

Evaluation Of Serum 1,5 - Anhydroglucitol Levels among Type 2 Diabetic Patients in Basrah

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ABSTRACT

Objective: To determine serum 1,5- anhydroglucitol (1,5-AG) levels among patients with type 2 diabetes (T2D) in Basrah, and to evaluate the changes in 1,5-AG levels with regard to the status of glycaemic control.

Methods: The present study included 76 patients with T2D, 33 males and 43 females, 30-78 years of age. Height, weight, waist circumference, systolic blood pressure, and diastolic blood pressure were measured. Fasting blood glucose (FBG), glycated haemoglobin (HbA1c) and serum 1,5-AG levels were determined.

Results: The study revealed that T2D patients have low serum 1,5-AG concentrations (3.62 ± 1.56) $\mu\text{g/ml}$. The comparative male and female values were (3.69 ± 1.55) $\mu\text{g/ml}$ and (3.57 ± 1.58) $\mu\text{g/ml}$. The vast majority of the included diabetic patients (90.8%) were in a state of poor glycaemic control, with 6.6% have an sub-optimal metabolic control. On the other hand, good glycaemic was documented in 2.6 % of patients. There were no significant differences in plasma 1,5-AG concentrations with regard to the status of glycaemic control ($P > 0.05$).

Conclusion: T2D patients have reduced serum 1,5-AG concentrations. Thus, it could be, potentially, valuable test for the diagnosis of diabetes mellitus. Diabetic patients were in poor glycaemic state. Therefore, they are at a substantial risk for the development of diverse diabetic complications.

Key words: Diabetes mellitus, 1,5-AG level, glycaemic control.

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Introduction:

In the 21st century, Diabetes mellitus (DM) is regarded as the most known non-communicable disease over the globe, occupying the 4th to 5th rank among death causing diseases in developed countries.¹ Diabetes prevalence had been studied in many countries over the world for adult over 20 years in 1995, the outcome of this study manifest that the prevalence of DM in this year scored 4% which equal to 135 million people. The same study also predict a rising in the prevalence to 5.4 % by the year of 2025 which is equal to 300 million people. This increment is especially occur in India, China, and US.² India showed the maximum increases in the last few years with 31.7 million. The prevalence of DM in rural population is one quarter that of urban population, and by this it will have the largest number of diabetic people all over the world.³

One, five-anhydroglucitol (1,5-AG) is a major polyol in the human serum.⁴

It is naturally occurring monosaccharide structurally similar to the D-glucose with an exception for the first position hydroxyl group which is reduced in 1,5-AG.⁵ There is a suggestion that serum level of 1,5-AG reflects glycemic control, and also it is changes sensitively to the alteration in plasma glucose level. In addition, it can act as mirror for postprandial hyperglycemia.⁴

In healthy individuals, the reference value of serum 1,5-AG ranging from 12-40 µg/ml and its half-life lasting for 1-2 weeks.^{6,7}

The concentration of 1,5-AG among diabetic patients may vary from 0.9 to 26.6 µg/ml.⁸ The degree of the reduction in the 1,5-AG serum level is directly proportional to the glycosuria severity.^{8,9} When the normal serum level of glucose has been

restored, the 1,5-AG increased again showing reversible relationship with the glycemic control recovery.^{10,11}

As 1,5-AG level show high stability in euglycaemic persons and doesn't affected by age, gender, and prandial state.^{12,13} Therefore, it is regarded as a sensitive marker for short term glycemic control as it reflect the glycemic control over a period ranging from two days to two weeks among diabetic patients.¹⁴ However, other studies reported that 1,5-AG reflect glucose excursions from 1-3 days to some weeks.¹⁵ These observations make it a powerful predictor for postprandial hyperglycemia, so occupying a plausible helpful role in glycemic control assessment.^{16,17}

The aims of this study were to estimate serum 1,5-AG levels among patients with type 2 diabetes (T2D) in Basrah, and to investigate the changes in 1,5-AG levels with regard to the status of glycaemic control.

Patients and Methods:

This is cross-sectional study conducted from November, 2017 throughout March 2018 and included 76 patients with T2D consulted Endocrinology and Diabetic Center in Al-Mawane General Hospital, Basrah, Southern of Iraq. They were 33 males and 43 females, 30 – 78 years of age. These patients were diagnosed by Consultant Physicains.

The information were obtained from each participant through an already prepared questionnaire form. The questionnaire was based on socio-demographic characteristics that include, age, gender, residency, educational level, smoking habits, and alcohol consumption. Regarding diabetic information, patients were enquired about

diabetes type, duration, current treatment whether insulin or oral anti-hyperglycaemic agents (OHA), and also the presence of diabetic complications, other systemic diseases and other types of treatment.

Physiological measurements were performed including systolic (SBP) and diastolic (DBP) blood pressure, weight and height for the estimation of body mass index (BMI), and waist circumference (WC).

Fasting blood glucose (FBG) was determined using enzymatic kit (GLUC-PAP) from RANDOX Laboratories, United kingdom. Estimation of Hb A1c level was performed by ion - exchange high-performance liquid chromatography (HPLC) using the VARIANT™ program form BIO-RAD. USA. Measurement of serum 1,5-AG level was done by using enzyme linked immunosorbent assay method (ELISA) using kit provided by My Biosource, USA

Data were analyzed in the computer by using SPSS "Statistical Package For Social Sciences Program" Version 23. The results are expressed as [mean + SD, range, percentage]. P value < 0.05 was considered the lowest limit for significance.

Results:

Table 1 presents to socio-demographic characteristics of diabetic patients. Most patients (75%) were between 45 and 64 years of age. The frequency of patient living in urban areas was distinctly greater than those living in rural areas with comparative figures of 72.4% 27.6% . With regard to the educational level, 52.6% of patients completed primary

school with only 2.6% just read and write. The vast majority of patients were non-smokers 82.9%, while current smokers and ex-smoker represented 13.2% and 3.9% respectively.

Clinical characteristics of the studied patients are described in Table 2. The mean levels of the SBP and DBP among males were 134.7 ± 23.2 and 84.4 ± 7.8 mm.Hg respectively. Among females, the comparative frequencies were 136.7 ± 19.4 and 86.1 ± 9.0 mm.Hg. Concerning BMI categories, overweight and grade I obesity were observed in 34.2% and 36.8% of diabetic patients respectively, while grade III obesity was recorded only in 3.9% of patients . On the other hand, most males have central obesity with $WC \geq 102$ cm and a mean of 104.9 ± 13.4 cm. Also, the vast majority of females have $WC \geq 88$ cm with a mean of 107.2 ± 15.1 cm.

Nearly half of patients (48.6%) have diabetes duration from 5-15 years, 28.9% with duration less than 5 years and only 22.4% with duration of more than 15 years. Regarding treatment modalities, the studied diabetic patients showed approximately equal frequencies of type of therapy, where 35.5 % treated by OHA, 31.6% by insulin and 32.9% by both modalities.

Table 3 demonstrated the measured biochemical parameters. The mean value of FBG was 235.33 ± 81.14 mg/dl. The overall mean of HbA1c was $10.47 \pm 1.96\%$. The highest proportion of patients (90.8%) have poor glycemic control ($HbA1c \geq 8\%$). Regarding serum 1,5-AG concentrations among diabetic patients, the reported value was 3.62 ± 1.56 μ g/ml. The male and female figure were 3.69 ± 1.55 and 3.57 ± 1.58 μ g/ml respectively.

As presented in Table 4, there were no significant differences in serum 1,5-AG

Discussion:

DM is considered as a universal health problem that may occur at any age.¹⁸

The prevalence of DM shows growing burden within the short future.¹⁹ In addition to the broad spectrum of complications frequently encountered in this syndrome.²⁰ These clinical consequences may appear even in pre-diabetic stage among those with impaired fasting glucose (IFG) and impaired glucose tolerance (IGT).²¹⁻²⁵ Thus an imperative need have been arisen for more intensive and sensitive marker that's not only predict the blood glucose level but also revealed a recent hyperglycemic excursions.²⁶

Unfortunately the vast majority of our diabetic patients where in poor glycemic status, where, 90.8% of the included patients have HbA1c \geq 8 %. This state of poor metabolic control implies that these patients at a considerable risk of macro- as well as micro- vascular complications.^{27,28} This finding is comparable to the observation of other workers.²⁹⁻³¹ In addition, several studies conducted earlier in Basrah revealed that the vast majority of diabetic patients have had distinctly hyperglycemic FBG values. Also, they were in a poor metabolic status reflected by the presence of considerably high HbA1c figures.³²⁻³⁶ Furthermore, it has been reported that the frequency of metabolic syndrome among diabetic patients in Basrah was considerably high.³⁷ This imposed a further increment in cardiovascular disease risk among our

concentrations among the studied patients with regard to the status of metabolic control ($P > 0.05$).

diabetic patients putting them at a substantial risk for the development of cardiovascular events.

This study obviously illustrated that diabetic patients have distinctly reduced serum 1,5-AG concentrations. This finding is consistent with the results of low serum 1,5-AG level reported by several workers.^{10,13,16,17,26,38-43} The present study demonstrated that the majority of the included patients showed profound hyperglycaemia as indicated by the distinctly high FBS. This fact of marked hyperglycaemia resulted in the reduction of the 1,5-AG level in blood among these patients. The reduction was attributed to the competition mechanism occurs between glucose and 1,5-AG on the reabsorption site in the proximal renal tubules.^{43,44} During hyperglycaemic episode, when the glucose excretion overwhelm its reabsorption, sodium glucose active co-transporter 4 (GLUT 4) system participated in the reabsorption process. This system for unknown reasons would favor glucose reabsorption rather than 1,5-AG, leading to a decrease 1,5-AG reabsorption, and hence plasma 1,5-AG level is consequently reduced.⁴⁴

Low plasma level of 1,5-AG among patients with T2D is associated with several advantages in clinical setting. Firstly, it can be valuable tool for screening of diabetes among subjects with high probability of DM.⁴⁵ It has been proposed that plasma 1,5-AG could be used as useful marker for DM screening especially when

combined with FBG.⁴⁶ Secondly, measuring plasma level of 1,5-AG may be helpful in the confirmation of the DM diagnosis among symptomatic individuals were the demonstration of low level is sufficient for the diagnosis. Several workers emphasize on the diagnostic significance of plasma 1,5-AG determination in the confirmation of the presence of DM.^{45,47} These two points, definitely required the removal of the current overlap existing in the lower part of the normal range of blood level of 1,5-AG with the diabetic range, and also the establishment of clear-cut value to differentiate between normal and abnormal 1,5-AG blood values.

The third point regarding the utility of measuring the level of blood 1,5-AG concentration, is that it may be particularly helpful in the assessment of the status of metabolic control among diabetic patients especially if serial determinations of serum 1,5-AG levels are performed in order to follow the changes in 1,5-AG homeostasis. This is of paramount importance during the period of hyperglycemic crisis or post prandial glycemic excursions. Several workers proposed that plasma 1,5-AG estimation may be particularly helpful in the assessment of the glycemic control among patients with DM.⁴⁸⁻⁵¹

The present study revealed no significant differences in serum 1,5-AG levels with regard to HbA1c. There is a wide area of controversy with regard to the pattern of association between HbA1c and blood levels of 1,5-AG. On one hand, some studies showed contradictory findings in comparison to the present study. These

emphasized that plasma 1,5-AG reflect the glycemic excursion and post prandial hyperglycemia more sensitively and robustly in patients with good glycemic control when HbA1c figures are 8% and below.^{9,17,50,52} Thus in patients with well to moderately glycemic control, 1,5-AG could be regarded as useful indicator of daily glycaemic excursions as well as an ancillary and even better marker than HbA1c in the evaluation of the deteriorating glycemic control.²⁶

On the other hand, other workers demonstrated different results. They illustrated that 1,5-AG level in the blood wasn't better than HbA1c as predictor for hyperglycemia.⁵³ In addition, several other reports also illustrated no relationship between 1,5-AG and HbA1c.^{54,55} This is in contrast with other studies that revealed that 1,5-AG show high specificity and sensitivity to even tiny glycemic excursions, even with slight increment in HbA1c.^{10,42,43}

We conclude that T2D patients have distinctly low serum 1,5-AG levels. This implies that measurement of serum 1,5-AG concentration could be a potential candidate as a diagnostic test for diabetes. Diabetic patients were obviously in poor glycaemic state. Thus, they are considerably at more risk for the occurrence and progression of diabetic complications.

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Table 1. Socio- demographic characteristics of diabetic patients.

Characteristic		No.	%
Age (years)	25-44	11	14.5
	45-64	57	75
	≥65	8	10.5
Gender	Males	33	43.4
	Females	43	56.6
Residency	Urban	55	72.4
	Rural	21	27.6
Educational Level	Illiterate	15	19.7
	Just read and write	2	2.6
	Primary school	40	52.6
	Secondary school and more	19	25
Smoking habit	Non-Smoker	63	82.9
	Current-Smoker	10	13.2
	Ex-Smoker	3	3.9

Table 2. Clinical characteristics of diabetic patients.

Characteristic		No.	%	Mean ± SD	
BP (mm.Hg)	SBP (males)			134.7 ± 23.2	
	DBP (males)			84.39 ± 7.8	
	SBP (females)			136.7 ± 19.4	
	DBP (females)			86.0 ± 9.0	
BMI (Kg/m²)	Overall			30.9 ± 4.9	
BMI groups	Normal range 18.5- 25	6	7.9		
	Over weight 25- 30	26	34.2		
	Grade I obesity 30- 35	28	36.8		
	Grade II obesity 35-40	13	17.1		
	Grade III obesity ≥40	3	3.9		
WC (cm)	Males	< 102	10	30.3	104.9 ±13.4
		≥102	23	69.7	
	Females	< 88	2	4.7	107.2 ± 15.1
		≥ 88	41	95.3	
Duration of DM (years)	< 5	22	28.9	9.4 ±5.5	
	5 – 15	37	48.6		
	≥ 15	17	22.4		
Treatment modality	Insulin	24	31.6		
	OHA	27	35.5		
	Both insulin and OHA	25	32.9		

Table 3. Biochemical characteristics of diabetic patients.

Parameter		No.	%	Mean ± SD	Range
FBG (mg/dl)	100-125.9	6	7.9	235.33 ± 81.14	100- 406.8
	≥ 126	70	92.1		
HbA1c (%)	< 7	2	2.6	10.47 ± 1.96	6.6 – 15.3
	7- 7.9	5	6.6		
	≥ 8	69	90.8		
1,5-AG (µg/ml)		76	100	3.62 ± 1.56	0.15 – 7.7

Table 4. Status of glycemic control and serum 1,5-AG levels among diabetic patients.

Glycemic status	HbA1c (%)	No.	%	1,5-AG (µg/ml)	P- value
Optimal control	< 7.0	2	2.6	5.04 ± 2.47*	0.271
Acceptable control	7.0 - 8.0	5	6.6	2.94 ± 1.49*	
Poor control	≥ 8.0	69	90.8	3.63 ± 1.53*	
Total	Total	76	100.0	3.62 ± 1.56*	

*Data of serum 1,5-AG are given as X ± SD

P > 0.05

تقييم مستويات ١,٥ انهاييروكلوسيتول عند مرضى السكري من النوع الثاني

كلية الصيدلة – جامعة البصرة

فرع الكيمياء الحياتية، كلية الطب | جامعة البصرة - البصرة | العراق

صفا كفاح قاسم

سلمان كاظم عجلان

الخلاصة:

الهدف: دراسة مستويات ١,٥ انهاييروكلوسيتول عند مرضى السكري من النوع ٢.

المواد و طرق العمل: في هذه الدراسة تم شمول ٧٦ من مرضى السكري من النوع ٢، وكانوا ٣٣ ذكرا و ٤٣ أنثى، تراوحت أعمارهم بين ٣٠-٧٨ سنة. تم قياس الطول، الوزن، محيط الخصر و ضغط الدم. تم تحديد مستويات سكر الدم، خضاب الدم السكري و ١,٥ انهاييروكلوسيتول في الدم.

النتائج: أظهرت الدراسة انخفاض مستويات ١,٥ انهاييروكلوسيتول عند مرضى السكري من النوع ٢ ($3,62 \pm 1,56$ مايكروغرام/مل)، وكانت المستويات لدى الذكور والإناث هي ($3,69 \pm 1,55$ مايكروغرام/مل) و ($3,57 \pm 1,58$ مايكروغرام/مل) على التوالي. كانت السيطرة السكرية سيئة عند الغالبية العظمى من المرضى (٩٠,٨%)، بينما كانت السيطرة السكرية مقبولة عند (٦,٦%) من المرضى، وكانت مثالية عند (٢,٦%) فقط من المرضى. لم تكن هنالك اختلافات معنوية في مستويات ١,٥ انهاييروكلوسيتول حسب درجة السيطرة السكرية ($p < 0,05$).

الاستنتاجات: كانت مستويات ١,٥ انهاييروكلوسيتول منخفضة عند مرضى السكري من النوع ٢، مما قد يشير الى دور محتمل له في تشخيص مرض السكري. كانت السيطرة السكرية سيئة عند المرضى مما يجعلهم و بشكل كبير أكثر عرضة للأصابة بالمضاعفات المتعددة للمرض.

مفاتيح الكلمات: مرض السكري، مستوى ١,٥ انهاييروكلوسيتول، السيطرة الأيضية.