Impact of Type-2 diabetes (T2DM) on cardiovascular disease in diabetic patients with COVID-19, positive family history of diabetes and consanguinity: A 12-Month cohort study in Khyber Pakhtunkhwa, Pakistan

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***Abstract*- Introduction:** The majority of people with diabetes have type 2 diabetes mellitus (T2DM), a form of disease that is not contagious and has serious health consequences. An important, non-modifiable risk factor for COVID-19 and cardiovascular disease is a family history of diabetes.

Objective: T2DM complications and their relationship to age, family history, consanguinity and COVID-19 in a 12-month cohort study in Khyber Pakhtunkhwa population.

Methods: We enrolled 150 people with type 2 diabetes who were taking the oral anti-diabetic medications metformin, glimepiride and their combination therapy for 12 months. There were 82 women and 68 men in the study, with ages ranging from 30 to 70. The Diabetes Hospital and Research Center Peshawar in Khyber Pakhtunkhwa, Pakistan, hosted the study and the hospital's Ethics Research Committee gave its blessing for its conduct. Clinical study data were collected via questionnaire using a non-probability purposive sampling strategy and analyzed with SPSS-23.

Results: Out of the total number of 150 diabetic subjects enrolled in the study, 57 (38%) had cardiovascular disease, 27 (18%) had diabetic neuropathy, 14 (9%) had retinopathy and 3 (2%) had nephropathy at baseline. In the first follow-up (after 4 months), 61 patients (41% of the total) were diagnosed with CVD, 32 (21%) with diabetic neuropathy, 17 (11%) with retinopathy and 3 (2%) with nephropathy. In the second follow-up (after 8 months), 66 patients (44% of the total) were diagnosed with CVD, 34 (23%) with diabetic neuropathy, 20 (13%) with retinopathy and 3 (2%) with nephropathy. After 12 months, 79 (52.7%) of patients had CVD, 41 (27.3%) had diabetic neuropathy, 24 (16.4%) had retinopathy and 6 (4%) had nephropathy. 48 (32%) had a positive family history of diabetes, 85.3% had diabetes-related complications and 22 (14.7%) in the sample had a history of consanguinity. Only 8 (5.3% of the total) of the study subjects tested positive for COVID-19 via polymerase chain reaction.

Conclusions: The results showed that a significant correlation existed between participants' age and a positive family history of type 2 diabetes (P = 0.041). And a non-significant relationship exists between a positive family history of T2DM and onset age (P = 0.075). In this study, people who had recently been diagnosed with diabetes were monitored to determine their susceptibility to the SARS-CoV-2 infection. Those with T2DM are more likely to acquire the COVID-19 infection and to develop complications, especially cardiovascular complications. Throughout the course of the 12-month cohort study, more than half of the patients were diagnosed with cardiovascular disease. It is likely that comorbidities associated with diabetes can be reduced through the provision of health education, particularly for cardiovascular health and T2DM, such as increasing physical activity and consuming a low-calorie diet to control the glycemic profile.

***Index Terms*-** Family history; T2DM; cardiovascular disease; consanguinity; SARS-CoV-2

I. Introduction

The vast majority of people with diabetes in Pakistan have type 2 (Rashid et al., 2019) and this is because it is a multifactorial disease with a complex interaction of modifiable and non-modifiable risk factors such as family history, obesity, ethnicity and age (Low et al., 2022). Cardiovascular disease (CVD), cancer and type 2 diabetes (T2DM) are just a few of the many chronic diseases for which a family history increases the risk (Li et al., 2020). According to recent statistics, type 2 diabetes is more common among first-degree relatives (88–95%) than it is among second-degree relatives (70–77%) (Hariri et al., 2006, Rossello et al., 2021). Therefore, reducing the future burden of these chronic diseases could be achieved through obtaining a thorough family history, which would facilitate risk classification and risk-specific disease prevention approaches. With the information collected from history and physical examination, better public health direction for chronic conditions can be attained facilitate risk classification and risk-specific disease prevention approaches. With the information collected from history and physical examination, better public health direction for chronic conditions can be attained. That's why it's so important to have a reliable screening tool for conditions like type 2 diabetes and its complications.

T2DM has been on the rise globally, especially among adolescents (Einarson et al., 2018), in Asian countries (Einarson et al., 2018) and among African Americans (Goran et al., 2003), especially among adolescents. One of the most significant barriers to preventing type 2 diabetes is our lack of understanding of the individual's role, as well as the contributions of genetics and environment. Despite the fact that healthy lifestyle choices can put off or even prevent diabetes and its complications, (Marzi, 2014). Complex disorders tend to cluster in families, proving that a person's genetic makeup isn't the only factor at play when a disease runs in their family (Murea et al., 2012). COVID-19, a SARS-CoV-2 virus, emerged in late 2019 and was traced back to its source in Wuhan, China, before spreading rapidly throughout the (Chawla et al., 2020, Wimalawansa, 2020, Ilkhani et al., 2021). Fever, dry cough (involvement of the lower respiratory tract), lethargy, and gastrointestinal symptoms are the hallmarks of a patient presenting with this syndrome (Pennington, 2020). In February of 2020, the WHO officially recognized it as a pandemic (Ferri and Lloyd-Evans, 2021). The severity of SARS-CoV-2-related respiratory illnesses is much lower than previously thought (Aucoin et al., 2020). The World Health Organization (WHO) officially named this particular coronavirus illness "COVID-19" on February 11, 2020 (Zhao et al., 2020). Among the 209 countries affected by the COVID-19 pandemic was Pakistan (Maffia et al., 2020, Hussain et al., 2021). The WHO reports a total of 226 844 344 confirmed cases, with 4,666,334 fatalities (Choudhury et al., 2022). The United States led the world in confirmed cases, with Italy and Spain close behind, according to the World Health Organization (Aouissi et al., 2022, Gerken et al., 2021). Feet, eyes, kidneys and skin aren't the only places where diabetes can cause complications. These signs may initially alert a person to the possibility that they have diabetes. Neuropathy, skin changes, calluses, foot ulcers, poor circulation and other serious conditions can develop as a result of foot problems (Said, 2013). Retinopathy, nephropathy and neuropathy are examples of micro-vascular defects seen in diabetic patients (Girach et al., 2006, Raman et al., 2012), similarly, cardiovascular disease and neuropathy are examples of complications caused by diabetes's impact on the brain and heart. One of the most important things you can do to prevent diabetes-related complications and death is to keep your blood sugar levels under control (Dungan et al., 2006, Boussageon et al., 2011).

There is an increased likelihood of ocular complications like glaucoma, cataracts and blindness in diabetic patients compared to the general population. Retinopathy, neuropathy and renal disease are micro vascular complications of diabetes that may be postponed or avoided altogether with reasonable metabolic control (Javadi and Zarei-Ghanavati, 2008, Kiziltoprak et al., 2019). Kidney failure is typically caused by either diabetes or high blood pressure (Atkins, 2005). However, the prevalence differs from one population to the next and is also proportional to the disease's intensity and duration (Group et al., 1995, Narres et al., 2016). Screening for diabetes and other risk factors can help reduce the severity of kidney damage caused by the disease, and prompt treatment can reduce the need for preventative measures (Hansen et al., 2002, Kavey et al., 2006).

Symptoms of neuropathy include numbness, tingling and a burning sensation in the extremities (Sen et al., 2019). It's also a leading cause of erectile dysfunction in men with (Boulton et al., 2005, Feldman et al., 2019). Common complications of diabetic foot disease caused by vascular and neuropathy include ulceration, persistent infection and eventual toe or limb amputation (Alavi et al., 2014). Problems with blood flow and nerve function are both (Chapman, 2014). Regular foot inspection and care can prevent diabetes, the leading cause of non-traumatic lower leg amputation (Boutoille et al., 2008). More than half of all cases of diabetes-related death in industrialized nations are caused by cardiovascular disease (Gaziano et al., 2010, Bitton and Gaziano, 2010). Diabetic heart disease risk factors include smoking, hypertension, high serum cholesterol and obesity (Smith Jr, 2007). The primary pathogenic mechanism in macro vascular disease is atherosclerosis, which results in the global narrowing and stiffening of artery walls (Fowler, 2011).

Oxidized lipid LDL particles accumulate in the endothelium of the artery wall after endothelial injury and inflammation, setting off a state of low-grade chronic inflammation. Foam cells are created when monocytes are drawn to an area, filtered into the arterial wall, and allowed to develop into macrophages, which then collect oxidized lipids. Foam cells, after forming, boost macrophage production and T-lymphocyte recruitment. Conversely, T-lymphocytes encourage smooth muscle proliferation and collagen accumulation in arterial walls. The fibrotic process results in the formation of a fibrous cap over a lipid-rich atherosclerotic lesion. Acute infarction occurs when this lesion ruptures and draws in platelets and blood cells (Dokken, 2008).

Hypercoagulability and increased platelet adhesion are also associated with type 2 diabetes, in addition to the development of atherosclerosis. It's possible that lowered nitric oxide production promotes platelet aggregation. Elevated and impaired fibrinolysis raise the risk of cardiovascular disease in people with type 2 diabetes (Kanase et al., 2009). Damage to the cardiovascular system is exacerbated when diabetes is not managed. The link between diabetes and CVD is strong, but the exact mechanisms by which diabetes increases the risk of atherosclerotic plaque development remain unknown. People with diabetes spend a disproportionately large amount of money on medical care due to cardiovascular disease, which is the leading cause of death in both types of diabetes(Fowler, 2008, DeBoer, 2013) and the highest cause of health care expenditure among people with diabetes(Ariza et al., 2010). Multiple studies, beginning with the Framingham study, have linked diabetes to macro-vascular complications like coronary heart disease (Fox et al., 2004). Researchers have found that diabetic patients have a MI risk that is on par with non-diabetic patients who have already had a MI (Kuusisto and Laakso, 2013). Recognizing diabetes as a risk equivalent for coronary artery disease is a recommendation of both the American Diabetes Association and the American Heart Association ((Fox et al., 2015). Abdominal obesity, hypertension, hyperlipidemia, and increased are all components of the metabolic syndrome, which is a major risk factor for type 2 diabetes, but other factors may also play a role in cardiovascular disease. Type 2 diabetes is a strong predictor of ischemic illness, stroke, and mortality, even when other risk factors are present. Potentially higher rates of coronary heart disease in females with T2DM have been found compared to males. A higher risk of developing coronary heart disease has also been associated with the micro-vascular disease (Al-Delaimy et al., 2002). Coronary artery disease is the best predictor of stroke and other cerebrovascular diseases (Weir et al., 2003). Patients with type 2 diabetes mellitus are at increased risk for stroke-related dementia and recurrence as well as increased stroke-related mortality (Pendlebury, 2009, Boehme et al., 2017). Better glycemic control in type 2 diabetes is associated with fewer macro-vascular disease events, according to a large, long-term, controlled study (Kipnes et al., 2001). Different statistical and computational analysis will also applicable for the genetic mutation of the diseases (Ullah et al., 2023, Jan et al., 2021). Multiple studies, however, have shown that reducing the risk of cardiovascular events by addressing other components of the metabolic syndrome is feasible and effective. Those with type 2 diabetes who take steps to reduce their blood pressure have a lower risk of cardiovascular disease and death (Hamilton et al., 2007). One of the earliest and best-known studies to show that treating hypertension in type 2 diabetes improved macro-vascular outcomes was the United Kingdom Prospective Diabetes Study (UKPDS) (Fowler, 2011). Patients with type 2 diabetes often need multiple medications to control their hypertension. One more target is the blood lipid concentration (Fowler, 2008, Mooradian, 2009). Treatment with lipid-lowering agents, especially statins, has been shown in numerous studies to reduce the risk of macro-vascular disease in patients with diabetes. Primary and secondary CVD prevention are both enhanced by these drugs, but the greatest potential benefit may be seen in patients with diabetes who also have preexisting CVD (Costa et al., 2006, Fowler, 2008, Fowler, 2011).

II. STUDY DESIGN AND METHODS

Ethical Considerations:

The review boards at both Islamia College University and Khyber Medical University in Peshawar gave their approval this research. All study subjects provided their voluntary, informed consent. Subjects with type 2 diabetes treated with sulfonylureas (glimepiride), biguanides (metformin), or a combination of the two were recruited from the Diabetic Hospital and Research Centre in Peshawar. Participants were followed for 12 months.

Study Inclusion Criteria:

Patients with type 2 diabetes enrolled in the clinical study had a disease duration of less than four years, were receiving metformin, glimepiride, or their combination therapy for glycemic control, and were aged 30-70. Diabetes is diagnosed when a person has a fasting blood sugar level that is greater than 11.1 mmol/L but less than 200 mg/dL. HbA1C levels range from 6.5 percent (48 mmol/mol) to 8.0 percent (64 mmol/mol), and fasting blood sugar levels range from 100 to 125 mg/dL (5.6 to 6.9 mmol/L).

Study Exclusion Criteria:

Excluded from the study were participants who were taking any medications besides sulfonylureas and biguanides, those who had been taking anti-diabetes medications for more than four years, women who were pregnant or nursing and participants aged more than 70 years; those with other serious diseases like liver and thyroid disorders were not allowed to participate.

Sample size calculation:

Demographic Characteristics:

Patients with type 2 diabetes mellitus (T2DM) ranging in age from 30 to 70 were included in the current study; women = 82 (55.66) of the participants and men 68 (45.33). T2DM patients in the population of Khyber Pakhtunkhwa were39.12 ±12 years old for women and 50.6 ±14.3 years old for men. Patients taking metformin had an average age of onset of 49.74 ±10.32 years; those taking glimepiride had an average age of 45.38 ±7.16 years and those taking both drugs together had an average age of 42.16 ±7.68 years (P = < 0.001).

Table 1 provides a summary of the demographics of T2DM patients. Nine percent of the participants in this study were between the ages of 30 and 40; 45 percent were between the ages of 41 and 50; 33 percent were between the ages of 51 and 60; 16 percent were between the ages of 61 and 70; the

Sample size = 150 (10% as dropouts) with open epi software for cohort study incidence rates of 95% CI and with 0.5% margin error.

Sample Collection:

Patients were followed for a total of 12 months, with blood samples taken at enrollment (the baseline) and then every four months thereafter. The KP Diabetic Hospital and Research Center in Peshawar provided the samples.

Obtaining the history and diabetic complications:

A standardized questionnaire was used to gather information on age, gender, onset age, family history, cousin marriage, COVID-19, and complications.

Statistical analysis: All of the data was logged into an Excel spreadsheet. It was sent over to IBM SPSS Version 23 for processing. IBM SPSS version 23 was used to conduct the required analysis. Descriptive statistics were used to report the dependent and independent variables (frequency and percentage). Frequency tables were used for categorical data, while mean and standard deviation (SD) were calculated for continuous data. Descriptive statistics were used to look into demographic and positive family history facts; Pearson correlation was used to investigate the connection between a positive family history and cousin marriage; age; the onset age of the disease; a positive family history and COVID-19; and a cousin marriage and COVID-19.

III. RESULTS

majority of the subjects were aged between 41 and 50, 68(45%). Forty eight subjects (32 percent) had a diabetes-positive family history, while 102 subjects (68 percent) did not (68 percent) of the participants, 141 (or 94 percent) were married couples, 4 (3 percent) were singles, 2 (or 1 percent) were divorced and 3 (or 2 percent) were widowed of the total sample, 44.6% were illiterate, 12 with primary education, 13% had some intermediate college education, 27.3% had some graduate education, and 2 % had some graduate school or higher education.

42 (28 percent) were unemployed, 90 (60 percent) were manual laborers, 11 (7.3 percent) were employed by the government and 7 (4.7 percent) were directly involved in the business. In terms of monthly income, the subjects had a socioeconomic status of 15000, with 13 (8.66 percent) in the range of 15000-40000. Of the

total, 53 (35.33 percent) were under 40,000, 54 (36 percent) were between 40,000 and 70,000, and 30 (20 percent) were 80,000 or more. Medication, dietary changes, and physical therapy were all used to help the patients. The full complement of 150 subjects all taking their prescribed medications, and 95.33 percent of the subjects were eating properly. There were (66percent) subjects who were getting enough exercise and 5 (3.33 %) who weren't eating well. In our population, 22 (14.7%) participants having consanguinity and 8 (5.3%) participants having been diagnosed with COVID-19 involved in the study. All 8 (or 5.5%) had recently been diagnosed with type 2 diabetes.

Subjects with a positive family history of diabetes were 48 (32 percent) and those with a negative family history were 102 (68 percent) (Table 2).

Those with a positive family history of diabetes and their age were subjected to a bi-variate, 2-tailed Pearson correlation test, the results of which were statistically significant (P = 0.041) in our sample. Our population's results from a Pearson co-relation bi-variate 2-tailed test on those with a positive family history of diabetes and age of onset were inconclusive (P = 0.075). When participants with a positive family history of diabetes and cousin marriage were subjected to a Pearson co-correlation bi-variate, a 2-tailed test, significant results (P = 0.002) were found. Significant results (P = 0.036) were found in our sample when participants with a positive family history of diabetes and COVID-19 were subjected to a Pearson Co-Relation bivariate, 2-tailed test. Results from a Pearson Co-Relation bivariate 2-tailed test for the association between COVID-19 and cousin marriage in the study population were not statistically significant (P = 0.069).

Diagnosed

In the present study, 8 (5.3%) of the participants were diagnosed with COVID-19, which showed that diabetes is a risk factor for COVID-19 in our population (Table 5).

IV. DISCUSSION:

With a diabetes prevalence of 10%, Pakistan is the sixth highest in the world among developing nations (Rahim et al., 2014). Low-income nations, like Pakistan (which has the fourth highest rate of diabetes in the world), are particularly vulnerable (Aslam et al., 2022).Pakistan is ranked third in the world for diabetes (Azeem et al., 2022). According to (Aslam et al., 2022) Khyber Pakhtunkhwa is one of Pakistan's less developed provinces, falling short of the national average on a number of economic and social indicators. In Pakistan, 7 million people are diabetic, according to data from the International Diabetes Federation (IDF) in 2015. Type 2 diabetes has an average prevalence of 11.77% in Pakistan. The prevalence rates are 11.60% in men and 9.20% in women. Khyber Pakhtunkhwa (KPK) Province: Khyber Pakhtunkhwa (KPK) Province was formerly known as the North West Frontier Province (NWFP). The rate of incidence of type 2 diabetes mellitus in the province of Khyber Pakhtunkhwa was calculated (Javed et al., 2019).There were 1035 adults (over the age of 25) enlisted. Most people in Khyber Pakhtunkhwa are economically poor, and because of a lack of education, they are not aware that type 2 diabetes is a long-term condition. The rising cost of caring for people with type 2 diabetes is aggravated by a health care system that is struggling to keep up with the epidemic. Many people don't realize that the medications they're taking for their health, particularly those used to treat diabetes, need to be taken exactly as prescribed. Disease risk factors include poor diet, lack of exercise, and genetic predisposition. Prevention and control of diabetes should be a top public health priority in Asia (Chan et al., 2009a), as the disease's prevalence has risen rapidly in recent years and is projected to rise by as much as 15% in South Indians (Unnikrishnan et al., 2007).Patients with type 2 diabetes (n = 150; 82 females and 68 males) between the ages of 30 and 70 years old participated in the current study. Type 2 diabetes diagnosis ages in Khyber Pakhtunkhwa were calculated to be 39 ±12 years for women and 50.6 ±14.3 years for men.

Out of the total number of participants, 68 (45%) were between the ages of 41 and 50, 33% were between the ages of 51 and 60, and 16% were between the ages of 61 and 70 (14 participants, or 9%, fell into this age range). The current study found that the prevalence of diabetes in the Khyber Pakhtunkhwa population was highest (63, 42%) in the middle-aged (41–60 years) age group and lowest (14, 9%) in the younger (30–40 years) age group. Participants' age and the presence of a positive family history of diabetes were tested using a bi-variate, 2-tailed Pearson correlation test, whose outcomes are statistically significant (P = 0.041) in our sample. The incidence of type 2 diabetes was studied in those between the ages of 51 and 60 (Aamir et al., 2019). (Sivaprasad et al., 2016) have also recorded a high prevalence of diabetes in the middle-aged (41–60) population. The most productive and active years of life (ages 45–64) were also reported to be the most affected by diabetes (Mohan et al., 2004). In this study, we find evidence that supports their conclusions. Forty-eight participants (32 percent) in the current study had a positive family history of diabetes, while 102 participants had no such history (68 percent).

Diabetic patients with consanguineous parents were more likely to have a positive family history of diabetes (77.4 %), with a particularly high prevalence of maternal history (45 percent). Non-consanguineous patients had a lower incidence (70.4 percent). Diabetes mellitus is on the rise among consanguineous couples, according to a recent study conducted in Qatar by Bener et al., (2013) (Bener et al., 2013). Forty-eight participants (32%) in the current study had a positive family history, and twenty-two (14.7%) were consanguineous. which yielded statistically significant outcomes (P = 0.002) in the sample we analyzed. According to the available data, consanguinity has been shown to increase the likelihood of a patient having a diabetic relative which yielded statistically significant outcomes (P = 0.002) in the sample we analyzed. According to the available data, consanguinity has been shown to increase the likelihood of a patient having a diabetic relative. Thus, having a parent or sibling who has diabetes mellitus is a strong indicator of the likelihood that a child will develop the disease. It was reported by Chee et al. that two patients who were already being treated for COVID-19 had a new diagnosis of diabetes. A 37-year-old man with a clean medical history presented with diabetic ketoacidosis (DKA) after being diagnosed with diabetes and the COVID-19 infection. He may have had preexisting DM that was exacerbated by COVID-19, as his HbA1C was 14.2 percent (Chee et al., 2020; Heaney et al., 2020) reported three cases of newly diagnosed diabetes that were reported to be associated with COVID-19. The HbA1C result for this patient was not available, but he could have had undiagnosed diabetes (Suwanwongse and Shabarek, 2021) reported three cases of newly diagnosed diabetes linked to COVID-19. The first case had COVID-19 and DKA simultaneously, while the second and third cases had DM after COVID-19 illnesses. Although the causal relationship between COVID-19 and diabetes cannot be established, it raises the question of whether COVID-19 can trigger the development of new-onset diabetes. In the present study, 8 (5.3%) participants had been diagnosed with COVID-19, and 22 (14.7%) participants had consanguinity involved in the study, which shows significant results (P = 0.036) in our population. All 8 (or 5.5%) had recently been diagnosed with type 2 diabetes, and their HbA1c levels ranged from 7.2, 8.4, and 9.1, 10. 10.5, 10.8, 11.2 and 12.5 percent. These eight patients included two females, ages 38 and 40, with HbA1c levels of 8.4 and 11.2 percent, respectively, and six males, ages 42, 45, 48, 50, 52, and 54, with HbA1c levels of 9.1, 10.5, 7.2, 10, 12.5, and 10.8 percent, respectively, who were treated with metformin, glimepiride, and their combination therapy, and then were followed by COVID-19. Similar results were found by us and by Suwanwongse and Shabarek (2021).

It appears that the high prevalence of first-cousin marriages in rural Punjab is to blame for the shockingly young age at which type 2 diabetes is developing there (Alvi, 1999). Indicators for screening people at risk of developing type 2 diabetes include the presence of a positive family history of the disease (Harrison et al., 2003, Lyssenko et al., 2005). One hundred forty-one (94%) of the participants were married, while only 4% were single. The divorce rate was 1%, and the widow/widower rate was 2%. Majority of people in the current study population were found to be overweight (BMI > 25) and were diagnosed with diabetes at a young age, indicating a higher risk of developing diabetes in Khyber Pakhtunkhwa (35 years). The diagnosis of T2DM in the Khyber Pakhtunkhwa population was typically made at a young age (39.12 ±12 years for women and 50.6 ±14.35 years for men) (35 years). Depending on factors such as culture, ethnicity, and urbanization, the onset of diabetes in Asia has been reported to occur at a relatively young age (Chan et al., 2009b). There are no statistically significant associations between T2DM diabetes and any of the studied risk factors in this investigation. The urban Indian population was found to be more predisposed to developing diabetes due to the role that lifestyle and environment play in the disease's onset (Shah and Afzal, 2013).

The current study found that the majority of participants were unaware of the risks associated with diabetes and its complications because the illiteracy rate was higher than the literacy rate. In addition, (Tang et al., 2008)) noted that his subjects' lack of education and knowledge contributed to the difficulties they encountered. Increasing Pakistan's literacy rate will help people better manage their diabetes and prevent complications from the disease. Unemployment is a major contributor to the difficulty of managing diabetes in Pakistan, after the disease itself. Thirteen participants (8.6 percent) had a monthly income of $15,000, and thirty participants (20 percent) had an income of $80,000 or more. Disease costs were highest for patients with incomes between 10,000 and 20,000 PKR, compared to those with lower and higher incomes.

Treatment and management costs vary by population due to differences in disease management, awareness, treatment (insulin or oral medication), complications, and the healthcare system (Soewondo et al., 2013),The estimated annual cost of managing diabetes ranges from $13 in Bangladesh to $11,157 in the United States, as documented by (Hirschl, 2020).When compared to the white population in the United States, the median annual direct medical cost for an African-American man with T2D was 82% higher (1,380 USD). The average monthly income of the participants in the current study was $33.33 percent, which was significantly lower than the subjects' treatment expenses. Inflation may make it possible to forgo routine treatment after a certain amount of time has passed. Currently, only the top 20%, or 30 people, who make $80,000 or more per month can afford to keep receiving adequate treatment. Due to differences in lifestyle, diabetes duration, and complications, the costs of disease care and management varied among patients. Patients with higher incomes and levels of education spent noticeably more on disease management than those with lower levels of both. Overall, it is cost-effective to manage T2D in the population over 45 and screen at younger ages in the United States (Group and JAMA, 1998). In line with our findings, (Khan and Khalid, 2016) reported that 42.3% of diabetes patients in Pakistan were illiterate and that many people in the country were poor. Those with less education and fewer resources in Italy have a higher risk of developing diabetes, making our research all the more important (Kankeu et al., 2013).To the tune of 70%, Pakistan, India, Vietnam, and Cambodia's low- and middle-income residents lose their lives to diabetes each year (Danaei et al., 2014).

There were 48 participants with a positive family history of diabetes (32%), and 102 participants without such a history (68 percent).There is a high prevalence of type 2 diabetes in families in Pakistan (Aamir et al., 2019).T2DM has been found to have a very strong association with a positive family history in the Punjab Province of Pakistan (Shera et al., 2010). Our findings are consistent with those of (Ahmedani et al., 2005), who found that 45% of Karachi, Pakistan, residents had a positive family history of T2DM. One in 123 Europeans and one in 192 Africans have type 2 diabetes. In 32.6% of those of European ancestry, at least one first-degree relative was affected, compared to 53.1% of those of African ancestry. Researchers (Al-Sharafi et al., 2021) found that among 612 people (32 percent male and 68 percent female) aged 30-70, 429 (70.1 percent) had a family history (FM) of DM due to consanguinity of parents, while 183 (29.9 percent) did not have a FM of diabetes. Individuals with class III obesity and those with a first-degree relative who has diabetes both have significantly increased risks of developing pre-diabetes and type 2 diabetes. The results we obtained are identical to those of (Al-Sharafi et al., 2021). Patients with a positive family history of diabetes were diagnosed with the disease at a BMI lower than normal (25) (Zuo et al., 2009).First-cousin marriages are very common in rural areas of Punjab and appear to be the cause of the early onset of T2D with a BMI of 25 in the rural population with a positive family history of diabetes. Indicators for screening people at risk of developing type 2 diabetes include the presence of a positive family history of the disease. The prevalence of diabetes-related complications increased in this analysis. Six people had nephropathy (4%), 24 had retinopathy (16%), 41 had neuropathy (27.3%), and 79 had cardiovascular disease (79.2%). (52.7 percent). Diabetes-related complications, such as retinopathy and nephropathy, were more prevalent in the rural population (37.5%) than in the urban population (11.8%) (Russell, 2013). More than 52.7% of the patients in this study had cardiovascular disease, and similarly, most of them came from rural areas of Khyber Pakhtunkhwa.

V. CONCLUSION

The study shows that participants who had a positive family history of T2DM were more susceptible to the early onset of the disease. Participants in our study had newly diagnosed diabetes, which was followed by COVID-19. Diabetes is also a risk factor for COVID-19 and cardiovascular problems. In the present study, more than 50% of patients were at risk for cardiovascular disease. A positive family history of diabetes is a major risk factor for type 2 diabetes and cardiovascular disease (CVD). Health education about increased physical activity, foot care, and a low-calorie diet can be advised to delay type 2 diabetes and cardiovascular problems in our population.

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Table 1: Demographic distribution of T2DM

Variables	No.	Percentage%
Age:		
30-40	14	09.0
41-50	68	45.0
51-60	49	33.0
61-70	24	16.0
Gender:		
Male	68	45.33
Female	82	54.66
Marital status:		
Married	141	94.0
Un-married	04	2.66
Divorced	02	1.33
Widowed	03	02.0
Education:		
Illiterate	67	44.6
Primary	18	12.0
Inter mediate	20	13.0
Graduate	41	27.3
Above graduation	03	02.0
Employment status:		
Un-employed	42	28.0
Labour	90	60.0
Government Job	11	07.3
Business	07	04.7
Socio-economic status:		
Up to 15000	13	08.66
15000-40,000	53	35.33
40,000-70,000	54	36.0
80,000 and above	30	20.0
Mode of treatment:		
Diet	143	95.3
Medication	150	100.0
Exercise	99	66
Cousin marriage:	22	14.7
COVID-19:	08	05.3

Table 2: Frequency and percentage of positive family history and complications of T2DM patients.

Family History of Diabetes Mellitus and complications		
	No	Percentage (%)
Positive family history	48	32 %
Negative family history	102	68 %
Complications present	128	85.3%
Complications absent	22	14.7%

Table 3: Percentage of complication of T2DM at Baseline (0 day), follow up-1 (4 months), follow up-2 (8 months) and follow up-3 (12-months).

	Baseline (0 day)	Followup-1 (4-months)	Followup-2 (8-months)	Followup-3 (12-months)
Nephropathy	2	2	2	4
Retinopathy	9	11	13	16
Cardiovascular	38	41	44	52.7
Neuropathy	18	21	23	27.3

Table 4: Pearson Co-Relation for age and Positive family history of diabetes.

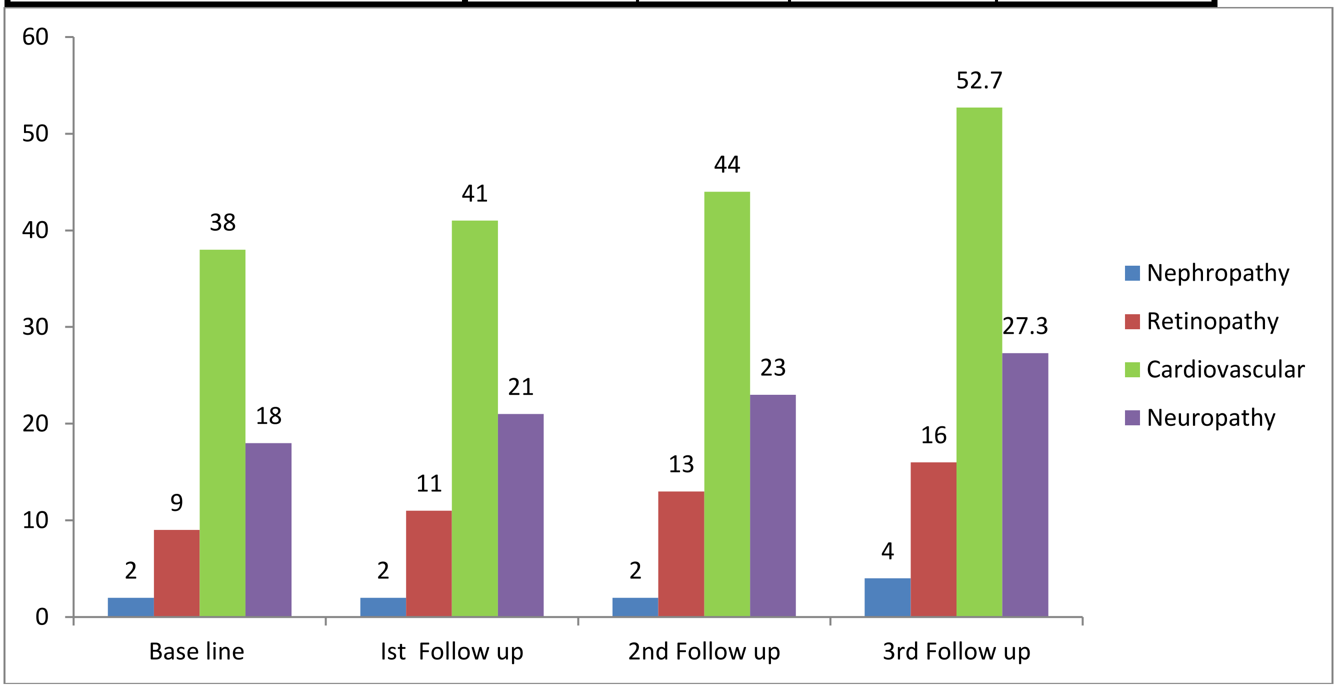
Correlation

		History	Age
History	Pearson Correlation	1	0.041
	Sig. (2-tailed)		.622
	N	150	150
Age	Pearson Correlation	.041	1
	Sig. (2-tailed)	.622	
	N	150	150
		History	Onset age
History	Pearson Correlation	1	.075
	Sig. (2-tailed)		.364
	N	150	150
onset age	Pearson Correlation	.075	1
	Sig. (2-tailed)	.364	
	N	150	150
		History	cousin marriage
History	Pearson Correlation	1	0.002
	Sig. (2-tailed)		0.984
	N	150	150
cousin marriage	Pearson Correlation	0.002	1.0
	Sig. (2-tailed)	0.984	*
	N	150	150
		Diagnosed COVID-19	History
Diagnosed	Pearson Correlation	1	0.036
	Sig. (2-tailed)		0.665
	N	150	150
History	Pearson Correlation	0.036	1.0
	Sig. (2-tailed)	0.665	*
	N	150	150
		Diagnosed	**cousin marriage**
Diagnosed	Pearson Correlation	1	0.069
	Sig. (2-tailed)		0.399
	N	150	150
cousin marriage	Pearson Correlation	0.069	1.0
	Sig. (2-tailed)	0.399	*
	N	150	150

Table 5: Diabetes as a risk factor for COVID-19.

Diagnosed

	Frequency	Percent	Valid Percent	Cumulative Percent
Diagnosed with Covid19	8	5.3	5.3	5.3
Undiagnosed	142	94.7	94.7	100.0
Total	150	100.0	100.0	*



Graph 1: Complication of T2DM at base line (0 day), follow up-1 (4 months), follow up-2 (8 months) and follow up-3 (12-months).