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Original Article

Determinants of Abnormal Kidney Function Tests in Diabetes Patient Type 2 in Libya

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Abstract

Introduction: Diabetes mellitus (DM) is among the most common non-communicable diseases. Humans around the world face many health threats. One of the most significant threats is DM, often simply referred to as diabetes. Although it has been centuries since DM was first recognized, it is still not fully understood and managed.

Materials and Methods: The target population was Type II diabetic males and females aged 40-60 years were selected at random among patients seeking medical care at the Hospital of El-Beida, Libya. The number of patients with Type II diabetic comprised 103 diabetic cases (79 males + 24 females). 39 healthy controls (29 males + 10 females), living under the same socio-economic conditions of the diabetic patients, were selected to serve as controls.

Results: Patients with diabetes 5 years were 60 (58.25%), whereas those with diabetic duration of 5-10 years were 27 (26.22%). The rest of patients 16 (15.53%) had diabetes for more than 10 years. The mean age of the patient was 56.10 ± 7.82 years. Type 2 diabetes is a disease associated with abnormal carbohydrate metabolism, which arises due to insulin deficiency as insulin is the key hormone responsible for glucose homeostasis in blood.

Conclusion: In conclusion, in Libya diabetic patients, we concluded that biochemical parameters of kidney functions are associated with a worsening in insulin action and predicts the development of Type 2 diabetes.

Key words: Diabetes mellitus, Kidney function, Libya diabetic patients

INTRODUCTION

Diabetes mellitus (DM) is among the most common non-communicable diseases. Humans around the world face many health threats. One of the most significant threats is DM, often simply referred to as diabetes. Although it has been centuries since DM was first recognized, it is still not fully understood and managed.[1] Diabetes now affects 7% of the world's adult population. Middle East occupies the second region after North America with the highest diabetes prevalence rates (9.3%), and this number is expected to double in <20 years.[2] However, the Libyan national non-communicable diseases survey in 2009 reported a prevalence of diabetes of 16.4%.[3] In Libya population, the Type II diabetes affected >70% in Libya which is the highest prevalence in North Africa and among Arabic nations. The most possible cause is eating habit.[4] Kadiki *et al.*[5] reported that DM is as frequent in Libya as in other Mediterranean countries. Libya has the uncertain destination of being home to the huge number of people suffering from diabetes like in any other country. In diabetes, the cells do not receive glucose and most of it is accumulated in the blood. Too much sugar in the blood can lead to serious health problems, including heart disease and damage to the nerves and kidneys. Failing to control diabetes can give rise to many complications.[6] Diabetic kidney disease takes many years to develop. Overall, kidney damage rarely occurs in the first 10 years of diabetes, and usually, 15-25 years will pass before kidney failure occurs. The kidneys excrete metabolic waste products and regulate the serum concentration of a variety of substances. At some stage during the course of renal disease, the following routinely measured substances often become abnormal and the extent of the abnormality generally depends on the severity of the disease.[7] Serum creatinine and urea concentrations

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change inversely with changes in chronic renal failure (glomerular filtration rate [GFR]) and are, therefore, useful in gauging the degree of renal dysfunction.[8] Urea, uric acid, and creatinine are the parameters to diagnose functioning of the kidney. Changes in serum creatinine concentration more reliably reflect changes in GFR than do changes in serum urea concentrations. Creatinine is formed spontaneously at a constant rate from creatinine, and blood concentrations depend almost solely upon GFR. Urea formation is influenced by a number of factors such as liver function, protein intake, and rate of protein catabolism.[8,9] Biologically, uric acid plays an important role in worsening of insulin resistance in animal models by inhibiting the bioavailability of nitric oxide, which is essential for insulin-stimulated glucose uptake.[10] Consequently, this study aims to evaluate the kidney function among diabetes patients compared to non-diabetic control group.

MATERIALS AND METHODS

The target population was Type II diabetic males and females aged 40-60 years were selected at random among patients seeking medical care at the Hospital of El-Beida, Libya. The number of patients with Type II diabetic comprised 103 diabetic cases (79 males + 24 females). 39 healthy controls (29 males + 10 females), living under the same socioeconomic conditions of the diabetic patients, were selected to serve as controls. They had no symptoms of diabetes and had fasting serum glucose levels <120 mg/dl. There was no evidence of any acute illness. The age distribution of the healthy controls was approximately similar to that of the patients. A meeting interview was used for filling in the questionnaire, which designated for matching the study need. All interviews were conducted face to face by the researcher himself. During the study, the interviewer explained to the participants any of the confused questions that will not clear to them. Most questions were the yes/no questions, which offer a dichotomous choice.

All participants were anonymized by numbering them and numbering the blood samples taken from them. All participants were asked to fast overnight for a period of about 8 h (12 pm - 8 am), during which no treatment (insulin or hypoglycemic drugs) was allowed to be taken. The patients were also given a questionnaire to fill in which contained several questions regarding their lifestyle habits and medical history for epidemiological study. Blood samples were collected from 103 Type II diabetic patients and 39 controls. Fasting overnight venous blood samples (about 7 ml) were drawn by the researcher himself into Vacutainer plane tubes from all individuals. The blood was left for a while without anticoagulant to allow blood to clot. Then, serum samples were obtained by centrifugation at room temperature at 4000 rpm/10 min.

Blood samples were obtained at recruitment (non-fasting) and measured at routine hospital laboratories using an automated biochemistry analyzer. Serum glucose concentration was measured by the method of Trinder,[11] and serum urea and creatinine were determined by methods of Patton and Crouch[12] and Henry *et al.*,[13] respectively. Serum uric acid was determined according to the method of Kayamori *et al.*[14]

All the data from despotic diabetic patients and age-matched controls from different experiments were analyzed and compared using Student's *t*-test. The results were expressed as mean ± standard deviation. The significant test was applied at $P < 0.05$.

The percentage difference was calculated according to the formula:

Percentage difference = (mean of patient-mean of control)/(mean of patient + mean of control/2) × 100. Range of minimum and maximum values was used.

RESULTS AND DISCUSSION

Distribution of the Study Population

Table 1 illustrates general characteristics of the study population. 142 participants were recruited to the study consisting of 103 patients with diabetes (cases) and 39 participants without diabetes (controls). The average age was 56.10 ± 7.82 years, ranging between 42 and 67 years in diabetic patients and 54.97 ± 6.34 years in a range of 39 through 61 in the control group. Among the patient's group, 79 patients were males representing 76.7% and 24 patients were females representing 23.3%, on the other hand, 29 of the control group were male (74.4%) and 10 were female (25.6%). The number of patients from each area was selected because the number of diabetic patient in El-Beida was not available.

Table 2 summarizes the distribution of diabetic patients by diabetes duration. Patients with diabetes 5 years were 60 (58.25%), whereas those with diabetic duration

Table 1: Participants recruited for this study

Characteristics	Healthy control	Diabetic
Number of Participants	39	103
Age group range (min-max)	54.97±6.34 (39-61)	56.10±7.82 (42-67)
Gender	29 males and 10 females	79 males and 24 females
Diabetic status	Non-diabetic	T2DM

of 5-10 years were 27 (26.22%). The rest of patients 16 (15.53%) had diabetes for more than 10 years. The mean age of the patient was 56.10 ± 7.82 years. It was reported that Type II DM usually develops after age 40 years.[15] The results that more than half of patients had diabetics since <5 years do confirm the idea that Type II diabetes has long asymptomatic pre-clinical phase, which frequently goes undetected. At the time of diagnosis, the patient could have one or more diabetes complications.[16] In the current study, the finding was not found any associated with complications (liver disease, cardiovascular disease, kidney disease, and recurrent infection) in relation to duration of diabetes. These findings are confirmed by self-report questionnaire. However, this point still needs further investigation. The prevalence of such symptoms was positively associated with the progress of the disease, i.e., the longer the duration of DM. Several studies reported similar diabetic complications with increasing rates upon disease progress.[17,18]

Serum Glucose of Diabetic Patients

Type 2 diabetes is a disease associated with abnormal carbohydrate metabolism, which arises due to insulin deficiency as insulin is the key hormone responsible for glucose homeostasis in blood (Kumar *et al*., 2005). As shown in Table 3, it was found that there was a significant ($P < 0.05$) increase in the mean serum glucose level in patients than that in controls (98.48 ± 8.97 vs. 210.0 ± 48.65 mg/dl, % difference = 84.20).

Table 2: Distribution of diabetic patients (*n*=103) by diabetes duration

Duration of diabetes (year)	Number (%)
<5	60 (58.25)
5-10	27 (26.22)
>10	16 (15.53)

Table 3: The results of serum glucose of diabetic patients and controls

Parameter	Healthy control (*n*=39)	Diabetic (*n*=103)	Percentage difference
Glucose (mg/dl)	98.48±8.97	210.0±48.65*	84.20
Range (min-max)	79-121	148-387	

*P<0.05 for diabetic compared to control group. All results are expressed as mean±SD. SD: Standard deviation

Diabetic patients are characterized by abnormalities in glucose metabolism in several organs, skeletal muscle glucose disposal is reduced, hepatic glucose production is increased, and insulin-independent glucose uptake into the lens and neural tissue are increased.[19] Although the actual mechanisms of insulin resistance in Type 2 diabetes remain unknown, several steps in the uptake and intracellular handling of glucose are probably affected.[20] Measuring blood glucose is one-way of monitoring diabetes. In this study, diabetic patients have an abnormal level in blood glucose compared with non-diabetics. High levels of blood glucose of diabetic patients due to lack of or resistance to insulin, same results were found by Abdelgadir[21] and Bergenstal *et al*.[22] In their studies of diabetic population, in which they conclude that the fasting blood glucose level is also elevated, and this indicates poor control of DM. In fact, DM is characterized by hyperglycemia together with biochemical alterations of glucose.[22]

Serum Urea, Uric Acid, and Creatinine of Diabetic Patients

Impairment in renal function is assessed by estimating the serum urea levels and the serum creatinine levels.[7] Impairment of renal function due to Type 2 diabetic mellitus was assessed by measurement of serum concentrations of urea and creatinine in diabetic patients and healthy controls. Data listed in Table 4 showed that the mean serum urea concentrations were significantly ($P < 0.05$) decreased in diabetic patients compared to controls (28.74 ± 2.13 vs. 47.24 ± 12.48 mg/dl, % difference = 48.70). Similar trend was found for creatinine and uric acid concentration (0.79 ± 0.04 vs. 1.19 ± 0.39 mg/dl, % difference = 40.40, 4.98 ± 0.81 vs. 8.19 ± 2.42 mg/dl, % difference = 48.80, respectively). This change was also significant ($P < 0.05$). Urea is formed by the liver as an end product of protein breakdown and is one marker of the kidney function.[23] An increase in serum urea observed here might be due to impairment in its synthesis as a result of impaired hepatic function and/or due to disturbance in protein metabolism.[23,24]

Creatinine is a waste product that is normally filtered from the blood and excreted with the urine. Higher creatinine levels in diabetic patients may be related to disturbance of kidney function.[23] In addition, the observed increases in urea and creatinine may be explained on the basis of glomerular hyper-filtration due to increase creatinine clearing from blood.[25]

Table 4: The results of the kidney function parameters measured in serum of healthy controls and diabetic patients

Parameters	Healthy control (*n*=39)	Diabetic (*n*=103)	Percentage difference
Urea (mg/dl) range (min-max)	28.74±2.13 (18.0-34.0)	47.24±12.48 (37.0-57.0)*	48.70
Creatinine (mg/dl) range (min-max)	0.79±0.04 (0.69-0.97)	1.19±0.39 (0.96-1.34)*	40.40
Uric acid (mg/dl) range (min-max)	4.98±0.81 (3.89-6.02)	8.19±2.42 (6.48-8.97)*	48.80

*P<0.05 for diabetic compared to control group. All results are expressed as mean±SD. SD: Standard deviation

Serum creatinine and urea are established markers of GFR. Although serum creatinine is a more sensitive index kidney function compared urea level. This is because creatinine fulfills most of the requirements for a perfect filtration marker.[23,26] The present results support by several studies, it has been reported that there is a clear association of serum urea with fasting blood sugar.[1,27,28] Manjunatha *et al.*[23] concluded in their study that blood urea and creatinine is accepted to assess the renal function.

As DM is the major cause of renal morbidity and mortality, so a good control over the sugar level can halt the progression of renal damage. Biologically, uric acid plays an important role in worsening of insulin resistance in animal models by inhibiting the bioavailability of nitric oxide, which is essential for insulin-stimulated glucose uptake.[10] Reports by Adler *et al.*[29] showed that raised plasma creatinine and urea levels in diabetic patient indicated a pre-renal problem such as volume depletion. Investigations by Judykay[30] suggested that high creatinine levels noted in diabetic patients might be due to impaired function of the nephrons. Increased serum creatinine and blood urea levels recorded in Type 1 and Type 2 DM patients could be attributed to a fall in the filtering capacity of the kidney thus leading to accumulation of waste products within the system. Although serum creatinine and blood urea tests can expose the patient's renal function, serum creatinine is a more sensitive indicator, as many extrarenal conditions such as dehydration, can increase urea levels. However, serum creatinine levels alter very little except in renal dysfunction.[31]

Serum uric acid is positively associated with serum glucose in healthy controls;[32] it is not clear whether raised serum uric acid predicts the risk of Type 2 diabetes.[33,34] This present study is investigated the association between serum uric acid and risk of diabetes in the El-Beida city. Table 4 presents the association between increasing serum uric acid levels and DM by hypertension status (48.80%). These results agree with previous studies, which reported that there is a positive association between high serum uric acid levels and diabetes,[35-37] whereas other studies reported no association [34] or an inverse relationship.[38,39]

Hence, it is recommended that these tests should be performed when patients are diagnosed as diabetics and at the time of follow-up, annually. A good control of blood glucose level is absolute requirement to prevent progressive renal impairment.

CONCLUSION

In conclusion, in Libya diabetic patients, we concluded that biochemical parameters of kidney functions are associated with a worsening in insulin action and predicts the development of Type 2 diabetes. These results support the hypothesis that the kidney is important in the pathogenesis of Type 2 diabetes, and that kidney parameter may be useful additional markers of patients at high risk for development of diabetes. Further studies on the kidney functions on diabetic patients need to be performed.

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