Prevalence of Type 2 Diabetes Complications and their Contributing Factors in Yazd Province

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Received: 15 June 2009 - **Accepted:** 20 July 2009

ABSTRACT

BACKGROUND: Type 2 diabetes is a common disorder recognized as a major health problem in Iran. Diabetes is a major source of morbidity, mortality and economic cost to society. Diabetic patients are at risk of experiencing macrovascular and microvascular complications of diabetes. The aim of this study was to assess the prevalence of type 2 diabetes complications and their contributing factors.

MATERIAL AND METHODS: This cross-sectional study was carried out on 1000 the type 2 diabetic patients referred to Yazd Diabetes Research Center. All diabetic patients underwent the specific tests for retinopathy, nephropathy, neuropathy, peripheral vascular diseases (PVD) and cardiovascular diseases (CAD). Logistic regression analysis was used to find out strength of association of risk factors with a specific complication.

RESULTS: In this study 1000 type 2 diabetic patients (457 male, 543 female) were studied. Nephropathy was diagnosed in 285 (28.5%), retinopathy in 519 (51.9%), CAD in 251 (25.1%), PVD in 143 (14.3%), CVA in 109 (10.9%) and foot ulcer in 84 patients (8.4%).

CONCLUSION: In this study the most important contributing factors in diabetic complications were age, duration of diabetes, systolic and diastolic blood pressure, glycated hemoglobin and Body Mass Index (BMI). So glycemic and blood pressure control can prevent diabetic complications or at least delay them.

KEY WORDS: Microvascular and macrovascular complications, type 2 diabetes.

INTRODUCTION

Type 2 diabetes is a common disorder recognized as a major health problem in Iran. It is estimated that more than 1.5 million people are affected by diabetes in Iran, (1) and the prevalence of diabetes in Yazd is evaluated as 14.52% (2). Diabetes is a major source of morbidity, mortality and economic cost to society. Diabetic patients are at risk of experiencing macrovascular and microvascular complications of diabetes (3).

The acute and chronic complications of diabetes are major causes of hospital admissions, blindness, renal failure, amputation, stroke and coronary heart disease (4,5). These conditions are the direct end-points of microvascular complications that are specific to diabetes and which include retinopathy, nephropathy and neuropathy (1). Diabetes mellitus is an independent risk factor for the development of atherosclerosis (6). On the other hand, atherosclerosis or macrovascular disease is responsible for more than 50% of all deaths in patients with type 2 diabetes (4). Cardiovascular disease accounts for most cases of diabetic macrovascular complications,

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the remainder are caused by cerebrovascular complication events and peripheral vascular disease (7). The results of a population-based study suggest that there is a 10-fold increase in coronary artery disease among diabetic patient when compared with the characteristically low rate among non-diabetic control (8). Identifying contributing factors of diabetic complications, makes it possible to control these complications and can lead to reduction in morbidity and health care costs (9,10 and 11). This study was performed to define more clearly the risk factors influencing susceptibility to chronic complications in type 2 diabetic patients.

METHODS

This cross-sectional study was carried out in type 2 diabetic patients referred to Yazd Diabetes Research Center. A total of 1000 type 2 diabetic patients, including new and review diabetes cases according to ADA criteria (12) were studied from June 2006 to June 2007. All diabetic patients registered at diabetic clinic were screened for diabetes and its complications. Blood glucose level estimation was done by colorimetry method in venous blood (in WL 546 nm). Glycosylated hemoglobin (GHb) was measured by HPLC method using DS5 analyzer. Each subject underwent a detailed history and complete clinical examination. Details regarding age, sex, socioeconomic status and duration of diabetes were recorded for all the patients. Blood pressure was recorded in lying down, sitting and standing positions at intervals of five minutes and compared in both arms. Mean values of both systolic and diastolic blood pressure were used to define blood pressure levels. Pregnant diabetic cases or gestational diabetes and type 1 diabetics were excluded from the study. The selected patients were evaluated for the presence of microvascular and macrovascular complications i.e. coronary artery disease, cerebrovascular disease, peripheral vascular disease, retinopathy, nephropathy and neuropathy by relevant test. Retinopathy was diagnosed by detailed fundus examination and classified according to Early Treatment Diabetic Retinopathy Study (ETDRS) (13). Incipient nephropathy was diagnosed by microalbumin test by combi-screen-9 kit with Clinitek 100. Incipient nephropathy was presumed to be present if any two readings out of three urinary albumin were ranging from 30 to 300 mg/day i.e. microalbuminuria. Overt nephropathy was diagnosed by elevated level of serum creatinine and blood urea, or presence of macroalbuminuria.

Neuropathy was diagnosed by history of numbness, parenthesis, tingling sensation, burning sensation and confirmed by touch sensation using 10 gm monofilament, vibration sense by biothesiometer (VTP at great toe >25 were considered significant) and ankle reflex. Painful peripheral neuropathy was diagnosed by history of pain worsening at night. Autonomic neuropathy was diagnosed by history of postural fall of blood pressure, history of constipation or diarrhea, gastroparesis and confirmed by Valsalva test, blood pressure in lying down and standing positions.

Peripheral Vascular Disease (PVD) was diagnosed by definitive history of intermittent claudicating or if one or more peripheral pulses were absent in both feet. PVD was diagnosed when ankle brachial index was less than 0.9. Coronary artery disease as diagnosed by history of angina, myocardial infarction or documented by previous treatment records. The diagnosis of cerebrovascular disease was made by documentation of sudden neurological deficit supported by the results of appropriate imaging techniques.

Informed consent was obtained from all subjects and the research had the approval of the Institutional Review Board and Ethics Committee of Shahid Sadoughi University of Medical Sciences and was carried out in accordance with the Declaration of Helsinki.

Statistical Analysis: Data were expressed as mean ± SD. Statistical analyses were performed using SPSS 12. Chi-square test was used for comparison between the two groups and regression analysis was done for finding the scientific risk factors' association with various complications. Logistic regression analysis was used to find out strength of association of risk factors with a specific complication.

RESULTS

In this study 1000 type 2 diabetic patients (457 male, 543 female) were studied (Table 1).

Table 1- Demographic profile of the study population

	Mean	SD
Age	55.91	10.02
Duration of diabetes	11.74	6.85
Systolic blood pressure	131.87	19.79
Diastolic blood pressure	80.49	6.58
FBS	198.82	70.99
HbA1c	9.37	2.20
2hpp	307.36	91.7
BMI	27.75	4.24

Nephropathy was diagnosed in 285 (28.5%), retinopathy in 519 (51.9%), CAD in 251 (25.1%), PVD in 143 (14.3%), CVA in 109 (10.9%) and foot ulcer in 84 patients (8.4%).

Patients were divided into 5 groups by age i.e. below 40, 41-50, 51-60, 60-69 and more than 70 years. When these results were put in logistic regression, we found strong association of age with specific complications, retinopathy [odds ratio 5.35 (CI 2.39-12)], neuropathy [odds ratio 2.09 (CI 1.01-4.35)] and diabetic foot [odds ratio 5 (CI 2.39-10.79)] (Table 2).

Table 2- Results of logistic regression analysis showing risk factors in micro and macrovascular complications

	Nephropathy	Retinopathy	Neuropathy	CAD	PVD	CVA	Diabetic foot
	Odds Ratio	Odds Ratio	Odds Ratio	Odds Ratio	Odds Ratio	Odds Ratio	Odds Ratio
Age	0.9	5.35	2.09	0.82	0.7	2.08	5
	0.4-1.94	2.39-12	1.01-4.35	0.38-1.77	0.26-1.87	0.9-4.79	2.39-10.79
Duration of diabetes	2.23	1.68	2.9	0.94	2.29	1.41	1.32
	1.67-2.98	1.29-2.18	2.23-3.77	0.7-1.26	1.57-3.33	0.94-2.1	0.83-2.1
HbA1c	1.05	2.29	1.2	0.96	5.53	0.68	1.36
	0.5-2.1	1.13-4.67	0.64-2.44	0.45-2.07	0.73-41.5	0.26-1.75	0.37-5
Systolic BP	1.19	0.7	1.19	1.31	0.92	1.3	1.25
	0.84-1.68	0.56-1.05	0.87	0.92-1.87	0.6-1.4	0.76-2.24	0.68-2.31
Diastolic BP	0.87	0.48	0.68	1.02	1	0.37	0.43
	0.56-1.35	0.32-0.72	0.46-1.03	0.64-1.63	0.58-1.72	0.2-0.68	0.21-0.86

According to duration of diabetes, patients were divided into 5 groups: below 5 years, 6-10, 11-15, 16-20, 21 and above. (Table 3)

On logistic regression we found statistically significant association between duration of diabetes and some vascular complications such as retinopathy [odds ratio 1.68 (CI 1.29-2.18)], nephropathy [odds ratio 2.23 (CI 1.67-2.98)], neuropathy [odds ratio 2.9 (CI 2.23-3.77)], PVD [odds ratio 2.29 (CI 1.57-3.33)]. (Table 4)

According to HbA1c, subjects were divided into 4 groups: below 8%, 8.1-9, 9.1-10, 10.1 and more. On logistic regression analysis a clear correlation was observed with HbA1c and retinopathy [odds ratio 2.29 (CI 1.13-4.67)] (Table 5). Also diastolic blood pressure showed a positive association with retinopathy [odds ratio 0.48 (CI 0.32-0.72)] and CVA [odds ratio 0.43 (CI 0.21-0.86)]. (Table 6)

On logistic regression it was found that high BMI was associated with retinopathy and CAD and PVD. (Table 7)

Results of this study showed that there was only a significant association between sex and nephropathy as prevalence of nephropathy was 34.1% in men (156) and 23.8% in women (129).

Table 3- Duration of diabetes and vascular complications of type 2 diabetes

	<5		6-10		11-15		16-20		>21		*P* value
	No.	%	No.	%	No.	%	No.	%	No.	%	
Nephropathy	41	20	65	21.2	78	31.8	46	34.8	55	49.5	0.0001
Retinopathy	72	35.1	141	45.9	138	56.3	61	46.2	77	69.4	0.0001
Neuropathy	66	32.2	133	43.3	158	64.5	90	68.2	72	64.9	0.0001
CAD	46	22.4	85	27.7	58	23.7	28	21.2	34	30.6	0.2
PVD	21	10.2	27	8.8	49	20	21	15.9	25	22.5	0.0001
CVA	12	5.9	34	11.1	23	9.4	21	15.9	19	17.1	0.008
Diabetic wound	7	¾	28	9.1	24	9.8	12	9.1	13	11.7	0.05
Hypertension	28	13.7	71	23.1	23	9.4	16	12.1	8	7.2	0.0001

Table 4- Systolic blood pressure and vascular complications of type 2 diabetes

	80-120		121-140		141-160		161		*P* value
	No.	%	No.	%	No.	%	No.	%	
Nephropathy	115	28.2	110	29.7	45	27.4	15	25.9	0.9
Retinopathy	227	55.6	154	41.6	80	48.8	28	48.3	0.002
Neuropathy	211	51.7	195	52.7	88	53.7	25	43.1	0.5
CAD	46	22.4	85	27.7	58	23.7	28	21.2	0.0001
PVD	63	15.4	53	14.3	23	14	4	6.9	0.3
CVA	50	12.3	38	10.3	14	8.5	7	12.1	0.5
Diabetic wound	36	8.8	27	7.3	19	11.6	2	¾	0.1

Table 5- Glycated hemoglobin and vascular complications of type 2 diabetes

	<8		8.1-9		9.1-10		>10		*P* value
	No.	%	No.	%	No.	%	No.	%	
Nephropathy	50	23.9	45	24.5	743	28.7	147	32.2	0.8
Retinopathy	85	40.7	98	53.3	75	50	231	50.5	0.05
Neuropathy	101	48.3	92	50	65	43.3	261	57.1	0.1
CAD	43	20.6	36	19.6	44	29.3	128	28	0.03
PVD	14	6.7	34	18.5	30	20	65	14.2	0.001
CVA	18	8.6	26	14.1	10	6.7	55	12	0.09
Diabetic wound	21	10	17	9.2	15	10	31	6.8	0.3
Hypertension	30	14.4	21	11.4	8	5.3	87	19	0.0001

Table 6- Diastolic blood pressure and vascular complications of type 2 diabetes

	<80		81-90		>91		*P* value
	No.	%	No.	%	No.	%	
Nephropathy	225	29.3	58	25.6	2	50	0.3
Retinopathy	381	49.5	104	45.8	4	100	0.07
Neuropathy	382	49.7	133	58.6	4	100	0.01
CAD	176	22.9	73	32.2	2	50	0.009
PVD	115	15	27	11.9	1	25	0.4
CVA	88	11.4	20	8.8	1	25	0.3
Diabetic wound	65	8.5	18	7.9	1	25	0.4

Table 7: BMI and vascular complications of type 2 diabetes

	<20 kg/m^2		20-25 kg/m^2		25-30 kg/m^2		30-35 kg/m^2		35-40 kg/m^2		>40 kg/m^2		*P* value
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	
Nephropathy	2	15.4	83	31.4	117	25.7	67	35.6	8	13.8	7	58.3	0.001
Retinopathy	13	100	138	52.3	230	50.4	84	44.7	13	22.4	7	58.3	0.0001
Neuropathy	9	69.2	133	50.4	216	47.4	125	66.5	22	37.9	9	51.9	0.0001
CAD	0	0	53	20.1	92	20.2	80	42.6	22	37.9	2	16.7	0.0001
PVD	0	0	50	18.9	59	12.9	25	13.3	4	6.9	0	0	0.03
CVA	1	7	32	12.1	44	9.6	27	14.4	4	6.9	1	8.3	0.4
Diabetic wound	4	30.8	24	9.1	35	7.7	15	8	4	6.9	1	8.3	0.1
Hypertension	0	0	28	10.6	52	11.4	45	24.5	12	20.7	8	66.7	0.0001

DISCUSSION

Diabetes mellitus is the most common metabolic disorder and has a high prevalence in Yazd province, Iran (2). There is no study regarding the micro and macrovascular complications in this part of Iran, hence we decided to undertake a cross-sectional study to record micro and macrovascular complications and contributing factors. This study was conducted on 100 patients with type 2 diabetes.

In this study of 1000 type 2 diabetic patients, 285 (28.5%) had nephropathy, 489 (48.9%0 had retinopathy, 519 (51.9%) had neuropathy, 251 (25.1%) had CAD, 143 (14.3%) had PVD, 109 (10.9%) had CVD and 84 (8.4%) had diabetic foot.

Retinopathy is an important complication of diabetes mellitus. The prevalence between 1990 and 1996 for patients with newly diagnosed type 2 diabetes mellitus has been estimated to be 22% in Hong Kong (14) and a population-based study performed in China in 1986 showed a prevalence of 31% (7). In a study by Agrawal et al. on 4400 type 2 diabetic patients, retinopathy was observed in 1176 individuals (28.9%). This study showed that age, duration of diabetes, hypertension and poor glycemic control are effective factors on retinopathy (15). In 1986, Knuiman et al. (16) reported the prevalence of retinopathy as 28% in a study from Perth (Western Australia). In a study by Rema et al. overall prevalence of DR was 17.6%. Logistic regression analysis showed that for every 5-year increase in the duration of diabetes, the risk for DR increased 1.89-fold and for every 2% elevation of glycated hemoglobin, the risk for DR increased by a factor of 1.7 (17). Randomized controlled trials such as the DCCT and the United Kingdom Prospective Diabetes Study (UKPDS) have shown conclusively that improving glycaemic control can decrease the incidence of Diabetic retinopathy (18,19). This concept is also supported by prospective follow-up studies among Japanese and Chinese patients with type 2 diabetes mellitus, (20,21).

In our study there was a significant association between prevalence of DR with age, duration of diabetes, systolic and diastolic blood pressure, and glycated hemoglobin. The risk of DR in HbA1c >7% was 2.29-fold to HbA1c <7%.

In our study 285 patients (28.5%) had nephropathy. A significant association was observed between prevalence of nephropathy with sex, age, duration of diabetes, glycated hemoglobin and BMI.

Diabetic nephropathy develops approximately between 15% and 60% of patients with the type 2 diabetes (22). It is the leading cause of chronic renal failure worldwide and is responsible for about one third of patients who undergo dialysis (23). WHO multicentric study of vascular disease (24) in diabetics, observed a wide geographic variation in prevalence of nephropathy i.e. 2.4% from Hong Kong, 23% from Delhi to 37% from Oklahoma, USA. In a study by Agrawal et al., prevalence of nephropathy was 32.5% (15). Many previous studies, (25, 26) found that age was the most important variable for renal impairment. In UKPDS study each 10 mmHg decrease in updated mean systolic blood pressure was associated with reductions in risk of 12% for any compli-

cation related to diabetes, 15% for deaths related to diabetes (11% for myocardial infarction, and 13% for microvascular complications (27). Rema et al. (28) and Ramachandra et al. (29) had also observed the positive association of hypertension with diabetic nephropathy. In a study in Hong Kong, the prevalence of microalbuminuria and macroalbuminuria was high in type 2 diabetic patients with hypertension, particularly in males and those with poorly controlled systolic blood pressure (30). Hyperglycaemia is an important determinant for the development of proteinuria in patients with type 2 diabetes. Studies showed that effective glycaemic control prevents the development of nephropathy and reverses established pathology (31). In a study by Yeung et al. predictive factors for macroalbuminuria included: above 70 years of age, male sex, known CV complications, and mild to moderate systolic hypertension (140-179 mmHg) (30). That was similar to our results.

Diabetic patients have an increased risk of the development of neuropathy (32). A study in the United States showed that one half of a group of patients who had had type 2 diabetes mellitus for more than 15 years also had diabetic neuropathy (33).

In our study 519 subjects (51.9%) had neuropathy. There was a significant association between age, duration of diabetes, Glycated hemoglobin, systolic and diastolic blood pressure. The risk of neuropathy in patients with history of diabetes more than 10 years was 2.99-fold. Also the risk of neuropathy in patients above 70 was 2.71.

Our results were consistent with findings of Knuiman et al. (1986) (16) who found that sensory Neuropathy is strongly related to both age at diagnosis and duration of diabetes. In a study by Phillips et al., of 15050 diabetic patients, prevalence of neuropathy was 47.9% (34). Nielsen et al. (35) observed neuropathy in 38% of their patients and Cheng et al. (36) in 33.9% of their Taiwanese diabetic patients.

Diabetic foot may develop, mainly because of the abnormal distribution of pressure owing to peripheral neuropathy .In our study prevalence of diabetic foot was 8.4% (84). There was a significant association between diabetic foot with age and duration of diabetes. The prevalence of diabetic foot in patients with history of diabetes more than 10 years was 4.9% and in less than 10 years was 3.5%.

In a study by Leelawattana et al., the prevalence of diabetic foot in the long-DM group was higher than that in the short-DM group (37). In a study by Basit et al. the prevalence of diabetic foot ulcer in patients with duration of diabetes more than 10 years was 14.82 and less than 10 years was 7.56% (38).

Cardiovascular disease accounts for most cases of diabetic macrovascular complications; the remainders are caused by cerebrovascular events and peripheral vascular disease (7). In our study CAD was found in 251 subjects (25.1%). There was a significant correlation between CAD and systolic and diastolic blood pressure, glycated hemoglobin and BMI.

Diabetes drafting group (39) also reported considerable influence of blood pressure on coronary artery disease. Similar results were shown by Harris MI et al. (1992), (40) and Fuller et al. (1996) (41). In UKPDS the incidence of myocardial infarction increased from 18 per 1000 patients per year in the group with the lowest systolic blood pressure to 33 per 1000 patients per year in the group with blood pressure >160 mmHg, with the comparable data for microvascular disease being 7 to 21 per 1000 patients per year (27). Mohan et al. concluded that age and LDL cholesterol were the risk factors for CAD (42). In a study by Basit et al., CAD in patients with duration of diabetes more than 10 years was 20.59% and less than 10 years was 11.7% (38), whereas in our study the relation between CAD and duration of diabetes was not significant. UKPDS and DCCT showed a strong association between glycemia and CAD (18, 19). In our study 50% with CAD had HbA1c more than 10%.

In our study prevalence of PVD was 14.3%. We found a significant association of peripheral vascular disease with the glycated hemoglobin, duration of diabetes and BMI. In Agrawal's study the prevalence of PVD was 18.1%. Also a significant association of PVD with age, duration of diabetes was seen. In a study by Basit et al., prevalence of PVD in patients with duration of diabetes more than 10 years was 8.02% and less than 10 years was

3.96 (387). Fowkes et al. (1992) (43), and Ramachandran et al. (1999) (29), found a clear association between PVD and glycemia which confirmed our results.

In our study prevalence of CVD was 10.9%. We found a significant association between age, duration of diabetes, HbA1c and CVD. In a study by Basit et al., a strong association was seen between CVD and duration of diabetes (38). In a study by Leelawattana et al. the prevalence of CVD in the long-DM group was 2-fold more than that in the short-DM group (37). In our study CVD in patients with duration of diabetes more than 10 years was 1.5-fold to duration of diabetes less than 10 years. The role of glycemic control in prevention of CVD was shown in UKPDS (19), but in our study relationship between HbA1c and CVD was not remarkable.

This study showed a high prevalence of microvascular and macrovascular complications in type 2 diabetic patients. Age, duration of diabetes, systolic and diastolic blood pressure, glycated hemoglobin and BMI were important risk factors in vascular complication. So glycemic control, weight loss and blood pressure control can prevent diabetes or at least delay its development.

ACKNOWLEDGMENT

This study was supported by Yazd Diabetes Research Center of Shahid Sadoughi University of Medical Sciences.

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