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Evaluation of Macro Minerals in Patients with Type II Diabetes Mellitus in Southern Nigeria

A. Z. Ogunleye[1*] and M. F. Asaolu[1]

[1]Department of Biochemistry, Ekiti State University, Ado Ekiti, Ekiti State, Nigeria.

Authors' contributions

This work was carried out in collaboration between both authors. Author MFA designed the study, wrote the protocol, supervised the work and edited the manuscript. Author AZO carried out all laboratories work, performed the statistical analysis, managed the analyses of the study, wrote the first draft of the manuscript and managed the literature searches. Both authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Aims: To evaluate serum sodium, potassium, calcium, chloride, magnesium, phosphorus and sulphur in patients with type II DM and compare with non-diabetic subjects.
Study Design: A cross sectional study.
Place and Duration of Study: Department of Chemical Pathology, Ekiti State University Teaching Hospital, Ado Ekiti and Federal Medical Centre, Ido Ekiti, Ekiti State, between April 2013 and February 2014.
Methodology: This study was conducted on 150 subjects, out of which 100 were type II diabetes mellitus patients and 50 were non diabetic (control) subjects. Glucose level was determined by Glucose oxidase –Peroxidase method, serum calcium, potassium, sodium and chloride

**Corresponding author: E-mail: ogunleyeadeoluz@gmail.com;*

concentrations were measured using Biolyte *Spin 6,* Full Automated Electrolyte Analyzer while magnesium was analyzed by Atomic Absorption Spectrophotometry. Phosphorus concentrations was determined by spectrophotometer using BioSystem reagent kit specific for phosphorus and Sulphur concentrations were measured using auto analyzer.

Results: The results showed that sodium, potassium, chloride, calcium, phosphorous and magnesium were significantly lower (*P<.001*) in diabetic subjects when compared with the control subjects whereas the mean sulphur concentration was significantly higher *(P<.001)* in diabetic subjects when compared with the non-diabetic (control) subjects.

Conclusion: This study showed Impair metabolism of macro minerals in diabetic group which result in variations in the levels of these minerals in diabetic male and female as well as in different diabetic age groups when compare with non-diabetic group.

Keywords: Macro minerals; diabetes mellitus; full automated electrolyte analyzer; Atomic Absorption Spectrophotometry (AAS); auto analyzer.

1. INTRODUCTION

Type II diabetes mellitus (DM2) is a chronic and progressive metabolic disorder characterized by insulin resistance and pancreatic beta islet cell failure. Diabetes mellitus is usually characterized by hyperglycaemia resulting from defects in insulin secretion, insulin action, or both [1]. Three specific abnormalities that contribute to hyperglycaemia in DM2 are: impaired insulin secretion, increased hepatic glucose production, and decreased insulin-stimulated uptake of glucose in peripheral tissues. Macro minerals (sodium, potassium, calcium, magnesium, chloride, sulphur and phosphorus) play an important role in intermediary metabolism and cellular function, including enzyme activities and electrical gradients [2]. Serum concentrations of these minerals have been shown to change with plasma glucose levels [3]. Disturbances in the levels of macro minerals were found to be associated with diabetes mellitus [4-6]. Potassium influences the release of insulin from the pancreas so it could be said that low potassium contributes to pancreatic stress and future insulin resistance leading to type II diabetes. Even slight decrease in potassium level in the blood reflects a larger decrease of potassium in the cells and this apparently impaired glucose metabolism and function [7]. Sodium depletion is another common feature of type II diabetes, reduction in serum sodium in diabetic subjects might be a result of electrolyte loss which arises due to dehydration or a result of kidney dysfunction and diabetic nephropathy. Also, several alterations in the renin-angiotensin system have been described in diabetes mellitus. In patients with established autonomic neuropathy, decreased plasma renin activity responses have been found, which suggests that neural control of renin release is altered in diabetes which may in turn alter sodium concentration in diabetes mellitus [8].

Glycosuria which is very common in diabetes might produce chloride depletion, in the absence of adequate fluid intake, the obligatory excretion of water necessary for the urinary excretion of glucose may result in a deficit of body water; under some circumstances this may be followed by a secondary depletion of the body stores of chloride. Insulin secretion which is a calcium-dependent process [9] may alter calcium flux and thus have adverse effects on β-cell secretory function. It may also be speculated that inadequate calcium intake may alter the balance between the extracellular and intra-cellular β-cell calcium pools, which may interfere with normal insulin release, especially in response to a glucose load. Sulphur containing compounds have also been established as risk factor for cardiovascular diseases and it occurs with high prevalence in patients with type II diabetes [10]. Diabetes is also known to be associated with various degrees of intracellular phosphate depletion, partially because of a shift of phosphorus from the intracellular to the extracellular compartments and because of prolonged and excessive hyperphosphaturia [11]. The occurrence of a paradoxical imbalance in phosphate metabolism from the early onset of diabetes mellitus have indicated that the imbalance may lead to a reduction of high energy phosphates and tissue hypoxia [11,12]. Mild changes in minerals such as low magnesium levels can predict mortality in type II DM [13], and supplementation of some of this mineral have been found to reduce fasting plasma glucose levels in DM patients [14]. Therefore, Several Studies have been carried out on the potential alteration of minerals in diabetes mellitus. However, results in these study have been

inconsistent and contradictory [15-18] in view of these conflicting reports, the present study was undertaken in order to investigate these parameters in diabetic patients and as well compare the result with age and sex matched non-diabetic patients.

2. MATERIALS AND METHODS

2.1 Study Subjects

The subjects used for the present study were made up of two groups. Group 1 comprised of 100 diagnosed type II diabetic patients and group 2 was made up of 50 non-diabetic aged matched control subjects. Among the total diabetic subjects, 43 were male and 57 were female while that of non-diabetic group were 26 males and 24 females. Both groups were of age range 35 – 80 years.

2.2 Inclusion and Exclusion Criteria

The study included diabetic patients and non-diabetic subjects.

Lactating mothers, patients with serious co-morbid diseases (stroke, major surgery, mal-absorption, myocardial infarction), Smoking and alcoholic individuals, history of using drugs that significantly affect glucose metabolism (glucocorticoids, oral contraceptives, high-dose thiazide diuretics), pregnant women, patients with other chronic illnesses or taking any other medications that could potentially affect levels of macro minerals were all excluded.

2.3 Sample Collection

5 ml of fasting blood sample was collected from antecubital vein into plain bottles from each of the subjects. The whole blood samples were allowed to clot and were centrifuged at 4000 rpm for 15 minutes. The supernatant serum was taken and delivered into plastic tubes with screw caps and was used for the analysis of macro-minerals (sodium, potassium, calcium, magnesium, chloride, sulphur and phosphorus).

2.4 Laboratory Analysis

Glucose level was determined by Glucose oxidase –Peroxidase method [19], calcium, potassium, sodium and chlorine concentration were measured using Biolyte *Spin 6,* Full Automated Electrolyte Analyzer, magnesium was analyzed by flame atomic absorption spectrophotometry, Serum phosphorus concentrations was determined by spectrophotometer using BioSystem reagent kit specific for phosphorus [20] and Serum Sulphur concentrations were measured using auto analyzer.

2.5 Statistical Analysis

Data analysis was performed using Statistical Package for Social Science (SPSS) for Windows version 16. The statistical significance was determined by one-way analysis of variance (ANOVA). The p-value less than .001 *(P<.001)* was considered as significant.

3. RESULTS AND DISCUSSION

3.1 Results

One hundred diabetic patients (43 Males and 57 Females) and fifty non-diabetic (control) subjects (26 Males and 24 Females) defined by clinical examination and with no history of any disease were compared for glucose levels and macro-minerals. Values were expressed as mean ±SD.

Table 1. Sex distribution

Parameter	Diabetic group	Control group
Male	43 (43%)	26 (52%)
Female	57 (57%)	24 (48%)
Total	100 (100%)	50 (100%)

Table 2. Age distribution

Age code (years)	Diabetic subjects	Control subjects
30-39	16 (16%)	16 (32.0%)
40-49	17 (17%)	11 (22.0%)
50-59	21 (21%)	10 (20.0%)
60-69	23 (23%	9 (18.0%)
70 and above	23 (23%)	4 (8.0%)
Total	100 (100%)	50 (100%)

3.2 Discussion

Type 2 Diabetes mellitus is one of the most serious public health problems being faced globally. It may therefore be prudent in medical practice to periodically monitor the macro minerals status of diabetics, because evaluation of these minerals may help in suggesting adequate management for type II diabetes mellitus patients. In the present study, serum

magnesium levels were found to be significantly reduced in the diabetic patients *(P<.001),* when compared with the control group this was in correlation with the findings of Berhane et al. [21], Chetan et al. [22], Diwan et al. [23], Tosiello [24], Walter et al. [25], Tripathy et al. [16], McNair et al. [26], Anetor et al. [27], Supriya et al. [28] and Sharma et al. [29]. It was also observed in this study that Magnesium levels of diabetic group differ between the different age groups but the difference was not statistically significant *(p>.05)*. Diabetic male has a slightly higher Magnesium levels than their female counterpart but the difference was not statistically significant *(p>.05)*. Magnesium is an essential element which is involved in glucose homeostasis at multiple levels; it is an integral part of the activated MgATP complex regulating protein kinases which is directly involved in the control of glucose metabolism. Low levels of magnesium can reduce secretion of insulin by the pancreas (Durlach et al. [30]. The cause of diabetic hypomagnesaemia is multifactorial; Osmotic actions of glycosuria are known to depress the net tubular reabsorption of magnesium in normal humans (Elaine et al. [31]; Ishrat et al. [32]; Nsonwu et al. [33].

Sodium depletion is another common feature of type II diabetes. In this study, sodium levels of diabetic group differ between the different age groups but the difference was not statistically significant *(p>.05)*. Sodium level in male diabetic group was slightly higher *(P>.05)* than their female counterpart. Despite the variation in sodium level among different ages and sexes of diabetic patients, the serum sodium levels were found to be significantly lower in diabetic group *(P<.001)* when compared with control subjects, this result was consistent with the findings of Hasan et al. [34], Al-Rubeaan et al. [5]. The sodium depletion might be due to inhibition of the renin-angiotensin-aldosterone system, which plays a key role in the regulation of fluid and electrolyte balance. This enzyme system has been reported to be affected in many endocrine and cardiovascular diseases particularly diabetes [35].

Potassium, the main intracellular cation in the human body is required for vital cellular processes. Recent research has led to renewed interest in low potassium as a possible risk factor for diabetes. In this study, the serum potassium levels were found to be significantly lower in diabetic group *(P<.001)* when compared with control subjects, which was in accordance with findings of Hasan et al. [34], (Ranee et al. [36], Al-Rubeaan et al. [5]. Potassium levels of diabetic group differ between the different age groups but the difference was not statistically significant *(p>.05)*. Also, potassium level in male diabetic group was significantly *(P<.05)* lower than their female counterpart. The observed depression in serum potassium in the diabetic cohort might be a result of electrolyte loss which arises due to dehydration or a result of kidney dysfunction and diabetic nephropathy. Potassium depletion was associated with a decrease in pancreatic β-cell sensitivity to hyperglycemia with a reduction in insulin release; it is a well-established correlate of disturbances in glucose metabolism. Potassium depletion might also occur due to activation of the renin-angiotensin-aldosterone system which plays a key role in the regulation of fluid and electrolyte balance in the body in type II diabetes mellitus patients. In type II diabetes low renin, low aldosterone responsiveness is associated with increased level of serum potassium [37]. In this study, serum chloride levels were also found to be significantly lowered in diabetic group *(P<.001)* when compared with control subjects, this result was in correlation with findings of Hasan et al. [34]. Chloride levels of diabetic group differ between the different age groups but the difference was not statistically significant *(p>.05)*, chloride level in male diabetic group was slightly higher than their female counterpart but the difference was not statistically significant *(p>.05)*. The observed lower serum chloride in the diabetic cohort might be a result of electrolyte loss which arises due to dehydration or a result of kidney dysfunction or diabetic nephropathy.

Sulphur containing compounds have been established as risk factor for cardiovascular diseases and occur with high prevalence in patients with type 2 diabetes. A large amount of evidence supports increased plasma sulphur containing compounds in type 2 diabetes, this can be found in the findings of Emoto et al. [10], Fiorina et al. [38], Hultberg et al. [39], Chico et al. [40], Stabler et al. [41], Buysschaert et al. [42]. In this study, serum sulphur concentrations were significantly higher *(P<.001)* in diabetic subject when compare with controls. Sulphur level among the diabetic group differs between the different age groups but the difference was not statistically significant *(p>.05)* whereas the level of Sulphur in both male and female diabetic group remain the same.

Table 3. Comparison between the glucose levels of diabetic group and control group

Parameter	Diabetic group N = 100 (MEAN±SD)	Control group N = 50 (MEAN±SD)	P-value
Glucose (Mg/dL)	160.94±61.81	67.41±7.95	<.001

The mean and SD of glucose in control group was (67.41±7.95) which was significantly lower (P<.001) than that of the diabetic group (160.94±61.82)

Table 4. Comparison between the ages of diabetic group and control group

Parameter	Diabetic group N = 100 (MEAN±SD)	Control group N = 50 (MEAN±SD)	P-value
Age(years)	58.11±13.51	47.65±9.03	0.000

The age range of these subjects was between 35 and 80years. The mean age and standard deviation of the control group was 47.65±9.03 years, while that of the diabetic group was (58.11±13.51) years. The mean age of the diabetic group is greater than that of the control group; the mean age difference was significant (p < 0.001)

Table 5. Association between serum macro-minerals, blood sugar and age of diabetic mellitus patients

Age range (year)	30-39	40-49	50-59	60-69	≥70	P-value
FBS (Mg/dL)	123.00±9.81	198.49±82.89	151.20±28.34	159.14±61.76	167.31±73.65	0.083
K (Mg/dL)	15.64±0.86	15.74±0.84	15.30±1.59	15.39±1. 68	14.93±1.59	0.589
Na (Mg/dL)	302.58±6.20	302.55±8.44	297.78±8.80	301. 61±9.34	303.27±6.52	0.306
Cl (Mg/dL)	349.48±8.89	348.22±4.62	344.35±9.80	346. 29±8.95	343.17±9.21	0.314
Ca (Mg/dL)	12.32±0.84	12.24±1.30	12.00±1.47	11.55±1 .40	12.25±1.43	0.427
Mg (Mg/dL)	0.73±0.14	0.89±0.16	0.87±0.29	0.83±0.21	0.91±0.20	0.337
P (Mg/dL)	1.73±0.71	2.35±0.65	2.19±0.93	1.96±1.14	2 .20±0.99	0.569
S (µg/dL)	3.80±0.32	3.49±0.74	3.70±0.65	3.94±1.07	3 .83±0.70	0.630

There was no significant difference (P>0.05) in FBS levels among the different age groups but the age range 30 39 has the lowest level of FBS whereas the age range 40-49 has the highest level.
There were no significant differences (P>0.05) in Potassium, Sodium, Chloride, Calcium, Magnesium, phosphorous and sulphur level among the different age groups, although the levels of these minerals vary between the different age ranges.

Table 6. Comparism between serum macro-minerals and blood sugar in Male and Female diabetic subjects

Parameters	Male N=43	Female N=57	P-value
Age (year)	63.64±11.30	54.02±14.06	0.002
FBS (Mg/dL)	177.11±74.45	149.59±48.87	0.049
K (Mg/dL)	14.94±1.80	15.60±1.12	0.046
Na (Mg/dL)	302.76±9.94	300.57±6.61	0.238
Cl (Mg/dL)	347.04±8.88	344.73±8.73	0.251
Ca (Mg/dL)	12.28±1.27	11.82±1.41	0.135
Mg (Mg/dL)	0.94±0.22	0.80±0.20	0.003
P (Mg/dL)	2.41±1.13	1.88±0.74	0.013
S (µg/dL)	3.78±0.74	3.78±0.82	0.972

The levels of Na, Cl, Ca, and S were slightly higher in diabetic male than in their female counterpart but the differences were not statistically significant. The levels of FBS, Mg and P were significantly higher (p<0.05) in diabetic male when compare with diabetic female whereas the K level was significantly higher (p<0.05) in diabetic female than in male

This study also showed that the mean levels of serum calcium were significantly lower *(p<0.01)* in the serum of types II diabetic patients when compared with the control group, similar results were recorded by Djalali et al. [43] and Anastassios et al. [44]. The loss of these elements might be attributed to impaired absorption and/or the excessive excretion of

Table 7. Comparison between serum macro-elements of diabetic group with control

Parameter (Mg/dL)	Diabetic group N = 100 (MEAN±SD)	Control group N = 50 (MEAN±SD)	P-value
Na	301.47±8.16	318.44±6.22	<.001
K	15.33±1.47	17.57±1.82	<.001
Cl	345.68±8.81	355.00±6.81	<.001
Ca	12.01±1.36	13.43±0.41	<.001
P	2.10±0.95	3.46±0.58	<.001
Mg	0.85±0.22	1.11±0.24	<.001
S	3.78±0.78	2.84±1.10	<.001

The results showed that, Sodium (301.47±8.16 mg/dL, P<.001), Potassium (15.33±1.47 mg/dL, P<.001), Chloride (15.33±1.47 mg/dL, P<.001), Calcium (12.01±1.36mg/dL, P<.001), Phosphorous (2.10±0.95 mg/dL P<.001) and Magnesium (0.85±0.22 mg/dL, P<.001) were significantly lower in diabetic subjects when compared with the control subjects (318.44±6.22 mg/dL), (17.57±1.82 mg/dL), (355.00±6.81mg/dL), (13.43±0.41 mg/dL), (3.46±0.58 Mg/dL) and (1.11±0.24 mg/dL)respectively. Conversely, the mean Sulphur (3.78±0.78 mg/dL, P<.001) was significantly higher in diabetic subjects when compared with the control group (2.84±1.10 mg/dL)

these elements in urine (glycosuria) in these patients, which may induce a deficiency or marginal state of these minerals in blood of diabetic patients. Brown et al. [45], Isbir et al. [46]. Calcium levels in diabetic group differ between the different age groups in both male and female but the differences was not statistically significant *(p>0.005)*. Moreover, calcium level in male diabetic group was slightly higher than their female counterpart but the difference was not statistically significant *(p>0.05)*.

Analysis of serum phosphorus in this study revealed a significantly lower level *(P<.001)* in diabetic patients when compared with control group, similar result has also been recorded by Djalali et al. [43]. Phosphorous level of diabetic group differs between the different age groups but the difference was not statistically significant *(p>0.05)*, and also male diabetic group has a slightly higher phosphorous level than their female counterpart but the difference was not statistically significant *(p>0.05)*. This reduction in phosphorus level may be due to loss as a result of increase glucosuria. The evidence of the occurrence of a paradoxical imbalance in phosphate metabolism from the early onset of diabetes mellitus has indicated that this imbalance may lead to a reduction of high energy phosphates. Cellular phosphorus depletion and hypophosphatemia have played a role in the development of acute, occasionally life-threatening complications in diabetic mellitus. When insufficient phosphate and oxygen are available for adenosine triphosphate (ATP) synthesis, cell homeostasis cannot be maintained and may result in cell lyses; this has been recognized as a cause of morbidity and mortality in Diabetic ketoacidosis [47].

4. CONCLUSION

I. Significantly reduced concentration of sodium, potassium, Chloride calcium, magnesium, phosphorus and sulphur were observed in diabetic group when compared with the non-diabetic group. The macro-minerals level also vary among the different age group and in both sexes but the differences were not statistically significant except calcium which was significantly reduced in female when compare with their male counterparts.

II. Alterations in Macro minerals levels may underlie many of the pathophysiologic and clinical characteristics of diabetes and as such must be routinely assayed in Diabetic patients so as to prescribe appropriate management which could prevent complications.

III. The impaired mineral elements metabolism of the present work may have a role in the pathogenesis and progression of diabetic mellitus type II. Imbalances in mineral elements level in the body may disturb antioxidants levels, hormone secretion, enzymatic activities and secretion of some enzymes e.g. the secretion of pancreatic amylase and it may also enhance lipid peroxidation.

IV. Sex related differences in serum minerals and mostly lipid fractions were observed in the diabetic population of this study. The differences observed in the diabetic males and female may be attributed to increased urinary excretion of these minerals, bone mineralization, physical activity, life style and hormonal imbalances may associate with the diabetic state in both sexes.

ETHICAL APPROVAL

This study was approved by the Department of Biochemistry of Ekiti State University, Ado Ekiti, Department of Chemical Pathology of Ekiti State University Teaching Hospital, Ado Ekiti and Federal Medical Centre of Ido Ekiti, Ekiti State, Nigeria. All procedures followed were in accordance with the ethical standards Ministry of Health, Nigeria.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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