Renal threshold of Sudanese with type 2 diabetes mellitus without glycosuria

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Abstract

Renal threshold of glucose is the blood glucose concentration; where glucose begins to be excreted by the kidneys into the urine. Our hypothesis is that, free glucose urine is it a good predictor for hyperglycemia in type 2 diabetes mellitus (T2DM), when it's the only sample available? To answer this question, this study was done at Haj Al Safi Hospital in Khartoum, Sudan, in the period from February to August 2014. The study included 93 subjects, of them 43 were known (T2DM) patients in their normal follow up visits, whose urine showed absence of glycosuria, while their blood showed hyperglycemia, in more than one occasion. Another 50 were age and sex matched healthy subjects as controls. Blood glucose was measured using automated chemical analyzer. The glucose content of the urine was semiquantitatively analyzed using test strips (Multistix 10 SG Bayer). Controls negative and positive were used parallel with all urine tests. The mean age of the type 2 DM with hyperglycemia without glycosuria was (54.58±4.94 years) versus (53.5±6.38years) in the control subjects, the mean random plasma glucose of T2DM was (231.06±26.94mg/dl), versus (97.01±11.80mg/dl) in the control subjects, the mean glycated hemoglobin (HbAIc) of T2DM was (7.6±0.72%), versus (5.5±0.70%) in the non-diabetic normal persons. Thirty tow (74.4%) of T2DM patients were non-insulin

dependents, while 11 (25.6%) were insulin dependents. Thirty three (76.7%) of the T2DM patients were normotensive, while 10 (23.3%) were hypertensive. The duration of diabetes among the patient's group was (11.70±4.80years).

The study suggests that these Sudanese T2DM patients most likely; carry gene mutations in the human gene SGLT1, whose individuals have defective renal threshold with little or no glycosuria.

Key words: Renal threshold, glucose, type2 diabetes mellitus, hyperglycemia, glycosuria, gene mutation, Sudan

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Introduction

The renal threshold for glucose (RTG) is determined by the nephron's reabsorptive capacity. Glucose is reabsorbed through sodium-coupled glucose cotransporters in the proximal tubules[1]. The kidney performs an important role in glucose homeostasis[2]. Renal glycosuria is a benign condition in patients with normal blood glucose levels[3]. Normal urine contains small amounts of glucose[4]. Glycosuria or glucosuria is the excretion of glucose into the urine[5]. This is due to a defect in the tubular threshold for reabsorption of glucose in the proximal tubules[3, 6]. Glucose is freely filtered at the glomerulus; renal glomeruli filter B180 g of D-glucose per day[2]. The average threshold for serum glucose varies widely; it might be as low as 120 to 130 mg/dl[7]. Patients with diabetes due to hepatocyte nuclear factor (HNF)-1alpha mutations, have a low renal threshold for glucose[8], while T2DM patients with peripheral vascular disease (PVD) tend not to have glycosuria[9]. Glycosuria might be a less efficient defense mechanism against hyperglycaemia in patients with diabetes mellitus, because glucose reabsorption is upregulated,

either as a result of chronic hyperglycaemia or an intrinsic defect of diabetes mellitus[10]. There may be glycosuria with normal blood glucose levels in some maturity-onset diabetes of the young (MODY), that suggests an additional renal manifestation of the respective genetic defect[11]. Measurement of glycosuria is still widely used for home monitoring of glycaemia control in non-insulin-dependent diabetes (NIDDM), even the renal threshold for glucose (RTglu) varies between subjects[12]. The degree of glycosuria is of value as an index of diabetic control only when the blood glucose/urinary glucose relationship is known[13]. Urine glucose testing by Clinitest provides reliable information for who cannot afford blood glucose monitoring [14]. In situations where urine is the only body fluid obtained, urine glucose levels are an effective risk predictor[7], glycosuria may be present when blood glucose levels are within the normal fasting or postprandial range, and it may be absent when the blood glucose is distinctly above normal[15]. In after meal ingestion; renal glucose release increases to a greater extent in people with T2DM than in people with normal glucose tolerance[16]. It is well established that in type 2 diabetes; the excessive release of glucose into the circulation is a major factor responsible for fasting hyperglycemia[17]. A molecular diagnosis of monogenic diabetes alters management and identifies affected or at-risk family members[18]. Different defects might be produced either by mutations on different gene loci, or by multiple alleles of the same gene locus that determines the synthesis of the glucose carrier[4]. The human SGLT1 gene, *SLC5A1*, is located on chromosome 22 q13.1. Mutations in *SLC5A1* drive intestinal glucose–galactose malabsorption, but individuals who carry these mutations have little or no glycosuria [10].

Materials and methods

The objective of the present study is to assess the renal glucose threshold in Sudanese patients diagnosed with type two diabetes mellitus (T2DM), whose urine showed absence of glycosuria while their blood showed hyperglycemia. The study was done between February to June 2014, in Haj Al Safi Hospital, which is a tertiary care hospital, in Khartoum North- Sudan. The study included 93 subjects, of them 43 were known type two diabetic patients in their normal follow up visits, whose urine showed absence of glycosuria, ketonuria or proteinuria, with blood hyperglycemia in more than one occasion, while another 50 were age and sex matched healthy

subjects as controls. Ethical clearance was taken from the authorities, while written consent was taken from all study subjects. Initially; random blood and urine sample were collected from patients with T2DM and their controls. Oral instruction was given to the T2DM patients to fast overnight for 10-12 hours. Fasting blood samples were collected in fluoride oxalate containers. Urine samples were collected in new sterile 50 ml plastic containers. Two hours postprandial blood and urine samples; were collected after full breakfast, followed with cup of tea without sugar or carbohydrate restrictions. Plasma was separated after centrifugation at 3000 RPM for 10 minutes. Blood glucose was measured using automated chemical analyzer (TOSOH AIA -360). Control samples used, were from Biosystem Company (Spain). The glucose content of the urine was semiquantitatively analyzed using test strips (Multistix 10 SG Bayer) - Germany). Controls negative and positive were used parallel with all urine tests. Data were analyzed using IBM SPSS Statistic version 20. A comparison of the means was performed using the Independent-Samples Student's *t*-test from the SPSS Statistic program.

Results

The study revealed that; out of the (43) T2DM participants; 29 (67.4%) were females and 14(32.6) were males. Among the 50 control subjects; 28(56%) were females, and 22(44%) males (Tabe.1). The entire T2DM group showed no glucose, no acetone and no protein in their urine. Thirty tow (74.4%) of T2DM patients were non-insulin dependents, while 11 (25.6%) were insulin dependents. Thirty three (76.7%) of the T2DM patients were normotensive, while 10 (23.3%) were hypertensive. The mean age of the type 2 DM with hyperglycemia without glycosuria was (54.58±4.94 years) versus (53.5±6.38years), and the mean random plasma glucose was (231.06±26.94mg/dl) inT2DM versus (97.01±11.80mg/dl) in their controls, with P value (0.01), the mean glycated hemoglobin (HbA_{IC}) of T2DM was (7.6±0.72%), versus (5.5±0.70%) in the non-diabetic normal persons Table (2), (3) & Figure (1). The duration of diabetes among the patient's group was (11.70±4.80years) as shown in (Table. 3). Twenty six (60.5%) of the patients group has no family history of diabetes, while 17(39.5%) had family history of diabetes.

Table (1) Descriptive table of the gender of the type 2 diabetes mellitus with hyperglycemia without glycosuria and their control

Subjects	Females	Males	Total
Patients	29(67.4%)	14(32.6%)	43
Control	28 *(56%)*	22*(44%)*	50
Total	57	36	93

Table (2) Comparative study of the type 2 diabetes mellitus with hyperglycemia without glycosuria and their control

Items	Patients (No=43) (mean±std)	Control (No=50) (mean±std)	P value
Age (years)	54.58±4.94	53.5±6.38	
Random blood glucose (mg/dl)	231.06 ±26.94	97.01±11.80	0.01
HbA_{1c} (%)	7.6±0.72	5.5±0.70	

Table (3) Descriptive table of plasma glucose (random, fasting and 2hour post prandial), glycated hemoglobin and duration of the disease in the type 2 diabetes mellitus with hyperglycemia without glycosuria

Parameters	Minimum	maximum	Mean	Std. Deviation
Random plasma glucose (mg/dl)	196	299	231.06	26.94
Fasting plasma glucose (mg/dl)	149	252	216.50	29.04
2hour post prandial plasma glucose (mg/dl)	220	287	261.4	26.14
HbA_{1c} (%)	6.2	8.6	7.6	0.72
Duration of T2DM (years)	4	25	11.70	4.80

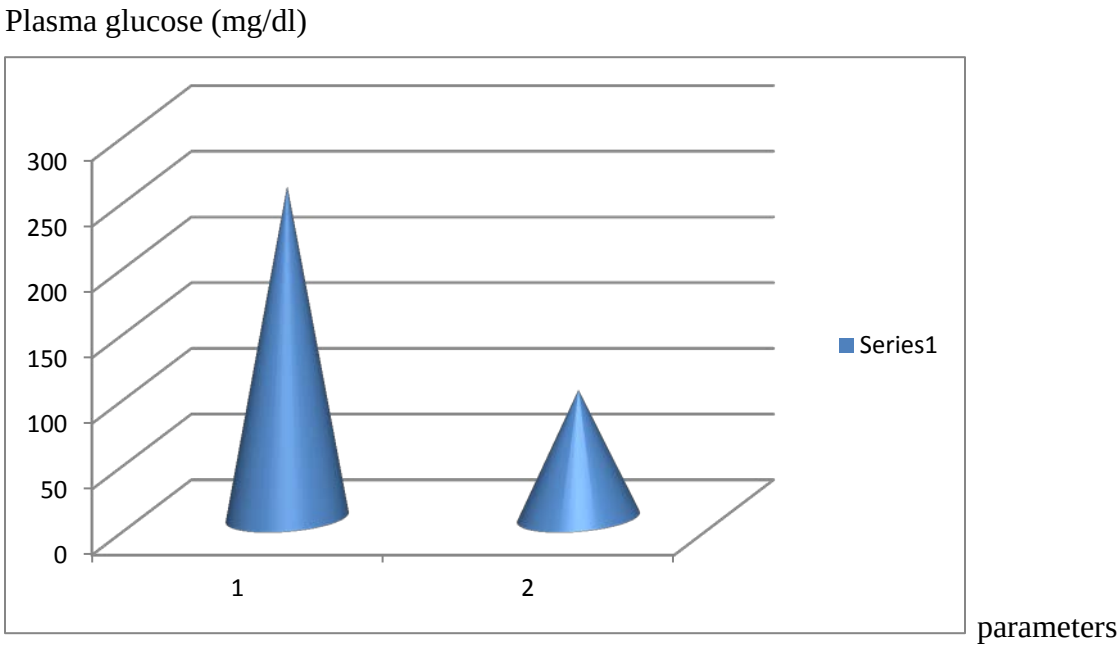

Figure 1 Random blood glucose in type2 diabetes mellitus (1) and their control (2).

Discussion

In the present study blood glucose and semiquantative urine glucose analysis was used to assess if free glucose urine, can be a misleading indicator for blood glucose levels in T2DM patients. In this study 0 % glycosuria is associated with average blood glucose concentrations (231.06±26.94mg/dl) in T2DM, this finding is in disagreement with that reported by Griffin et al (1979)[19], and in their study 0% glycosuria is only occurred in the diabetic patients with blood glucose less than (115 mg/dl), while in agreement for some extent with Ethiopian study done by Feleke & Abdulgadir (1998)[14], who said that semiquantative urine testing in T2DM may be suitable for only about 70% of patients. Even type 2DM is associated with genetic predisposition, according to WHO (2006)[6] guidelines, in this study only 39.5% of T2DM have family history, here the role of many factors raised, like sodium glucose transporter 2 (SGLT2) gene, as reported by Asimina (2011)[17] and Amanda & Carol (2011)[2], or liver cells abnormalities like hepatocyte nuclear factor (HNF)-1alpha mutations accompanied by beta-cell deficiency as reported by Stride and colleagues (2005)[8]. Ketone body assessment is indicated in all diabetic

patients when the risk of ketotic decompensation exists as indicated by Guerci et al (2005)[20], all the T2DM involved in this study do not proved ketosis. As HbA1c is a worldwide gold standard for glycemic assessment and even diagnosis of diabetes as concluded by a recent Japanese study written by Sato (2014)[21], in our study the mean HbA1c is (7.6±0.72%), means that even there is no glucose in the urine, some extent of glycation is occurring in this type of T2DM.

Conclusion

In treating type 2 diabetes mellitus with no glycosuria associated with hyperglycemia another genetic factors including liver and kidney abnormalities, should be considered. It seems plausible that the different defects might be produced either by mutations on different gene loci, or by multiple alleles of the same gene locus that determines the synthesis of the glucose carrier.

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