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The Correlation of HbA1c with Serum Electrolytes among Type 2 Diabetic Patients in Atbara, River Nile State, Sudan

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Abstract: ***Background***: Diabetes mellitus in Sudan is a growing health problem that is associated with poor glycemic control in all socio-economic classes. This is a study that was conducted in Naserldeen Karamalla diabetic center located at Atabara River Nile state. ***Aims***: The study aimed to evaluate the relationship between glycated hemoglobin (HbA1c) and serum electrolytes in type 2 diabetic patients. ***Methods***: The present study was a Cross-sectional, descriptive hospital-based study. A total of 500 type 2 diabetics with ages ranging from 15 to 87 years volunteered to participate in this study. The glycated hemoglobin (HbA1c), and serum electrolyte & were measured with standard procedure. The statistical analysis was done by using SPSS version 20. ***Results***: The mean HbA1c was 10.8±6.6 %. (96.6%) of the patients who had poor glycemic control (HbA1c >60.5) the mean Mg, Ca, Na, K, and Cl was 2.06±0.68, 9.1 ±3.7, 140.9 ±7.0, 3.9 ±0.41 and101.04 ±7.7 respectively. In this study, the correlation between Mg+2 and HbA1c was statistically insignificant (*P. value* =0.765) and between Ca 2+ and HbA1c was statistically insignificant (*P. value* = 0.586). Insignificant correlation between Na+ and HbA1c *P value* = 0.283). An inverse relation between HbA1C and K+ (*P. value* = 0.020). ***Conclusion***: HbA1c and serum potassium were negatively correlated while sodium, calcium, magnesium, and chloride had an insignificant correlation.

Keywords: Glycated hemoglobin, diabetes mellitus, electrolytes, management, healthcare, correlation.

Research Paper

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INTRODUCTION

Diabetes mellitus (DM) is a chronic, metabolic disease characterized by elevated levels of blood glucose (or blood sugar), which leads over time to serious damage to the heart, blood vessels, eyes, kidneys, and nerves [1]. The origin and etiology of DM can vary greatly but always include defects in either insulin secretion or response or in both at some point in the course of the disease [2]. (DM) prevalence was higher in urban areas than in rural areas due to changes in lifestyle, physical activity, and dependence on high carbohydrate diet and beverages [3]. The prevalence is higher in low and middle-income communities. Diabetes prevalence ranged from 2.6% in rural Sudan to (20%) in urban Egypt [3]. There is a high prevalence of diabetes (19.1%) among the urban population of North Sudan [4]. Insulin affects electrolyte balance. Electrolytes are chemical substances when dissolved in water will be dissociated into electrically charged particles. The principal positively charged ions in the body fluid (cations) are sodium Na+, potassium K+, calcium ca2+, and magnesium Mg2+. The negatively charged anion is chloride (Cl-). Electrolytes are essential to normal body functions. The concentration of each electrolyte differs between intracellular and extracellular fluid and electrolyte imbalance exists when the concentration of any one is too low or too high [5]. Magnesium (Mg2+) is an essential ion for human health, as it is involved in virtually every mechanism in the cell, including energy homeostasis, protein synthesis, and DNA stability [6]. (Mg2+) is a co-factor in several pathways, including glucose transport, insulin sensitivity, and insulin secretion, providing a molecular basis for its involvement in the pathogenesis of DM [7]. In the body, the majority of calcium (Ca2+) is located within the skeleton (99%), where it provides structural support and helps maintain Ca2+ balance through extra-skeletal exchange. A positive association between elevated serum Ca2+ and DM has been observed in several cross-sectional studies [8]. Potassium (K+) is the most abundant cation in the body. It is predominantly restricted to the intracellular space, such that only (2%) is located extracellularly and the remaining (98%) is in the intracellular compartment. Serum K+ is normally regulated around the narrow range of (3.5–5.0 mmol/l) [9]. Although short periods of mild potassium depletion are typically well tolerated in healthy individuals, severe K+ depletion can result in glucose intolerance, serious cardiac problems, renal impairment, and neurologic dysfunction, including death [10]. The most important factors regulating this movement under normal conditions are insulin and catecholamines [11]. Sodium is essential for cellular homeostasis and physiological function. Hyponatremia is a common electrolyte disorder that arises from disturbances in water metabolism [12]. Hyponatremia is defined by a serum Na+ concentration of less than (136 mmol/L) When the sodium level in the blood becomes too low, extra water enters the cells and causes them to swell. Swelling in the brain is especially dangerous because the brain is confined by the skull and unable to expand without causing symptoms [13]. Hypernatremia Na+> 145 mmol/L is caused by primary water deficit (with or without Na+ loss) and commonly occurs from inadequate access to water or impaired thirst mechanism. Chloride (Cl-) is the major strong anion in blood accounting for approximately one-third of plasma tonicity, (97 to 98%) of all strong anionic charges, and two-thirds of all negative charges in plasma. The normal serum range for chloride is 98 - 108 mmol/L. Chloride is distributed in the three major body fluid compartments, plasma, interstitial fluid (ISF), and intracellular fluid [14]. It functions importantly in many fundamental biological processes, including regulation of pH, maintenance of intracellular volume resting membrane potential, and cell differentiation [15]. Hyperglycemia results in nonenzymatic glycosylation commonly referred to as glycation [16]. Glycation is the nonenzymatic attachment of free aldehyde groups of carbohydrates (such as glucose) to the unprotonated free amino groups of proteins (such as hemoglobin). Glycation alters the structure and function of several soluble and insoluble proteins, as well as the structure and function of isolated basement membrane components. These changes are slow and cumulative, resulting in a long time lag between the diagnosis, the onset, and the progression of the complications of DM [17].

MATERIALS AND METHODS

Study Design: Prospective, quantitative, analytical, laboratory-based study.

Study Area:

Sudan, River Nile state, Atbara town, Naser Eldeen Karamalla Diabetic Center. River Nile state lies in Northern Sudan, covering an area (124ooo m2) boarding the capital Khartoum and extending to the border of Egypt in the north. Atbara is one of the important towns. Its geographical coordinates are (17° 41' 50" North, 33° 58' 42" East). Naser Eldeen Awad Karamalla Diabetes Centre was established in 2001, and the number of patients registered is 2787. There is a daily clinic to review the patients by a medical officer besides specialists of internal medicine and pediatrician the center provides advisory services in nutrition and nursing in addition to psychological counseling.

Study Population: All T2DM patients revising diabetic centers.

Sample Size: Five hundred diabetic patients

Sample Size Calculation Method:

Previous studies in the River Nile State (RNS) showed that the prevalence of DM is (19.1%). To obtain a confidence interval of (95%) and a margin of error of (5%). Taking into consideration the total adult population of RNS about (800,000). The estimated sample size that represents the diabetic patients in RNS is: (384) (SurverySystem.com), to allow for non-response and design effect we increased the sample to 500 patients.

Laboratory analysis of HbA1c:

The standard Operating Procedures (SOPs) were adhered to, in the pre-analytical phase by collecting a sufficient amount of sample, at least 3mls of blood for measuring serum electrolytes and at least 3mls for measuring glycosylated hemoglobin levels. Request forms were filled properly with unique patient identification numbers. Blood samples for measuring HbA1c levels were collected in EDTA vacutainers and transported to the laboratory for analysis using an automated HbA1c analyzer machine which used Ichroma α^{TM} It is a fluorescence immunoassay (FIA) for the quantitative determination of HbA1c.

Laboratory analysis of electrolytes:

Venous blood for determination of serum electrolytes was collected in plain red-top vacutainers, labeled properly, and delivered to the laboratory immediately. Upon delivery to the laboratory, the samples were allowed to settle to allow complete clotting then put in a centrifuge and spun at 3000rpm for 5 minutes, the serum was transferred into sample cups and labeled appropriately. The samples were analyzed for electrolyte levels (sodium, calcium, phosphorus, potassium, and chlorides). This was done by use of an automated Selectra prom biochemistry analyzer which is based on the Ion Selective Electrode (ISE) method. The results were then recorded.

Tools of Data Collection:

A questionnaire filled by participants consists of socioeconomic information, diabetes history, type, and treatment name.

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Data Analysis:

All collected data were analyzed using SPSS for Windows, version 20.0. A paired Student t-test was used for calculating the degree of variation, with a P value (≤0.05) considered significant. Analysis of variance (ANOVA) was used for continuous data and the statistical results were presented as means ± SD.

Ethical Clearance and Consent:

Ethical approval was obtained before the study from the Ministry of Health Research Committee. Verbal consent was taken from each respondent before blood collection and questionnaire administration. Respondents were briefed on a full description of the study including benefits and fully entitled to confidentiality and voluntary participation.

RESULTS

In this study, (500) diabetic patients were enrolled and investigated. Clinical and biochemical variables were studied, primarily determining the correlation between the degree of DM control and the serum electrolyte level. The most common age group was (56-60) years accounted for (26.8%). There were (180), (36%) males and (320), (64%) were females (64%). There 210 (58%) were from rural areas and 290 (42%) from urban areas (Table 1). Among diabetic patients (96.6%) had poor glycemic control and 17 (3.4%) had good glycemic control (Table 2). The Pearson correlation test showed that there was an inverse significant relationship between the Hba1c level and K+ level (*P. value* =0.020). The linear model of the relation if HbA1c is an independent variable modified as K=4.070 + (-.007* HbA1c), the ANOVA test proved the linearity with *P. value* (0.020). The R2 of the model was 0.02 (2%). The residuals were not completely independent (Durbin Watson =1.579), and normally distributed (0.00±0.99), but some higher values of data showed as extremes (the case-wise diagnostic -9.176 to 3.18 in comparison to -3 to 3 (Figure 1).

Table 1: Socio-demographic characteristics of diabetic patients (n=500)

Variable	Features	Frequency	Percentage
Sex	Male	180	36.0
	Female	320	64.0
Educational level	Illiterate	136	27.5
	primary/khalwa	208	41.6
	Secondary	115	23.0
	College	41	8.2
Residence	Urban	290	58.0
	Rural	210	42.0
Age of the patient when s/he got DM	15 years	3	0.6
	16 – 20	3	0.6
	21 – 30	30	6.0
	31 – 40	108	21.6
	41 – 50	139	27.8
	51 – 60	129	25.8
	More than 60 years	88	17.6
Duration (years)	Less than one year	10	2.0
	1 - 10	355	71.0
	11 - 20	112	22.4
	21 - 30	15	3.0
	More than 30 years	8	1.6
Type of treatment	Dietary control only	39	7.8
	Insulin	156	31.2
	Hypoglycemic agents	305	61.0
	Poor	12	2.4
Compliance with treatment	Medium	90	18.0
	Excellent	398	79.6

Table 2: Characteristics of glycated hemoglobin (HbA1c) among diabetic patient (n = 500)

HbA1c level	Frequency	Percent (%)
Less than or equal to 6.5	17	3.4
More than 6.5 Poorly controlled	483	96.6
Total	**500**	**100.0**

Mean= (10.8±6.6)

Table 3: Characteristics of serum electrolytes (Mg^{++}, Ca^{++}, Na^{+}, K^{+} and Cl^{-}) in diabetic patients

Ion	Conc.	Frequency	Mean ± Std
Mg^{++} group	less than 1.6 (hypo)	50(10%)	Mean= (2.06±0.68)
	1.6 - 2.4 (Normal)	379 (75.8%)	
	More than 2.4	71(14.2%)	
Ca^{++} group	less than 8 (hypo)	35 (7.0%)	Mean= (9.1±3.7)
	8 - 10 (Normal)	464 (92.8%)	
	More than 10	1 (0.2%)	
Na^{+} group	less than 135 (hypo)	16 (3.2%)	Mean= (140.9±7.0)
	135 - 145 (Normal)	441 (88.2%)	
	More than 145	43 (8.6%)	
K+ group	less than 3.5 (hypo)	33 (6.6%)	Mean= (3.9±0.41)
	3.5 - 5.3 (Normal)	467 (93.4%)	
Cl^{-} group	less than 95 (hypo)	13 (2.6%)	Mean= (101.04±7.7)
	95 - 105 (Normal)	443 (88.6%)	
	More than 105	44 (8.8%)	

Table 4: Relationship between HbA1c and serum electrolytes

Characteristic	Variable	HbA1cgroup		X^2	*P value*
		<6.5 Good	**>6.5 bad**		
Mg^{++} group	less than 1.6 (hypo)	4(7.8%)	47(92.2%)	3.596	0.166
	1.6 - 2.4 (Normal)	25 (6.4%)	363 (93.6%)		
	More than 2.4	1(1.3%)	77 (98.7%)		
Ca^{++} group	less than 8 (hypo)	1 (2.8%)	35 (97.2%)	0.714	0.700
	8 - 10 (Normal)	29 (6.0%)	451 (94.0%)		
	More than 10	0 (0.0%)	1 (100.0%)		
Na^{+} group	less than 135 (hypo)	0 (0.0%)	19 (100.0%)	2.523	0.283
	135 - 145 (Normal)	29 (6.4%)	424 (93.6%)		
	More than 145	1 (2.2%)	44 (97.8%)		
K+ group	less than 3.5 (hypo)	1 (2.9%)	34 (97.1%)	0.569	0.440
	3.5 - 5.3 (Normal)	29 (6.0%)	453 (94.0%)		
Cl^{-} group	less than 95 (hypo)	0 (0.0%)	14 (100.0%)	3.115	0.211
	95 - 105 (Normal)	25 (5.5%)	432 (94.5%)		
	More than 105	5 (10.9%)	41 (89.1%)		

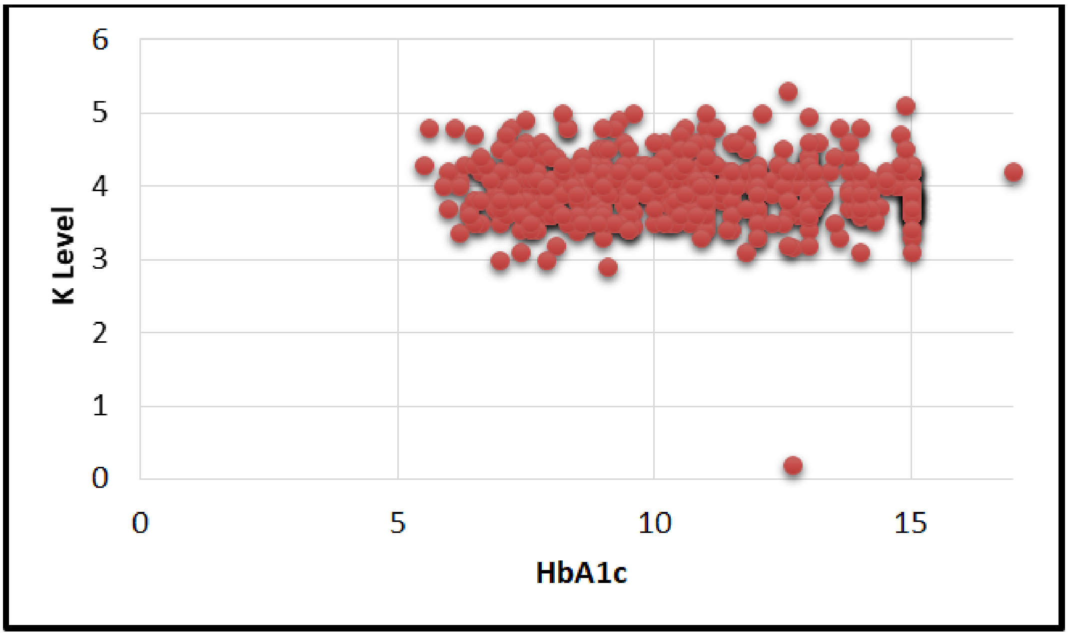

Figure 1: The Scatter Dots of the relationship between HbA1C and K levels

DISCUSSION

Diabetes mellitus (DM) is a systemic metabolic disorder that can lead to diabetic nephropathy (DN), a leading cause of end-stage renal disease around the world [26]. This study was the first to be conducted in River Nile State during the period (January 2016 to June 2018), aiming to determine the relationship between glycated hemoglobin (HbA1c) and serum electrolytes in type 2 diabetic patients. The study included (500) diabetic patients, 180 (36%) were males, while 320 (64%) of the patients were females. The ratio of male to female was consistent with a previous study conducted by Saeed M. Omar and his colleagues [18] who found the ratio was (69.9 to 30.1) and also consistent with a study performed by Wadie M and his colleagues, 2016 [4] who found that the ratio was (45.7 to 53.3). The results of this recently performed study might have a similar explanation as that of a study done by Awad Mohammed and his colleagues 2011 [19] who stated that females cope less with diabetes and have metabolically less control than men also may be due to physiological characteristics of females as they were subjected to hormonal and emotional changes during their life. Concerning the residency, (58%) of the participants were from urban areas. This may be attributed to the migration from poor rural areas to urban areas where most of the services are found allocated there, especially health services. The findings of this present study revealed that the glycemic control indicator (HbA1c > 6.5) was poor in (96.6 %) of the patients. These findings follow a previous study conducted by Noor SK. his colleagues 2017 [20] found that (85%) of their study population (387) had poor glycemic control (HbA1c >7). The results of this study showed a significant increase in the mean of HbA1c (10.82±6.56) of the diabetic patients with (HbA1c > 6.5) compared to the patients with HbA1c <6.5, (*P value* < 0.001). This may be attributed to bad food consumption habits and dependence on carbohydrate-rich meals like Kira, acids, and gorasa, as the same time this explanation possibly might be in harmony with other results and verifications demonstrated by a previous study performed by Moawi 2016 [21]. Furthermore, in addition to all that, sugar consumption is increasing nowadays as in confectionaries, beverages, juices, and other different types of foods in both urban and some rural areas Awad Mohammad and his colleagues 2011[19]. This research depicted that there were no significant differences between the mean± std versus the reference values of (Mg2+, Ca2+, Na+, Cl-). This may be attributed to the duration of diabetes; most of the patients (71%) had diabetes for (1-10) years besides their high consumption of salt (NaCl), moreover, River Nile Water has a high concentration of Ca2+ and Mg2 (www.miracosta.edu/earth_science). The study revealed an inverse relation between HbA1c and K+ (*P value*= 0.020). This result was found to be consistent with Nabil A and his colleagues 2016 [22], who found a significant decrease in the serum levels of Na+ and K+ in all diabetics(*P value* < 0.001). On the other hand different from the results obtained by Khalid Al-Rbean 2011 [23], who found that the association between HbA1c and K+ was insignificant (*P value* = 0.50). Moreover, this study elucidated an insignificant correlation between (Na+ and HbA1c), (*P value* = 0.283), at the same time the result was found to be consistent with Khalid Al-Rbean 2011 [23], who found an insignificant association between Na+ and HbA1c (*P value* =0.120), on the other hand, this result was contradicting the findings of Shenqi Wang 2013 [24], who found that serum Na+ level was negatively correlated with HbA1c (*P value* < 0.010). So, this may be attributed to ethnicity because two studies were conducted in different ethnic groups with different food cultures; Arab world and China. In this study, the correlation between Mg+2 and HbA1c was statistically insignificant (*P value* = 0.166). This result was in disagreement with that obtained by Shenqi Wang 2013 [24], who found that serum Mg+2 level was negatively correlated with HbA1c (*P value* < 0.01) also the result contradicting that obtained by (Osman Evliyaoğlu 2004) [25], who found a strong negative correlation (*P value* <0,001) with serum Mg ve blood HbA1c. This present study showed that the correlation between Ca2+ and HbA1c was statistically insignificant (*P value*= 0.700). This result contradicts that obtained by Shenqi Wang 2013) [24], who demonstrated that serum Ca2+ level was positively correlated with HbA1c (*P value* < 0.050).

CONCLUSIONS

The study found that there is HbA1c and serum potassium were negatively correlated while sodium, calcium, magnesium, and chloride had an insignificant correlation. The findings underscore the need for all-encompassing diabetes management approaches that tackle both electrolyte balance and glucose control.

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Conflict of Interest: The authors have declared that no competing interests exist.

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