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The Impact of Serum Manganese, Molybdenum and Selenium Levels on Pathogenesis of Preeclampsia.

Nadia Mudher Al-Hilli*, Haydar Hashim Al-Shalah, and Mohammed Abbas Hasan.

College of Medicine, University of Babylon, Hilla, Babylon, Iraq.

ABSTRACT

Preeclampsia is a disease that is peculiar to pregnancy, It affect women after twenty weeks of gestation and resolve completely after peurperium. In this study we tried to find any association of changes in serum levels of trace and ultra-trace elements manganese, molybdenum, and selenium with the development of pre-eclampsia. The study included 120 women, half of them (60) were diagnosed as preeclamptic in the third trimester while the other sixty were healthy pregnant women (controls) in the last trimester. Measurement of serum levels of these substances was done using graphite furnace atomic absorption spectrophotometer technique. The results were expressed as mean ± standard error of mean. Statistically significance is defined at a P value < 0.05. Serum Manganese and selenium levels were significantly lower in patients with pre-eclampsia compared to control groups, (7.617 ± 0.293µg/dl vs. 10.847 ± 0.356µg/dl) and (2.546 ± 0.068µg/dl vs. 4.306 ± 0.050µg/dl), (P. value <0.05) respectively. while molybdenum level was not significantly different (2.304 ± 0.173 µg/dl vs. 2.670 ± 0.172 µg/dl), (P. value > 0.05). As conclusion, Deficient levels of manganese and selenium could have a role in the pathogenesis of PE.

Keywords: Pre-eclampsia, Manganese, Molybdenum, Selenium, Graphite Furnace Atomic Absorption Spstrophotometry.

Corresponding author:

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INTRODUCTION

Preeclampsia is a syndrome that affect pregnant women after the 20th week of gestation and consist of hypertension and proteinuria and it resolve after the 6th postpartum week[1]. It is associated with fetal and maternal complications that lead to increased morbidity and mortality[2].In UK, the prevalence of preeclampsia is 3-5%[3]. Its etiology remains unclear and many theories have been considered.

In normal placental implantation, the extra villous trophoblast proliferates from an anchoring villous. The cytotrophoblast invade the uterine spiral arteries in the inner part of the myometrium. Invasion of the spiral arteries is associated with degeneration of the tunica media and replacement by fibrinoid material resulting in loss of resistance and marked dilatation of the spiral artery and increased intervillous blood flow [4]. In pre-eclamptic patients, the placenta suffers from defective implantation. The disease process is composed of two phases. The first phase is characterized by patchy trophoblast invasion so that the spiral arteries retain their muscular walls which will prevent the development of high-flow, low-impedence uteroplacental circulation. The pre-eclamptic placenta will get high resistance, so the flow of blood will be decreased and the perfusion will be inefficient. These will cause ischemia and hypoxia of the placenta. This stressful condition will result in production of reactive oxygen species. Normal endogenous antioxidants will try to scavenge these radicals but failure to do so as they are overwhelmed will result in a condition of oxidative stress. This is fundamental to the pathogenesis of the clinical syndrome of pre-eclampsia[5].

Oxidative stress and release of vasoactive substances from the placenta, lead to activation of the vascular endothelium all over the body. In the second phase of pre-eclampsia, all maternal organs are affected by the general vascular endothelial dysfunction[6].

Cell growth and differentiation in both the mother and her fetus increase the demand for micronutrients, therefore, both of them are liable for deficiency in trace element levels once the dietary supply is inadequate. Essential trace elements are required for various biochemical actions[7].The most specific and important functions of trace elements are the catalytic role of enzymes in chemical reactions and in structural function of large molecules such as hormones [8]. Changes in concentrations and homeostasis of any of these micronutrients in body can contribute in the pathophysiology of various disorders and diseases [7]. Manganese is a component of certain enzymes (e.g. pyruvate carboxylase, mitochondrial superoxide dismutase, arginase) and is also an activator of many others (e.g. hydrolases, glycosyltransferases, kinases, decarboxylases), so deficiency could potentially affect the metabolism of carbohydrates, glycosaminoglycans and cholesterol [9]. Molybdenum is bound to molybdoprotein by two sulfur atoms, this is a substituted pterin which is involved in synthesis of xanthine oxidase and aldehyde oxidase . Molybdenum deficiency causes impaired xanthine oxidase activity, increased xanthine excretion and decreased excretion of uric acid [10].Selenium has an important role in glutathione peroxidase enzyme function. This enzyme act as a scavenger of free radicals and also maintain the red blood cells membranes stability. In addition, selenium has vital role in vitamin E metabolism. It enhance its absorption from the gut and maintain its level in blood. Selenium is also involved in the biosynthesis of thyroid hormones[11].

Aim of Study

The of aim of present study was an attempt to assess the role of some essential trace elements namely manganese, molybdenum and selenium in the development of PE and hence its pathogenesis .

Subjects and Methods:

This case control study was achieved on subjects recruited from Babylon Teaching Hospital for Gynecology & Pediatrics, City of Hilla . Samples were obtained during the period between November 2014 till February 2015, included 120 pregnant women, 60 of them identified with PE by gynecologist expert in the third trimester and other 60 were apparently healthy pregnant women taken as a controls in the same period of pregnancy.

Complete evaluation of pregnant women was undertaken which involve history, physical examination, laboratory investigations, and ultrasound. Pregnant women more than 40 years old, body mass index > 30,

smoking, prior history of PE ,family history of PE , prior hypertension or kidney disease , previous history of vascular disease, and multiple pregnancy were excluded from this study .

The Anthropometric measurements involving age, gestational age, and body mass index of PE group were comparable to control group, where there was no significant differences (P> 0.05).

Ethical considerations:

Legal agreements from research related offices had been taken , in addition , verbal acceptance from all participants involved in this study was undertaken.

Sample collection:

From each subject enrolled in the study. about 5 ml of blood was obtained by vein puncture. However, The patient diagnosed with AMI, the blood was aspirated within 24 hours to avoid changes in parameters results. The aspirated blood was put in gel separating tube, centrifuged at 6000 X g for 10 minutes. The obtained serum was stored in eppendorf and kept freezing until time of analysis.

Estimation of Serum Mn, Mo and Se Concentration:

Serum Mn, Mo and Se concentrations was estimated by Furnace Graphite Atomic Absorption Spectrometer provided by PG Instruments Ltd (United Kingdom) with usage of Serum Mn, Mo and Se hollow cathode lamps supplied by Varian.

RESULTS

Demographic characteristics in patients and control

For the purpose of testing the demographic characteristics matching between patients and control groups, maternal age, gestational age, body mass index were tested. No statistical difference was found in all these characteristics, P value > 0.05, (27.72 ± 0.66 years vs. 26.85 ± 0.53 years), (36.93± 0.46 weeks vs.37.28± 0.28 weeks), (28.30 ± 0.20 Kg/m^2 vs.27.83 ± 0.24 Kg/m^2) respectively, as shown in Table 1. However, parity was significantly different between both groups with (51%) of patients being primigravida while (6.666 %) only were primigravida in the control group this result can be explained by the fact that preeclampsia occur more frequently in primigravid ladies.

Statistically significant differences were found between the mean diastolic blood pressure of patients (106.42 ± 2.03 mmHg) and the mean diastolic blood pressure of controls (77.60 ± 0.69 mmHg), (P. value < 0.05) as shown in Table 1.

The differences between the mean systolic blood pressure of patients and the mean systolic blood pressure of control was also statistically significant (159.63 ± 2.63mmHg, 115.62 ± 0.90mmHg), (P. value < 0.05) .

Table 1 also shows a statistically significant difference between mean of urinary total protein/creatinine ratio for patients (38.82 ± 0.31 mg/mmol) and control (27.94 ± 0.19 mg/mmol), (P. value <0.05).

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Table 1 : Demographic characteristics of pre-eclamptic and healthy women.

NO.	Characteristics	Control	Patient	P. Value
1	Maternal Age (Years) Mean ± SEM	26.85 ± 0.53	27.72 ± 0.66	> 0.05
2	Gestational Age(Weeks) Mean ± SEM	37.28± 0.28	36.93± 0.46	> 0.05
3	BMI (Kg/m^2) Mean ± SEM	27.83 ± 0.24	28.31 ± 0.20	> 0.05
4	Diastolic BP(mmHg) Mean ± SEM	77.60 ± 0.69	106.42 ± 2.03	< 0.05
5	Systolic BP(mmHg) Mean ± SEM	115.62 ± 0.90	159.63 ± 2.63	< 0.05
6	Protein/Creatinine Ratio (mg/mmol) Mean ± SEM	27.94 ±0.19	38.82 ± 0.31	< 0.05
7	Parity			
	ParityCharacteristics	Control		Patient
		No.	%	No.	%
	0	4	6.666	31	51.666
	1-3	54	90	22	36.666
	≥ 4	2	3.333	7	11.666
8	Number of samples	60		60	

Trace and Ultra Trace Elements Studies in patients and control.

Manganese (Mn) Concentrations in Patients and Control.

Figure (1) showed that the mean serum manganese level was significantly lower in patients than in control (7.617 ± 0.293µg/dl vs. 10.847 ± 0.356µg/dl), (P. value < 0.05).

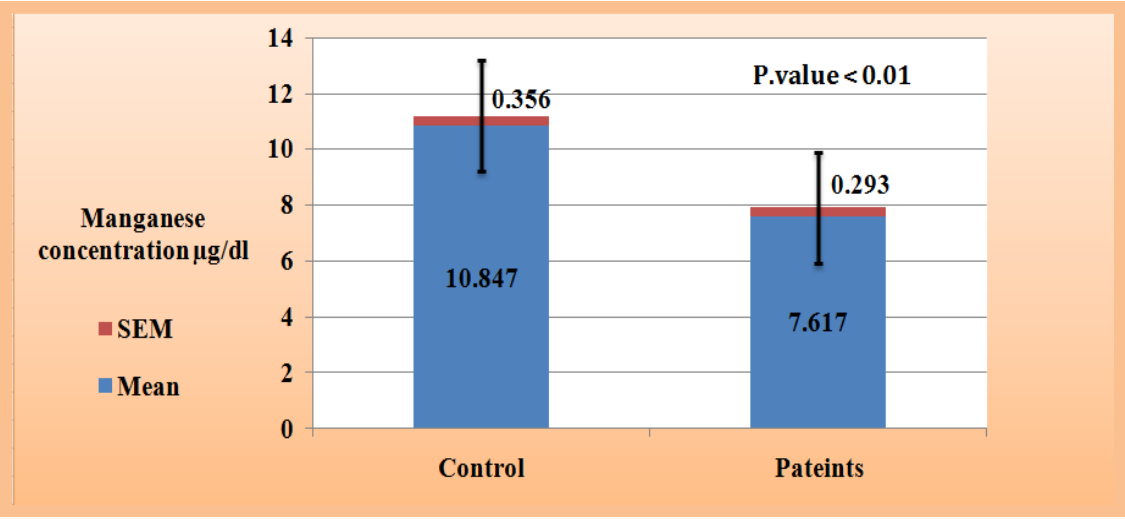

Figure (1): Serum manganese concentrations (µg/dl) in patients and control (mean ±SEM).

Molybdenum (Mo) Concentrations in Patients and Control.

There was no statistically significant difference between the mean serum molybdenum concentrations of patients (2.304 ± 0.173 µg/dl) and the mean serum molybdenum concentrations of controls (2.670 ± 0.172 µg/dl), (P. value > 0.05) as described in Figure (2).

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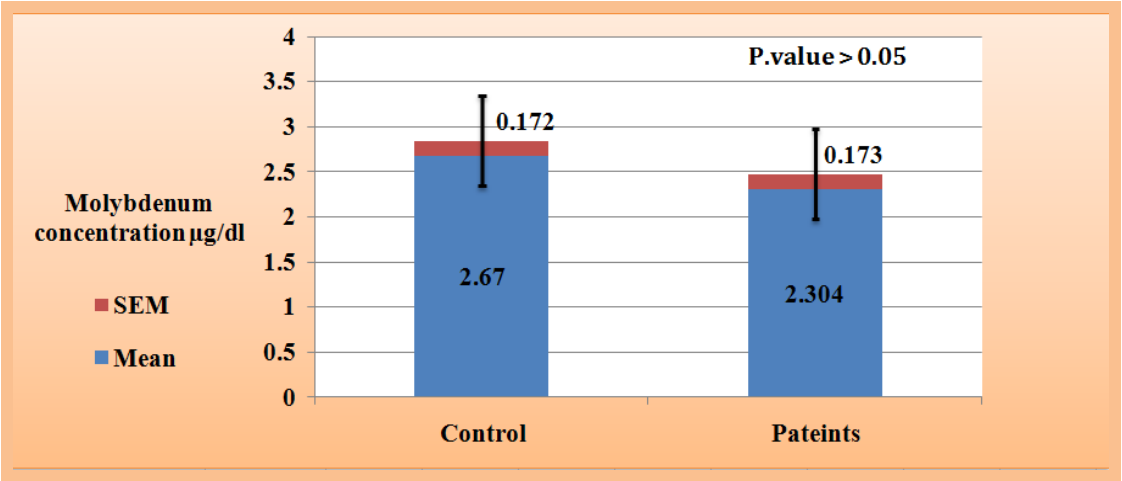

Figure (2): Serum molybdenum concentrations (µg/dl) in patients and control (mean ±SEM).

Selenium (Se) Concentrations in Patients and Control.

Figure (3) illustrated that the mean serum selenium level was significantly lower in patients than in control (2.546 ± 0.068µg/dl vs. 4.306 ± 0.050µg/dl), (P. value <0.05).

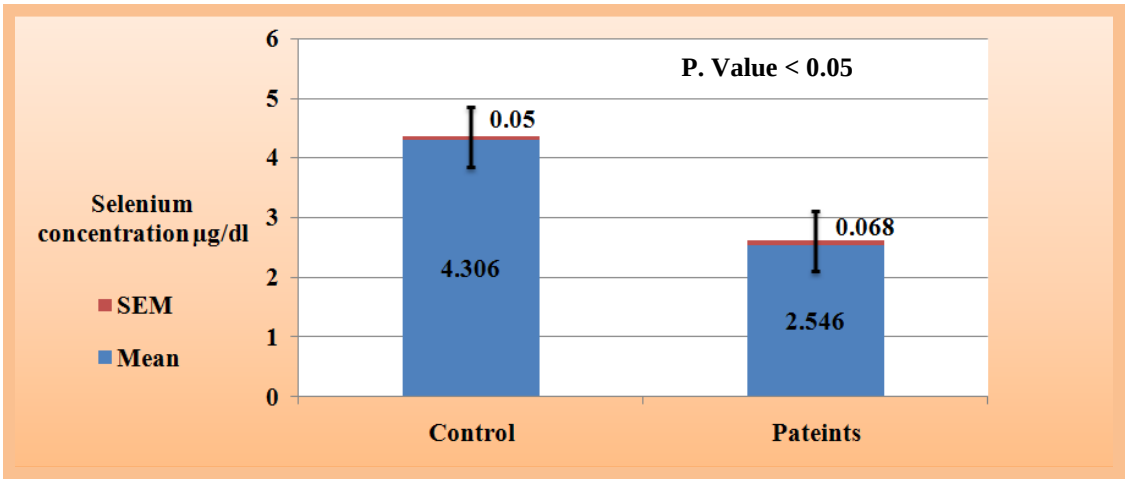

Figure (3): Serum selenium concentrations (µg/dl) in patients and control (mean ±SEM).

DISCUSSION

Manganese (Mn) Concentrations in patients and control.

In this study manganese was found to be significantly decreased in women with preeclampsia when compared to healthy pregnant women. Several studies reported that low level of manganese in serum may cause accumulation of superoxides and other oxygen radicals that may lead to preeclampsia and its consequences, Hofmeyr G, et al[13] Lou G, et al. [14]. Results of this study agree with earlier findings by Mohammed K, et al. [15] and Ohad K, et al. [16].

Manganese also has a role in maintaining endothelial function as it is involved in the synthesis of arginine which is required for the production of nitric oxide. Also manganese is involved in biosynthesis of metalloproteinases and other enzyme and its deficiency will affect many vital cell functions [14]. These observation suggest that manganese deficiency in pregnant women diagnosed with preeclampsia is likely to be a cause rather than an effect.

Molybdenum concentration in patients and controls:

In this study no significant difference was found in the serum concentration of molybdenum between patients and controls. This may be explained by the rare incidence of molybdenum deficiency as only very tiny amounts are needed by human body to maintain its functions. Deficiency only occur in those with genetic defect that lead to impaired absorption of molybdenum from the gut and in those with prolonged total parenteral nutrition. [17] However, no studies found, that assess the molybdenum levels in preeclampsia, in order to compare with our results.

Selenium (Se) Concentrations in patients and control.

This study showed that serum selenium concentration was significantly lower in preeclamptic women compared to control group. Results of this study were in agreement with that of Rayman M et al [18] and Mistry H. et al. [19].

Selenium has an important antioxidant activity. It is a component of several enzymes that act as scavenger for free radicals. Selenium deficiency is associated with free radicals accumulation and oxidative stress and this agree results of a study done by Witzum[20] who stated that free radical accumulation which result from low density lipoproteins peroxidation is one of the pathogenic mechanisms of pre-eclampsia. On the other hand, decreased incidence of pre-eclampsia was found in those with normal serum selenium concentration in a study done by Vanderlelie J [21]. Supplementation with selenium may help reduce the incidence of preclampsia and its complications [22].

CONCLUSION

Deficiency in the maternal manganese and selenium could have an important role in pathogenesis of pre-eclampsia.

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