

Over 27% of Type II Diabetic Patients Studied at Parirenyatwa Diabetic Clinic in Zimbabwe Have Evidence of Impaired Renal Function

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Abstract: Diabetes mellitus is a chronic metabolic disorder characterized by hyperglycemia and is the most prevalent non communicable disease in the world. Progressive kidney damage is one of the major complications of diabetes mellitus and has significant mortality and morbidity. The aim of our study was to analyze renal function in Type II diabetics that have been on treatment for more than 12 months. Our laboratory based cross-sectional study was done on 239 patients who have been diagnosed as Type II diabetics for more than 12 months, who routinely attend the Parirenyatwa Diabetic Clinic. Serum sample were used for urea and creatinine analysis. Of the 239 patients studied, 65 (27.2 %) were found to have elevated values of creatinine and/or urea. Creatinine is usually elevated when the kidneys have lost about 50% of their function. Therefore, the prevalence of impaired renal function found in patients attending Parirenyatwa Diabetic clinic was approximately 27.2%. All patients with impaired renal function were hypertensive. Males had a greater percentage of elevated urea and creatinine levels compared to females. Age and period on treatment were found to be significantly associated with impairment of renal function.

Index Terms: Creatinine, Diabetics, Parirenyatwa, Renal Function, Type II Diabetes mellitus, Urea, Zimbabwe

1 INTRODUCTION

Diabetes mellitus has become a global health problem due to urbanization, increasing prevalence of obesity and physical inactivity [1]. Diabetes mellitus is characterized by chronic hyperglycemia, that is, high blood glucose due to derangement in carbohydrate, fat, and protein metabolism. Diabetes mellitus is associated with absolute or relative deficiencies in insulin secretion, insulin action or both [2], [3]. When levels of glucose fall to a normal range, production of insulin is stopped until the level of glucose is high again. When the body fails to lower blood glucose on its own, Diabetes mellitus, a chronic health condition develops. Diabetic patients normally develop symptoms such as: weight loss, polyuria (frequent urination), polydipsia (increased thirst) and polyphagia (increased hunger) as a compensatory way of maintaining osmolality in the body [4]. According to the World Health Organization (WHO), Diabetes mellitus affects more than 170 million people worldwide, and this number will rise to 370 million by 2030 [5], [6]. In Zimbabwe there is no current statistics on Diabetes mellitus prevalence but it is among the top five chronic conditions seen in the out-patients clinic. The latest survey done in 2005 reported that the prevalence of Diabetes mellitus among the Zimbabwean adult population was 10%, although a large number of people were not aware that they had raised blood sugar levels [7]. Diabetes mellitus is classified primarily into Type I and Type II. Type I Diabetes mellitus is mainly idiopathic (of unknown causes) or caused by autoimmune disorders. Autoimmune disorders cause destruction of islets cells in the pancreas which synthesize the hormone insulin leading to an absolute insulin deficiency [8]. Type I develops over a short period of time and over 95 percent develop the disease before the age of 25 [9]. Type II Diabetes mellitus arises from insufficient production of the hormone insulin from beta cells of the pancreas or in conditions where the peripheral receptors; primarily muscles, liver and fat tissue do not respond adequately to normal insulin levels. This condition is known as insulin resistance [8]. Instead of the body converting glucose into energy, glucose builds up in the bloodstream causing hyperglycemia. Type II diabetes makes up about 90% of cases of diabetes and has a slow and insidious onset [3], [10]. It usually occurs in people who are over forty years of age, are obese, with a sedentary

life style, poor diet, hypertension and family history of diabetes. Type II Diabetes mellitus was formerly known as adult onset but now it is increasingly found in young people especially in the 21st Century [11]. Women with a history of gestational diabetes, which is defined as any degree of glucose intolerance which is first recognized during pregnancy, are at an increased risk of developing Type II diabetes [9]. Available epidemiological data shows that about 80% of Type II diabetic patients are obese, with a body mass index (BMI) of 30 kg/m² or more, whereas the other 20% have a BMI of 25 to 29.9 kg/m² which is above expected BMI [12]. Other epidemiological data shows there are increasing incidences of Type II Diabetic mellitus and diabetic patients are at an increased risk of developing complications such as: nephropathy, retinopathy, neuropathy and atherosclerosis [13], [14]. About one third (33%) of Type II diabetics are found to have a progressive deterioration of kidney function, making diabetes a global health concern [6], [10]. The kidneys are important organs in the body serving as a natural filter of the blood, and keeping the body chemically balanced. The kidney regulates the concentration of water and soluble substances like sodium salts by filtering the blood, reabsorbing water, glucose and amino acids. It also excretes wastes such as urea, creatinine, uric acid, electrolytes and extra water, thereby regulating blood volume, blood pressure, levels of electrolytes, metabolites and blood pH, which is a homeostatic function [15]. If the kidneys fail to remove wastes, these wastes accumulate in the blood and the body, damaging the body and the kidneys themselves leading to renal failure [16], [17], [18]. Kidney damage usually starts 2 to 5 years after onset of hyperglycemia, if hyperglycemia is not controlled [19]. Hence diabetes mellitus is the most common cause of chronic kidney failure and end stage renal disease (ESRD) throughout the world in both developed and emerging nations [20], [21]. Over 40% of the newly diagnosed cases of end stage renal disease are attributed to diabetes [22]. Renal disease is progressive and is more frequent in men than in women because of differences in lifestyle (smoking is a risk factor) and testosterone deficiency that is common in men who are diabetic [23], [24]. Renal dysfunction leads to accumulation of nitrogenous waste products in the blood above their normal ranges, some of which are toxic. These products include

creatinine and urea [25], whilst urinary albumin excretion rate exceeds 200 mg/minute. Early detection at this stage is vital to preserve kidney function and to delay or prevent end stage renal disease [1]. Males have greater proportions of skeletal muscles as compared to women resulting in proportionally elevated values of creatinine. Normal serum creatinine is usually 74-110 $\mu\text{mol/l}$ in men less than 50 years, 72-127 $\mu\text{mol/l}$ in men more than 50 years and 58-96 $\mu\text{mol/l}$ in women [26]. Normally urea is filtered out of the blood and controlled to a range of 2.86 - 8.57 mmol/L for men and 2.14 - 7.50 mmol/L for adult women [26]. In pregnancy urea values are decreased by 25%. Intensive treatment of Diabetes mellitus reduces the risk of renal complications development in the long term. In Zimbabwe there is need to update and obtain current statistics to reduce renal morbidity in diabetics and this forms the basis of our study. This study therefore sought to determine the prevalence of impaired renal function in Type II diabetic patients attending Parirenyatwa Diabetic Clinic using relatively inexpensive renal function tests (urea and creatinine serum levels).

2 MATERIALS AND METHODS

2.1 Study Design

A laboratory based cross-sectional study

2.2 Study Setting

The study was carried out on serum samples of consenting diabetic patients attending the Diabetic Clinic at Parirenyatwa Group of Hospital in Harare, Zimbabwe. Patients with a history of kidney problems and congestive heart failure, liver failure, pregnancy and smoking were excluded from the study.

2.2 Ethical Considerations

Permission to carry out the project was sought from authorities in charge of the Diabetic Clinic, including the Consultant and the Ward Manager. Ethical approval was obtained from the Joint Research Ethics Committee of the College of Health Sciences and Parirenyatwa Group of Hospitals (JREC/346/12). All samples were de-identified by giving each sample numerical codes.

2.3 Sample Size Calculation

The minimum sample size of 239 was determined using the following formula: $S = Z^2 pq / E^2$, Where Z= Test statistics, E= Standard Error, P= Population proportion with characteristic, q = 1-p, S= minimum sample size

$$S = \frac{1.645^2 \times 0.33 \times 0.667}{0.05^2} = 239.32$$

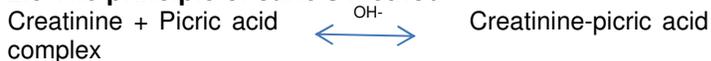
i. e. minimum sample size = 239

2.4 Sample Processing

Blood samples were centrifuged at 3000rpm to separate serum and serum samples were stored at -38°C . Urea and creatinine were assayed on the Mindray® BS 120 (Mindray® Medical International Limited, Shenzhen, China) at the University of Zimbabwe, College of Health Sciences, Department of Medical Laboratory Sciences. To ensure quality results the analyser was calibrated and control samples were assayed first. Estimation of plasma creatinine was done using modified Jaffe's method [9, 10]. Serum urea was estimated

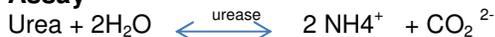
using the Urease-Glutamate Dehydrogenase, UV method.

2.5 The principle of Jaffe's method



Under alkaline conditions, creatinine combines with picric acid to form an orange-red colored complex. The absorbance at 510nm increases and the increase is directly proportional to the concentration of creatinine in the sample.

2.6 The principle of Urease-Glutamate Dehydrogenase Assay



Urea is hydrolyzed by urease, and one of the products, ammonia, converts NADH to NAD^+ under the catalysis of glutamate dehydrogenase (GLDH). The absorbance decreases in direct proportion to the concentration of urea, at 340nm.

2.7 Data and Statistical Analysis

Impaired renal function was defined as: values of creatinine, greater than 96 $\mu\text{mol/l}$ for women, greater than 127 $\mu\text{mol/l}$ for males and urea values of greater than 7.5mmol/l for women and greater than 8.57 mmol/l, for males. The data acquired from the study was used to calculate prevalence of impaired renal function. Analysis of the data was done using STATA 11 statistical package. The descriptive statistics were computed with standard methods and presented as mean and standard deviations. Association of variables and results was calculated using Pearson's Chi square and a p value of <0.05 was considered to be statistically significant.

3 RESULTS AND ANALYSIS

The results of our study on patients attending Parirenyatwa Diabetic clinic showed the prevalence of elevated creatinine and/or urea levels in Type II diabetics (Figure 1). The age of the participants studied ranged from 35 years to 86 years of age. Out of 239 patients, 52% were male.

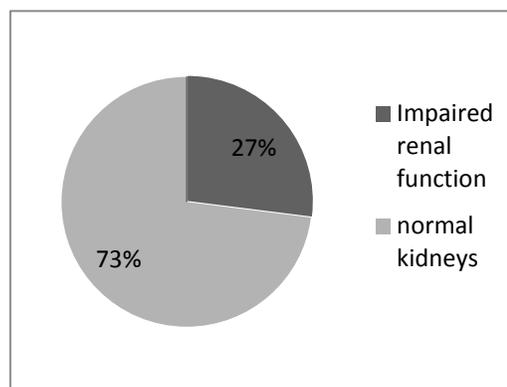


Figure 1: Prevalence of Impaired Renal Function (Elevated Creatinine And/Urea Levels) in Type II Diabetic Patients Attending Parirenyatwa Diabetic Clinic

Table 1: Serum Creatinine and Urea Levels in Type II Diabetic patients (Values are expressed in mean ± SD)

Variables	Males	Females
Age (in years)	63 ± 10.17	56 ± 12.01
Number of years on treatment	10.22 ± 7.93	9.17 ± 7.61
Creatinine (µmol/l)	110.51 ± 22.83	89.06 ± 21.18
Urea (mmol/l)	5.78 ± 1.95	5.00 ± 2.08

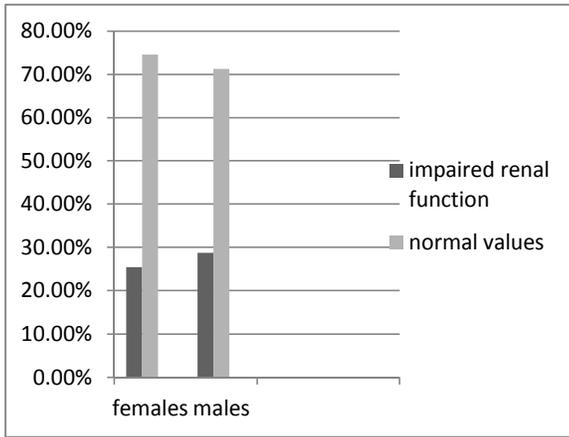


Figure 2: The Percentages of Diabetic Patients with Impaired Renal Function by Sex

Duration of intake of medication (most were on Metformin® and Glibenclamide®) ranged from 1 year to 35 years. It is apparent (Figure 3) that those who had been on treatment for more than 20 years were more likely to have elevated serum creatinine levels compared to those below 5 years on treatment, OR = 36.4 at 95% Confidence Interval (11.7; 112.9), p < 0.001. Therefore we found a significant association between impaired renal function and period on treatment in this group of Type II Diabetics.

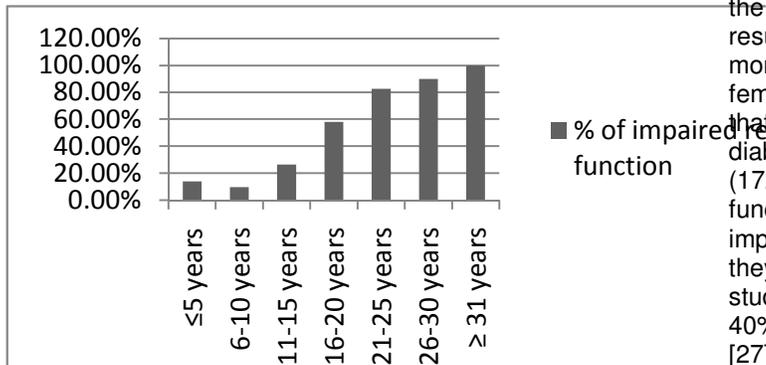


Figure 3: Distribution of Impaired Renal Function with Period on Treatment

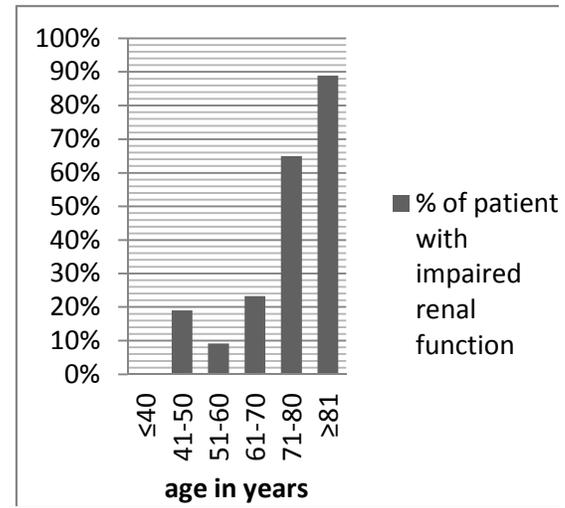


Figure 4: Relationship between Impaired Renal Function and Age of Study Subjects.

Our data showed that patients older than 70 years were 17.4 times more likely to develop impaired renal function compared to those below 50 years in this group of patients (O.R = 17.4 at 95% Confidence Interval (6.9;49.4), p < 0.001). There was evidence of significant association between age of patient and impaired renal function (Figure 4).

4. DISCUSSION AND CONCLUSION

Impairment of renal function due to type II Diabetes mellitus was assessed by measurement of serum concentration of urea and creatinine. Creatinine is usually elevated when the kidneys have lost about 50% of their function. Therefore, the prevalence of impaired renal function found in patients attending Parirenyatwa Diabetic clinic may in fact be more than the 27.2 % reported here. The males had a slightly greater percentage of impaired renal function, (28.7%) compared to females (25.4%) as shown in Figure 2. In this study, impairment of renal function was found to be significantly associated with age of the patient (p < 0.001) and the number of years on treatment (p < 0.001). There is no current statistics on diabetes and its complications in Zimbabwe therefore our research study gives an indication of the prevalence of diabetes complications in our setting. The results from this Parirenyatwa Diabetic Clinic study show that more diabetic males have impaired renal function compared to females. This agrees with current literature which suggests that male sex is a risk factor for impaired renal function in diabetic patients [27], [28]. Out of the 239 study subjects 72% (172) were hypertensive. All the subjects with impaired renal function were found to be hypertensive. Out of 65 patients with impaired renal function, 36% developed hypertension before they were diagnosed of diabetes. This correlates with previous studies that showed that hypertension is usually present in 30-40% of patients when they are first diagnosed with diabetes [27]. The combination of systemic hypertension and diabetes is dangerous as this accelerates damage to the remaining nephrons compared to diabetes alone. Therefore intensive treatment of both diabetes and hypertension is necessary to retard impairment of renal function [29]. The major limitation of this study is because creatinine values may remain within range even when the kidneys have lost more than half of

function. Patients may, therefore, be misdiagnosed as having normal kidney function, when in fact they have lost some function. Therefore, the results of this study should be interpreted with caution. We conclude that prevalence of impaired renal function in Type II diabetic patients attending Parirenyatwa Diabetic Clinic is above 27.2 %. Age and long duration on Diabetes treatment are associated with risk of kidney damage. In our study, age was associated with impaired renal function. Therefore, screening for Diabetes mellitus and renal impairment should be standard practice for those over 40 years of age in Zimbabwe. Earlier detection of Diabetes mellitus may lead to tighter control of blood glucose levels and a reduction in the severity of complications associated with Diabetes mellitus.

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