Risk Factors and Chronic Complications Among Type 2 Diabetes Patients of Southern Punjab, Pakistan.

Pakiza. M[1*], Aftab. A[1], Naeem. M[1], Azmi. UR[2], Irfan.M[3], Nadeem. Z[4]

[1*]Department of Biochemistry, University of Agriculture, Faisalabad
[2]Department of Plant Breeding and Genetics, University of Agriculture, Faisalabad
[3]Department of Botany, University of Agriculture, Faisalabad
[4]Institute of Biochemistry and Biotechnology, University of the Punjab, Lahore

Abstract- About half of the diabetic population in Pakistan is unidentified and almost half of the initially characterized diabetic patients are seen to have diabetic complications. The purpose of the current study was to evaluate the frequency of chronic complications of Diabetes Mellitus Type 2 in patients attending a primary care center at Jampur, Pakistan. Patientshavingtheir initial appointment at outpatient Department of Iqbal Diabetes Clinic from February 2017 to March 2018. A total of 100 diabetic patients were taken from February to June 2018. A detailed review of medical history, physical inspection and clinical and laboratory tests of blood samples were performed to recognize the dyslipidemia and related complications. A neuropathy disability scores greater than zero was used to classify peripheral neuropathy as low, medium and high. An opthalmoscopic detailed observation of dilated retina was performed. Hyperglycemia was observed in 85%, hypertension in 62%, dyslipidemia in 58%, obesity in 52%, retinopathy in 15%, neuropathy in 47%, nephropathy was in 42% of diabetic patients. Obesity, low HDL, High LDL and total cholesterol were significantly higher in females (p at 0). Neuropathy was seen higher in patients with shorter diabetes duration while all other complications were high in patients with longer diabetes duration and of longer age group. The current study will be fruitful for the management and control of secondary complications in diabetic patients of Pakistan.

Index Terms- Type 2 diabetes, Chronic complications, Neuropathy, Retinopathy, Nephropathy.

I. INTRODUCTION

The Global prevalence of Diabetes is 8.8% of which 80% victims are from low to middle income countries[1,2].Type 2 diabetes mellitus (T2DM) is the most common type of diabetes that covers 90% of the diabetic occupants. Still more than half of the diabetic population is declared to be undiagnosed. High infirmity and fatality rate by diabetes type 2 has lessened the caliber of life, IDF reports 5M deaths by the year 2015, likewise it casts a huge economic burden to check and cure the acute and chronic complications. Type II diabetes shows a direct alliance with complications, until then on identification [3,4]. Firstly, there can be two or more indications of disorder or may be not any. It holds up the identification, aggregating the chance of comorbidities that are often chronic micro and macrovascular complications.

Macrovascular complications contain cardiovascular heart disease, cerebrovascular disease, and peripheral vascular disease, quite linked with the disease and are likely to direct to demise. More than half of the diabetic patients die of cardiovascular diseases, primarily heart attack and stroke[5,6]. Microvascular complications are described by maligned eyes (retinopathy), renal illness (nephropathy) and neurological abrasion (neuropathy). These are the major familiar reasons of visual impairnesss, renal illness and leg amputation [7]. About 30–45% of patients with Type 2 Diabetes Mellitus have microvascular complications[8].

Well-known risk factors for both types of complications include poor glycemic control, diabetes duration, hypertension and dyslipidemia. Age, gender and duration of Diabetes are also major risk factors to flourish the diabetic complications in patients. Over weight and obesity are found huge risk indicators for Diabetes. Proper management and early screening of Diabetes type can be a good outcome for the patients to combat the diabetic complications [9].

II.   MATERIAL AND METHODS

A cross sectional study was carried out in Outpatient Department at Iqbal Diabetes Clinic (IDC), Jampur, Dist. Rajanpur. A total of 100 diabetic patients were included in this study and all of them had their first visit at IDC. The inclusion criteria were: (1) T2DM diagnosed in accordance with international standards (WHO 1999), i.e. fasting plasma glucose (FPG) $\geq$ 7.0 mmol/L and/or 2 hours' postprandial plasma glucose (PPG) or casual plasma glucose $\geq$ 11.1 mmol/L, under regular anti-diabetic drug treatment for at least 6 months,>18 years old, resident of the same district, provided written informed consent to participate in the study. The majority of patients belonged to the low and middle socio-economic class. Only chronic complications such as cardiovascular conditions, cerebrovascular conditions, nephropathy, retinopathy, neuropathy, and diabetic foot problems that develop mostly after the proper diagnosis of T2DM were considered in this study. All the patients were interviewed via a full structured questionnaire to grab information about their demographics, diabetes related complications and medical history.All the information deduced from patients were kept confidential. Medical records and prescription reviews were done to know if they had cardiovascular and cerebrovascular complications. Moreover, to assess various complications blood and urine tests such as serum creatinine level, FPG, lipids were also performed in certified labs. Following is the detail of methods used to assess the diabetic complications: All the patients were tested for Fasting Plasma Glucose for free of charge. A standard digital Glucometer was used to check the blood glucose levels and for successive visits of patients to OPD these values were averaged. Hyperglycemia was defined to be $\geq$126mg/dl in fasting conditions. Blood pressure was measured with a standard mercury sphygmomanometer. Hypertension was defined as a systolic blood pressure of at least 140 mm Hg and/or a diastolic blood pressure of at least 90 mm Hg or current use of any treatment with antihypertensive medications. Blood pressure of each patient was measured after making sure that he took rest of at least 10 minutes. The average of two or more readings separated by 2 min wastaken [10].

Body mass index (BMI) was calculated using the formula: weight (kg)/height squared (in m2). BMI between 18.5 and 24.9 was considered normal, while that of >25.0-26.9 as overweight. The WHO protocol for measuring waist/hip was followed, a value $\leq$90 for male and $\leq$80 for females was considered to be normal. An Ophthalmoscope was used by the Diabetologist for testing Diabetic Retinopathy. The structures present in the innermost facet of the eye ball mostly named as the eye ground/ retina, blood vessels of retina were examined. Detailed medical history of patients was also examined for previous cataract or laser therapy. The glomerular filtration rate (GFR) was estimated on the basis of serum creatinine levels. Spot urine samples were tested for microalbuminuria. Severe nephropathy was defined as a doubling of the serum creatinine level, a creatinine level of more than 3 mg per deciliter (265 µmol per liter), or a GFR of less than 15 ml per minute. The lipid profile of each patient was recorded for this reason; laboratory tests for Total Cholesterol,Triglycerides,LDL and HDL were performed. To check the Diabetic Neuropathy patient's detailed interviews, review of medical history and a lower extremity physical examination was done by the same investigator to assure the uniformity. Neuropathy Disability Score andmonofilaments (10 g) were used to identify peripheral sensory neuropathy as previously described by Boulton[11].

The Achilles tendonreflexes were assessed. 0 was used if the reflex could be detected positively by the patient with closed eyes and a score of 1 was marked if the response was negative. Sensory tests were also performed by using a pinprick usinga neuro-tip over the hallux dorsal area proximal to   toe. Vibration testing was done with attuning fork on the pulp of the hallux and temperature perception over hallux dorsal area proximal to the toe. The sum of scores presented the neuropathy disability score. If DNS was >6 indicated high risk for neuropathy. A patient detected to be irresponsive to the 10 g monofilament pressure was reported to be at high risk to develop foot ulcer. All the data and information were arranged on Microsoft Excel sheet and results were drawn. To analyze the data statistically SPSS version 25 was used. One sample t-test was done to assess the statistical significance of the sample mean with standard cutoff values. Frequency of chronic complications in young age group and old age patients; comparatively and in patients

with little and long duration of diabetes was measured. The significance of these differences was evaluated by performing Chi square test[12].

III.   RESULTS

A total of 100 diabetic patients were included in these study 68% males and 32% females. Mean age of the patients for male was 51.6±11.3 years (p at 0) and for females it was 48.6±11.4 years (p at 0). Age of patients was recorded as 27% patients were between -39 years, 25% were between 40-49 years, 26% were between 59-60 years, 14% were between 60-69 years and 8% were 70 and above 70 years old. The patients diagnosed with DM 2 at the age of 30 were 3%, 30-39 years were 27%, above 40 were 25%, at 50 were 27% and after 60 were 10%. The patients had different occupations 28% were home maker, 10% were school teachers, 15% were farmers and 19% were retired. About 80% of females were house wives. As a whole 52% patients were found with positive diabetes family history, 35% patients reported single diabetic parent, 13% had both diabetic parents and 4% had their siblings with diabetes. Fifteen percent were reported to be ex-smokers and 35% were smokers including 3% female smokers.

Table 1: Mean Values For Metabolic Risk Factors of Patients (N=100)

Parameters	Marked Value	Differences From Marked Values Specify Metabolic Risk Factors											
		Sex of Patients											
		Male						Female					
		Mean	SD	T	p value	95% CI of difference		Mean	SD	T	p value	95% of CI of difference	
Age		51.65	11.46	284.88	0	48.863	54.373	48	11.24	106.19	0	205.72	213.78
BMI (kg/m2)	25	27.7	5.21	24.53	0	90.202	91.475	29.3	5.51	86.67	0	156.63	164.18
Waist to Hip Ratio	M 90, F 80	90.94	2.5	67.06	0	177.01	208.37	84.87	3.46	29.35	0	42.454	48.796
FPG (mg/dl)	144	193	65.13	110.58	0	146.11	155.07	21.8	73.98	118.55	0	103.81	107.44
systolic BP (mmHg)	85	83	10.5	90.86	0	194.43	201.57	80	22.6	85.4	0	51.5	54
Diastolic BP(mmHg)	130	130	20.3	35.09	0	154.96	161.92	136	21.7	115	0	47.5	46.5
Cholesterol (mg/dl)	200	197.6	14.62	76.74	0	38.405	43.037	210	11.14		0.0003	155.8	162.5
Triglycerides (mg/dl)	150	158.11	14.23	6.64	0	107.21	112.94	161	10.68	4.91	0	0.2558	0.6192
Low HDL (mg/dl)	130	40.5	9.57	0.34	0	0.2777	0.5164	45.7	8.68	4.91	0	0.2558	0.6192
High LDL (mg/dl)	M 40, F 50	110	11.85	2.034	0.01	0.123	0.532	105	5.05	4.03	0	0.1698	0.5177

At reporting time 15% patients had diabetes duration more than 5 years, 35% had between 5-10 years and 12% had more than 10 years. Patients adhered to diabetic food were ≤45%. Table 1 shows the comparison of mean values of variables with the standard values that elucidates metabolic risk factors for patients, analyzed by one sample t-test. The mean values for variables and their statistical significance is given in table 1.

Table 2: Occurance of diabetes complications with respect to Gender

Complications	Gender			Chi square test
	Overall %	Male	Female	p-value
Metabolic risk factors				
FPG>144 (mg/dl)	86	83.8	90.6	Ns
TGL>150 (mg/dl)	68	60.3	84.4	0.016
HDL<40 male,<50female	70	67.6	75	0
LDL>130 (mg/dl)	57	47	78	Ns
Obesity (BMI>25)	59	55.9	65.6	0
Systolic HTN>130	90	89.7	90.6	0
Diastolic HTN>85	51	51.5	50	0.031
Total Chl.>200 (mg/dl)	36	27.9	53.1	0.014
Microvascular				
Neuropathy	60	60.3	59.4	Ns
Retinopathy	43	42.6	43.8	ns
Nephropathy	36	39.7	28.1	ns
Macrovascular				
Stroke	5	7.4	0	Ns
CVD	6	7.4	3.1	Ns

The frequency of complications overall and in male and female is shown separately. The most frequent risk factor calculated was Hyperglycemia 86% accompanied by other risk factors 59% were obese, 58% had abnormal lipids.

Table 3: Frequency of Diabetes Complications according to Age

Complications	Age		Chi square test
	< 40 Years	≥ 40 Years	p-value
Metabolic Risk Factors			
FPG>144mg/dl	92.6	83.6	Ns
TGL>150mg/dl	85.2	61.6	0.025
HDL<40 male,<50female	63	72.6	Ns
LDL>130mg/dl	52	61.5	Ns
Obesity (BMI>25)	55.6	60.3	Ns
Systolic HTN>130mmHg	81.5	93.2	0.084
Diastolic HTN>85mmHg	37	56.2	0.089
Total Chl.>200mg/dl	37	35.6	Ns
Microvascular			
Neuropathy	59.3	60.3	Ns
Retinopathy	29.6	47.9	Ns
Nephropathy	14.8	43.8	0.007
Macrovascular			
Stroke	0	6.8	Ns
Cardiovascular disease	11.1	4.1	Ns

Frequency of microvascular complications was as follows: retinopathy 43%, neuropathy 60%; nephropathy was 36% and more than three fourth of diabetic patients had high blood pressure. 75% of the patients were taking diabetic medications orally, 10% were taking insulin injections and 15% were on diet control. Occurrence of triglycerides, total Cholesterol and Hypertension was high in females

(p at 0). High triglycerides were found in younger age group of patients while High systolic blood pressure and nephropathy were more frequent in older group. Data is given in table 3.

Table 4: Frequency of Diabetes Complications according to Duration of Diabetes

Complications	Duration of Diabetes		Chi square test
	< 10 Years	≥ 10 years	P-value
Metabolic Risk Factors			
FPG>144 (mg/dl)	84.4	91.3	Ns
TGL>150 (mg/dl)	71.4	56.5	Ns
HDL<40 male,<50female	67.5	78.3	Ns
LDL>130 (mg/dl)	57.2	72.1	0.056
Obesity (BMI>25)	54.5	73.9	0.097
Systolic HTN>130mmHg	89.6	91.3	Ns
Diastolic HTN>85	49.4	56.5	Ns
Total Chl.>200mmHg	37.7	30.4	Ns
Microvascular			
Neuropathy	61	56.5	Ns
Retinopathy	40.3	52.2	Ns
Nephropathy	18.2	95.7	0
Macrovascular			
Stroke	1.3	17.4	0.002
CVD	6.5	4.3	Ns

The occurrence of complications according to duration of diabetes. High LDL and hypertension were found to be frequent in patients with longer duration of diabetes.Hypertension was recorded as most prominent risk factor for the patients. Total cholesterol also indicated high risk factor with clearly being higher in females than in males. The progression of complications with diabetes duration could not be clearly demonstrated, even some patients with recently diagnosed with diabetes had developed some complications. It was related to low economic status of patients, high illiteracy and latent period of diabetes diagnosis. Much more studies are needed to check these complications in this area.

IV. DISCUSSIONS

About 35% of the diabetic patients are found to have diabetic complications even at the time of diagnosis. Hence it is crucial to explain the epidemiology of Diabetes Mellitus 2 complications and its co-morbidities. To our familiarity this could be the first record for survey of prevalence of chronic complications of Diabetes Mellitus 2 in rural areas of Southern Punjab, Pakistan. The results of this study report the frequency of many chronic complications in Diabetes type 2 patients attending a primary care unit in Jampur (Dist.Rajanpur). Our discoveries are relative and not fixed so the results cannot always be compared. Twenty-seven percent of patients were ≤40 years of age. This tendency of occurring of DM2 at younger age in this region is proportionate to other studies. The high frequency of diabetes in the 40-60 age group patients showed that more than half of diabetics were at diabetes in their most fertile years of life. Mean age of the diabetics in this study group was 47 years whereas a study done in Karachi it was 52. As the study was district based and combines previous undiagnosed diabetes patients, it could be supposed that district based surveys describe a substantial reduced mean age of the diabetics.

More than 50% of our study population showed positive family history for Diabetes Mellitus type 2, showed a firm inherited increase of the disease in this locality. Moreover, certain other factors such as eating patterns also affected BMI and other risk factors to develop the illness and its associated complications. About three-fourth of the patients had poor glycemic control on their first visit

to the OPD and more than half of the diabetic population had diabetes for > 5 years. This showed the high liability of diabetes and its associated complications for > 5 years. A higher proportion of diabetic patients was instructed to take exogenous insulin but only 10% of patients were going through insulin treatment. This focused the demand of revolutionizing the care centers for diabetes and creating responsiveness among the public about this disaster and its worseness. Our study showed eloquently higher triglycerides and low a HDL were measured that is consistent with diabetes dyslipidemia studied in India[13].

However, patient's social and demographic background may have effects on these dissimilarities. As well as expert ophthalmologists and better monitoring of retinopathy in specific care centers is necessary to find out the exact number.Our study showed the frequency of macrovascularcomplications overall as 7%, cardiovascular diseases being 6% and 1% stroke that are comparatively lower than the results of another study who found 18% of the diabetic patients to have macrovascularcomplications 12% CVDs cases and 6% were found to have strokes [14].

The Frequency of neuropathy was 60% with no gender differences. A recent study in India conducted by showed the same results 59% for neuropathy. High prevalence of foot ulcers was also recorded about 20% of total of 60%. This is because a large proportion of patients belonged to backward areas and had poor life style. Knowledge about the complications and life style improvements can reduce the number of diabetic patients with peripheral neuropathy and foot problems. Total cholesterol, triglycerides, obesity and Hypertension was recorded more prevalent in females than in male. While microvascular complications showed no significant gender differences. In our study prevalence of diabetic nephropathy was 36% comparable to that conducted in India was 40% . The calculations were based on the values of estimated glomerular filtration rates by measuring serum-creatinine ratio and urine test for micro albuminuria. 5% patients were detected with end stage renal disease. Timely detection and proper treatment can reduce the kidney failures. Triglycerides and hypertension increased with the age but diabetes duration had no significant effect on these variables, indicating that these risk factors emerged in latent period of diabetes. Detection of more than half of diabetics with hypertension declares it to be a major risk factor towards a number of diabetes related complications.

V.   CONCLUSION

The higher frequency of the diabetic complications is worsening the caliber of life in this area. It demands a high need for advanced health care centers and alertness in patients to take greater self-care and revolutionize their lifestyles. The screening methods for diabetes should be made improved to combat the chronic complications of diabetes. Further research with improved methodology is needed to hit upon the exact frequencies of these complications and to find the relation between several risk factors and the complications.

REFERENCES

[1]   Abougalambou S, Abougalambou A . Risk factors associated with diabetic retinopathy among type 2 diabetes patients at teaching hospital in Malaysia.2015 :9(2), 98-103.
[2]   Basit A, Hydrie M, Hakeem R, Ahmedani M ,Masood Q. Frequency of chronic complications of type II diabetes. Journal of the College of Physicians and Surgeons, Pakistan,2004; 14(2), 79-83.
[3]   Chatterjee S , Khunti K ,Davies M. J. Type 2 diabetes. Lancet, 2010;389(10085), 2239-2251
[4]   Cho N, Shaw J , Karuranga S, Huang Y. IDF Diabetes Atlas: global estimates of diabetes prevalence for 2017 and projections for 2045.2018 , 138, 271-281.
[5]   Santos J, Moreira T. Risk factors and complications in patients with hypertension diabetes in a regional health district of northeast Brazil. Revista da Escola de Enfermagem da USP,2012 : 46(5), 1125-1132.
[6]   Herman W. H, Zimmet P. J. Type 2 diabetes: an epidemic requiring global attention and urgent action.2012: 35(5), 943-944.
[7]   Heydari I, Radi V, RazmjouS. Chronic complications of diabetes mellitus in newly diagnosed patients.2010; 2(1), 61-63.
[8]   Hussain S, Qamar M. R, Iqbal M. A, Ahmad A. Risk factors of retinopathy in type 2 diabetes mellitus at a tertiary care hospital, Bahawalpur Pakistan.2013; 29(2), 536.
[9]   Ikem R, Ikem I, Adebayo O. An assessment of peripheral vascular disease in patients with diabetic foot ulcer.2010; 20(4), 114-117.
[10] Khanam P. A, Hoque S, BegumT, Habib S. H, Latif,Z. A. J. D, Research M. S. C., & Reviews. Microvascular complications and their associated risk factors in type 2 diabetes mellitus. 2011;11, S577-S581.

[11] Maniarasu K, Muthunarayanan M & HealthP. Prevalence of certain chronic complications of diabetes among type 2 diabetic patients in rural population of Kancheepuram district, Tamil Nadu-A cross sectional study. 2017;7(1),132-138

[12] Miah. M, Yousuf. M. Analysis the significant risk factors on type 2 diabetes perspective of Bangladesh. 2018;24(5), 111-116.

[13] Ogurtsova K, Fernandes J, Huang Y, Linnenkamp U, Guariguata, L. IDF Diabetes Atlas: Global estimates for the prevalence of diabetes for 2015 and 2040.2017; 128, 40-50.

[14] Oliveira. A,Valente. J, Leite. I, Schramm. J, Azevedo A. Global burden of disease attributable to diabetes mellitus in Brazil.2009; 25(6), 1234-1244.

AUTHORS

First Author – Maryam Pakiza, M.Phil. Biochemistry, University of Agriculture, Faisalabad, maryampakiza07@gmail.com.

Second Author – Aftab Ahmad, Assistant Professor, Department of Biochemistry, University of Agriculture, Faisalabad,aftab.ahmad@uaf.edu.pk.

Third Author – Muhammad Naeem, M.Phil. Biochemistry, University of Agriculture, Faisalabad,naeemsaleem413@gmail.com.

Correspondence Author – Maryam Pakiza, maryampakiza07@gmail.com, +923333153666