

# Major Complication Associated With Diabetes Mellitus Type II in Punjab and Khyber Paktunkhwa Population

Samreen Riaz<sup>1</sup>, Shagufta Naz<sup>2</sup>, Umera kousar<sup>2</sup>, Zil E Huma Malik<sup>2</sup> and Rasheeda Bashir<sup>2\*</sup>

<sup>1</sup>Department of Microbiology and Molecular Genetics, University of the Punjab, Pakistan

<sup>2</sup>Department of Biotechnology, University of the Punjab, Lahore, Pakistan

\*Corresponding author: Rasheeda Bashir, Department of Biotechnology, University of the Punjab, Lahore, Pakistan, Tel: +923004351979; E-mail: rashidasb@yahoo.com

Received date: June 05, 2018; Accepted date: October 29, 2018; Published date: October 31, 2018

Copyright: © 2018 Riaz S, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

## Abstract

Type-II diabetes mellitus is a particularly heterogeneous and multifactorial metabolic disorder that is characterized by a combination of insulin insufficiency and insulin resistance. The prevalence of diabetes mellitus has risen exponentially over the last three decades, with resultant increase in morbidity and mortality mainly due to its complications. Data of 400 individuals affected with diabetes mellitus type II were collected from different hospitals of Lahore (Punjab) and Dera Ismail Khan (KPK) during the year 2016-2017. Two hundred individual data recruited from Punjab out of them 90 (45%) were male; while from KPK 107 (53.5%) were male. The age of these patients were range between 17 to 90 years but most of the patients fall in the range between 40-60 years. The mean age of patients of Punjab  $52.6 \pm 11.2$  and KPK  $50.31 \pm 12.0$ . Patients are mostly belonging to urban areas (70%) in Punjab while in KPK from rural areas (62.5%). In Punjab 45% patients have the knowledge about diabetes management and complication while in KPK only 25% affected individuals have awareness about the disease. Results showed that cardiovascular risk in the population of Khyber Pakhtunkhwa is 40%, nephropathy and foot ulcer is present in same percentage (9%). On the other side, the percentage of cardiovascular complication in Punjab is 26%, nephropathy is 14% and foot ulcer is 12%. There is need of increases awareness of these complications among patients and populations, this facilitate early detection and prevention of these diseases. The earlier diagnosis, timely appropriate treatment may help in avoiding severe, irreversible disability and deformity, which can be done with the tool of patient education and conducting seminar to increase awareness.

**Keywords:** Diabetes; KPK (Khyber Paktunkhwa Population); Punjab

## Introduction

Diabetes mellitus type II is a long term metabolic disorder that is characterized by high blood sugar, insulin resistance and relative lack of insulin. Common symptoms include increased thirst, frequent urination and weight loss.

The prevalence of type II diabetes differ in different countries like in Africa 0.3 to 17.9%, in Asia, 1.2 to 14.6%, in Europe 0.7 to 11.6%, in the Middle East 4.6 to 40%, in North America, 6.69 to 28.2% and 2.01 to 17.4% in South America [1]. The world population will increase by 37% and the number of people with diabetes will increase by 114% between 2000 and 2030 according to World health Organization [2]. In the United States more than 5 million individuals remains undiagnosed 20 million individuals are having diabetes [3]. The prevalence rate during 1998-2000 is higher in women and this prevalence is changed from 1998-2000 to 2013-2015 and increase in men. In developed countries during 2010 and 2030, DM will rise to 20% and 69% increase in numbers of individuals with diabetes in developing countries [4].

In the developing countries, Diabetes mellitus is a common and severe problem and in 2030, it is rapidly evolving as a global health care problem that may reach pandemic levels [2]. The incidence rate of diabetes mellitus including type I and type II is growing worldwide but the incidence of type-2 diabetes is increasing much more rapidly than type I because of reduced activity levels and rising obesity [5]. In Asian

populations the incidence of diabetes has increased rapidly in recent decades and more than 110 million person in Asia were suffering with diabetes during 2007. Pakistan was ranked at 8th number. During 1995, 4.3 million persons are suffering with diabetes mellitus and it will be expected that in 2025 Pakistan will be at 4th number having 14.5 million individuals suffering with diabetes mellitus type II [6]. Rural areas of Pakistan like NWFP the prevalence rate is high and is same in Sindh and Baluchistan. In the urban and the rural areas the incidence rate of diabetes mellitus is 3.5% in women and 6.0% in men [7].

Diabetes mellitus can be classified as type I, type II and gestational diabetes. Type I diabetes mellitus is linked with immunological tolerance to self-antigens. Type I diabetes is a T-cell-mediated disease. Diabetes mellitus is the disturbances of metabolism for which the main finding is chronic hyperglycaemia. The cause is either impaired insulin secretion or impaired insulin action or both. Gestational diabetes mellitus (GDM) can develop during pregnancy due to glucose intolerance.

Micro-vascular and Macro-vascular complications are the division of chronic complications. Diabetes Mellitus have acute complications that's include hyperglycaemia hyperosmolar state (HONK), diabetic ketoacidosis (DKA), hypoglycaemic diabetic coma, infections like respiratory infections and periodontal diseases. Diabetic nephropathy, Diabetic neuropathy (sensory, motor and autonomic) and Diabetic retinopathy are Chronic micro-vascular complications. On the other hand peripheral vascular disease (PAD), cerebrovascular incidence like stroke and transient ischemic attack (TIA), diabetic encephalopathy and diabetic foot are macrovascular complications. Those people in

which well controlled sugar level is present have minimum chances to develop the complication of diabetes mellitus [8].

This study will provides the consciousness of severe complication of diabetes and help the population for early mediation and then point outs the significance of cardiovascular, kidney and foot ulcer risk factor for various diseases in diabetic patients. This study will provide great information to diabetic patients with better and more actual care with chronic diseases.

## Material and Methods

For this retrospective case-control association study, patients with Diabetes type II that are affected with other complications will be recruited from different hospitals of Lahore and KPK. All subjects will undergo Diabetic examination and medical records of all subjects will be carefully reviewed. Questionnaire detailing are fulfill by patients which are affected with other complication like cardiovascular, kidney and Foot ulcers. Medical history of patients including family history is also check that includes parents, children, and grandparents information regarding diabetes and its complications. The doctors related to these diabetic centers will take into confidence about the details of research project and they proved very instrumental in the enrolment of diabetic patients.

Patients who were suffering with diabetic complications (cardiovascular, nephropathy, foot ulcer, neuropathy and retinopathy) are included in the study criteria. Patients who are included in the study are both male and female and age of these patients is between 17 to 90 years. Information regarding diabetes and complication was obtained by using Performa. In the Performa, questions were present and patients asked to reply with either a Yes, No. Questions were asked by the researcher themselves and history of cigarette smoking, cardiovascular, nephropathy, foot ulcer, neuropathy and retinopathy were noted. Those patients which do not have diabetes mellitus type II and those who are not interested in taking part in research are excluded. SPSS (Statistical Package for Social Sciences) version 17.0 was used to enter and analyze data. The Quantitative variables were expressed as mean  $\pm$  standard deviation (S.D), whereas qualitative data was presented by frequency and percentages. P-value of  $<0.05$  was considered statistically significant.

## Results

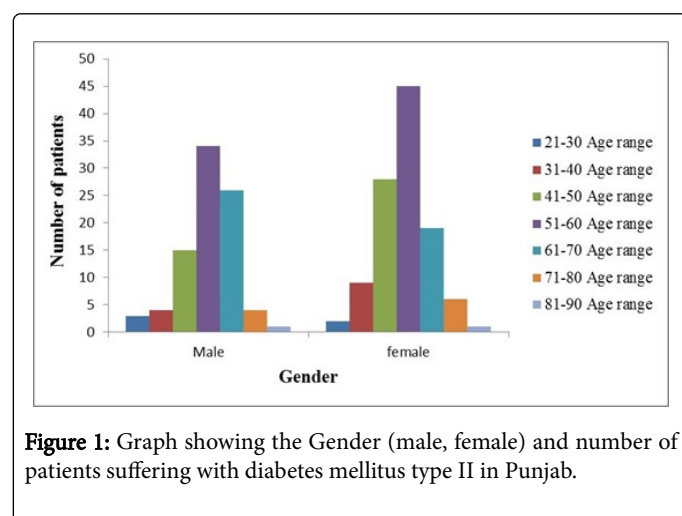
Data of 400 individuals affected with diabetes mellitus type II were collected from Services Institute of Medical Sciences of Lahore (Punjab) and Government hospital of Dera Ismail khan (KPK) during the year 2016-2017. The mean age of patients of Punjab  $52.6 \pm 11.2$  and KPK  $50.31 \pm 12.0$ . In Punjab 45% patients have the knowledge about diabetes management and complication while in KPK only 25% affected individuals have awareness about the disease.

Clinical features of the patients of Khyber Pakhtunkhwa and Punjab is shown in Table 1. The age of these patients are range between 20 to 90 years and most of the patients fall in the range of 40-60 years. In Khyber Pakhtunkhwa, the number of male patients is 107 and females are 93 while in Punjab total number of male patients is 90 and females was 110.

The duration of diabetes mellitus is less than 1 year to more than 10 years. According to the smoking status 70 smoker are present in KPK and 110 in Punjab (Table 1 and Figure 1).

Parameters	Patients of KPK	Patients of Punjab
Age	50.31 $\pm$ 12.0 (min 20 max 74)	52.6 $\pm$ 11.2 (min 20 max 85)
20 to 30 years	15	5
31 to 40 years	36	13
41 to 50 years	45	43
51 to 60 years	65	79
61 to 70 years	35	47
71 to 80 years	4	10
81 to 90 years		3
<b>Sex</b>		
Male	107	90
Female	93	110
Duration of Diabetes Mellitus	40 $\pm$ 23.8 (min 9 max 67)	40 $\pm$ 22.15 (min 11 max 71)
Less than 1 year	33	45
1 to 3 years	61	52
4 to 6 years	67	71
7 to 9 years	30	21
More than 10	9	11
<b>Smoking status</b>		
Smoker	70	110
Non-smoker	130	90

**Table 1:** Clinical features of the patients of Khyber Pakhtunkhwa and Punjab.



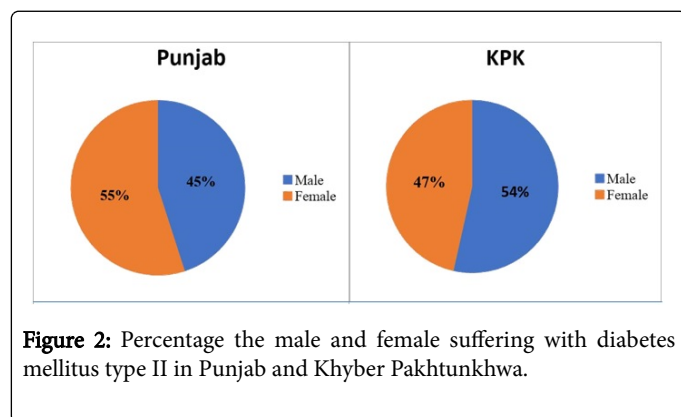
**Figure 1:** Graph showing the Gender (male, female) and number of patients suffering with diabetes mellitus type II in Punjab.

## Complications

There are some common complications which are associated with diabetes. Diabetes mellitus are associated different types of alignments of heart but the most common complication linked with diabetes mellitus is cardiovascular diseases (CVD). Nephropathy is also known as End Stage Renal Disease. In this disease the kidney completely stop its function and the end stage of chronic renal failure. Patients with type II diabetes mellitus are suffering with foot ulcers and there are many factors present in diabetic patients, the most important factor is neuropathy then this is major reason of ulceration [9]. A common complication of diabetes is diabetic peripheral neuropathy that can cause major illness and death. The major risk factor is hyperglycemia. Among working age groups retinopathy is the leading reason of visual impairment and blindness (Figures2-4).

Complications	Positive Response	Negative Response
Cardiovascular disease	132	268
Nephropathy	45	355
Foot ulcer	42	358
Neuropathy	205	195
Retinopathy	196	204

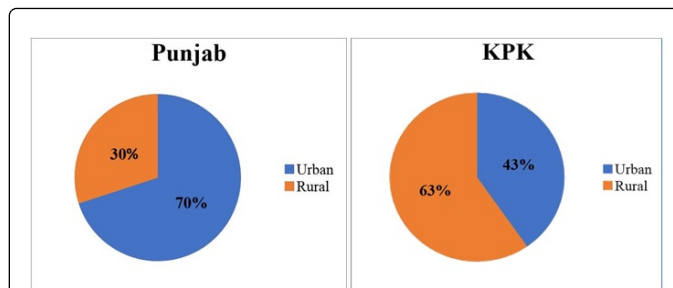
**Table 2:** Complications of Diabetes Mellitus with respect to positive and negative response.



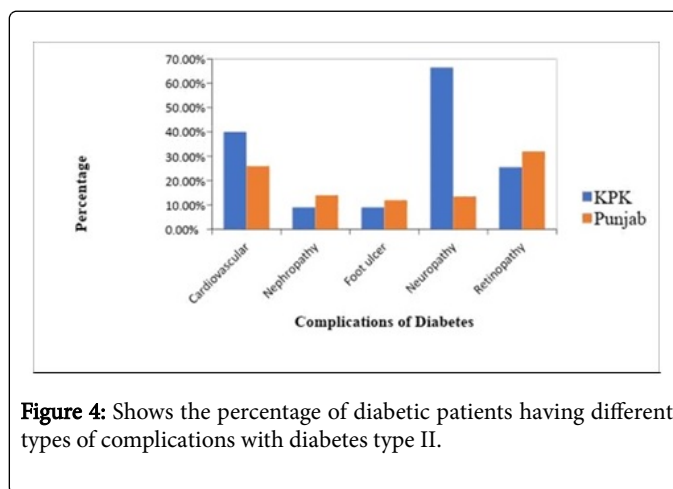
**Figure 2:** Percentage the male and female suffering with diabetes mellitus type II in Punjab and Khyber Pakhtunkhwa.

Complications with diabetes associated	Frequency of Complication in KPK region	Frequency of Complication associated with Diabetes Mellitus in Punjab
Cardiovascular	80 (40%)	52 (26%)
Nephropathy	18 (9%)	27 (14%)
Foot ulcer	18 (9%)	23 (12%)
Neuropathy	133(66.50%)	144(32%)
Retinopathy	61(25.5%)	63(56%)

**Table 3:** Frequency of complications associated with DM in KPK and Punjab.



**Figure 3:** Graph showing that patients belonging to different areas (rural or urban) of the Punjab and KPK.



**Figure 4:** Shows the percentage of diabetic patients having different types of complications with diabetes type II.

Complications of Diabetes Mellitus type II with respect to different response is shown in the Table 2. The patients give positive and negative response according to specific complication like cardiovascular, Nephropathy and Foot ulcer. The patients give positive response about the cardiovascular disease (132), nephropathy (45) foot ulcer (42) neuropathy (205) and retinopathy 196 while 268 patients give negative response for the cardiovascular disease, 355 patients for nephropathy 358 for foot ulcer, 195 for neuropathy and 204 for retinopathy (Figures 2-4).

## Discussion

Diabetes Mellitus is a complex metabolic disorder characterized by inappropriate hyperglycaemia as a result of either an absolute or relative deficiency of insulin and/or insulin resistance.

According to Shera et al. [9] the incidence of diabetes was higher in urban as compared to the rural areas. Diabetes mellitus type II in urban areas was 3.5% in females and 6.0% in male population. When compared with rural areas 2.5% female and 6.9% males. However, the diabetes which was recently identified in urban areas among males was 5.1% and 6.8% in females and in rural areas 5.0% males and 4.8% females were suffering with diabetes in Sindh province [10]. Another study was conducted to see the incidence of diabetes mellitus type II in only rural areas of Pakistan. The total patients was present in the study was 2119 and aged of these patients was started from 20 years or more. Result showed a total of 5.8% the incidence of diabetes among female was 6.9% and 3.7% in males [11]. It is reported that the diabetes mellitus were mostly occurred in the age of 50-60 years in Indian

population [12]. While study conducting in another regions of Pakistan described in Peshawar 79.16% patients do not have proper knowledge as compared to other patients lived in different regions of the other countries. Because of lack of education in maximum of patients and particularly female patients [13]. In other developing countries like Kenya population it is reported that only 26% awareness was present among patients regarding to diabetic complications [14]. It is described that approximately 75% do not have proper awareness of DM and also about the diet. The patients suffering with diabetes do not avoid sweets, rice and consume more ragi, millet and wheat chapattis [15].

### Cardiovascular complications

There are various complications associated with diabetes mellitus type II. In this study we compare the cardiovascular risk in Punjab and KPK region of Pakistan. It is reported that diabetes mellitus was the major cause cardiovascular complication and in under developed countries it is main reason of morbidity and mortality [16]. Our results showed that the risk of cardiovascular complication in Punjab is 26% while in Khyber Pakhtunkhwa the ratio of cardiovascular complication is 49%. 75.5% females are affected with cardiovascular disease and 24.5% male while in KPK in 65% male and 45% females are affected.

Macrovascular complications are major risk associated with long term diabetes mellitus type II. Long term diabetes was due to hypertension, smoking habits, physical inactivity, obesity and unhealthy dietary habits [17]. Patients suffering with diabetes have greater chance of developing myocardial infarction, hypertension and level of cholesterol was also very high. Ischaemic stroke was more common in diabetic patients than non-diabetic patients [18].

Fructose play an important role in cardiovascular disease, stroke, and mortality. Reducing the amount of uric acid in patients suffering with diabetes can also reduce the risk of cardiovascular complication [19]. It was described that chronic heart disease (CHD) was most common in males aged 40 years and diabetes, hypertension and smoking are the major cause of CHD. The level of glucose is much higher in patients suffering with diabetes mellitus [20]. It was discussed that in South Asians the incidence rate of Coronary Artery Disease (CAD) was very high and Coronary Artery Disease was most commonly present in female population rather than males [21,22].

Our results showed cardiovascular risks are high in Punjab than KPK the reason may that mostly data collected from Punjab from urban areas as compared to KPK which was from rural area. People from urban area are less likely involve in physical activity and obese while individual belongs to rural areas has more physical activity comparatively. Besides this smoking is less prevalent in rural area as compared to urban. Females are more susceptible to heart diseases may be due to life style i.e. less physical activity habit, diet and obesity etc.

### Nephropathy

Diabetic Nephropathy is a complex pathophysiological process involving various cellular and molecular mechanisms. Diabetes mellitus type II play an important role in the development of chronic kidney disease (CKD) and diabetic nephropathy is the leading cause of End-Stage Renal Disease (ESRD). In some studies kidney injury was due to metabolic syndrome along with microalbuminuria [23]. It was discussed in European Group for the study of Insulin Resistance (EGIR) was hypertension and diabetes is two major factor of chronic

kidney disease [24]. It is also seen that poor metabolic control is important in the progression of diabetic nephropathy [25]. Higher level of glucose play major role in kidney lesions and acting as a marker for metabolic abnormality which can cause nephropathy [26].

Results of our study showed that the risk of nephropathy in Punjab was 13.5% while in Khyber Pakhtunkhwa the ratio of nephropathy was 9%. 12.7% females are affected with nephropathy and 11% male while in KPK 6.5% male and 12.9% female are affected.

Frequency of Chronic kidney disease is 15.65% in diabetic patient and 18.54% were present in smokers and 9.35% announced in ethanol consumption and 7.14% had a background associated with CV complication [27]. There are five factors which play major role in chronic kidney diseases and in the developing countries chronic glomerulonephritis and interstitial nephritis are the major reason for chronic kidney disease [28]. Diabetic nephropathy (DN) may be due to some change in RAAS gene and various drugs in diabetic nephropathy are used to control RAAS like Angiotensin Converting Enzyme (ACE) inhibitors [29].

Life style, particularly diet is a critical component of treatment for these conditions. A range of dietary manipulations has been reported to reduce risk factors and decrease risk of CVD and CKD outcomes [30]. Lastly, increased awareness of renal disease among the population is needed, as are strategies to facilitate early detection and prevention to delay the onset of ESRD [31].

High carbohydrate diet promote diabetes and kidney failure. The ratio is high in Punjab as compared to KPk which is may be due to taking processed sugary diet as well as life style habits. The risk of CKD resulting in kidney failure depends on level of kidney damage. If kidney disease is found early, medication, combined with diet and lifestyle changes, can prolong the life of your kidneys.

### Foot ulcers

Patients with type II diabetes mellitus are suffering with foot ulcers and there are many factors present in diabetic patients, the most important factor is neuropathy then this is major reason of ulceration [9]. The symptoms of peripheral neuropathy included loss of the protective sensations of pressure, dry skin, dry skin along with joint mobility [32]. There are certain causes which help in the growth of certain subsequent amputation and foot ulceration. These causes might be Peripheral neuropathy, deformity, and macro vascular disease [33].

Our results showed that Diabetic foot ulcer in Punjab is 13.5%. On the other hand in Khyber Pakhtunkhwa the ratio of Diabetic foot ulcer is 8.00%.

There are many factor which play an important role in diabetic foot wounds and these wounds can be checked by using simpler, cheap apparatus placed in medical location [34]. Offloading devices are used for curing foot ulcers. Large number of ulcer was managed with "gold standard" and shoe mollifications [35]. The main reason of diabetic wounds is that doctors do not cooperate with the patients and as a result patients do not pay heed on foot ulceration [36]. This study is conducted in Lahore to check that in every one in three patient do not have any awareness about the diabetic foot ulcers and the knowledge about these ulcers is essential among these patients [37]. Foot care education play important role for preventing lower leg amputation. Thus low cost, low technology evaluation and preventive processes are enough to reduce the rates of risk. An individualized educational intervention can lead to improved foot care knowledge, self-care

practices and confidence in performing foot related self-care is important. There is a need to redirect and motivate health personnel in educating diabetic peoples about self-care and also practicing by themselves proper foot examination. Print and electronic media must be engaged in order to enhance the public awareness of diabetes and its complications. Strategies must be worked out to develop a countrywide network of diabetes centers with implementation of primary prevention programs regarding foot care [37]. While the study conducted in Islamabad. It demonstrated that exclusive 38% patients with diabetes were educated about foot protection strategies. They stayed insensible about the significance and strategies for foot protection even after hospitalization for foot diseases. Out of 16% patients who were admitted because of foot disease, just 8% got foot mind training in healing center [38]. It is explained that patients who got foot instruction and had foot examination by specialists were altogether more prone to check their feet consistently [39].

In another review different educational methodologies were utilized to clarify diabetic patients about foot examination, foot washing and appropriate foot wear. It was found that a serious instruction program enhanced the foot learning and performance of high hazard patients [40]. However, different reviews indicated opposing outcomes [41].

When results regarding foot care were compared between two provinces it is examine that in both areas ratio of foot ulcer is nearly same which suggest that there is need of foot care education in both provinces.

## Neuropathy

Diabetic neuropathy is perceived by the American Diabetes Association (ADA) as "the nearness of manifestations and additionally indications of fringe nerve brokenness in individuals with diabetes after the prohibition of different causes" [42]. As with other miniaturized scale vascular difficulties, danger of creating diabetic neuropathy is relative to both the greatness and span of hyperglycemia, and a few people may have hereditary properties that influence their inclination to growing such complexities. There are many long haul complexities of diabetes. Neuropathies are the commonest among them. Overseeing incessant sensorimotor distal symmetric polyneuropathy is the most critical restorative challenge [43,44]. The clinical introductions of Diabetic fringe neuropathy (DPN) are various that incorporates troublesome neuropathic torment toward one side and there might be unfeeling foot on the flip side which is additionally at danger of ulceration. This influences personal satisfaction due to paresthetic side effects that can be both new and painful [45]. In propelled fringe diabetic neuropathy (PDN) there is raised vibration and warm discernment limits that prompts tangible misfortune and degeneration of a wide range of filaments in fringe nerve [46].

## Retinopathy

The study was directed in Karachi at diabetic relationship of Pakistan (a world wellbeing association teaming up focus). Aftereffect of this investigation demonstrates that of aggregate enlisted diabetic patients (n=11, 158) (96.5%) were screened for Diabetic retinopathy. General diabetic retinopathy was found in 2661 (24.7%) patients. Diabetic retinopathy was found in diminishing request of recurrence in patients with type II (n=2555, 23.7%) trailed by patients with type I diabetes (n=101, 0.93%). From this examination it is reasoned that type II patients with brief time type I patients with long history of diabetes most every now and again had Diabetic retinopathy.

Diabetic Retinopathy (DR) is an all-around perceived entanglement of diabetes mellitus. Out of 39 million worldwide visual deficiency because of different eye infections, 4.8% (1.8 million) is because of Diabetic Retinopathy (DR) Nationally every fourth patient with diabetes has some level of DR with enhanced care the diabetics are living longer and are presented to the danger of unending entanglements like DR bringing about expanding visual deficiency.

In Oman predominance of diabetic retinopathy is 14.39%. Men had fundamentally higher rate of retinopathy than women. The retinopathy rate is higher in age bunches 50-59 years and 60-69 years. From this examination it is presumed that Patients with type I diabetes are known to have higher danger of diabetic retinopathy than those with type II diabetes (19.8%) (Figure 5 and 6) [47].

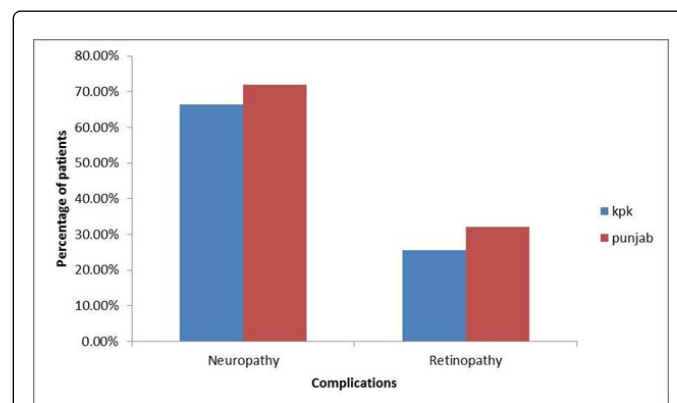


Figure 5: Graph showing the complications of percentage of patients with type 1 diabetes with diabetic neuropathy and diabetic retinopathy.

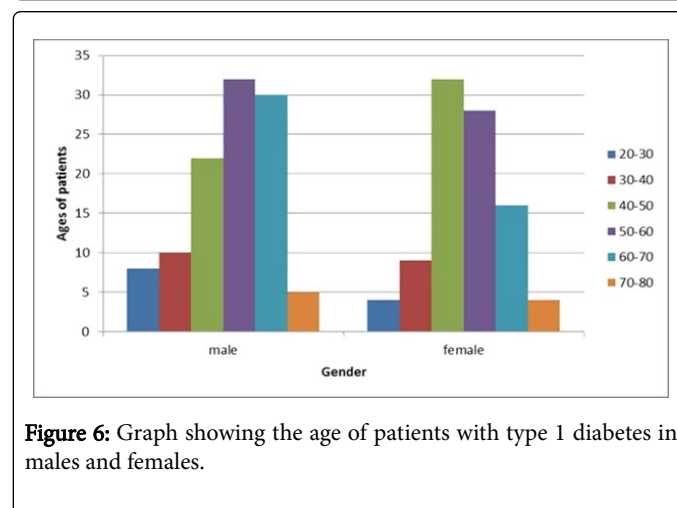


Figure 6: Graph showing the age of patients with type 1 diabetes in males and females.

## Conclusion

Our study showed that diabetes mellitus was frequently present in patients with cardiovascular diseases. The frequency was found to be nearly 40% in both provinces of the Pakistan. Therefore proportion of diabetics among the patients with cardiovascular complications is one out of every three (1:4). Diabetes is more prevalent in female as compared to male but cardiovascular risk is high among female. Similarly nephropathy was found to 13.2% among diabetes patients

and high prevalence among females. Foot ulcer is also common among women and found to be 10% among diabetic patients.

Increases awareness of these complications among patients and populations is need, this facilitate early detection and prevention of these diseases. Early diagnosis forward to appropriate therapy which may lead to prolong survival among diabetic patient. The earlier diagnosis, timely appropriate treatment may help in avoiding severe, irreversible disability and deformity, which can be done with the tool of patient education and conducting seminar to increase awareness.

Proper care and management of the diabetes and its related complications is not adequate therefore it us the responsibility of the stake holders to design and implement diabetes education programmes with special emphasis on cardiovascular, nephropathy and foot care education. In this regard, epidemiological information helps in the design of better programs for disease control.

We recommend screening of high risk groups and emphasize importance of early diagnosis of diabetes and detection chronic complications so that appropriate treatment initiated at the earliest as possible.

Keeping in view the total population of Pakistan, Pakistan needs large sample size studies that represent both genders, rural and urban population with different age groups to highlight the actual prevalence of type 2 diabetes mellitus from all the provinces of Pakistan. In Pakistan, diabetes mellitus is gradually increasing, therefore, it is suggested that, Pakistani health officials should include the diabetes preventive measures in their national health policy to minimize the burden of the disease. Public education, regular physical exercise, nutritional knowledge of foods must be provided to the community to control diabetes in the country. Diabetes and its complications should be frequently discussed in scientific, academic assemblies and both in electronic and print media to improve public awareness to minimize the prevalence of the disease.

## References

1. Adegate E, Schattner P, Dunn E (2006) An update on the etiology and epidemiology of diabetes mellitus. *Ann N Y Acad Sci* 1084: 1-29.
2. Rathmann W, Giani G (2004) Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care* 27: 2568-2569.
3. Winer N, Sowers JR (2004) Epidemiology of diabetes. *J Clin Pharmacol* 44: 397-405.
4. Shaw JE, Sicree RA, Zimmet PZ (2010) Global estimates of the prevalence of diabetes for 2010 and 2030. *Diabetes Res Clin Pract* 87: 4-14.
5. Cali AM, Caprio S (2008) Prediabetes and type 2 diabetes in youth: an emerging epidemic disease? *Curr Opin Endocrinol Diabetes Obes* 15: 123-127.
6. Iqbal F, Naz R (2005) Pattern of diabetes mellitus in Pakistan; An overview of the problem. *Pak J Med Res* 44: 59-64.
7. Shera AS, Jawad F, Maqsood A, Jamal S, Azfar M, et al. (2004) Prevalence of chronic complications and associated factors in type 2 diabetes. *J Pak Med Assoc* 54: 54-59.
8. Weissman AJ, Ross P, Nathan D, Genuth S, Lachin J, et al. (2006) Intensive diabetes treatment and cardiovascular disease. *N Engl J Med* 354: 1751-1752.
9. Reiber GE, Vileikyte L, Boyko EJ, del Aguila M, Smith DG, et al. (1999) Causal pathways for incident lower-extremity ulcers in patients with diabetes from two settings. *Diabetes Care* 22: 157-162.
10. Shera AS, Rafique G, Khwaja IA, Ara J, Baqai S, et al. (1995) Pakistan national diabetes survey: prevalence of glucose intolerance and associated factors in Shikarpur, Sindh Province. *Diabet Med* 12: 1116-1121.
11. Zahid N, Claussen B, Hussain A (2008) High prevalence of obesity, dyslipidemia and metabolic syndrome in a rural area in Pakistan. *Diabetes Metab Syndr* 2: 13-19.
12. Raheja BS, Kapur A, Bhoraskar A, Sathe SR, Jorgensen LN, et al. (2001) DiabCare Asia-India Study: diabetes care in India--current status. *J Assoc Physicians India* 49: 717-722.
13. Ullah F, Afridi AK, Rahim F, Ashfaq M, Khan S, et al. (2015) Knowledge of diabetic complications in patients with diabetes mellitus. *J Ayub Med Coll Abbottabad* 27: 360-363.
14. Maina WK, Ndegwa ZM, Njenga EW, Muchemi EW (2010) Knowledge, attitude and practices related to diabetes among community members in four provinces in Kenya: a cross-sectional study. *Pan Afr Med J* 7: 1-10.
15. Muninarayana C, Balachandra G, Hiremath SG, Iyengar K, Anil NS (2010) Prevalence and awareness regarding diabetes mellitus in rural Tamaka, Kolar. *Int J Diabetes Dev Ctries* 30: 18-21.
16. Veiraiiah A (2005) Hyperglycemia, lipoprotein glycation, and vascular disease. *Angiology* 56: 431-438.
17. Gul A, Rahman MA, Salim A, Simjee SU (2008) Advanced glycation end-products in senile diabetic and non-diabetic patients with cardiovascular complications. *Age (Dordr)* 30: 303-309.
18. Zafar A, Shahid SK, Siddiqui M, Khan FS (2007) Pattern of stroke in type 2 diabetic subjects versus non diabetic subjects. *J Ayub Med Coll Abbottabad* 19: 64-67.
19. Johnson RJ, Segal MS, Sautin Y, Nakagawa T, Feig DI, et al. (2007) Potential role of sugar (fructose) in the epidemic of hypertension, obesity and the metabolic syndrome, diabetes, kidney disease, and cardiovascular disease. *Am J Clin Nutr* 86: 899-906.
20. Bansilal B, Ali N, Afzal N, Khan TS, Shahjahan S (2007) Antioxidant status in coronary heart disease (CHD) patients with type 2 diabetes mellitus. *J Ayub Med Coll Abbottabad* 19: 98-101.
21. McKeigue PM, Ferrie JE, Pierpoint T, Marmot MG (1993) Association of early-onset coronary heart disease in South Asian men with glucose intolerance and hyperinsulinemia. *Circulation* 87: 152-161.
22. Enas EA, Mehta J (1995) Malignant coronary artery disease in young Asian Indians: thoughts on pathogenesis, prevention, and therapy. *Clin Cardiol* 18: 131-135.
23. Humphrey LL, Ballard DJ, Frohner PE, Chu CP, O'Fallon WM (1989) Chronic Renal Failure in Non-Insulin-Dependent Diabetes Mellitus: A Population-Based Study in Rochester, Minnesota. *Ann Intern Med* 111: 788-796.
24. Alberti KG, Zimmet P, Shaw J, IDF Epidemiology Task Force Consensus Group (2005) The metabolic syndrome-a new worldwide definition. *Lancet* 366: 1059-1062.
25. Deferrari G, Repetto M, Calvi C, Ciabattini M, Rossi C, et al. (1998) Diabetic nephropathy: from micro-to macroalbuminuria. *Nephrol Dial Transplant* 13: 11-15.
26. Shahid SM, Nawab SN, Shaikh R, Mahboob T (2012) Glycemic control, dyslipidemia and endothelial dysfunction in coexisted diabetes, hypertension and nephropathy. *Pak J Pharm Sci* 25: 123-129.
27. Wang C, Li Y, Zhang J, Ye Z, Zhang Q, et al. (2016) Prognostic Effect of Isolated Nocturnal Hypertension in Chinese Patients with Nondialysis Chronic Kidney Disease. *J Am Heart Assoc* 5: 4105-4198.
28. Barsoum RS (2006) Chronic kidney disease in the developing world. *N Engl J Med* 354: 997-999.
29. Zain M, Awan FR (2014) Renin Angiotensin Aldosterone System (RAAS): Its biology and drug targets for treating diabetic nephropathy. *Pak J Pharm Sci* 27: 1379-1391.
30. Nazar CM, Bojerenu MM, Safdar M, Ahmed A, Akhtar MH, et al. (2016) Efficacy of dietary interventions in end-stage renal disease patients; a systematic review. *J Nephropharmacol* 5: 28-40.
31. Sakhuja V, Kohli HS (2006) End-stage renal disease in India and Pakistan: incidence, causes, and management. *Ethnicity and Disease* 16: 20-23.
32. Fernando DJ, Masson EA, Veves A, Boulton AJ (1991) Relationship of limited joint mobility to abnormal foot pressures and diabetic foot ulceration. *Diabetes Care* 14: 8-11.

33. Edmonds ME, Blundell MP, Morris ME, Thomas EM, Cotton LT, et al. (1986) Improved survival of the diabetic foot: the role of a specialised foot clinic. *Q J Med* 60: 763-771.
34. Wu SC, Driver VR, Wrobel JS, Armstrong DG (2007) Foot ulcers in the diabetic patient, prevention and treatment. *Vasc Health Risk Manag* 3: 65-76.
35. Wu SC, Jensen JL, Weber AK, Robinson DE, Armstrong DG (2008) Use of pressure offloading devices in diabetic foot ulcers. *Diabetes Care* 31: 2118-2119.
36. Ali R, Farooq U, Jalal-ud-din M, Jadoon RJ, Alam MA, et al. (2016) Are we telling the diabetic patients adequately about foot care? *J Ayub Med Coll Abbottabad* 28: 161-163.
37. Hasnain S, Sheikh NH (2009) Knowledge and practices regarding foot care in diabetic patients visiting diabetic clinic in Jinnah Hospital, Lahore. *J Pak Med Assoc* 59: 687-690.
38. Saeed N, Zafar J, Atta A (2010) Frequency of patients with diabetes taking proper foot care according to international guidelines and its impact on their foot health. *The J Pak Med Assoc* 60: 1- 732.
39. Keast D, Goetti K (2005) Foot care for persons with type 2 Diabetes: Can a teaching video improve compliance. *Wound Care Canada* 3: 19 -26.
40. Ward A, Metz L, Oddone EZ, Edelman D (1999) Foot education improves knowledge and satisfaction among patients at high risk for diabetic foot ulcer. *Diabetes Educ* 25: 560-567.
41. Chan YM, Molassiotis A (1999) The relationship between diabetes knowledge and compliance among Chinese with non-insulin dependant diabetes mellitus in Hong Kong. *J Adv Nurs* 30: 431-438.
42. Zinman B, Harris SB, Neuman J, Gerstein HC, Retnakaran RR, et al. (2010) Low-dose combination therapy with rosiglitazone and metformin to prevent type 2 diabetes mellitus (CANOE trial): a double-blind randomised controlled study. *Lancet* 10 : 103-111.
43. Boulton AJ, Malik RA, Arezzo JC, Sosenko JM (2004) Diabetic somatic neuropathies. *Diabetes Care* 27: 1458-1486.
44. Boulton AJ, Vinik AI, Arezzo JC, Bril V, Feldman EL, et al. (2005) Diabetic neuropathies: a statement by the American Diabetes Association. *Diabetes Care* 28: 956-962.
45. Vileikyte L, Rubin RR, Leventhal H (2004) Psychological aspects of diabetic neuropathic foot complications: an overview. *Diabetes Metab Res Rev* 20: S13-S18.
46. Iftikhar IH, Kline CE, Youngstedt SD (2014) Effects of exercise training on sleep apnea: a meta-analysis. *Lung* 192: 175-184.
47. Khandekar S, Charoensawan P, Groll M, Terdtoon P (2003) Closed loop pulsating heat pipes Part B: visualization and semi-empirical modeling. *Appl Therm Eng* 23: 2021-2033.