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ASSESSMENT OF UREA AND CREATININE LEVELS IN TYPE 2 DIABETIC PATIENTS AT INSTITUTE OF KIDNEY DISEASES PESHAWAR, PAKISTAN

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Abstract

The Type 2 Diabetes Mellitus (T2DM) is a widespread disease that is generally linked to kidney-related diseases. This paper focused on evaluating the blood sugar levels and renal function indicators- urea and creatinine in persons having T2DM.The cross-sectional study was done in a period of six months (February 1 to July 30) at Chemical Pathology Department of Institute of Kidney Diseases (IKD) Peshawar, Hayatabad. A group of T2DM patients aged 40 to 60 years was included into the study in non-random convenience technique with 150 blood samples being taken. The Cobas c311 Chemistry Analyzer was used to analyze blood samples in terms of serum glucose, creatinine, and urea. Manual interpretation of data in SPSS version 22 was done. Sixty percent of 150 participants had a serum glucose level ranging between 150 to 300 mg/dL, 30.7 percent had levels between 300 to 450 mg/dL and 9.3 percent had levels above 450 mg/dL. Sixty-six-point seven percent of the sample were male, and 33.3 percent were female. The age range of most of the respondents (60.7%) was 50-60 age category. Concerning kidney functions, 56.7 percent had normal levels of urea (0-40 mg/dL) and 43.3 percent were elevated to different levels. Equally, 63.3 percent had normal values of creatinine (0.6-1.3 mg/dL) and 36.7 percent had an abnormal level which may indicate renal impairment in a large proportion of patients. The results reveal a large percentage of patients with T2DM experiencing poor glycemic control with the resultant renal dysfunction especially in males among the aged. Such findings explain why it is important to observe renal function within a patient with diabetes on a regular basis to avoid such complications as diabetic nephropathy. Key words: Creatinine, Urea, Type 2

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Diabetes,

INTRODUCTION

Diabetes Mellitus

Diabetes mellitus is a condition in which hyperglycemia is characterized by decrease or insufficient production of insulin. The pancreas is the organ which are responsible for insulin production any abnormality in the Beta cells of pancreas can lead to decrease insulin production. The persistence high level of glucose in blood can affect different body organs including Kidneys, Retina, Heart, Blood vessels and Nervous system. So therefore we called Diabetes mellitus a heterogeneous group of disorder.(Suryasa*et al.*, 2021).Diabetes mellitus can cause different diseases like Diabetic Nephropathy, Diabetic Retinopathy, Diabetic Neuropathy and Heart stroke. But the most common Diabetic Nephropathy which lead to cause chronic kidney diseases (CKD) (Sun *et al.*, 2021)The common symptoms in Diabetes mellitus is excessive thirst, urination, hunger, weight loss and blurred vision. In some patients with Diabetes hyperglycemic condition can be control with weight loss, excessive exercise, or oral glucose lowering agents. The patients who can do this so they do not required insulin. Some common drugs are used to decrease concentration of glucose in the blood to reduce risks of diseases associated with Diabetes mellitus. There is no permanent treatment of Diabetes mellitus but insulin therapy is used to treat Diabetes mellitus. It is a life long term disease (Pandey *et al.*, 2020).

Types of Diabetes Mellitus

There are three main types of Diabetic Mellitus.

Type 1 Diabetes

Type 1 Diabetes is an autoimmune disorder in which the immune B cells produce antibodies against Beta cells of pancreas and destroy Beta cells completely and progressively leads to insulin deficiency and resultant hyperglycemia. If type 1 Diabetes is untreated insulin deficiency progressive metabolic derangement with hyperglycemia, ketoacidosis, starvation and death. It is also known as Insulin Dependent Diabetes ((Powers *et al.*, 2021).

In healthy person pancreas beta cells is responsible to produce insulin hormone which Basically convert glucose into glycogen but in type 1 Diabetes the pancreatic beta cells is completely destroy which do not produce insulin so therefor we called it Insulin Dependent Diabetes (Alam *et al.*, 2021).

There are some other pathogenic factors of T1DM have include genetic and environmental factors which have effect on Type 1 Diabetes mellitus. The type 1 diabetes is caused due to the genetic predisposition of HLA. the HLA are located on chromosome 6p21 which are responsible for the formation of protein that presents antigens to Cytotoxic T cells which involve in immune response. HLA genes include HLA-DR, HLA-DQ and HLA-DP when defect in these genes cause Type 1 Diabetes Insulin VNTR is an insulin Gene located on chromosome 11p15. Insulin VNTR are classified in three classes on the basis of number repeats Class 1 (26 -63 repeats) Class 2 (intermediate) and Class 3 (140 -210 repeats). the Insulin VNTR genes is polymorphic DNA region it plays important role in gene expression in thymus and pancreas .it regulate how much Insulin mRNA is transcribed and also controls expression of insulin levels in thymus and pancreatic beta cells. When there is defect in insulin VNTR genes cause Type 1 Diabetes. Environmental factors include Viral infections such as Enterovirus Coxsackievirus B which have strong linked with Type 1 Diabetes. Family History of type 1 Diabetic patients have high risks of this condition in sibling and identical twins (.Paschou *et al.*, 2018).

Type 2 Diabetes mellitus

Type 2 Diabetes Mellitus is one of the major leading disorders worldwide and its leading tendency is caused by a combination of two main factors so first is impaired secretion of insulin from Beta cells of pancreas and second when body show resistance response to insulin so therefor hyperglycemic condition is developed.

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Insulin is release but properly glucose metabolism is not occurred because insulin play important role to maintain glucose levels in blood (Galicia-Garcia *et al.,* 2020).

The ratio of type 2 diabetic patient is up to 90%. Overtime type 2 Diabetes can cause serious complication such as cardiovascular diseases, diabetic nephropathy, Retinopathy and Neuropathy. Type 2 Diabetes is due to overweight, Obesity, lack of exercise, family history, Genetics, Aging, Beta cells dysfunction, medication, hormonal Disorders and insulin resistance(Ruze *et al.,* 2023)**.**

Gestational Diabetes Mellitus

The name Gestational Diabetes mellitus is given due to hyperglycemic condition during pregnancy. Gestational Diabetes Mellitus mostly occurs in pregnant females which impacts on million women health worldwide**.**(Ye *et al.,* 2022)**.**The first case of gestational diabetes mellitus was appeared in pregnant women in 1824 according to German researcher and lambie reported the first diabetes signs in fifth or sixth month of pregnancy in 1926. (Bogdanet *et al.,* 2020)Some complication of Gestational Diabetes mellitus has included Cardiovascular Disease, Obesity and impaired carbohydrate metabolism which leading to cause Gestational Diabetes Mellitus. (Li *et al.,* 2020).

Causes of Diabetes Mellitus

The main causes of type 1 Diabetes have included Autoimmune Reaction, predisposition of HLA, Abnormality in insulin VNTR genes, Family history, environmental Factors have included viruses (Paschou *et al.,* 2018).Type 2 Diabetes Mellitus causes have included overweight, Obesity, lack of exercise, family history, Genetics, Aging, Beta cells dysfunction, medication, hormonal Disorders and insulin resistance (Ruze *et al.,* 2023)**.**Gestational Diabetes Mellitus have included Increase insulin Resistance, Imbalance of pregnancy Hormones, Obesity, Family history, Previous Gestational Diabetes mellitus and hypertension (Modzelewski *et al.,* 2022)

Risks Factors for Diabetes Mellitus

Risks Factors for Diabetes Mellitus have included Genetics Disorder, lack of physical exercise, Smoking, uses of Alcoholic Beverages, Dyslipidemia, reduce Beta cells Sensitivity, Hyperinsulinemia**,**(Arya P*et al.,* 2023)Type 1 diabetes mellitus risks factors have included autoimmune reaction, Family History, predisposition of HLA, Genetic Defects and Environmental Factors (Paschou *et al.,* 2018)**.**IN Type 2 Diabetes mellitus 90% cases is occur due to excessive Body weight. increase intake of high amount of glycemic ingredients have a risk for diabetes mellitus. Soft drinks contain high ratio of fructose which cause Obesity and increase BMI which leads to developed Type 2 Diabetes Mellitus, sedentary life, smoking, insulin resistance, ethnicity and genetics. Gestational Diabetes mellitus have included several risks factors which are Obesity, maternal over ages, polycystic ovary syndrome, hormonal disorder, previous history of GDM and high blood pressure related with pregnancy (Arya P *et al.,* 2023).

Prevalence of Diabetes Mellitus

According to international Diabetes federation in 2024 prevalence was about 589 million adults were lived with diabetes mellitus worldwide. The IDF also estimated that number of adults with diabetes is projected to reach 853 million in 2050 According to IDF 9 to 10% cases is type 1 Diabetes while 90% cases is type 2 Diabetes Mellitus (Risk & Collaboration*et al.,* 2024).

According to World Health Organization state that about 830 million people worldwide with Diabetes mellitus. WHO state that in 2017 about 9 million people have Type 1 Diabetes. WHO estimates that number may increase up to 13.5 to 17.4 million in 2024. WHO say that 14% adult having aged 18 or above were living with type 2 Diabetes in 2022. American Diabetes Association and Centers for Disease and Control and Prevention reported that the prevalence of Diabetes in American population was 38.4 million or 11.6% in 2021. 2 million Americans living with type 1 Diabetes in which 304,000 are children and Adolescents and current estimation

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of type 2 Diabetes is 8.5% in adults. According to international Diabetes Federation the current prevalence of Diabetes Mellitus in Adult is 31.4% in Pakistan. IDF reported the rate of type 1 Diabetes is 0.5% in 100,000 in 2019. In 2021 the estimated ratio was 26.7% of Diabetes. Recent study show that Pakistan has the highest ratio of type 2 diabetes mellitus compare to type 1 Diabetes. On the basis of regions Punjab have 16%, Baluchistan 15%, Sindh 14%, KPK 11% type 2 Diabetes prevalence in Pakistan(Diabetes Rates by Country*et al.,2025*).

Urea

The ammonia production takes place due to break down of amino acid or any gut bacteria in Human. increase level of ammonia in blood cause toxicity to brain. The ammonia is removed from the blood through urea cycle which convert ammonia into urea. The hepatocytes of the liver is carried out by urea cycle. The urea formation is occurred through urea cycle in two stages one is Mitochondrial Stage and second is cytosolic stage. In Mitochondrial stage ammonia and Bicarbonate is convert into carbamoyl phosphate with help of carbamoyl phosphate synthetase enzyme. Carbamoyl phosphate and ornithine are condensing into citrulline by ornithine transcribe amylase enzyme. In cytosolic Stage citrulline and aspartate convert to Arginine succinate by arginine succinate synthetase enzyme. Arginine and Fumarate is Formed from arginine succinate through arginine succinate lyase. In the last Arginine is convert into urea by Arginase Enzyme. Urea is excreted from the body through urine. the urea or ammonia levels increase in the blood due to Renal disfunction (Hajaj et al., 2021).

Creatinine

Creatine and phosphocreatine richly found in the muscle of skeleton. The formation of creatine and phosphocreatine is mainly occurred in liver and kidneys from amino acids like arginine, glycine, and methionine. Creatine and phosphocreatine are converted into creatinine compound by creatine Phosphokinase and energy is produced. Kidney plays important role to remove waste product from blood. So, creatinine is filter from blood plasma through glomerular filtration (Akpotaire & Seriki *et al.,* 2023).

In Different condition the value of creatinine is increases which have include Atrophy of skeletal muscle, congestive heart failure, urinary tract infections (UTIs)and kidney diseases. So, creatinine is used for renal biomarker. The normal range of creatinine is 0.7–1.4 mg/dL. In Men usually have higher serum creatinine than women because of greater muscle mass (Ullah *et al.,* 2023).

Effect of RFTS in Type 2 Diabetes Mellitus

There are different types of Diabetes Mellitus but type 2 Diabetes Mellitus is more prominent as compared type 1 Diabetes Mellitus. Diabetes Mellitus Causes Different Condition such as Diabetic Retinopathy, Diabetic Nephropathy, Cardiovascular Disease and Diabetic Neuropathy. So therefore type 2 Diabetes have highly affected kidney and cause a condition known as Diabetic Nephropathy. Diabetic nephropathy result to cause of chronic kidney disease (CKD) and end-stage renal disease (ESRD) worldwide. In this condition protein leaking into the urine cause (proteinuria or albuminuria) and result increasing blood pressure with hypertension. loss of protein in the urine damage of the glomeruli of nephron, and decrease serum albumin which cause so called nephrotic syndrome. On the other end estimated glomerular filtration rate (eGFR) may progressively reduce from a normal range at this point we called it end-stage renal disease(Thipsawat et al., 2021).In Diabetes mellitus patients the urea and creatinine levels increase due to poor treatment of hypertension and result cause Diabetic Nephropathy (Akpotaire & Seriki *et al.,* 2023).

METHODOLOGY

Study Design

The current study was descriptive cross-sectional study.

Study Place

The current study was conducted within the pathology department of Institute of Kidney

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Diseases (IKD) located in Peshawar Hayatabad.

Study Duration

The current study was completed with in duration of 6 months from 1st Feb to 30 July.

Sample Size

Total 150 blood sample were collected from Type II Diabetics patients by using statistical Cochran's formula:

$$n = Z^2 p. (1-P) / e^2$$

Sampling Technique

Non-Probability convenient sampling technique was used to take the sample from the research subject.

Sample Selection Criteria

Inclusion Criteria

Both male and female only Type II diabetics patients whose age was between 40 to 60 years ages were included in the current study.

Exclusion Criteria

Patients with chronic kidney diseases or other kidney disease patients were excluded.

Patients who were unwilling to give sample were excluded from the current study

Sample Collection and processing

Proper inform consent was taken from Type 2 Diabetic Mellitus patients to give us venous blood. Venous blood was taken by using 5ml of sterile disposable syringe and collected in yellow and gray top tube. Sample send to chemical pathology section for further processing first of all yellow top tube blood was centrifuge in centrifuge machine and glucose, creatinine and urea test was run on Cobas c 311 Chemistry analyzer.

Statistical Analysis

All the statistical analysis of the current study was performed by using SPSS version 22.

RESULTS

1. Sugar levels among Type 2 Diabetes Mellitus

The tableno 4.1 present the distribution of blood sugar levels among a group of 150 individuals. The majority of participants, 90 individuals have 60.0%, had blood sugar levels ranging from 150 to 300 mg/dL have shown in the table. This indicates that most individuals in the sample had moderately elevated glucose levels, which may suggest poor glycemic control but not extreme hyperglycemia. A smaller portion of the group, 46 individuals have 30.7%, exhibited higher sugar levels within the 300 to 450 mg/dL range, that shown in the table reflecting a more severe level of hyperglycemia that could pose significant health risks if not managed appropriately. The remaining 14 individuals, accounting for 9.3% of the sample, had blood sugar levels above 450 mg/dL that shown in the table.

Table No 4.1 shows Serum Sugar Level of Type II Diabetics Individuals

Sugar Level	Frequency	Percent
150-300 mg/dL	90	60 %
300-450 mg/dL	46	30.7
above 450 mg/dL	14	9.3
	150	100.0

2. Gender wise distribution of Type 2 Diabetes

The figure no 4.2 shown the gender distribution of participants with type 2 diabetes mellitus shows that out of 150 individuals, (66.7%) were100 male shown in Blue Bar chart and (33.3%) were 50 females shown in Red Bar chart. This indicates that type 2 diabetes was more

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prevalent among males in this sample, suggesting a possible gender-related difference in risk factors, lifestyle, or health-seeking behaviors associated with the condition.

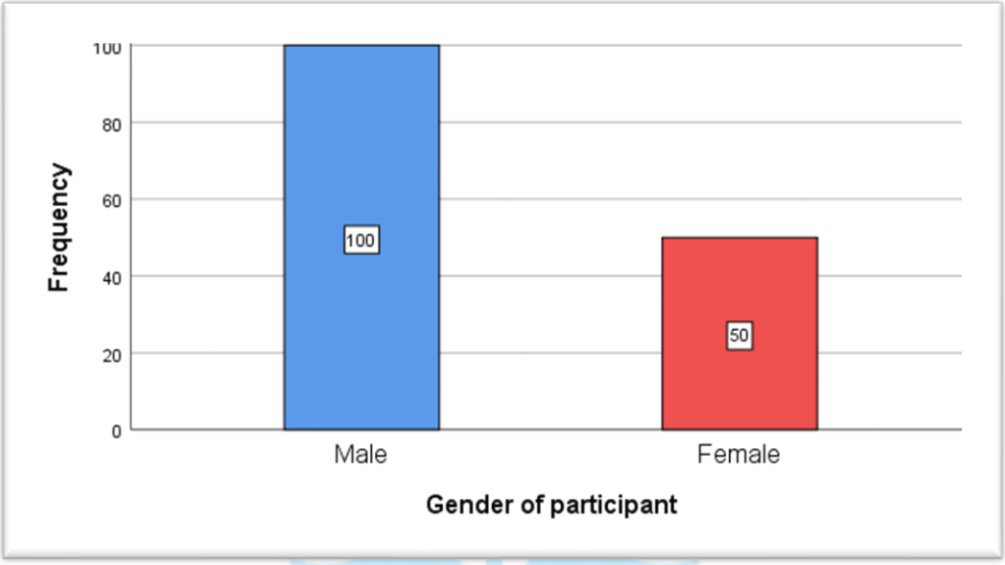

Fig. no 4.2gender wise distribution of Type 2 Diabetes

3. Age wise Distribution of Type 2 Diabetes

The tableno 4.3 shown the age wise distribution of participants with type 2 diabetes mellitus reveals that the majority, 91 individuals have (60.7%), were between 50–60 years old, shown in the table while 59 individuals have (39.3%) were between 40–50 years old shown in the table. This suggests that type 2 diabetes is more common in the older age group within the sample, highlighting increased risk with advancing age.

Table no 4.3 shown age wise Distribution of Type 2 Diabetes

Age of Participant (in Years)		
Age of Participant	**Frequency**	**Percent**
40-50	59	39.3
50-60	91	60.7
Total	150	100.0

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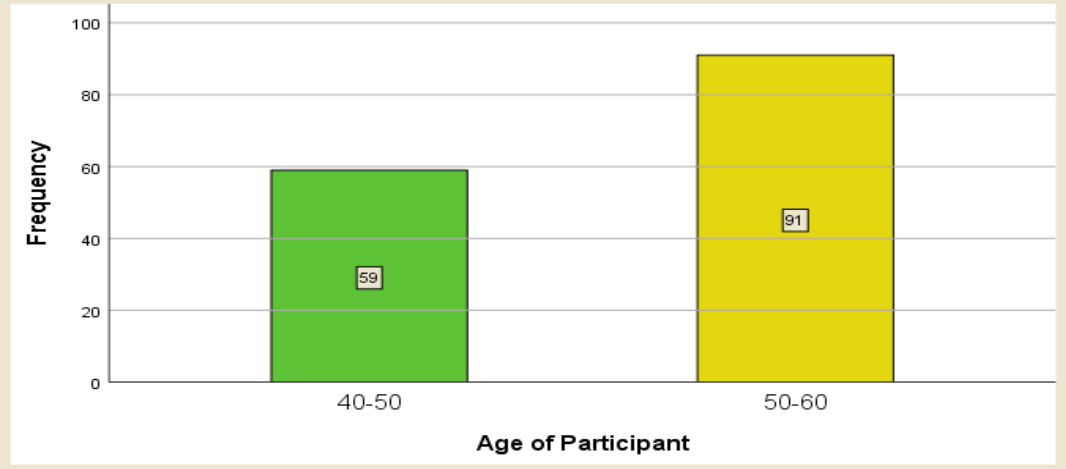

4. Urea Levels Distribution among Type 2 Diabetes

TheFigure no 4.4 shown urea level distribution among type 2 diabetes mellitus patients shows that the majority, 85 individuals have (56.7%), had urea levels within the normal range of 0–40 mg/dL shown in the Red Bar chart. However, 39 participants have (26.0%) had moderately elevated levels (40–140 mg/dL) shown in Green Bar chart, while 18 individuals have (12. %) had significantly high levels (140–280 mg/dL) shown in yellow Bar chart. A smaller group of 8 participants have (5.3%) critically high urea levels above 280 mg/dL shown in Blue Bar chart. These findings suggest that while over half of the patients maintained normal kidney function, a considerable proportion showed signs of renal impairment, which is a common complication of poorly controlled diabetes.

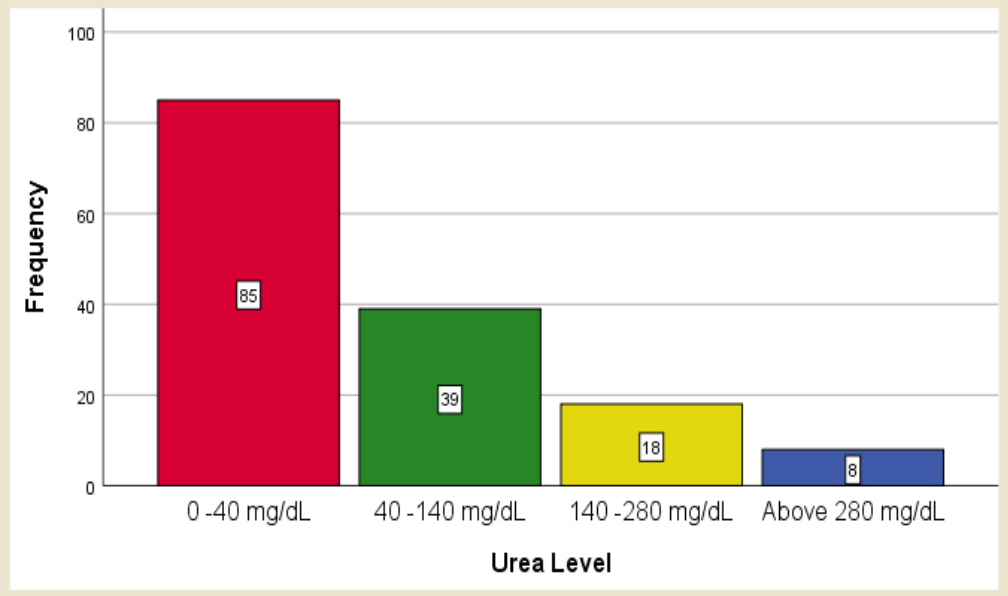

Fig no 4.4 Urea levels among Type 2 Diabetes

5. Creatinine levels Distribution among Type 2 Diabetes

The Figure 4.5 shown the distribution of creatinine levels among type 2 diabetes mellitus patients indicates that the majority, 95 individuals have (63.3%), which have normal levels ranging from 0.6 to 1.3 mg/dL shown in Green Bar chart. However, 11 participants have

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(7.3%) which have mildly elevated levels (1.3–3.0 mg/dL) shown in yellow Bar chart, while 23 individuals have (15.3%) showed moderately high levels (3.0–7.0 mg/dL) shown in pink Bar chart. Notably, 21 patients have (14.0%) had critically elevated creatinine levels above 7.0 mg/dL shown in Red Bar chart. This data suggests that while most patients maintained normal kidney function, a significant portion experienced impaired renal function, highlighting the risk of diabetic nephropathy associated with type 2 diabetes.

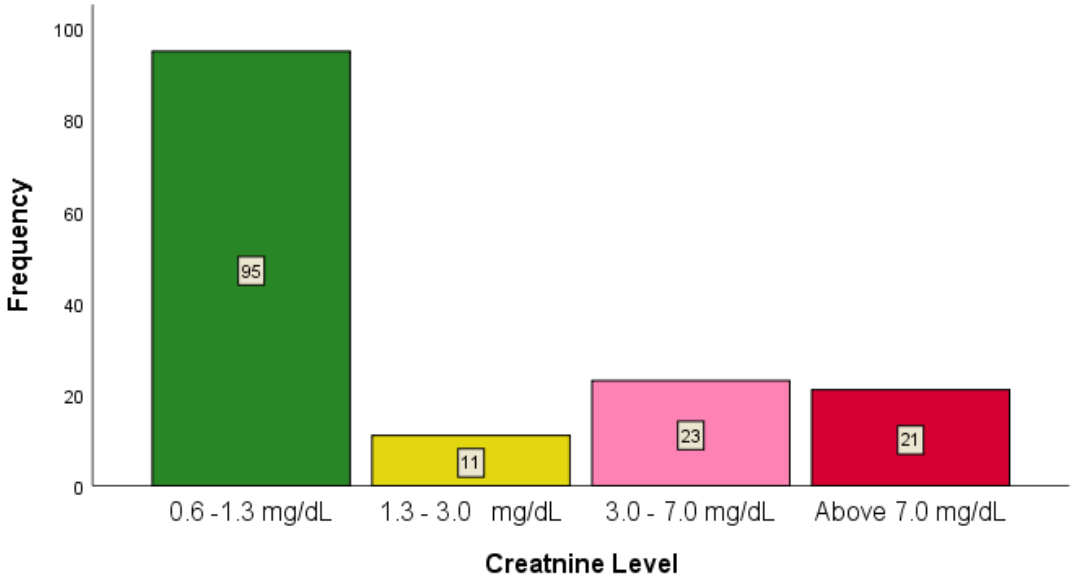

Fig. no 4.5 Creatinine levels among Type 2 Diabetes

DISCUSSION

This research assessed the serum glucose, urea and creatinine concentrations in the population with Type 2 Diabetes Mellitus (T2DM) to determine the trends of glycemic control and kidney status in a Pakistani community. As shown in the results, Hyperglycemia and different extents of renal dysfunction were as well found to be significantly prevalent especially among males and between the age range of (50 - 60) years. It is also consistent with the past research done in such South Asian populations, where there is a lack of access to healthcare, poor health literacy, and inappropriate glycemic control explain the lack of control of diabetes (Das & Dhar*et al.,* 2022). The main cause of microvascular and macrovascular complications, in particular, diabetic nephropathy is chronic hyperglycemia.

Gender distribution analysis of the study reflected that prevalence of diabetes was high among the males (66.7%) compared to the females (33.3%). Such gender difference is not surprising since regional studies that have already been conducted also confirm that T2DM is more frequently developed by males, owing to excessive accumulation of fat in the abdomen, sedentary behavior, and prevalence of smoking(Mohammadi Arvanag *et al.,* 2019). Also, social and community factors can either impact the health-seeking behavior whereby men tend to visit clinics and health screening programs more as compared to their female counterparts.

The age factor was also important since 60.7 percent of respondents were age (51-60 years). Age is a solid risk factor of T2DM because of changes that occur with age; that is, insulin resistance, impairment of beta-cells efficiency, and exposure to the hazards of lifestyle (Lohsiriwat*et al.,* 2022). These findings indicate the necessity of the diabetes screening and intervention approaches that are age-specific.

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Evaluation of the renal functions demonstrated that normal levels of urea were recorded in 56.7 percent of the patients; whereas, the value was above normal which revealed the compromised clearance rates of the functions in 43.3 percent patients. Similarly, 36.7 of the sample showed an elevation in the creatinine level, and 14 of this percentage showed a seriously high creatinine level of more than 7.0 mg/dL. These results indicate that diabetic nephropathy or other renal dysfunctions are observed in significant number of the research population. Thenephropathy in patients with diabetes is a severe complication of long-term uncontrolled diabetes and the most common cause of end stage renal disease (ESRD) globally(Arora *etal.,* 2024).The same trends have been documented in one of the studies by Afkarian et al., and elevated serum creatinine and urea reported to be significantly associated with poor glycemic control and the prevalence of diabetes (Bogdanet *et al.,* 2020). Diagnosis and subsequent intervention of kidney dysfunction at an early stage are therefore very essential to avoid development into ESRD. This necessitates the screening of serum creatinine and urea regularly in patients with diabetes, especially resource poor countries such as Pakistan. Elevated renal markers were also common in this study, which makes it agree on the findings of Ritz and Orth, who defined the significance of maintaining strict glycemic and blood pressure control to preserve renal functioning in patients with T2DM. Because of the large number of patients with aberrant renal parameters in our study, there is definite need of integrative management by endocrinologists, nephrologists, and primary care physicians.

To conclude, this paper highlights the relationship between renal dysfunction and suboptimal glycemic control in T2DM patients especially among older males. The proposed findings will help to highlight the significance of the early diagnosis of the disease, patient education, systematic control, monitoring of the level of blood glucose and renal functioning, and a multidisciplinary approach to diabetes treatment. The tracking of renal outcomes in diabetic populations in the long-term should be emphasized in the future studies as well as the changes introduced by those targeted interventions, including change in diet, medicine consumption and physical exercises.

CONCLUTION

The results reveal a large percentage of patients with T2DM experiencing poor glycemic control with the resultant renal dysfunction especially in males among the aged. Such findings explain why it is important to observe renal function within a patient with diabetes on a regular basis to avoid such complications as diabetic nephropathy.

RECOMMENDATION

The routine monitoring of blood urea and creatinine should be done on all T2DM patients.
Train patients into diet, medication and lifestyle to enhance blood sugar control.
Considering managing diabetes and preventing kidney damage, it is possible to use a team-based approach.

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