The impact of maternal overweight on hair essential trace element and mineral content in pregnant women and their children

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Abstract
The aim of the present study was to investigate hair essential trace elements and mineral levels in 105 pregnant normal-weight (control) and 55 overweight and obese women in the third trimester of pregnancy, as well as in their children at the age of 9 months. The hair essential trace elements and mineral levels were assessed using inductively-coupled plasma mass-spectrometry. Overweight pregnant women had significantly reduced Cr (-24%; p = 0.047) and Zn (-13%; p = 0.008) content, as well as elevated hair Na and K levels as compared to the controls. Children from overweight and obese mothers had lower hair Mo (-18%; p = 0.017), Se (-8%; p = 0.043), and V (-24%; p = 0.028) levels, as well as elevated Sr content (19%; p = 0.025). Correlation analysis revealed a significant relationship between maternal and child hair levels of Co (r = 0.170; p=0.038), Cu (r = 0.513; p<0.001), Mn (r = 0.240; p=0.003), and Na (r = 0.181; p=0.027) in the whole sample. Pre-pregnancy maternal body mass index (BMI) positively correlated with maternal hair K (r = 0.336; p<0.001) and Na (r = 0.212; p=0.008), and negatively correlated with V (r = -0.204; p=0.011) and Zn (r = -0.162; p=0.045) levels. The results indicate that impaired trace element and mineral metabolism may play a role in the link between maternal obesity, complications of pregnancy and child's postnatal development. Hypothetically, dietary improvement may be used as a tool to reduce these risks. However, further experimental and clinical studies are required to investigate the relationship between obesity and trace element metabolism in pregnancy.

Key words: maternal obesity; chromium; vanadium; zinc; pregnancy.

Introduction

Essential trace elements and minerals play a significant role in male [1,2] and female [3,4] reproductive health. Specifically, in females variations of zinc and copper [5], as well as selenium [6] are related to menstrual cycle. Impaired trace element metabolism may be involved in polycystic ovarian syndrome pathogenesis [7].

Adequate nutritional status of trace elements and minerals is also required for normal embryogenesis and pregnancy [8,9]. Particularly, in view of the role of selenium in pregnancy [10], altered Se metabolism may be associated with adverse pregnancy outcomes [11], including higher risk of gestational diabetes [12] and pre-eclampsia [13]. Adequate selenium status and selenoprotein metabolism is also essential for fetal development [14]. In addition, selenium may also play a protective role against hazardous environmental pollutants in pregnancy [15].

Zinc also plays a crucial role in pregnancy, as well as prenatal and postnatal development [16]. Poor maternal Zn status is associated with reduced linear growth and psycho-motor development in children [17], although the existing data are inconsistent [18]. The results of a meta-analysis demonstrate that Zn supplementation may reduce the rate of preterm birth [19].

Other trace elements and minerals including copper, magnesium [20], iron [21], calcium [22], also play a role in normal pregnancy and fetal development. A significant relationship has been demonstrated between trace element status and risk of infertility [23], as well as pre-eclampsia [24] and other adverse outcomes [25]. It has been also noted that altered trace element status may be also involved in pathogenesis of postpartum depression [26].

Essential elements have also been linked to obesity, which itself negatively affects female reproductive system and pregnancy. For example, a study of 287,213 pregnancies demonstrated the association between obesity and gestational diabetes, pre-eclampsia, intrauterine death and other adverse pregnancy outcomes [27]. In addition, obese women are characterized by a higher rate of placental vascular lesions [28]. Research has demonstrated links between obesity pathogenesis and metabolism of iron [29], zinc [30], magnesium [31], as well as other essential elements. Correspondingly, multiple studies have demonstrated altered trace element and mineral levels in hair [32, 33], blood [34, 35], and urine [36] of obese patients.

Given the role of metal-ligand homeostasis both in obesity and reproduction, as well as the adverse effects of maternal obesity on pregnancy and fetal development, it is hypothesized that altered trace element and mineral metabolism play a role in the link between obesity and pregnancy complications and outcomes. The existing data are insufficient to test this hypothesis [17, 24, 37]. Therefore, the present study aims to address this issue by evaluating hair essential trace elements and mineral levels in pregnant non-overweight and overweight women and their children at the age of 9 months.

Materials and methods

Participants

A total of 159 mother-children pairs, living in the Siberian Federal District of the Russian Federation, were involved in the present study. The present study was performed in agreement with the principles of the Declaration of Helsinki and its later amendments. The protocol of the study was approved by the Ethics Committee for Interdisciplinary Investigations (Tomsk State University, Russia). All women participated in the investigation on a voluntary basis and were informed about the objectives and procedures of the study. The women signed informed consent for their own and their children's participation. Hair sampling procedures involving children were performed in the presence of one of the parents.

Measures

Pre-pregnancy body mass index (BMI) was assessed using a standard formula: BMI = weight (kg) / height^2 (m^2). Based on BMI values, all women were divided into two groups: normal-weight controls (n = 104; BMI =18 - 25) and overweight (n = 55; BMI > 25).

Demographic information, obstetric anamnesis, as well as information about the pregnancy were recorded for all women (Table 1). Prenatal monitoring of fetal condition (Table 2) was performed regularly in agreement with the program of prenatal screening (Ministry of Health of the Russian Federation, No. 572n). Specifically, chronic fetal hypoxia was assessed using doppler ultrasonography. Blood serum levels of human chorionic gonadotropin (hCG) and pregnancy-associated plasma protein (PaPP) as markers of eclampsia and adverse pregnancy outcome [38, 39] were assessed in the first trimester of pregnancy using enzyme-linked immunosorbent assay (ELISA). Threatened miscarriage (ICD-10: O20.0), being characterized by vaginal bleeding and increased risk of premature delivery [40] was registered regularly (each trimester). At delivery, newborn health status information including body weight, height, head and chest circumference, as well as Apgar 1 and 5 scores was recorded by neonatologist in the delivery room (Table 3).

Hair sampling and preparation

Maternal hair sampling was performed in the third trimester of pregnancy, whereas hair from their children were collected at the age of 9 months. 9-month-old children were examined in order to investigate the impact of maternal overweight and obesity not only during gestation, but also at breastfeeding. Proximal parts of hair samples were collected from 3 sites of the occipital region using ethanol-precleaned stainless steel scissors in a quantity of 0.05–0.1 g. All examinees have washed their hair in the morning before sampling using usual commercial shampoos. Earlier data demonstrate that commercial shampoos not enriched with trace elements (zinc, selenium) do not affect hair trace element levels [41].

In the laboratory the obtained hair samples were washed with acetone and rinsed three times with deionized water (18 MΩ · cm) from DVS-M/1HA-1(2)-L electric distiller (Mediana-Filter, Podolsk, Russia). Washed hair samples were dried on air at 60°C to a stable weight. Microwave degradation of hair samples (50 mg) was performed in the presence of concentrated HNO_3 (Sigma-Aldrich Co., St. Louis, MO, USA) in Teflon tubes using Berghof SW-4 DAP-40 (microwave frequency, 2.46 GHz; power, 1450 W) microwave system (Berghof Products + Instruments GmbH, 72800 Eningen, Germany) at 170–180°C for 20 minutes. The obtained solutions were adjusted to 15 ml with distilled deionized water and transferred into polypropylene test tubes for further analysis.

Hair analysis and quality control

The levels of essential trace elements (Co, Cr, Cu, Fe, I, Mn, Mo, Se, Si, Sr, V, and Zn) and minerals (Ca, K, Mg, Na, P) were established using inductively-coupled plasma mass-spectrometry in dynamic reaction cell mode (ICP-DRC-MS) at NexION 300D (PerkinElmer Inc., Shelton, CT, USA) equipped with 7-port FAST valve and ESI SC-2 DX4 autosampler (Elemental Scientific Inc., Omaha, NE, USA). The system was calibrated via external calibration using standard solutions containing 0.5, 5, 10 and 50 μg/l of the studied elements prepared from Universal Data Acquisition Standards Kit (PerkinElmer Inc.). Internal online standardization was performed using 10 μg/l yttrium-89 and rhodium-103 solutions prepared from Yttrium (Y) and Rhodium (Rh) Pure Single-Element Standard (PerkinElmer Inc. Shelton, CT, USA) on a matrix containing 8% 1-butanol (Merck KGaA, Gernsheim, Germany), 0.8% Triton X-100 (Sigma-Aldrich Co., St. Louis, MO, USA), 0.02% tetramethylammonium hydroxide (Alfa Aesar, Ward Hill, MA, USA) and 0.02% ethylenediaminetetraacetic acid (Sigma-Aldrich Co., St. Louis, MO, USA). Laboratory quality control was performed twice a day (before and after a set of analysis) using GBW09101 human hair certified reference material (Shanghai Institute of Nuclear Research, Shanghai, China). The recovery rates for the studied trace elements and minerals varied from 92% to 111%. The laboratory is also a participant of the Occupational and Environmental Laboratory Medicine External Quality Assessment Schemes (OELM EQAS).

Statistical analysis

Statistical analyses were performed using Statistica 10.0 (Statsoft, Tulsa, OK, USA). Data distribution was assessed using Shapiro-Wilk test. As data on hair trace element and mineral levels were characterized by non-Gaussian distribution, median and 25–75 percentile boundaries (interquartile range, IQR) were used as descriptive statistics. Demographic and anthropometric data from both mothers and their children were normally distributed, therefore mean and standard deviation (SD) were used for data expression. Significance of group differences was assessed using the non-parametric Mann-Whitney U test for paired-group comparisons and one-way ANOVA. False Discovery Rate (FRD) adjustment for p-value was applied due to multiple comparisons. Correlation analysis was performed using Spearman's rank correlation coefficient. The level of significance of $p < 0.05$ was used for all statistical analyses.

Results

The data demonstrate that pregnant women in the overweight group had 34% higher values of pre-pregnancy body weight and of BMI, as compared to the control group (Table 1). Women in the overweight group also had earlier age of menarche and first sex. No significant group differences were found in age, pre-pregnancy body height, as well as other parameters.

The results of prenatal monitoring of fetal health (Table 2) indicate that the risk of spontaneous abortion (miscarriage) in the first trimester was more likely in overweight and obese women. However, no significant group differences in relation to the risk of miscarriage in the second and third trimesters was observed. The rate of chronic fetal hypoxia as assessed by Doppler studies was similar for the two groups. The circulating levels of PaPP and hCG in blood of overweight women were significantly lower than those in the control group by 33% and 41%, respectively.

Assessment of children's health at delivery (Table 3) did not reveal any significant group differences. Pregnancy duration, as well as the rate of Cesarean section, were similar in the two groups.

The data demonstrate that overweight status was associated with altered hair trace element and mineral levels in pregnancy (Table 4). Specifically, hair Cr and Zn levels were significantly reduced in overweight women, as compared to the women with normal weight by 24% and 13%, respectively. In contrast, hair K and Na content was severely elevated, being higher than the respective values in the control group by 104% and 55%. It is also notable that hair Fe levels in the overweight group were 26% lower than the control values, with marginal significance.

Differences were observed in the level of several hair trace elements and minerals in children of overweight vs. non-overweight mothers (Table 5). In particular, hair Mo, Se, and V content in children from overweight women was 18%, 8%, and 24% lower as compared to the respective control values. In contrast, hair Sr in this group of children exceeded the control levels by 19%. No significant group differences in hair Cr, Zn, K, and Na content were revealed.

Correlation analysis was performed to investigate the association between maternal and children's hair trace elements and minerals (Table 6). In the full cohort (non-overweight and overweight groups combined), a significant correlation was observed between maternal and child hair levels for the following elements: Co ($p = 0.038$), Cu ($p<0.001$), Mn ($p = 0.003$), and Na ($p = 0.027$). In the control group of mother-child pairs, a significant correlation was observed for only hair Mn ($p = 0.005$). In contrast, in the overweight group, significant correlations between mothers and children were revealed for Co ($p<0.001$), Cu ($p < 0.001$), I ($p = 0.002$), and Na ($p = 0.006$).

Correlation analysis also demonstrated the association of hair trace element and mineral content with BMI values in women (Table 7). In the full cohort of women, BMI directly correlated with hair K ($p<0.001$) and Na ($p = 0.008$) content. In contrast, hair V ($p = 0.011$) and Zn ($p = 0.045$) were inversely associated with BMI values. Similarly to the total sample, BMI was inversely related to hair V ($p = 0.016$) and Zn ($p = 0.029$) levels in the normal weight group. In the overweight group, only hair Fe ($p = 0.007$) and Si ($p = 0.049$) correlated with BMI values. No significant associations between maternal BMI and hair trace elements in children's hair were observed.

Discussion

The results of this study showed no significant association between maternal overweight status and adverse outcomes in pregnancy and offspring at 9 months. Nevertheless, overweight status was related to both maternal and offspring hair essential trace element and mineral content. The only adverse parameters that differed between study groups were reduced hCG and PaPP levels, as well as significantly increased risk of spontaneous abortion in the first trimester in the overweight group as compared to the controls. The observed decrease in hCG levels in pregnant overweight women is in agreement with the earlier data [42]. The observed association may be related to the interplay between adipokines and hCG [42, 43]. Lower PaPP-A [38] and h-CG [39] levels were associated with increased risk of preeclampsia and premature delivery.

The obtained data on hair trace elements in overweight pregnant women are in agreement with the existing studies. Hair Zn levels were found to be reduced in overweight women. Several studies have demonstrated that obese individuals are characterized by reduced hair, as well as urinary [44] and serum/plasma [45] zinc levels. Plasma zinc was found to be reduced in pregnant underweight, overweight, obese women [46]. Moreover, Zn status is also associated with metabolic profile in obese patients [47] and experimental animals [48]. Zn supplementation was shown to be effective in improving metabolic health in obesity [49]. The association between low Zn stores, its protective effect, and obesity may be mediated by antioxidant and anti-inflammatory effects of zinc, as well as by its role in regulation of adipogenic signals [30].

Pregnancy is associated with modulation of Zn kinetics including increased Zn absorption and reduced loss in order to provide fetus with sufficient levels of the nutrient [50]. Although data on the association between Zn and pregnancy complications are rather contradictory [51], the existing studies demonstrate the role of altered Zn metabolism on prenatal and postnatal development [16]. Particularly, the association between Zn deficiency and fetal growth restriction [52] and neural tube defects [53] has been revealed. The underlying mechanisms may involve altered regulation of transcription factors in fetal brain [54]. In addition, the results of meta-analysis demonstrated that Zn supplementation may reduce preterm birth [55].

Chromium content was also decreased in overweight women as compared to controls. Low Cr status in overweight/obese patients may be associated with the intake of refined foods especially those enriched with sugars that contain low levels of Cr and increase its excretion [56]. Diet-induced obesity was shown to result in reduced hair and adipose tissue chromium levels in experimental animals, being also associated with metabolic parameters [57]. Moreover, multiple studies have considered chromium as the potential tool for metabolic improvement in obesity and diabetes [56].

Data on the potential role of chromium and its deficiency in pregnancy and its complications are limited. However, it has been demonstrated that reduced chromium levels are associated with gestational diabetes [58], which may be at least partially associated with increased chromium loss [59]. The existing data on the impact of maternal chromium deficiency on fetal development are also insufficient. Particularly, experimental studies demonstrated that maternal chromium restriction results in increased body adiposity in the offspring [60] through modulation of methylation status of hepatic genes involved in insulin signaling [61].

The present findings of higher hair Na and K levels in overweight pregnant women are in agreement with our earlier data demonstrating increased hair Na and K levels in both obese postmenopausal women [62] and high-fat-fed animals [63]. The underlying mechanism of the observed alterations may involve modulation of mineralocorticoid secretion in obesity [64]. It has been also demonstrated that dietary intake as well as urinary Na levels were associated with increased adiposity [65]. Conversely, potassium intake was proposed to be effective in reduction of the obesity risk [66].

The results of the present study also found links between maternal overweight status and trace element status of children, although the changes were not similar to those in their mothers. Data on prenatal programing of trace element status by maternal obesity are limited. However, earlier studies demonstrated the impact of maternal overweight and obesity in pregnancy on placental nutrient transport [67]. Impaired trace element metabolism may be associated with modulation of hepatic metallothionein expression in the offspring [68]. Specifically, umbilical vein Zn levels were found to be altered in the obese group of maternal-fetal pairs [69].

In a recent study it has been revealed that children from obese women are characterized by reduced hair Mo, Se, Sr, and V levels. Earlier data by [70] demonstrated a negative correlation between maternal body mass and amniotic fluid V and Sr levels (r = - 0.31), however the correlation did not reach significance [70]. We propose that the reduced levels of these trace elements in offspring hair may be at least partially associated with impaired processing of these elements during pregnancy in obese women. The physiological effect of vanadium is mainly related to its insulin mimetic effects being beneficial in both diabetes and obesity [71]. Correspondingly, obese children were characterized by significantly reduced serum vanadium levels [72]. Strontium is also shown to play a significant role in improvement of insulin sensitivity, as well as in bone physiology [73]. In turn, selenium is essential for various functions due to its role in selenoproteins. Particularly, selenium plays a significant role in brain development, mediating the immune-thyroid interplay [74]. Selenium also has an impact on glycemic control [75] although high Se exposure may disrupt insulin signaling through modulation of redox environment [76]. Molybdenum deficiency, although being rather rare in humans, is also known to be associated with brain dysfunction [77]. The observed findings of impaired metabolism of vanadium, selenium, and strontium all playing a role in carbohydrate metabolism in children of obese women are in agreement with the experimental observation of insulin resistance in adult offspring from obese ewes [78].

Limitations

The present study has a number of limitations that should be addressed in further studies. First, nutritional intake of trace elements and minerals was not assessed in pregnant women. Monitoring of maternal diet could indicate whether the observed changes in hair trace elements and mineral content are associated with insufficient dietary intake or increased excretion of the elements. Second, data on serum and urine levels of the studied elements would be beneficial in order to elucidate the mechanisms of the observed group differences. Third, in this study, analysis of hair was performed in children at 9 months. This allowed to investigate the impact of maternal weight not only during gestation, but also breastfeeding. However, the absence of hair analysis at delivery precludes disentangling effects of prenatal environment and breast feeding from potential influence of postnatal environmental factors. Finally, the sample size was relatively small and unequal for the two groups. As the study is ongoing, in the future we plan to replicate and extend our findings in a bigger sample.

Conclusions

The results demonstrated that maternal overweight status is associated with impaired hair trace element and mineral content in both mothers and their children. Specifically, overweight pregnant women were characterized by significantly reduced Cr and Zn content alongside elevated hair Na and K levels. Their children had lower Mo, Se, and V levels, and increased Sr content in hair, as compared to the control values. It is possible that impaired trace element and mineral metabolism provides an additional link between maternal overweight and complications of pregnancy and postnatal development. Hypothetically, dietary improvement may be used as a tool to reduce these risks. However, further experimental and clinical studies are required to investigate the complex relationship between weight and trace element metabolism in pregnancy.

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Compliance with Ethical Standards

The present study was performed in agreement with the principles of the Declaration of Helsinki and its later amendments. The protocol of the study was approved by the Ethics Committee for Interdisciplinary Investigations (Tomsk State University, Russia) (project No. 8.1.11.2018). All women participated in the investigation on a voluntary basis and were informed about the objectives and procedures of the study. The women signed informed consent for their own and their children's participation. Hair sampling procedures involving children were performed in the presence of one of the parents.

Conflict of interest

The authors declare no conflict of interest

References

1. Yamaguchi S, Miura C, Kikuchi K, Celino FT, Agusa T, Tanabe S, Miura T (2009) Zinc is an essential trace element for spermatogenesis. Proc Natl Acad Sci USA 106(26):10859-10864. https://doi.org/10.1073/pnas.0900602106
2. Ahsan U, Kamran Z, Raza I, Ahmad S, Babar W, Riaz MH, Iqbal Z (2014) Role of selenium in male reproduction. A review. Anim Reprod Sci 146(1-2):55-62. https://doi: 10.1016/j.anireprosci.2014.01.009
3. Kontic-Vucinic O, Sulovic N, Radunovic N (2006) Micronutrients in women's reproductive health: II Minerals and trace elements. Int J Fertil Womens Med 51(3):116-124
4. Mistry HD, Pipkin FB, Redman CW, Poston L (2012) Selenium in reproductive health. Am J Obstet Gynecol 206(1):21-30. https://doi.org/10.1016/j.ajog.2011.07.034
5. Michos C, Kalfakakou V, Karkabounas S, Kiortsis D, Evangelou A (2010) Changes in copper and zinc plasma concentrations during the normal menstrual cycle in women. Gynecol Endocrinol 26(4):250-255. https://doi.org/10.3109/09513590903247857
6. Ha EJ, Smith AM (2003) Plasma selenium and plasma and erythrocyte glutathione peroxidase activity increase with estrogen during the menstrual cycle. J Am Coll Nutr 22(1):43-51. https://doi.org/10.1080/07315724.2003.10719274
7. Chakraborty P, Ghosh S, Goswami SK, Kabir SN, Chakravarty B, Jana K (2013) Altered trace mineral milieu might play an aetiological role in the pathogenesis of polycystic ovary syndrome. Biol Trace Elem Res 152(1):9-15. https://doi.org/10.1007/s12011-012-9592-5
8. Wu G, Imhoff-Kunsch B, Girard AW (2012) Biological mechanisms for nutritional regulation of maternal health and fetal development. Paediatr Perinat Epidemiol 26:4-26. https://doi.org/10.1111/j.1365-3016.2012.01291.x
9. Spencer BH, Vanderlelie JJ, Perkins AV (2015) Essentiality of trace element micronutrition in human pregnancy: a systematic review. J Preg Child Health 2(157):1-7. https://doi.org/10.4172/2376-127X.1000157
10. Pieczyńska J, Grajeta H (2015) The role of selenium in human conception and pregnancy. J Trace Elem Med Biol 29:31-38. https://doi.org/10.1016/j.jtemb.2014.07.003
11. Mariath AB, Bergamaschi DP, Rondó PH, Ana CAT, de FragasHinnig P, Abbade JF, Diniz SG (2011) The possible role of selenium status in adverse pregnancy outcomes. Br J Nutr 105(10):1418-1428. https://doi.org/10.1017/S0007114510005866
12. Hawkes WC, Alkan Z, Lang K, King JC (2004) Plasma selenium decrease during pregnancy is associated with glucose intolerance. Biol Trace Elem Res 100(1):19-29
13. Rayman MP, Bode P, Redman CW (2003) Low selenium status is associated with the occurrence of the pregnancy disease preeclampsia in women from the United Kingdom. Am J Obstet Gynecol 189(5):1343-1349
14. Hatfield DL, Tsuji PA, Carlson BA, Gladyshev VN (2014) Selenium and selenocysteine: roles in cancer, health, and development. Trends Biochem Sci 39(3):112-120. https://doi.org/10.1016/j.tibs.2013.12.007
15. Kantola M, Purkunen R, Kröger P, Tooming A, Juravskaja J, Pasanen M, Vartiainen T (2004) Selenium in pregnancy: is selenium an active defective ion against environmental chemical stress? Environ Res 96(1):51-61
16. Uriu-Adams JY, Keen CL (2010) Zinc and reproduction: effects of zinc deficiency on prenatal and early postnatal development. Birth Defects Res B Dev Reprod Toxicol 89(4):313-325. https://doi.org/10.1002/bdrb.20264
17. Scheplyagina LA (2005) Impact of the mother's zinc deficiency on the woman's and newborn's health status. J Trace Elem Med Biol 19(1):29-35
18. Aydemir F, Çavdar AO, Söylemez F, Cengiz B (2003) Plasma zinc levels during pregnancy and its relationship to maternal and neonatal characteristics. Biol Trace Elem Res 91(3):193-202. https://doi.org/10.1385/BTER:91:3:193

19. Ota E, Mori R, Middleton P, Tobe Gai R, Mahomed K, Miyazaki C, Bhutta ZA (2015) Zinc supplementation for improving pregnancy and infant outcome. Cochrane Database Syst Rev 2. https://doi.org/10.1002/14651858.CD000230.pub5
20. Pathak P, Kapil U (2004) Role of trace elements zinc, copper and magnesium during pregnancy and its outcome. Indian J Pediatr 71(11):1003-1005/
21. Cao C, O'brien KO (2013) Pregnancy and iron homeostasis: an update. Nutr Rev 71(1):35-51. https://doi.org/10.1111/j.1753-4887.2012.00550.x
22. Kovacs CS (2011) Calcium and bone metabolism disorders during pregnancy and lactation. Endocrinol Metab Clin 40(4):795-826. https://doi.org/10.1016/j.ecl.2011.08.002
23. Skalny AV, Tinkov AA, Bohan TG, Shabalovskaya MB, Terekhina O, Leshchinskaia SB, Kovas Y (2018) Toxicological and nutritional status of trace elements in hair of women with in vitro fertilization (IVF) pregnancy and their 9-month-old children. Reprod Toxicol 82:50-56. https://doi.org/10.1016/j.reprotox.2018.10.004
24. Al-Jameil N, Tabassum H, Ali MN, Qadeer MA, Khan FA, Al-Rashed M (2017) Correlation between serum trace elements and risk of preeclampsia: A case controlled study in Riyadh, Saudi Arabia Saudi. J Biol Sci 24(6):1142-1148. https://doi.org/10.1016/j.sjbs.2015.02.009
25. Shen PJ, Gong B, Xu FY, Luo Y, Zhou B, Wang C (2015) Four trace elements in pregnant women and their relationships with adverse pregnancy outcomes. Eur Rev Med Pharmacol Sci 19(24):4690-4697
26. Etebary S, Nikseresht S, Sadeghipour HR, Zarrindast MR (2010) Postpartum depression and role of serum trace elements. Iran J Psychiatry 5(2):40
27. Sebire NJ, Jolly M, Harris JP, Wadsworth J, Joffe M, Beard RW, Robinson S (2001) Maternal obesity and pregnancy outcome: a study of 287 213 pregnancies in London. Int J Obes 25(8):1175-1182
28. Kovo M, Zion-Saukhanov E, Schreiber L, Mevorach N, Divon M, Ben-Haroush A, Bar J (2015) The effect of maternal obesity on pregnancy outcome in correlation with placental pathology. Reprod Sci 22(12):1643-1648. https://doi.org/10.1177/1933719115592712
29. Nikonorov AA, Skalnaya MG, Tinkov AA, Skalny AV (2015) Mutual interaction between iron homeostasis and obesity pathogenesis. J Trace Elem Med Biol 30:207-214. https://doi.org/10.1016/j.jtemb.2014.05.005
30. Olechnowicz J, Tinkov A, Skalny A, Suliburska J (2018) Zinc status is associated with inflammation, oxidative stress, lipid, and glucose metabolism. J Physiol Sci:1-13. https://doi.org/10.1007/s12576-017-0571-7
31. Nielsen FH (2010) Magnesium, inflammation, and obesity in chronic disease. Nutr Rev 68(6):333-340. https://doi.org/10.1111/j.1753-4887.2010.00293.x
32. Fatani SH, Saleh SA, Adly HM, Abdulkhaliq AA (2016) Trace element alterations in the hair of diabetic and obese women. Biol Trace Elem Res 174(1):32-39. https://doi.org/10.1007/s12011-016-0691-6
33. Skalnaya MG, Skalny AV, Grabeklis AR, Serebryansky EP, Demidov VA, Tinkov AA (2018) Hair Trace Elements in Overweight and Obese Adults in Association with Metabolic Parameters. Biol Trace Elem Res 186(1):12-20. https://doi.org/10.1007/s12011-018-1282-5
34. Yerlikaya FH, Toker A, Arıbaş A (2013) Serum trace elements in obese women with or without diabetes. Indian J Med Res 137(2):339-345. https://doi.org/10.1186/1824-7288-40-20
35. Zhang H, Yan C, Yang Z, Zhang W, Niu Y, Li X, Su Q (2017) Alterations of serum trace elements in patients with type 2 diabetes. J Trace Elem Med Biol 40:91-96. https://doi.org/10.1016/j.jtemb.2016
36. Błażewicz A, Klatka M, Astel A, Partyka M, Kocjan R (2013) Differences in trace metal concentrations (Co, Cu, Fe, Mn, Zn, Cd, And Ni) in whole blood, plasma, and urine of obese and nonobese children. Biol Trace Elem Res 155(2):190-200. https://doi.org/10.1007/s12011-013-9783-8
37. Kocyłowski R, Grzesiak M, Gaj Z, Lorenc W, Bakinowska E, Barałkiewicz D, Suliburska J (2018) Evaluation of Essential and Toxic Elements in Amniotic Fluid and Maternal Serum at Birth. Biol Trace Elem Res:1-10. https://doi.org/10.1007/s12011-018-1471-2
38. Ranta JK, Raatikainen K, Romppanen J, Pulkki K, Heinonen S (2011) Decreased PAPP-A is associated with preeclampsia, premature delivery and small for gestational age infants but not with placental abruption. Eur J Obstet Gynecol Reprod Biol 157(1):48-52. https://doi.org/10.1016/j.ejogrb.2011.03.004
39. Korevaar TI, Steegers EA, Chaker L, Medici M, Jaddoe VW, Visser TJ, Peeters RP (2016) The risk of preeclampsia according to high thyroid function in pregnancy differs by hCG concentration. J Clin Endocrinol Metab, 101(12):5037-5043. https://doi.org/10.1210/jc.2016-2397

40. Johns J, Jauniaux E (2006) Threatened miscarriage as a predictor of obstetric outcome. Obstet Gynecol 107(4):845-850.
41. LeBlanc A, Dumas P, Lefebvre L (1999) Trace element content of commercial shampoos: impact on trace element levels in hair. Sci Total Environ 229(1-2):121-124
42. Eskild A, Fedorcsak P, Mørkrid L, Tanbo TG (2012) Maternal body mass index and serum concentrations of human chorionic gonadotropin in very early pregnancy. Fertil Steril 98(4):905-910. https://doi.org/10.1016/j.fertnstert.2012.06.011
43. Połeć A, Fedorcsák P, Eskild A, Tanbo TG (2014) The interplay of human chorionic gonadotropin (hCG) with basic fibroblast growth factor and adipokines on angiogenesis in vitro. Placenta 35(4):249-253. https://doi.org/10.1016/j.placenta.2014.02.002
44. Ozturk P, Kurutas E, Ataseven A, Dokur N, Gumusalan Y, Gorur A, Inaloz S (2014) BMI and levels of zinc, copper in hair, serum and urine of Turkish male patients with androgenetic alopecia. J Trace Elem Med Biol 28(3):266-270. https://doi.org/10.1016/j.jtemb.2014.03.003
45. Konukoglu D, Turhan MS, Ercan M, Serin O (2004) Relationship between plasma leptin and zinc levels and the effect of insulin and oxidative stress on leptin levels in obese diabetic patients. J Nutr Biochem 15(12):757-760
46. Ugwuja EI, Akubugwo EI, Obidoa O, Ibiam AU (2010) Maternal BMI during pregnancy: effect on trace elements status and pregnancy outcomes. Int J Environ Health Res 3(2):71-78. https://doi.org/10.4314/ijhr.v3i2.70270
47. Ferro F, Lima VB, Soares N, Cozzolino S, Marreiro D (2011) Biomarkers of metabolic syndrome and its relationship with the zinc nutritional status in obese women. Nutr Hosp 26(3):650-654. https://doi.org/10.1590/S0212-16112011000300032
48. Tinkov AA, Popova EV, Gatiatulina ER, Skalnaya AA, Yakovenko EN, Alchinova IB, Nikonorov AA (2016) Decreased adipose tissue zinc content is associated with metabolic parameters in high fat fed Wistar rats. Acta Sci Pol Technol Aliment 15(1):99-105. https://doi.org/10.1 7306/J.AFS.2016.1.10
49. Capdor J, Foster M, Petocz P, Samman S (2013) Zinc and glycemic control: a meta-analysis of randomisedplacebo controlled supplementation trials in humans. J Trace Elem Med Biol 27(2):137-142. https://doi.org/10.1016/j.jtemb.2012.08.001
50. Donangelo CM, King JC (2012) Maternal zinc intakes and homeostatic adjustments during pregnancy and lactation. Nutrients 4(7):782-798. https://doi.org/10.3390/nu4070782
51. Wilson R, Grieger J, Bianco-Miotto T, Roberts C (2016) Association between maternal zinc status, dietary zinc intake and pregnancy complications: a systematic review. Nutrients 8(10):641. https://doi.org/10.3390/nu8100641
52. Wang H, Hu YF, Hao JH, Chen YH, Su PY, Wang Y, Tao FB (2015) Maternal zinc deficiency during pregnancy elevates the risks of fetal growth restriction: a population-based birth cohort study. Sci Rep 5:11262. https://doi.org/10.1038/srep11262
53. Dey AC, Shahidullah M, Mannan MA, Noor MK, Saha L, Rahman SA (2010) Maternal and neonatal serum zinc level and its relationship with neural tube defects. J Health Popul Nutr 28(4):343. https://doi.org/10.3329/jhpn.v28i4.6040
54. Aimo L, Mackenzie GG, Keenan AH, Oteiza PI (2010) Gestational zinc deficiency affects the regulation of transcription factors AP-1, NF-κB and NFAT in fetal brain. J Nutr Biochem 21(11):1069-1075. https://doi.org/10.1016/j.jnutbio.2009.09.003
55. Chaffee BW, King JC (2012) Effect of zinc supplementation on pregnancy and infant outcomes: a systematic review. Paediatr Perinat Epidemiol 26:118-137. https://doi.org/10.1111/j.1365-3016.2012.01289.x
56. Lau FC, Bagchi M, Sen CK, Bagchi D (2008) Nutrigenomic basis of beneficial effects of chromium (III) on obesity and diabetes. Mol Cell Biochem 317(1-2):1-10. https://doi.org/10.1007/s11010-008-9744-2
57. Tinkov AA, Popova EV, Polyakova VS, Kwan OV, Skalny AV, Nikonorov AA (2015) Adipose tissue chromium and vanadium disbalance in high-fat fed Wistar rats. J Trace Elem Med Biol 29:176-181. https://doi.org/10.1016/j.jtemb.2014.07.006
58. Sundararaman PG, Sridhar GR, Sujatha V, Anita V (2012) Serum chromium levels in gestational diabetes mellitus. Indian J Endocrinol Metab. 16(1):70-73. https://doi.org/10.4103/2230-8210.94266
59. Morris BW, Samaniego S, Fraser R, MacNeil S (2000) Increased chromium excretion in pregnancy is associated with insulin resistance. J Trace Elem Exp Med 13(4):389-396. https://doi.org/10.1002/1520-670X(2000)13:4<389::AID-JTRA7>3.0.CO;2-Q

60. Padmavathi IJ, Rao KR, Venu L, Ganeshan M, Kumar KA, Rao CN, Raghunath M (2010) Chronic maternal dietary chromium restriction modulates visceral adiposity: probable underlying mechanisms. Diabetes 59(1):98-104. https://doi.org/10.2337/db09-0779
61. Zhang Q, Sun X, Xiao X, Zheng J, Li M, Yu M, Wang X (2017) Dietary chromium restriction of pregnant mice changes the methylation status of hepatic genes involved with insulin signaling in adult male offspring. PloS one 12(1), e0169889. https://doi.org/10.1371/journal.pone.0169889
62. Skalnaya MG, Demidov VA (2007) Hair trace element contents in women with obesity and type 2 diabetes. J Trace Elem Med Biol 21:59-61
63. Tinkov AA, Popova EV, Polyakova VS, Skalny AV, Nikonorov AA (2014) Effect of high fat diet on macroelement content in hair and adipose tissue of Wistar rats. Trace Elem Electroly 31(4):156-59. https://doi.org/10.5414/TEX01351
64. Ehrhart-Bornstein M, Arakelyan K, Krug AW, Scherbaum WA, Bornstein SR (2004) Fat cells may be the obesity–hypertension link: human adipogenic factors stimulate aldosterone secretion from adrenocortical cells. Endocrine Res 30(4):865-870
65. Lee SK, Kim MK (2016) Relationship of sodium intake with obesity among Korean children and adolescents: Korea National Health and Nutrition Examination Survey. Br J Nutr 115(5):834-841. https://doi.org/10.1017/S0007114515005152
66. Rafie N, Hamedani SG, Mohammadifard N, Feizi A, Safavi SM (2018) 24-h urinary sodium to potassium ratio and its association with obesity in children and adolescents. Eur J Nutr 1-7. https://doi.org/10.1007/s00394-018-1645-x
67. Jones HN, Woollett LA, Barbour N, Prasad PD, Powell TL, Jansson T (2009) High-fat diet before and during pregnancy causes marked up-regulation of placental nutrient transport and fetal overgrowth in C57/BL6 mice. FASEB J 23(1):271-278. https://doi.org/10.1096/fj.08-116889
68. Lomas-Soria C, Reyes-Castro LA, Rodríguez-González GL, Ibáñez CA, Bautista CJ, Cox LA, Zambrano E (2018) Maternal obesity has sex-dependent effects on insulin, glucose and lipid metabolism and the liver transcriptome in young adult rat offspring. J Physiol 596(19):4611-4628. https://doi.org/10.1113/JP276372
69. Al-Saleh E, Nandakumaran M, Al-Harmi J, Sadan T, Al-Enezi H (2006) Maternal-fetal status of copper, iron, molybdenum, selenium, and zinc in obese pregnant women in late gestation. Biol Trace Elem Res 113(2):113-123. https://doi.org/10.1385/BTER:113:2:113
70. Suliburska J, Kocyłowski R, Komorowicz I, Grzesiak M, Bogdański P, Barałkiewicz D (2016) Concentrations of mineral in amniotic fluid and their relations to selected maternal and fetal parameters. Biol Trace Elem Res 172(1):37-45. https://doi.org/10.1007/s12011-015-0557-3
71. Pessoa JC, Etcheverry S, Gambino D (2015) Vanadium compounds in medicine. Coord Chem Rev 301:24-48. https://doi.org/10.1016/j.ccr.2014.12.002
72. Tascilar ME, Ozgen IT, Abaci A, Serdar M, Aykut O (2011) Trace elements in obese Turkish children. Biol Trace Elem Res 143(1):188-195. https://doi.org/10.1007/s12011-010-8878-8
73. Nielsen SP (2004) The biological role of strontium. Bone 35(3):583-588
74. Schomburg L (2012) Selenium, selenoproteins and the thyroid gland: interactions in health and disease. Nat Rev Endocrinol 8(3):160-171. https://doi.org/10.1038/nrendo.2011.174
75. Wiernsperger N, Rapin J (2010) Trace elements in glucometabolic disorders: an update. Diabetol Metab Syndr 2(1):70. https://doi.org/10.1186/1758-5996-2-70
76. Zhou J, Huang K, Lei XG (2013) Selenium and diabetes—evidence from animal studies. Free Radic Biol Med 65:1548-1556. https://doi.org/10.1016/j.freeradbiomed.2013.07.012
77. Gupta UC, Srivastava PC, Gupta SC (2011) Role of micronutrients: Boron and molybdenum in crops and in human health and nutrition. Curr Nutr Food Sci 7(2):126-136. https://doi.org/10.2174/157340111795713807
78. Long NM, George LA, Uthlaut AB, Smith DT, Nijland MJ, Nathanielsz PW, Ford SP (2010) Maternal obesity and increased nutrient intake before and during gestation in the ewe results in altered growth, adiposity, and glucose tolerance in adult offspring. J Anim Sci 88(11):3546-3553. https://doi.org/10.2527/jas.2010-3083

Table 1. Demographic and obstetric characteristics of the examined women with normal and excessive body mass index

Parameter	Normal weight (n = 104)	Overweight (n = 55)	P value
Age, years	32.5±4.0	33.0±5.3	0.151
Pre-pregnancy height, cm	166.0±5.7	166.0±5.8	0.972
Pre-pregnancy weight, kg	58.0±6.3	77.5±11.2	< 0.001 *
Pre-pregnancy BMI	21.0±1.7	28.1±3.7	< 0.001 *
Age of menarche, years	13.2±1.3	12.6±1.2	0.014 *
Age of first sex, years	18.7±2.5	17.9±2.0	0.043 *
Use of Fe supplements, %	43%	35%	0.288
Special diet	13%	24%	0.118
First pregnancy	44%	25%	0.021 *
Number of pregnancies	2.3±1.5	2.5±1.2	0.235
Planned pregnancy	85%	91%	0.268
Anemia	61%	53%	0.481
Thyroid pathology	19%	39%	0.839

Data expressed as mean ± SD or % (% is indicative of the respective number of women with particular characteristics from the total number of women in the group); * Significant difference at $p < 0.05$.

Table 2. Prenatal monitoring of fetal condition in normal weight and overweight pregnant women

Parameter	Normal weight mothers (n = 104)	Overweight mothers (n = 55)	P value
Chronic hypoxia	10%	16%	0.568
Risk of spontaneous abortion			
I trimester	27%	49%	0.043 *
II trimester	33%	37%	0.700
III trimester	26%	29%	0.804
Whole pregnancy	13%	31%	0.121
PaPP, IU/L	3.361 (2.203 - 4.829)	2.258 (1.048 - 4.317)	0.012 *
hCG, IU/L	59.5 (37.6 - 78.2)	35.0 (20.4 - 55.4)	0.004 *

Data expressed as Median (IQR) or % (% is indicative of the respective number of women with particular characteristics from the total number of women in the group); * Significant difference at $p < 0.05$.

Table 3. Children's health at delivery in relation to maternal body mass index

Parameter	Normal weight mothers (n = 104)	Overweight mothers (n = 55)	P value
Gender, F/M (%)	46/54	64/36	0.115
Pregnancy duration, wk	39.2±1.6	38.9±2.5	0.825
Cesarean section	38%	49%	0.316
Apgar score 1, pts	8.2±0.5	8.1±0.6	0.375
Apgar score 5, pts	9.0±0.6	8.8±0.6	0.265
Body weight, g	3349.1±535.8	3261.5±898.7	0.954
Height, cm	52.3±2.8	52.5±4.3	0.319
Head circumference, cm	34.3±1.5	34.3±2.4	0.714
Chest circumference, cm	33.6±2.0	33.8±3.0	0.388

Data expressed as mean ± SD or % (% is indicative of the respective number of women with particular characteristics from the total number of women in the group); * Significant difference at $p < 0.05$.

Table 4. Hair essential trace element and electrolyte levels in normal weight and overweight women (µg/g)

Element	Normal weight mothers (n = 104)	Overweight mothers (n = 55)	P value
Ca	1947.9 (1143.6-3222.0)	1561.2 (813.0-2631.4)	0.193
Co	0.019 (0.009-0.056)	0.015 (0.009-0.028)	0.151
Cr	0.098 (0.052-0.166)	0.074 (0.043-0.118)	0.047 *
Cu	13.66 (11.05-21.75)	14.99 (11.25-24.45)	0.333
Fe	16.85 (9.07-32.94)	12.44 (9.08-21.17)	0.079
I	0.307 (0.193-0.514)	0.323 (0.215-0.482)	0.739
K	92.2 (44.2-190.3)	188.1 (106.0-573.4)	< 0.001 *
Mg	113.2 (75.2-198.9)	99.2 (59.3-221.5)	0.608
Mn	0.919 (0.468-1.704)	0.767 (0.558-1.39)	0.994
Mo	0.022 (0.016-0.027)	0.021 (0.016-0.03)	0.921
Na	73.3 (43.2-133)	113.8 (70.1-267.4)	0.002 *
P	162.3 (146.2-178)	164 (148.5-200.9)	0.256
Se	0.423 (0.328-0.483)	0.376 (0.261-0.486)	0.255
Si	32.6 (19.71-45.46)	26.36 (16.06-39.18)	0.141
Sr	6.937 (4.089-11.518)	6.393 (3.097-11.205)	0.645
V	0.010 (0.005-0.024)	0.007 (0.005-0.014)	0.177
Zn	229.2 (190.7-303.6)	198.2 (152.0-246.0)	0.008 *
Data expressed as Median (IQR); * Significant difference at p < 0.05.			

Table 5. Essential trace elements and minerals in hair of children of normal weight and overweight women (μg/g)

Element	Normal weight mothers (n = 104)	Overweight mothers (n = 55)	P value
Ca	324.4 (239.5-438.7)	341.0 (259.7-565.0)	0.233
Co	0.009 (0.006-0.017)	0.008 (0.005-0.014)	0.337
Cr	0.182 (0.125-0.302)	0.152 (0.105-0.263)	0.242
Cu	10.43 (7.97-12.90)	9.922 (8.019-12.740)	0.800
Fe	13.95 (10.02-20.13)	13.73 (9.34-18.34)	0.596
I	0.804 (0.449-1.390)	0.605 (0.430-1.036)	0.176
K	869.5 (349.7-1644.4)	687.4 (330.4-1691.4)	0.815
Mg	19.43 (15.41-28.39)	23.15 (17.49-29.47)	0.101
Mn	0.319 (0.226-0.475)	0.334 (0.242-0.524)	0.689
Mo	0.050 (0.033-0.066)	0.041 (0.026-0.055)	0.017 *
Na	275.8 (133.2-627.3)	334.4 (135.0-703.0)	0.366
P	160.2 (131.0-185.9)	158.0 (135.8-176.0)	0.794
Se	0.469 (0.400-0.540)	0.433 (0.368-0.483)	0.043 *
Si	25.05 (14.65-51.43)	30.46 (18.44-59.00)	0.410
Sr	0.800 (0.565-1.187)	0.955 (0.734-1.629)	0.025 *
V	0.021 (0.012-0.055)	0.016 (0.007-0.040)	0.028 *
Zn	67.22 (43.84-111.86)	84.03 (51.62-118.99)	0.219

Data expressed as Median (IQR); * Significant difference at $p < 0.05$.

Table 6. Correlation between maternal and children's hair trace elements and minerals

Element	General cohort (n = 159)	Normal weight (n = 104)	Overweight (n = 55)
Ca	-0.086	-0.095	-0.255
Co	0.171 *	0.110	0.745 *
Cr	-0.048	-0.064	-0.071
Cu	0.514 *	0.084	0.803 *
Fe	-0.082	-0.107	0.019
I	0.121	0.072	0.431 *
K	0.049	0.045	0.048
Mg	-0.109	-0.089	-0.176
Mn	0.241 *	0.279 *	0.303 *
Mo	-0.020	-0.025	-0.003
Na	0.180 *	-0.003	0.435 *
P	-0.056	-0.006	-0.141
Se	-0.026	-0.077	0.052
Si	0.036	0.061	0.009
Sr	-0.079	-0.083	-0.145
V	0.088	0.071	0.160
Zn	0.006	-0.007	0.089

Data expressed as correlation coefficient (r); * - correlation is significant at $p < 0.05$

Table 6. Correlation between maternal hair trace element and mineral content and pre-pregnancy BMI values

Element	General cohort (n = 159)	Normal weight (n = 104)	Overweight (n = 55)
Ca	0.006	-0.012	0.167
Co	0.040	0.093	0.173
Cr	-0.143	-0.188	0.095
Cu	0.021	-0.085	0.067
Fe	-0.097	-0.083	0.376 *
I	-0.080	-0.014	-0.071
K	0.336 *	0.056	0.068
Mg	0.073	0.019	0.154
Mn	-0.003	-0.080	0.158
Mo	-0.021	0.075	0.122
Na	0.212 *	-0.015	0.090
P	0.131	0.127	-0.076
Se	-0.092	-0.050	0.018
Si	-0.025	-0.103	0.277 *
Sr	-0.065	-0.083	0.171
V	-0.204 *	-0.237 *	-0.105
Zn	-0.162 *	-0.215 *	0.044

Data expressed as correlation coefficient (r); * - correlation is significant at $p < 0.05$