

Risk Factors Associated with Diabetes Mellitus in Local Population of Lahore, Pakistan

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Abstract

Background: Diabetes is the leading cause of morbidity and mortality amongst the people of Pakistan. In 2015, 7 million people had diabetes and the number is still on raise. Family history of diabetes, high body mass index, and other sociodemographic factors are the risk factors of diabetes. Persistent exposure to excessive glucose may be a reason behind diabetic complications like nephropathy, neuropathy, retinopathy, cardiomyopathy and gestational diabetes mellitus.

Methods: For the evaluation of laboratory parameters, 600 blood samples were collected at Akhuwat Diabetic Centre and from Jinnah Hospital, Lahore. Demographic data of the participants was collected by filling a questionnaire. Lipid profile, liver enzymes, and renal function tests were performed and statistical analysis was done.

Results: Type 2 diabetes mellitus among other types is the most prevalent form of diabetes in our population. Family history of diabetes ($p=0.002$), Body Mass Index (>25) $p<0.001$, high cholesterol ($p=0.04$), high triglyceride $p<0.001$, high LDL $p<0.001$ and low HDL $p<0.001$ are significantly associated with the incidence of diabetes. Hypertension among the other comorbidities is more common in diabetic patients.

Conclusion: Type 2 Diabetes Mellitus is highly prevalent in the local population. Improved lifestyle and proper medical monitoring can help to manage diabetes in our population.

Keywords: T2DM, BMI, lipid profile, liver enzymes, renal profile

1. Introduction

Diabetes Mellitus a metabolic disorder arises if body is incapable to synthesize sufficient insulin for metabolism, it could be due to improper insulin secretion, improper insulin action, or both. Persistent exposure to excessive glucose could be a dominant reason for cardiomyopathies nephropathies, retinopathies, neuropathies and a variety of different sorts of tissue injury. Diabetes mellitus additionally leads to vascular disease, hypertension, dyslipidemia, and obesity (Leech et al., 2011; Malandrino, Wu, Taveira, Whitlatch, & Smith, 2012; Zimmet, Magliano, Herman, & Shaw, 2014) (Figure 1).

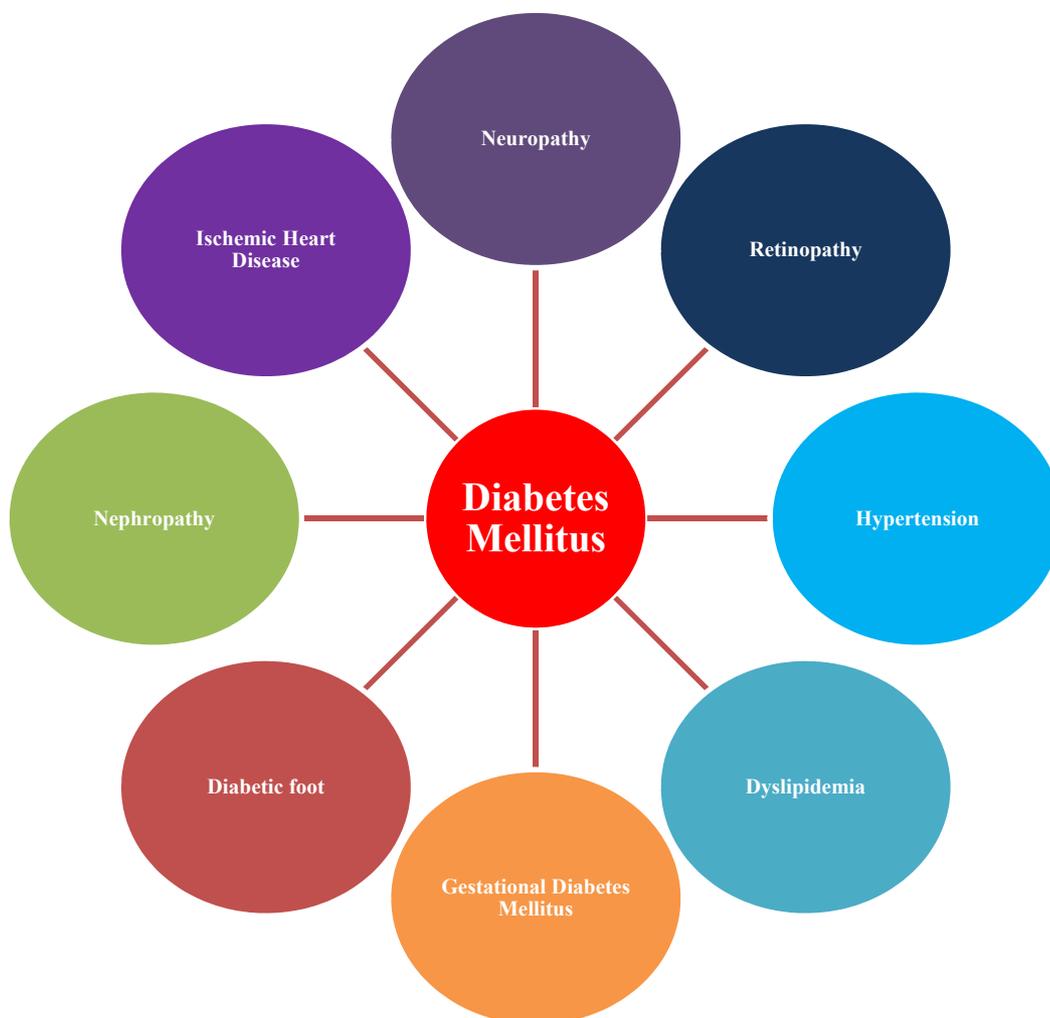


Figure 1: Diabetes-related complications

The most common type of diabetes is Type 2 (95%), while Type 1 only contributes 4-5% (Model, 2015; World Health, 2016). According to WHO in 2014, 422 million adults have diabetes worldwide (World Health, 2016). International Federation of Diabetes (IDF) reported that approximately 415 million people had diabetes in 2015 (*IDF Diabetes Atlas*, 2017) and almost 1.5 million deaths are directly attributed to diabetes each year (World Health, 2016). In Pakistan diabetes is one of the most prevalent metabolic disorder. In 2015, National Diabetes Action Plan of Pakistan reported over 7 million people suffering from diabetes (Sherin, 2015). According to International Diabetes Federation (IDF) report, the prevalence of diabetes in Pakistan in 2014 was approximately 7% ("International Diabetes Federation", 2015). A diagnostic criterion for the diagnosis of diabetes mellitus defined by World Health Organization (WHO) and International Diabetes Federation (IDF) is presented in figure 2 (*IDF Diabetes Atlas*, 2017).

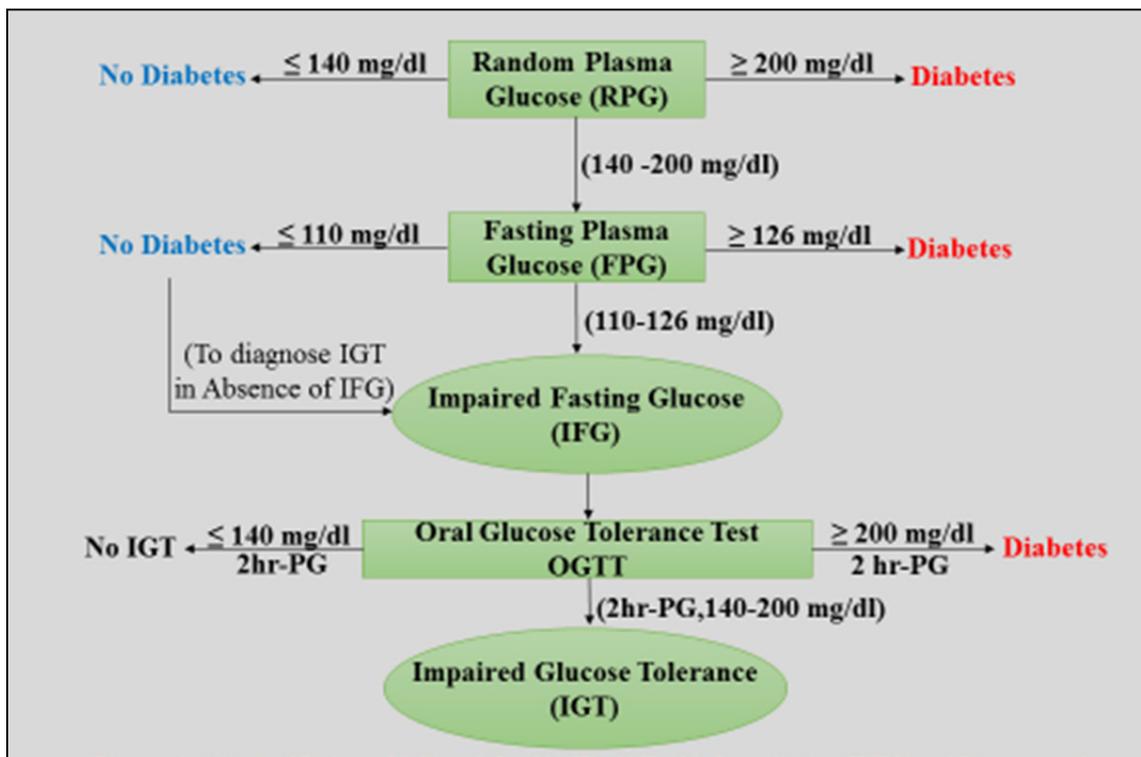


Figure 2. Diagnostic criteria of Diabetes Mellitus defined by World Health Organization (WHO) and International Federation of Diabetes (IFD)

Numerous studies on the prevalence and risk factors related to T2DM are disbursed in the Asian nation within the past, however, most of them are restrained to South Indian populations (Sethi, Kumar, Gupta, & Bhanwer, 2011). So this study was conducted to compare social and demographic features among diabetic and non-diabetic individuals in our local population. Another important aim of this study was to compare lipid profile, renal function tests and liver function tests in diabetic and non-diabetic individuals.

2. Materials and Methods

2.1 Study Design

A cross-sectional study was designed, in which 600 blood samples were collected from the participants visited Akhuwat Diabetic Centre, Township Lahore, and Jinnah Hospital Lahore from December 2016 to April 2017.

2.2 Sample Size

According to International Diabetes Federation (IDF) report, the prevalence of diabetes in Pakistan in 2014 was approximately 7% so using open epi software a minimum sample size for this study was 101 with 95% confidence interval ("International Diabetes Federation ", 2015; Sherin, 2015).

2.3 Sample Collection, Transportation, and Storage

From all the subjects including in the study, 5ml blood was drawn from the median cubital vein of the arm with the help of sterilized 5cc syringe and collected in EDTA-containing tube, serum separating tube and sodium fluoride containing tube. Samples were carefully transported to Laboratory and stored at 2-8°C for further processes.

2.4 Demographic Data

Demographic data of the participants was collected by filling a questionnaire, including the following particulars: age, gender, smoking, alcohol consumption, family history of diabetes, family history of hypertension, surgical history of the participants and any other comorbidity. Body mass index (BMI) of the participants was calculated by the following formulae:

$$BMI = \frac{\text{Weight of the person in Kgs}}{\text{Height of the person in m}^2}$$

2.5 Laboratory Analysis

Blood Sugar Random (BSR)

Blood Glucose of all participants was estimated by using kits of Cobas ® c311 by Roche Diagnostics, USA.

HbA1c

For all those participants who had elevated levels of Blood Glucose, estimation of blood glycated hemoglobin (HbA1c) was done (Cobas ® c311, Roche Diagnostics USA).

Lipid Profile:

Serum Cholesterol, Triglyceride, High Density Lipoprotein (HDL) and Low Density Lipoprotein (LDL) were measured in all blood samples (Cobas ® c311 by Roche Diagnostics USA).

Renal Function Tests (RFTs)

For renal function test Serum Urea, Serum Creatinine and Serum Uric Acid were measured and kits of Cobas ® c311 by Roche Diagnostics USA were used.

Liver Function Test (LFTs)

Serum Total Bilirubin, Serum Alanine Aminotransferase (ALT), Serum Aspartate Aminotransferase (AST) and Serum Alkaline Phosphatase (ALP) were estimated by using kits of Cobas ® c311 by Roche Diagnostics USA.

2.6 Statistical Analysis

Data was stored in Microsoft EXCEL and analyzed using the Statistical Package for Social Sciences (SPSS 21.0. version). Descriptive analysis was done for the calculation of frequencies of different variables. Chi-square test was done to evaluate any significant association among qualitative variables and Independent T-test was done to compare mean difference between diabetic and non-diabetic group. Regression analysis was done to find out Odd Ratio (OR) and 95% Confidence Interval (CI) for different variables. P value less than 0.05 was considered as significant in this study.

3. Results

In this cross sectional study, blood samples from 600 participants were collected, of which 83% were diabetic and only 17 % were non diabetic. Table 1 presents the comparison of diabetic patients vs. non-diabetic group; of 500 diabetic patients 221 (44%) were male and 279 (56%) were females while 45% were non-diabetic males and 55% were non-diabetic females. Results of chi-square analysis indicate diabetes is gender independent. Diabetes was more prevalent in married people as 99% of the diabetic patients were married (p value <0.001). Two-hundred and eighty-two (56%) of diabetic patients with >10,000 PKR income were moderate while rest (44%) were with the poor socioeconomic background (\leq 10,000 PKR monthly income). Socio-economic status showed a borderline significant relation with the high prevalence of diabetes (p value = 0.05).

Smoking and Alcohol consumption did not show any statistical significance with diabetes. Results of this study indicate body mass index (BMI) was significantly associated with diabetes. Among 600 participants 362 were obese and 96% of these obese participants had diabetes (p value <0.001).

Table 1. Comparison of Diabetic and Non-Diabetic Group

Characteristics		Diabetic Group n= 500	Non-Diabetic Group n=100	p value
Gender	Male	221 (44%)	45 (45%)	0.88
	Female	279 (56%)	55 (55%)	
Marital Status	Married	497 (99%)	82 (82%)	<0.001
	Unmarried	3 (1%)	18 (18%)	
Socio-economic Status	Poor	218 (44%)	33 (33%)	0.05
	Moderate	282 (56%)	67 (67%)	
Smoking	Non-smoker	457 (91%)	88 (88%)	0.28
	Smokers	43 (9%)	12 (12%)	
Alcohol Consumption	Non-alcohol Consumer	498 (99.6%)	99 (99%)	0.43
	Alcohol Consumer	2 (0.4%)	1 (1%)	
BMI	Normal (≤ 25)	149 (30%)	89 (89%)	<0.001
	Obese (>25)	351 (70%)	11 (11%)	

Out of 500 diabetic patients 96.8% had Type-2 Diabetes Mellitus and others had Type-1 Diabetes Mellitus. Glycated hemoglobin (HbA1c) was raised ($>6.0\%$) in 464 (93%) of the diabetic patients and only 36 (7%) of the diabetic patients had their normal HbA1c (4.0-6.0%).

Hypertension is highly prevalent in diabetic patients (45%) among all other comorbidities (Table 2).

Table 2. Prevalence of Comorbidities in Diabetic Patients

Comorbidities	Frequency (Percentage)
Hypertension (HTN)	226 (45%)
Surgical History	180 (36%)
Dyslipidemia	39 (8%)
Ischemic Heart Disease (IHD)	32 (6%)
Nephropathy	26 (5%)
Neuropathy	22 (4%)
Liver Disease	17 (3%)
Diabetic Foot	5 (1%)
Infectious Diseases	3 (0.6%)
Retinopathy	2 (0.4%)

Results indicate Lipid Profile (Serum Cholesterol, Triglyceride, HDL and LDL) was statistically associated with the incidence of diabetes mellitus. Serum Cholesterol (p value: 0.04; OR: 1.56; 95% CI: 1.00-2.45), Serum Triglyceride (p value: <0.001 ; OR: 3.86; 95% CI: 2.23-6.70), Serum HDL (p value: <0.001 OR: 3.24; 95% CI: 1.68-6.24) and Serum LDL (p value: <0.001 ; OR: 2.63; 95% CI: 1.43-3.89). Statistically Liver Function Tests (Serum Total Bilirubin, ALT, AST and ALP) and Renal Function Tests (Serum Urea, Creatinine and Uric Acid) did not show any association with diabetes mellitus (Table 3).

Table 3. Comparison of Lab Parameters among Diabetic and Non-Diabetic Group

Lab Parameter		Diabetic Group	Non-Diabetic Group	OR (95% CI)	p value
		n= 500	n= 100		
Cholesterol	≤200 mg/dL	229 (87%)	35 (13%)	1.56 (1.00-2.45)	0.04
	>200 mg/dL	271 (81%)	65 (19%)		
Triglycerides	30-200 mg/dL	279 (77%)	83 (23%)	3.86 (2.23-6.70)	<0.001
	>200 mg/dL	221 (93%)	17 (7%)		
HDL	35-65 mg/dL	357 (80%)	89 (20%)	3.24 (1.68-6.24)	<0.001
	<35 mg/dL	143 (93%)	11 (7%)		
LDL	60-130 mg/dL	293 (80%)	77 (20%)	2.63 (1.43-3.89)	<0.001
	>130 mg/dL	207 (90%)	23 (10%)		
Total	≤1.1 mg/dL	415 (84%)	81 (16%)	0.87 (0.50-1.51)	0.63
Bilirubin	>1.1 mg/dL	85 (82%)	19 (8%)		
ALT	≤42 IU/L	389 (84%)	76 (16%)	1.10 (0.60-1.83)	0.69
	>42 IU/L	111 (82%)	24 (18%)		
AST	≤41 IU/L	392 (84%)	75 (16%)	1.21 (0.73-1.99)	0.45
	>41 IU/L	108 (81%)	25 (19%)		
ALP	35-130 IU/L	367 (85%)	64 (15%)	1.55 (0.98-2.44)	0.058
	>130 IU/L	133 (79%)	36 (21%)		
Serum Urea	10-50 mg/dL	469 (83%)	93 (17%)	1.13 (0.48-2.66)	0.76
	>50 mg/dL	31 (82%)	7 (18%)		
Serum Creatinine	0.7-1.2 mg/dL	452 (83%)	93 (17%)	0.41 (0.61-3.21)	0.41
	>1.2 mg/dL	48 (87%)	7 (13%)		
Serum Uric Acid	3.4-7.0 mg/dL	445 (84%)	84 (16%)	1.54 (0.84-2.81)	0.16
	>7.0 mg/dL	55 (77%)	16 (23%)		

In this study family history of hypertension did not show any significant relation with the commencement of diabetes mellitus (p value: 0.11; OR: 1.44 and 95% CI: 0.91-2.26). However, family history of diabetes mellitus is significantly associated with the incidence of diabetes mellitus (p= 0.002, OR: 1.97 95% CI: 1.27-3.04). Results presented in Table 4.

Table 4. Comparison of Family History of Diabetes and Hypertension among Diabetic and Non-Diabetic Group

Characteristics		Diabetic Group	Non-Diabetic Group	OR (95% CI)	p value
		n= 500	n= 100		
Family history of HTN	Yes	287 (81%)	66 (19%)	1.44 (0.91-2.26)	0.11
	No	213 (86%)	34 (14%)		
Family history of Diabetes	Yes	343 (87%)	52 (13%)	1.97 (1.27-3.04)	0.002
	No	157 (77%)	48 (23%)		

4. Discussion

This study was designed to investigate the association of sociodemographic factors with the incidence of diabetes mellitus and to throw light on the relationship of diabetes mellitus with the lipid profile, liver function tests, and renal function tests.

Results of this study suggest a high prevalence of diabetes in a local population of Lahore, Pakistan. It has been showed in the National diabetic survey conducted by Diabetes Association of Pakistan (DAP) and World Health Organization (WHO) that the prevalence of diabetes was 11% in Pakistan in 1990s ("Milestones of the Diabetic Association of Pakistan," ; Sherin, 2015; World Health, 2016). According to International Diabetes Federation (IDF) report, the prevalence of diabetes in Pakistan in 2014 was approximately 7% ("International Diabetes Federation ", 2015; Sherin, 2015). According to WHO and IDF reports 422 million adults have diabetes in 2014 and 415 million people had diabetes in 2015 respectively (*IDF Diabetes Atlas*, 2017; World Health, 2016). In this study, although the percentage of diabetes is much higher than previously reported. This study has strength that it reflects the association of not only social demographic characteristics but also laboratory parameters with family history of diabetes. However, there is some limitation as samples were collected from the specialized therapeutic clinic, which may a reason behind the high frequency of diabetes in our participants. The data of this was not randomly collected from population which is a limitation of this current study.

Findings of this study suggest that diabetes is more prevalent in adult age (mean age 49.05 years). Study of Dai *et al* in 2012 supported this fact that aging is an important risk factor for diabetes. Mitochondrial dysfunction starts with the aging, which disturbs the cellular physiology and helps in the development of pathological conditions like insulin resistance (D. F. Dai, 2012). The results of this study suggests that diabetes is prevalent in married people as compared to unmarried individuals, these results are in accordance with the earlier (Azimi-Nezhad *et al.*, 2008; Corsi & Subramanian, 2012)

Current findings suggest that smoking and alcohol are not significant for the onset of diabetes in accordance with the previous reports (Carter *et al.*, 2015; Holmes *et al.*, 2014; Mokdad *et al.*, 2003).

Body mass index (BMI) is significantly associated with the commencement of diabetes mellitus. Multi-various studies showed the positive connection of high BMI with the diabetes mellitus. Overweight/obesity contribute to fatty liver or insulin resistance and also disturbs body metabolism thus helps in the progression of diabetes (Sung, Jeong, Wild, & Byrne, 2012). Modern lifestyle, physical inactivity or psychological stress are the causes of abnormal BMI which leads to diabetes mellitus. Studies showed that there are 42% more risk for diabetes if BMI of a person is above 30.

It was also observed that Type 2 diabetes mellitus is the most prevalent type of diabetes among others. Dey *et al* in 2011 reported that 5-10% cases are suffering from Type 1 diabetes while 90-95% cases are of Type 2 diabetes mellitus (Dey & Attele, 2011). This high prevalence of Type 2 diabetes may be due to psychological behavior, hypertension, stress, obesity, moderate lifestyle with less physical activities and improper glycemic control. All these factors considered as risk factors for the diabetes mellitus (Sethi *et al.*, 2011).

We reported a significant association of Lipid profile (Cholesterol, triglyceride, HDL and LDL) with diabetes. Results indicate Cholesterol, Triglyceride, and LDL were elevated whereas HDL which is considered as a good cholesterol was less in diabetic patients. Our results are consistent with previous reports (Khan, Sobki, & Khan, 2007; Meikle *et al.*, 2013) those suggested hypercholesterolemia, hypertriglyceridemia, high LDL and low HDL levels are the significant risk factors for the cardiovascular disorders in diabetic patients (VinodMahato *et al.*, 2011) and 8% of diabetic patients of this study have diabetic lipidus. In the study of Pandya *et al*, 82% of diabetic patients showed dyslipidemia (Pandya, Lakhani, Dadhania, & Trivedi, 2012). Major etiology behind diabetic lipidus is insulin resistance due to the interaction of insulin with apolipoproteins and adipocytes in obesity (Meikle, Wong, Barlow, & Kingwell, 2014). Dyslipidemia together with diabetes mellitus is the leading cause of Ischemic heart disease (IHD) as indicated by the prevalence of IDH in diabetic patients of the current study is 6%.

In contrast to previous studies our results did not suggest any association of Liver enzymes (ALT, AST, and ALP) with diabetes (Harris, 2005; Nannipieri *et al.*, 2005; Vozarova *et al.*, 2002). Liver enzymes are not directly linked with diabetes however abnormal liver enzymes may be due to obesity or any other complication that arise after diabetes. Similarly in our samples renal function test also did not show any statistical significant association with diabetes.

Bamanikar *et al* concluded that serum urea and serum creatinine are the predictors of the nephropathy in diabetic patients (Bamanikar, Bamanikar, & Arora, 2016). Though mostly studies reported that renal function tests are associated with diabetes, the reason behind the results of this current study may be a short duration of diabetes onset, as nephropathy occurs after the prognosis of diabetes.

Uric acid is the metabolic end product of purines their levels raised in nephropathies. The current finding is supported by the results of Bandaru and Taniguchi they found a negative association between serum uric acid and diabetes while contradicted by others (Bandaru & Shankar, 2011; Kodama *et al.*, 2009; Kramer, Von Mühlen,

Jassal, & Barrett-Connor, 2009; Taniguchi et al., 2001). Results of this study also showed that prevalence of nephropathy in diabetic patients is 5%.

Though studies have reported that there is a significant relationship between prognosis of diabetes and nephropathy. Studies have also revealed that presence of HTN in diabetic patients also trigger this relationship. Results of our study did not show any significance association between diabetes and nephropathy. So we further examined the relationship between hypertension and RFTs.

A high prevalence of hypertension in diabetic patients in contrast to other complications was also observed in this study. Increased body mass index is the main reason behind high prevalence of hypertension, as this study has indicated a high prevalence of increased BMI in diabetic patients. Colosia *et al*, in 2013 reported hypertension with or without obesity is very much prevalent in diabetic patients (Colosia, Palencia, & Khan, 2013). Other studies showed same results in Romania and Japan (Dorobantu, Darabont, Badila, & Ghiorghe, 2010; Nakano et al., 2004). Blood glucose damages the arteries and makes them hard (atherosclerosis), result in the high blood pressure and cardiovascular disorders.

The family history of diabetes was observed as a significant factor in the onset of diabetes. A person has 1.97% more chances if first degree relatives have a positive history of diabetes as showed in this study. The family history of diabetes and hypertension is important in the individuals with metabolic syndrome for the commencement of Type 2 diabetes mellitus (Das, Pal, & Ghosh, 2012; Ranasinghe, Cooray, Jayawardena, & Katulanda, 2015). Family history of diabetes is an independent risk factor for diabetes in the Local Population of Lahore, as reported in the study of Zafar *et al*, in 2013 (Zafar, Qureshi, & Sandhu).

Diabetic individuals are at high risk for developing complications like cardiovascular disease, nephropathy, neuropathy, retinopathy, dyslipidemia, diabetic foot, infectious diseases, and pregnancy complications (*IDF Diabetes Atlas*, 2017). Deshpande *et al* in 2008 also reported high prevalence of complications in diabetic patients (Deshpande, Harris-Hayes, & Schootman, 2008). There is no exact estimation of complication in diabetic patients, but many studies showed the prevalence of individual complication of diabetes.

5. Conclusion

Type 2 Diabetes Mellitus is highly prevalent in the local population of Lahore, Pakistan. Family history along with other risk factors like high Cholesterol, Triglyceride, Body Mass Index (BMI >25) and low High-Density lipoproteins (HDL) contributes to the development of diabetes. An improved lifestyle and medical monitoring can manage to control diabetes in the local population. Further studies with a large cohort and to evaluate genetic risk factors are required in this population.

Competing Interests Statement

The authors declare that there are no competing or potential conflicts of interest.

Author's Contribution

SA perform lab work and draft this manuscript, ST, BT design this study and did sampling, NT, TR, SM and AM recruitment of patients and lab work, KJ design this study, statistical analysis and final revision of the manuscript.

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