Journal of Biosciences and Medicines, 2017, 5, 49-56
http://www.scirp.org/journal/jbm
ISSN Online: 2327-509X
ISSN Print: 2327-5081

Variations of Hair Trace Element Contents in Diabetic Females

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How to cite this paper: Saleh, S.A.K., Fatani, S.H., Adly, H.M., Abdulkhaliq, A.A. and Al-Amodi, H.S. (2017) Variations of Hair Trace Element Contents in Diabetic Females. *Journal of Biosciences and Medicines*, **5**, 49-56.
http://dx.doi.org/10.4236/jbm.2017.51004

Received: December 19, 2016
Accepted: January 21, 2017
Published: January 24, 2017

Abstract

Background: Alterations of trace elements, could induce metabolic disorders as they forthwith participating in the metabolic pathways and play different roles modulating it as well as many enzymes require trace elements for their activation and functions. Of these elements, selenium (Se), zinc (Zn), copper (Cu) and manganese (Mn) have been recognized as essentials for metabolism. Hyperglycemia and diabetes mellitus are important causes of mortality and morbidity worldwide, and their global prevalence are growing from 2.8% in 2000 projecting to be 4.4% in 2030. Diabetes is prevalent in Saudi Arabia with high incidence in urbanized areas and its prevalence is estimated to expand 3 times by 2030. Patients and Methods: In total, 75 diabetic women and 80 aberrantly healthy women were recruited. Clinical and familial history was recorded. Hair Se, Zn, Cu and Mn levels were analyzed as well as fasting blood sugar (FBS), glycated hemoglobin (HbA1c). Results: Our findings revealed a marked decrease of Zn and Mn levels in diabetic women hair compared to control group ($p < 0.05$, $p < 0.005$ respectively). Otherwise, Se and Cu levels were significantly elevated in hair of diabetic patients ($p < 0.005$, $p < 0.05$ respectively). Conclusion: Diabetes may disrupt the trace elements balance as well as their alterations can affect glucose metabolism and insulin action. Chronic hyperglycemia can cause disturbance of some trace elements which, in turn, can modulate glucose homeostasis. The metabolic dysregulation occurring in hyperglycemia may influence trace element status by increasing excretion, diminishing availability or redistribution of trace elements among different body pools. Hair trace elements can be useful long-term markers for metabolic disturbance; however, larger prospective studies are required to validate their role in diagnosis and follow up applications.

Keywords

Hair, Trace Elements, Diabetes Mellitus, Women, Saudi Arabia

1. Introduction

Diabetes and hyperglycemia are leading causes of worldwide morbidity and mortality. In 2014, the global prevalence of diabetes was estimated to be 9% among adults. It has been reported that Saudi Arabia is facing a diabetes epidemic, as the overall adult prevalence increased from 16.8% in 2010 to 18.3% in 2014, with the prevalence in women increasing from 15.9% to 16.9% [1] [2].

Many trace elements are directly involved in metabolic pathways, as many enzymes require them for their activation and functions like selenium (Se), zinc (Zn), copper (Cu), and manganese (Mn). Some elements appear as antioxidants, inhibit membrane peroxidation or straightway affect glucose metabolism [3] [4]. Mn, as a cofactor or activator for many enzymes, is involved in different metabolic pathways through regulation of carbohydrates and lipids metabolism, regulation of blood glucose and cellular energy and participation in synthesis of insulin as well as normal immune functions and the defense mechanisms against free radicals [5] [6]. Many enzymes required Cu ions for their activation, like superoxide dismutase, involved in protection against superoxide radicals and cytochrome oxidase for electron transport [7]. Se appeared to be important antioxidant through its involvement as selenocysteine—containing enzymes as glutathione peroxidase and thioredoxin reductase [8]. Zn plays an essential role as a cofactor for many liver enzymes and it has a substantial function in glucose metabolism [9] [10]. Zn has been found to promote effect of insulin *in vitro* and it has been assumed that its deficiency may trigger the insulin resistance in non-insulin dependent diabetes [11].

Remarkably, diabetes may disrupt the elemental balance thus affecting glucose metabolism and insulin function [12]. Chronic hyperglycemia can induce similar alterations which affect glucose homeostasis [13]. A complex relationship between diabetes and trace elements content had been reported that this disease and its complications can promote metabolic alterations of trace element pools [14] [15].

Conventional blood analysis can indicate the trace elements content at the day of sample or a few days prior to the blood analysis [16]; however, trace element analysis in hair can determine the metal content for the past 3 - 6 months prior to analysis. Hair analysis can overcome fluctuation due to daily food intake and may provide non-invasive, low cost and measurement of large number of elements at a time. On the other hand, some limitations may interfere the accuracy of results, such as age, gender, ethnicity and inter-individual variability [17]. There is an increased interest towards effectiveness of trace elements on metabolic pathways [18]. Thus, this study demonstrated the content of hair trace elements as long-term markers and their alterations in diabetes among Saudi female patients.

2. Patients and Methods

This study was performed between February and September 2016 and included randomly recruited 75 diabetic volunteer women from Diabetes and Endocri-

nology Centre, Al-Noor Specialized Hospital, Makkah, Saudi Arabia and 80 apparently healthy non-diabetic women of similar socio-economic status as control group. Clinical and familial history was recorded; women with renal or liver diseases, smokers or taking mineral supplements for the previous three months were excluded from the study.

2.1. Hair Analysis

Scalp hair specimens were collected, weighed, and stored at 25˚C till washed, digested and analyzed within 3 weeks of sample collection. For each sample of 5 mg hair, successive washes of acetone, deionized water and 0.5% Triton X-100 solution were performed then hair sample was digested by nitric acid, hydrogen peroxide, and deionized water followed by dilution to 10 mL [19]. Analysis of hair trace elements (Se, Zn, Cu and Mn) concentrations were carried out by ICP-MS (Perkin Elmer 7300, Perkin Elmer, USA), according to manufacturer's instructions.

2.2. Blood Analysis

A 10-mL fasting blood sample was collected from all subjects and into plain tube and EDTA tube. Serum samples were separated, from plain tube after clotting, in aliquots and fasting blood sugar (FBS) concentration was measured by using HUMAN Clinical Chemistry Reagents (HUMAN Gesellschaftfür Biochemica und Diagnostica mbH, Germany) according to manufacturer's instructions. EDTA whole-blood tube was used to analyze glycated hemoglobin (HbA1c) by using HumaStar HbA1c liquidirect Immunoassay kits (HUMAN Gesellschaftfür Biochemica und Diagnostica mbH, Germany), according to manufacturer's instructions. FBS and HbA1c levels were used for to confirm a diagnosis of diabetes.

2.3. Statistical Analysis

Data are expressed as the mean ± standard deviation (SD) for different studied parameters and possible associations between them. Data between groups were compared using one-way analysis of variance (ANOVA), and the differences between means of two of three studied groups were analyzed using an independent-sample t-test. The level of significance was set at a $p < 0.05$. IBM SPSS Statistics v20 (IBM, USA) was used for the statistical analyses.

3. Results

FBS and HbA1c levels were significantly elevated in the diabetic group compared to those of control group ($p < 0.005$, **Table 1** and **Figure 1**). Hair Se and Cu levels were increased in diabetic group compared the normal one ($p < 0.005$ and $p < 0.05$ respectively, **Table 1** and **Figure 1**). In contrast, Zn and Mn levels in hair samples were significantly lower in diabetic group than in the control group ($p < 0.05$, $p < 0.005$, respectively) and negatively their levels were correlated with FBS and HbA1c levels ($p < 0.05$, **Table 1** and **Figure 1**).

Table 1. Clinical chemistry parameters, and hair trace element concentrations in diabetic and healthy studied groups.

Groups	Control Group Mean ± SD	Diabetic Group Mean ± SD	p value
Number (n)	80	75	-
Age (yrs.)	36.6 ± 5.5	38.4 ± 5.3	>0.05
FBS (mg/dl)	85.9 ± 4.9	165.4 ± 12.1	<0.005
HbA1c (%)	4.96 ± 0.16	9.24 ± 0.52	<0.005
Hair Se (μg/g)	0.425 ± 0.038	1.029 ± 0.087	<0.005
Hair Zn (μg/g)	234.6 ± 16.9	153.2 ± 11.9	<0.05
Hair Cu (μg/g)	12.95 ± 1.14	17.72 ± 1.20	<0.05
Hair Mn (μg/g)	4.086 ± 0.294	2.561 ± 0.223	<0.005
Hair Zn/Cu ratio	18.72 ± 2.04	9.13 ± 1.25	<0.005

FBS: fasting blood sugar; HbA1c: glycated hemoglobin; Se: selenium; Zn: zinc; Cu: copper; Mn: manganese.

Zn/Cu ratio in the hair samples were inversely related to blood hyperglycemia represented by FBS and HbA1c levels ($p < 0.005$, **Table 1** and **Figure 1**). Moreover, Zn/Cu ratio effectively differentiated between diabetic and non-diabetic groups ($p < 0.005$, **Table 1** and **Figure 1**).

4. Discussion

Diabetes development and progression may include metabolic dysregulation of trace elements. Zn is essential for the processing, storage, secretion, and action of insulin in beta (β)-cells where six insulin molecules coordinate with two Zn ions to produce a hexameric-structure based molecule for insulin crystals [20]. Our findings indicated marked diminish of hair Zn concentration in diabetic women. Since Zn inhibited glycogen synthase kinase 3; Zn deficiency may be related to diabetes as a result of increased excretion resulting from polyuria. Moreover, Zn deficiency impairs insulin release as it is an essential cofactor for insulin synthesis and release [21] [22] [23].

Cu ions are involved in oxidation-reduction reactions and have dominant roles in diverse enzymes such as cytochrome oxidase and cytoplasmic superoxide dismutase. As of many other elements, Cu and Zn may have antagonistic effect [24] [25]. The present study indicated that hair Cu levels were elevated in diabetic women, in agreement with previous results, thus supporting the hypothesis of Cu involvement in oxidative stress. The elevated Cu levels in diabetic patients may be referred to hyperglycaemia that stimulate glycation and release of Cu ions which accelerate the oxidative stress which lead to diabetic complications by reinforce direction towards advanced glycation end products [26].

Glutathione peroxidase and thioredoxin reductase enzymes constitute an important type of selenoproteins through which Se contributes to many metabolic pathways, including antioxidant defence systems, immune function, and activation of thyroxin [8] [27]. In contrast, high-Se diets may trigger the release of glucagon, reinforcing hyperglycaemia, or may stimulate glutathione peroxidase overexpression, leading to insulin resistance and storage of fat [28].

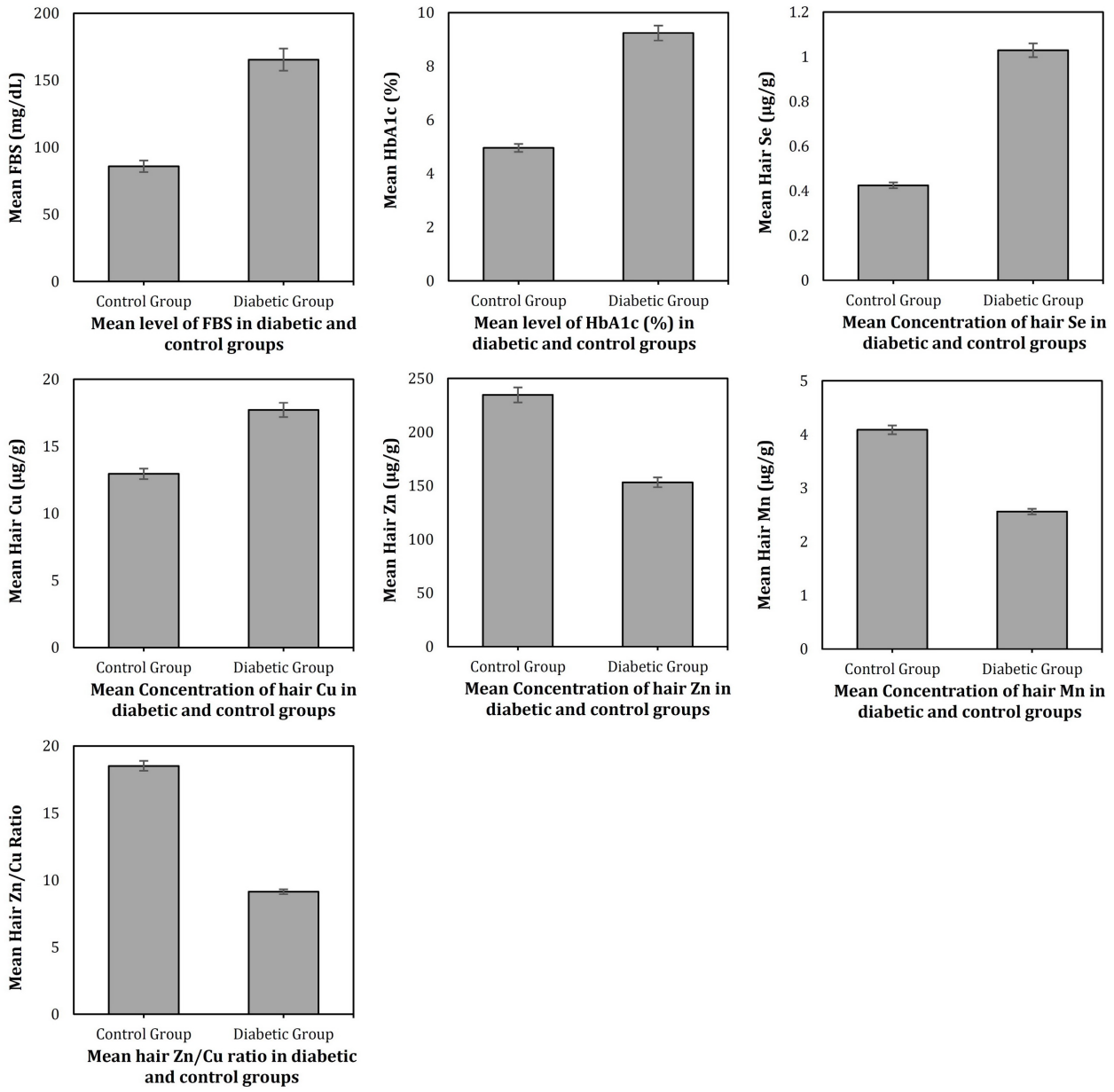

Figure 1. FBS, HbA1c and mean hair trace element levels in diabetic and control groups.

Mn acts as a cofactor and catalyst in many biochemical reactions and metabolic pathways, in addition, Mn is a cofactor of the antioxidant enzyme superoxide dismutase [29]. Our results showed that diabetic women had significantly lower hair levels of Mn than those in the controls, which agrees with the results of previous studies [12] [24] [30].

Hyperglycemia is commonly associated with hyperzincuria thus increased urinary excretion of Zn ions, leading decreasing overall body Zn [31] [32]. In the present study, there is an antagonistic relationship between levels of hair Cu and Zn in diabetes and the ratio of hair Zn/Cu was inversely related to hyperglycemia and diabetes and may provide more useful information. Thus, the role of trace elements in diabetes become important and studies on the changes of var-

ious element ratios and their association with hyperglycemia may provide beneficial information for diabetes control.

4. Conclusion

Diabetes may disrupt the trace elements balance as well as their alterations can affect glucose metabolism and insulin action. Chronic hyperglycemia can cause disturbance of some trace elements which, in turn, can modulate glucose homeostasis. The metabolic dysregulation occurring in hyperglycemia may influence trace element status by increasing excretion, diminishing availability or redistribution of trace elements among different body pools. Hair trace elements can be useful long-term markers for metabolic disturbance; however, larger prospective studies are required to validate their role in diagnosis and follow up applications.

Acknowledgements

The authors thank the Institute of Scientific Research and Revival of Islamic Culture, Umm Al-Qura University, Makkah, Saudi Arabia, for funding this project.

Authors' Contributions

All authors equally contributed in the article. All authors read and approved the final manuscript.

Conflict of Interests

The authors declare that they have no competing interests regarding the publication of this manuscript.

Compliance with Ethical Standards

The study protocol was approved by Ethics Review Board for Human Studies at Faculty of Medicine, Umm Al-Qura University and conformed to the ethical guidelines of the 1975 Helsinki declaration.

Limitations

Although hair analysis may have advantages such as non-invasiveness, low cost, and the ability to measure a large number of biologically essential elements, some factors may limit the interpretation and reliability of results, such as hair growth rate, age, sex, ethnicity, and inter-individual variability.

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