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Comparison between Fructose Amine and Hemoglobin A1C Level to Evaluate Glycemic Control in Sudanese Diabetic Control.

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Abstract

Background: Diabetes mellitus (DM), commonly referred to as diabetes, is a group of metabolic diseases with high blood sugar levels over a prolonged period, and is one of the most severe and frequent human disorders. ***Fructosamine*** is a generic name given to a compound known as plasma protein ketoamines. ***Fructosamine*** together with glycated haemoglobin (HbA1c) are used to monitor the state of hyperglycaemia in diabetics.

Objectives: This study aimed to compare between ***HeamoglobinA1c*** and ***Fructosamine*** in Sudanese diabetic patients in Omdurman Teaching Hospital and Diabetic and Endocrine center in Bahri.

Materials and Methods: This is a cross-sectional study. Automated colorimetric determination of fructosamine for each of the 50 blood samples of the study group was carried out according to specific procedure. Latex enhanced immuno-assay method for hemoglobinA1c (HbA1c) determination based on the interaction between antigen molecules (HbA1c) and HbA1c specific c antibodies coated on latex beads was carried out according to a specific procedure. Control group criteria should be clear because it is confused.

Results: HbA1c% and Fructose amine were measured on the same sample in 50 diabetic patients. There is a significantly direct positive correlation between levels of fructose amine (mmol/L) and HbA1c% among the studied group (P-value = 0.001 < 0.05). Sensitivity and specificity of fructosamine and HbA1c to detect blood glucose. hemoglobin A1C has (86%) sensitivity and (25%) specificity while fructosamine has (63%) sensitivity and (55%) specificity.

Conclusion: In diabetes serum fructosamine assay can better reflect average blood glucose concentration over the previous 2-3 weeks and $HbA1_c$ is better reflective over the previous 8-10 weeks there for fructosamine can be used as routine test while HbA1C as a first -line screening test.

Keywords: Diabetes, Controlled, fructosamine , HbA1c, Sudan

Introduction

Diabetes is one of the most severe and frequent human disorders. According to recent statistics, this condition afflicts as many as 382 million persons around the globe, with an estimated prevalence of approximately 8.3% in 2013. At variance with other frequent pathologies such as cardiovascular disease and bacterial infections, the trend toward an increased prevalence is not expected to reverse soon. Worldwide, as many as 592 million individuals may be affected by diabetes in 2035, a remarkable 55% increase in prevalence over the next 2 decades. Due to its high global prevalence and severe, frequently life-threatening complications (eg, retinopathy, nephropathy, neuropathy, and cardiovascular disease), diabetes must be regarded as a serious and increasing global health burden [1].

Recent reports have shown that diabetes and its related complications were major health problem in Sudan [2].

Diabetes and lesser forms of glucose intolerance, impaired glucose tolerance (IGT) and impaired fasting glucose (IFG), can now be found in almost every population in the world and epidemiological evidence suggests that, without effective prevention and control programs, the burden of diabetes is likely to continue to increase globally.

Because diabetes is now affecting many in the workforce, it has a major and deleterious impact on both individual and national productivity.

The socioeconomic consequences of diabetes and its complications could a seriously negative impact the economies of developed and developing nations.

The most recent Standards of Medical Care in Diabetes published by the American Diabetes Association (ADA) emphasize that early diagnosis and monitoring are critical for preventing or delaying the onset of acute complications and lowering the risk of long-term complications of diabetes . The A1C test should be performed using a certified method by the National

Glycohemoglob in Standardization Program (NGSP) and standardized or traceable to the Diabetes Control and Complications Trial (DCCT) reference assay. Although point-of-care (POC) A1C assays may be NGSP-certified, proficiency testing is not mandated for performing the test, so the use of these assays for diagnostic purposes may be problematic.

Epidemiological data show a similar relationship of A1C with the risk of retinopathy as seen with FPG and 2-h PG. The A1C has several advantages to the FPG and OGTT, including greater convenience (fasting not required), possibly greater pre-analytical stability, and fewer day-to-day perturbations during stress and illness. These advantages must be balanced by greater cost, the limited availability of A1C testing in certain regions of the developing world, and the incomplete correlation between A1C and average glucose in certain individuals [3].

FPG is highly vulnerable to a number of pre analytical variables including recent food ingestion, sample storage, high within-subject biological variability, acute stress and diurnal variations, common drugs which influence glucose metabolism such as corticosteroids, fibrates, cyclosporine, beta-blockers, sulfamethoxazole, thiazide diuretics, and thyroid hormones, among others. With regard HbA1c, well-recognized drawbacks include a lower diagnostic performance in specific populations such as pregnant women, the elderly and non-Hispanic blacks, the risk of over diagnosing diabetes in the presence of iron deficiency anemia (i.e , hemoglobin level lower than 130 g/L in males and 120 g/L in females, respectively), and in subjects genetically predisposed to hyperglycation, the uncertain significance of this measure in subjects with increased red blood cell turnover (e.g , hemolytic anemia, major blood loss, athletes), end-stage renal disease or heavy alcohol consumption, the interference from hemoglobin variants, potentially larger analytical imprecision when not using high pressure liquid chromatography (HPLC), and the higher costs compared to glucose measurement. In particular, genetic variants such as hemoglobin S and C traits or elevated fetal hemoglobin along with chemically modified derivatives of hemoglobin (eg, carbamylated hemoglobin in patients with impaired renal function) can substantially reduce the accuracy of HbA1c measurements. The bias is mainly dependent on the specific hemoglobin variant and method used for measuring HbA1c [4].

Glycaemic control status was defined according to the HbA1c target of < 7% as recommended by the American Diabetes Association for non-pregnant adults [5].

Interestingly, the American Diabetes Association ADA has acknowledged that in patients in whom HbA1c and blood glucose are unreliable (especially those with hemoglobinopathies, altered red cell

turnover or impaired renal function), the assessment of other indices of chronic glycemia may be advisable, although their relation with average glucose and prognosis remains uncertain. These alternative measures essentially include Fructosamine and glycated albumin (GA) [6].

The A1C test should be performed using a method that is certified by the NGSP and standardized or traceable to the Diabetes Control and Complications Trial (DCCT) reference assay. Although point-of-care (POC) A1C assays may be NGSP certified, proficiency testing is not mandated for performing the test, so use of POC assays for diagnostic purposes may be problematic and is not recommended.

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The A1C has several advantages to the FPG and OGTT, including greater convenience (fasting not required), greater pre analytical stability, and less day-to-day perturbations during stress and illness. These advantages must be balanced by It is important to take age, race/ethnicity, and anemia/ hemoglobinopathies into consideration when using the A1C to diagnose diabetes [7].

Glycated haemoglobin (HbA1c) was initially identified as an “unusual” hemoglobin in patients with diabetes over 40 years ago. After that discovery, numerous small studies were conducted correlating it to glucose measurements resulting in the idea that HbA1c could be used as an objective measure of glycaemic control. The A1C-Derived Average Glucose (ADAG) study included 643 participants representing a range of A1C levels. It established a validated relationship between A1C and average glucose across a range of diabetes types and patient populations. HbA1c was introduced into clinical use in the 1980s and subsequently has become a cornerstone of clinical practice [8].

The A1C has several advantages compared with the FPG and OGTT, including greater convenience (fasting not required), greater preanalytical stability, and less day-to-day perturbations during stress and illness. However, these advantages may be offset by the lower sensitivity of A1C at the designated cut point, greater cost, limited availability of A1C testing in certain regions of the developing world,and the imperfect correlation between A1C and average glucose in certain individuals.

National Health and Nutrition Examination Survey (NHANES) data indicate that an A1C cut point of 6.5% (48 mmol/mol) identifies a prevalence of undiagnosed diabetes that is one-third of that using glucose criteria [9].

Fructosamine measurement was able to confirm poorly-controlled diabetes and assist in improving diabetes control. Fructosamine is unaffected by disorders of red blood cells, which have a profound potential influence on HbA1c. Fructosamine also has the advantage of accurately reflecting shorter-term changes in glycemia that correspond to the half-life of albumin. In diabetic patients with HbA1c values below the lower limit of normal, a routine Fructosamine level should be performed [10].

One such marker is fructosamine which relates to average levels of glucose during the preceding 1 to 3 weeks. Fructosamine may give an earlier indication of poorly controlled glucose compared to HbA1c. It is a simple, robust and inexpensive biomarker that could potentially be a useful tool in large epidemiological and clinical studies either as a standalone indicator of hyper glycaemia or in combination with glucose and HbA1c [11]. Importantly, fructosamine may be reliably measured irrespective of fasting or non-fasting. However, fructosamine is rarely used in clinical practice and has not been extensively evaluated as an indicator of diabetes and its micro-and macro vascular complications in large population based studies. Various cut-offs for fructosamine as well as correlations to glucose and HbA1c have been published based on rather small cohorts of patients [12]. Recently, fructosamine has been showed to be an independent biomarker to predict incident diabetes and its microvascular complications [13].

Previously, monitoring long-term glycaemic control relied on tests such as ‘24 hour urinary collections’ and ‘daily blood glucose profiles’ and fructosamine. [14]. In comparison, HbA1c is a more reliable measure of glucose control, no fasting is required and only requires a single venous blood sample [15].

Results

Fifty Sudanese diabetic patients aged from 30 to 60 years old , 33 males (66%) and 17 females (34 %). Each subject of the study group was identified based on the duration of diabetes from which 22 subjects are less than 5 years duration and 28 subjects are 5 years duration or more. According to the use of treatment of which 24 subjects are insulin dependent , 22 subjects are using other treatments and 4 subjects are not using any treatment for diabetes. On the basis of diabetic complications 5 subjects of the study group are suffering from retinopathy , 10 subjects suffering from nephropathy , and 7 subjects have being suffered from non ketotic hyperglycemia.

Table(1) sensitivity and specificity of HbA1C and fructosamine.

	Sensitivity	**Specificity**
HbA1c	86%	25%
FA	63%	55%

Table (1) show that hemoglobin A1C have (86%) sensitivity and (25%) specificity while fructosamine have (63%) sensitivity and (55%) specificity.

Table (2) according to HbA1c results identify how many diabetic patients are glycemic controlled or glycemic uncontrolled

	HbA1c	
Controlled(HbA1c < 6.5%)		Uncontrolled(HbA1c ≥ 6.5%)
N=	10	40
Total	50	

Table (3) according to fructosamine results identify how many diabetic patients are glycemic controlled or glycemic uncontrolled

	Fructosamine	
Controlled(1.9-2.9mmol/l)		Uncontrolled(>2.9mmol/l)
N=	21	29
Total	50	

Table (4) How many member of the study group according to HbA1c and Fructosamine results correlation

	HbA1c controlled but fructosamine uncontrolled	Fructosamine controlled but HbA1c uncontrolled	HbA1c controlled and fructosamine controlled	HbA1c uncontrolled and fructosamine uncontrolled
N=	4	14	6	26
Total	50			

Table (5) Mean values of HbA_{1c}% differences according to duration of the disease

Duration of DM	N	Mean	Std. Deviation
< 5 years	22	6.37	1.45
5 years and more	28	8.36	1.79

Table (5) shows that the mean of HbA1c% among study subjects with duration of disease less than 5 years was 6.37±1.45, compared to 8.36±1.79 in subjects with duration of disease 5 years and more.

Table (6) Mean values of fructose amine (mmol/L)differences according to duration of the disease

Duration of DM	N	Mean	Std. Deviation
< 5 years	22	3.53	1.00
5 years and more	28	5.20	0.99

Table (6) shows that the mean value of fructose amine (mmol/L) among study subjects with duration of disease less than 5 years was 3.53±1.00, compared to 5.20±0.99 in subjects with duration of disease 5 years and more.

Discussion

Our study that aimed to correlate between fructosamine and hemoglobinA1c in Sudanese diabetic patients in Omdurman Teaching Hospital and Diabetic and Endocrine Center in Bahri . In this

study found that fructoseamine has a specificity of 55% and sensitivity of 63%, while HbA1c has a specificity of 25% and a sensitivity of 86%. Therefore fructosamine is of high specificity but low sensitivity compared with hemoglobin A1c, this study disagrees with a study made in comparison of HbA1c and fructosamine in diagnosis of glucose tolerance abnormalities found good specificity of HbA1c and fructosamine (100 and 97% respectively) but low sensitivity (15 and 19% respectively) [16]. The study concluded that neither HbA1c nor fructoseamine seems suitable for diagnosing of mild abnormalities in glucose tolerance.

Significant differences between the two groups were found, higher levels of HbA1c% among those with duration of disease 5 years and more. Significant differences between the two groups were found, higher levels of fructose amine (mmol/L) among those with duration of disease 5 years and more. Both tests are useful-and state that fructosamine may be considered as a substitute in situations where HbA1C cannot be reliably measured instance where fructosamine may be a better monitoring choice than HbA1c include: rapid monitoring effectiveness of diet or medication adjustment,and diabetic pregnancy , shortened red blood cells life span such as hemolytic anemia or blood loss, in abnormal form of hemoglobin. Fructosamine have short life span (14 days) therefor it could be used for routine diabetic glycemic control tests to avoid the complication specially in gestational and juvenile diabetets.

Conclusion:

Due to limitations of the test, HbA1c is a dynamic test affected by age, pregnancy, different laboratory standards and co-morbid disease such as haemoglobinopathies, renal failure and the long duration of the test. Therefore, fructosamine able to used instead of HbA1c for most routine purposes while retaining occasional HbA1c estimation . In diabetes serum fructosamine assay can better reflect average blood glucose concentration over the previous 2-3 weeks and HbA1c is better reflective over the previous 8-10 weeks there for fructosamine can be used as routine test while HbA1C as a first -line screening test.

Recommendations:

We recommended to investigate more sample size and investigate juvenile and gestational diabetes to aid in the avoiding of diabetic complications.

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