



# **A Comparative Study of Micronutrient Levels in the Women with Hypertensive Gestational Diabetes with and without Preeclampsia**

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ARTICLE INFO	ABSTRACT
<i>Article type:</i> Research Paper	<b>Introduction:</b> Diabetes is a common metabolic disease during pregnancy. Preeclampsia is the most prevalent disorder that accompanies gestational diabetes. Recent studies have demonstrated the role of micronutrients in diabetic women with preeclampsia. The present study aimed to compare the levels of micronutrients in the women with gestational and hypertensive diabetes with and without preeclampsia.
<i>Article History:</i> Received: 21 Aug 2018 Accepted: 05 Sep 2018 Published: 20 Jan 2019	<b>Methods:</b> This descriptive study was conducted on 72 women with gestational and hypertensive diabetes with and without preeclampsia, who were in the third trimester of pregnancy. Demographic characteristics and data on the previous and current pregnancies were obtained using a questionnaire. In addition, blood samples were collected, and the levels of micronutrients were measured, including iron, zinc, magnesium, and lipid profile. Data analysis was performed in SPSS version 19 using t-test and Chi-square at the significance level of 0.05.
<i>Keywords:</i> Iron Zinc Magnesium Copper Lipid Profile Preeclampsia Diabetes	<b>Results:</b> Among 72 participants, 32 cases had gestational diabetes and hypertension with preeclampsia, and 40 cases were without preeclampsia. Mean iron level in the group with preeclampsia was $108.91 \pm 64.58$ , while it was $79.75 \pm 53.33$ in the group without preeclampsia. The level of zinc in the group with preeclampsia was $65.73 \pm 24.40$ , while it was $53.17 \pm 19.23$ in the group without preeclampsia. The level of copper in groups with and without preeclampsia was $220.59 \pm 61.92$ and $192.83 \pm 47.46$ , respectively. Differences between the groups in terms of the levels of iron ( $P=0.39$ ), zinc ( $P=0.02$ ), and copper ( $P=0.035$ ) were considered significant. In addition, the levels of magnesium, cholesterol, and triglyceride had no significant differences between the groups ( $P>0.5$ ).
	<b>Conclusion:</b> According to the results, the levels of micronutrients such as iron, zinc, and copper were higher in the women with gestational and hypertensive diabetes with preeclampsia compared to those without preeclampsia.

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## **Introduction**

Diabetes is the most common metabolic disorder across the world. During pregnancy, the serum level of insulin physiologically increases twice, which could be due to the increased levels of diabetogenic hormones, such as cortisol, placental lactogenic hormone, and progesterone. On the other hand, lipolysis has been reported to increase in overweight pregnant women due to the higher acid level. The function of insulin at the end of the

gestational period is 50-70% higher in pregnant women compared to non-pregnant women, which in turn increases the serum level of insulin.

According to the literature (1,2), preeclampsia is more prevalent in diabetic mothers compared to non-diabetic pregnant women. Preeclampsia is a severe disorder, which affects 8% of pregnant women and may lead to maternal and neonatal death, thereby

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increasing the risk of preterm birth and intrauterine growth restriction (IUGR) (4).

Evidence suggests that with the increased gestational age, the anoxic environment of the placenta changes into an environment filled with oxygen, leading to the high production of oxygen free radicals. With the presence of metals such as iron as the catalyst, these active species initiate cellular impairments such as the impairment of red blood cells (5).

Iron and heme play a key role in preeclampsia as the catalysts in the lipid peroxidation of tissues. According to reports, the presence of the iron ion and lipid peroxidase gives rise to the lipid peroxidation of phospholipid in the cell membrane, which may cause cellular dysfunction. As a result, the simultaneity of two hyperlipidemia factors during the second half of the gestational period and increased serum iron in the mother may lead to oxidative stress and disorders in the endothelial cells of the placenta. Recent studies have indicated that the level of zinc decreases in the women with gestational diabetes due to its high excretion, as well as its key role in the production and storage of insulin.

Zinc requirement increases during pregnancy. Considering the high requirement of zinc for natural growth and development during pregnancy, lack of zinc increases the risk of various gestational complications, such as diabetes. On the other hand, some studies have discussed the effects of the changes in several minerals (e.g., increased zinc levels) in the etiology and pathology of preeclampsia (3, 6). Rare metals (e.g., copper) play a biological role similar to catalysts (antioxidant enzymes); as a result, they are involved in the etiology of preeclampsia and other gestational complications. Moreover, magnesium is considered to be a secondary carrier of insulin; in fact, lack of magnesium in cells occurs simultaneously with the deficiency in the function of several enzymes that are involved in the ATPase activity. These enzymes are also involved in the metabolism of glucose, requiring magnesium as the cofactor. Furthermore, increased level of copper has been reported to have a significant impact on the manifestation of the symptoms of cardiovascular diseases. Regarding the increase in the requirements of these micronutrients during the gestational

period, the mentioned effects may be more significant due to the lack of these micronutrients. The present study aimed to investigate the effects of micronutrient levels on the incidence of preeclampsia in the pregnant women with gestational diabetes and hypertension based on the studies focused on the correlations between the levels of various micronutrients (iron, copper, zinc, and magnesium) with the incidence of preeclampsia and gestational diabetes.

## Material and methods

This descriptive study was conducted during autumn 2016-2017 in Imam Reza and Omolbanin hospitals in Mashhad, Iran. The study was registered at the Research Gate of Mashhad University of Medical Sciences (date: 09-03-2016, code: 941059, ethical code: IR.MUMS.fm.REC.1394.668). Sample population consisted of 72 pregnant women referring to the obstetric and maternity clinics of Imam Reza and Omolbanin hospitals (hospitalized or outpatient). The patients were diagnosed with gestational diabetes and hypertension in the third trimester of pregnancy. The inclusion criteria being in the third pregnancy trimester and blood pressure of  $\geq 140/90$  mmHg without proteinuria. Women with a minimum of one abnormal glucose level in 75-gram glucose tolerance test who had been diagnosed with gestational diabetes were presented with the objectives of the study and provided written informed consent for enrollment. The participants completed a questionnaire containing demographic data and obstetrical data, including the age at pregnancy (week), current and previous obstetric status, current and previous simultaneous diseases and their consequences, type of previous deliveries, symptoms of preeclampsia, duration of diabetes and hypertension during pregnancy (week), and blood pressure. During the stay of the subjects in the hospital for delivery, their difference in terms of preeclampsia was examined, and they were divided into two groups of women with and without preeclampsia. Data analysis was performed in SPSS version 19 using t-test and Chi-square, and the P-value of less than 0.05 was considered significant.

## Results and Discussion

In total, 72 women were enrolled in the

research and examined until the end.

**Table 1.** Comparing the means of age level of education and job in preeclampsia and non-preeclampsia people

variables	affected by preeclampsia n(32)	not affected by preeclampsia 40( n)	P value
	Percent (n)	Percent (n)	
Age	5/7±32/94	6/01±32/95	0/99**
Levels of education			
elementary	72/8(%24)	63(%25)	0/828*
Diploma- Higher than diploma	27/2(%8)	27(%15)	
job			
housewife	71(%23)	90(%36)	0/80*
CON	29(%9)	10(%4)	

\* Resulted from an independent Chi square test

\*\* resulted from T-student test

As it can be observed in table 1, there is no meaningful difference between the mean of age, level of education, and job in the two groups

Among the participants, 32 women with gestational diabetes and hypertension were diagnosed with preeclampsia, while 40 women were not diagnosed as such. In the comparison of the mean levels of iron, zinc, copper, and magnesium in the subjects with and without preeclampsia, the results of independent t-test showed no statistically significant difference in the mean level of iron between the groups ( $P=0.039$ ). On the other hand, the mean level of iron was higher in the women with preeclampsia compared to those without preeclampsia. In addition, the level of iron was 29.16 units higher in the subjects with preeclampsia compared to the other group.

Our findings are in line with the results obtained by Tasneem Zafar, who concluded that the levels of iron, hemoglobin, and serum ferritin were significantly higher in the women with preeclampsia compared to the pregnant women with normal blood pressure (16). In another research by Taheripanah, the level of serum ferritin was reported to increase in the women with preeclampsia (17). The results of the present study are consisted with the findings of Haji Mardani et al. and Kym et al. In the latter, the risk of preeclampsia was higher in the pregnant women with higher serum levels of iron. On the other hand, Haji Mardani et al. reported that the serum level of iron was significantly higher in the subjects with preeclampsia compared to those with normal pregnancy ( $P>0.001$ ). Furthermore, the serum level of ferritin level was observed to be significantly higher in the women with preeclampsia in the mentioned research, while total iron-binding capacity(TIBC) was reported to be lower in the subjects with preeclampsia

compared to those with normal pregnancy ( $P<0.001$ ). According to the findings of the current research and previous studies in this regard, the iron profile, including the serum levels of iron and ferritin and degree of transfer in saturation, was higher in the patients with preeclampsia compared to normal subjects (18).

In the present study, the P-value of 0.02 indicated a significant difference between the mean levels of zinc between the two groups. Correspondingly, the level of zinc was significantly higher in the subjects with preeclampsia compared to those without preeclampsia. In the study by Kym et al. (2012), the serum level of zinc in the pregnant women with preeclampsia was reported to be lower compared to those with normal blood pressure (7), while the risk of preeclampsia was lower in the pregnant women with higher serum levels of zinc. In another research, Harma et al. claimed that the serum level of zinc was higher in the women with higher blood pressure compared to those without hypertension, which is in congruence with the results of the present study (8).

According to the study by Bahadoran et al., the zinc levels in pregnant women had a significant, negative correlation with gestational hypertension and preeclampsia; in other words, reduced serum level of zinc was associated with the severity of preeclampsia (9). In contrast, Adam et al. stated that the mean level of zinc in normal women had no statistically significant difference with hypertensive pregnant women. The discrepancy between the results of the present study and other studies in this regard could be attributed to the differences in trophic

levels, age, and age at pregnancy. The level of copper in groups with preeclampsia was  $220.59 \pm 61.92$  higher than groups without preeclampsia  $192.83 \pm 47.46$  ( $P$  value=0.035). So In the current research, the  $P$ -value of 0.035 was an indicator of the significant difference in the mean level of copper between the two groups. Based on the findings in this respect, it could be stated that the level of copper was higher in the women with preeclampsia compared to those without preeclampsia. This finding is in line with the study by Ranjkesh et al., which compared the level of copper in the serum and 24-hour urine of pregnant women with preeclampsia with healthy individuals. Furthermore, their findings demonstrated that the density of copper in the serum and 24-hour urine of the women with preeclampsia was significantly higher compared to the women with normal blood pressure (15). The results of

the present study also showed an association between the increased density of copper in the serum and urine with preeclampsia. However, this increment did not reveal the severity of preeclampsia. Further examinations could be performed to predict preeclampsia based on this test.

In the current research, comparison of the mean level of magnesium in the women with preeclampsia and those without this condition was performed using independent t-test, and the mean level of magnesium was similar in the two groups. In addition, the level of magnesium had no effect on the incidence of preeclampsia in the pregnant women ( $P=0.37$ ). The results of independent t-test regarding the comparison of the cholesterol level between the study groups indicated no statistically significant difference in this regard ( $P=0.04$ ).

**Table 2.** Comparing the Means of Micronutrients between Preeclampsia and Non-preeclampsia People

variables	affected by preeclampsia n (32)	not affected by preeclampsia n (40)	P value*
	standard-deviation $\pm$ mean	standard-deviation $\pm$ mean	
Iron (micro/dl)	64/58 $\pm$ 108/91	53/33 $\pm$ 79/75	0/039
Zinc (micro/dl)	24/40 $\pm$ 65/73	19/23 $\pm$ 53/17	0/02
copper(micro/dl)	61/92 $\pm$ 220/59	47/46/ $\pm$ 192/83	0/035
magnesium(mg/dl)	1/11 $\pm$ 2/04	0/76 $\pm$ 1/84	0/37

\* Resulted from an independent T-test

The results of the present study are consistent with the study by Adam et al. (10). In the mentioned study, the serum level of magnesium was evaluated in three groups, including pregnant women, women with normal pregnancy, and women with severe preeclampsia. The comparison of the groups revealed no significant difference in this regard. In another research, Kanagal et al. investigated the serum levels of magnesium between pregnant women with normal blood pressure and women with preeclampsia. The obtained results showed no significant difference in the serum levels of magnesium.

Our findings are in line with the studies by

Adam et al. and Waffy et al. (11). In the former, the mean level of magnesium had no significant differences between normal and hypertensive women. The difference observed between the results of the present study and other studies in this regard could be due to the more differentiated groups in the previous studies. In the current research, the level of cholesterol was predicted to be similar in the two groups. Moreover, the  $P$ -value of 0.04 indicated no significant difference in the mean triglyceride of the women with and without preeclampsia, and the triglyceride level was observed to be almost equal in the study groups.

**Table 3.** Comparing the means of cholesterol and triglyceride in preeclampsia and non-preeclampsia people

variables	affected by preeclampsia n (32)	not affected by preeclampsia n (40)	P value*
	standard-deviation $\pm$ mean	standard-deviation $\pm$ mean	
cholesterol	59/16 $\pm$ 214/82	49/51 $\pm$ 224/73	0/4
triglyceride	93/13 $\pm$ 263/28	99/85 $\pm$ 262/28	0/97

\* Resulted from an independent T-test

As it can be observed in table 3, there is no meaningful difference between the mean of cholesterol and triglyceride in the two groups

In the present study, the mean levels of micronutrient (iron, zinc, and copper) were higher in the women with preeclampsia and gestational diabetes compared to those without these conditions. However, the magnesium level was similar in the study groups with no significant difference. In the present study, the mean levels of micronutrients (e.g., zinc) in the subjects with preeclampsia and gestational diabetes compared to those without these conditions.

According to the study by Kym et al. (2012), the serum level of zinc in the pregnant women with preeclampsia was lower compared to those with normal blood pressure (7), and the risk of preeclampsia was lower in the pregnant women with higher serum levels of zinc. In the mentioned research, the mean serum level of zinc in the mothers was estimated at 95.7-116.6 mg/dl based on the evaluation of the serum level of zinc in 1,033 pregnant women during the first half of the gestational period.

In the current research, the serum zinc in 27.4% of the samples was less than 51 mg/dl, while 7.26% of the samples had a normal status in terms of serum zinc ( $P=0.05$ ). Moreover, the results of independent t-test indicated a significant difference in the mean serum zinc between the women with and without preeclampsia, and the mean level of zinc was lower in the women with preeclampsia. According to the findings of the mentioned research, the reduced level of serum zinc is associated with the incidence of preeclampsia, which is consistent with the results of the present study. On the other hand, Harma et al. stated that the level of serum zinc was higher in the women with higher blood pressure compared to those without hypertension, which is in line with our findings (8).

The findings of the current research are in line with the studies by Adam et al. and Waffy et al. (11). In the former, the mean magnesium level between normal and hypertensive women had no significant difference. Similarly, in a study by Vafaei et al., no significant difference was reported in the serum levels of calcium, magnesium, and zinc. In contrast with the present study, Das et al. stated that the serum level of magnesium was significantly higher in hypertensive pregnant women compared to those with normal pregnancy (12).

The results of the present study are inconsistent with the findings Roudsari et al., which indicated that serum magnesium was significantly lower in the women with preeclampsia compared to those with normal pregnancy (13). Another study in this regard was carried out by Kazemian et al. in order to compare the trophic status of hypertensive pregnant women with those with normal pregnancies. According to the obtained results, the risk of gestational hypertension increased with the consumption of magnesium (95% CI: 84.04-49.0; OR=0.64) (14).

In the present study, the mean level of copper in the women with preeclampsia was higher compared to the other group, which is in line with the study by Ranjkesh et al. In the mentioned research, the serum and 24-hour urine copper levels were compared between the pregnant women with preeclampsia pregnant and healthy individuals. The density of copper in the serum and 24-hour urine samples of the group with preeclampsia was reported to be significantly higher compared to the women with normal blood pressure (15). The findings of the current research showed the increased density of copper in the serum and urine samples of the women with preeclampsia, which could not indicate the severity of preeclampsia. Further examinations are required to employ this test to predict preeclampsia.

In the present study, the mean level of iron was observed to be higher in the women with preeclampsia compared to those without preeclampsia, which is consistent with the results obtained by Tasneem Zafar. In the mentioned study, it was concluded that the levels of iron, hemoglobin, and serum ferritin were significantly higher in the women with preeclampsia compared to the pregnant women with normal blood pressure (16). In another research conducted by Taheripanah, the serum level of ferritin was reported to increase in the women with preeclampsia (17).

Our findings are in line with the studies by Haji Mardani et al. and Kym et al. In the latter, the risk of preeclampsia was reported to be higher in the pregnant women with higher serum levels of iron. Similarly, Haji Mardani et al. claimed that the serum levels of iron were significantly higher in the patients with preeclampsia compared to those with normal



pregnancy ( $P > 0.001$ ). In addition, the serum level of ferritin was observed to be significantly higher in the patients with preeclampsia, while the TIBC was lower in these patients compared to the women with normal pregnancy ( $P < 0.001$ ).

Based on the findings of the current research and previous studies in this regard, the iron profile (serum iron and ferritin and degree of transferrin saturation) is higher in the women with preeclampsia compared to normal subjects (18). Given the importance of preeclampsia in pregnancy and its association with several maternal and fetal complications, Dr. Akhlaghi, Dr. Malekizadeh, and Dr. Aram have performed a research to evaluate and compare the levels of micronutrients between three groups of pregnant women, including women with overt diabetes, gestational diabetes, and healthy women. In the mentioned study, the incidence of preeclampsia was investigated based on the levels of micronutrients in a larger sample size.

## Conclusion

According to the results, the levels of micronutrients in the women with diabetes are correlated with the incidence of preeclampsia. The comparison of the levels of micronutrients (iron, zinc, and copper) in the women with gestational diabetes and hypertension showed significant differences with the women with gestational diabetes without hypertension. However, the serum levels of magnesium, cholesterol, and triglyceride had no significant differences between the groups.

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