Endocrinology & Metabolic Syndrome

Hammouda SAI, et al., Endocrinol Metab Syndr 2017, 6:2
DOI: 10.4172/2161-1017.1000262

Research Article — OMICS International

Serum Levels of Zinc, Magnesium and Selenium among First Trimester Pregnant Saudi Women with Pre-Diabetes and Diabetes

Sahar A Ibrahim Hammouda[1], **Eman A Sultan**[2*] **and Ahmed M Mohamadin**[3]

[1]*Faculty of Applied Medical Sciences, Clinical Nutrition Department, Taibah University, Saudi Arabia*

[2]*Clinical Nutrition Department, National Nutrition Institute, Cairo, Egypt*

[3]*Deanery of Academic Services, Chemistry for Health Sciences Department, Taibah University, Saudi Arabia*

[*]**Corresponding author:** Emam A, Clinical Nutrition Department, National Nutrition Institute, Cairo, Egypt, Tel: +20 2 23643522; E-mail: emansoltan@gmail.com

Received date: March 01, 2017; **Accepted date:** March 06, 2017; **Published date:** March 10, 2017

Abstract

Background: Glycosylated hemoglobin (HbA1c) was found to be a valuable predictor of the risk of congenital malformations. Other studies documented diabetic complications in subjects with HbA1c at the pre-diabetic levels.

Objectives: This study was done to compare serum levels of zinc, magnesium and selenium between pregnant women with normal glycemic control, diabetes and pre-diabetes.

Subjects/Methods: The data was part of a large prospective cohort study aimed at identifying some preventable risk factors that cause congenital malformations among Saudi women. 1103 healthy first trimester pregnant were randomly selected from antenatal clinics in twenty one health care centers and two hospitals at Al-Madinah Al-Monawarah, KSA. Clinical history, examination and lab analysis were done (serum levels of magnesium, zinc, selenium, and HbA1c). Subjects were classified by their HbA1c levels as normal (HbA1c<5.7%), pre-diabetic (HbA1c 5.7<6.5%), and undiagnosed type 2 diabetics (HbA1c≥6.5%), comparison in the lab results was done between the groups.

Results: About 78. 9% (870 subjects) had normal HbA1c, 19.1% (211 subjects) had HbA1c in the range of pre-diabetes and 1.99% (22 subjects) had HbA1c>6.5% denoting undiagnosed type 2 diabetes

Serum levels of nutrients were significantly lower among pre-diabetics compared to normal subjects, same results were obtained when comparing diabetics and pre-diabetics and diabetics and normal subjects. There was a significant negative correlation between the levels of HbA1c and zinc, magnesium and selenium.

Conclusion and Recommendations: Changes in serum levels of zinc, magnesium and selenium occurs at the pre-diabetic stage and precedes the development of diabetes & may be responsible for medical complications that are recently reported at this stage. Studies should be done for re-establishment of safe target levels of HbA1c.

Keywords: Pre-diabetic; Congenital malformations; Diabetes; Pregnancy

Introduction

Diabetes Mellitus (DM) is a major public health problem worldwide; amongst the most common chronic disorders of modern time. It remains unique because of its systemic micro and macrovascular complications. The complications of Diabetes Mellitus have far reaching effects on the lives of people, and have a big constraint on the budget for health services [1]. Saudi Arabia has the second highest rate of diabetes in the Middle East, and the seventh highest rate in the world [2].

With an estimated number of 3.8 million people diagnosed with the disease in KSA by 2014, this represents more than 25% of the population, and that figure is expected to exceed by more than double by 2030. Half of the population over 30 years of age is prone to diabetes [3].

Pre-diabetes is defined as the elevation of blood glucose and glycated Hb (HbA1c), above the normal range, but below levels of diabetes. Insulin resistance and b-cell dysfunction are characteristics of this disorder. Recently, pre-diabetes was found to be associated with disorders that were considered to be restricted to established diabetes. These disorders include micro vascular disease, metabolic syndrome, cardiovascular disease, cognitive dysfunction, blood pressure abnormalities, fatty liver disease, periodontal disease, obstructive sleep apnea, low testosterone, cancer [4], and birth defects [5].

In early pregnancy, HbA1c elevations close to the reference range may identify women with both underlying hyperglycemia, and association with adverse pregnancy outcomes [6].

Diabetic women with elevated blood glucose and glycosylated hemoglobin levels in the first trimester have been significantly associated with increased risk of adverse pregnancy outcomes (e.g., abortion, stillbirth, and congenital abnormalities) [7,8]. This is also true for those with insulin resistance, obesity, and even lesser degrees of hyperglycemia, which affect the intrauterine metabolic environment

Citation: Hammouda SAI, Sultan EA, Mohamadin AM (2017) Serum Levels of Zinc, Magnesium and Selenium among First Trimester Pregnant Saudi Women with Pre-Diabetes and Diabetes. Endocrinol Metab Syndr 6: 262. doi:10.4172/2161-1017.1000262

and have long-term implications on the future health of the offspring, so that achieving optimal outcomes in mothers can no longer be simply measured by whether or not maternal glucose values are at goal. Thus, the pregnant women with undiagnosed diabetes are a high-risk group that may benefit from early intervention [9].

The relation between zinc, diabetes and insulin was discovered in the 1930s, a decade following discovery of the hormone, when a study showed that crystallized insulin contains zinc and that zinc, along with other metal ions, could induce insulin crystallization [10].

Later on, zinc was found to prolong insulin action when co-injected with the hormone [11]. More recent findings show association between type 2 diabetes (T2D) risk, and the inheritance of gene variants encoding a critical β cell zinc transporter [12]. This documented the role of zinc in diabetes aetiology, and as a possible therapeutic target [13].

Globally, scientists observed beneficial outcomes in decreasing HbA1c levels with zinc supplementation. However, it is still unclear if dietary zinc supplementation would have an effect in preventing T2D [14,15].

Hypomagnesemia was found to be associated with the development of impaired glucose tolerance (IGT) and T2D [16].

Prospective studies have found that Mg intake can reduce the risk of developing pre-diabetes among those with normal glucose regulation [17], and can also improve glycemic status in adults with pre-diabetes [18] However, a cross-sectional study has failed to demonstrate a relationship between serum Mg and precursor states of diabetes, including impaired fasting glucose and IGT [19].

Selenium has contradictory effects in diabetes; the antioxidant property of selenium prevents the development of complications in diabetic patients. Some studies found that higher serum selenium concentrations were associated with a higher prevalence of diabetes [20]. More convincing data focuses on specific selenoproteins in glucose metabolism. Recently, a study showed that both selenoprotein deficiency and a high expression of selenoproteins cause glucose disturbances [21] Selenium has been shown to have insulin-like properties, [22] which qualify it as a potential anti-diabetic agent.

Subjects/Methods

This study was done to compare serum levels of zinc, magnesium and selenium between pregnant women with different glycemic status, (normal, pre-diabetic and diabetic).

The data was part of a large prospective cohort study with the aim of identifying some preventable risk factors that can cause congenital malformations among Saudi women.

A total of 1,180 healthy first trimesters pregnant were randomly selected from antenatal clinics in two hospitals, and 21 primary health care centres in Al-Madinah Al-Monawarah, KSA. Inclusion criteria included the following factors:

- Pregnant women in the first trimester
- Agreeability to participate until delivery
- Absence of systemic diseases that are known to cause birth defects such as diabetes (type 1 and 2) epilepsy, heart diseases etc.

Clinical history, examination, and lab analysis were done (serum levels of magnesium, zinc, selenium and HbA1c). Subjects were classified by their HbA1c levels as normal (HbA1c<5.7%), pre-diabetic (HbA1c 5.7<6.5%), and undiagnosed T2D (HbA1c ≥ 6.5%). Comparison in the lab results was done between the groups [23].

Laboratory methods: Blood samples

Fasting blood samples were taken after an overnight fast, placed into EDTA tubes, and centrifuged at 3000 x g for 10 minutes. The plasma obtained was frozen at -80°C until the time of analysis.

Blood HbA1c levels were measured by using standard biochemical procedures, and the results were identified with the use of reference ranges in this laboratory. NycoCard HbA1c is a boronate affinity assay.

Zinc and magnesium were measured using Bioassay Systems' kits that measured zinc and magnesium directly in biological samples without any pre-treatment. The present method utilizes a chromogen that forms a colored complex. The intensity of the color measured at 425 nm, and 500 nm for zinc and magnesium respectively.

Statistical analysis

Descriptive analysis (mean, standard deviation, and Student's t test) was done using Statistical Package for Social Sciences (SPSS17). The comparative outcome of lab data was analyzed by using T-test for paired samples for continuous data. The minimal level of significance was set at $P<0.05$. Correlation coefficients were determined by linear regression analysis.

Results

A total of 1,103 cases were enrolled in the study, and 77 dropped out for various reasons. The mean age of the participants was 27.9 ± 6.25 years.

About 78.9% (870 subjects) had normal HbA1c, 19.1% (211 subjects) had HbA1c in the range of pre-diabetes and 1.99% (22 subjects) had HbA1c>6.5% denoting undiagnosed type 2 diabetes.

Serum levels of zinc, magnesium and selenium were significantly lower among pre-diabetics compared to normal subjects. The same results were obtained when comparing both diabetics and pre-diabetics, and diabetics and normal subjects. There was a significant negative correlation between the levels of HbA1c and all the studied minerals.

Discussion

The cause-and-effect relationship of the deficiency of certain nutrients with pre-diabetes and diabetes remains unclear. In our study, mineral levels in pregnant women at the pre-diabetes stage were significantly lower than that of women with normal glycemic control, but higher than those with diabetes. It has been shown that various trace elements such as Ca, P, Mg, Zn, Cu, Fe, etc. are metabolically interrelated, and there is an alteration in their concentration during pregnancy [24].

Several studies have linked the deficiency of certain nutrients with glycemic control and a possible interaction of multiple nutrients' deficiencies; each of which may have a contributing effect.

In the complex processes of development or progression of diabetes mellitus, micronutrients are involved in several different areas. Some are components of antioxidant enzymes (e.g., Cu, Zn and Mn in the case of the superoxide dismutases, and Selenium for GSHPx), and cofactors in a variety of enzymatic processes of importance in glucose and lipid metabolism (e.g., Zn, Mn, Cu). Evidence for changes in trace mineral and vitamin metabolism as a consequence of diabetes pathophysiology is proved especially among micronutrients which have a recognized antioxidant or pro-oxidant functions, with consideration of the relevance of these changes to current hypotheses regarding the onset of secondary complications in the progression of diabetes [25]. Hyperglycemia also results in overproduction of oxygen free radicals, which contributes to the progression of diabetes [26].

Zinc has been shown to have insulin-like action and anti-diabetic effects; it is required for insulin storage and secretion and it has antioxidant properties. Chronic low intake of zinc is associated with an increased risk of diabetes, and conversely, diabetes also impairs zinc metabolism [27] Comparable to our study, diabetic patients were found to have significantly lower serum zinc levels compared with healthy controls [28].

A recent study reported an improvement in glucose handling in subjects with pre-diabetes supplemented with zinc, and this could potentially be a safe way to prevent the progression of the pre-diabetes stage to diabetes [29]. Previous studies on dietary and supplemental zinc showed a potential protective effect on type 2 diabetes [30].

Results from a recent study suggested that a low magnesium level is an independent risk factor for the development of pre-diabetes and type 2 diabetes [31].

Magnesium is an essential ion involved in multiple levels in insulin's secretion, its binding, and its activity, and it is also a critical cofactor of many enzymes in carbohydrate metabolism. Magnesium plays an important role to improve insulin resistance [32].

The increased incidence of hypomagnesemia among patients with T2D is presumably multifactorial. Altered insulin metabolism, poor glycemic control, and osmotic diuresis may be contributory factors [33].

Plasma selenium concentrations corresponding to optimal health are highly dynamic and based on a combination of factors that need to be considered when assessing epidemiological data, such as the findings linking serum selenium and T2D [34].

Comparable with our study, Ruiz et al found that mean plasma selenium content in diabetic patients was significantly lower than the controls, and that there was a negative correlation between plasma contents of selenium and glycosylated hemoglobin [35].

Studies have shown that selenium can protect against oxidative damage attributable to unregulated blood sugar [36, 37].

Conclusion and Recommendations

Changes in serum levels of some lab parameters occur at the prediabetic stage and precedes the development of diabetes, and may be responsible for medical complications that are recently reported at this stage. Studies should be done for re-establishment of safe target levels of HbA1c.

Further researches should be done on the exact relation between those altered micronutrients in pre-diabetes, and the possible role of their correction on the development and progression of diabetes.

Acknowledgement

The investigators are deeply indebted and wish to express their sincere thanks to King Abdul Aziz City for Science and Technology (KACST) for the generous funding throughout this research. This project was made possible by Grant Number AT. 28-113 from KACST.

References

1. Nozha M, Maatouq M, Mazrou Y, Harthi S, Arafah M, et al. (2004) Diabetes Mellitus in Saudi Arabia. Saudi Med J 25: 1603-1610.
2. (2013) World Health Organization. Country Cooperation Strategy at a glance. Saudi Arabia.
3. International Diabetes Federation (2014) Saudi Arabia URL: http://www.idf.org/membership/mena/saudi-arabia.
4. Buys schaert M, Medina J, Bergman M, Shah A, Lonier J (2015) Prediabetes and Associated Disorders. Endocrine 48: 371-393.
5. Hammouda S, Hakeem R (2015) Role of HbA1c in Predicting Risk for Congenital Malformations. Primary Care Diabetes 9: 458-464.
6. Hughes R, Rowan J, Florkowski C (2016) Is There a Role for HbA1c in Pregnancy? Curr Diab Rep 16: 5.
7. Mills J, Simpson J, Driscoll S, Peterson J, Van Allen M, et al. (1988) Incidence of Spontaneous Abortion among Normal Women and Insulin-dependent Diabetic Women Whose Pregnancies were Identified Within 21 days of Conception. N Engl J Med 319: 1617-1623.
8. Greene MF (1999) Spontaneous Abortions and Major Malformations in Women with Diabetes Mellitus. Semin Reprod Endocrinol 17: 127-136.
9. Barbour LA (2014) Changing Perspectives in Pre-existing Diabetes and Obesity in Pregnancy: Maternal and Infant Short- and Long-term Outcomes. Curr Opin Endocrinol Diabetes Obes 4: 257-263.
10. Scott D (1934) Crystalline insulin. Biochem J 2: 1592.
11. Rabinowitch MI, Foster GS, Fowler AF, Corcoran AC (1936) Clinical Experiences with Protamine-Zinc-Insulin and Other Mixtures of Zinc and Insulin in Diabetes Mellitus. Can Med Assoc J 35: 239-252.
12. Sladek R, Rocheleau G, Rung J, Dina C, Shen L, et al. (2007) A Genome-wide Association Study Identifies Novel Risk Loci for Type 2 diabetes. Nature 445: 881-885.
13. Rutter GA, Chimienti F (2015) SLC30A8 Mutations in Type 2 Diabetes. Diabetologia 58: 31-36.
14. El Dib R, Gameiro OL, Ogata MS, Modolo NS, Braz LG, et al. (2015) Zinc Supplementation for the Prevention of Type 2 Diabetes Mellitus in Adults with Insulin Resistance. Cochrane Database Syst Rev 5: CD005525.
15. Vardatsikos G, Pandey NR, Srivastava AK (2013) Insulino-mimetic and Anti-diabetic Effects of Zinc. J. Inorg. Biochem 120: 8-17.
16. Guerrero-Romero F, Rascon-Pacheco RA, Rodriguez-Moran M, de la Pena JE, Wacher N (2008) Hypomagnesaemia and Risk for Metabolic Glucose Disorders: A 10-year Follow-up Study. Eur J Clin Investig 38: 389-396.
17. Hruby A, Meigs JB, O'Donnell CJ, Jacques PF, McKeown NM (2014) Higher Magnesium Intake Reduces Risk of Impaired Glucose and Insulin Metabolism and Progression from Prediabetes to Diabetes in Middle-aged Americans. Diabetes Care 37: 419-427.
18. Guerrero-Romero F, Simental-Mendía LE, Hernández-Ronquillo G, Rodriguez-Morán M (2015) Oral Magnesium Supplementation Improves Glycaemic Status in Subjects with Prediabetes and Hypomagnesaemia: A Double-blind Placebo-controlled Randomized Trial. Diabetes Metab 41: 202-207.
19. Simmons D, Joshi S, Shaw J (2010) Hypomagnesaemia is Associated with Diabetes: Not Pre-diabetes, Obesity or the Metabolic Syndrome. Diabetes Res Clin Pract 87: 261-266.
20. Rayman MP, Stranges S (2013) Epidemiology of Selenium and Type 2 Diabetes: Can We Make Sense of it? Free Radical Biology and Medicine 65: 1557-1564.
21. Labunskyy VM, Lee BC, Handy DE, Loscalzo J, Hatfield DL, et al. (2011) Both Maximal Expression of Selenoproteins and Selenoprotein Deficiency can Promote Development of Type 2 Diabetes-like Phenotype in Mice. Antioxid. Redox Signal 14: 2327-2336.
22. Stapleton SR (2000) Selenium: An Insulin-mimetic. Cell Mol Life Sci 57: 1874-1879.

23. Silverman R, Thakker U, Ellman T, Wong I, Smith K, et al. (2011) Hemoglobin A1c as a Screen for Previously Undiagnosed Prediabetes and Diabetes in an Acute-Care Setting. Diabetes Care 34: 1908-1912.
24. Khoushabi F, Shadan MR, Miri A, Sharifi-Rad J (2016) Determination of Maternal Serum Zinc, Iron, Calcium and Magnesium During Pregnancy in Pregnant Women and Umbilical Cord Blood and Their Association with Outcome of Pregnancy. Mater Sociomed 28: 104-107.
25. Thompson K, Godin D (1995) Micronutrients AND Antioxidants in the Progression of Diabetes. Nutrition Research 15: 1377-1410.
26. Song Y, Cook N, Albert C, Van Denburgh M, Manson J (2009) Effect of Homocysteine-Lowering Treatment with Folic Acid and B Vitamins on Risk of Type 2 Diabetes in Women: A Randomized Controlled Trial. Diabetes 58: 1921-1928.
27. Wang S, Liu GC, Wintergerst KA, Cai L (2015) Metals in Diabetes: Zinc Homeostasis in the Metabolic Syndrome and Diabetes. In Molecular Nutrition and Diabetes: A Volume in the Molecular Nutrition Series. Elsevier Inc 169-182.
28. Al-Maroof RA, Al-Sharbatti SS (2006) Serum Zinc Levels in Diabetic Patients and Effect of Zinc Supplementation on Glycemic Control of Type 2 Diabetics. Saudi Med J 27: 344-350.
29. Islama R, Attiaa J, Alib L, McEvoya M, Selimc S, et al. (2016) Zinc Supplementation for Improving Glucose Handling in Pre-diabetes: A double Blind Randomized Placebo Controlled Pilot Study. Diabetes Research and Clinical Practice 115: 39-46.
30. Khoushabi F, Shadan MR, Miri A, Sharifi-Rad J (2016) Determination of Maternal Serum Zinc, Iron, Calcium and Magnesium During Pregnancy in Pregnant Women and Umbilical Cord Blood and Their Association with Outcome of Pregnancy. Mater Sociomed 28: 104-107.
31. Fang C, Wang X, Wu W, Gu X, Ye T, et al. (2016) Association of Serum Magnesium Level with Odds of Prediabetes and Diabetes in a Southern Chinese Population: a Prospective Nested Case. Biol Trace Elem Res 172: 307-314.
32. Volpe SL (2008) Magnesium, the Metabolic Syndrome, Insulin Resistance, and Type 2 Diabetes Mellitus. Critical Reviews in Food Science and Nutrition 48: 293-300.
33. Pham PC, Pham PT, Pham SV, Miller JM, Pham PT (2007) Hypomagnesemia in Patients with Type 2 Diabetes. Clin J Am Soc Nephrol 2: 366-373.
34. Rocourt C, Cheng W (2013) Selenium Supranutrition: Are the Potential Benefits of Chemoprevention Outweighed by the Promotion of Diabetes and Insulin Resistance? Nutrients 5: 1349-1365.
35. Ruiz C, Alegria A,Barbera R, Farre R, Lagarda J (1998) Selenium, Zinc and Copper in Plasma of Patients with Type 1 Diabetes Mellitus in Different Metabolic Control States. J. Trace Elem. Med. Biol 12: 91-95.
36. Naziroglu M, Cay M (2001) Protective Role of Intraperitoneally Administered Vitamin E and Selenium on the Antioxidative Defense Mechanisms in Rats with Diabetes Induced by Streptozotocin. Biol Trace Elem Res 79: 149-159.
37. Guney M, Erdemoglu E, Mungan T (2011) Selenium-vitamin E Combination and Melatonin Modulates Diabetes-induced Blood Oxidative Damage and Fetal Outcomes in Pregnant Rats. Biol. Trace Elem Res 143: 1091-1102.