Contents lists available at ScienceDirect

Asian Pacific Journal of Tropical Disease

journal homepage: www.elsevier.com/locate/apjtd

Document heading doi: 10.1016/S2222-1808(14)60475-8

Retrospective correlation of fasting glucose and glycated hemoglobin with serum electrolytes, urea and creatinine in diabetic patients

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PEER REVIEW

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Comments

It is a good study for publication as alterations in electrolyte levels in diabetes mellitus is generally not looked into routinely. It also gives further scope of research in this line particularly the status of kidney and its function in diabetes mellitus.
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ABSTRACT

Objective: To assess the relationship of fasting blood glucose and glycated hemoglobin with serum electrolytes *i.e.* sodium and potassium, urea and creatinine in patients with diabetes mellitus for at least a period of ten years.

Methods: One hundred and forty diabetic individuals between the age group 45-70 who were diabetic since at least past 10 years and visited the outpatient department at Kasturba Hospital, Manipal. All the data were obtained from the Kasturba Medical College and Hospital records section. Potassium and sodium levels were estimated by ion selective electrodes indirect method (Cobas 6000). Fasting glucoses were estimated by hexokinase method, serum urea by urease method and serum creatinine by Jaffe´s method (Cobas 6000). Glycated hemoglobins were estimated by ion exchange chromatography using HPLC Variant II Turbo.

Results: The association between sodium with glycated Hb and sodium with fasting glucose is inversely related and their association were statistically significant. The association between potassium with fasting glucose, urea with fasting glucose and creatinine with fasting glucose was found to be statistically insignificant.

Conclusions: Hyperglycaemic hyperosmolar state in diabetes may influence the levels of various serum analytes such as sodium, potassium, urea and creatinine due to dilutional effects. Hence before interpretation of these results, it is suggested that they have to be correlated with serum/urine osmolarity levels.

KEYWORDS

Diabetes mellitus, Dilutional hyponatremia, Osmotic diuresis, Glycated hemoglobin

1. Introduction

Diabetes mellitus is a diverse group of chronic and degenerative metabolic disorders that is characterized by chronic hyperglycemia[1]. Hyperglycemia can predispose to increased blood volume due to osmotic effect which in turn can alter the electrolyte balance due to dilutional effects. Also excessive glucose in urine can draw water resulting in osmotic diuresis which also may influence water and electrolyte balance of our body[2]. Glucose being osmotically active results in a fluid shift from the intracellular spaces causing cellular dehydration. Studies have shown that insulin decreases extracellular potassium which may be by its action on Na-K ATPase. These osmotic effects of glucose can thus alter cationic balance in diabetics which may influence progression and management of diabetes[3].

Glycated hemoglobin (also known as HbA1c) is a form of hemoglobin which is mainly used to identify the average plasma glucose concentration over prolonged duration. When hemoglobin is exposed to plasma glucose, it is converted to glycated hemoglobin by a non enzymatic

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Foundation Project: Supported by the Kasturba Medical College and Hospital (IEC No-65/2013).

Article history:
Received 20 Nov 2013
Received in revised form 30 Nov, 2nd revised form 8 Dec, 3rd revised form 17 Dec 2013
Accepted 27 Dec 2013
Available online 28 Jan 2014

glycation pathway. Normal levels of glucose produce a normal amount of glycated hemoglobin. As the average amount of plasma glucose increases, the fraction of glycated hemoglobin increases in a predictable fashion. This serves as a marker of average blood glucose levels over the previous three months[4].

Long term diabetes can influence the functioning of kidneys and predispose to development of nephropathy. Chronic hyperglycemia is known to affect the filtering system of the kidney which may gradually affects its function. Both serum urea and creatinine are widely used to regularly assess the renal function in diabetics[5].

The aim of this study is to assess the relationship of fasting blood glucose and glycated hemoglobin with serum electrolytes *i.e.* sodium and potassium, urea and creatinine in patients with diabetes mellitus for at least a period of ten years.

2. Materials and methods

Ethics clearance for this study was obtained from the Institutional Ethics Committee, Kasturba Medical College, Manipal. One hundred and forty diabetic individuals not suffering from any renal disease or any other inflammatory conditions were included in the study (Table 1). The subjects were between the age group 45-70 who were diabetic since at least past 10 years and visited the outpatient department at Kasturba Hospital, Manipal. All the data were obtained from the Kasturba Medical College and Hospital records section.

Table 1

Number of males and females (total=140) with mean age of males and females in years.

Gender	Number (%)	Age (in years) (Mean±SD)
Male	95 (67.90)	53.77±13.51
Female	45 (32.10)	56.69±13.51

Potassium and sodium levels were estimated by ion selective electrodes indirect method (Cobas 6000). Fasting glucose were estimated by hexokinase method, serum urea by urease method and serum creatinine by Jaffe's method (Cobas 6000). Glycated hemoglobin were estimated by ion exchange chromatography using HPLC Variant II Turbo. HbA1c was expressed in percentage while fasting blood sugar, urea and creatinine were expressed in milli grams per deciliter (mg/dL) and sodium, potassium were expressed in milliequivalent per litre (mEq/L).

Data were analyzed using statistical package for the Social Sciences (SPSS 20).

3. Results

The level of significance was fixed at 5%. Hence a '*P*' value lesser than 0.05 will be considered as statistically significant.

All the statistical analyses were carried out using SPSS version 20.

3.1. Association between fasting glucose and sodium

Spearman's correlation coefficient was used to determine the association between the variables fasting glucose and sodium. Spearman's correlation coefficient's (rs) value was found to be "-0.72", indicating an inverse relationship and a highly significant association ($P<0.001$) as shown in Figure 1.

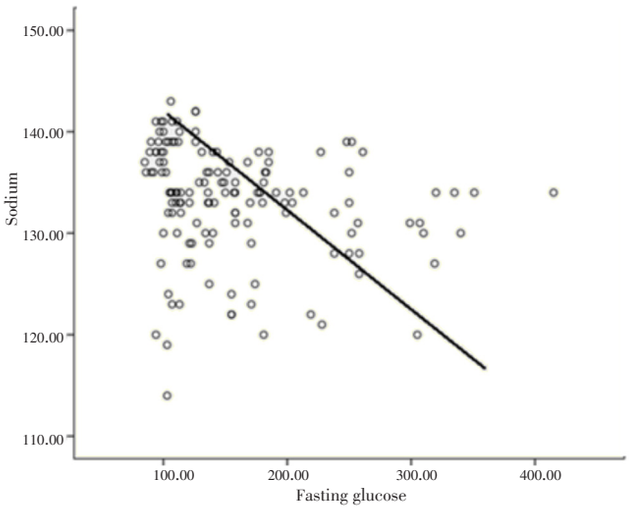

Figure 1. Scatter plot to indicate the association between the variables fasting glucose and sodium.

3.2. Association between sodium and glycated hemoglobin

The value of the Spearman's correlation coefficient (rs) was found to be "-0.70" and the *P* value was found to be <0.001. This shows that the variables sodium and glyco Hb are inversely related and their association is statistically significant as shown in Figure 2.

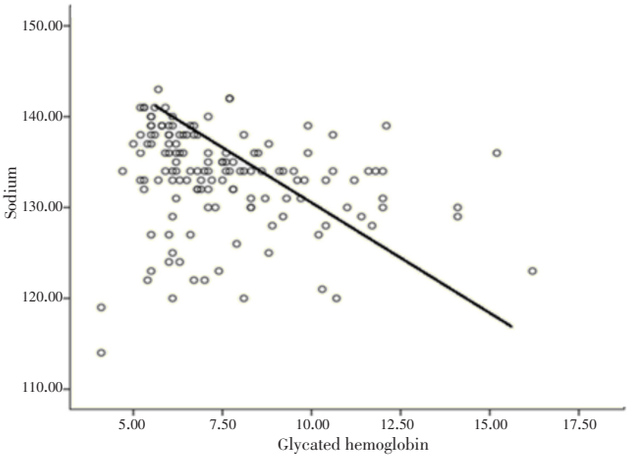

Figure 2. Scatter plot to show the association between the variables sodium and glycated hemoglobin.

3.3. Association between fasting glucose, potassium, urea and creatinine

No significant association was found between fasting glucose, potassium, urea and creatinine as shown in Table 2.

Table 2
Correlation between fasting plasma glucose with potassium, urea and creatinine.

Variables	rs	*P* value
Fasting glucose-Potassium	0.020	0.79
Fasting glucose-Urea	−0.090	0.28
Fasting glucose-Creatinine	−0.004	0.96

4. Discussion

Studies have already shown that hyperglycemia, hyperosmolarity and acidosis are responsible for the electrolyte imbalance associated with diabetes[6,7]. Hyperglycaemia is restricted to the extracellular space so water moves from the intracellular to the extracellular compartment initially, diluting plasma sodium. During the accompanying osmotic diuresis, water is generally lost in excess of sodium until eventually the loss of water is similar for both extracellular and intracellular compartments. Therefore, in diabetes mellitus, plasma sodium concentrations may be artificially lowered. This study demonstrates a notable decrease in the serum sodium levels in the diabetic subjects and this decreased sodium levels has a significant inverse correlation with fasting blood glucose levels. Also when compared with glycated hemoglobin which indicates the average plasma glucose concentration over prolonged duration, the results still remain highly significant. These findings were also demonstrated by Khalid Al-Rubeaan *et al*. in Saudi Arabian diabetic population[8].

On the contrary, the serum potassium levels did not show any significant alteration or correlation with the fasting blood glucose levels.

As already mentioned, serum urea and creatinine are widely used to assess renal function. Studies have shown a significant positive correlation of serum urea and creatinine with blood glucose status[9-15]. However, this present study does not show any significant correlation between the fasting blood glucose and urea and/or creatinine and this variation in results may be due to various factors like duration of diabetes, age or population and relative dilutional effects of hyperglycemia. In diabetics electrolyte disorders occurred often even if the renal function is normal and this fact is supported by our study.

This study therefore shows a strong positive correlation of blood glucose status with serum sodium levels where the potassium levels seem to be unaffected along with urea and creatinine levels.

Hyperglycaemic hyperosmolar state in diabetes may influence the levels of various serum analytes such as sodium, potassium, urea and creatinine due to dilutional effects. Hence before interpretation of these results, they have to be correlated with serum/urine osmolarity levels. If these analytes can be expressed in terms of ratio with respect to osmolarity observed, it may help us to eliminate possible confounders.

Limitations: One of the limitation of this study is that data regarding the osmolarity of serum and urine of all subjects were not available and hence further studies need to be done to support the hypothesis of expression of analytes in terms of ratio with respect to osmolarity. Also studies can be done to verify whether local temperature, humidity conditions and average water intake will have an influence on these analytes.

Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgements

This study is supported by the Kasturba Medical College and Hospital (IEC No-65/2013).

Comments

Background

Hyperglycemia, in diabetes mellitus can predispose to increased blood volume due to osmotic effect which in turn can alter the electrolyte balance due to dilution effects. Also excessive glucose in urine can draw water resulting in osmotic diuresis which also may influence water and electrolyte balance of our body.

Research frontiers

This study has been performed to know the effects

of hyperglycemia particularly in relation disturbances in electrolyte levels in diabetes mellitus subjects. Hyperglycemia is known to cause many adverse effects. Due to its effect on kidneys and fluid balance, it can have an effect on electrolyte levels as well. This study has attempted to know its association.

Related reports

There are not many studies related the hypothesis the authors have formulated for this study. However, the study design is done well. Sample size is fairly adequate. Standard methods have been applied for sample analysis. Appropriate statistical tools have been employed. Results obtained have been presented well.

Innovations & breakthroughs

As such there are no innovations as such. However, based on the defined objectives of the study, a sincere attempt has been made to procure the data and analyse accordingly by application of proper statistical tools. The presentation of results is satisfactory.

Applications

The study focuses on hyperosmolar state as a result of hyperglycemia in diabetes mellitus and its effect on various biochemical analytes, electrolytes in particular. It suggests that such alterations can exist and the need that it must be kept in mind while interpretation of the results.

Peer review

It is a good study for publication as alterations in electrolyte levels in diabetes mellitus is generally not looked into routinely. It also gives further scope of research in this line particularly the status of kidney and its function in diabetes mellitus.

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