ISSN: 2073-8854
Magazin of Al-Kufa University for Biology / VOL.5 / NO.2 / year : 2013

Total Iron Binding Capacity (TIBC), free Iron , Ceruloplasmin,Transferrin and ferritin concentration, in pregnant women with pre-eclampsia

RanaM.Hameed* **Wasan Gh. Aboud****
*Department of Biochemistry college of Medicine, Kerbala University
**Head of Department of Obstetrics and Gynecology, college of Medicine, Kerbala University

Background: Preeclampsia is one of the most important complications of pregnancy that is associated with increased morbidity and mortality. The evidence of increased oxidative stress due to endothelial dysfunction in preeclampsia has been well established. The increased oxidative stress is catalyzed in the presence of free transitional metals. Therefore, the relationship of iron status with preeclampsia was under investigation. The objective of the study was to compare Total Iron Binding Capacity (TIBC), Iron ,ceruloplasmin,Transferrin and ferritin concentration, in pre-eclamptic and healthy pregnant women, and to investigation the relation between these factors and preeclampsia.
Method: Blood samples were collected from 40 pregnant women diagnosed as preeclampsia and 30 normal pregnant females at the hospital of Obstetrics and Gynecology between February 2012 and January 2013. We recorded TIBC count, Iron concentration, serumceruloplasmin, ferritinand Transferrin levels in both groups.
Result: Mean serum iron in preeclamptic group was 97.0 ± 7.83, while 94.35± 11.81in normal group ($p \leq 0.01$). Similarly, mean serum TIBC concentration in normal pregnant and preeclamptic women were 319.65± 32.35 and 292.3 ±30.86, respectively ($p \leq 0.01$). The mean serum ferritin was 0.33± 0.056 in preeclamptic women and in normal pregnant women was0.29±0.039,significant differences were found among ceruloplasminconcentration in both groups, while the mean Transferrin in preeclamptic and in normal pregnant women were 204.61 ± 21.60584 and 223.75 ± 22.64877, respectively.
In conclusion, ischemic placental tissue may be a primary source of potentially toxic iron in preeclampsia and the released iron species may contribute to the etiology and endothelial cell injury, which may be abated by antioxidant supplementation.
Keywords: preeclampsia , Iron, Ferritin , ceruloplasmin, Total Iron Binding Capacity

Introduction

Hypertensive disorders complicating pregnancy are common. They are responsible for a large number of maternal deaths [Roberts et al 2005,MARK et al, 2001]. The development of hypertension and proteinuria and/or edema induced by pregnancy after 20th week of gestation is described as preeclampsia and if convulsion or coma is added, it is named as eclampsia. It is one of the components of the deadly triad along with hemorrhage and thromboembolism during pregnancy and found in 3–7% of pregnancies [Roberts et al, 1998]. It is associated with increased maternal and fetal mortality and 18% of maternal deaths are attributed to preeclampsia [Duley L et al2009].

Other major complications of preeclampsia are premature delivery resulting in the need of intensive care admission for neonates, intracranial hemorrhage, acute renal tubular or cortical necrosis, heart failure, pulmonary edema, rupture of the liver,

disseminated intravascular coagulopathy (DIC), hemolysis, increased liver enzymes, and in about 10% of preeclampsia and eclampsia HELLP syndrome develops[Rahman et al 2002]. Some risk factors for development of preeclampsia are documented like nulliparity, age more than 40, positive family history of preeclampsia, chronic hypertension, chronic renal failure, diabetes mellitus and multiple gestation [Xiao et al 2003].

Preeclampsia is best described as blood pressure of ≥140/90 mmHg after 20th week of gestation [North et al 1999]. Despite decades of intensive researches, these disorders remain among the most important unsolved problems in obstetrics but evidences point to the placenta as a key source of factors that lead to the maternal endothelial cell dysfunction in preeclampsia because the clinical signs and lesions of preeclampsia remit after delivery, implicatingthe placenta as a main culprit in the disease [Roberts et al 2000,Redman et al 2001]. The disease can occur in anembryonic pregnancy, suggesting that the presence of a fetus is not strictly necessary. In rare cases of extrauterine (abdominal)pregnancy, in which delivery of the fetus is not followed by delivery of the placenta, the signs of preeclampsia persist postpartum until the placenta is resorbed [Rampersad et al 2007].

An initiating event in preeclampsia has been postulated to be the reduced placental perfusion that leads to widespread dysfunction of the maternal vascular endothelium by mechanisms that are not well defined [Gilbert et al 2008]. With increasing gestational age, hypoxic environment of placenta changes into oxygen rich environment, leading to the production of reactive oxygen species (ROS). These ROS initiate the cellular damage including destruction of red blood corpuscles (RBCs) in the presence of transitional metals like iron [Entman1987,Balla et al 2005].

MATERIAL AND METHODS

This study was carried out in the department of biochemistry, College of Science for Women, Baghdad university with collaboration of Kerbala maternity hospital. This analytic case-control study included seventy pregnant women , 40 of them diagnosed to have preeclampsia and 30 normal pregnant ladies , from February 2012 to January 2013. The study was performed on pregnant women of age ranging between 15-35years and having gestational age between 28 to 34 weeks. Forty obstetric patients were identified as having pre-eclampsiaaccording to specific criteria as pre-clampsiais defined as an increase of 30 mm Hgsystolic or 15 mm Hg diastolic blood pressure with proteinuria, thirty healthy pregnant subjects were taken as controls, having uncomplicated pregnancies and were normotensive throughout gestation [Tietz et al1986]. The clinical characteristics recorded were maternal age, gestational age at the time of blood sampling, systolic and diastolic blood pressure , ten ml of blood was collected from all the selected women. Blood was centrifuged at 3000 rpm for 5 minutes. The supernatant was used to quantify the Serum TIBC and iron level by spectrophotometeric methods supplied by Biolabo, France. The ceruloplasmin levels in human serum by turbidimetric method supplied by Fortress Diagnostics Limited.

To calculate the unsaturated binding capacity (UIBC), the serum iron concentration was subtracted from the TIBC.

UIBC = TIBC – Serum iron concentration

ISSN: 2073-8854
Magazin of Al-Kufa University for Biology / VOL.5 / NO.2 / year : 2013

Transferrin can be estimated indirectly from the TIBC value by the following equation [Tietz, 1988]:
Transferrin (g/dl) = 0.7 × TIBC (g/dl)

The percentage of saturation of transferrin with iron is determined by the following equation :

$$\%\,\text{Saturation} = \frac{\text{Serum iron}}{\text{TIBC}} \times 100$$

All statistical analyses in studies were performed using SPSS version 17.0 for Windows (Statistical Package for Social Science, Inc., Chicago, IL, USA). Descriptive analysis was used to show the mean and standard deviation of variables. The significance of difference between mean values was estimated by Student T-Test. The probability P< 0.05 = significant, P> 0.05 = non-significant . Correlation analysis was used to test the linear relationship between parameters .ANOVA test was used to show the differences between variables of differentiated groups.

Results

The results were observed as follows; of the 70 pregnant women, 40 were pre-eclamptic and 30 were normal pregnant women. Inpregnancy with pre-eclampsia , the free iron &ceruloplasmin concentration were statistically significantly increased ($p<0.01$) as compared to normal pregnant ones. Serum ferritin concentration was observed to be significantly raised ($p<0.01$) in pre-eclampsia . On comparison of the pre-eclamptic and normal pregnancy,the Total iron binding capacity was significantly lower ($P<0.01$) , but no statistically significant variations was observed in serum Transferrin level.

Table 1: Comparison of Iron states and ceruloplasmin level in pre-eclamticand normal pregnancy

S.NO.	Parameter	Pre-eclamptic pregnancies	Normal pregnancies
1-	TIBC (µg/dl)	292.3±30.8*	319.6±32.3
2-	Ceruloplasmin (mg/dl)	51.3±6.89*	43.0±7.80
3-	Iron (µg/dl)	97.0±7.83*	94.3±11.8
4-	Transferrine (µg/dl)	204.6±21.6	223.7±22.6
5-	Ferritin (µg/dl)	0.33±0.05*	0.29±0.03

Normal pregnancies (n=30), Pre-eclamptic pregnancies (n=40)
Value was mean ± SD;
*p <0.01 pre-eclamptic pregnancies as compared to normal pregnancies

Discussion

Pregnancy is a period of rapid growth and cell differentiation for both the mother and fetus. Consequently, in this period both are vulnerable to changes in dietary supply, especially of those micronutrients that are marginal under normal

circumstances. In developed countries this vulnerability applies mainly to micronutrients. Iron deficiency is a common disorder, especially in pregnancy [Gambling et al 2004].

Pre-eclampsia is the most common medical complication of pregnancy associated with increased maternal and infant mortality and morbidity. The exact etiology and pathogenesis is not known, although several evidences indicate that various iron stats might play an important role in pre-eclampsia [Jain et al 2007]

Some evidences suggest that serum iron level in pre-eclampsia is more than normal.Increased serum iron promotes lipid peroxidase activity and induces endothelial cell damage .Other evidences suggest that increased serum iron level plays a pathogenic role in the development of pre-eclampsia [Hubel et al 2008,Walsh et al 1994].

In this study we found that there is a significant increase in the level of serum iron which act as an oxidative substance and has a role in the endothelial destruction and pathogenesis of pre-eclampsia , this iron comes from the destruction of red blood cells in such patients.Iron status markers such as serum iron and ferritin are considered to be an acute phase reactant [Milman et al 2004]. In normal pregnancy serum ferritin concentration depicts replaceable iron storage that is in the liver, spleen and bone marrow. Serum ferritin level changes during the pregnancy with advancing gestation and reaches the minimum at the third trimester. Increased concentration of serum ferritin during third trimester may be part of an acute phase response, which suggests maternal infection and increased risk of poor pregnancy outcome[Theresa 1998].

Total iron binding capacity (TIBC) is low in pre eclamptic group as compared to Control[Rayman et al 2002]. Similarly, unsaturated iron binding capacity, a measure of the iron binding reserve of serum is also significantly lower in women with pre eclampsia relative to normal pregnancy[Rayman et al 2002]. Similar findings regarding the TIBC and UIBC were observed[Basher et al 2006]. The results allude to the possible contribution of released iron free radicals from ischemic placenta in pre eclampsia to its etiology[Migneco et al 2004].

Ceruloplasminhas also ferroxidase action, and its ferroxidatic activity is an important function of this enzyme because even trace amount of iron can produce hydroxyl radicals through the fenton reaction which can destroy cellular architecture . Ferroxidatic activity of Ceruloplasmin is known to convert toxic ferrous iron to less toxic ferric iron ,which reduces oxidative damage to lipids ,proteins and DNA [Hellman et al 2002]. The high Ceruloplasmin levels in late gestations suggest an enhanced catecholamine breakdown during the stress alarm reaction .In agreement with other finding previous studies showed that ceruloplasmin levels are significantly elevated not only in pre-eclampsia but also in patients with essential hypertension [Griffin et al 1987].

The antioxidant activity of pre-eclampsia decreases with increasing transferrin saturation by iron .Increases transferrin saturation and decreases unsaturated iron-binding capacity in pre-eclampsia may occur consequently to oxidative stress and this further promote oxidative stress by decreasing serum antioxidant buffering against redox-active iron these findings are compatible with our study results [Bernardi et al 2008]

References

Balla J, Vercellotti GM, Jeney V, Yachie A, Varga Z, Eaton JW et al (2005) Heme, hemeoxygenaseand ferritin in vascular endothelial cell injury. MolNutr Food Res 49(11):1030–1043

Basher K, Deb K. (2006) Alteration in iron status in pre eclampsia. Mymensingh Med J. Jan; 15(1): 22-420.
Bernardi , F., F.Guolo.T . Bortolin, F. Petronilho and F.Dal-Pizzol,(2008).Oxidative stress and inflammatory markers in normal pregnancy and preeclampsia .J.Obstet.Gynaecol.Res.,34:948-951

Duley L (2009),The global impact of pre-eclampsia and eclampsia. SeminPerinatol 33(3):130–137

Gambling L, McArdle HJ. (2004) Iron, Copper and Fetal Development. ProcNutrSoc; 63: 553-62.

Gilbert JS, Ryan MJ, LaMarca BB, Sedeek M, Murphy SR, Granger JP (2008) Pathophysiology of hypertension during preeclampsia: linking placental ischemia with endothelial dysfunction. Am J Physiol Heart CircPhysiol 294(2):H541–H550

Griffin,J.F.,(1983). Pregnancy-associated plasma protein level at term in normal pregnancy ,preeclampsia and essential hypertension. Aust. N. Z. J. Obstet.Gynaecol.,23:11-14.

Hellman, N.E. and J.D. Gitlin (2002). ceruloplasmin metabolism and function .Ann.Rev. Nutr.,22:439-458.

Hubel CA, Robert JM ,Taylor RN,(2008) Lipid peroxidation in pregnancy :new perspectives on preeclampsia .Am J Obstet Gynecol;161(4):1025-1034

Hubel CA Bodnar LM, Many A, Harger G, Ness RB, Roberts IM.(2004)Nonglycosylated ferritin predominantes in the circulation of women with pre eclampsia but not intra utrine growth restriction. ClinChern 50: 948- 951.

increased red cell turnover in preeclampsia. Am J ObstetGynecol 156(5):1169–1173

Jain S, Sharma P, Kulsheshtha S, Mohan G, Singh S. (2009) The Role of Calcium, Magnesium, and Zinc in Pre-Eclampsia. Biol Trace Elem Res; 22: 104-109.

MARK A. ZAMORSKI, M.D. , and LEE A. GREEN, M.D. NHBPEP on High Blood Pressure in Pregnancy: A Summary for Family physicians(2001) AmFam Physician 64(2);263-271.

. Migneco A et al. (2004) Hypertensive crises. Diagnosis and management in the emergency room.Eur Rev Med pharmacolSc; 8:143

. Milman N, Sengel V, H and Dombernowsky P. (2004)Iron status markers in preeclampsia .Clin Chem;50(5):948-951

ISSN: 2073-8854
Magazin of Al-Kufa University for Biology / VOL.5 / NO.2 / year : 2013

North RA, Taylor RS, Schellenberg JC (1999) Evaluation of a definition of pre-eclampsia. Br J ObstetGynaecol 106(8):767–773

. Rahman TM, Wendon J (2002), Sever hepatic dysfunction in pregnancy. QJM 95(6):343–357
Rampersad R, Nelson DM (2007) Trophoblast biology, responses to hypoxia and placental dysfunction in preeclampsia. Front Biosci 12:2447–2456

Rayman MP, Barlis I, Evans RW. Redman CWG, King IJ. (2002)Abnormal iron parameters in the pregnancy syndrome pre eclampsia. Am J ObstetGynaecol 2002; 187: 412-8.

Redman CW, Sargent IL (2001) The pathogenesis of preeclampsia. GynecolObstetFertil 29(7–8):518–522

Roberts CL, Algert CS, Morris JM, Ford JB, Henderson-Smart DJ (2005) Hypertensive disorders in pregnancy: a population-based study. Med J Aust 182(7):332–335

. Roberts JM, Taylor RN, Musci TJ, Rodgers GM, Hubel CA, McLaughlin MK (1989) Preeclampsia: an endothelial cell disorder. Am J ObstetGynecol 161(5):1200–1204

Roberts JM (2000) Preeclampsia.SeminPerinatol 24(1):24–28

Tietz, NW., (1986),"In; Text book of clinicalchemistry, Edited by N W Tietz, W B Saunders company,Philadelphia, London, Toronto", pp: 960-962.

Tietz. N.W,(1988),"Fundamentals of Clinical Chemistry", 3rded., Eds. Philadelphia, W.S. Sounders.
Theresa OS.(1998) High third trimester ferritin concentration. Association with very preterm delivery, infection and maternal nutritional status.Obstet, Gynaecol 1998;92:161-6

Walsh SC.(1994)Lipid peroxidation in pregnancy Hypertens .pre;131:1

Xiao R, Sorensen TK, Williams MA, Luthy DA (2003) Influence of pre-eclampsia on fetal growth. J Matern Fetal Neonatal Med 13(3):157–162

مجموع سعة الحديد المرتبط ، الحديد الحر ، سيرولوبلازمين ، تركيز الترانسفيرين ,الفيريتين، في حالات تسمم الحمل

**وسن غازي الصافي .د م رنا مجيد حميد* .م
فرع الكيمياء الحياتية / كلية الطب / جامعة كربلاء رئيس فرع النسائية / كلية الطب / جامعة كربلاء

خلفية :تسمم الحمل او كما يعرف بالضغط الحملي هو واحد من أهم مضاعفات الحمل مقترن بزيادة المرضى والوفيات ، والدليل على زيادة الاكسدة بسبب ضعف البطانية في حالات ارتفاع الضغط .يتم تحفيز زيادة في الاجهاد التأكسدي في وجود المعادن الانتقالية الحرة .ولذلك، فإن العلاقة بين حالة الحديد مع ارتفاع الضغط كانت تحت الهدف. الهدف من هذه الدراسة هو مقارنة معدل TIBC والحديد،ceruloplasmin ، والتركيز Transferrine ومعدلFerritin ، في حالات ارتفاع ضغط النساء الحوامل بالمقارنة مع المجموعة الضابطة.والتحقيق العلاقة بين هذه العوامل وارتفاع ضغط الحمل الطريقة :تم جمع عينات الدم من 40 الإناث

ISSN: 2073-8854
Magazin of Al-Kufa University for Biology / VOL.5 / NO.2 / year : 2013

الحوامل تشخيص تسمم الحمل و 30 من الإناث الحوامل الطبيعي في مستشفى التوليد وأمراض النساء بين شباط 2012و كانون الثاني .2013 سجلنا تركيز TIBC و تركيز الحديد، ceruloplasmin المصل، ومستويات الفيريتين Transferrine في مجموعات على حد سواء.وكان متوسط الحديد في مصل الدم في الحوامل المصابة بارتفاع ضغط الدم97) ، 7 ± 0،(83، في حين94) ،(11.81 ± 35مجموعة الاصحاء :(0.01 \ (p نتيجة . وبالمثل، يعني تركيزTIBC في مصل الاصحاء و الحوامل ذات الضغط المرتفع كانت319)،32 ± 65، (35 ± 292 30.86)،(3، على التوالي .(p\ 0.01) يعني مصل الفيريتين كان0 ،0 ± 33، .056في المرضى وعند النساء الحوامل الطبيعية كانت0 ± 0.29) ، (039تم العثور على ، فروق ذات دلالة إحصائية بين تركيز ceruloplasminفي المجموعات على حد سواء، في حين أن متوسط Transferrine في المرضى وعند النساء الحوامل الطبيعية كانت204) ،21 ±223،61) (60584،22 ± 75، (64877وعلى التوالي.في الختام، قد يكون نقص تروية الأنسجة المشيمة المصدر الرئيسي للحديد في حالات ارتفاع ضغط الم الحملي وأنواع الحديد التي يمكن يمكن أن تسهم في المسببات المرضية وإصابة الخلية البطانية، والتي يمكن ان ينقص تاثيرها من خلال مضادات الأكسدة التكميلية.