Original Article

Diabetes and Associated Cardiovascular Risk Factors in Iran: The Isfahan Healthy Heart Programme

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Abstract

Introduction: Diabetes mellitus (DM) is one of the major health problems worldwide. The aim of this study was to detect the prevalence of DM and its associated risk factors in Iran. Materials and Methods: This cross-sectional study was performed in 3 cities in the central part of Iran on participants over the age of 19 years. Sampling was conducted by multi-stage randomised cluster method. Initially, a questionnaire consisting of demographic information, drug intake and smoking status was filled out. Later, a physical examination was performed, including the measurement of systolic blood pressure (SBP) and diastolic blood pressure (DBP), body mass index (BMI) and waist-to-hip ratio (WHR). Fasting blood sample was drawn and analysed for sugar, total cholesterol (TC), triglyceride (TG) and 2-hour postprandial glucose. A fasting blood sugar (FBS) of >126 mg/dL or a 2-hour plasma glucose of over 200 mg/dL was considered an indication of diabetes. The impaired glucose tolerance test (IGTT) was defined with 2-hour plasma glucose of 140 to 200 mg/dL and FBS <126 mg/dL. The collected data were analysed with Student's *t*-test, chi-square test and multiple logistic regression analysis. Results: This study was performed on 12,514 subjects (48.9% males and 51.1% females). The total prevalence of DM was 6.7% and 5.3% in urban and rural areas and 5.4% and 7.1% in males and females, respectively. The mean blood glucose rose with age in both sexes, and blood glucose was higher in females and in urban areas. IGTT, known and new DM heightens as age increased and more than half of the diabetes cases in all age groups were newly diagnosed. The mean blood pressure, age, BMI, waist circumference and serum lipids were higher in people with DM and IGTT especially in females. Obesity, a family history of DM, high blood pressure, high WHR and ageing were associated with a higher probability of DM, but sex had no effect on this probability. Discussion and Conclusion: Considering the high prevalence of DM in the central regions of Iran, providing vast educational programme to prevent this disease is essential and screening FBS tests, especially for obese subjects and those with a family history of DM, should be taken into account.

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Key words: Diabetes mellitus, Glucose tolerance test, Iran, Prevalence, Risk factor

Introduction

The incidence and prevalence of diabetes mellitus (DM) worldwide is increasing, due almost exclusively to an increase in non-insulin-dependent (type 2) DM, which represents more than 90% of all cases of diabetes.[1] Presently, there is a global pandemic of type 2 DM and its clinical sequelae. The World Health Organization (WHO) estimates that there will be 300 million people with diabetes worldwide by the year 2025, which is more than twice the estimated prevalence reported in 1995.[2] These figures are most likely a gross underestimation of the problem, given that as many as half of affected patients remain undiagnosed.[3] Historically, type 2 diabetes has been a public health problem principally in developed countries due to its close association with the "Western" lifestyle, though the greatest anticipated threat of diabetes over the next several decades

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belongs to developing countries.[2] Modernisation has resulted in increased rates of diabetes, primarily because of a decrease in physical activity, an increasing prevalence of obesity, and an increasing consumption of high-caloric diets in these nations.[4] In addition, increases in life expectancy will most likely translate into an increasing prevalence of DM in developing countries. DM is strongly associated with cardiovascular disease (CVD) risk, which is the primary cause of morbidity and mortality among patients with diabetes, accounting for more than 80% of deaths in this population.[5]

Given that the leading cause of morbidity and mortality for patients with diabetes is atherosclerotic vascular disease, knowledge of the epidemiology of diabetes and its associated cardiovascular complications is essential for targeting interventions designed to improve health outcomes in this high-risk population.

This study was performed as the baseline survey of a longitudinal community-based programme entitled the Isfahan Healthy Heart Program (IHHP) in the population of the central parts of Iran who were over 19 years of age. It aims to assess the current situation to facilitate the formulation of appropriate policies.

Materials and Methods

The survey was conducted in 3 cities in the central part of Iran (Arak, Isfahan and Najafabad) as part of the IHHP.[6]

The subjects were selected by multi-stage random sampling with clusters in the urban and rural areas. The number of clusters was in accordance with the total population of the 3 cities. Having resided for more than 10 years in these cities, not being pregnant for females and being mentally healthy were the criteria for participating in this study. Written informed consent was obtained from subjects after full explanation of the procedure involved.

Initially, a questionnaire was completed at each subject's home by trained nurses. It contained demographic information, previous history of DM, consumption of relevant medication and family history of diabetes in first-degree relatives.

The subjects then proceeded to certain centres, where blood samplings and clinical check-ups after 12 to 14 hour fasting were carried out. In addition to fasting blood sugar (FBS), 2-hour plasma glucose (2hPG) was also measured after 2 hours and afer consumption of 75 g of glucose. Serum lipids, including total cholesterol (TC) and triglyceride (TG), were also measured using the relevant fasting blood sample. All the blood sampling procedures were performed in the central laboratory of the Isfahan Cardiovascular Research Center using the enzyme-linked method.

Subjects were weighed with light clothes and no shoes, and their waist and hip measurement and weight were also noted. The blood pressures of the individuals were measured twice with a standard barometer, with the subjects in a sitting position, and the average blood pressure was taken into consideration.

The definition of impaired plasma glucose levels was in accordance with the criteria of the World Health Organization.[7] A FBS of ≥126 mg/dL or a 2-hour blood sugar of >200 mg/dL or the consumption of blood sugar-reducing medications defined DM. If a person had a previous history of diabetes and/or was under the treatment of insulin and/or an oral blood sugar reducing medication, they would be considered as a known DM (KDM). If the patient did not have any previous history of the disease or consumption of medication, they would then be considered as a new DM (NDM). Impaired glucose tolerance test (IGTT) applied to cases in which the patient was not a KDM and his FBS was <126 mg/dL, but the 2-hour plasma glucose was 140 to 200 mg/dL. If the FBS was in the range of 110 to 126 mg/dL and the 2-hour plasma glucose was <140 mg/dL, it was considered as impaired fasting glucose (IFG); whereas, if the FBS was below 110 mg/dL and the 2-hour plasma glucose <140 mg/dL, it was considered a sign of normal glucose tolerance (NGT). Any subject who reported smoking cigarettes of any number was considered a current smoker.[8]

In terms of physical activity, if a person exercised at least 2 times a week for at least 15 minute regularly, this would then be identified in the research as regular physical activity.[9] Blood pressure was measured twice and if the average was >140/90, this was defined as high blood pressure.[10] A waist-to-hip ratio (WHR) of <80 in women and <95 in men was considered normal.[11]

Body mass index (BMI) was calculated based on the formula weight/height^2 and subjects were considered to be of normal weight if their BMI was <25 kg/m^2, overweight if their BMI was 25 kg/m^2-29.9 kg/m^2 and obese if their BMI was 30 kg/m^2.[12]

Statistical Analysis

The data were analysed by SPSS 11.5 software and analysed with Student's *t*-test, chi-square test and multiple regression analysis.

Results

This cross-sectional study involved 12,514 subjects who provided informed consent.

In this cohort, there were 6391 (51.1%) women and 6123 (48.9%) men. They were divided into 6 age groups: 19-24 years, 25-34 years, 35-44 years, 45-54 years, 55-64 years and ≥65 years. In addition, they were divided into 2

Table 1. Mean and Standard Deviation of Fasting Blood Sugar (mg/dL) Based on Age, Sex and Area of Residence

Age group (y)	Sex		Area of residence		Total
	Female	Male	Urban	Rural	
19-24	75.84 ± 10.56	76.62 ± 21.42	76.16 ± 18.66	76.41 ± 10.21	77.94 ± 19.75
25-34	78.62 ± 26.11	79.69 ± 23.64	79.34 ± 27.75	78.61 ± 14.82	80.23 ± 27.37
35-44	84.51 ± 33.86	83.46 ± 29.93	83.80 ± 29.43	84.72 ± 83.33	83.77 ± 32.21
45-54	90.21 ± 43.94	87.57 ± 30.10	89.92 ± 41.79	86.40 ± 25.21	88.15 ± 38.17
55-64	95.11 ± 36.86	93.89 ± 40.43	95.56 ± 39.59	91.89 ± 36.05	92.85 ± 36.91
≥65	98.14 ± 52.29	94.74 ± 41.93	98.70 ± 51.25	89.72 ± 32.44	91.94 ± 42.81
Total	84.02 ± 33.57	53.54 ± 29.92	84.19 ± 33.48	82.74 ± 26.84	83.80 ± 31.84

subgroups of urban and rural subjects, based on their place of residence.

Table 1 shows the mean FBS based on sex, area of residence and age. The mean FBS rose with age and was higher in the urban areas.

Table 2 demonstrates the prevalence of DM and impaired blood sugar levels based on age groups, sex and area of residence. The total prevalence of DM in the central regions of Iran was 6.3%. The prevalence of DM in urban and rural areas was 6.7% and 5.3%, respectively, 5.4% in men and 7.1% in women.

Impaired fasting glucose, IGTT, KDM and NDM cases increased with age and more than half of all diabetic patients in all age groups had been newly diagnosed. BMI, WHR, SBP, DBP, total cholesterol, serum triglyceride and family history of DM of subjects with normal blood sugar was lower than those diabetics or those who had IGTT (Table 3).

Table 4 shows the relationship between the variables and the existence of DM specifies that obesity, a family history of DM, high BP, abdominal obesity and ageing is associated with a higher probability of diabetes but sex has no significant effect on this probability.

Discussion

DM is one of the major CVD risk factors worldwide The first systematic epidemiologic studies on diabetes in Iran started from 1992 in Eslamshahr, Tehran, Isfahan and then Boushehr. According to the primary studies, it was estimated that at least 1.2 million people suffer from DM in Iran.[13] Based on these studies, the prevalence of DM in the over 30-years-old population of Tehran was 7.2% (7.6% of women and 7.1% of men). According to numerous reports, adult diabetes is considered a general health hazard in Iranian and other third-world communities.[14]

In European societies, the prevalence of age-uniformed type II diabetes in people over 25 years of age is 3% to 10%. Western societies and Indian immigrants in the US, the Chinese and Hispanic Americans are considered high-risk population and the prevalence of DM is 14% to 20%. The highest reported prevalence is among the Pima/Papago Indians – 50%.[15] The prevalence of diabetes in the US is approximately 7%.[16] The prevalence of DM of 6.3% as reported in this study is considerable and requires serious consideration since diabetes is a debilitating chronic disease. The prevalence of DM is higher in urban areas, highlighting the fact that lifestyles in these areas must change.

As for the relation between sex and DM, the prevalence of DM is higher in women than in men, partly due to the higher predisposition of women to this disease, and higher prevalence of unhealthy lifestyle habits in women than men.[17] According to studies conducted in Isfahan, the prevalence of type II diabetes in women who were overweight or obese was higher than that of men who were

Table 2. Percentage of Subjects with Diabetes and Percentage with Impaired Fasting Glucose Overall by Sex, Area of Residence, and Age Group

Parameters	IFG (%)	IGTT (%)	NDM (%)	KDM (%)	Total DM (%)
Sex					
Men	0.4	3.7	2.1	3.3	5.4
Women	0.5	6.2	2.5	4.6	7.1
Area of residence					
Urban	0.4	4.4	2.6	4.1	6.7
Rural	0.5	6.7	2	3.3	5.3
Age group (y)					
19-24	0.1	1.2	0.4	0.3	0.7
25-34	0.3	2.7	0.9	0.7	1.6
35-44	0.2	6.2	2.1	3.4	5.5
45-54	0.8	7.0	4.2	6.7	10.9
55-64	1.0	9.1	5.9	10.5	16.4
≥65	1.2	10.9	6.1	12.7	18.8
Total	0.5	5.0	2.3	4.0	6.3

DM: total cases of diabetes mellitus; IFG: impaired fasting glucose; IGTT: impaired glucose tolerance test; KDM: known diabetes mellitus; NDM: new diabetes mellitus

Table 3. Risk Factor Levels Among Individuals with Normal Blood Sugar, Diabetics and Those who Have Impaired Glucose Tolerance Test

	NGT	IFG	IGTT	NDM	KDM
Age (y)	37.45 ± 14.31	49.19 ± 15.88	48.08 ± 15.15	50.79 ± 14.11	54.60 ± 12.85
Proportion male (%)	49.8	44	36.2	43.3	43.4
Mean BMI (kg/m^2)	25.49 ± 5.46	27.81 ± 7.02	27.55 ± 5.38	27.54 ± 5.49	27.78 ± 6.20
Mean waist-to-hip ratio	0.89 ± 0.91	0.92 ± 0.11	0.93 ± 0.09	0.94 ± 0.10	0.96 ± 0.09
Mean systolic blood pressure (mm Hg)	114.12 ± 18.11	119.48 ± 19.57	121.77 ± 21.50	129.09 ± 23.85	131.64 ± 23.32
Mean diastolic blood pressure (mm Hg)	74.76 ± 10.75	77.66 ± 12.76	78.24 ± 11.84	81.13 ± 12.90	82.81 ± 12.75
Mean total cholesterol (mg/dL)	195.31 ± 54.60	219.14 ± 54.21	222.01 ± 70.40	229.69 ± 58.89	229.76 ± 57.99
Mean triglyceride (mg/dL)	162.11 ± 101.25	197.07 ± 134.72	203.87 ± 127.22	252.36 ± 164.83	255.90 ± 161.80
Current active smoker (%)	14.5	15.8	7.6	8.4	10.5
Family history of diabetes mellitus (%)	14.8	15.8	19.7	20.7	37.9
Regular physical activity (%)	15.3	19.3	9.6	11.7	11.1

IFG: impaired fasting glucose; IGTT: impaired glucose tolerance test; KDM: known diabetes mellitus; NDM: new diabetes mellitus; NGT: normal glucose tolerance

Table 4. Multiple Logistic Regression Model of Variables Associated with Type 2 Diabetes

Parameter	Logistic regression coefficient	OR	95% CI	ρ
Age (y)	0.05	1.05	1.05-1.06	≤0.0001
Sex				
Female		1*		
Male	0.09	0.91	0.72-1.11	0.36
BMI (kg/m^2)				
<25		1*		
25-29.9	0.25	1.29	1.07-1.55	0.008
≥30	0.52	1.69	1.37-2.08	≤0.0001
WHR				
Normal		1*		
High	0.53	1.29	1.35-2.14	≤0.0001
Hypertension				
No		1*		
Yes	0.51	1.67	1.39-2.00	≤0.001
Family history of diabetes mellitus				
No		1*		
Yes	1.16	3.20	2.68-3.83	≤0.0001

95% CI: 95% confidence interval; BMI: body mass index; OR: odds ratio; WHR: waist-to-hip ratio

* Reference category: multiple logistic regression model includes age, sex, BMI, WHR, family history of DM, hypertension, total cholesterol and triglyceride: as risk factors. Statistically significant variables shown, except for sex and BMI.

overweight and obese.[18] DM is directly associated with a few cardiovascular risk factors, including age, obesity, high blood pressure and previous family history.[19]

As observed from the results, there was also a significant relationship in this study between the increase of FBS and age, family history, BMI and high BP. In this study, samples of lower age groups had lowest prevalence of DM. The prevalence of diabetes rose with age.[20] In NHANES III, the prevalence of diagnosed and undiagnosed diabetes was 1.6% in men aged 20 to 39 years, rising to 21.1% in men older than 75 years of age.[21] Similarly, in the Framingham Study, glucose intolerance or diabetes was present in 30% to 40% of study subjects older than 65 years of age.[22]

Consistent with these studies, we found that the prevalence of DM was higher in the over 50 years age group compared to other groups. Concurring with our study, in developing countries, the largest population of diabetics fell into the 45- to 64-years category.[23]

This study showed a relationship between high blood sugar and positive family history of DM. Type 2 diabetes appears to have strong genetic associations. Studies in twins have demonstrated that the concordance rates of type 2 diabetes in monozygotic twins range between 34% and 83%. [24] The broad range of observed correlations suggests both a complex genetic predisposition and an interaction between environmental and genetic factors in the pathogenesis of type 2 diabetes. People who have one first-degree relative suffering from diabetes have a 40% risk of having this disease. If diabetes is seen in both parents, this risk is doubled.[25]

Several longitudinal cohort studies have demonstrated the association between obesity and glucose intolerance.[26] Data from NHANES III show that 67% of those with type 2 DM have a BMI that meets the criteria for being overweight, and almost half have a BMI that meets the definition of obesity.[27] In the Iowa Women's Health Study, women in the highest quintile of BMI had a relative risk of 29 for the development of diabetes over the 12-year follow-up period.[28] Waist circumference and WHR may be even

better markers of diabetes risk than either weight or BMI alone.[29] Even among non-obese patients, abdominal distribution of fat and increased WHR are independently associated with the risk for diabetes.[30] Although the molecular mechanisms by which obesity contribute to glucose intolerance remain elusive, they most likely involve a combination of genetic factors and mechanisms in which skeletal myocytes and central adipocytes play a deterministic role.[31] Basu et al[32] showed that obesity is one of the major risk factors in the incidence of diabetes. In our study, there was a positive correlation between obesity and diabetes prevalence.

In this study, there was a significant association between an increase in systolic and diastolic blood pressure and an increase in blood sugar. Epidemiological studies report at least 2-fold incidence of high blood pressure in diabetics.[33] In the NHANES II study, the prevalence of hypertension, defined as blood pressure >160/95 mm Hg among individuals aged 65 to 74 years, increased with decreasing glucose tolerance. Approximately 60% of subjects with diabetes, 50.7% of those with IGT, and 38.3% of those with normal glucose were affected.[34] In NHANES II, with hypertension defined as blood pressure >140/90 mmHg, 71% of patients with diabetes had hypertension.[35]

In addition, the considerable percentage of diabetics who were not diagnosed in this study and similar studies could reflect how little people know about diabetes, physicians' little attention towards the signs and symptoms of the disease and the necessity of diabetes screening. Due to the specific nature of type II diabetes, an approximate figure of 50% of the total cases were not diagnosed even in the US.[36] This might be caused by the lack of versatility in the health systems for early diagnosis and management of DM, due to the burden caused by other complications and problems of this disease.

Data from the Nurses' Health Study demonstrated that even physical activity of moderate intensity and duration was associated with a decreased risk for diabetes.[37] The favourable impact of physical activity on diabetes risk extends beyond issues of weight management. Physical activity is directly associated with improved glyco-metabolism, as demonstrated by decreased insulin levels, increased insulin sensitivity, and a lower incidence of diabetes.[38] We found that a low percentage of our population had adequate physical activity.

Even with good control, type 2 DM patients often have elevated triglycerides and depressed HDL-C, which is likely to be accompanying abnormalities of lipids in type 2 diabetes. It develops concomitantly with the failure of insulin activity, which in turn leads to the release of fatty acids from adipose tissue, increased delivery of free fatty acids to the liver, and increased hepatic synthesis of very low-density lipoproteins.[39] This abnormal lipid profile, as seen in this study, is characterised by modestly elevated LDL cholesterol, high triglyceride levels, and is associated with markedly increased cardiovascular risk among diabetic patients.[40]

In conclusion, this study showed a meaningful relationship between CVD risk factors and DM in the central regions of Iran. Therefore, identifying and reducing these factors are of great importance to the health of the general population. The matters discussed above highlights the necessity to pay more attention and have more programmes towards the control of this important public health problem. The high prevalence of DM and the considerable percentage of non-diagnosed diabetics in these regions make it necessary to generalise the screening methods of the disease for the population at risk and for those who have risk factors such as positive previous family history, are overweight or obese and older than 30 years of age. In addition, promoting the level of general knowledge on the risk factors of DM or its symptoms and side effects can play an effective role in the prevention and control of the disease, and timely diagnosis. This can be done through the mass media or the distribution of educational pamphlets or books written in simple language.

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