

Diabetic Complications: Influence of Age, Sex, Family History, Duration, Glycemic Control and Obesity

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Abstract: This study was undertaken to find prevalence of diabetic complications and influence of age, sex, family history, duration, glycemic control and obesity on these complications in 1104 diabetic patients. Late diabetic complications were present in 76% cases. The prevalence of hypertension was 28.846%, retinopathy 25.962%, neuropathy 24.038%, nephropathy and ischemic heart disease 8.654%, polyarthritis 6.731%, angina and urinary track infection 5.769%, dermatitis 4.808% and atherosclerosis 1.923%. Overall 74% cases had poor glycemic control. An increase in mean (SD) (227.722 (74.521) vs. 222.360 (64.386) mg/dl) and most frequent (mode) (340 vs. 200 mg/dl) random blood glucose of complicated cases compared with non complicated cases was observed. There was no difference in mean (SD) age (50.768 (13.715) vs. 50.800 (12.845) years) and median age (50 vs. 50 years) of complicated and non-complicated cases while most frequent age (mode) (45 vs. 40 years) was higher in complicated cases. The mean (SD) (43.240 (12.965) vs. 46.760 (13.694) years), median (43 vs. 49 years) and most frequent age at diagnosis of diabetes (mode) (40 vs. 46 years) was lower in complicated cases compared with non-complicated cases. The prevalence of diabetic complications was low (66.667%) in diabetic patients with family history of diabetes as compared to diabetic patients without family history of diabetes (79.221%). An increased percentage of complicated cases in males (80.33%) as compared to female patients (72.09%) were observed. Mean (SD) duration of diabetes was higher in complicated diabetic patients (7.585 (5.730) years) as compared to non-complicated diabetic patients (4.080 (4.551) years). There was an increase in percent-complicated cases with an increase in duration of diabetes and both parameters showed a positive regression ($R^2 = 0.84$). Obese diabetic patients have 13.555 and 14.461% more chance of developing diabetic complications compared with normal and lean diabetic patients respectively. It was concluded that poor glycemic control, early age at diagnosis, gender (male), duration of diabetes and obesity are the factors which can increase the risk of developing diabetic complications.

Key words: Diabetic complications, age, sex, family history, duration, glycemic control, obesity

Introduction

Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both (Alberti and Zimmet, 1998, 1999). It is one of the leading causes of death and disability in the world (Turner et al., 1999). The International Diabetes Federation (IDF) and World Health Organization (WHO) have declared diabetes as a global epidemic (Zimmet and McCarty, 1995).

Diabetes is the major cause of premature mortality (Guk et al., 1998). If the diabetes is poorly controlled it can lead to diabetic complications. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction and failure of various organs, especially the eyes, kidneys, nerves, heart and blood vessels. It damages the vessels and the basement membrane, causing impaired delivery of nutrients and hormones to the tissues, resulting in tissue damage. The most sites affected are the retina, renal glomerulus and the nerve sheath. Vascular complications of diabetes occur in both micro and macro vascular vessels. Microvascular complications include retinopathy, nephropathy and neuropathy. Macro vascular complications comprise peripheral vascular disease and cardiovascular complications, such as ischemic heart disease and hypertension. These are all chronic illnesses, which take 10-20 years to manifest. One of the most important factors in the pathogenesis of diabetic complications is the metabolic milieu of the diabetic patients, the main causative factor being hyperglycemia (Anonymous, 1993). The severity of complications is modified by genetic factors. Many of the diabetic patients do not develop complications even when their glycemic control is not optimal (Rosenstock and Raskin, 1988).

The main aim of diabetes management is to achieve a normal glycemic state. Large follow-up studies have shown that good glucose control may prevent or delay the manifestation of complications despite the long duration of the disease (Reichard et al., 1993; Anonymous, 1993; Wang and Chalmers, 1993). Diabetes is a chronic health condition that requires tremendous

energy and care throughout the patient's life span. Clinically, it is easier to prevent glucose excursions than to treat them once they occur. There are data to suggest that control of blood glucose levels will prevent damaging glucotoxicity, preventing or delaying diabetes-related complications. New treatment goals of the American Diabetes Association are the following: fasting plasma glucose levels of 80 to 120 mg dl⁻¹, initial treatment of diet, self-care management, education and exercise (Nicollerat, 2000). This study was conducted to find the prevalence of diabetic complications. Other objective was to find influence of age, sex, age at diagnosis, family history, duration of diabetes, glycemic control and obesity on prevalence of these complications.

Materials and Methods

A total of 1104 physician's clinically diagnosed diabetic patients attending out door or admitted in emergency at National Hospital Faisalabad from Feb 2000 to April 2002 with complete history of disease were included in this study. This is a retrospective study using data from patient's history files. Basic demographic information from diabetic patients was collected using a standard questionnaire, interviewing and browsing patient's history files. Main objective was to document late diabetic complications diagnosed by physicians on the bases of multiple laboratory investigations. Various parameters, which can influence the appearance and severity of diabetic complications, were also included. Different epidemiological parameters included were age, sex, age at on set of diabetes, family history of diabetes (one or more diabetic patient in grand parents, parents or offspring) and duration of diabetes. While pathological parameters like glycemic control and obesity were also included in this study. Diabetic patients were classified in to different types on the bases of 1998 WHO criteria (Alberti and Zimmet, 1998).

Mean random blood glucose (RBG) level was used to find out glycemic control. Mean was calculated by taking average of multiple readings of RBG level from patient's clinical history files.

Then patients were classified as having good, satisfactory, or poor glycaemic control according to their mean RBG level. Patients with mean RBG ranging up to 140 mg dl⁻¹ were regarded as having good glycaemic control and from 141-180 mg dl⁻¹ as having satisfactory glycaemic control, while from 181 to above as having poor glycaemic control.

Diabetic patients were classified as lean, normal and obese on basis of their body mass index (BMI). The patients with BMI ranging from 19-25 kg m⁻² (Lloyd, 1991) were classified as normal, less than this as lean and greater than this as obese.

Diabetic patients included in this study were screened for family history of diabetes. While collecting data for family history of diabetes, the patients with one or more diabetic in grand parents, parents and siblings were categorized as having family history of diabetes.

For variables like age, age at diagnosis of diabetes, glycaemic control and duration of diabetes, descriptive statistics including mean, mode, median, standard deviation (SD), minimum, maximum values, range and sample variance were applied for complicated and non complicated cases separately. All these descriptive statistical parameters were calculated using Microsoft Excel 2000.

Results

Progression of diabetes mellitus and uncontrolled hyperglycemia may lead to various complications in later stage of diabetes. These late diabetic complications were very common in diabetics included in this study. At least one or more diabetic complications were reported in 76% diabetic patients and remaining 24% diabetic patients were with out any diabetic complication.

Different pathological complications common in diabetics included in this study were listed and arranged from top to bottom in decreasing order of their prevalence (Table 1). The prevalence of hypertension was 28.846%, retinopathy 25.962%, neuropathy 24.038%, nephropathy and ischemic heart disease (IHD) 8.654%, polyarthritis 6.731%, angina and urinary track infection (UTI) 5.769%, dermatitis 4.808% and atherosclerosis 1.923%.

Therefore most common complications were hypertension, retinopathy, neuropathy, while other complications are less common in this study

Glycaemic control and complications: The mean (SD) value for glycaemic control of diabetic patients was 226.433 (71.949) mg dl⁻¹. The descriptive statistics was to applied RBG level of complicated and non-complicated diabetic patients (Table 2) separately. The mean (SD) value for random blood glucose level of non-complicated diabetic patients was 222.360 (64.385) mg dl⁻¹ and for complicated diabetic patients value was 227.722 (74.521) mg dl⁻¹. The random blood glucose level in non-complicated diabetic patients ranged from 96-340 mg dl⁻¹ while in complicated diabetic patients it ranged from 56-360 mg dl⁻¹. The most frequent value (mode) of random blood glucose in non-complicated diabetic patients was 200 mg dl⁻¹ and for complicated diabetic patients was 340 mgdl⁻¹. The median value of random blood glucose for non-complicated and complicated diabetic patients was 211 and 226 mg dl⁻¹ respectively.

Only 14.423% diabetic patients had good glycaemic control (mean random blood glucose up to 140 mg dl⁻¹) and 11.538% had satisfactory glycaemic control (141-180 mg dl⁻¹). On the other hand 74.038% diabetic patients had poor glycaemic control (> 181 mg dl⁻¹). This was also evident from this study (Table 1) that prevalence of complications was more in diabetics with poor glycaemic control.

Diabetes types and complications: On the bases of 1998 WHO criteria 96.154% diabetic patients were classified as having type 2 diabetes. The remaining 3.846% diabetics included in this study were classified in type 1 diabetes mellitus. Prevalence of complications in type 2 diabetes was 71.154%. In type 1 diabetes all cases were complicated.

Age and complications: The age of diabetic patients ranged from

5 to 82 years with mean (SD) value 50.798 (13.449) years. The descriptive statistics was also applied to age of complicated and non-complicated diabetic patients (Table 2) separately. The mean (SD) age of non-complicated diabetic patients was 50.800 (12.845) years and for complicated diabetic patients 50.768 (13.715) years. The most frequent age (mode) of non-complicated diabetic patients was 40 years and for complicated diabetic patients 45 years. The median age for both non-complicated and complicated diabetic patients was 50 years.

Gender and complications: Fig. 1 illustrates an increased percentage of complicated cases in males (80.33%) as compared to female patients in which 72.09% cases were complicated. This shows that male diabetic patients had 8.26% more risk to develop diabetic complications than female diabetic patients.

Age at diagnosis of diabetes and complications: The age at diagnosis of diabetes ranged from 3 to 80 years with mean (SD) value 44.086 (13.163) years. The mean (SD) age at diagnosis of diabetes in non-complicated diabetic patients was 46.760 (13.694) years (Table 2) and for complicated cases was 43.240 (12.965) years. The most frequent age at diagnosis (mode) of non-complicated diabetic patients was 46 years and for complicated diabetic patients 40 years. The median age at diagnosis for non-complicated diabetic patients was 49 years and for complicated diabetic patients 43 years.

This shows that mean, median and most frequent age at diagnosis of diabetes (mode) was lower in complicated cases compared with non-complicated diabetic patients.

Duration of diabetes and complications: For duration of diabetes in diabetic patients the mean (SD) value was 6.744 (5.668) years. The mean (SD) duration of diabetes in non-complicated diabetic patients was 4.080 (4.551) years (Table 2) and for complicated cases was 7.585 (5.753) years. The most frequent duration (mode) of diabetes in non-complicated diabetic patients was 1 years and for complicated diabetic patients it was 10 years. The median duration of diabetes in non-complicated diabetic patients was 3 years and for complicated diabetic patients it was 6 years.

Therefore mean duration of diabetes was much higher in complicated diabetic patients (7.585 years) as compared to non-complicated diabetic patients (4.080 years).

Diabetic patients were divided in to four groups based on duration of diabetes (Fig. 2). There was an increase in percent-complicated cases with an increase in duration of diabetes and both parameters showed a good positive regression (R² = 0.84). This is also evident from data that 11.538% diabetic patients did not develop any complication after 10 years duration of diabetes and even after 15 years duration 3.293% diabetic patients did not develop any complication.

Family history of diabetes and complications: Diabetic patients were also screened for family history of diabetes (one or more diabetic patient in grand parents, parents or offspring). Family history of diabetes was reported in 25.962% diabetic patients. To check whether family history of diabetes have any influence on prevalence of complications or not, diabetic patients with or without family history of diabetes were screened for prevalence of complications separately in both groups. A less No. of complicated cases (66.667%) was reported (Table 3) in diabetic patients with family history of diabetes as compared to diabetic patients without any history diabetes (79.221%).

Obesity and complications: The diabetic patients were also divided in to different groups on the bases of their physique (Table 4). Prevalence of obesity on bases of body mass index was 32.692% while 23.077% diabetics were lean and remaining 44.231% were normal in physique. In diabetic patients with normal physique any type of diabetic complications were present in 71.739% diabetic patients. In lean diabetic patients any type of diabetic complications were present in 70.833% cases. Furthermore in obese diabetic patients there was an increase in percent-

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Table 1: Influence of glycemic control on prevalence of late diabetic complications in diabetes

Complications	Glycemic control (%)			Total
	Good μp to 140 mg dl ⁻¹	Satisfactory 141 to 180 mg dl ⁻¹	Poor above 180 mg dl ⁻¹	
Hypertension	2.884	4.808	21.154	28.846
Retinopathy	6.731	4.808	14.423	25.962
Neuropathy	3.846	3.846	16.346	24.038
Nephropathy	0.000	2.885	5.769	8.654
Ischemic heart disease (IHD)	2.884	0.962	4.808	8.654
Polyarthritits	0.962	0.000	5.769	6.731
Angina	0.962	1.923	2.884	5.769
Urinary track infection (UTI)	0.000	0.961	4.808	5.769
Dermatitis	0.000	1.923	2.885	4.808
Atherosclerosis	0.000	0.961	0.962	1.923

Table 2: Descriptive statistical analysis of age, age at diagnosis, duration of diabetes and glycemic control.

	Age (years)		Age at diagnosis (years)		Duration of diabetes (years)		Glycemic control (mg dl ⁻¹)	
	Comp.	NonC.	Comp.	NonC.	Comp.	NonC.	Comp.	NonC.
Mean	50.797	50.8	43.240	46.76	7.585	4.08	227.722	222.360
Median	50.000	50.0	43.000	49.00	6.000	3.00	226.000	211.000
Mode	45.000	40.0	40.000	46.00	10.000	1.00	340.000	200.000
Standard deviation	13.714	12.845	12.965	13.694	5.753	4.552	74.521	64.385
Sample variance	188.087	165.0	168.082	187.523	33.097	20.716	5553.383	4145.490
Range	77.000	45.0	77.000	56.000	29.900	17.900	304.000	244.000
Minimum	5.000	30.0	3.000	15.000	0.100	0.100	56.000	96.000
Maximum	82.000	75.0	80.000	71.000	30.000	18.000	360.000	340.000

Comp = Complicated diabetic patients, NonC = Non Complicated diabetic patients.

Table 3: Influence of family history on prevalence of diabetic complications

Case conditions	With family history (%)	No family history (%)
Complicated cases	66.667	79.221
Non complicated cases	33.333	20.779

Table 4: Prevalence of obesity in diabetic patients on bases of body mass index

Physique	Obese	Lean	Normal
Diabetic patients (%)	32.692	23.077	44.231
Complicated Cases (%)	85.294	70.833	71.739

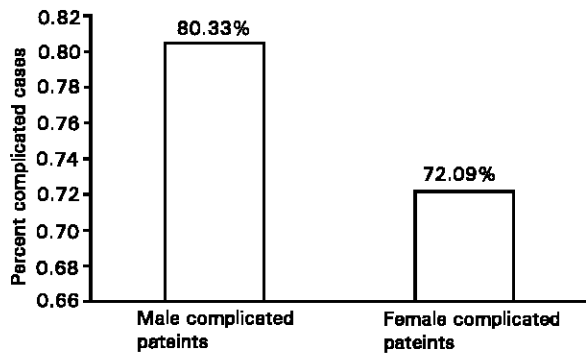


Fig. 1: Influence of gender on prevalence of diabetic complications

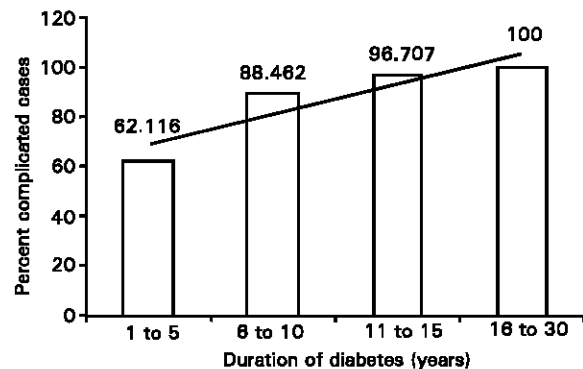


Fig. 2: Influence of duration of diabetes on appearance of late diabetic complications

complicated cases. In obese diabetic patients complications were present in 85.294% cases. Obese diabetic patients have 13.555 and 14.461% more chance of developing diabetic complications compared with diabetic patients with normal and lean physique respectively. This means obesity was associated with higher prevalence of complications and disease becomes more serious in presence of obesity.

Discussion

Diabetes is a chronic health condition that requires tremendous energy and care throughout the patient's life span. Clinically, it is easier to prevent glucose excursions than to treat them once they occur (Nicollerat, 2000). Progression of diabetes mellitus and uncontrolled hyperglycemia may lead to various complications in later stage of diabetes. In present study 76% diabetic cases were complicated and only 24% cases were free of complications. This prevalence of diabetic complications was much higher in Pakistani population as compared to other populations reported previously (Tai *et al.*, 1991).

In this study the prevalence of retinopathy was 25.962%, neuropathy 24.038% and hypertension 28.846%. Similarly high prevalence of hypertension (26%) (Haider *et al.*, 1980) and retinopathy, (26%) (Khan, 1991) was also reported previously in Pakistan. High prevalence of retinopathy (24.0%) and neuropathy (23.5%) has also been reported previously in population of Taipei city (Tai *et al.*, 1991).

Insulin-resistant type 2 diabetic subjects have more cardiovascular risk factor and this is only partially related to increased obesity and an adverse body fat distribution. (Haffner *et al.*, 1999) Diabetes mellitus and obesity play critical roles collectively and individually in increasing coronary heart disease, morbidity and mortality (Potts and Thomas, 1999). Therefore high prevalence of cardiovascular problems (16.346%) in this study may also be regarded due to obesity in diabetic patients.

It has been reported that diabetic neuropathy is independently associated with body weight and retinopathy (Cohen *et al.*, 1998). Comparable prevalence of neuropathy (24.038%) and retinopathy (25.962%) along with high prevalence of obesity in Pakistani

population (32.692%) also indicates a strong association among these conditions.

In this study random blood glucose levels were used to analyze glycemic control in diabetic patients. Poor glycemic control was found in 74.038% diabetic patients. Similar results were also documented previously (Levitt *et al.*, 1997, Hawthorne and Tomlinson, 1999). Previously it was pointed out that only 24% Pakistani moslems with type 2 diabetes mellitus knew how to manage persistent hyperglycemia. Women were worse than men and had poorer glycaemic control overall. They were less likely to understand why glucose levels should be monitored (Hawthorne and Tomlinson, 1999).

The role of social support in promoting diabetes management and improved glycemic control is a little-explored area (Ford *et al.*, 1998). Lower-income is one of problems for proper glycemic control in black children with diabetes (Delamater *et al.*, 1999). In diabetics included in present study lower-income may also be one of the problems for maintaining good glycemic control.

Poor glycemic control contributes to the high incidence of late diabetic complications (Harris *et al.*, 1998). It has been reported that poor metabolic control is associated with development and high blood pressure with progression of diabetic complications (nephropathy) in type 2 diabetic patients (Torffvit and Agardh, 2001; Saum *et al.*, 2002). This aspect was also evident from this study. As mentioned above, late diabetic complications were present in 76% cases and know 74% cases had poor glycemic control so there was strong relation between glycemic control and late diabetic complications. This is also clear from this study that prevalence of complications was more in diabetics with poor glycemic control.

The comparison of clinical and biochemical data of diabetic patients with and without complications, has shown significant difference in fasting plasma glucose (Tai *et al.*, 1991). Difference in mean (SD) random blood glucose levels of diabetic patients with and without complications (227.722 (74.521) vs. 222.360 (64.386) mg dl⁻¹) and most frequent (mode) glucose level (340 vs. 200 mg dl⁻¹) was also found in this study.

Diabetes is known to be increasing in prevalence and incidence, particularly among the elderly (Black *et al.*, 1999; Alessandro *et al.*, 1999). There is evidence that the prevalence of diabetes mellitus appeared to increase steadily with age (Mangia *et al.*, 1998). There was no difference in mean (SD) age (50.768 (13.715) vs. 50.800 (12.845) years) and median age (50 years) of complicated and non-complicated diabetic patients. While the most frequent age (mode) (45 years) of complicated diabetic patients was higher than non-complicated diabetic patients (40 years). Diabetic patients with family history of diabetic complications should be screened for complications in this period of life. Older age diabetics have more risk to develop complications than younger age diabetic patients. An increased percentage of complicated cases in males (80.33%) as compared to female patients (72.09%) was observed. This shows that male diabetic patients had 8.26% more risk to develop diabetic complications than female diabetic patients.

The mean (SD) (43.240 (12.965) vs 46.760 (13.694) years), median (43 vs. 49 years) and most frequent age at diagnosis of diabetes (mode) (40 vs. 46) was lower in complicated cases compared with non-complicated diabetic patients. Therefore it was conclude that diabetic patients with early age at diagnosis of diabetes has more potential to develop complications and should be screened for complications at different time intervals in their life.

Duration of diabetes mellitus is an important determinant of diabetic complications in diabetic patients (Wan *et al.*, 1999; Motala *et al.*, 2001). The comparison of clinical and biochemical data of diabetic patients with and without complications, has shown significant difference in diabetic duration (8.2 ± 6.7 vs. 4.1 ± 2.7, years) (Tai *et al.*, 1991). These result are in agreement with these findings as mean (SD) duration of diabetes was much higher in complicated diabetic patients (7.585 (5.730) years) as compared to non-complicated diabetic patients (4.080 (4.551) years). There was an increase in percent-complicated cases with an increase in

duration of diabetes and both parameters showed a good positive regression (R² = 0.84). Similar association between duration of diabetes, development and progression of diabetic complications has also been reported recently (Rewers *et al.*, 2002; Torffvit and Agardh, 2001).

Large follow-up studies have shown that good glucose control may prevent or delay the manifestation of complications despite the long duration of the disease (Reichard *et al.*, 1993; Anonymous, 1993; Wang and Chalmers, 1993). The severity of complications is modified by genetic factors, since many of the diabetic patients do not develop complications even when their glycemic control is not optimal (Rosenstock and Raskin, 1988). This was also evident from data as 11.538% diabetic patients did not develop any complication after 10 years duration of diabetes and even after 15 years duration 3.293% diabetic patients did not develop any complication.

A less number of complicated cases (66.667%) was reported in diabetic patients with family history of diabetes as compared to diabetic patients without any history of diabetes (79.221%). This indicates that diabetic patients who apparently develop diabetes due environmental factors (no family history of diabetes) have 12.554% more risk of developing diabetic complications as compared to those with family history of diabetes. Association between diabetes mellitus and family history of diabetes has also been reported in Sindh (Shera *et al.*, 1995) and NWFP provinces of Pakistan (Shera *et al.*, 1999) and in children of Pakistani, Indian or Arabic origin residing in UK (Ehtisham *et al.*, 2000). No literature regarding association between family history of diabetes and complications in Pakistan is available.

Obese diabetic patients have 13.555 and 14.461% more chance of developing diabetic complications compared with diabetic patients with normal and lean physique respectively. This means obesity was associated with higher prevalence of complications and disease becomes more serious in presence of obesity. Substantial reduction in diabetes complications in men and women is achievable if the waist size is decreased (Okosun *et al.*, 1998) with an aerobic exercise program (Sowers, 1998) in high risk populations.

Finally it was concluded that poor glycemic control, early age at diagnosis, gender (male), duration of diabetes and obesity are the factors which can increase the risk of developing diabetic complications. Diabetic patients with these risk factors should be screened for diabetic complications. This practice may be of great help in early diagnosis and then after in proper management of diabetic complications. The clear message to both patients and diabetes care providers is that aggressive and early therapeutic intervention in diabetes is the key to improving and maintaining continued glycemic control and preventing micro- and macro vascular complications. It is proposed that emphasis should be given to health education of diabetes along with pharmacological therapy.

Acknowledgments

This project was greatly facilitated by splendid cooperation of Dr. Hasan Akhtar Bukhari and staff at National Hospital Jinnah colony, Faisalabad, Pakistan, from where the samples were collected.

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