1.10; 2.98]) and low HDL-cholesterol in men alone were significant independent predictors of DM. Diabetes mellitus was a significant and independent predictor of fatal and nonfatal CHD, with a RR of 1.81 (95%CI 1.19; 2.75), after adjustment for sex, age, hypertension, waist circumference, serum total cholesterol and smoking status.

Conclusions: The annual incidence of DM in Turkey rises very rapidly, currently stands at 300,000, and, hence, its prevalence also rises correspondingly. Insulin resistance appears to be a weak determinant of DM in Turkish women while abdominal obesity is the main determinant. Multivariately adjusted DM is a significant independent predictor of fatal and nonfatal CHD. These observations emphasize that measures to reverse or stop the "epidemic" of abdominal obesity are severely required. *(Anadolu Kardiyol Derg 2006; 6: 314-21)*

Key words: Abdominal obesity, coronary heart disease, diabetes type 2, diabetes incidence, prospective population-based study, Turkish adults

ÖZET

Amaç: Türk erkek ve kadınlarını temsil eden bir örneklemde, tip 2 diyabetin insidansı, bazı öngördürücüleri ile akıbetini prospektif biçimde, prevalansını da kesitsel olarak araştırmak.

Yöntemler: Ortalama yaşı 48 (±12) olan 3401 kişilik bir örneklem 19,050 kişi-yılı tutan bir izlemede öne dönük olarak değerlendirildi. Diyabetes mellitüs'lü (DM) bireylerin tanısı Amerikan Diyabet Cemiyeti kriterlerine göre kondu. Fatal ve fatal olmayan koroner kalp hastalığı (KKH) klinik bulgu ve istirahat elektrokardiyografisinin Minnesota kodlarıyla belirlendi. Abdominal obezite için erkekte ≥95 cm, kadında ≥91 cm'lik sınırlar uygulandı. Öne dönük değerlendirmelerde, başlangıçtaki DM ve KKH vakaları dışlandı.

Bulgular: Nüfusu ≥35 yaş olan kesim için %11.0'e karşılık gelen bir DM prevalansı (tahminen 2.89 milyon) saptandı. Ortalama 5.9 yıllık takipte 223 kişide yeni DM gelişmesi karşılığında, 1000 kişi-yılında kadında 11.0, erkekte 12.4'lük bir insidans hesaplandı; bu da ülke bazında yılda 300 bin kişilik insidans ifade eder. Geri kalanlara kıyasla, yeni gelişen diyabetli kişilerde başlangıçtaki HDL-kolesterol benzer olup şu risk değişkenleri anlamlı farklıydı: Yaş (5 yıl), bel çevresi (7 cm), kan basıncı (12/6 mmHg), apolipoprotein B (7 mg/dl), total kolesterol (14 mg/dl), açlık trigliseridleri (yalnız kadında, 52 mg/dl). Diyabetes mellitüs'ün anlamlı bağımsız öngördürücüleri olarak abdominal obezite (RR 2.61 [%95GA 1.87; 3.63]) ile yaş her iki cinsiyette, erkekte ise hipertansiyon (RR 1.81 [%95GA 1.10; 2.98]) ve düşük HDL-kolesterol ortaya çıktı. Cinsiyet, yaş, hipertansiyon, bel çevresi, total kolesterol ve sigara içimi için ayarlandıktan sonra, DM 1.81'lik (%95GA 1.19; 2.75) bir nisbi risk ile fatal ve fatal olmayan KKH'nın anlamlı bağımsız bir öngördürücüsüydü.

Sonuçlar: Halkımızda halen 305 bin olan DM insidansı hızla artmakta, prevalansı da benzer şekilde yükselmektedir. Diyabetin kadınlarda esas belirleyicisi abdominal obezite iken, insülin direnci bu bağlamda daha zayıf görünmektedir. Çok değişkenli ayarlamada DM, fatal ve fatal olmayan KKH'nın anlamlı bağımsız öngördürücüsüdür. Bu gözlemler, göbeklilik "salgını"nı durdurucu veya tersine dönüştürücü önlemlere şiddetle ihtiyaç olduğunun altını çizmektedir. *(Anadolu Kardiyol Derg 2006; 6: 314-21)*

Anahtar kelimeler: Abdominal obezite, diyabet, diyabet insidansı, koroner kalp hastalığı, prospektif popülasyona-dayalı çalışma, Türk yetişkinleri

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Introduction

The incidence of diabetes mellitus, type 2 (DM), has been increasing in the past decade worldwide. It affects approximately 8% of adults in the United States (1). Reducing its incidence with lifestyle-intervention programs in subjects with impaired glucose tolerance (2) or at high risk for the development of DM (3) has been shown. In Turkey, the prevalence of DM has been rising at an unprecedented rate, along with the obesity "epidemic", according to data provided by both TURDEP (4) and the Turkish Adult Risk Factor Study (TEKHARF) (5, 6). However, knowledge is scarce in regard to the incidence of DM among Turkish adults, as well as to its predictors and its role in the outcome such as coronary heart disease (CHD) or death. Also, features of atherogenic dyslipidemia among diabetic Turks warrant investigation since we have the impression that its magnitude is attenuated as compared with Western populations.

Hence, the aim of the present study is to investigate prospectively the incidence, certain predictors and outcomes of DM, as well as determine its prevalence cross-sectionally, in a representative sample of Turkish men and women.

Methods

Population sample

Population sampled included participants of the nationwide survey 1997/98 of the Turkish Adult Risk Factor Study and followed up thereafter till 2004/2005, numbered 3401, among whom 1718 were women. This is a prospective survey on the prevalence of cardiac disease and risk factors in a representative sample of adults in Turkey carried out periodically almost biennially since 1990 in 59 communities scattered throughout all geographical regions of the country (7). Details of sampling were described previously (8). Since combined measurements of waist circumference, high-density lipoprotein (HDL)-cholesterol and apolipoprotein (apo) B were first performed at the follow-up visit in 1997/98, the latter examination formed the baseline. Participants were 28 years of age or older at baseline examination. Of the survivors, 8% were examined up to the survey 2001/02, 14% up to 2003, the remainder having been examined lastly in the survey 2004/05. Individuals of the cohort were visited in their addresses on the eve of the examination and were requested to give written consent for participation after having read an explanatory note, manifesting by their voluntary participation the next morning. The survey conformed to the principles embodied in the Declaration of Helsinki. Data were obtained by history of the past years via a questionnaire, physical examination of the cardiovascular system, sampling of blood and recording of a resting electrocardiogram.

Measurements of risk variables

Blood pressure was measured in the sitting position on the right arm after 5 min of rest, and the mean of two recordings 3 min apart was recorded. Weight was measured without shoes in light indoor clothes using scales. Waist circumference was measured with a tape (Roche LI95 63B 00) - the subject standing and wearing only underwear, at the level midway between the lower rib margin and the iliac crest. Body mass index was calculated as weight divided by height squared (kg/m^2). Physical activity was graded by the participant himself into four categories of increasing order with the aid of the following scheme: Grade 1: white-collar worker, sewing-knitting, walking ≤1 km daily; Grade 2: repair worker, house work, walking 1-2 km daily; Grade 3: mason, carpenter, truck driver, cleaning floors and windows, walking 4 km daily; Grade 4: heavy labour, farming, regular sports activity (8).

Plasma concentrations of cholesterol, fasting triglycerides, HDL -cholesterol and glucose were determined at baseline examination by the enzymatic dry chemistry method using a Reflotron apparatus (Roche Diagnostics, Mannheim, Germany). External quality control was performed with a reference laboratory in a random selection of 5-6% of participants and adjustments were made. Blood samples were spun at 1000g for 10 minutes and also shipped within a few hours on cooled gel packs at 2-5°C to Istanbul to be stored in deep-freeze at -75°C, until analyzed at a central laboratory. Concentrations of serum apo B were measured by Behring nephelometry (Behring Diagnostics, Marburg, Germany), those of insulin by the chemiluminescent immunometric method using Roche kits and Elecsys 1010 immunoautoanalyzer (Roche Diagnostics, Mannheim, Germany). Homeostatic model assessment (HOMA) was calculated with the following formula (9): insulin (mIU/L)* glucose (in mmol/L)/ 22.5.

Definitions and outcomes

Never smokers, past smokers and current smokers formed the categories in cigarette smoking. Current smokers of >10 cigarettes daily were designated as heavy smokers. Anyone consuming alcohol once a week or more was considered as alcohol user. Hypertension was defined as being under antihypertensive treatment or having a blood pressure ≥140 mmHg systolic and/or ≥90 mmHg diastolic. Individuals with diabetes and prediabetes were diagnosed with criteria of the American Diabetes Association (10), namely by self -report or when plasma fasting glucose was ≥126 mg/dl or 2-h postprandial glucose was >200 mg/dl. Impaired fasting glucose denoted fasting glucose values of 100-125 mg/dl. Same criteria were utilized for new diabetes developing over the follow-up period. Hypercholesterolemia was defined as a serum total cholesterol level ≥200 mg/dl. Abdominal obesity was defined in this study in terms of waist circumference in agreement with this anthropometric measure emerging as the most appropriate one to reflect visceral adiposity among Turks (11); ≥95 cm in males and ≥91 cm in females were cutpoints selected for abdominal obesity based on results of receiver operating characteristics (ROC) related to CHD, DM, and metabolic syndrome (12). Metabolic syndrome (MS) was defined in accordance with the ATPIII criteria, modified for the mentioned criteria of abdominal obesity.

Information on the mode of death was obtained from first degree relatives and/or health personnel of local health office. Diagnosis of nonfatal coronary heart disease (CHD) was based on the presence of angina pectoris, of a history of myocardial infarction with or without accompanying Minnesota codes of the ECG (13) or on a history of myocardial revascularization. Typical angina and age >45 years were prerequisite for a diagnosis in women when angina was isolated. Electrocardiographic changes of "ischemic type" of greater than minor degree (Codes 1.1-2, 4.1-2, 5.1-2, 7.1) were considered as myocardial infarct sequelae or myocardial ischemia, respectively.

Data analysis

Values of the baseline examination were used to evaluate prospective developments. All subjects known to have DM at baseline were excluded from analyses for the incidence of DM. Descriptive parameters were shown as mean ± SD and in percentages. Two-sided t-tests and Pearson's Chi-square tests were used to analyze the differences in means and proportions between groups. In multivariate prediction of the incidence of a dependent variable, the cohort in whom that particular variable existed at baseline examination was excluded from multivariate analysis. Estimates (and 95% confidence intervals) for relative risk (RR) of a dependent variable were obtained by use of logistic regression analysis in models that controlled for potential confounders. Hazard ratio (HR) estimate was obtained for abdominal obesity, the major determinant of diabetes, by taking into account that the mean gradient across the dichotomization (16 cm) represented 1.45 standard deviations (SD). A value of $p<0.05$ on the two-sided test was considered statistically significant. Statistical analyses were performed using SPSS-10 for Windows (SPSS Inc., Chicago, Ill., Nr. 9026510).

Extrapolation from the cohort data to the population: Estimates for the prevalence and incidence of DM are based on the consideration that the adult Turkish population in 2003 aged 35 or over was 26.1 million. Sex-specific prevalences obtained for each decade were standardized for the related sex-specific proportion of the population to determine the overall diabetes prevalence.

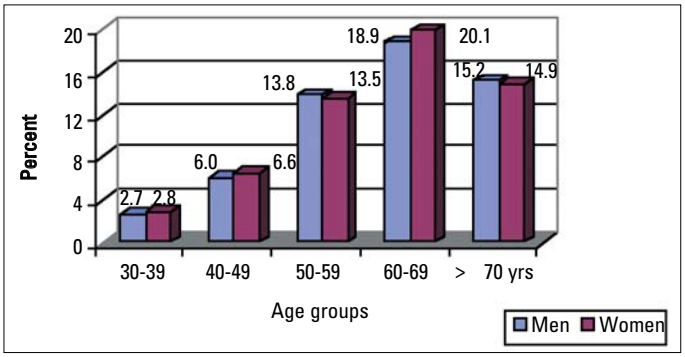

Figure 1. Prevalence of diabetes in Turkish men and women, by age groups. Number of participants in age groups 30-39 through ≥70 years was 402, 1114, 811, 610 and 464, respectively

Results

Mean age of the study sample was 48.2 ±11.9 years at baseline.

Sex-specific prevalence of diabetes in 2004/2005, by age groups and geographic regions

In the study sample, 195 men and 209 women received a diagnosis of DM (Fig. 1). This constituted 11.9% (11.0% age-standardized for the Turkish population aged ≥35 years), with no significant difference (p= 0.87) between men and women. A peak was reached in the age group 60-69 years with a prevalence of 20%, after which it declined to 15%, again similarly in both sexes.

Table 1 depicts the prevalence of diabetes in the various regions. While Southeast Anatolia and the Black Sea regions had above-average prevalence, East Anatolia and the Aegean regions exhibited the lowest prevalence. The Marmara, Central Anatolia and the Mediterranean regions constituted the regions with roughly the mean prevalence. Significant difference among the sexes was noted only in Central (and Eastern) Anatolia with females demonstrating higher prevalence, the Mediterranean with males.

Dyslipidemia and insulin resistance (IR) associated with diabetic subjects and some risk factors preceding diabetes

After exclusion of subjects with diabetes at baseline examination, 223 adults developed new diabetes over a mean follow-up of 5.9 years. Levels of certain parameters in individuals with and without DM are presented in Table 2, which shows that all 8 risk factors excepting HDL-cholesterol are significantly elevated in diabetic subjects. These comprise, on average, being 5 years older, having 7 cm wider waist girth, a BP 12/6 mmHg higher, apo B and total cholesterol concentrations by 7 and 14 mg/dl, respectively, higher. Fasting triglycerides were significantly higher (by 49 mg/dl) in women but not in men, regardless of the baseline or the final survey (Table 3).

At baseline median fasting insulin levels were 7.4 mIU/L, HOMA index 1.44 in nondiabetic subjects. At the final survey these values were only slightly higher. In diabetic subjects, fasting insulin median (interquartile range) levels were 9.1 (6 to 14.7) mIU/L, HOMA index values were 3.2 (1.8 to 5.9). Thus in diabetic persons, HOMA index was roughly twice as high and fasting insulin values by only about 14 to 25% higher than in nondiabetic persons.

Table 1. Prevalence of diabetes in the sample, by regions

	Total			Men			Women			
	DM	Cohort	%	DM	Cohort	%	DM	Cohort	%	p
Southeast Anatolia	55	285	19.3	26	145	17.9	29	140	20.7	ns
Black Sea	55	400	13.8	29	201	14.4	26	199	13.1	ns
Mediterranean	44	356	12.4	27	161	16.8	17	195	8.7	0.022
Marmara	107	904	11.8	54	463	11.7	53	441	12.0	ns
Central Anatolia	77	731	10.5	28	352	8.0	49	379	12.9	0.029
East Anatolia	26	277	9.4	9	139	6.5	17	138	12.3	0.095
Aegean	40	448	8.9	22	222	9.9	18	226	8.0	ns
Total	404	3401	11.9	195	1683	11.6	209	1718	12.2	ns

DM- diabetes mellitus, NS- nonsignificant

Incidence of DM

Over a mean follow-up of 5.9 years (total 19,050 person-years) incident type 2 diabetes developed in 105 women (11.0 per 1000 person-years) and 118 men (12.4 per 1000 person-years). This corresponds to an annual 300,000 incidence of DM (155,000 in men, 145,000 in women) in the year 2003. The mean (SD) age of onset of DM was 52.8 ±11 years.

Predictors of newly developing diabetes

Factors predicting the development of DM were examined in a logistic regression model comprising 2840 adults and sex, age, abdominal obesity, hypertension, smoking status, low HDL-cholesterol, high total cholesterol levels and physical activity grade (Table 4). Abdominal obesity (RR 2.61 [95%CI 1.87; 3.63]) and age (RR 1.023 [95%CI 1.01; 1.036]) were two significant independent predictors in both genders combined. Among men, hypertension (RR 1.81 [95%CI 1.10; 2.98]) and HDL-cholesterol (RR 1.54 [95%CI 1.02; 2.33]), furthermore independently predicted DM.

We have also examined the relative roles of MS and IR as predictors of DM (Table 5). Since insulin concentrations were first measured in 2001, the follow-up was inadequate to yield significant results except for the group with both variables at baseline in which RR was 4.47 (95%CI 1.69; 11.3) compared with the group having neither abdominal obesity nor IR. The number of total incident cases of DM was 29. The group of abdominal obesity

Table 2. Baseline levels of certain risk parameters in subjects without and with new diabetes

Parameters	No diabetes (n=2995)			Diabetes newly developed (n= 223)			
	n	mean	SD	n	mean	SD	p<
Age, years	2995	47.7	12.8	223	52.8	11.1	0.001
Fasting triglycerides, mg/dl	2399	139.9	89.7	192	172.3	96.9	0.001
HDL-cholesterol, mg/dl	2895	41.2	12.8	222	40.8	13.2	0.68
Apolipoprotein B, mg/dl	1819	112.7	35.8	161	119.4	36.1	0.023
Total cholesterol, mg/dl	2919	182.9	38.8	210	197.3	42.8	0.001
Waist circumference, cm	2972	91.7	11.9	223	98.6	10.9	0.001
Systolic blood pressure, mmHg	2993	128.8	24.4	223	141.2	24.7	0.001
Diastolic blood pressure, mmHg	2993	81.3	13.6	223	87.1	14.4	0.001
Fasting insulin, mIU/L*	1618	7.4	5.2/10.4				

*Median, interquartile range
181 diabetes existing at baseline excluded
HDL- high density lipoprotein cholesterol, SD- standard deviation

Table 3. Mean values for dyslipidemia and insulin resistance in final survey

Parameters	Nondiabetic participants (n=2995)			All cases with diabetes† (n= 223)			
	n	mean	SD	n	mean	SD	p<
Fasting triglycerides, mg/dl	2373	154.8	93	340	**188.2**	113.7	0.001
HDL-cholesterol, mg/dl	2556	43.6	12.3	369	44.0	11.7	0.62
Apolipoprotein B, mg/dl	2236	108.8	36.8	333	**116.6**	44.2	0.002
Men							
Fasting triglycerides, mg/dl	1119	167.5	103	159	183.2	119.6	0.079
HDL-cholesterol, mg/dl	1253	39.6	10.8	180	40.9	11.8	0.15
Apolipoprotein B, mg/dl	1082	110.0	37.7	158	107.5	37.7	0.44
Fasting insulin, mIU/L	801	7.5	4.9/12.2	113	8.96	5.6/13.6	1.19
HOMA index	728	1.47	1.01/2.4	41	3.43	1.71/6.35	2.33
Women							
Fasting triglycerides, mg/dl	1254	143.5	81	181	**192.6**	108.5	0.001
HDL-cholesterol, mg/dl	1303	47.6	12.4	189	47.0	10.9	0.54
Apolipoprotein B, mg/dl	1154	107.6	36	175	**124.9**	48	0.001
Fasting insulin, mIU/L*	925	8.21	5.6/11.4	128	**9.25**	6.4/15.8	1.13
HOMA index*	873	1.65	1.10/2.44	50	2.90	1.83/5.53	1.76

*Median, interquartile range
† includes cases existing at baseline with determined level of specific parameter in final survey
HDL- high density lipoprotein cholesterol, HOMA- homeostatic model assessment, SD- standard deviation

alone exhibited excess risk (RR 1.8) without attaining significance, while the smallest group of IR alone tended to show no excess risk. Notably, in none of 83 females with IR alone did diabetes develop in contradistinction to 4 new diabetes cases developing in 210 men with abdominal obesity alone.

Diabetes in the prediction of CHD

Table 6 shows the results of a logistic regression model in predicting the development of 313 cases of CHD; the model comprised 7 independent variables including DM. Apart from age, hypertension, waist circumference and serum total cholesterol at baseline, DM was a significant and independent predictor of fatal and nonfatal CHD. Relative risk amounted to 1.81 (95%CI 1.19; 2.75) which exceeded 2.0 in women, but was only at borderline significance among males with an RR 1.70. Adjusted only for age, RR for CHD in men was a significant 1.98 (95%CI 1.07; 3.66), again lower than the 2.57 in women.

Diabetes as predictive factor of all-cause mortality

For overall mortality, DM was not a significant age-adjusted risk factor, nor after additional adjustment for three major risk factors and waist girth (Table 7) in a regression model including over 3200 subjects and 219 deaths.

Discussion

Though the overall DM prevalence in the TURDEP study (4) among adults aged 30 or over was 9.83%, apparently lower than our prevalence of 11.6%, it is in very close agreement when one considers that the age-group 30-39 years formed a nearly 3-fold share of their cohort than of the current study. Indeed, analyzing the number of subjects comprised in each age group in the TURDEP study by the prevalence specific to each age group in the present analysis, it is clear that, from age 40 onwards the overall prevalence in our study is slightly, namely by 12%, lower (14). Therefore, our findings are by no means overestimates, and it is considered that 1.31 million men and 1.58 million women, in sum 2.89 million Turkish adults (11% of the population aged ≥35 years) had DM at the beginning of the 21st century. Of this prevalence 790,000 persons are estimated to have age <50 years, and 2.1 million ≥50 years.

The gender difference in the prevalence in the TURDEP study (8% women vs 6.2% men) was somewhat greater than the difference in sex-specific prevalence obtained herein. As concerns geographic regions, these were defined differently in the two stated studies so as to preclude valid comparisons, but Western, Central and Eastern Turkey displayed lower rates (than North and South Turkey) with which our findings are in general agreement.

The incidence of DM has not been studied thus far except in the TEKHARF study (6). The current estimate is based on both a larger cohort and a longer follow-up. Expressed per 1000 person-years, overall incidence was 11.7 (12.4 in men compared to 11.0 in women). This corresponds to an annual development of new DM in 300,000 Turkish adults. Our previous estimate in females has been confirmed though the one in males had previously been low,

Table 4. Risk factors in prediction of new diabetes at 6-year follow-up

Parameters	Adults (n=204/2840*)		Men (n=112/1452)		Women (n= 92/1388)	
	RR	95% CI	RR	95% CI	RR	95% CI
Sex, F	0.65	0.46; 0.93				
Age, years	**1.023**	1.009; 1.036	**1.024**	1.007; 1.041	1.02	0.999; 1.041
Abdominal obesity >91/95 cm	**2.61**	1.87; 3.63	**2.87**	1.75; 4.71	**2.97**	1.78; 4.93
Hypertension >140/90 mm Hg at baseline	1.41	0.996; 2.00	**1.81**	1.10; 2.98	1.09	NS
Current smoking at baseline	0.75	0.51; 1.10	0.73	NS	0.80	NS
HDL-cholesterol <40/45 mg/dl	1.09	NS	**1.54**	1.02; 2.33	0.73	NS
Physical activity grade I-IV	0.97	NS	1.03	NS	0.86	NS
Hypercholesterolemia >200 mg/dl at baseline	1.22	NS	1.07	NS	1.48	0.95; 3.32

782 men & 279 women current smokers
*Missing values in 5.2% of sample
CI - confidence interval, F- female, HDL- high density lipoprotein cholesterol, NS - nonsignificant, RR - relative risk

Table 5. Abdominal obesity and insulin resistance in prediction of new diabetes at 2-years

Parameters	Adults (n=29/1470)		Men (n=13/661)		Women (n= 16/809)	
	RR	95% CI	RR	95% CI	RR	95% CI
Sex, F	1.033	NS				
Age, years	1.026	0.995; 1.058	1.043	0.998; 1.09	1.009	NS
AO+/NoIR	1.81	0.62; 5.33	1.64	NS	2.12	NS
NoAO/IR+	0.82	NS	2.28	NS	0.004	NS
AO+/IR+	**4.47**	1.69; 1128	3.22	0.75; 13.7	**6.23**	1.62; 23.9

AO- abdominal obesity, CI- confidence intervals, F- female, IR- insulin resistance by HOMA, NS- nonsignificant, RR- relative risk

likely a consequence of a small sample size then. The higher incidence of DM in men than in women, though not reaching a significant level, was more pronounced when adjustment was made for age, abdominal obesity, hypertension and other confounders. The higher incidence but similar prevalence suggests that Turkish men with DM survive a slightly shorter period than women. Diabetes incidence in Turkey may be compared with that of the United States which has been given in the age bracket 18-79 years as 7 per 1000 population (10.1 for Hispanics, 10.8 for African Americans) (15). The age-adjusted rate rose by 39% in the preceding 5 years. Turkey's incidence - even considering the different age structure - is estimated already to be higher than that of the US, and is set to continue to rise rapidly in the next decade, in view of the aging population, additionally exhibiting a rise in abdominal obesity.

The dyslipidemia of DM among Turks

Among those identified as DM at the final examination, it was noteworthy that diabetic dyslipidemia, including apo B levels in men were not significantly different from over 1200 nondiabetic men. A significant difference did not emerge in women also regarding HDL-cholesterol levels but did so in regard to fasting triglycerides and apo B values. The lack of a difference of HDL-cholesterol levels in DM combined with the lack of their predictive value for DM in females, suggests that some Turkish women may harbor defects in HDL, i.e. they may have a higher proportion of the smaller less cardioprotective HDL_3 subclass (16) corresponding to the lipoprotein A (LpA)-I/A-II particles. This possibility is supported by our previous observation that HDL-cholesterol is not as good a predictor of CHD in women as in men (17). Mahley and associates (18) showed that the frequency distribution of HDL-cholesterol levels was skewed toward bimodality in Turkish women, as were also LpA-I levels. Women stood in contrast to Turkish men in whom HDL-cholesterol did predict independently the development of DM, despite displaying similar concentrations among diabetic and nondiabetic participants.

Predictors of diabetes

Abdominal obesity (RR 2.6) and age (RR 1.25 per decade) were the two significant independent predictors of DM in both genders, in addition to hypertension (RR 1.8) and low HDL-cholesterol levels (RR 1.54) in men. These observations suggested that Turkish women may harbor defects in HDL composition. Altered composition of HDL in DM may alter its antiatherogenic properties (19). The gradient of risk with respect to abdominal obesity is similar in magnitude to the DM risk in men of the Health Professionals Follow-up study (20) across the quintiles of waist circumference. Our finding of an RR 2.61 across a mean gradient of 16 cm means that every 6 cm increment in waist girth elevates the diabetes risk by 43%.

Table 6. Prediction of incident fatal & nonfatal CHD by diabetes and other risk factors at baseline

Parameters	Adults (n=313/3122)*		Men (n=160/1534)		Women (n=153/1588)	
	RR	95% CI	RR	95% CI	RR	95% CI
Sex, F	0.86	NS				
Age, years	**1.064**	1.053; 1.075	**1.065**	1.049; 1.081	**1.064**	1.047; 1.081
Diabetes mellitus	**1.81**	1.19; 2.75	1.70	0.89; 3.28	**2.06**	1.19; 3.56
Hypertension >140/90 mmHg	**1.84**	1.39; 2.44	**2.29**	1.51; 3.48	**1.61**	1.10; 2.35
Waist circumference, cm	**1.018**	1.007; 1.29	**1.019**	1.002; 1.036	**1.019**	1.003; 1.34
Total cholesterol, mg/dl	**1.007**	1.004; 1.011	**1.010**	1.006; 1.015	**1.005**	1.001; 1.010
Current smoking	1.32	0.95; 1.84	**1.89**	1.19; 3.00	0.93	0.53; 1.65

In total, 154 subjects with diabetes and 565 with hypertension existed at baseline, after exclusion of 171 cases with CHD
*Missing values in 3.3% of sample
CHD- coronary heart disease, CI- confidence interval, F- female, NS- nonsignificant, RR- relative risk

Table 7. Prediction of overall mortality by diabetes and other risk factors at baseline

Parameters	Adults (n=219/3268)		Men (n=133/1614)		Women (n=86/1654)	
	RR	95% CI	RR	95% CI	RR	95% CI
Sex, F	**0.61**	0.415; 0.906				
Age, years	**1.114**	1.099; 1.13	**1.099**	1.081; 1.118	**1.139**	1.113; 1.166
Diabetes mellitus	0.63	NS	**0.52**	NS	0.71	NS
Hypertension >140/90 mmHg	**1.90**	1.36; 2.66	**2.34**	1.50; 3.66	1.515	0.91; 2.51
Waist circumference, cm	**0.986**	0.973; 1.000	**0.98**	0.962; 0.998	0.994	NS
Total cholesterol, mg/dl	1.002	NS	1.003	NS	1.000	NS
Current smoking	**1.73**	1.145; 2.61	**1.77**	1.074; 2.91	1.32	NS

Diabetes existed at baseline in 174, hypertension in 633, current smoking in 1149 persons
CI- confidence interval, F-female, NS- nonsignificant, RR- relative risk

In 892 non-diabetic Finnish subjects aged 65-74 years, 69 subjects developed diabetes over a follow-up of 3.5 years (21). The risk of developing diabetes was 3.5-fold among subjects with triglycerides above than with those below 221 mg/dl, 2.5-fold in those with HDL-cholesterol < 38.7 mg/dl, 2.1-fold in those with BMI > 30 kg/m^2, 1.9-fold among those in the highest quartile of fasting insulin distribution, 1.8-fold in those having hypertension.

Among 872 participants with normal or impaired glucose tolerance enrolled at baseline in the Insulin Resistance Atherosclerosis Study, 143 developed type 2 diabetes in 5 years. Significant risk factors for developing type 2 diabetes included plasminogen activator inhibitor (PAI)-1, hypertension, high triglycerides, low levels of HDL-cholesterol, and impaired glucose tolerance. Each of these sex- and age-adjusted risk factors increased the risk of diabetes at an odds of 2.1, and at an odds of 1.81 (95%CI 1.49-2.20) after further adjustment of insulin resistance and waist circumference. Thus, individuals with multiple risk factors are at increased risk of diabetes, which is only partially mediated by insulin resistance or central obesity (22). Our preliminary data may be interpreted as diabetes risk in Turkish women being less determined by IR than by central obesity and in the sense that IR alone may not sufficiently predispose them. Low sex hormone-binding globulin levels might be related in this phenomenon (as yet unpublished observation).

Of 559 Chinese subjects without diabetes at baseline as reported by Wang et al. (23), 129 developed diabetes during the 5-year follow-up. Fasting insulin and waist to hip ratio, postload and fasting glucose levels and serum insulin predicted diabetes in factor analysis. IR alone did not underlie all features of MS. Different physiological processes associated with various components of the MS contained unique information about diabetes risk (23).

Diabetes as a Risk Factor for CHD and Mortality

In adults with diabetes, risk for incident fatal and nonfatal CHD proved to be 81% in excess of subjects without diabetes adjusted for conventional risk factors. In a study from Finland (24), compared with nondiabetic subjects with no prior myocardial infarction, those with diabetes and no prior myocardial infarction had a 6-fold incidence of cardiovascular events in the follow-up, after adjustment for sex and age alone.

Diabetes mellitus did not turn out to confer excess age-adjusted risk for all-cause mortality in this cohort with or without further adjustments. Though this may surprise, it is recognized that diabetic individuals generally die of cardiovascular complications, not at a premature age. In the USA, diabetes prevails in 6.7% of the population but deaths from DM represent 3% of all deaths (15).

In conclusion, the annual incidence of DM provided in this study is high and rising rapidly. Abdominal obesity is its main modifiable determinant, followed in men by hypertension and low HDL-cholesterol levels, which are markers of IR. Diabetic subjects exhibit similar levels of serum HDL-cholesterol and men exhibit similar fasting triglyceride levels as the nondiabetic population. Some observations suggested that Turkish women may harbor defects in HDL composition. Diabetes mellitus predicted fatal and nonfatal CHD with an RR of 1.8 independent of sex, age, hypertension, waist circumference, total cholesterol and smoking status. Implementation of measures to reverse the tide of abdominal obesity is badly needed.

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