



Investigating the Complications Associated with Diabetic Foot Ulcer Patients through a Retrospective Case-Control Association Mechanism

Dr. Muhammad Siddique

Assistant Professor
Department of Public Administration
Gomal University, Dera Ismail Khan,
Pakistan
Email: mpasiddique@gmail.com

Dr. Syed Zulqarnain Mehdi

MPH Program (Research Scholar)
Department of Public Administration
Gomal University DIKhan, Pakistan
Email: mehdi_sz@gmail.com

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ABSTRACT:

The study aimed to find the complications associated with diabetic patients with its different parameters. This study is based on the retrospective case-control association, in which patients with Diabetes type II along other complications were the sample taken from different hospitals in Pakistan. They will undergo Diabetic examination whereas their medical records will be assessed carefully. The research has identified that diabetes mellitus is frequently found among the patients with cardiovascular syndromes with its frequency around 40% in KP and Punjab provinces of Pakistan. This proportion of diabetics among patients with cardiovascular diseases one out of every three is very high i.e., 1: 4. The study reported that Diabetes is more dominant among the female in comparison to the male. However, it is found that the cardiovascular risk is higher among the females. Similarly, study has identified 13.2% nephropathy in the diabetes patients; again, its prevalence was high in the females. The study found that foot ulcer is also found in the women i.e., 10% among diabetes patients. The study concludes to create awareness among patients for such complication. It could be helpful in early detection and prevention of such diseases because it will help improve the life of diabetic patients. This study was helpful to see the complications in the diabetic patients and help in its control. The objectives of this study included: Survey to Government General Hospital Faisalabad from Punjab and Government hospital of Dera Ismail Khan from Khyber Pakhtunkhwa. Enrollment of Diabetic patients type II from Punjab and KPK. Determine diabetes with its different types of risks and parameters in the patients.

Key words: Investigating Complications, Diabetic Patients, Foot Ulcer, Retrospective Case-Control Association Mechanism

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Introduction

Diabetes Mellitus is a heterogeneous and multifactorial metabolic disorder. Which is regarded as the combination of insulin deficiency and resistance respectively (Rossoth, Lechleitner, & Oberaigner, 2021). Those people who have diabetes are at high risk of severe health problems like premature death, depression, cardiovascular disease (CVD), blindness, kidney failure, amputations, and cognitive decline (Abd El-Khalik, Hafez, & Elkholy, 2020). The incidence rate of type II diabetes varies among various countries i.e., 14.6% in Asia, 0.7% to 11.6% in Europe, 6.69 to 28.2% in North America, and 2.01 to 17.4% in South America, 0.3 to 17.9% in Africa, and 4.6 to 40% in the Middle East (Adeghate, Nurulain, Tekes, Fehe´r, Kala´sz, & Adeghate 2017). The incidence rate of diabetes mellitus type II is increasing over time. During the years 2000 and 2030, the population of the world will increase by 37% and people suffering from diabetes will increase by 114% according to World Health Organization (Aldana & Khachemoune, 2020). Around five million people are reported undiagnosed in the US while 20 million have been reported to be diabetic patients (Al-Rubeaan, Al Derwish, & Ouizi, *et al.*, 2015). The prevalence rate was higher among females during 1998-2000 as compared to 1998-2000 to 2013-2015 with every increase among males (Bonilla, Hornsby, Pannone, Case, Aviles, & Apolinario Carrasco *et al.*, 2019). Among the developed countries, DM is expected to rise to 20%, whereas, a 69% increase is expected among individuals in the developing nations (Armstrong, Boulto, & Bu, 2017).

Diabetes mellitus will be one of the most common and severe problems among developing countries in 2030. As evolving fast as a global healthcare issue could be declared at a pandemic level diseases (Bakker, Apelqvist, Lipsky, van Netten, & Schaper, 2016). The occurrence of diabetes mellitus in both type I and type II has mushroom growth throughout the globe yet the pace of Diabetes II is spreading faster as compared to type. Bauersachs, Debus, Nehler, Huelsebeck, Balradj, Bowrin, *et al.* (2020) reported that the cause behind this rapid growth is the reduced activity levels and rise in obesity. In this connection, Pakistan is standing at the eighth number. According to Naz, Rabia, Fatima Saqib, Samir Awadallah, Muqet Wahid, Muhammad Farhaj Latif, Iram Iqbal, and Mohammad S. Mubarak (2023), 4.3 million persons were reported to have diabetes mellitus in Pakistan, which is expected to 14.5 million in 2025 Pakistan. In Pakistan, around 6.9 million cases of diabetes mellitus were recorded in 2014 among patients who fell in the age range of 20-79 years (Armstrong, Boulto, & Bus, 2017). Furthermore, the current incidence rate of type II diabetes mellitus in Pakistan is reported, as be 11.77%. The incidence of diabetes in males is 11.20 percent and 9.19% in females (Bakker, Apelqvist, Lipsky, van Netten, & Schaper, 2016). In Khyber Pakhtunkhwa, the prevalence rate is high however in Sindh and Baluchistan province the ratio is almost the same (Rafique, Azam, & White, 2006). In urban and rural areas, the incidence rate of diabetes mellitus is 3.5% in women and 6.0% in men (Jampol, Glassman, & Sun, 2020). 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. Maintenance of peripheral tolerance is present in the mechanism, which includes a par subset of regulatory T-cells (Treg) within the CD4+CD25+ T-cell population. In type 1 diabetes function and phenotype of these cells have not been understood as a result trouble will occur in the balance of the CD4+CD25+ population which leads to type I diabetes (Abd El-Khalik, Hafez, & Elkholy, 2020). Type-II Diabetes mellitus is a state in which patients do not depend on insulin for immediate survival and hardly develop ketoacidosis (Kurniawati, Ismiarto, & Hsu, 2019). Type-II diabetes mellitus is predominantly a heterogeneous and multifactorial metabolic disorder because of a combination of insulin inadequacy and resistance (Verdecchi, Reboldi, & Angeli, 2020). On the other hand, Gestational diabetes mellitus (GDM) is generally developed during the period of pregnancy because of the intolerance of glucose. In healthy individuals, GDM is the product of routine glucose tolerance. Just like hyperglycemia, this condition is due to pancreatic β -cell defects that do not produce sufficient body insulin. Thus, GDM often represents diabetes in evolution and, as such, holds great potential as a condition in which to study the pathogenesis of diabetes and to develop and test strategies for diabetes prevention (Adeghate, Nurulain, Tekes, Fehe´r, Kala´sz, & Adeghate 2017). Those people who have diabetes are at high risk of severe health problems like premature death, depression, cardiovascular disease (CVD), blindness, kidney failure, amputations, and cognitive decline (Aldana & Khachemoune, 2020). It is reported that

Micro-vascular and Macro-vascular problems are chronic ones. Diabetes Mellitus brings acute complications, for example, hyperglycemia hyperosmolar state (HONK) as well as diabetic ketoacidosis (DKA). Diabetic neuropathy and retinopathy are also protracted micro-vascular problems. On the other side, peripheral vascular disease (PAD), for example, the cerebrovascular incidence i.e., strokes inter alia the transient ischemic attack (Tm), and diabetic foot ulcers are the macrovascular associated with diabetic disease. People with well-controlled diabetes levels have the minimum likelihood of developing complications because of diabetes mellitus (Bauersachs, Debus, Nehler, Huelsebeck, Balradj, Bowrin, *et al.*, 2020).

It is a clear fact that diabetes is one of the strongest CVD risk factors (Chaudhary, Bhansali, & Rastogi, 2019). Those people who are suffering from diabetes have greater chances to develop several diseases including cardiovascular disease (CVD) (Bonilla, Hornsby, Pannone, Case, Aviles, & Apolinario Carrasco *et al.*, 2019). In diabetes, the most common complication is cardiovascular disease (CVD). This is the major cause of death in patients suffering from diabetes mellitus (Al-Rubeaan, Al Derwish, & Ouizi, *et al.*, 2015). In DM patients, cardiovascular diseases are common and major cause of death. There is an increased chance of having diabetes and cardiovascular disease in such patients with first-degree Relatives (FDRs) (Jalilian, Ahmadi Sarbarzeh, & Oubari, 2020). The important risk factor for cardiovascular disease (CVD) is endothelial dysfunction, which leads to mortality and morbidity (Verdecchi, Reboldi, & Angeli, 2020). Atherosclerotic changes in the vessels can cause Peripheral arterial disease (PAD) (Abd El-Khalik, Hafez, & Elkholy, 2020). On diabetic patients, new studies are being conducted for introducing new cardiovascular protective treatments, which is, consist of personalized CHD complications. In diabetes mellitus, the Complication Engine is a tool that is used for diagnosing the complication of cardiovascular complications (CVD) (Kurniawati, Ismiarto, & Hsu, 2019). cardiovascular diseases and mortality can occur due to chronic kidney disease and diabetes. The prevalence of cardiovascular disease (CVD) is higher in blacks as compared to whites. Certain regions of the United States such as Mississippi where blacks reside have a larger number of cardiovascular (CV) mortality than those residing elsewhere in the country (Harreiter & Roden, 2019).

In Rheumatoid Arthritis, Ischemic heart disease and heart failure are the most common and major causes of death. Like diabetes mellitus, in ischemic heart disease, RA appears as an independent risk factor (Jampol, Glassman, & Sun, 2020). Certain risk factors are present in patients who are suffering from type II diabetes mellitus. These risk factors are hypertension and smoking and this factor can cause coronary heart disease CHD (Bakker, Apelqvist, Lipsky, van Netten, & Schaper, 2016). Over the last three decades, the incidence of diabetes mellitus has increased exponentially due to its complications, which lead the morbidity and mortality. For a decrease in morbidity and mortality linked with diabetes mellitus hospital and community-based awareness programs should be launched (Harreiter & Roden, 2019). In Pakistan, people with type II diabetes are at high risk of Peripheral arterial disease. Early diagnosis of the disease by medical professionals can help to avoid other complications that develop soon (Rossboth, Lechleitner, & Oberaigner, 2021). Pakistani patients suffering from type II diabetes have an incidence of atherogenic dyslipidemia and poor glycemic control (Rossboth, Lechleitner, & Oberaigner, 2021). In poorly controlled diabetic patients, cardiovascular autonomic neuropathy (CAN) gives potentially life-threatening outcomes (Tolossa, Mengist, Mulisa, Fetensa, Turi, & Abajobir, 2020). Another complication associated with diabetes mellitus is nephropathy. ESRD known as End Stage Renal Disease is another stage of this disease, in which an individual's kidney completely ceases its function leading to a chronic renal failure. Less urine output, swelling of the legs, and face, nausea, and vomiting are the symptoms of ESRD. A high risk of developing End Stage Renal Disease (ESRD) is associated with Diabetic nephropathy (DN). In the beginning of diabetic nephropathy, several factors are involved like glomerular hyperactive filtration, which leads to nephropathy and renal injury (Yazdanpanah, Shahbazian, Nazari, Arti, Ahmadi, & Mohammadianinejad *et al.*, 2018). In chronic kidney disease, failure of the glomerular filtration rate (GFR) may be due to obesity (Armstrong, Boulton, & Bus, 2017). Chronic kidney disease (CKD) is a growing task for healthcare systems worldwide (Harreiter & Roden, 2019). Older adults are at high risk of developing chronic kidney disease (Verdecchi, Reboldi, & Angeli, 2020). In contrast in developing countries, CKD occurs due to diabetes and hypertension and occurs during middle-aged and elderly patients (Jalilian, Ahmadi Sarbarzeh, &

Oubari, 2020). Cardiovascular disease (CVD), chronic kidney disease (CKD), and diabetes mellitus form the triad and this triad shares the most basic disease pathway. Healthcare costs are excessively contributed by these patients suffering from this condition (Aldana & Khachemoune, 2020). Vascular diseases and diabetes are the major causes of CKD (Abd El-Khalik, Hafez, & Elkholy, 2020). Development of CKD might be slow so patients who have cardiovascular disease can die before the ESRD can be reached (Chaudhary, Bhansali, & Rastogi, 2019). However, the incidence of chronic kidney disease is essential for the prediction of the prevalence of ESRD (Rossboth, Lechleitner, & Oberaigner, 2021). The chance of developing microalbuminuria is increasing with smoking which leads to the development of nephropathy (Al-Rubeaan, Al Derwish, & Ouizi, *et al.*, 2015). The decline in deaths and massive advances in the treatment of acute complications of diabetes, amputations, or coronary heart disease has resulted in enhanced survival (Jaramillo-Bustamante, Piñeres-Olave, & Gonza lez-Dambrauskas, 2020). Renal insufficiency and renal biopsies renal biopsies from type-II diabetic patients displayed a heterogeneous pattern of renal disease. One-third of diabetic patients are suffering from non-diabetic renal diseases (Bauersachs, Debus, Nehler, Huelsebeck, Balradj, Bowrin, *et al.*, 2020). With type II Diabetes, renal biopsy is beneficial in the complete management of patients (Tolossa, Mengist, Mulisa, Fetensa, Turi, & Abajobir, 2020). Diabetic nephropathy is a very common problem, which is related to severe morbidity, and mortality (Verdecchi, Reboldi, & Angeli, 2020). In End Stage Renal Disease (ESRD) patients, there are several causes, which are associated to affect the survival time. Diabetes, hypertension & glomerulonephritis are the three major risk factors that have a strong association with ESRD (Tolossa, Mengist, Mulisa, Fetensa, Turi, & Abajobir, 2020). In the beginning of diabetic nephropathy, several factors are involved like glomerular hyperfiltration, which leads to nephropathy and renal injury (Kurniawati, Ismiarto, & Hsu, 2019). Levels of serum nitric oxide and sialic acid are used as strong biochemical indicators in micro and macrovascular complications of diabetes (Rossboth, Lechleitner, & Oberaigner, 2021). In the pathogenesis of 1) N several molecular and biochemical pathways have been implicated. A key pathway that is considered is Renin Angiotensin Aldosterone System (RAAS). In RAAS mutation will occur in many genes, which causes the development of diabetic nephropathy (Jampol, Glassman, & Sun, 2020). A variety of nutritional control has been reported to lessen CVD and CKD outcomes. During the fixing, the dose of any diet with multiple co-morbid conditions linked with ESRD, made the scenario worse (Yazdanpanah, Shahbazian, Nazari, Arti, Ahmadi, & Mohammadianinejad *et al.*, 2018). There are 15% Pakistanis who are suffering from diabetic diseases are completely diagnosed and millions of people are present who remain unaware that they have the disease (Kurniawati, Ismiarto, & Hsu, 2019).

According to Yazdanpanah, Shahbazian, Nazari, Arti, Ahmadi, & Mohammadianinejad *et al.* (2018), 15% of diabetic patients who have foot ulcers are reported to fall in the category of type II diabetes mellitus. When many factors act together, the most important factor is neuropathy which is the major reason for ulceration (Adeghate, Nurulain, Tekes, Fehe ´r, Kala ´sz, & Adeghate 2017). Whereas the main symptoms among the peripheral neuropathy patients have issues of dry skin, loss of sensations, and joint mobility (Hicks, Canner, Mathioudakis, Lippincott, Sherman, & Abularrag, 2020). The causes of foot ulcers might be peripheral neuropathy, macrovascular disease, and deformity (Tolossa, Mengist, Mulisa, Fetensa, Turi, & Abajobir, 2020). Foot ulcer is the major factor, which leads to hospitalization (Chaudhary, Bhansali, & Rastogi, 2019). In particular, hospitals, and patients suffering from diabetic foot ulceration need immediate consultation with professional doctors. Telemedicine is considered telehealth technology (Bakker, Apelqvist, Lipsky, van Netten, & Schaper, 2016). In primary and specialized care, Telemedicine supports distant interaction among healthcare professionals. Telemedicine minimizes the chances of patients suffering from diabetes visiting certain hospitals (Al-Rubeaan, Al Derwish, & Ouizi, *et al.*, 2015). Lower limb amputations are very common in diabetic patients. Foot ulceration patients' 85% Lower limb amputations have been recorded (Tolossa, Mengist, Mulisa, Fetensa, Turi, & Abajobir, 2020). As compared to nonsmokers or prior smokers, the chances of wound injury are much higher in smoker-diabetic patients. Therefore, doctors recommend please stopping smoking because it has an impact on vascular factors (Harreiter & Roden, 2019). The risk of depression can be higher in patients having diabetes mellitus, and especially neuropathy. Depressed diabetic patients do not pay attention to poor foot care. Therefore, the chances of developing foot ulceration are much higher in depressed patients (Aldana & Khachemoune, 2020). For the

management of diabetic foot ulcers, different types of growth factors are used to recover healing. Some diabetic foot ulcers cannot respond to conventional care. Growth factors originating from platelets might be effective in chronic, non-healing neuropathic ulcers (Bonilla, Hornsby, Pannone, Case, Aviles, & Apolinario Carrasco *et al.*, 2019). For the management of diabetic foot ulceration, platelet release is the most commonly used treatment developed by wound care centers (WCCs) (Jaramillo-Bustamante, Piñeres-Olave, & González-Dambrauskas, 2020). For the treatment of diabetic foot ulcers, Graft skin is proven very useful for the recovery of healing (Bauersachs, Debus, Nehler, Huelsebeck, Balradj, Bowrin, *et al.*, 2020). During diabetes, Exendin 4 (Ex 4) a glucagon like the one peptide 1 receptor is used that gives many positive effects. For the treatment of wounds, healing mesenchymal stem cells are used for recovery of diabetic foot ulcers. Stem cells, growth factors, skin substitutes, and gene therapy are advanced therapeutic products (Abd El-Khalik, Hafez, & Elkholy, 2020). Diabetic foot complications have been caused by several factors like poor glycemic control, duration of diabetes, and Lack of awareness (Kurniawati, Ismiarto, & Hsu, 2019). The incidence of foot washing is linked with fungal infection. In our society, particularly housewives always have wet feet. Knowledge of drying wet feet is very rare in diabetic patients, their number is only 23% and in this minority, the web spaces remain wet (Yazdanpanah, Shahbazian, Nazari, Arti, Ahmadi, & Mohammadianinejad *et al.*, 2018). The complication of diabetic foot ulcer is very costliest and only 37% of doctors can force the patient to take care of their feet. Finally, this complication is very disheartening (Al-Rubeaan, Al Derwish, & Ouizi, *et al.*, 2015).

Aims and Objectives

The study aimed to find the complications associated with diabetic patients with its different parameters and its comparison between the population of Punjab and Khyber Pakhtunkhwa regions in Pakistan. This study helped see the complications in diabetic patients and helped its control. The objectives of this study included a survey of the Government General Hospital Faisalabad in the province of Punjab and the Government hospitals in Dera Ismail Khan from Khyber Pakhtunkhwa. Enrollment of Diabetic patients types II from Punjab and KPK. Determine diabetes with its different types of risks and parameters in the patients. Assessment of complication by Questionnaire. Compare the sample of both areas.

Literature Review

Diabetes mellitus type II is considered a long-standing metabolic disorder that is caused by high blood sugar, insulin resistance, or deficiency of insulin. The most common symptom of this disease includes an increased thirst coupled with frequent urination and loss of weight. The pancreas is formed from the protuberance of the primordially foregut, and it is larger, comparatively flat, and has adjacent cooperation with the upper duodenum. The color of the pancreas organ is white to pink. The pancreas is a collective endocrine and exocrine gland.

Anatomy

The pancreas is a vital organ of the human body. The weight of the individual pancreas gland is 70 to 110g. The structure of the pancreas is like a lobe and at the back of the peritoneum of the abdominal wall; the head of the pancreas is present. The pancreas is present within the bending region of the duodenum and the position of the pancreas head is on the right side. The pancreas has a neck, body, and tail region and the region of the tail is continuing in the spleen. The pylorus is the first fragment of the duodenum and the pancreas head is present together with the pylorus. The uncinate process is defined as the elongation of pancreatic tissue with different sizes and shapes, this elongation moves out from the pancreas head, and the spreading of this will occur left and upward. The tail of the pancreas is moveable and the top portion of this reaches the hilus of the spleen (Bonilla, Hornsby, Pannone, Case, Aviles, & Apolinario Carrasco *et al.*, 2019).

Function

The pancreas performs both endocrine and exocrine functions. In the gastrointestinal tract, the exocrine gland can secrete many digestive enzymes, ions, and water into the intestine. The meal is consumed along the lining

of the gastrointestinal tract. The digestive enzyme plays the most important role in the breakdown of the food. Secretion of digestive enzymes will occur from the salivary gland, stomach, and lining epithelium of the gastrointestinal tract. The disorder and disturbance of metabolism causes Diabetes mellitus for which the main finding is severe hyperglycinemia because of either compromised insulin secretion or lessened insulin action, and in some cases both (Adeghate, Nurulain, Tekes, Fehe' r, Kala'sz, & Adeghate 2017).

Major complications associated with Diabetes Mellitus

Micro-vascular and Macro-vascular difficulties are the kinds of severe complications. Diabetes Mellitus has serious problems that comprise the hyperglycemia hyperosmolar state (HONK) and inter alia the diabetic ketoacidosis (DICA). Diabetic neuropathy, nephropathy, and retinopathy are a few of the severe micro-vascular issues. On the other hand, peripheral vascular disease (PAD), the cerebrovascular incidence for example, stroke along with the transient ischemic attack (TIA) and diabetic foot ulcers show macrovascular difficulties. Patients with well-controlled sugar levels have lesser chances of developing such complications from diabetes mellitus (Aldana & Khachemoune, 2020).

Cardiovascular Complication

Diabetes mellitus is associated with various kinds of diseases of the heart. The most common among them is cardiovascular diseases (CVD). It is a clear fact that diabetes is one of the strongest CVD risk factors (Al-Rubeaan, Al Derwish, & Ouzi, *et al.*, 2015). Those people who are suffering from diabetes, have greater chances to develop several diseases including cardiovascular disease (CVD) (Bakker, Apelqvist, Lipsky, van Netten, & Schaper, 2016). A study conducted in a Swiss medical institute describes that Diabetes and cardiovascular patients have an impressively high likelihood of cardiovascular complications and comparatively low respiratory ailments (Hicks, Canner, Mathioudakis, Lippincott, Sherman, & Abularrag, 2020).

It is reported in one study that many other diseases occurred due to the combination of three complications like chronic kidney disease, cardiovascular and diabetes mellitus and patients with these complications contribute extremely to healthcare costs (Jaramillo-Bustamante, Piñeres-Olave, & Gonzalez-Dambrauskas, 2020). The burden of diabetes, cardiovascular disease, and chronic kidney disease is high in the South Asian population (Hicks, Canner, Mathioudakis, Lippincott, Sherman, & Abularrag, 2020). It is described that when the level of HS-CRP increases then the danger of cardiovascular disease and mortality also increases with time (Bauersachs, Debus, Nehler, Hulsebeck, Balradj, Bowrin, *et al.*, 2020). Type II diabetes mellitus is expanding around the world just because of the advancement of cardiovascular (CV) complications. There are two new ways to deal with bringing down glucose levels, one is the "incretin effect" and sodium-glucose co-transporter 2 (SGLT-2) in the tubules of the kidney to enhance glycosuria (Harreiter & Roden, 2019). Diabetes complications can occur due to advanced glycation end products (AGEs) and their receptors and when AGEs are activated, the receptors can cause inflammation (Tolossa, Mengist, Mulisa, Fetensa, Turi, & Abajobir, 2020). In females, early puberty timing is related to higher dangers for type II diabetes and cardiovascular disease, and both early and late menarche were related to higher dangers for early normal menopause in women (Armstrong, Boulton, & Bu, 2017). Besides this dysfunction of endothelial is a major factor considered for cardiovascular complications (CVD) related to injury and death among people (Jalilian, Ahmadi Sarbarzeh, & Oubari, 2020). Moreover, the threat of CVD in people with type II diabetes mellitus was related to increased levels of Von Willebrand factor in the Framingham population (Aldana & Khachemoune, 2020).

In the South Asian population, there is a great risk of cardiovascular and diabetes diseases. In one study it is reported that 30 transients from Pakistan to the UK, 30 British-conceived British Pakistani ladies, and 25 British-conceived ladies of European birthplace are included, and it is concluded that the risk of diabetes and cardiovascular disease is higher in British-conceived British Pakistani ladies than in vagrant British Pakistani women (Bakker, Apelqvist, Lipsky, van Netten, & Schaper, 2016). The endemic of cardiorenal illness keeps on

expanding at a high rate. Corpulence influences 33% of individuals and one of six kids in the United States and keeps on expanding; despite that, dietary intercessions are regularly fruitful, and they frequently flop after some time due to attrition (Jampol, Glassman, & Sun, 2020). Hypertension is also a major reason for cardiovascular mortality (Kurniawati, Ismiarto, & Hsu, 2019). In DM type II patients cardiovascular complication is one of the major factor and first-degree relatives (FDRs) of such patients are in danger of having cardiovascular disease diabetes (van Netten, Bus, & Apelqvist *et al.*, 2019). In CED patients with hypertension and diabetes, levels of vitamin C, vitamin B, and antioxidant is higher as compared to those patients with CHD having no hypertension and diabetes (Mohammad Zadeh, Lingsma, van Neck, Vasilic, & van Dishoeck, 2019).

In Pakistan, various studies have reported complications related to diabetes type II. A study conducted in Khyber Teaching Hospital, Peshawar describes foot ulcers at 72.91%, stroke at 56.25%, renal illnesses at 66.66%, and side effects of diabetic neuropathy running from 47-65% (Shabana, Ullah Shahid, & Wah Li, et al., 2016). Diabetes is also associated with endothelial irregularities (Saboor *et al.*, 2014). This study was undertaken in Faisalabad to check that microalbuminuria is a dependent factor for the cause of cardiovascular morbidity and the result showed that microalbuminuria in type II diabetic patients is reduced due to the Angiotensin receptor blockers (ARB), and Angiotensin-converting enzyme inhibitor (Rossboth, Lechleitner, & Oberaigner, 2021). Increased serum leptin levels play an important role in diabetes mellitus type II. In diabetic patients, hyperleptinemia shows that the development of cardiovascular disease in diabetic patients is due to the contribution of leptin. In the Pakistani population. It is reported that concentrations of Serum adiponectin are an indicator of cardiovascular diseases in diabetic patients (Mohammad Zadeh, Lingsma, van Neck, Vasilic, & van Dishoeck, 2019). The studies report that Dyslipidemia is the major source of cardiovascular diseases and managing the concentration of dyslipidemia reduces the chance of cardiovascular diseases. The incidence of dyslipidemia among diabetic males was 97.18% while for females 87.15% (Sarfraz, Sajid, & Ashraf, 2016).

Nephropathy

Nephropathy is End Stage Renal Disease, in which kidneys completely cease function coupled with end-stage severe renal failure. Less urine output, swelling of the legs, and face, nausea, and vomiting are the symptoms of ESRD. Diabetic nephropathy is a well-known cause in Europe, the United States, and Japan (Hicks, Canner, Mathioudakis, Lippincott, Sherman, & Abularrag, 2020). Severe kidney disease (CKD) is an expanding challenge for the medicinal services frameworks worldwide (Bakker, Apelqvist, Lipsky, van Netten, & Schaper, 2016). Major reasons for CKD are diabetes and vascular diseases (Aldana & Khachemoune, 2020). CKD is an advancing complication and in the situation where the kidney work deteriorates, dialysis and transplantation might be required (van Netten, Bus, & Apelqvist *et al.* (2019). The prevalence of type II diabetes mellitus along with chronic kidney disease and expenses of renal therapy has increased over time (Al-Rubeaan, Al Derwish, & Ouizi, *et al.*, 2015). The occurrence of CKD in China is 10.8% (Bauersachs, Debus, Nehler, Huelsebeck, Balradj, Bowrin, et al., 2020). Hypertension is among the most grave modifiable hazard variables for CKD progression (Jalilian, Ahmadi Sarbarzeh, & Oubari, 2020). It is reported that in CKD patients, 15.64% had DM, 18.55% were present smokers 9.45% proclaimed ethanol ingesting and 7.14% had a family marked by CV difficulty (Armstrong, Boulton, & Bu, 2017). Different stages of renal damage could prompt distinct changes in urinary protein structure and the need to discover urinary competitor peptide biomarkers in type II diabetic patients with various degrees of kidney harm (Jalilian, Ahmadi Sarbarzeh, & Oubari, 2020). Five factors are considered responsible for chronic kidney diseases, while in developing nations, chronic glomerulonephritis inter alia interstitial nephritis is the main cause of prolonged kidney disease (Rossboth, Lechleitner, & Oberaigner, 2021). An Indian study reported a continuous increase in complications related to diabetes mellitus continuously and stressed preventive measures (Bonilla, Hornsby, Pannone, Case, Aviles, & Apolinario Carrasco *et al.*, 2019). Where in Africa, chronic kidney disease is reported 3-4 times more common in contrast to other developing nations. Kurniawati, Ismiarto, & Hsu (2019) reported hypertension as a critical factor in the failure of kidney among the diabetic patients. In several developing nations, diabetic nephropathy (DNP) has been identified as the major cause of end-stage renal disease (ESRD). Jampol, Glassman, & Sun (2020) reported that 43.1% of patients with arterial hypertension, 69.4% with proliferative retinopathy, and 44.4% with clinical neuropathy in the Gulf region.

Studies reported that failure of the glomerular filtration rate (GFR) during End Stage Renal Disease (ESRD) could occur due to obesity (Bauersachs, Debus, Nehler, Huelsebeck, Balradj, Bowrin, *et al.*, 2020). Obesity, hypertension, and excessive glucose intake play an important role in cardiorenal disease and excessive glucose intake will increase the level of uric acid which also increases the prevalence of cardiorenal disease in the American population (Jampol, Glassman, & Sun, 2020). In the entire cohort, there about were 136 males and 75 females with an average age range of 60.1 (30-82) years. Nearly 56% of the patients belonged to Caucasia, 10% Asian, and 34% Afro-Caribbean. 46% were nonsmokers and 77% were getting treatment with inhibitors of the renin-angiotensin-aldosterone system. Around 73% were administering oral antidiabetic agents beside 27% were on insulin treatment. An established analysis of diabetic retinopathy exists in 47% of patients while 5% had a history of baseline cardiovascular disease. At this baseline, 49% were normoalbuminuric (ACR <3 mg/mmol), 37% had microalbuminuria (ACR 3 - 30 mg/mmol), and 14% had ACR >30 mg/mmol in the target population (Aldana & Khachemoune, 2020). In Pakistani populations, various studies have reported the complications associated with diabetes type II. This study is conducted in Karachi to check kidney failure associated with type II diabetes mellitus and renal biopsy is also done among three groups of patients to find the renal injury and provide awareness for patient management. Results showed that 27.3% had diabetic glomerulosclerosis 23.3% showed the occurrence of vascular changes 49.3% had non-diabetic renal diseases (Arif *et al.*, 2009). At the beginning of diabetic nephropathy, several factors were involved like glomerular hyperfiltration which lead to nephropathy and renal injury (Jalilian, Ahmadi Sarbarzeh, & Oubari, 2020). In Peshawar, it is found that end-stage renal disease (ESRD) is more common in diabetic patients as compared to non-diabetic patients. A close relationship was found between different risk factors i.e., diabetes, hypertension, and glomerulonephritis (van Netten, Bus, & Apelqvist *et al.*, 2019). Nitric oxide and sialic acid are biochemical indicators used in many screening processes that are helpful in micro and macrovascular complications for example, hypertension and nephropathy (Yazdanpanah, Shahbazian, Nazari, Arti, Ahmadi, & Mohammadianinejad *et al.*, 2018). Diabetic nephropathy (ON) can occur due to some changes in RAAS gene. Various drugs in diabetic nephropathy are used to control RAAS like Angiotensin Converting Enzyme (ACE) inhibitors (Lain & Awan, 2014). Cardiovascular disease (CVD) and chronic kidney disease (CKD) could be controlled through proper diet and adopting good and healthy lifestyles (Mohammad Zadeh, Lingsma, van Neck, Vasilic, & van Dishoeck, 2019). There is a close association of diabetes type II mellitus with glycemic control and nephropathy, abnormal lipid metabolism, endothelial dysfunction, and hypertension reported (Yazdanpanah, Shahbazian, Nazari, Arti, Ahmadi, & Mohammadianinejad *et al.*, 2018). This study is conducted in Karachi to check the incidence of non-diabetic renal disease (NDRD) in diabetic patients and renal biopsy can be performed for the treatment of this disease. Patients were grouped into Groups, II, and III. Group II isolated NDRD; NDRD with underlying DN; and Group III, isolated DN. Diabetes was significantly less in Group I compared with Group II and Group III (Ashraf *et al.*, 2011). This study was conducted in Karachi to check that the percentage of retinopathy is 43% neuropathy at 39.6% foot ulcers at 4% and Nephropathy was found in 20.2%. Patients with poor glycemic control are at high risk of these complications (Rosboth, Lechleitner, & Oberaigner, 2021). This study was conducted in Islamabad to check that Angiotensin-converting enzyme (ACE) gene is the major cause of diabetic nephropathy. Different types of inhibitors like ACE inhibitors and angiotensin receptor blockers (ARBs) can be used for the reduction of diabetic nephropathy. Family history and neuropathy were strongly related to the onset of diabetic nephropathy (van Netten, Bus, & Apelqvist *et al.* (2019). This study was conducted in Peshawar. According to this study, microvascular, complications like nephropathy can occur more rapidly in patients suffering from diabetes mellitus type II (Wang, Lv, Cheng, Ma, Wang, & Gui *et al.*, 2020). It is reported that the risk of nephropathy was present in one in three patients (Mohammad Zadeh, Lingsma, van Neck, Vasilic, & van Dishoeck, 2019).

Diabetic Foot ulcer

It is well reported in the literature that patients with type II diabetes mellitus suffer from foot ulcers for which several factors are accountable. The critical of them is neuropathy and the cause of ulceration (Bonilla, Hornsby, Pannone, Case, Aviles, & Apolinario Carrasco *et al.*, 2019). The symptoms of peripheral neuropathy include loss of protective sensations of pressure, dry skin, as well joint mobility (Jampol, Glassman, & Sun, 2020). There are

certain factors, which account for the growth of certain subsequent amputation and foot ulceration. These might include peripheral neuropathy, macrovascular disease, and deformity (Aldana & Khachemoune, 2020). Foot ulcers occur because of neuropathy and have a maximum prevalence of microvascular complications (Jalilian, Ahmadi Sarbarzeh, & Oubari, 2020). Diabetic foot ulceration can occur due to certain causes and these causes are peripheral vascular disease, callus, edema, and deformity (Jampol, Glassman, & Sun, 2020). In diabetic patients, foot ulcers can occur naturally and despite therapy, it may result in the loss of legs and fingers. Those ulcers, which can be cured in the past, have a chance to develop into chronic wounds (Armstrong, Boulton, & Bu, 2017). It is reported that many factors play an important role in diabetic foot wounds and could be checked through simple and cheap apparatus (Bakker, Apelqvist, Lipsky, van Netten, & Schaper, 2016).

Diabetic foot ulcers are an economic problem that has increased with the passage of time and the cost of treating one foot ulcer is expected to be about two-year period is \$28,000 (Jampol, Glassman, & Sun, 2020). The skin graft is used in the treatment of diabetic foot ulceration, which is more effective than currently available treatment and therapies with no side effects (Al-Rubeaan, Al Derwish, & Ouizi, *et al.*, 2015). The prevalence of diabetic foot ulcers is 2.0% per year and the price for the cure of diabetic foot ulcers is \$27,987 for the first 2 years after diagnosis in the American population (Jampol, Glassman, & Sun, 2020). It is reported that the Diabetic Foot Ulcer Scale (DES-SF) has been used for the evaluation of ulcers. The size of the ulcer was about 5.5cm in those patients suffering from diabetic foot ulcers and during diabetic foot ulcers, only one limb was commonly damaged (Bonilla, Hornsby, Pannone, Case, Aviles, & Apolinario Carrasco *et al.*, 2019). Telemedicine can be used in the treatment of diabetic foot ulcers and increase the knowledge and skill among patients suffering from DFU (Jaramillo-Bustamante, Piñeres-Olave, & González-Dambrauskas, 2020). This form of new care technology in diabetes foot care often involves healthcare professionals working across different settings with different management systems and organizational cultures (Kurniawati, Ismiarto, & Hsu, 2019). Another study conducted in China reports that Mesenchymal stem cells (MSCs) are also an effective treatment for diabetic foot ulcers. It helps in the cessation of wounds with reduced amputation (Lechleitner *et al.*, 2019). Depositing devices are applied to cure foot ulcers. A large number of ulcers were managed with "gold standard" and shoe modifications (Aldana & Khachemoune, 2020). This study was conducted in California. In this study different types of therapies are used, the first is maggot therapy and the other one is conventional therapy. It is concluded that maggot therapy is more effective than conventional therapy (Mohammad Zadeh, Lingsma, van Neck, Vasilic, & van Dishoeck, 2019).

Multidrug-resistant organisms can cause disease in patients suffering from diabetic foot ulcers. Therefore, to avoid different complications it is necessary to control the bacteria (Lechleitner *et al.*, 2019). Research conducted in Karachi found that both micro and macrovascular complications are very common in diabetic foot ulcers which stresses creating awareness among such patients (van Netten, Bus, & Apelqvist *et al.*, 2019). Similarly, a study in Rawalpindi was undertaken to investigate the ratio of ischemic ulcers, it reported its existence with 18.3%, whereas, 22.6% of patients were neuropathic, and 59% of patients were neuro-ischemic (Ashraf *et al.*, 2011). Like, a study in Peshawar reported that every patient among the three was unaware of diabetic foot ulcers (Lechleitner *et al.*, 2019). This research was conducted in Islamabad to find that only a small number of patients can pay heed to their diabetic foot ulcer according to the instructions given by ADA Guidelines (Saeed *et al.*, 2010). This study was conducted in Abbottabad to find that diabetic foot ulcer is the most damaging and depressing complication of diabetes mellitus. The major problem concerning diabetic wounds is that in most cases, the physicians are non-cooperative to patients consequently; patients do not give importance to foot ulceration (Mohammad Zadeh, Lingsma, van Neck, Vasilic, & van Dishoeck, 2019).

Method

Identification and Enrollment

The study in hand used the retrospective case-control association method. The patients with Diabetes type II complications were the subjects under study from hospitals in Punjab and Khyber Pakhtunkhwa. All of them went through a Diabetic examination together reviewing their medical record. A structured questionnaire was used to collect the opinions of the sample. The medical history related to family history was also checked (parents, children, and

grandparents) for diabetes and its complications. The physicians from these diabetic centers were taken into confidence by explaining the purpose of the study which proved instrumental in the enrolment of the subjects.

Inclusion Criteria

The patients who did not show interest or those who were not suffering from diabetic complications (cardiovascular, nephropathy, foot ulcer) were excluded, which included both males and females between the ages of 17 to 90 years. Data was collected through a proforma. The researchers administered the proforma by themselves among the patients with a history of smoking and hypertension; the items included the height, weight and waist, foot ulcer, nephropathy, and cardiovascular circumference.

Exclusion criteria

Those patients who do not have diabetes mellitus type II and those who are not interested in taking part in research were excluded.

Clinical Assessment of Diabetes Mellitus Type H

Glucose testing

Different types of tests can be performed to check diabetes, which includes.

- Blood glucose level
- Urine testing
- HbA1c and fructosamine
- Blood fat (lipids)

For glucose testing, after the fasting state of about 10- hours blood was collected, and samples were taken by venous puncture. After taking tubes, added EDTA and heparin. Placed the sample immediately on ice. Now, the centrifugation process has been done by using clotted blood. For 30 min, clotted blood was centrifuged at 1,500 rpm and after that, the serum was separated. Before analysis it was stored at -70C. The Glucose oxidase method was used for monitoring blood glucose was measured calorimetrically using an HbA1c kit. People suffering from diabetes can check the level of sugar present in their blood by using testing strips at their homes. This test will provide accurate results of blood glucose. It involves pricking a finger with the help of a finger-pricking device and then putting a drop of blood on a testing strip.

Cardiovascular risk assessment tests

Deep Breathing test

In the deep breathing test, an Electrocardiogram (ECG) was done on an ECG machine and the ECG was done for 30 seconds. The patient was allowed to take deep and slow inspiration and expiration. As a result, ECU was traced.

Valsalva maneuver

Valsalva maneuver was performed when the patient was in a sitting position and the patient was trained to blow into a mouthpiece attached to a sphygmomanometer. The expiratory rate was kept for 15 seconds at 40 mmHg. After 15 seconds, the patient released the pressure.

Holter Monitoring

A portable device that is used for the recording of ECG. Heart rhythm irregularities can be found with the help of Holter monitoring.

Echocardiogram

In an Echocardiogram, the ultrasound of your chest is done and the result shows the complete structure and function of the heart.

Cardiac Catheterization

In Cardiac catheterization, a small tube known as a catheter was inserted in the veins and arteries of the leg and arm. As shown the catheter is a deep, elastic, and large tube. With the help of an X-ray image on the monitor, the catheter moves toward the heart. In this method, the dye was also used. This dye will help to find the rate of blood flow in the heart and blood vessels for the finding of any abnormalities.

Cardiac Computerized Tomography

(CT) Cardiac computerized tomography (CT) scan was used to find heart abnormalities. It is a doughnut-shaped machine. In this machine, an X-ray tube is present. This rotates around the body and gives an image of the chest and heart.

Cardiac Magnetic Resonance Imaging (MRI)

Magnetic resonance imaging gives detailed pictures of internal body structure by producing a strong magnetic field. For this test, patients lie on a table inside a long tube-like machine that produces a magnetic field.

Clinical Assessment of Nephropathy

Various types of tests are performed in diabetic nephropathy.

Urine Test

The urine test was used to find early kidney damage. Early kidney damage does not have any kind of symptoms. A small amount of protein named microalbuminuria can be checked. With appropriate treatment, one can prevent the kidney from being damaged.

Determining glomerular filtration rate

The Glomerular filtration rate is a measure of how well kidneys filter blood. Creatinine cannot be removed from the blood during kidney damage as a result creatinine starts to deposit in muscle tissue and blood. There are five stages of kidney disease and treatments depend upon the stage of kidney disease.

Clinical Assessment of Foot ulcer

The ulceration and gangrene were observed with the color of limb, skin, nail, and hair present in patients suffering from diabetic foot ulcer. A standard neurological examination was performed by testing the sensation of touch, pain, and vibration with the help of a tuning fork. If three senses were absent out of four then Peripheral neuropathy was present. Reduction of diabetic foot ulcers and wounds was achieved with regular care and by using various kinds of antibiotics.

Examination

A full systemic and physical examination was performed. In dorsalispedis, arterial pulse and posterior tibial arteries were examined and compared bilaterally.

Charcot Osteoarthropathy

The lower limb was checked by physical examination. Charcot Osteoarthropathy of the foot was based on history and clinical examination. Different sides of the foot as dorsal and plantar surfaces were examined for erythema increase in temperature and any deformity was analyzed by using X-rays.

Assessment for Neuropathy

The patient's examination is carried out with the presence of neuropathy, the position of the joint, and vibration. By taking halluces as a standard point, a tuning fork was used for sensation. If patients feel that vibration produced by the tuning fork then the result will be positive, and the result will be negative if patients do not feel any type of vibration. According to standard clinical practice, the sense of position was checked which is dorsal and plantar flexion.

Semmes-Weinstein (SW) Monofilament

To check the pressure sensation among diabetes mellitus type II patients, we used the Semmes-Weinstein monofilament. There are four sites namely 1st, 3rd, and 5th metatarsal heads and plantar surface of distal hallux. The pressure along with 10 g monofilament was used perpendicularly for 2 seconds. The test is abnormal if the patients do not sense the monofilament.

Statistical Analysis

For the analysis of data, SPSS version 17.0 was used. The mean \pm standard deviation (S.D) was found and results were expressed using frequency and percentages methods. The P-value of <0.05 was considered significant.

Patient Analysis

Diabetes mellitus in particular is a heterogeneous and multifactorial metabolic disorder due to a lack of insulin sufficiency and resistance (Lechleitner *et al.*, 2019) along with associated type II diabetes mellitus. People with diabetes are at high risk of various kinds of severe health issues i.e., untimely demise, downheartedness, cardiac disease (CVD), loss of sight, kidney botch, amputations besides a cognitive decline (Al-Rubeaan, Al Derwish, & Ouizi, *et al.*, 2015). Data from the 400-persona suffering from diabetes mellitus type II was gathered from government hospitals in Faisalabad and Dear Ismail Khan during 2022- October 2023, whose average age was between 52.6-111.2 in Punjab and 50.31 ± 12.0 in Khyber Pakhtunkhwa. Around 45% of patients in the Punjab province were aware of how to manage diabetes complications as compared to Khyber Pakhtunkhwa's 25%. The clinical topographies of the patients of Punjab and Khyber Pakhtunkhwa whose ages range from 20 to 90 years where the majority of them fall in the 40-60 years category including 107 males and 93 females in Khyber Pakhtunkhwa as compared to 107 and 110 females in Punjab respectively. As for the duration of diabetes mellitus is concerned it was set from less than 1 year to more than 10 years. Furthermore, 70 of the patients were smokers from Khyber Pakhtunkhwa and 110 were smokers from the Punjab.

Complications associated with Diabetes Mellitus

The common complications associated with diabetes include cardiovascular diseases (CVD) and Nephropathy in which the kidney ceases to function resulting in chronic renal failure. The other symptoms include decreased urination, swelling of the face and legs, nausea and vomiting, etc. Furthermore, in most cases, patients with type II diabetes also suffer mellitus foot ulcers for which neuropathy is responsible (Armstrong, Boulton, & Bu, 2017). Similarly, other symptoms also include peripheral neuropathy resulting in the loss of the defensive senses of pressure, skin dryness, and joint mobility (Bonilla, Hornsby, Pannone, Case, Aviles, & Apolinario Carrasco, *et al.*, 2019). As for patients' responses were concerned, they showed positive responses for cardiovascular disease (132), nephropathy (45), and foot ulcer (42) while 268 patients showed a negative response for cardiovascular disease, 355 for nephropathy and 358 patients for foot ulcer.

Discussion

Type II diabetes or non-insulin-dependent diabetes is one of the diseases in which the level of glucose increases in the blood of an individual and they are at a high risk of severe health complications for example, untimely demise, downheartedness, cardiac disease (CVD), sightlessness, kidney-failure, cognitive decline, etc. (Bakker, Apelqvist, Lipsky, van Netten, & Schaper, 2016). The findings of the study are based on the data collected from 400 individuals suffering from diabetes mellitus type II. According to Jaramillo-Bustamante, Piñeres-Olave, & Gonza'lez-Dambrauskas (2020), the prevalence of diabetes is generally higher in urban than rural areas as could be observed from the results for Urban, where 3.5% in females and 6.0% in males were found with this disease in contrast to 2.5% female and 6.9% males in rural areas. These results also have the support of Jampol, Glassman, & Sun (2020). In a study on the incidence of diabetes mellitus, type II in the rural areas of Pakistan. The study finds 2119 patients in the 20 years or above. The study portrays a 5.8% prevalence of diabetes with 6.9% females and 3.7% males respectively (Zahid *et al.*, 2008). van Netten, Bus, & Apelqvist, *et al.* (2019) assert that diabetes mellitus is more common among individuals in the age category of 50-60 years in the Indian sub-continent as compared to the results of a Pakistani study in Peshawar. According to the results, 79.16% of patients have no basic information about the disease due to a lack of education in the majority of patients in general and female patients in particular. Approximately 75% of the patients are unaware of DM and proper diet, and they do not avoid sweets, consume extra millet and wheat chapattis, etc. (Al-Rubeaan, Al Derwish, & Ouizi, *et al.*, 2015).

Cardiovascular Complications

Diabetes mellitus was reported as the principal cause of cardiovascular diseases in most of the less developed and developing countries and one of the reasons for high morbidity and mortality (Armstrong, Boulton, & Bu, 2017). The results of the study are evident in this, according to our results there are 26 % cardiovascular complications in Punjab and 26% in Khyber Pakhtunkhwa comparatively 49% for males and 75.5% for females. It is further identified that Macrovascular complication is the main risk connected with long-term diabetes mellitus type II due to hypertension and smoking inter alia physical laziness, fatness, and unhealthy diets (Gul *et al.*, 2008). Patients with diabetes are at greater risk of developing myocardial infarction, and hypertension with increased levels of cholesterol that causes Ischaemic stroke and cardiac arrest (Lechleitner *et al.*, 2019). Jampol, Glassman, & Sun (2020) observed that decreasing the amount of uric acid in diabetic patients can reduce the cardiovascular risk and associated complications. van Netten, Bus, & Apelqvist *et al.* (2019) have found that higher-level glucose is found in diabetes mellitus patients. Further, 5.5% of macrovascular complications are reported along with 15.1% coronary artery disease (CAD), & peripheral arterial disease (PAD) 4.4% among such patients. Likewise, Bonilla, Hornsby, Pannone, Case, Aviles, & Apolinario Carrasco *et al.* (2019) reported similar results in an Indian study. As for results of the existing study are concerned, a high cardiovascular is reported in Punjab as compared to Khyber Pakhtunkhwa province because most of the data was assembled from the urban areas of the Punjab province due to lack of participation in physical activity that causes obesity inter alia smoking. Furthermore, it is found that females are more vulnerable to cardiovascular diseases due to household lifestyle i.e., less physical activity and no control over diet etc.

Nephropathy

It is a complex pathophysiological process concerning several cellular as well as molecular mechanisms (Mohammad Zadeh, Lingsma, van Neck, Vasilic, & van Dishoeck, 2019), in which diabetes mellitus type II plays an instrumental part resulting in chronic kidney disease (CKD) which is considered as the prime reason for End-Stage Renal Disease (ESRD). Although Jaramillo-Bustamante, Piñeres-Olave, & Gonza'lez-Dambrauskas (2020) reported metabolic syndrome along with microalbuminuria caused a kidney injury. Yet, van Netten, Bus, & Apelqvist *et al.* (2019) reported hypertension and diabetes as the main causes of chronic kidney diseases. Where, a high amount of glucose found in kidney lesions is the cause of metabolic abnormality, which can cause nephropathy (Wang, Lv, Cheng, Ma, Wang, & Gui *et al.*, 2020). Our results highlighted that 13.5% risk of nephropathy in Punjab and 9% in Khyber

Pakhtunkhwa, 12.7% among females and 11% in males in Punjab, and 6.5% male and 12.9% female in Khyber Pakhtunkhwa. 15.65% in diabetic patients was the reported frequency of chronic kidney disease, 18.54% smokers, 9.35% ethanol consumption, and 7.14% cardiovascular complications (Jampol, Glassman, & Sun, 2020). Five elements have a significant role in developing chronic kidney disease, whereas chronic glomerulonephritis and interstitial nephritis are considered significant in developing nations that cause chronic kidney disease (Bakker, Apelqvist, Lipsky, van Netten, & Schaper, 2016). Diabetic nephropathy might also occur because of changes in the RAAS gene and the use of different drugs to control RAAS for example, angiotensin-converting enzyme (ACE) inhibitors (Kurniawati, Ismiarto, & Hsu, 2019) besides lifestyle and diet in specific are the critical factors to treat with such conditions (Lechleitner *et al.*, 2019). The study found that increasing awareness concerning renal disease is needed time together with adequate strategies that could facilitate timely detection and prevention to avoid the onset of ESRD (Wang, Lv, Cheng, Ma, Wang, & Gui *et al.*, 2020). Further, our study finds that a high carbohydrate diet is one of the main causes of diabetes and kidney failure in Pakistan.

Foot Ulcers

Studies have reported that many factors account for patients suffering foot ulcers due to type II diabetes mellitus; the significant is that neuropathy is the principal cause of ulceration (Jaramillo-Bustamante, Piñeres-Olave, & Gonza'lez-Dambrauskas, 2020). Moreover, the main symptom of peripheral neuropathy consists of loss of defensive sensations of pressure, skin dryness, and skin dryness inter alia mobility of joints (Al-Rubeaan, Al Derwish, & Ouizi, *et al.*, 2015; Yazdanpanah, Shahbazian, Nazari, Arti, Ahmadi, & Mohammadianinejad *et al.*, 2018). Some factors could result in growing certain subsequent amputation and foot ulceration including peripheral neuropathy, macrovascular disease, and deformity (Kurniawati, Ismiarto, & Hsu, 2019). The result of this research shows that 13.5% of patients in Punjab and 8.00% in Khyber Pakhtunkhwa were suffering from diabetic foot ulcers. Further, several factors account for diabetic foot wounds that could be checked by simpler and inexpensive apparatus (Armstrong, Boulton, & Bu, 2017). Likewise, offloading devices could be used for curing the foot (Bakker, Apelqvist, Lipsky, van Netten, & Schaper, 2016; Lechleitner *et al.*, 2019). The study finds that a lack of awareness is tripling the effects of the disease (Hasnain & Sheikh, 2009). The findings of the study explained that patients who received guidance for foot protection and had a history of foot examination were altogether more susceptible to consistently checking their feet (Armstrong, Boulton, & Bu, 2017). Therefore, it is required to initiate a comprehensive instruction program to promote learning about foot care and cures for ulcers due to diabetes, especially among the more vulnerable patients (Al-Rubeaan, Al Derwish, & Ouizi, *et al.*, 2015). When we compared the results concerning foot care between Punjab and Khyber Pakhtunkhwa the ratio of foot ulcers in both provinces was about the same, which suggests education for foot care.

Conclusions

The frequent prevalence of diabetes mellitus has been recorded in patients together with cardiovascular diseases; the frequency was around 40% in Punjab and Khyber Pakhtunkhwa Pakistan. Consequently, the ratio of diabetics in patients with cardiovascular disease was recorded as 1:4. Diabetes is more rampant among females than males with a high risk of cardiovascular complications. Furthermore, 13.2% of patients were found with nephropathy and again it was reported high for the females. Foot ulcer was also common in females i.e., 10% of the diabetic patients. The lack of awareness concerning these complications suggests the need for awareness to detect and prevent them early and to improve the lives of such patients. Timely and adequate treatment could help patients to prevent severe abnormalities associated with diabetes mellitus type II. Likewise, proper care and management of the disease together with its complications are required thus, all stakeholders must design and implement diabetes education programs focusing on cardiovascular, foot care education, and nephropathy and as well. Here, epidemiological information could be used to design result-oriented programs to control the disease. The research study in hand recommends regular screening of vulnerable groups for early diagnosis and detection of chronic complications for timely and proper treatment. This study was conducted small sample size, however considering the large population of the country, future researcher needs a large sample size including both genders from the rural and urban areas among the different age categories,

therefore, this study suggest that health authorities must include the diabetes preventive measures in country's health policy to lessen the liability of this disease.

Declaration of Interest

The authors declare that there is no clash of interest.

References

- Abd El-Khalik, S.R., Hafez, Y.M., & Elkholy, R.A. (2020). The role of circulating soluble FMS-like tyrosine kinase-1 in patients with diabetic foot ulcer: A possible mechanism of pathogenesis via a novel link between oxidative stress, inflammation, and angiogenesis. *Microvasc Research*, 130:103987.
- Adeghate, J., Nurulain, S., Tekes, K., Fehe' r, E., Kala'sz, H., & Adeghate, E. (2017). Novel biological therapies for the treatment of diabetic foot ulcers. *Expert Opin Biol Ther*. 17: 979-87.
- Aldana, P.C., & Khachemoune A. (2020). Diabetic Foot Ulcers: Appraising standard of care and reviewing new trends in management. *Am J Clin Dermatol*. 21: 255–64.
- Al-Rubeaan, K., Al Derwish, M., Ouizi, S., *et al.* (2015). Diabetic foot complications and their risk factors from a large retrospective cohort study. *PLoS One*. 10(5): e0124446.
- Armstrong, D.G., Boulton, A.J.M., & Bus, S.A. (2017). Diabetic foot ulcers and their recurrence. *N Engl J Med*. 376: 2367–75.
- Ashraf, R., Khan, R. A., & Ashraf, I. (2011). Garlic (*Allium sativum*) supplementation with standard antidiabetic agent provides better diabetic control in type 2 diabetes patients. *Pakistan Journal of Pharmaceutical Sciences*, 24(4): 565-570.
- Bakker, K., Apelqvist, J., Lipsky, B., van Netten, J., & Schaper, N. (2016). The 2015 IWGDF guidance documents on prevention and management of foot problems in diabetes: development of an evidence-based global consensus. *Diabetes/metab Res Rev*. 32: 2-6.
- Bauersachs, R., Debus, S., Nehler, M., Huelsebeck, M., Balradj, J., Bowrin, K., *et al.* (2020). A targeted literature review of the disease burden in patients with symptomatic peripheral artery disease. *Angiology*, 71: 303-14.
- Bonilla, G.A., Hornsby, P.P., Pannone, A.F., Case, S.K., Aviles, E.S., Apolinario Carrasco, M.E., *et al.* (2019). Demographic and clinical characteristics of Dominican adults admitted to a diabetic foot clinic in the Dominican Republic in 2015. *Diabetes Metab Syndr*. 13: 1727-32.
- Chaudhary, S., Bhansali, A., & Rastogi, A. (2019). Mortality in Asian Indians with Charcot's neuroarthropathy: a nested cohort prospective study. *Acta Diabetol*. 56(12): 1259-1264.
- Harreiter, J., Roden, M., (2019). Diabetes mellitus—definition, Klassifikation, diagnose, screening und prävention (update 2019). *Wien Klin Wochenschr*. 131(1): 6-15.
- Hicks, C.W., Canner, J.K., Mathioudakis, N., Lippincott, C., Sherman, R.L., & Abularrage, C.J. (2020). Incidence and risk factors associated with ulcer recurrence among patients with diabetic foot ulcers treated in a multidisciplinary setting. *J Surg Res*. 246: 243-250.
- Jalilian, M., Ahmadi Sarbarzeh, P., & Oubari, S. (2020). Factors related to severity of diabetic foot ulcer: A systematic review. *Diabetes Metab Syndr Obes*. 13: 1835-1842.
- Jampol, L.M., Glassman, A.R., & Sun, J. (2020). Evaluation and care of patients with diabetic retinopathy. *N Engl J Med*. 382: 1629-37.
- Jaramillo-Bustamante, J.C., Piñeres-Olave, B.E., & Gonza'lez-Dambrauskas, S. (2020). SIRS or not SIRS: Is that the infection? A critical review of the sepsis definition criteria. *Bol Med Hosp Infant Mex*. 77: 293-302.
- Kurniawati, A., Ismiarto, Y.D., & Hsu, I.L. (2019). Prognostic factors for lower extremity amputation in diabetic foot ulcer patients. *J Acute Med*. 9: 59-63.
- Lechleitner, M., *et al.* (2019). Diabetic neuropathy and diabetic foot syndrome (update 2019). *Wien Klin Wochenschr*. 131(1): 141-150.
- Mohammad Zadeh, M., Lingsma, H., van Neck, J.W., Vasilic, D., & van Dishoeck, A.M. (2019). Outcome predictors for wound healing in patients with diabetic foot ulcer. *Int Wound J*. 16: 1339-46.



- Naz, Rabia, Fatima Saqib, Samir Awadallah, Muqet Wahid, Muhammad Farhaj Latif, Iram Iqbal, and Mohammad S. Mubarak. (2023). Food polyphenols and type ii diabetes mellitus: Pharmacology and mechanisms. *Molecules*, 28(10): 3996.
- Rafique, G., Azam, S.I. & White, F. (2006). Diabetes knowledge, beliefs, and practices among people with diabetes attending a university hospital in Karachi, Pakistan. *EMHJ - Eastern Mediterranean Health Journal*, 12(5): 590-598.
- Rosboth, S., Lechleitner, M., & Oberaigner, W. (2021). Risk factors for diabetic foot complications in type 2 diabetes—a systematic review. *Endocrinol, Diabetes Metab.* 4(1): e00175.
- 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. *JPMA. The Journal of the Pakistan Medical Association*, 60(9): 732.
- Sarfraz, M., Sajid, S., & Ashraf, M.A. (2016). Prevalence and pattern of dyslipidemia in hyperglycemic patients and its associated factors among Pakistani population. *Saudi Journal of Biological Sciences*, 23(6):761-766.
- Shabana, Ullah Shahid, S., Wah Li, K. et al. (2016). Effect of six type II diabetes susceptibility loci and an FTO variant on obesity in Pakistani subjects. *Eur J Hum Genet.* 24: 903-910.

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