ORIGINAL ARTICLE

Screening of Microvascular Complications of Type-1 Diabetes Mellitus In A Tertiary Care Hospital

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ABSTRACT

Objectives*:* To study the biochemical status and screening of microvascular complications of type-1 diabetic patients.

Study design and settings: It was a descriptive study carried out at Diabetic Clinic of PMRC Research Centre, FJMC, Lahore.

Patients and Methods*:* Eight years case records of type-1 diabetic patients seen at the PMRC Research Centre FJMC Lahore from 1999-2006 were reviewed Out of 1265 diabetic patients sixty five were known type-1 diabetic. A 12 hours fasting blood sample was collected from each patient for serum total cholesterol , triglycerides , low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, urea, creatinine, uric acid and glucose as well as glycosylated hemoglobin (HbA1c) by using standard methods performed at Biochemistry laboratory of the research centre. Body mass index (BMI) was calculated. HbA1c<6.1 was considered as poor glycemic control. Relevant information of all patients was recorded with the help of a pre-designed proforma. They were also investigated for type-1 diabetic complications. Data was analyzed by using statistical software SPSS-15.

Results: Sixty five type-1 diabetic patients mean age of 36±12.5 years of both sexes were screened. These patients were mostly illiterate or having primary education and poor family background and has family history of CHD, diabetes mellitus, hypertension, stroke and gout. Glycemic status (blood glucose level ≥11.1 mmol/l) was noted in 10.8% and mean level of HDL-cholesterol was 0.95 ± 0.09 mmol/l. Rate of complications of reproductive, skin and gastrointestinal tract infection was higher in these patients i.e. 20%, 13.8%, and 10.8% respectively.

Conclusion*:* The study indicates the prevalence of microvascular complications which were common in our type-1 diabetic patients and low HDL-cholesterol was a commonly associated condition among them, while duration of diabetes has significant association with retinopathy and respiratory complications.

Key words: Type-1 diabetes mellitus, Complications, Coronary artery disease, nephropathy, neuropathy, renal, reproductive

INTRODUCTION

Type-1 diabetes mellitus is a multisystem disease with both biochemical and anatomical/structural consequences. It is a chronic disease of carbohydrate, fat and protein metabolism caused by the lack of insulin, which results from the marked and progressive inability of the pancreas to secrete insulin because of autoimmune destruction of the beta cells[1]. It occurs most commonly in juveniles but can also occur in adults, especially in those in their late 30s and early 40s[2].

Unlike people with type-2 diabetes mellitus, those with type-1 diabetes generally are not obese and may present initially with diabetic ketoacidosis. The distinguishing characteristic of a patient with type-1 diabetes is that if his or her insulin is withdrawn, ketosis and eventually ketoacidosis develop. Therefore, these patients are dependent on exogenous insulin[3].

Chronic and progressive nature of the disorder, which is associated with obesity, hypertension, advancing age[4] and inadequate screening[5], leads to deposition of harmful substances in the vascular endothelium ultimately causing development of micro vascular complications[6]. These complications include retinopathy, nephropathy and peripheral neuropathy, which produce early death and increased morbidity and health care costs[7]. These complications vary in prevalence in different populations depending on various factors such as genetic predisposition, ethnicity, type of diabetes, associated predisposing factors and

even definition of the respective complications[8]. The aim of our study was to assess the frequency and biochemical changes occurring leading to macrovascular as well as microvascular complications in type-1 diabetics. In view of the proper non-availability of such data in our local population, the presence of these abnormalities was assessed.

PATIENTS AND METHODS

It was a descriptive study where 1265 diabetic patients were studied of which 65 had diagnosed type-1 diabetes mellitus. Eight years case records of type-1 diabetic patients seen at the PMRC Research Centre FJMC Lahore from 1999-2006 were reviewed and these patients were called for physical examination; laboratory investigations and for checking any complication related to type-1 diabetes. Patients with type-2 diabetes mellitus and seriously ill patients were excluded from the study. Current American Diabetes Association (ADA) definitions and Adult Treatment Panel III (ATP III) guidelines were used to label patients as type-1 diabetics and to assess the associated complications[9].

The patient's personal data, medical, family, dietary history and daily physical activities were recorded according to a pre-designed questionnaire. The height and body weight of each subject were measured. Body mass index (BMI) was calculated in metric units as weight (kg)/height^2 (m^2).

Physical activity was defined as sedentary lifestyle; the patient had no regular physical activity i.e. usually sitting reading or using computer, mild activity; doing little physical activity as walking in the street or doing minor household work, moderate activity those involved in doing some regular exercise as jogging or brisk walk and vigorous physical activity those doing hectic work such as laborers[10].

Blood samples (5ml) were collected after an overnight fast of 12 hours in all patients. Serum isolated and collected in serum tubes and preserved for batch analysis except blood sugar and HbA1c which were analyzed on the same day in blood samples. Blood glucose level was measured by glucose oxidase method.[11] Hemoglobin A_1c was determined after hemolysed whole blood mixed with cation-exchange resin, which bound non-glycosylated hemoglobin, leaving HbA1c in the supernatant measured by calorimetrically[12]. Revised ADA guidelines classify people with HbA1c levels in the range of 5.7 to 6.4 percent as "at very high risk" for developing diabetes over 5 years. The range of 5.5 to 6 percent is the appropriate level to initiate preventive measures. Glycemic control is considered to be poor with glycosylated hemoglobin level >6.1% and good at <6.1 level[13.] Serum total cholesterol concentration was determined by enzymatic CHOD-PAP method[14] using reagent kit from Randox, U.K. Serum HDL-cholesterol was measured by precipitation method (HDL-cholesterol precipitant, and cholesterol concentration was determined by enzymatic CHOD-PAP method using reagent kit from Randox, U.K[15]. The LDL cholesterol concentration in serum was calculated according to the Friedewald formula [LDL cholesterol (mmol/l) = Total cholesterol – (Triglycerides/2.2 + HDL Cholesterol)] [16]. Serum triglycerides concentration was determined by GPO- PAP method using reagent kit from Randox, U.K[17].

Statistical Analysis

Data was analyzed by using SPSS version 15.0. All quantitative variables like age, cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol and BMI were described by using mean and standard deviation. For association of dyslipidemia with age, BMI, duration of disease and glycemic control were calculated by using Chi-square test. P-value ≤ 0.05 was considered statistically significant.

RESULTS

Out of sixty five type-1 diabetic patients 38.5% were male and 61.5% female with average age of 36±12.58 years. Most of the patients were illiterate or having primary education 26.2% and 26.2% respectively. Financially 47.7% belong to poor class and mode of onset of disease was symptomatic in 56.9 % type-1 diabetics. Family history of CHD was present in 35.4%, diabetes mellitus 64.6%and hypertension 49.2% as depicted in table2.

Glycemic status of type-1 diabetics mean ± SD values of blood sugar fasting and random (9.32±3.39 and 13.71±3.38) has shown respectively. Poor glycemic control blood sugar level ≥ 11.1 mmol/l was observed in 10.8% while average (8.8-11.1 mmol/l) and excellent (< 8.8 mmol/l) was noted in 18.5% and 70.80% respectively. Mean level of HDL-cholesterol was 0.95±0.09 mmol/l as depicted in table-3.

Table-4 shows the macrovascular and microvascular complications most commonly occurred among type-1 diabetic.

It is clear that duration of diabetes have significant relationship with diabetic eye and respiratory complications. There is significant relationship between BMI and gastrointestinal tract infection at 5 % level of significance. Other clinical and baseline characteristics with type-1diabetic complication are insignificant with P values reported in table 5

Table-1: Physical and family characteristics of type-1 diabetic patients

		n	%	Mean ± SD
Sex	Male	25	38.5	
	Female	40	61.5	
Age				36.00±12.58
Duration of Diabetes (years)				11.71 ±6.43
Education	Illiterate	17	26.2	
	Primary	17	26.2	
	Matric	16	24.6	
	Above Matric	15	23.1	
Occupation	Unemployed	7	10.8	
	House wife	31	47.7	
	Labour	7	10.8	
	Service	9	13.8	
	Business	9	13.8	
	Technical hand	2	3.1	
Monthly Income	Lower class	31	47.7	
	Middle class	24	36.9	
	Upper class	10	15.4	
Mode of onset	Symptomatic	37	56.9	
	Asymptomatic	28	43.1	
Physical Activity	Sedentary	2	3.1	
	Light	27	41.5	
	Moderate	35	53.8	
	Severe	1	1.5	
BMI				24.7 ±4.7
Systolic B.P				123.8±19.5
Diastolic B.P				82.4±10.4
Family History				
	C.H.D.	23	35.4	
	Diabetes Mellitus	42	64.6	
	Hypertension	32	49.2	
	Stroke	11	16.9	
	Gout	4	6.2	

Table-2: Biochemical characteristics of type-1 diabetes mellitus

		n	%	Mean ± SD
Blood Sugar Fasting mmol/l				9.32 ± 3.39
Blood sugar Random mmol/l				13.71± 3.38
Triglyceride mmol/l				1.77 ± 0.63
Cholesterol mmol/l				4.74 ± 0.89
HDL-cholesterol mmol/l				0.95 ± 0.09
LDL-cholesterol mmol/l				2.96 ± 0.71
Creatinine (µmol/l)				83.09 ± 38.89
Urea(µmol/l)				11.49 ± 3.17
Uric Acid(µmol/l)				230.19 ±53.53
HbA1c	Less than 6.1	11	16.9%	
	Greater than 6.1	54	83.1%	
Glycemic Control	Blood glucose level ≥11.1 mmol/l	7	10.8%	

Table-3: Complications of patients with type-1 diabetes mellitus

Parameter	n	Percentage
Cardiovascular complications	5	7.7%
Retinopathies	4	6.2%
Neuropathy	4	6.2
Nephropathy	5	7.7%
Skin	9	13.8%
Respiratory	2	3.2%
Reproductive	13	20%
Gastrointestinal tract infections	7	10.8%

Table-4: Association of clinical and baseline characteristics with type-1 diabetic complication

	Retinopathy	Neuropathy	Renal	Skin	Respiratory	Reproductive	GIT
Age	0.2898	0.4164	0.1851	0.6313	0.7349	0.9224	0.8015
BMI	0.8840	0.7146	0.8931	0.2585	0.4652	0.3841	0.0224*
Duration of Diabetes	0.0170*	0.0890	0.4970	0.8090	0.0370*	0.5930	0.8560
HbA1c	0.3511	0.3593	0.1520	0.1572	0.4958	0.1406	0.2062

*significant at 5% level of significance

DISCUSSION

Diabetes is a chronic condition with numerous potential complications that considerably affect patients, healthcare providers, society and has been taken as one of the most prevailing disease in recent years. The chronic hyperglycemia in diabetic patients leads to chronic complications of organs like heart, nerves, eyes, kidneys and blood vessels[18], some of the complications related with diabetes have caused death directly or indirectly[19]. Diabetes affects 10% of adult population in Pakistan and has the potential to become 3rd most important cause of blindness in Pakistan [20].

Coronary heart disease is the leading cause of mortality in patients with type-1 diabetes. Cardiovascular complications observed in a study conducted in Pakistan [21] indicated 7.14 % rate while in our study the rate of this complication was 7.7% which is in close association with the study. In our study prevalence percentage of complication especially macrovascular were lower in type-1 diabetic patients [22].

A study conducted to determine the prevalence of microvascular and nacrovascular complications in Asian Indian type-1 diabetic subjects has revealed retinopathy in 13.4% diabetics[23]. The frequency of diabetic retinopathy varies with age of

onset and duration of diabetes. In some of earlier studies in Pakistan, the frequency of retinopathy was reported to be 15%[24], while it ranges from 20-40% in studies from India [25], Sri Lanka [26], UK [27] and USA[28]. In our study retinopathy was observed in 6.2% cases.

Diabetic nephropathy is the most common cause of renal failure in many Eastern Mediterranean region countries[29] and a major cause of premature death in diabetic patients. Diabetic patients are 17 times as prone to kidney disease as non-diabetic people. The cumulative risk of diabetic nephropathy in type-1 diabetes mellitus is about 30%–40% after duration of 25–30 years. 7.1 % nephropathy rate was observed in a study conducted in India [30]. In our study nephropathy was observed in 7.7 % cases.

Diabetic neuropathy is a nerve disorder that may be clinically evident or subclinical and which occurs in diabetics in the absence of other evident etiology[31] .Manifestations may occur in both the peripheral and the autonomic nervous systems. Investigators have reported that 30% of patients with type-1 diabetes mellitus and 36% to 40% with type-2 diabetes mellitus experience neuropathic symptoms[26]. Sensory neuropathy at a rate of 3% was observed in India[32]. In our study 6.2 % diabetics were neuropathic.

Skin complications are the result of a combined effect of hyperglycaemia, neuropathy and vascular abnormalities which include both microvascular and macrovascular angiopathy [33]. In our study 13.6% had cutaneous complication.

Pulmonary function may be adversely affected by diabetes mellitus. The mechanical function of the lungs has been evaluated in a number of studies, but the results are contradictory. Some studies have shown reduction in forced vital capacity, forced expiratory volume in 1 second, total lung capacity, and end-expiratory volume, all of which are the result of decreased elastic recoil[34], however, other studies have shown that pulmonary function is predominantly preserved in persons with diabetes mellitus[35]. In our study pulmonary complications were observed in 3.2 %.

The prevalence of male impotence in diabetics reported range from 20-50% increasing with patient age and duration of diabetes[36]. In our study reproductive disorders were seen in 20%. In Pakistan, diabetes is on rise and if proper intervention and preventive strategies were not adopted the epidemic of diabetes will prove fatal. The present study has limitations due to the small number of patients.

Duration of diabetes showed positive association with retinopathy, neuropathy and neuropathy[37] . In our study association with respect to duration of disease was noted with retinopathy and respiratory disease only. In our study prevalence of complication especially macrovascular were lower in type-1 diabetic patients.

From this study it was observed that neuropathy is generally the first complication to appear, nephropathy and retinopathy soon entering into the race. This combination may leave the patient in a highly morbid condition.

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