# DIABETIC COMPLICATIONS AND RISK FACTORS IN RECENTLY DIAGNOSED TYPE II DIABETES: A CASE-CONTROL STUDY

MH Khazai<sup>(1)</sup>, B Khazai<sup>(2)</sup>, Z Zargaran<sup>(3)</sup>, Z Moosavi<sup>(4)</sup>, F Khadivi Zand<sup>(5)</sup>

## **Abstract**

INTRODUCTION: Due to a worldwide increase in the incidence of type II diabetes, it will likely continue to be a major cause of morbidity and mortality in the future. Given that usually a mean of 4-7 years has passed from the initial onset of type II diabetes until the time of diagnosis, a great number of patients have already been affected by one or more diabetic complications by the time of diagnosis. Our objective was to evaluate the prevalence of diabetic complications and risk factors in recently diagnosed type II diabetic patients in the city of Mashhad, Northeast Iran.

METHODS: This cross-sectional prevalence study was performed between March, 2002 and September, 2002. The study group included 200 type II diabetics whose disease had been diagnosed within one year prior to the start of our study. The collected data included medical history, physical examination and clinical tests, including urinalysis (for evaluation of macroproteinuria), blood sampling (for evaluation of serum glucose and lipid levels), and electrocardiography (EKG). Several common indicators of diabetic complications were analyzed.

RESULTS: Of the 200 patients studied, 66 were male and 134 were female. The mean age of the patients was 52.2 years for men and 46.8 for women at the time of diagnosis. Overall, 74.2% of the patients were shown to have been affected by one or more diabetic complications prior to diagnosis with type II diabetes.

CONCLUSIONS: Formulating a new screening program may help us diagnose type II diabetes earlier and control it more effectively. This may lead to a reduction in morbidity and mortality in type II diabetes patients.

**Keywords:** Type II diabetes mellitus, retinopathy, neuropathy, nephropathy, macrovascular complications, body mass index.

ARYA Journal, 2006, 2(2): 79-83

### Introduction

Diabetes mellitus is the most common cause of endstage renal disease, non-traumatic lower extremity amputations and working-age adult blindness in the United States.<sup>1</sup> Type II diabetes accounts for 90-95% of total diabetes cases. Because of its gradual progression, usually a mean of 4-7 years has passed from the initial onset of type II diabetes until the time of diagnosis. About 50% of type II diabetes patients have already been affected by one or more of the main diabetic complications at the time of diagnosis.<sup>2</sup> Diabetes mellitus has a relatively high incidence in Iran. The Tehran Lipid and Glucose Study reported in 2001 that 9.8% of males (5.7% undiagnosed and 4.1% diagnosed) and 11.1% of females (5.7% undiagnosed and 5.4% diagnosed) over 20 years of age are affected by this disease in Tehran.<sup>3</sup> Type II diabetes mellitus risk factors have been defined to a large extent<sup>1</sup> and mainly include a positive family history of diabetes, obesity,<sup>4</sup> age, race, a history of impaired fasting blood glucose (FBS) level or impaired glucose tolerance test, a positive history of gestational diabetes mellitus (GDM) and delivery of a fetus weighing more than 9 pounds, hypertension,<sup>5</sup> and dyslipidemia.

- (1) Mohammad Hassan Khazai, Khorasan Diabetes Center, Mashhad University of Medical Sciences, Mashhad, Iran
- E-mail: bahram\_khazaee@yahoo.com Tel: +98 (511) 7680999 (2) Bahram Khazai, Khorasan Diabetes Research Center
- (3) Zahed Zargaran, Khorasan Diabetes Research Center
- (4) Zohreh Moosavi, Department of Internal Medicine, Emam Reza Medical Center, Mashad University of Medical Sciences
- (5) Farhad Khadivi Zand, Bu-Ali Research Institute

Corresponding author: Mohammad Hassan Khazai Date of submission: July 11, 2006 Date of acceptance: October 24, 2006 The CDC (Center for Disease Control) recommends that individuals over 45 years of age undergo screening with FBS levels every three years regardless of the presence of other risk factors for the development of diabetes.

If other risk factors are present, recommendations are that the testing intervals should be shortened, although this is not accepted by the American Diabetes Association (ADA). Presently, the ADA recommends screening only of selected populations of patients seen in office-based practices, specifically patients having one or more risk factors of type II diabetes. Because the incidence of diabetes is low in asymptomatic risk-free people, ADA maintains that screening of whole populations is not justified.<sup>6</sup>

Considering these facts and the high prevalence of diabetes in Iran, we decided to evaluate the complications and risk factors for the development of diabetes in recently diagnosed type II diabetic patients in the city of Mashhad, Iran, in hopes that these results will lead to improved screening programs. Our results allow us to make suggestions for the screening of high-risk individuals. This may lead to earlier diagnosis and more effective control of type II diabetes, reduction of its morbidity and mortality and potentially delayed onset of its complications.

## Materials and methods

We conducted a cross-sectional prevalence study of 200 recently diagnosed (less than a year before the study) type II diabetic patients in Mashhad.

The subjects were selected from among patients receiving treatment at Khorasan Diabetes Center, as well as patients directly referred to us by their endocrinologists. The inclusion criterion was being diagnosed with type II diabetes within one year prior to the start of the study.

All patients provided their written informed consent and a form was completed for each patient using the same protocol. Patients were interviewed to collect information on family history, history of sedentary life, and history of GDM.

Height and weight of patients were measured and body mass index (BMI) was calculated.

Blood pressure was measured in both supine and sitting positions and neurological examination was done for each patient.

Sensory deficits were evaluated by means of a tuning fork and fixed monofilament test.

Swallowing problems, periodic diarrhea and constipation, orthostatic hypotension and impotency

were assessed for the evaluation of autonomic nervous system complications. The patients were referred to an ophthalmologist for fundoscopy. We looked for macroproteinuria in two different urine analyses to diagnose nephropathy (we did not look for microproteinuria). We used EKG to detect cardiopathy and performed pulse examinations (with palpation) to evaluate peripheral blood vessel involvement.

We also looked for other symptoms such as intermittent claudication and sexual dysfunction. We looked for history of cerebrovascular accident (CVA) and its signs and symptoms and examined the patients' feet to exclude diabetic foot. We examined the patients for diabetic dermopathy and skin infections. 14,15

Serum levels of low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and triglyceride (TG) were measured for every patient. These data were evaluated according to the criteria of the World Health Organization (WHO) and were analyzed using Chi square test (for the proportion of patients having complications or the risk factors).

#### Results

One-hundred thirty-four (67%) patients were female and 66 (33%) were male. This pattern of the female-to-male ratio was due to the fact that for cultural reasons, females had been more likely to use the facilities of Khorasan Diabetes Center.

Polyuria, polydipsia and weight loss (classic diabetes symptoms) were the most common symptoms and were detected in 79% of the patients (Table 1).

Forty-three (21.5%) of the patients complained of weakness and fatigue and 17.5% mentioned a history of transient blurred vision. These symptoms had been experienced by the patients before the diagnosis of the disease.

In 3% of the patients the disease was diagnosed by diabetic complications (mainly resistant skin infections). Ninety-one patients (40% of the men and 48% of the women) had a history of diabetes in their first-degree relatives (Table 2). The mean age was 52.2 years in men and 46.8 years in women. The ages of the patients ranged between 14 and 77 years. 76% of men and 86% of women had a BMI equal to or greater than 25.

22.5% of the patients had abnormal systolic blood pressure (BP) and 17.5% had abnormal diastolic blood pressure (BP).

**TABLE 1.** Prevalence of symptoms in type II diabetic patients at the time of diagnosis and before that

Symptoms	Men	Women	Total
Diagnosed regardless of symptoms (accidentally)	18%	18%	18%
Polyuria, polydipsia, weight loss	81%	78%	79%
Weakness and fatigue	18%	24%	21%
History of blurred vision	12%	20%	17.5%
Presentation with long-term diabetic complications	3%	3%	3%

TABLE 2. Prevalence of risk factors in type II diabetic patients

Risk factors	Men	Women	Total	
Sedentary life	41%	50%	47%	
Positive family history	40%	48%	45.5%	
Age ≥45	52.2 years	46.8 years	48.6 years	
BMI ≥25	76%	86%	82%	
Abnormal diastolic blood pressure	16%	18%	17.5%	
Abnormal systolic blood pressure	21%	22.5%	22.5%	
Low HDL-C	30%	45%	36.5%	
High LDL-C	24%	36%	32%	
High TG	21%	25.5%	24.5%	

(BMI=body mass index; HDL-C=high-density lipoprotein cholesterol; LDL- C=low-density lipoprotein cholesterol; TG=triglyceride)

**TABLE 3.** Prevalence of diabetic complications in type II diabetic patients at the time of diagnosis

Complications			Men	Women	Total
Microvascular	Retinopathy (	Retinopathy (Mild to moderate NPDR)		7.5%	11%
	Neuropathy	Autonomic	6%	18%	14%
		Mononeuropathy	0%	1.6%	1.1%
		Superficial sensory deficit	12%	24%	20%
		Deep sensory deficit	3%	8%	6.5%
	Nephropathy	Nephropathy (macroproteinuria)		0%	3%
Macrovascular	IHD		1.5%	2.2%	2%
	History or syr	History or symptoms of CVA		0.7%	0.5%
	Peripheral blo	Peripheral blood vessel defects		4.4%	4%
Sexual complications		12%	1.5%	5%	
Diabetic foot		0%	3%	2%	
Dermatologic complications		5%	6%	5.5%	

(NPDR=Nonproliferative diabetic retinopathy; IHD=Ischemic heart disease; CVA=Cerebrovascular accident)

24.5% of the patients had high triglyceride (TG) levels, 32% had high low-density lipoprotein cholesterol (LDL-C) and 36.5% had low high-density lipoprotein cholesterol (HDL-C). Retinopathy was detected in 18% of the males and 7.5% of the females (mild to moderate non-proliferative diabetic retinopathy) (Table 3).

Macroproteinuria was detected in 9% of the men and none of the women. 6% of the men and 18% of the women had autonomic neuropathy including orthostatic hypotension. 12% of the men and 1.5% of the women had sexual dysfunction. Mononeuropathy was detected in none of the men and 1.6% of the women; impaired superficial sensation was detected in

12% of the men and 24% of the women, while 3% of the men and 8% of the women had deep sensory deficits. One of the patients was a 35-year-old woman from Sabzevar who had presented with Charcot's joints in both ankles and feet.

This was the symptom which had led to the diagnosis of type II diabetes. 1.5% of the men and 2.25% of the women had evidence of ischemic heart disease (IHD) in EKG and 3% of the men and 4.45% of the women had peripheral blood vessel involvement. None of the men and 0.7% of the women had a history of CVA.

5% of the men and 7% of the women had dermatologic complications including persistent fungal infections and diabetic dermopathy.

#### Discussion

Type II diabetes has reached epidemic proportions and is projected to continue to increase in prevalence in the future, especially in developing countries.<sup>18</sup> This upward trend is mainly attributed to a so-called "nutritional transition" (increased availability of food combined with reduced physical activity).

For example, obesity has become a pandemic phenomenon and the prevalence of overweight has doubled in children aged 6-11 years and tripled among those aged 12-17 years from 1980 to 2000 alone in the United States. More importantly, 60% of overweight children and adolescents have at least one additional risk factor such as elevated BP and 25% have 2 or more risk factors.

Type II diabetes mellitus has been estimated to account for 8-45% of all new cases of diabetes mellitus in children and adolescents.

In addition, adults have also demonstrated this disturbing combination of obesity combined with lack of exercise.<sup>19</sup> In our study, we found that nearly all of our patients had one or more than one of the diabetic risk factors, especially high BMI and low physical activity. The majority of our patients (79%) had classic diabetes symptoms or associated symptoms of type II diabetes mellitus and in total, 74.2% of our patients had been affected by one or more than one diabetic complications.

In a study performed in 1999-2000 in Slovakia (the Slovak population) on 3424 recently diagnosed type II diabetics aged up to 70 years, 95.2% had a positive history of sedentary lifestyle, 87.6% were overweight or obese, 44.7% had a positive family history of type II diabetes mellitus, 67.3% had hypercholesterolemia, 66.5% had hypertriglyceridemia, and 67.9% had hypertension. 25.5% of these patients had microvascular complications and 22.8% had IHD.<sup>16</sup> In another study performed in 2001 in the United

Kingdom, 165 Asian and 127 European type II diabetic patients were evaluated. In these groups the prevalence of macrovascular complications was 15.7% in Asians and 9.4% in Europeans. Retinopathy was detected in 17.5% of Asians and 7.9% of Europeans, while nephropathy was detected in 18.1% of Asians and 7.8% of Europeans.

The difference in prevalence rates between Asians and Europeans was due to inadequate blood glucose control in Asians compared with Europeans, as well as the lower level of HDL-C and higher BP in Asians.<sup>17</sup>

Considering the high prevalence of diabetic complications and the mean age at the time of diagnosis (48.6 years) in our population, we propose that periodic FBS screening testing (every three years) be performed for Iranians aged 40 years or older with at least one diabetic risk factor (nearly all of our patients had at least one risk factor).

It is obvious that the proposed screening interval should be shortened in those with several risk factors of type II diabetes mellitus. Screening can be done by physicians encountering such patients in the office and may lead to timely diagnosis.

The screening strategy we propose is consistent with the basic objective of modern diabetic management, the prevention of complications.<sup>20</sup>

## Acknowledgements

We appreciate the financial support of the Research Deputy of Mashhad University of Medical Sciences and the cooperation of the staff of the Khorasan Diabetes Center; Dr. Farzin Majid Fayyaz, Mr. Firoozi and Miss Pooreskandari. We also thank Dr. Byrd James Brian who assisted us in editing this article.

# References

- 1. Sherwin RS. Diabetes mellitus. In: Cecil RL, Goldman L, Bennett JC, editors. Cecil textbook of medicine. 21st ed. Philadelphia: WB Saunders, 2000:1263-1285.
- 2. Powers AC. Diabetes mellitus. In: Braunwald E, Fauci AS, Kasper DL, Hauser SL, Longo DL, Jameson JL, editors. Harrison's principles of internal medicine. 15th ed. New York: McGraw-Hill, 2001:2109-2138.
- 3. Endocrine Research Center (Iran). Tehran lipid and glucose study. Tehran: National Research Council and Ministry of Health and Medical Education, 2001.
- 4. Bray GA. Obesity. In: Fauci AS, Longo DL, Kasper DL, Braunwald E, Martin JB, Isselbacher KJ, et al., editors. Harrison's principles of internal medicine. 14th ed. New York: McGraw-Hill,1998:454-62.
- 5. Williams GH. Approach to the patient with hypertension. In: Fauci AS, Longo DL, Kasper DL, Braunwald E, Martin JB, Isselbacher KJ, et al., editors. Harrison's principles of internal medicine; 14th ed. New York: McGraw-Hill,1998:35-203.
- 6. American Diabetes Association (US). Report of the expert committee on the diagnosis and classification of diabetes mellitus. Diabetes Care, Supplement 1; 2003:26.
- 7. Macleod AF, Sonksen PH. Diabetic neuropathy. In: Shaw KM, editor. Diabetic complications. Chichester, England: John Wiley & Sons,1996:27-52.
- 8. Jaspan JB. The neuropathies of diabetes. In: Degroot LJ, Jameson JL, editors. Endocrinology. Philadelphia: WB Saunders; 1989:1484-1491,1498.
- 9. International Diabetes Federation (IDF), (European Region). Guide Lines for Diabetes Care. Brussels: IDF; August, 1998:14-23.

- 10. Alberti KGMM, Zimmet P, Defronzo RA, editors. International textbook of diabetes mellitus, 2nd edition. Chichester, England: John Wiley & Sons; 1997.
- 11. Veves A, editor. Clinical management of diabetic neuropathy (contemporary endocrinology). Totowa, New Jersey: Humana Press; 1998.
- 12. Hasslacher C, editor. Diabetic neuropathy. Chichester, England: John Wiley & Sons; 2001.
- 13. Dyck PJ, Thomas PK, editors. Diabetic neuropathy. Philadelphia: WB Saunders; 1999.
- 14. Mackool BT, Lowitt MH, Dover JS. Skin manifestations of diabetes mellitus. In: Kahn CR, Weir GC, editors. Joslin's diabetes mellitus. 13th ed. Philadelphia: Lea & Febiger;
- 1. 1994:49-90.
- 15. Williams R, Herman W, Kinmonth AL, Wareham NJ, editors. The evidence base for diabetes care. Chichester, England: John Wiley & Sons; 2002.

- 16. Krahulec B, Vozar J. Pracovana Skupina Pre Detekciu Vascularynch Komplikacii. Diabetu Na Slovensku. Vnitr Lek 2002; 48(11):1031-8.
- 17. Chowdhury TA, Lasker SS. Complications and cardiovascular risk factors in South Asians and Europeans with early-onset type II diabetes. QJMed 2002; 95:241-246
- 18. Taylor R. Causation of type II diabetes--The Gordian Knot unravels. NEJM 2004;350:639-641.
- 19. Dietz WH. Overweight in childhood and adolescence. NEJM 2004;350:855-857.
- 20. Keen H. Therapeutic objectives and their practical achievement in type II diabetes. Journal of Diabetes and Its Complications 2000;14:180-184.