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ORIGINAL ARTICLE

The Relationship Between Glucose Intolerance and Blood Pressure, Body Mass Index, and Waist to Hip Ratio in Tehran Urban Population: "Tehran Lipid and Glucose Study"

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Glucose intolerance, hypertension, and obesity are important risk factors for cardiovascular diseases. In this study we aim at assessing the association between WHR, BMI, and blood pressure and glucose tolerance status.

Materials and Methods: Of 15000 urban individuals, 3-69 years old, chosen by cluster random sampling in the cross-sectional phase of a longitudinal study in the east of Tehran, 2886 men and 4013 women, between 30-69 years of age, underwent a 2-hour oral glucose tolerance test. Diabetes mellitus (DM) and impaired glucose tolerance (IGT) were defined using WHO criteria. Blood pressure, weight, height, and hip and waist circumferences were measured according to standard protocols, and BMI and WHR were calculated.

Results: 911 subjects (13.2%) had IGT and 372 (5.4%) had diabetes. Obesity (BMI≥30 kg/m^2) was more common in DM and IGT than healthy individuals (45.1% and 39.1% vs 22.9%, respectively, p<0.001). There was no significant difference among the prevalence of overweight (25<BMI<30 kg/m^2) in different glucose tolerance categories. Truncal obesity (WHR>0.8 in females and WHR>0.95 in males) was present in 82.7, 75.6 and 53.7% of diabetics, IGT, and normal subjects respectively (p<0.001). In forward stepwise logistic regression adjusted for age and sex, the following variables, in order of entering the model, were significantly associated with DM: age OR=4.4) 95% CI: 3-6.5, p<0.001); Truncal obesity OR=1.8 (95% CI: 1.3-2.4, 0.001); obesity OR=3 (95% CI: 2-4.3, p<0.001); and overweight OR=2 (1.4-2.9, P<0.001). Prevalences of hypertension in DM, IGT, and healthy subjects were 51.9, 39.5, and 18.8%, respectively (p<0.001) and when adjusted for age, sex, BMI, and WHR, all types of glucose disorders were significantly associated with hypertension: IGT OR=1.8 (95% CI: 1.5-2, p<0.001) and DM OR=2.4 (95% CI: 1.9-3, p<0.001).

Conclusion: Hypertension, obesity, and high WHR are more prevalent in individuals with diabetes and IGT than in normal population. Furthermore, truncal obesity is more often associated with glucose intolerance than with generalized obesity.

Key Words: Blood pressure, Body mass index, Diabetes mellitus, Impaired glucose tolerance, Waist to hip ratio, Glucose intolerance

Introduction

Hyperglycemia has long been recognized as a strong risk factor for cardiovascular diseases (CVD). Increased liability to atheroscelerotic vascular disease occurs with abnormal glucose tolerance.[1-3] However, identification of the glucose thresholds above which the risk of CVD begins to increase has been controversial.[4,5] A recent systemic over-

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view and metaregression analyses of several epidemiologic studies also confirmed a graded relationship between fasting and post-prandial glucose levels and cardiovascular risk.[6] Asymptomatic hyperglycemia is a significant public health problem. Those with undiagnosed diabetes may develop micro- or macrovascular complications and are especially prone to CVD. For people with impaired glucose tolerance (IGT) or undiagnosed diabetes, cardiovascular risk factors are equal and in some cases, greater than in patient with diagnosed diabetes.[7-9] Although several studies reported strong effects of WHR, BMI, and blood pressure on the development of diabetes,[10-14] there are a few studies focusing on the association of IGT with these CVD risk factors.[15-18]

Over the last few years, diabetes and CVD have been accorded priority status in Iranian communities,[19,20] as some previous studies have clearly shown a high prevalence of diagnosed and especially undiagnosed diabetic and IGT patients in Iran.[21,22]

The objective of this study is to investigate the association between blood pressure, BMI, and WHR and different glucose tolerance status in an adult Iranian population.

Materials and Methods

Study population

The Tehran Lipid and Glucose Study (TLGS) is a study to determine the risk factors for atherosclerosis among Tehran's urban population and to develop population-based measures to change the life-style of the population and to prevent the rising trend of diabetes mellitus and dyslipidemias.[23] The design of this study encompasses two major components: phase 1 is a cross-sectional prevalence study of coronary artery disease (CAD) and associated risk factors and phase 2 is a prospective interventional study, currently underway planned for the most 20 years. A cluster random sampling was used to recruit 15000 people aged 3-69 years from urban district 13 of Tehran, the capital of the Islamic Republic of Iran.

Among this population, 6899 adults, aged 30-69 years, including 2886 men and 4013 women were the subjects of this study. All subjects were studied at the TLGS clinic between February 1999 and Aug 2001.

The appropriate Research Ethics Committee approved this study.

Medical history and clinical examination

All participants invited, after signing informed written consent, were examined by trained physicians according to a uniform protocol. Demographic, and lifestyle information were obtained by the use of a standard and validated questionnaire.

For blood pressure calculation, the participants remained seated for 15 minutes, when a qualified physician measured blood pressure two times after one more measurement for determining peak inflation level using a standard mercury sphygmomanometer calibrated by the Iranian Institute of Standards and Industrial Researches. The cuff was placed on the right arm, at the heart level, and inflated at as high a rate as possible, until the cuff pressure was 30 mmHg above the level at which the radial pulse disappeared. There was at least a 30 second interval between these two separate measurements, and the mean of two measurements was considered to be the participant's blood pressure. The systolic blood pressure was defined as the appearance of the first sound (Korotkoff phase 1), and the diastolic blood pressure was defined as disappearance of the sound (Korotkoff phase 5) during deflation of the cuff at a 2-3 mm per second decrement rate of mercury column.

Anthropometric measurements were made with shoes removed and the participant wearing lightweight clothing. Weight and height were measured according to the standard protocol. Waist circumference was measured at the level of the umbilicus and hip circumference was measured over light clothing at the widest girth of the hip. Body mass index was calculated by dividing the weight in kilograms by the square of height in meters.

According to the JNC-VI (Joint National Committee) criteria,[24] hypertension was defined as mean systolic blood pressure (SBP) $\geq$ 140 mmHg, mean diastolic blood pressure (DBP)$\geq$ 90 mmHg, or current treatment with antihypertensive medications at the time of interview or in the previous one month. Awareness of hypertension reflects any prior diagnosis of hypertension by a physician and was defined as a positive answer to the relevant question at the time of the interview. A BMI of 25 to 29.9 kg/m^2 was considered as overweight and BMI equal to or more than 30 kg/m^2 was defined as obesity. Truncal obesity was defined as WHR more than 0.95 in men and WHR more than 0.8 in women.

Serum glucose analysis

A blood sample was drawn between 7:00 and 9:00 AM into vacutainer tubes from all study participants after a 12-14 hour overnight fast. 82.5 g glucose monohydrate solution (equivalent to 75 g anhydrous glucose; Cerestar EP, Spain) was administered orally. Blood sample was obtained 120 minutes after the ingestion of of glucose load. Blood samples were taken in sitting position according to the standard protocol and centrifuged within 30 to 45 minutes of collection. All blood glucose analyses were carried out at the TLGS research laboratory on the day of blood collection by Selectra 2 auto-analyzer (Vital Scientific, Spankeren, Netherlands), using glucose kits (Pars Azmun Inc., Iran). Glucose was assayed using enzymatic colorimetric method with glucose oxidase technique. Assay performance was monitored every 20 tests using the glucose control serum, Precinorm (normal range) and Precipath (pathologic range) wherever applicable (Boehringer Mannheim, Germany; cat. no. 1446070 for Precinorm and 171778 for Precipath). Glucose standard (C.f.a.s, Roche, Germany; cat. no. 759350) was used to calibrate the Selectra 2 auto-analyzer each day of laboratory analyses. All samples were analyzed when internal quality control met the acceptable criteria. Inter- and intra-assay coefficient of variations were both 2.2%.

The results of the oral glucose tolerance test of each subject were used to classify glucose metabolism status according to WHO criteria,[25] and subjects were classified as normal glucose (2h postload plasma glucose-2hPG<140 mg/dl), IGT (200>2 hPG $\geq$ 140), or diabetic (2h PG $\geq$ 200 mg/dl).

Statistical analysis

For analysis of the data, the study population was divided into 4 age groups: 30-39, 40-49, 50-59, and 60-69 years. Serum fasting glucose concentration and the prevalence of diabetes mellitus and IGT were compared among different age strata in both sexes. Because of history of drug cosumption and probability of related interventions in known DM patients, they were excluded from our analyses. Statistical analysis was performed using the SPSS 9.05 statistical software package (SPSS Inc., Chicago, IL), and quantitative data were presented as mean and standard deviation and qualitative data as number and percentage. Mean values were compared by t-test and analysis of variance (ANOVA). Forward stepwise logistic regression controlling for age and sex was undertaken to identify the associated variables with diabetes mellitus. P<0.05 were considered to be statistically significant.

Results

There were 6899 adults, 2886 males and 4013 females. Thirty-five percent of the study population was between 30-39 years, 26% between 40-49 years, 21% between 50-59 years, and 18% between 60-69 years. The age distribution in different oral glucose tolerance statuses appeared uneven (Table 1). Accordingly, age was introduced as a covariate in the data analysis.

Table 1. Characteristics of subjects in different oral glucose tolerance categories; TLGS

	N	Age (year)	BMI (Kg/m^2)
All			
Healthy	5242	44 (11)	27 (4)
IGT	911	50 (11)*	29 (5)*
New DM	372	52 (10)*	31 (12)*
Known DM	374	55 (10)*	28 (5)*
Total	6899	47 (11)	28 (5)
Males			
Healthy	2282	45 (11)	26 (4)
IGT	337	52 (11)*	28 (4)*
New DM	144	53 (10)*	29 (4)*
Known DM	123	56 (10)*	27 (4)*
Total	2886	47 (12)	26 (4)
Females			
Healthy	2960	44 (11)	28 (5)
IGT	574	49 (10)*	30 (5)*
New DM	228	52 (10)*	32 (15)*
Known DM	251	54 (10)*	29 (5)*
Total	4013	46 (11)	29 (6)

IGT: Impaired glucose tolerance; BMI: Body mass index (adjusted for age).
Values are means (SD).
* P<0.001, Compared with healthy subjects.

The prevalence (95% CI) of newly diagnosed diabetes was 5% (4.2-5.8) in males and 5.7% (5-6.4) in females, and that of IGT was 11.7% (10.5-12.9) and 14.3% (13.2-15.4) in males and females, respectively. The prevalence of known diabetes was 4.1% (3.9-4.2) in males and 6.1% (5.9-6.3) in females. Age specific prevalence rates of glucose disorders are shown in Table 2. As shown in this Table, there is a consistent increase in 2hPG with age, in both males and females.

Mean systolic and diastolic blood pressures were greater in the DM and IGT subjects as compared to the healthy group: 131±19 mmHg in DM and 125±18 mmHg in IGT vs 116±16 mmHg in healthy group for systolic and 84±11 mmHg in DM and 81±11 in IGT vs 77±10 mmHg in healthy for diastolic BP, respectively, $p<0.001$ (Table 3). The overall prevalence of hypertension was significantly higher in DM and IGT than in the healthy group: 51.9% in DM and 39.5% in IGT vs 18.8% in healthy, $p<0.001$ (Fig. 1). The prevalence of hypertension increased by age in all three groups (Table 4).

The mean BMI was higher in DM and IGT than in healthy subjects: 31±4 Kg/m^2 in DM and 29±5 in IGT vs 27±4 kg/m^2 in healthy individuals, $p<0.001$. Age-specific prevalence rates of obesity and overweight in different oral glucose categories in men and women are shown in Table 5. The prevalence of obesity was significantly higher in DM and IGT than in normal subjects; males: 33.1% in DM and 24.7% in IGT vs 12.9% in healthy, $p<0.001$; and females: 52.7% in DM and 47.7 %in IGT vs 30.8% in healthy subjects, $p<0.001$.

The prevalence of truncal obesity was significantly higher in DM and IGT than in the healthy group: 82.7% in DM and 75.6% in IGT vs 53.5% in healthy, $p<0.001$. Age-specific prevalence of truncal obesity in men and women is illustrated in Table 6.

In forward stepwise logistic regression adjusted for age and sex, the following variables were significantly associated with DM: age OR=4.4 (CI %95, 3-6.5, $p<0.001$); truncal obesity OR=1.8 (95% CI: 1.3-2.4, $p<0.001$); obesity OR=3 (95% CI:2-4.3, $p<0.001$); and overweight OR= 2 (95% CI:1.4-2.9, $p<0.001$).

Table 2. Age-specific prevalence rate of oral glucose tolerance categories and mean, SD, and percentiles of 2hPG for each age group in men and women (adjusted for age and BMI): TLGS

Age groups (Years)	IGT (%)*	New DM (%)	Known DM (%)	2hPG percentiles (mg/dL)						
				Mean#	SD	10	25	50	75	90
All										
30-39	8.2 (196)	1.6 (39)	0.6 (16)	105†	37	71	83	100	118	140
40-49	14.2 (258)	6.2 (113)	3.4 (65)	124‡	56	76	93	111	138	182
50-59	16.2 (234)	8 (116)	8.4 (126)	134§	64	80	97	118	149	203
60-69	18 (223)	8.4 (104)	13.2 (167)	145	78	84	103	124	160	226
Total	13.2 (911)	5.4 (372)	5.2 (374)	122	58	75	90	109	135	176
Males										
30-39	6.1 (60)	1.3 (13)	0.4 (4)	99†	37	64	77	93	114	134
40-49	11.7 (87)	5.3 (39)	2.3 (18)	117‡	60	68	85	103	127	170
50-59	14 (78)	9 (50)	6.0 (35)	132¶	70	73	92	114	146	215
60-69	18.8 (112)	7 (42)	10.8 (66)	141	80	78	96	120	159	218
Total	11.7 (337)	5 (144)	4.1 (123)	118	62	68	84	104	129	174
Females										
30-39	9.7 (136)	1.9 (26)	0.8 (12)	109†	36	76	88	102	122	145
40-49	15.8 (171)	6.9 (74)	4.2 (47)	128‡	53	84	98	115	142	186
50-59	17.5 (156)	7.4 (66)	10.0 (91)	136§	60	86	101	122	151	200
60-69	17.3 (111)	9.7 (62)	15.5 (101)	149	76	92	107	128	161	229
Total	14.3 (574)	5.7 (228)	6.1 (251)	126	55	81	95	113	138	178

*Numbers in parenthesis show number of subjects; †P<0.001, compared with 40-49, 50-59, 60-69 age groups; ‡P<0.001, compared with 50-59 and 60-69 age groups; §P<0.001, compared with 60-69 age groups; ¶P<0.05, compared with 60-69 age group.; #Previously diagnosed diabetic patients not included because OGTT was not performed for them

Table 3. Age and BMI adjusted mean systolic and diastolic blood pressures in different glucose tolerance categories in Tehran urban population: TLGS

	Healthy	IGT	New DM	Known DM
All				
SBP (mmHg)	116 (16)	125 (18)*	131 (19)*	128 (20)*
DBP (mmHg)	77 (10)	81 (11)*	84 (11)*	81 (10)*
Males				
SBP (mmHg)	117 (16)	126 (18)*	132 (21)*	127 (20)*
DBP (mmHg)	77 (10)	81 (12)*	83 (12)*	80 (11)*
Females				
SBP (mmHg)	115 (15)	124 (18)*	130 (18)*	128 (19)*
DBP (mmHg)	77 (10)	81 (10)*	84 (10)*	81 (10)*

SBP: systolic blood pressure; DBP: diastolic blood pressure
Values are mean (SD)
*p<0.001, compared with healthy subjects

Table 4. Age-specific prevalence of hypertension in different oral glucose categories: TLGS

Age groups (Years)	Number	Healthy (%)	IGT* (%)	New DM* (%)
All				
30-39	2392	7	13	33
40-49	1822	16	33	32
50-59	1448	32	50	60
60-69	1237	46	60	71
Total	6899	19	40	52
Males				
30-39	991	8	15	31
40-49	742	14	27	34
50-59	557	25	45	58
60-69	596	42	53	62
Total	2886	17	38	50
Females				
30-39	1401	7	12	35
40-49	1080	18	36	31
50-59	891	37	52	61
60-69	641	49	66	77
Total	4013	20	41	52

*The prevalence of hypertension was higher in IGT and diabetic than healthy subjects in all age strata and both sexes, p<0.001.

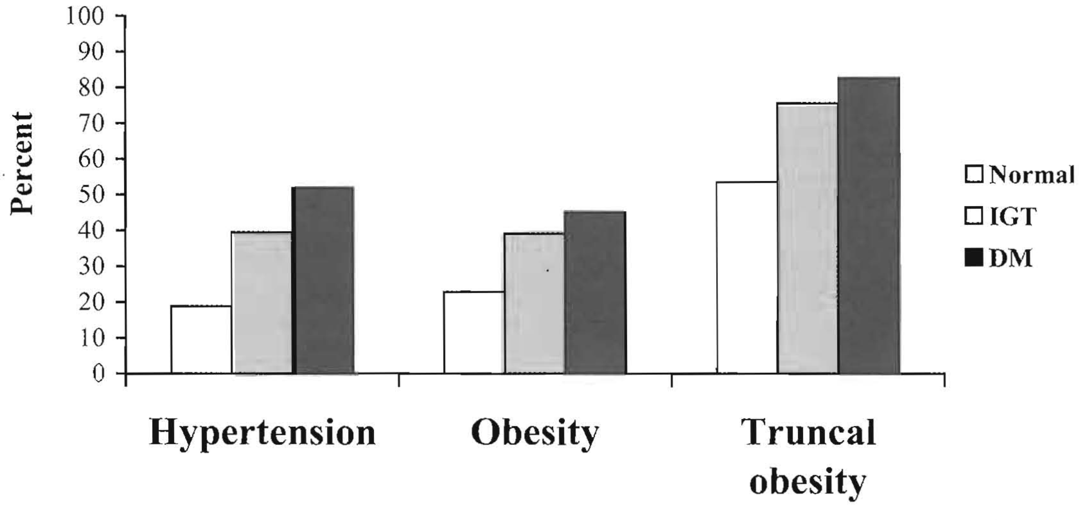

Fig. 1. The prevalence of hypertension, obesity, and truncal obesity in various oral glucose tolerance categories in Tehran's urban population: TLGS

Table 5. Age-specific prevalence of obesity (BMI≥30 kg/m^2) and overweight (25<BMI<30 Kg/m^2) in different oral glucose categories in men, women, and total population in Tehran urban population: TLGS

Age groups (years)	Healthy			IGT			New DM		
	Normal (%)	overweight (%)	obese (%)	Normal (%)	overweight (%)	obese (%)	Normal (%)	overweight (%)	obese (%)
All									
30-39	40	42	19	25	41	34*	8	51*	41*
40-49	30	46	25	10	44	46*	13	42	45*
50-59	24	46	30	15	40	45*	7	38	55*
60-69	33	43	24	23	47	30†	16	49†	35*
Total	33	44	23	18	43	39*	11	44	45*
Males									
30-39	43	43	14	35	38	27*		69*	31*
40-49	43	46	11	14	57†	29*	18	53	29*
50-59	39	47	14	23	48	29*	6	50	44*
60-69	44	44	12	26	56†	18†	17	59*	24*
Total	42	45	13	24	51†	25*	12	55†	33*
Females									
30-39	37	41	22	20	43	37*	12	43	46*
40-49	20	45	35	8	38	54*	10	36†	54*
50-59	14	45	41	10	37†	53*	8	29†	63*
60-69	21	42	36	20	38	42	15	43	43
Total	26	43	31	14	39	48*	11	37†	53*

DM: diabetes mellitus

*p<0.001, †p<0.05, compared with healthy subjects

Table 6. Age-specific prevalence of truncal obesity (WHR>0.95 in men and WHR>0.8 in women): TLGS

Age groups (years)	Number	Healthy (%)	IGT* (%)	New DM* (%)
All				
30-39	2392	40.6	64.6	71.8
40-49	1822	55.8	77.4	87.0
50-59	1448	69.3	79.0	82.6
60-69	1237	69.6	79.4	82.4
Total	6899	53.5	75.6	82.7
Males				
30-39	991	21.6	33.3	46.2
40-49	742	31.4	54.8	73.7
50-59	557	44.7	59.7	72.0
60-69	596	49.0	66.7	61.0
Total	2886	32.0	56.0	66.9
Females				
30-39	1401	55.1	79.1	84.6
40-49	1080	75.0	88.7	94.3
50-59	891	85.9	88.5	90.8
60-69	641	91.2	92.5	96.7
Total	4013	70.3	87.1	92.8

*p<0.001, compared with healthy subjects in all age starata and both sexes

Discussion

In this study we found a close relationship between truncal and generalized obesity and the glucose intolerance state in an adult population of Tehran. Impaired glucose tolerance is a heterogeneous state and may predispose to CVD and in subjects with glucose intolerance, a higher BP, FPG, and BMI is present as compared to subjects with normal glucose tolerance.[7,26-31] Since IGT subjects comprise approximately 80% of the total glucose intolerant population,[32-36] it is important to consider if IGT subjects are at increased cardiovascular risk. The results of this study demonstrate a linear upward trend in age, WHR, BMI, and systolic and diastolic blood pressure, with a shift from normal glucose metabolism to IGT and DM in the Tehran adult residents.

The proportion of IGT and DM in this study i.e. 3-12% for DM and 7-15% for IGT was not much different from those reported in adults elsewhere in Iran and other countries.[21,37,38]

Impaired glucose tolerance is more frequent in obese than in non-obese subjects and is frequently associated with hyperinsulinemia and insulin resistance.[39] It has been almost consistently reported that truncal obesity is equally or more important than generalized obesity in the development of DM in men and women in both cross-sectional and prospective studies.[40-42] In the present study, WHR was the strongest modifiable factor associated with DM. In a cross-sectional study in Japan, Iso et al[43] found a significant positive correlation between WHR and HbA1c, which reflects the condition of plasma glucose. Few studies have examined the relation between WHR and IGT.[41-43] Silverstein reported a highly significant association between WHR and IGT and a positive, insignificant association between BMI and IGT in separate analyses for WHR and BMI.[42] In our study the association of IGT with WHR was stronger than with BMI.

In the present study, the prevalence of hypertension was significantly higher in DM and IGT than normal subjects. This finding is in accordance with findings of other studies.[44,45] Some investigations have implicated insulin resistance as the mechanisms that mediates BP elevation through the action of insulin on increasing sympathetic nervous system activity[46-48] or on increasing renal sodium reabsorption.[49] On the other hand, in subjects with normal glucose tolerance, insulin has a vasodilator effect, resulting in an increase in blood flow and a decrease in vascular resistance.[50] Studies by Baron et al have shown that, there is a blunted vasodilator response to insulin as well as an attenuated effect of insulin in decreasing vascular resistance in insulin resistance associated with diabetes. Moreover endothelium-dependent vasodilation is abnormal in diabetic patients.[50,51] Endothelial dysfunction may be secondary to underlying mechanisms that result in reduced bioavailibility of nitric oxide.[52]

In conclusion, our data suggest that truncal obesity is an important contributor not only for diabetes mellitus but also to impaired glucose tolerance. Primary prevention of cardiovascular disease at the community level using simple and inexpensive tools, to screen and control truncal and generalized obesity, two modifiable risk factors, may prove to be highly cost-effective.

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References

1. Gerstein HC. Is glucose a continuous risk factor for cardiovascular mortality? Diabetes Care. 1999 May;22 (5):659-60.
2. Coutinho M, Gerstein HC, Wang Y, Yusuf S. The relationship between glucose and incident cardiovascular events. A metaregression analysis of published data from 20 studies of 95,783 individuals followed for 12.4 years. Diabetes Care. 1999 Feb;22 (2):233-40.
3. Balkau B, Bertrais S, Ducimetiere P, Eschwege E. Is there a glycemic threshold for mortality risk? Diabetes Care. 1999 May;22 (5):696-9.
4. Klein R, Klein BE, Moss SE. Prevalence of microalbuminuria in older-onset diabetes. Diabetes Care. 1993 Oct;16 (10):1325-30.
5. Wingard DL, Barrett-corner E. Heart disease and diabetes. In: Diabetes in America. 2nd ed. National diabetes data group, editors. Bethesda, MD, National Institutes of Health, National Iinstitute of Diabetes and Digestive and Kidney Diseases; 1995.p.429-48.
6. Eastman RC, Cowie CC, Harris MI. Undiagnosed diabetes or impaired glucose tolerance and cardiovascular risk. Diabetes Care. 1997 Feb;20 (2):127-8.
7. McPhillips JB, Barrett-Connor E, Wingard DL. Cardiovascular disease risk factors prior to the diagnosis of impaired glucose tolerance and non-insulin-dependent diabetes mellitus in a community of older adults. Am J Epidemiol. 1990 Mar;131 (3):443-53.
8. Burchfiel CM, Hamman RF, Marshall JA, Baxter J, Kahn LB, Amirani JJ. Cardiovascular risk factors and impaired glucose tolerance: the San Luis Valley Diabetes Study. Am J Epidemiol. 1990 Jan;131 (1):57-70.
9. Rewers M, Shetterly SM, Baxter J, Marshall JA, Hamman RF. Prevalence of coronary heart disease in subjects with normal and impaired glucose tolerance and non-insulin-dependent diabetes mellitus in a biethnic Colorado population. The San Luis Valley Diabetes Study. Am J Epidemiol. 1992 Jun 15;135 (12):1321-30.
10. Pyorala K, Savolainen E, Lehtovirta E, Punsar S, Siltanen P. Glucose tolerance and coronary heart disease: Helsinki policemen study. J Chronic Dis. 1979;32 (11-12):729-45.
11. Kannel WB, McGee DL. Diabetes and cardiovascular risk factors: the Framingham study. Circulation. 1979 Jan;59 (1):8-13.
12. Fuller JH, Shipley MJ, Rose G, Jarrett RJ, Keen H. Mortality from coronary heart disease and stroke in relation to degree of glycaemia: the Whitehall study. Br Med J (Clin Res Ed). 1983 Sep 24;287 (6396):867-70.
13. Cassano PA, Rosner B, Vokonas PS, Weiss ST. Obesity and body fat distribution in relation to the incidence of non-insulin-dependent diabetes mellitus. A prospective cohort study of men in the normative aging study. Am J Epidemiol. 1992 Dec 15;136 (12):1474-86.
14. Iso H, Kiyama M, Naito Y, Sato S, Kitamura A, Iida M, et al. The relation of body fat distribution and body mass with haemoglobin A1c, blood pressure and blood lipids in urban Japanese men. Int J Epidemiol. 1991 Mar;20 (1):88-94.
15. Tominaga M, Eguchi H, Manaka H, Igarashi K, Kato T, Sekikawa A. Impaired glucose tolerance is a risk factor for cardiovascular disease, but not impaired fasting glucose. The Funagata Diabetes Study. Diabetes Care. 1999 Jun;22 (6):920-4.
16. Rodriguez BL, Curb JD, Burchfiel CM, Huang B, Sharp DS, Lu GY, et al. Impaired glucose tolerance, diabetes, and cardiovascular disease risk factor profiles in the elderly. The Honolulu Heart Program. Diabetes Care. 1996 Jun;19 (6):587-90.
17. Tuomilehto J, Schranz A, Aldana D, Pitkaniemi J. The effect of diabetes and impaired glucose tolerance on mortality in Malta. Diabet Med. 1994 Mar;11 (2):170-6.
18. Butler WJ, Ostrander LD Jr, Carman WJ, Lamphiear DE. Mortality from coronary heart disease in the Tecumseh study. Long-term effect of diabetes mellitus, glucose tolerance and other risk factors. Am J Epidemiol. 1985 Apr;121 (4):541-7.
19. Barzigar A, Shojaei H. prevalence of atherosclerosis risk factors in Sowmesara district of Gilan in 1996. Journal ofKerman University. 1997 Winter;4 (4): 182-9.
20. Sharifi F, Azizi F. Prevalence of hyperlipidemia, overweight, and hypertension in diabetic and IGT patients comparing with normal subjects in Zanjan rural area. Pajouhesh Dar Pezeshki. 1997 Winter;21 (4): 41-50.
21. Azizi F. Diabetes mellitus in the Islamic Republic of Iran. IDF Bulletin. 1996; 4: 38-39.
22. Amini M, Afshin-Nia F, Bashardoost N, Aminorroaya A, Shahparian M, Kazemi M. Prevalence and risk factors of diabetes mellitus in the Isfahan city population (aged 40 or over) in 1993. Diabetes Res Clin Pract. 1997 Dec;38 (3):185-90.
23. Azizi F, Rahmani M, Emami H. Tehran Lipid and Glucose Study: Rationale and Design. CVD Prevention 2000.3 : 242-7.
24. The sixth report of the Joint National Committee on prevention, detection,evaluation, and treatment of high blood pressure.Arch Intern Med. 1997 Nov 24;157 (21):2413-46. Erratum in: Arch Intern Med 1998 Mar 23;158 (6):573.
25. World Health Organization: Diabetes mellitus: report of a WHO Study Group. Geneva, world

Health Organization. 1985 (Tech Rep. Ser. No 727).
26. Manolio TA, Savage PJ, Burke GL, Liu KA, Wagenknecht LE, Sidney S, et al. Association of fasting insulin with blood pressure and lipids in young adults. The CARDIA study. Arteriosclerosis. 1990 May-Jun;10 (3):430-6.
27. Modan M, Or J, Karasik A, Drory Y, Fuchs Z, Lusky A, et al. Hyperinsulinemia, sex, and risk of atherosclerotic cardiovascular disease. Circulation. 1991 Sep;84 (3):1165-75.
28. Morales PA, Mitchell BD, Valdez RA, Hazuda HP, Stern MP, Haffner SM. Incidence of NIDDM and impaired glucose tolerance in hypertensive subjects. The San Antonio Heart Study. Diabetes. 1993 Jan;42 (1):154-61.
29. Mitchell BD, Haffner SM, Hazuda HP, Valdez R, Stern MP. The relation between serum insulin levels and 8-year changes in lipid, lipoprotein, and blood pressure levels. Am J Epidemiol. 1992 Jul 1;136 (1):12-22.
30. Chu NF, Lee MM, Wang DJ, Chen LM, Ding YA, Shieh SM. The interrelationship between impaired glucose tolerance and other risk factors for cardiovascular disease: is it a predictor for cardiovascular disease? J Clin Epidemiol. 1994 May;47 (5):485-93.
31. Stern MP, Rosenthal M, Haffner SM. A new concept of impaired glucose tolerance. Relation to cardiovascular risk. Arteriosclerosis. 1985 Jul-Aug;5 (4):311-4.
32. Harris MI. Impaired glucose tolerance in the U.S. population. Diabetes Care. 1989 Jul-Aug;12 (7):464-74.
33. Harris MI, Hadden WC, Knowler WC, Bennett PH. Prevalence of diabetes and impaired glucose tolerance and plasma glucose levels in U.S. population aged 20-74 yr. Diabetes. 1987 Apr;36 (4):523-34.
34. Harris MI, Flegal KM, Cowie CC, Eberhardt MS, Goldstein DE, Little RR, et al. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults. The Third National Health and Nutrition Examination Survey, 1988-1994. Diabetes Care. 1998 Apr;21 (4):518-24.
35. Olatunbosun ST, Ojo PO, Fineberg NS, Bella AF. Prevalence of diabetes mellitus and impaired glucose tolerance in a group of urban adults in Nigeria. J Natl Med Assoc. 1998 May;90 (5):293-301.
36. Elbagir MN, Eltom MA, Elmahadi EM, Kadam IM, Berne C. A population-based study of the prevalence of diabetes and impaired glucose tolerance in adults in northern Sudan. Diabetes Care. 1996 Oct;19 (10):1126-8.
37. Sekikawa A, Tominaga M, Takahashi K, Eguchi H, Igarashi M, Ohnuma H, et al. Prevalence of diabetes and impaired glucose tolerance in Funagata area, Japan. Diabetes Care. 1993 Apr;16 (4): 570-4.
38. Ohmura T, Ueda K, Kiyohara Y, Kato I, Iwamoto H, Nakayama K, et al. Prevalence of type 2 (non-insulin-dependent) diabetes mellitus and impaired glucose tolerance in the Japanese general population: the Hisayama Study. Diabetologia. 1993 Nov;36 (11):1198-203.
39. Lillioja S, Mott DM, Howard BV, Bennett PH, Yki-Jarvinen H, Freymond D, et al. Impaired glucose tolerance as a disorder of insulin action. Longitudinal and cross-sectional studies in Pima Indians. N Engl J Med. 1988 May 12;318 (19):1217-25.
40. Ohlson LO, Larsson B, Svardsudd K, Welin L, Eriksson H, Wilhelmsen L, et al. The influence of body fat distribution on the incidence of diabetes mellitus. 13.5 years of follow-up of the participants in the study of men born in 1913. Diabetes. 1985 Oct;34 (10):1055-8.
41. Haffner SM, Stern MP, Hazuda HP, Pugh J, Patterson JK. Do upper-body and centralized adiposity measure different aspects of regional body-fat distribution? Relationship to non-insulin-dependent diabetes mellitus, lipids, and lipoproteins. Diabetes. 1987 Jan;36 (1):43-51.
42. Kritz-Silverstein D, Barrett-Connor E, Wingard DL. The effect of parity on the later development of non-insulin-dependent diabetes mellitus or impaired glucose tolerance. N Engl J Med. 1989 Nov 2;321 (18):1214-9.
43. Iso H, Kiyama M, Naito Y, Sato S, Kitamura A, Iida M, et al. The relation of body fat distribution and body mass with haemoglobin A1c, blood pressure and blood lipids in urban Japanese men. Int J Epidemiol. 1991 Mar;20 (1):88-94.
44. Falkner B, Sherif K, Sumner AE, Kushner H. Blood pressure increase with impaired glucose tolerance in young adult American blacks. Hypertension. 1999 Nov;34 (5):1086-90.
45. Report of the Expert Committee on the diagnosis and classification of diabetes mellitus. Diabetes Care. 1998; 21 (suppl): 5-19.
46. Rowe JW, Young JB, Minaker KL, Stevens AL, Pallotta J, Landsberg L. Effect of insulin and glucose infusions on sympathetic nervous system activity in normal man. Diabetes. 1981 Mar;30 (3):219-25.
47. Anderson EA, Hoffman RP, Balon TW, Sinkey CA, Mark AL. Hyperinsulinemia produces both sympathetic neural activation and vasodilation in normal humans. J Clin Invest. 1991 Jun;87 (6):2246-52.
48. Anderson EA, Balon TW, Hoffman RP, Sinkey CA, Mark AL. Insulin increases sympathetic activity but not blood pressure in borderline hypertensive humans. Hypertension. 1992 Jun;19 (6 Pt 2):621-7.

49. DeFronzo RA. The effect of insulin on renal sodium metabolism. A review with clinical implications. Diabetologia. 1981 Sep;21 (3):165-71.
50. Baron AD, Brechtel-Hook G, Johnson A, Hardin D. Skeletal muscle blood flow. A possible link between insulin resistance and blood pressure. Hypertension. 1993 Feb;21 (2):129-35.
51. Laakso M, Edelman SV, Brechtel G, Baron AD. Impaired insulin-mediated skeletal muscle blood flow in patients with NIDDM. Diabetes. 1992 Sep;41 (9):1076-83.
52. Williams SB, Cusco JA, Roddy MA, Johnstone MT, Creager MA. Impaired nitric oxide-mediated vasodilation in patients with non-insulin-dependent diabetes mellitus. J Am Coll Cardiol. 1996 Mar 1;27 (3):567-74.