

## Assessment of Plasma B2-Microglobulin among Sudanese with Type 2 Diabetes Mellitus

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### Abstract

**Background:** Diabetic nephropathy cause gradual renal impairment that may end stage renal failure. In glomerular kidney disease, the glomeruli can't filter B2-microglobulin out of the blood, so levels increase in the blood and decrease in the urine. In tubular kidney disease, the tubules can't reabsorb it back into the blood, so urine levels rise and blood levels fall.

**Objectives:** To assess the plasma levels of B2-microglobulin, creatinine clearance, blood HbA1c% and body mass index in Sudanese patient with type 2 diabetes.

**Materials and methods:** This is a case-control study conducted in two diabetic centers in Khartoum state, Sudan, from March 2010 to November 2013. A total of 300 Sudanese patients with type2 diabetes mellitus as a test group, and 150 healthy subjects as a control group were enrolled in this study. Both groups were matched for gender and age. The plasma levels of Beta2-microglobulin, blood HbA<sub>1c</sub> and plasma creatinine were measured using Nephelometry, and creatinine clearance was calculated for each participant. SPSS was used for analysis of data.

**Results:** The means of the plasma levels of Beta2-microglobulin, HbA<sub>1c</sub>% and the body mass index were significantly raised in the diabetic group when compared to the control group ( $p < 0.05$ ). The study showed a significant moderate inverse correlation between Beta2-microglobulin and creatinine clearance ( $r = -0.56, p = 0.04$ ) in the diabetic group, and also showed a significant moderate positive correlation between the plasma levels of Beta2-microglobulin and HbA<sub>1c</sub>% ( $r = 0.50, p = 0.03$ ).

**Conclusion:** The present data indicates that among Sudanese patients with Type 2 Diabetes Mellitus, the plasma levels of Beta2-microglobulin is significantly raised and has a significant moderate positive correlation with glycated haemoglobin % and a significant moderate inverse correlation with creatinine clearance.

**Keywords:** Type 2 Diabetes, Beta2-microglobulin, Glycated Haemoglobin

## 1-Introduction

Diabetes mellitus is a group of metabolic diseases characterized by high blood glucose levels, which result from defects in insulin secretion, action, or both<sup>1</sup>. Over time, Diabetes can lead to blindness, kidney failure, and nerve damage. These types of damage are the result of damage to small vessels, referred to as micro vascular disease. Diabetes is also an important factor in accelerating hardening and narrowing of the arteries (atherosclerosis), leading to strokes, coronary heart disease, and other large blood vessel disease<sup>2</sup>. Diabetes affects approximately 17 million (about 8% of the population) in the United States. In addition, an estimated additional 12 million people in the United States have diabetes and don't even know it. From an economic perspective, the total annual cost of diabetes in 1997 was estimated to be 98 billion dollars in the United States<sup>3</sup>. Diabetes is the third leading cause of death in the United States after heart disease and cancer<sup>4</sup>. Diabetes, the most common non-communicable disease in Sudan, is having an increasing impact on rates of morbidity and mortality. The spread of sedentary lifestyles and adoption of western dietary habits that is high in refined carbohydrates and fat are driving an increase in the number of people with obesity-related type 2 diabetes. Knowledge of the diabetes epidemic in Sudan is limited, and the most recent data come from a small-scale study indicated a prevalence of 3.4%, but recent research estimates about four millions, around 95% of whom have type 2 diabetes mellitus<sup>5</sup>.

Beta2-microglobulin is plentiful on the surface of many cells. Increased production or destruction of these cells causes Beta2-microglobulin levels in the blood to increase. This increase is seen in people with cancers involving white blood cells, but it is particularly meaningful in people newly diagnosed with multiple myeloma<sup>6</sup>. Change in the plasma levels of B2-microglobulin can also be detected kidney disease.

When kidney disease is suspected, comparing blood and urine levels of Beta2-microglobulin helps identify where the kidney is damaged. Beta2-microglobulin normally is filtered out of the blood by the kidney's glomeruli, only to be partially reabsorbed back into the blood when it reaches the kidney's tubules<sup>7</sup>.

## 2-Materials and Methods

This is an analytical, case-control and hospital-based study, that conducted in Jabir Abualizz and Almolazmeen diabetic centers in Khartoum state, Sudan, during the period from march 2010 to November 2013. A total of 300 Sudanese patients with type 2 diabetes mellitus were enrolled in this study as a test group, in contrast to 150 healthy volunteers as a control group. Both groups were matched for age and gender. Patients with type 1 diabetes, gestational diabetes, secondary diabetes, renal insufficiency, cancer, cytomegalovirus and human immunodeficiency virus were excluded from this study.

A venous blood sample (4mls) was collected from each participant by standard procedures and divided into two containers, 2mls in EDTA container for HbA1c (whole blood) and 2mls in lithium heparin container, which was centrifuged at 300rpm for 3 minutes to get plasma that kept at -20C<sup>0</sup> until used. The plasma level of Beta2-microglobulin was measured using nephelometry, and HbA<sub>1c</sub> for each sample was measured using cobas system (SIEMENS nephelometry). Serum creatinine was measured using jaffe reaction and then creatinine clearance for each participant was calculated using the Cockcroft-Gault formula<sup>8</sup>.

$$\text{Creatinine clearance (GFR estimation)} = \frac{(140 - \text{age}) \times \text{weight (kg)} \times 1.23 \text{ (0.85 for female)}}{\text{Serum creatinine (mol/L)}}$$

The body mass index for each participant was calculated by measuring the weight in Kg and the height in meters, and using the formula (BMI = Wt./higet<sup>2</sup>). SPSS (version 11.5) computer software was used for data analysis and the significant level was set at p ≤ 0.05. (t) test was used for comparison of groups and Pearson's correlation was used or assessment of correlation between variables.

## 3-Results

This study was conducted on 300 Sudanese patients with type 2 diabetes mellitus (49% males and 51% females) as a test group and 150 healthy subjects (48% males and 52% females) as a control group. The test group and the control group were matched in terms of gender and age. The mean age of the test group was 58.40 ± 7.20 year and that of the control group was 56.8 ± 10.0 year, (p = 0.094). In the current study the majority of diabetic patients were obese (71%), with long standing diabetes (65%) and had uncontrolled diabetes (69%). Table (1) shows a significantly raised means of the plasma levels of Beta2-microglobulin, HbA<sub>1c</sub>% and body mass index of the diabetic group when compared with the control group. It also shows a significant reduction of creatinine clearance of the test group when compared with the control group.

Figure (1) shows a significant moderate inverse correlation between the plasma levels of Beta2-microglobulin and creatinine clearance. Figure (2) shows a significant moderate positive correlation between the plasma levels of Beta2-microglobulin and HbA<sub>1c</sub>%. Figure (3) shows insignificant weak positive correlation between the plasma levels of Beta2-microglobulin and the body mass indexes.

**Table 1: Comparison of the Plasma Levels of B2-Microglobulin, Creatinine Clearance Hba<sub>1c</sub>% and Body Mass Index of the Diabetic Group and the Control Group**

Variables	diabetic group (n=300)	Control group (n=150)	(P)
Plasma β <sub>2</sub> microglobulin (mg/ml)	2.38±1.22 (0.82-4.00)	1.31±0.48 (1.12- 2.00)	0.0351*
Creatinine clearance ml/min	( 80.66±33.17) (71.91- 120.00)	(93.37±30.61) (90.90- 138.89)	0.015*
Blood HbA <sub>1c</sub> %	8.51±1.74 (3.75-11.32)	3.22±4.31 (2.35-5.11)	0.0157*
BMI kg/m <sup>2</sup>	(27.69±3.77) (18.62-34.68)	(23.43±4.31) (18.43-35.42)	0.043*

The table shows the mean ±StD and probability (P). Independent t-test was used for comparison. P-value ≤0.05 was considered significant.

#### 4-Discussion

In the present study the results showed that the means of the plasma levels of Beta2-microglobulin, blood HbA<sub>1c</sub>% and body mass indexes were significantly raised in the diabetic group when compared to the control group. Increased level of B2-microglobulin may be an early indication of diabetic nephropathy and reflect glomerular kidney disease. This result agrees with the results of the study done by Askumet al<sup>9</sup> who reported significant high levels of B2-microglobulin in patients with type 2 diabetes. In our study the majority of patients (71%) were obese and 69% were found to have uncontrolled diabetes with HbA<sub>1c</sub>% ≥ 6.5%. In the current study, the glomerular filtration rate assessed by creatinine clearance was significantly reduced, this could be due to the impact of long standing diabetes mellitus on the kidney, that cause progressive diabetic nephropathy. The current study showed moderate negative correlation between creatinine clearance and plasma Beta2-microglobulin levels, that means reduction of creatinine clearance is associated with raised serum levels of Beta2-microglobulin. In the present study HbA<sub>1c</sub>% has a significant moderate positive correlation with the plasma levels of B2-microglobulin, this means uncontrolled diabetes with abnormal raised glycated hemoglobin is associated with high serum Beta2-microglobulin levels.

Two large studies<sup>10,11</sup> with consistent results found that Beta2-microglobulin is influenced by many variables (age, sex, body mass index, smoking, hypertension, coronary heart disease and C-reactive protein level) rather than renal function alone. Both studies excluded patients with moderate and severe renal failure, and in both Beta2-microglobulin levels were highly correlated with age. In conclusion, although multiple factors in addition to renal function may influence Beta2-microglobulin, our study provides convincing evidence that Beta2-microglobulin is significantly raised and positively correlated with HbA<sub>1c</sub>% and inversely correlated with creatinine clearance in patients with diabetes mellitus, so it can be used as a marker of renal damage in diabetic patients<sup>10</sup>. These results are remarkable in light of data suggesting that Beta2-microglobulin is a useful indicator of the association of mild kidney dysfunction with increased risk for cardiovascular events, peripheral arterial disease, heart failure, and death<sup>11</sup>.

## 5-References

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