Asian Journal of Pharmaceutical and Clinical Research

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 12, Issue 10, 2019

Online - 2455-3891
Print - 0974-2441

Research Article

SERUM LIPID AND TRACE MINERAL PROFILES AMONG TYPE 2 DIABETICS AND HYPERTENSIVE DIABETICS AT THE BAMENDA REGIONAL HOSPITAL

LUKONG HUBERT SHALANYUY[1]*, SAMJE MOSES[2]

[1]Department of Medical Laboratory Sciences, School of Medical and Biomedical Sciences – Kesmonds International University, National Polytechnic University Institute, Bamenda, Cameroon. [2]Department of Biomedical Sciences, University of Bamenda, Bamenda, Cameroon. Email: lukong.hubert@gmail.com

Received: 08 June 2019, Revised and Accepted: 24 August 2019

ABSTRACT

Objective: Diabetes mellitus has become a clinical condition of public health importance, especially in developing countries due to its high mortality and morbidity. The aim of this study was to measure and compare the lipid and serum trace mineral profile among type 2 diabetics and hypertensive diabetics with controls.

Methods: This cross-sectional study was carried out at the Regional Hospital, Bamenda, involving 50 diabetic normotensives, 50 hypertensive diabetics, and 50 normal recruited subjects. Serum levels of lipids and minerals were determined using standard methods.

Results: Of the four trace elements assessed, except for copper (Cu) whose mean values in diabetics were abnormally increased ($p=0.01$), zinc (Zn), magnesium (Mg), and chromium (Cr) showed significantly decreased mean values in diabetics compared to the controls ($p<0.05$). The mean levels of these trace elements were also significantly reduced in hypertensive diabetic patients ($p<0.05$). In diabetics, there was no significant difference in the lipid levels. However, only total cholesterol (TC) and low-density lipoprotein mean values were significantly higher in hypertensive diabetic patients compared to the normal controls. There was also a positive significant correlation between the body mass index and Cr ($r=+0.3$, $p=0.045$) in diabetics.

Conclusion: This study saw statistically significant differences in the serum lipid and trace element levels between diabetics, hypertensive diabetics, and controls: With diabetic and diabetic hypertensive patients having higher serum Cu levels and decreased serum Mg, Zn, and Cr levels compared to the normal controls. The lipid profile levels in diabetics and hypertensive diabetics were not significant differences within the study groups for all lipid profile estimations except for TC and LDL which were significantly higher only in hypertensive diabetic patients.

Keywords: Trace elements, Lipid profile, Type 2 diabetes, Hypertension.

 DOI: http://dx.doi.org/10.22159/ajpcr.2019.v12i10.34501

INTRODUCTION

The World Health Organization (WHO) [1] defined diabetes mellitus (DM) as a metabolic disorder of multiple etiology, characterized by chronic hyperglycemia with disturbances of carbohydrate, fat, and protein metabolism resulting from defects in insulin secretion, insulin action, or both [2]. The WHO estimated that the number of people with diabetes worldwide in the year 2000 was 177 million, which will increase to at least 336 million by the year 2030 [1]. With an annual prevalence of about 5.4%, major concerns are that much of this increase will be experienced in developing countries (approximately 75% of all persons). Chronic hyperglycemia is associated with the long-term consequences of diabetes that include damage and dysfunction of the cardiovascular system, eyes, kidneys, and nerves [3,4]. The complications of diabetes are often divided into two groups: Microvascular (retinopathy, nephropathy, and neuropathy) and macrovascular (ischemic heart disease, stroke, and peripheral vascular disease) [5].

Garg and Grundy [6] had identified the relationship between diabetes, hypertension, and dyslipidemias. Dyslipidemia according to them is common in diabetes and diabetic hypertensives and is a significant risk factor of cardiovascular disease among patients with type 2 diabetes and those with hypertension. Dyslipidemia is a preferable term to hyperlipidemia because it includes risk factors such as a decreased concentration of high-density lipoprotein (HDL) cholesterol as well as qualitative changes in low-density lipoprotein (LDL), together with raised triglycerides (TGs), which are features of the metabolic syndrome, increasingly recognized as a harbinger of congenital heart disease [5]. Confirmatory associations between diabetes and dyslipidemia have been reported in Africa [7-10].

Direct association of trace elements with diabetes has been observed in many research studies [11]. There is accumulating evidence that the metabolism of several essential elements is altered in diabetes and that these nutrients might have specific roles in the pathogenesis and progress of this disease [12,13]. Zinc (Zn), for example, is required for insulin synthesis and storage and insulin is secreted as Zn crystals [14]. It is also involved at multiple levels in insulin secretion, binding and enhancing the ability of insulin to activate tyrosine kinase [15]. Copper (Cu) is an important trace element associated with a number of metalloproteins which involves oxidation-reduction reactions. Chromium (Cr) functions in the control of glucose and lipid metabolism. Insulin resistance may be a consequence of Cr deficiency and insulin is apparently ineffective as a glucose regulator without Cr [16]. Many studies have indicated that excessive insulin in the body increases Cr excretion and thus Cr deficiency. This can be noticed in type 2 DM due to the excessive insulin in the body due to insulin intolerance; thus, Cr supplementation in diabetics is essential to improve glucose tolerance [16,17]. According to Martin [18], reduced magnesium (Mg) intake is associated with hypertension and insulin resistance [18]. It has also been implicated in carbohydrate intolerance, dyslipidemia, and complications of diabetes [19]. Evidence shows that Zn has a biphasic effect in that it is required for insulin storage and cellular binding, although high concentrations can lead to a reduction in insulin release [17]. The present study was aimed at contributing to the proper management of type 2 diabetes by providing data on both the serum lipid and trace mineral levels among type 2 diabetics and hypertensive diabetics compared to the controls among patients attending the Bamenda Regional Hospital, Cameroon.

METHODS

The study was carried out at the Bamenda Regional Hospital involving 50 diabetic normotensives, 50 hypertensive diabetics, and 50 normal subjects. All type 2 diabetic patients were aged 52.42±7.10 years and were those who came to the Bamenda Regional Hospital for diabetes control. All hypertensive diabetic patients were aged 49.84±5.81 years. Subjects with type 1 diabetes, diabetic patients on insulin, chronic liver disease, chronic renal disease, and chronic and acute infections and those who refused to give their consent were excluded from the study. Two milliliters of freshly collected blood were dispensed into fluoride oxalate bottles and centrifuged for glucose estimation using glucose oxidase method [20]. Two milliliters of blood were also left to clot, spun, retracted and the serum separated into aliquots to be used for lipid profile, sodium, potassium, and trace element estimations. Lipid profile (total cholesterol [TC], HDL cholesterol, LDL cholesterol, and TG), sodium, and potassium were estimated using colorimetric enzymatic method [16]. The trace elements (Mg, Zn, Cu, and Cr) were evaluated by atomic absorption at the standard medical diagnostic and research center, Douala, where the element was dissociated from its chemical bonds and placed in an unexcited or ground state (neutral atom) and a hollow cathode lamp with a cathode made of the material to be analyzed, used to produce a wavelength of light specific for the material. When the light from the hollow cathode lamp entered the flame, part of it was absorbed by the ground state atoms in the flame, resulting in a net decrease in the intensity of the beam from the lamp referred to as atomic absorption. Weight was measured using the Taylor Precision Digital Scale from Taylor Company Ltd. Height was measured in standing position using a tape meter with the shoulders in a normal position. Body mass index (BMI) was defined as weight in kilograms divided by height in meters squared. Overweight was defined as BMI 25.0–29.9 kg/m^2 and obese as BMI ≥30 kg/m^2 [21]. All statistical analyses were done using SPSS version 21 (IBM SPSS Statistics, IBM Corporation, Chicago, IL). The data were analyzed using the independent sample t-test (to compare significant differences between the means of two independent groups); analysis of variance which was used to check if the means of two or more groups are significantly different from each other. The Chi-square analysis and the Spearman correlation coefficients were used to test the relationship between categorical variables with the strength and direction of association between two ranked variables, respectively. p<0.05 was considered statistically significant. Ethical approval was obtained from the Institutional Review Board (IRB) of the Bamenda Regional Hospital (Approval No: 021/APP/RDPH/RHB/IRB).

RESULTS

Of the total of 150 patients divided into 50 diabetic normotensives, 50 hypertensive diabetics, and 50 normal subjects in this study, there was no significant difference in BMI distribution score between diabetic patients, hypertensive diabetic patients, and the control group (p=0.08).

Cu values in diabetics were significantly higher compared to the controls (p=0.01). Zn, Mg, and Cr also showed significantly lower values in diabetics, compared to the controls (Table 1). Just like Cu in hypertensive diabetics which were significantly higher (p=0.0001), Zn, Mg, and Cr values were also significantly low in hypertensive diabetics. Despite the differences in the mean values of these elements, there was no significant difference in the lipid levels of diabetics compared with the controls in this study (Table 2).

Even though the plasma lipid mean concentrations tended to be higher among the hypertensive diabetics as compared to the diabetic patients, there was no significant difference in the mean values between the diabetics and hypertensive diabetics for the lipid profile estimations except for TC and LDL which were significantly higher only in hypertensive diabetic patients (Table 2).

Table 1: Trace elements in diabetic and hypertensive diabetic patients versus controls

Diabetics, hypertensive and controls	Trace elements			
	Cu (μg/dl)	Zn (μg/dl)	Mg (mmol/L)	Cr (μg/dl)
Diabetics	183.27±16.9	60.3±8.4	0.90±0.12	0.07±0.01
Control	135.8±14.8	102.3±5.6	1.0±0.1	0.09±0.01
p-value	0.010*	0.001*	0.0001*	0.0001*
Hypertensive diabetic patients	70.9±14.6	48.1±6.7	0.3±0.1	0.05±0.02
Control	135.8±14.8	102.3±5.6	1.0±0.1	0.09±0.01
p-value	0.0001*	0.0001*	0.001*	0.0001*

*Statistically significant at 0.05 significance level. Reference ranges: Mg – 0.7 – 1.1 mmol/L, Cr – 0.05–1.50 μg/L, Zn – 55–150 μg/dl, Cu in males – 70–140 μg/dl, Cu in females – 80–155 μg/dl. Zn: Zinc, Mg: Magnesium, Cr: Chromium, Cu: Copper

Table 2: Lipid profile in diabetic patients versus controls

Diabetics, hypertensive and controls	Lipid levels			
	TC (mmol/L)	HDL (mmol/L)	LDL (mmol/L)	TG (mmol/L)
Diabetics (DM)	4.19±0.87	1.33±0.62	2.48±0.73	1.27±0.71
Control	3.72±0.37	1.18±0.25	1.56±0.53	1.02±0.37
p-value	0.210	0.431	0.101	0.174
Diabetics	4.19±0.87	1.33±0.62	2.48±0.73	1.27±0.71
Hypertensive diabetic patients	4.60±0.98	1.27±0.12	2.72±0.44	1.26±0.51
F-value	1.433	5.091	2.061	2.814
p-value	0.043*	0.498	0.017*	0.141

*Statistically significant at 0.05 significance level. TC: Total cholesterol, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, TG: Triglyceride. Reference ranges: TC – <5.17 mmol/L (desirable blood cholesterol), 5.17–6.18 mmol/L (borderline-high blood cholesterol), ≥6.20 mmol/L (high); HDL – up to 0.91 mmol/L (high risk), 1.56 mmol/L (low risk); LDL – up to 2.59 mmol/L (optimal), 2.59–3.34 mmol/L (above optimal), 3.37–4.12 mmol/L (borderline); TG – 1.71 mmol/L (suspect), 2.29 mmol/L (increased). DM: Diabetes mellitus

Within diabetic patients, only TC and HDL significantly differed (p<0.05) in gender with females showing even higher odds ratio (OR) values (1.24 and 1.51) in all the above significant parameters. Cu, Mg, and Zn levels in diabetic patients were significantly different between males and females in the present study with p=0.019, 0.001, and 0.008, respectively. Women had significantly higher mean Cu and Mg levels than males (while males had significantly higher mean Zn levels than females). With respect to marital status, Cu and Cr values were significantly increased in married than non-married respondents (p=0.005 and 0.001, respectively). All other parameters were not statistically significant (Table 3).

There was a significant difference in TC (Fig. 1) and LDL between males and females within hypertensive diabetic group (p=0.012 and 0.005, respectively), with females showing higher mean values than males (Fig. 2). TG was significantly different between the age groups with the age group of 56–60 years statistically different from all other age groups (p=0.046, OR=1.04, confidence interval [CI]=0.535–6.482). Only TC differed significantly between the married and the unmarried participants (Fig. 1). Interestingly, there was also a significant difference between TC, TG, and LDL values with respect to the educational levels of the study participants with respondents having attained only primary level of education, having higher mean values of TG, TC, and LDL when compared to those with higher educational levels (p=0.041, 0.02, and 0.001; OR=1.70, 1.02, and 1.51; CI=1.204–5.620) (Figs. 1 and 2). With respect to elements, there was a significant difference in Cu, Mg, and Zn distribution between males and females. Only Cu and Zn mean values were

Table 3: Common trace elements and lipid profile in diabetic patients according to gender and marital status

Trace elements				
Socio-demographics	**Cu (µg/dl)**	**Zn (µg/dl)**	**Mg (mmol/L)**	**Cr (µg/dl)**
Gender				
Male	138.27±06.1	98.4±2.8	0.80±0.01	0.05±0.18
Female	195.80±09.2	99.8±6.3	1.10±0.12	0.08±0.05
p value	0.019*	0.008*	0.001*	0.087
Marital status				
Married	156.90±9.24	110.51±7.1	0.76±0.20	2.10±0.20
Not married	127.54±10.3	108.24±5.7	0.84±0.01	0.05±0.04
p value	0.005*	0.102	0.084	0.001*
Lipid levels	TC (mmol/L)	HDL (mmol/L)	LDL (mmol/L)	TG (mmol/L)
Gender				
Male	3.92±0.72	1.05±0.24	1.68±0.57	1.24±0.24
Female	5.22±0.64	2.60±0.13	2.01±0.33	1.07±0.32
p value	0.012*	0.046*	0.061	0.089

*Statistically significant at 0.05 significance level. TC: Total cholesterol, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, TG: Triglyceride, Zn: Zinc, Mg: Magnesium, Cr: Chromium, Cu: Copper

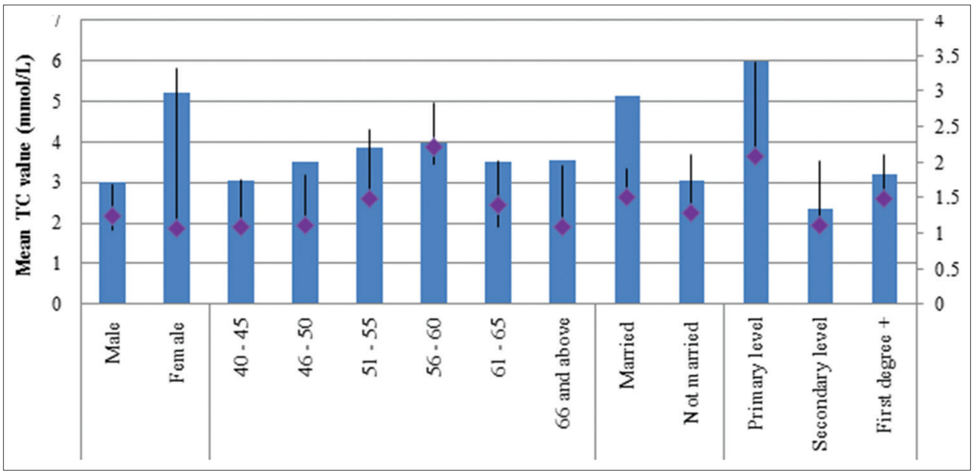

Fig. 1: Mean total cholesterol distribution with respect to sociodemographics

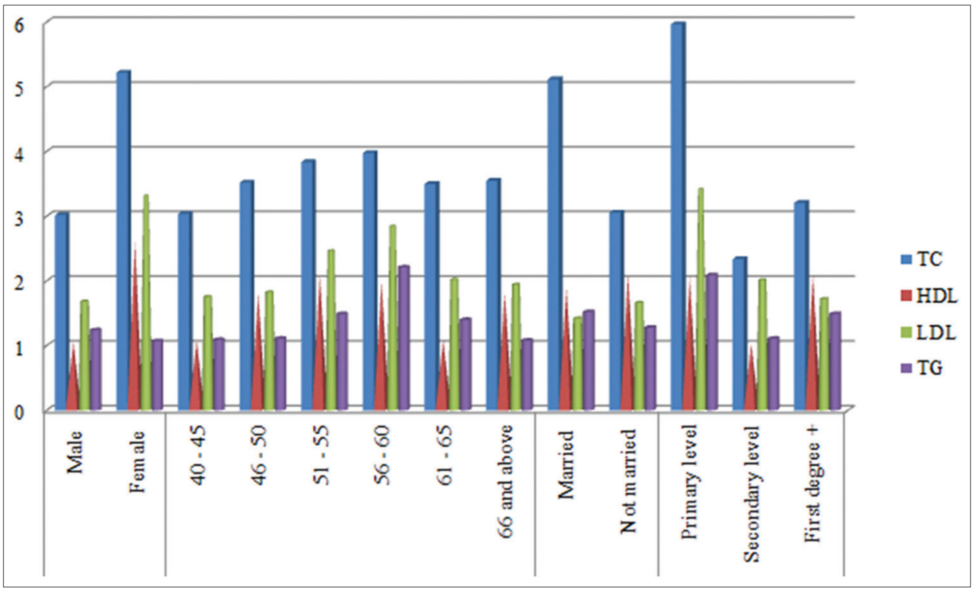

Fig. 2: Mean distribution of lipid profile with respect to sociodemographics

significantly different in age group. Interestingly, only Mg mean values significantly differed with respect to marital status. There was also a positive significant correlation between the BMI and Cr (r=+0.3, p=0.045) in diabetics.

DISCUSSION

There was a statistically significant difference in the serum lipid and trace element levels between diabetics, hypertensive diabetics, and controls within this study. Cu being an essential element that is important for energy production is also a component of the mitochondrial cytochrome oxidative phosphorylation system [22]. In this study, there was a significant difference in mean Cu levels between diabetics and controls within the study population with diabetic patients having higher Cu levels compared to the normal controls. These results corroborated with that of Qiu *et al.* [23]. They stated overall that the DM patients showed higher Cu levels than the healthy controls. However, these results did not tie with that of Edan [24], who showed in their study that serum Cu levels are significantly decreased in diabetic patient as compared to normal controls. Other studies showed that increase in plasma Cu levels was reported in Taiwan [22], Brazil [25], and Egypt [26], whereas decrease or no change in Cu levels was reported in studies from the USA [27] and Germany [28]. The discrepancy could be due to differences in lifestyles, dietary habits, different populations or sample sizes, and associated conditions with the type 2 diabetes patients.

Mg is an essential ion for all organisms and it is present in every cell in the human body [29]. The role of Mg in glucose metabolism, transport, and homeostasis is well documented [30,31]. The results of the current investigation showed low levels of Mg in patients with diabetes compared to the normal controls. These results tie with that of Lin and Huang [30] and Chen *et al.* [32], who reported a decreased Mg level in diabetic patients compared to their normal controls. Disturbance of Mg levels in patients with diabetes also agrees with the previous reports that were conducted in other areas such as that of Odusan *et al.* [33], in India and Pokharel *et al.* [34], in Pakistan. Factors that might contribute to the low levels of Mg (also known as hypomagnesemia) in diabetes include impairment of tubular reabsorption of Mg by the action of glycosuria and hyperglycemia [35]. In addition, disturbance in insulin levels affects cellular Mg uptake [36,37]. Although diabetes *per se* may induce hypomagnesemia, higher Mg intake may confer a lower risk for type 2 diabetes.

Eshak *et al.* [38] reported that abnormal Zn metabolism is suggested to play a role in the etiology of diabetes and some of its complications. In the present study, serum Zn levels were found to be significantly lower in patients with diabetes compared to their normal controls. This was consistent with the previous findings such as that of Chausmer [14] and Viktorínová *et al.* [39]. Conversely, Zn was reported to be elevated in erythrocytes of children with DM in a study by Kruse-Jarres and Rükgauer [40]. Thus, hyperglycemia seems to play a major role in the determination of Zn levels in patients with diabetes.

The results found decreases in Cr levels in type 2 diabetic patients compared to the normal controls. This is in agreement with most previous studies [32,41,42]. Cr is involved in insulin action and its Cr deficiency is related to glucose intolerance and insulin resistance in patients with diabetes [43]. In addition, some studies have reported a lower risk of non-insulin-dependent DM in adults who were taking Cr-containing supplements [42]. This suggests that insulin might play a role in Cr balance inside the body. However, one previous study from Germany has shown increases in Cr in plasma and polymorphonuclear cells of DM patients [40]. Cr level was found to be lowest in hypertensive diabetics perhaps as a result of the two conditions occurring together. In type 2 diabetics, there is excessive production of unutilized insulin and elevated glucose level, thus resulting in high excretion of Cr and this result in Cr deficiency invariably [16,17].

The study on lipid profile levels in diabetics, hypertensives, and diabetic hypertensives shows that there was no significant difference observed within the diabetic patients and controls for all the lipid profile estimations, respectively, perhaps due to the fact that the patients were already on medications. This study agrees with the study carried out in Nigeria, in 2003, by Isezuo and Badung who stated that the TC, HDL cholesterol, LDL cholesterol, and TG levels did not differ significantly among patients with diabetes compared to normal controls [10].

There was a significant difference in Mg levels in diabetic females and males, respectively. This may be attributed to hormonal changes, particularly high estrogen seen, especially in menopausal women. Estrogens circulate in the body bound mainly to the sex hormone-binding globulin (SHBG); however, only unbound estrogens can enter target tissue cells and induce biological activity. Any change in the concentration of SHBG will alter estrogen metabolism by inducing changes in the availability of estrogen to the target cell [44].

The fact that the study respondents were already on medications may have had effects on the results. Again, only some trace elements which have been proven to be greatly affected in type 2 diabetes were analyzed. However, the scope of the study was on some trace elements in patients coming for diabetes treatment and management such that the relationship between the analyzed trace elements and type 2 diabetes will give a wider basis on the need to consider trace elements in the effective management of type 2 DM.

CONCLUSION

Understanding the impact of micronutrient deficiencies and the potential utility of supplementation is relevant to the prevention and/or management of type 2 DM. There was a statistically significant difference in the serum lipid and trace element levels between diabetics, hypertensive diabetics, and controls within this study with diabetic and hypertensive diabetic patients having higher serum Cu levels and decreased serum Mg, Zn, and Cr levels compared to the normal controls. With respect to the lipid profile levels in diabetics and hypertensive diabetics, there was no significant difference observed within the study groups for all lipid profile estimations except for TC and LDL which were observed to be significantly higher only in hypertensive diabetic patients. The utilization of these trace elements and lipids as an aid to improve glucose control and management cannot, therefore, be sidelined.

ACKNOWLEDGMENTS

We wish to thank the Bamenda Regional Hospital authorities for granting us permission to carry out the work.

AUTHORS' CONTRIBUTIONS

The first author performed the procedure, while the second author guided through the procedure. All authors discussed and contributed to the final manuscript.

CONFLICTS OF INTEREST STATEMENT

There are no conflicts of interest in this project.

REFERENCES

1. World Health Organization. Prevention of Diabetes Mellitus. WHO Technical Report Series. Geneva: World Health Organization; 1994.
2. Scoppola A, Montecchi FR, Menzinger G, Lala A. Urinary mevalonate excretion rate in Type 2 diabetes: Role of metabolic control. Atherosclerosis 2001;156:357-61.
3. Tierney LM, Phee MC, Papadakis SJ. Diabetics. In: Current Medical Diagnosis and Treatment. 48th ed. New York: Lange Medical Books/McGraw-Hill; 2002. p. 120.
4. Rother KI. Diabetes treatment – bridging the divide. N Engl J Med 2007;356:1499-501.
5. Naway LM. Lipid Profile in Sudanese Diabetic Patients. Thesis; 2011.
6. Garg A, Grundy SM. Management of dyslipidemia in NIDDM. Diabetes Care 1990;13:153-69.
7. Aduba O, Onwuamaeze I, Oli J, Udeozo K. Serum cholesterol and high density lipoprotein cholesterol in Nigerian diabetics. East Afr Med J 1984;61:35-9.
8. Adedeji OO, Onitiri AC. Plasma lipids in Nigerian hypertensives. Afr J Med Med Sci 1990;19:281-4.
9. Anaja HP, Isah HS, Abdu-Aguye I, Obura NA. Lipid profiles in diabetic Nigerians: A Zaria update. Int Diabet Dig 1995;6:90-3.
10. Isezuo AS, Badung SL. Plasma lipids among Northwestern Nigerian

hypertensives. Sahel Med J 2001;4:181-6.

11. Nourmohammadi I, Shalmani IK, Shaabani M, Gohari L. Zinc, copper, chromium, manganese and magnesium levels in serum and hair of insulin independent diabetics. Arch Iran Med 2000;2:88-91.
12. Murray CJ, Lopez AD. Global mortality, disability, and the contribution of risk factors: Global burden of disease study. Lancet 1997;349:1436-42.
13. Vincent JB. Quest for the molecular mechanism of chromium action and its relationship to diabetes. Nutr Rev 2000;58:67-72.
14. Chausmer AB. Zinc, insulin and diabetes. J Am Coll Nutr 1998;17:109-15.
15. Suarez Z. Decreased insulin sensitivity in skeletal muscle of hypomagnesaemia rats. Diabetologia 1993;36:82.
16. Burtis AC, Ashwood RE. Trace elements. In: Tietz Fundamentals of Clincal Chemistry. 5th ed. India: Saunders; 2003. p. 570-5.
17. Mertz W. Chromium in human nutrition: A review. J Nutr 1993;123:626-33.
18. Martin AC. Calcium, phosphate and magnesium. In: Clinical Chemistry and Metabolic Medicine. 7th ed. London: Hodder Arnold; 2006. p. 113.
19. Resnick LM, Gupta RK, Bhargava KK, Gruenspan H, Alderman MH, Laragh JH, *et al.* Cellular ions in hypertension, diabetes, and obesity. A nuclear magnetic resonance spectroscopic study. Hypertension 1991;17:951-7.
20. Yuen VG, McNeill JH. Comparison of the glucose oxidase method for glucose determination by manual assay and automated analyzer. J Pharmacol Toxicol Methods 2000;44:543-6.
21. Altekin E, Coker C, Sişman AR, Onvural B, Kuralay F, Kirimli O, *et al.* The relationship between trace elements and cardiac markers in acute coronary syndromes. J Trace Elem Med Biol 2005;18:235-42.
22. Lowe J, Taveira-da-Silva R, Hilário-Souza E. Dissecting copper homeostasis in diabetes mellitus. IUBMB Life 2017;69:255-62.
23. Qiu Q, Zhang F, Zhu W, Wu J, Liang M. Copper in diabetes mellitus: A meta-analysis and systematic review of plasma and serum studies. Biol Trace Elem Res 2017;177:53-63.
24. Edan HH. Serum copper level in non insulin diabetes mellitus. Mustansiriya Med J 2006;6:36-41.
25. Abou-Seif MA, Youssef AA. Evaluation of some biochemical changes in diabetic patients. Clin Chim Acta 2004;346:161-70.
26. Chen MD, Lin PY, Tsou CT, Wang JJ, Lin WH. Selected metals status in patients with noninsulin-dependent diabetes mellitus. Biol Trace Elem Res 1995;50:119-24.
27. Rohn RD, Pleban P, Jenkins LL. Magnesium, zinc and copper in plasma and blood cellular components in children with IDDM. Clin Chim Acta 1993;215:21-8.
28. Leonhardt W, Hanefeld M, Müller G, Hora C, Meissner D, Lattke P, *et al.* Impact of concentrations of glycated hemoglobin, alpha-tocopherol, copper, and manganese on oxidation of low-density lipoproteins in patients with Type I diabetes, Type II diabetes and control subjects. Clin Chim Acta 1996;254:173-86.
29. Wu J, Xun P, Tang Q, Cai W, He K. Circulating magnesium levels and incidence of coronary heart diseases, hypertension, and Type 2 diabetes mellitus: A meta-analysis of prospective cohort studies. Nutr J 2017;16:60.
30. Lin CC, Huang YL. Chromium, zinc and magnesium status in Type 1 diabetes. Curr Opin Clin Nutr Metab Care 2015;18:588-92.
31. Veronese N, Watutantrige-Fernando S, Luchini C, Solmi M, Sartore G, Sergi G, *et al.* Effect of magnesium supplementation on glucose metabolism in people with or at risk of diabetes: A systematic review and meta-analysis of double-blind randomized controlled trials. Eur J Clin Nutr 2016;70:1354-9.
32. Chen S, Jin X, Liu J, Sun T, Xie M, Bao W, *et al.* Association of plasma magnesium with prediabetes and Type 2 diabetes mellitus in adults. Sci Rep 2017;7:12763.
33. Odusan OO, Familoni OB, Odewabi AO, Idowu AO, Adekolade AS. Patterns and correlates of serum magnesium levels in subsets of Type 2 diabetes mellitus patients in Nigeria. Indian J Endocrinol Metab 2017;21:439-42.
34. Pokharel DR, Khadka D, Sigdel M, Yadav NK, Kafle R, Sapkota RM, *et al.* Association of serum magnesium level with poor glycemic control and renal functions in Nepalese patients with Type 2 diabetes mellitus. Diabetes Metab Syndr 2017;11 Suppl 1:S417-23.
35. Djurhuus MS, Skøtt P, Vaag A, Hother-Nielsen O, Andersen P, Parving HH, *et al.* Hyperglycaemia enhances renal magnesium excretion in Type 1 diabetic patients. Scand J Clin Lab Invest 2000;60:403-9.
36. Matsunobu S, Terashima Y, Senshu T, Sano H, Itoh H. Insulin secretion and glucose uptake in hypomagnesemic sheep fed a low magnesium, high potassium diet. J Nutr Biochem 1990;1:167-71.
37. Rodríguez-Morán M, Guerrero-Romero F. Insulin secretion is decreased in non-diabetic individuals with hypomagnesaemia. Diabetes Metab Res Rev 2011;27:590-6.
38. Eshak ES, Iso H, Maruyama K, Muraki I, Tamakoshi A. Associations between dietary intakes of iron, copper and zinc with risk of Type 2 diabetes mellitus: A large population-based prospective cohort study. Clin Nutr 2018;37:667-74.
39. Viktorínová A, Toserová E, Krizko M, Duracková Z. Altered metabolism of copper, zinc, and magnesium is associated with increased levels of glycated hemoglobin in patients with diabetes mellitus. Metabolism 2009;58:1477-82.
40. Kruse-Jarres JD, Rükgauer M. Trace elements in diabetes mellitus. Peculiarities and clinical validity of determinations in blood cells. J Trace Elem Med Biol 2000;14:21-7.
41. Lin CC, Tsweng GJ, Lee CF, Chen BH, Huang YL. Magnesium, zinc, and chromium levels in children, adolescents, and young adults with Type 1 diabetes. Clin Nutr 2016;35:880-4.
42. Doddigarla Z, Parwez I, Ahmad J. Correlation of serum chromium, zinc, magnesium and SOD levels with hbA1c in Type 2 diabetes: A cross sectional analysis. Diabetes Metab Syndr 2016;10:S126-9.
43. Wang ZQ, Cefalu WT. Current concepts about chromium supplementation in Type 2 diabetes and insulin resistance. Curr Diab Rep 2010;10:145-51.
44. Douglas HC. Nutritional influences on oestrogen metabolism. Fem Res J 2004;4:20-8.