Research Article

Predictive Value of Glycated Albumin in Haemodialysis Diabetic Patients

Fatma El-Zahraa S. El-Bokhary, Elham A. Mohamed, Waleed Mohamed, and Samar E. Mohamed
Department of Internal of Medicine, El-Minia Faculty of Medicine

Abstract
Diabetes mellitus is a condition primarily defined by the level of hyperglycaemia giving rise to risk of microvascular damage (retinopathy, nephropathy and neuropathy). Diabetes mellitus is already the leading cause of end-stage kidney disease (ESKD). The aim of management of diabetic patients is to avoid acute and to prevent the long-term complications. Challenges in improving glycemic control in patients with advanced CKD (including ESRD). While HbA1c is well established as a marker for diabetes complications, Glycated albumin is a measurement of a marker directly linked to serious DM complications. Glycated albumin is better correlated to fasting plasma glucose than HbA1c, and it is a more sensitive indicator of short-term variations of glycemic control.
Keywords: Glycated Albumin, Haemodialysis

Introduction
Diabetes mellitus is a chronic disease caused by inherited and/or acquired deficiency in production of insulin by the pancreas, or by the ineffectiveness of the insulin produced. Such a deficiency results in increased concentrations of glucose in the blood, which in turn damage many of the body's systems, in particular the blood vessels and nerves (WHO, 2018).

DM is a condition primarily defined by the level of hyperglycaemia giving rise to risk of microvascular damage (retinopathy, nephropathy and neuropathy). It is associated with reduced life expectancy, significant morbidity due to specific diabetes related microvascular complications, increased risk of macro vascular complications (ischaemic heart disease, stroke and peripheral vascular disease), and diminished quality of life (WHO, 2018).

DM is associated with a number of complications acute metabolic and chronic complications.

In Both type 1 and type 2 diabetes, various genetic and environmental factors can result in the progressive loss of β cell mass and/or function that manifests clinically as hyperglycaemia. Once hyperglycaemia occurs, patients with all forms of diabetes

are at risk for developing the same chronic complications, although rates of progression may differ. The identification of individualized therapies for diabetes in the future will require better characterization of the many paths to Beta cell demise or dysfunction (Skyler et al., 2017).

patients with type 2 DM may have insulin levels that may be normal or elevated, the higher blood glucose levels in these patients would be expected to result in even higher insulin values had their B cell function been normal. Thus, insulin secretion is defective in these patients and insufficient to compensate for insulin resistance. Insulin resistance may improve with weight reduction and/or pharmacologic treatment of hyperglycemia but is seldom restored to normal (Marselli et al., 2014)

These complications develop over many years due to chronic hyperglycemia affect blood vessels include microvascular due to damage to small blood vessels like retinopathy leading to blindness, kidneys (nephropathy) leading to renal failure and to

nerves (neuropathy) , and macrovascular due to damage to larger blood vessels leading to impotence and diabetic foot disorders (which include severe infections leading to amputation and cardiovascular diseases such as heart attacks, strokes.
There is evidence from large randomized-controlled trials that good metabolic control in both type 1 and 2 diabetes can delay the onset and progression of these complications Diabetic kidney disease is defined by elevated urine albumin excretion or reduced glomerular filtration rate (GFR) or both is a serious complication that occurs in 20% to 40% of all diabetics. Approximately one-third of diabetic patients showed micro albuminuria after 15 years of disease duration and less than half develop real nephropathy. Early and tight control of diabetes is the corner stone for the management of diabetic kidney disease (DKD) (Gheith et al., 2016).

The measurement of the non-enzymatically glycated deriIvatives of haemoglobin and plasma proteins has provided a reliable index of long term blood glucose control of proven value to the management of patients. Despite serious consideration, however, their measurement has not been shown to be reeliable in the diagnosis of diabetes mellitus.(Eva Lester, 1989)

Glycemic management in patients with type 2 diabetes and CKD has become increasingly complex over the last 2 decades. Challenges in improving glycemic control in patients with advanced CKD (including ESRD) include therapeutic inertia, monitoring difficulties, and the complexity of available treatments. (Williams et al., 2014)

HbA1c is the most predominant fraction of HbA1, and it is formed by the glycation of terminal valine at the β-chain of hemoglobin. It reflects the patient's glycemic status over previous 3 months. HbA1c is widely used as a screening test for diabetes mellitus, and American Diabetes Association has recently endorsed HbA1c $\geq$ 6.5% as a diagnostic criterion for diabetes mellitus

Albumin is the most common protein found in serum, making up about 80% of the circulating blood plasma. It is replaced in the body approximately every 20-25 days. As with other proteins in the body, it is subject to glycation by excess sugar. Glycated albumin measurement monitors diabetes complications by showing damage to proteins over the previous 2-3 weeks. A comparison with total albumin provides a simple, stable index of glycation over the test period, and closes the information gap that now exists between daily blood glucose testing and glycated hemoglobin testing

Plasma glycated albumin is better correlated to fasting plasma glucose than HbA1c, and it is a more sensitive indicator of short-term variations of glycemic control than HbA1c is during treatment of diabetic patients. Analyzing the serum albumin levels which have been glycated allows for the accurate measurement of glycemia. Moreover, glycated albumin plays a dual role in diabetes complications. It acts as an indicator or marker of intermediate glycation and as a causative agent of the damage of diabetes complications. Glycated albumin has been specifically implicated as a casual factor in atherosclerosis and kidney damage

Materials and Methods

This prospective cross sectional study included 40 ESRD DM patients after informed written consent. Patients were selected from Minia University haemodialysis unit the patients were followed at the start and after 6m of regular haemodialysis. patient group were subdivided in to 2 groups according to diabetic complications.

Exclusion criteria:

Any patient with any of the following criteria were excluded from the study:

- Type- 1DM
- HCV Abs positive patients
- Conditions that affect blood homeostasis such as acute and chronic blood loss, hemolytic anemia, and splenomegaly, haemoglobinopathies.

Clinical Study

All patients were subjected to

- Full history taking and clinical examination.
- Patients were interviewed according to a standard questionnaire about clinical characteristics that included;
- Smoking status (non-smokers, ex-smokers or current smokers),
- Duration of diabetes, treatment (oral hypoglycaemic drugs/ insulin) dose of medication after start haemodialysis, history of hypoglycaemia or diabetic complication (IHD, recurrent infections, retinopathy and diabetic foot).
- History of hypertension or presence of cardiovascular disease (CVD) (defined as previous myocardial or cerebral infarction) & current medication of angiotensin-converting enzyme inhibitors (ACEI) and/or angiotensin II receptor blockers (ARBs), or statins and erythropoietin stimulating agents.
- Hemodialysis history (duration of HD, dry weight, UF volume and HD complication).
- Calculation of body mass index Liver cirrhosis

Laboratory investigations:

Consent for the collection of 10 ml of blood for laboratory tests was obtained from all study subjects and were subjected to:

1) Hemoglobin A1c (glycated haemoglobin).
2) Glycated albumin .
3) Fasting blood sugar:
4) Fasting insulin
5) Lipid profile: Serum total cholesterol, and triglyceride concentrations

Sampling

5ml of blood was withdrawn by sterile venipuncture after 12 hours of fasting, before starting haemodyalysis session. samples are left to be clotted then centrifuged and the separated serum was divided into aliquates. One was designated for the immediate assessment of fasting blood glucose ,s.insulin and lipid profile . The rest of serum was stored at -20 c for subsequent assay of glycated albumin .Another 2ml of blood sample was withdrawn for assessment of HBA1c

Statistical method

The collected data were coded, tabulated, and statistically analyzed using SPSS program (Statistical Package for Social Sciences) software version 25. Descriptive statistics were done for parametric quantitative data by mean ± standard deviation, and for non-parametric quantitative data by median and interquartile range (IQR), while they were done for categorical data by number and percentage. Distribution of the data was done by Shapiro Wilk test.

Results

Table (1): Comparison of glucose level between control and patients' groups

Variables		Patients	Control	P value
		NO=40	NO=20	
HbA1c %	Range Mean ± SD	(5.8-10.4) 6.9±1.5	(4-5.5) 4.7±0.5	<0.001*
GA (Umol/L)	Range Mean ± SD	(2.7-6.9) 3.4±0.8	(0.7-1.9) 1.0±0.2	<0.001*

Table (2): Comparison of clinical data between patients' subgroups

Variables		Controlled DM group NO=18	Uncontrolled DM group NO=22	P value
HD complications	No Hypoglycemia Hypotension Cramps	12(66.7%) 5(27.8%) 1(5.6%) 0(0%)	13(59.1%) 2(9.1%) 6(27.3%) 1(4.5%)	0.136
Erythropoietin dosage	Range Mean ± SD	(2-3) 2.6±0.5	(2-3) 2.6±0.5	0.827

Discussion

Improve glycemic control reduces micro- and macro-vascular complications in patients with diabetes mellitus. HbA1c has been a cornerstone in the evaluation of haemodialysis diabetic patients (Williams et al., 2014). According to the NKF-KDOQI (National Kidney Foundation–Kidney Disease Outcomes Quality Initiative) guidelines, HbA1c targets are no different in diabetic patients with and without CKD. However, it now is well understood that HbA1c level may overestimate glycemic control in kidney patients: HbA1c levels appear to be lower, leading to underestimation of hyperglycemia. A lack of correspondence in clinical studies between HbA1c level and other measures of glycemia has inspired concerns about the validity of the latter in predicting outcomes in patients with advanced CKD (including ESRD). Other measures of glycemic control, such as glycated albumin, may be more useful in CKD (Am J Kidney Dis. 2014).

Intensive glycemic control was analogous to conventional glycemic control In the general population, the landmark Diabetes Control and Complications Trial (DCCT) and the follow-up Epidemiology of Diabetes Interventions and Complications (EDIC) studies demonstrated that intensive vs. standard glycemic control reduces microvascular complications and cardiovascular disease, respectively, in type 1 diabetic, intensive treatment was observed to reduce microvascular complications among type 2 diabetic patients with in the 10-year follow-up, a reduction in myocardial infarction and all-cause death was also observed in the intensive treatment group despite an attenuation in glycemic differences between the intensive and standard treatment groups over time. HbA1c is the most predominant fraction of HbA1, and it is formed by the glycation of terminal valine at the β-chain of hemoglobin. It reflects the patient's glycemic status over previous 3 months. HbA1c is widely used as a screening test for diabetes mellitus, and American Diabetes.
Association has recently endorsed HbA1c ≥6.5% as a diagnostic criterion for diabetes mellitus Iron defecency anemia affect A1c level.

Glycated albumin is better correlated to fasting plasma glucose than HbA1c, and it is a more sensitive indicator of short-term variations of glycemic control than HbA1c is during treatment of diabetic patients (Danese et al., 2015).

References

1. American Diabetes Association. (2018). 2. Classification and diagnosis of diabetes: standards of medical care in diabetes—2018. Diabetes care, 41 (Supplement 1), S13-S27.
2. American Diabetes Association. (2018). 8. Pharmacologic approaches to glycemic treatment: Standards of Medical Care in Diabetes-2018. Diabetes care, 41(Suppl 1), S73.
3. Williams, M.E. &Garag, R.(2014). Glycemic management in ESRD and earlier stages of CKD. American GOurnal of Kidney Disease 63 (2), S22-S38.

4. Danese, E., Mntagnana, M., Nouvenne A., & Lippi, G. (2015) .Advantage and pitfalls of fructosamine and glycated albumin in the diagnosis and treatment of diabetes. Journal of diabetes science and technology ,9(2),169-176.
5. Gheith, O., Farouk, N., Nampoory, N., Halim, M. A., & Al-Otaibi, T. (2016). Diabetic kidney disease: world wide difference of prevalence and risk factors. Journal of nephropharmacology, 5(1), 49.
6. Skyler, J. S., Bakris, G. L., Bonifacio, E., Darsow, T., Eckel, R. H., Groop, L., ... & McElvaine, A. T. (2017). Differentiation of diabetes by pathophysiology, natural history, and prognosis. Diabetes, 66(2), 241-255.
7. Marselli L, Suleiman M, Masini M, Campani D, Bugliani M, Syed F, et al. Are we overestimating the loss of beta cells in type 2 diabetes? Diabetologia. 2014;57:362–5. doi: 10.1007/s00125-013-3098-3.[PubMed]