

Above observations inspired our study.

The aim of this study was the comparative analysis of the soluble homocysteine in pregnancies complicated by preeclampsia and in normotensive pregnancies.

The study was given the approval of the Board for Supervising Ethics in Medical Experiments at the Medical University of Lublin.

PATIENTS AND METHODS

The study was carried out on 54 patients with severe preeclampsia (group Pre). The control group consisted of 44 healthy normotensive pregnant patients with singleton uncomplicated pregnancies, without any renal, heart and vascular diseases and with normal laboratory tests (group K). All arterial blood pressure measurements in the control group were normal and did not exceed 135/85mmHg. None of the patients from this group suffered from proteinuria. All patients in the study were non-smokers.

Preeclampsia was determined by increased blood pressure >140mmHg systolic and >90 mmHg diastolic in women who were normotensive before 20 weeks of gestation accompanied by proteinuria defined as the urinary excretion of more than 0.3g protein in 24 hour specimen. Severe preeclampsia was defined as blood pressure >160/110mmHg on at least 2 occasions 6 hours apart with proteinuria >2g in a 24-hour urinary protein excretion and when hypertension and proteinuria were associated with one or more of the following clinical manifestations: renal abnormalities, hematologic abnormalities (thrombocytopenia, microangiopathic hemolysis) or HELLP syndrome (hemolysis, elevated liver enzymes, low platelet count, right-upper quadrant pain), or neurologic symptoms (headache, visual disturbances, seizures).

Five milliliters of blood were collected by venipuncture from each preeclamptic patient and from each woman from the control group and placed in sterile test-tubes. They were centrifuged for 15 min at 500xg.

The maternal serum homocysteine concentrations were estimated using a sandwich ELISA assay according to the manufacturer's instructions (human sandwich ELISA kit Bender MedSystems, Vienna, Austria).

Data were expressed as mean +/- SD and were statistically analyzed with the computer program "Statistica" using the Shapiro-Wilk test for normal distribution of data, and equality of variance by Levene test and, subsequently one-tailed Student's t-tests, or (in unequal variance) the Cochran-Cox test, (absence of normal distribution and non-parametric data) the Mann-Whitney U test and ANOVA Kruskal-Wallis test. The level of statistical significance was established as $p < 0.05$.

RESULTS

There were no statistically significant differences in gravidity and parity in patient profiles between groups. Creatinine and urea levels were normal in all patients. Systolic and diastolic blood pressure and mean arterial blood pressure were higher in the study group in comparison with the control group. These differences were statistically significant ($p < 0.000001$).

The mean systolic blood pressure values were 168.426 +/- 16.755 mmHg in the group of preeclamptic patients and 113.886 +/- 10.627 mmHg in the control group. The mean diastolic blood pressure values were 110.019 +/- 21.089 mmHg in women with pregnancy complicated by preeclampsia and 72.114 +/- 6.875 mmHg in the healthy controls.

Data presented in table 1.

Table 1. Analysis of obtained results.

Data	Group Pre (n=50)	Group K (n=34)	p value
Systolic blood pressure (mmHg)	168.426 +/- 16.755	110.019 +/- 21.089	p<0.000001*
Diastolic blood pressure (mmHg)	113.886 +/- 10.627	72.114 +/- 6.875	p<0.000001*
Maternal Homocysteine levels ($\mu\text{mol/L}$)	10.386 +/- 3.459	7.615 +/- 2.764	p=0.000040*

Data presented as a mean +/- SD

* Statistical significance (p<0.05)

Groups of studied pregnant women:

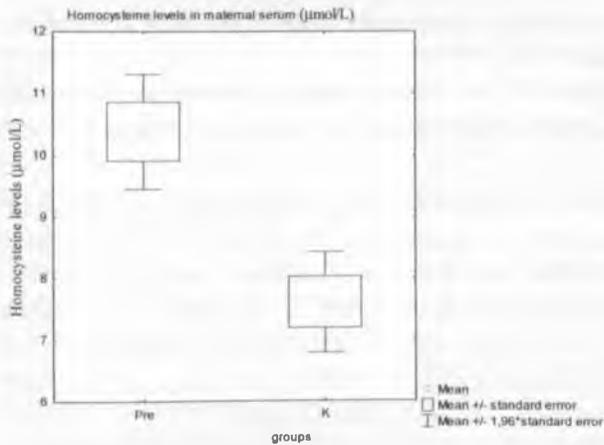
Pre – women with pregnancies complicated by severe preeclampsia

K – healthy normotensive pregnant women

Pregnant women with severe preeclampsia had higher maternal serum homocysteine levels than the normotensive controls. This difference was statistically significant (p=0.000040). The mean values of maternal homocysteine were 10.386 +/- 3.459 $\mu\text{mol/L}$ in group Pre compared with 7.615 +/- 2.764 $\mu\text{mol/L}$ in the control group respectively.

Data presented in Figure 1.

Figure 1. Homocysteine levels in maternal serum from women with pregnancy complicated by severe Preeclampsia and in control subjects ($\mu\text{mol/L}$).



DISCUSSION

Preeclampsia has been called the disease of theories and remains a challenging enigma to researchers.

Our study revealed significantly higher levels of homocysteine in preeclamptic women than in healthy normotensive pregnant patients.

A special role of homocysteine in the etiology of vascular disturbances, which are important in preeclamptic pregnancies, seems to be consistent with these observations.

Our results also suggest that hyperhomocysteinemia during pregnancy may contribute to endothelial cells activation or dysfunction observed in pregnancy complicated by severe preeclampsia. Further studies are needed to clarify this increase in homocysteine level which could be also caused by the decrease in maternal renal function that is common in atherosclerosis which is one of the changes observed in preeclamptic pregnancy.

Similar findings were presented by Hogg et al. [13]. They observed that women with pregnancy induced hypertension or preeclampsia had higher homocysteine concentrations in comparison with control subjects. But in their studies the homocysteine levels in the second trimester of pregnancy did not differ in women with pregnancy complicated by preeclampsia or pregnancy – induced hypertension from women with uncomplicated pregnancies. They concluded that plasma homocysteine concentrations in the second trimester do not predict the subsequent complications of pregnancy such as pregnancy induced hypertension or preeclampsia.

Also Wang et al [14] demonstrated elevated levels of maternal plasma homocysteine in preeclamptic pregnancies. They concluded that elevated plasma homocysteine plays a role in pathogenesis of the vascular disturbances in the utero-placental circulation and due to placental insufficiency.

Similar results higher homocysteine levels in serum from preeclamptic women were presented by López-Quesada et al. [15].

Mao et al. [16] observed a highly significant positive correlation between plasma concentrations of homocysteine and asymmetric dimethylarginine (ADMA) and concluded that homocysteine-ADMA-NO pathway may be responsible for etiology of preeclampsia and could be regarded for the severity of the disease.

Steeegers-Thenissen et al. [17] observed that higher levels of homocysteine were associated with an approximately 2 to 3-fold increased risk of pregnancy hypertension, previous abruption of placenta and intrauterine fetal growth restriction

Also Herrmann et al. [18] observed elevated homocysteine levels in women with preeclamptic pregnancies. These authors concluded that the adverse effect of homocysteine on endothelial function might be related to ADMA in early-onset preeclampsia. They suggest that hyperhomocysteinemia indicate poor status of the B vitamins during pregnancy and that more emphasis should be placed on increasing the intake of B vitamins in all pregnant women, but especially from developing countries.

On the basis of our findings and reports from literature it seems that higher levels of homocysteine may be responsible for the development of preeclampsia.

Further studies are needed to explain above aspects and evaluate the role of homocysteine in preeclampsia in order to improve the management and therapeutic strategies for preeclamptic patients.

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STRESZCZENIE

CEL PRACY: Celem pracy była analiza porównawcza poziomu homocysteiny w ciąży powikłanej ciężkim stanem przedzucawkowym w odniesieniu do zdrowych kobiet ciężarnych.

PACJENTKI I METODY: Badaniami objęto 54 pacjentki z ciążą powikłaną ciężkim stanem przedzucawkowym (grupa Pre) oraz 44 zdrowe kobiety ciężarne z niepowikłanym przebiegiem ciąży i prawidłowymi wartościami ciśnienia tętniczego krwi (grupa K). Ocenę stężenia homocysteiny w surowicy krwi matczynej przeprowadzono metodą ELISA.

WYNIKI: Badane grupy pacjentek nie różniły się w sposób istotny statystycznie pod względem płodności i rodności. Zaobserwowano wyższe wartości skurczowego i rozkurczowego ciśnienia tętniczego krwi w grupie badanej w odniesieniu do zdrowych kobiet ciężarnych z grupy kontrolnej. Odnotowano istotnie podwyższone poziomy homocysteiny w surowicy krwi u kobiet z ciążą powikłaną ciężkim stanem przedzucawkowym w odniesieniu do zdrowych kobiet ciężarnych. Średnie poziomy homocysteiny w surowicy krwi matczynej u pacjentek z ciężką preeklampsją wynosiły 10.386 +/- 3.459 $\mu\text{mol/L}$ w odniesieniu do wartości 7.615 +/- 2.764 $\mu\text{mol/L}$ w grupie kontrolnej.

WNIOSKI: Wyniki naszych badań sugerują kluczową rolę prawidłowych poziomów homocysteiny dla niepowikłanego przebiegu ciąży oraz sugerują, iż hypehomocysteinemia może stanowić jeden z istotnych czynników odpowiedzialnych za dysfunkcję komórek śródbłonna naczyniowego w ciąży powikłanej stanem przedzucawkowym. Konieczne są dalsze badanie powyższych aspektów i oceny roli homocysteiny w preeklampsjii w celu lepszego poznania patogenezы schorzenia i wdrożenia nowych możliwości terapeutycznych.

Słowa kluczowe: ciężki stan przedzucawkowy, homocysteina

SUMMARY:

OBJECTIVE: The aim of this study was the comparative analysis of the homocysteine levels in pregnancies complicated by severe preeclampsia and healthy normotensive pregnant women.

PATIENTS AND METHODS: The study was carried out on 54 patients with pregnancy complicated by severe preeclampsia (group Pre). The control group consisted of 44 healthy normotensive pregnant patients with singleton uncomplicated pregnancies (group K).

Maternal serum homocysteine levels were estimated using a sandwich ELISA assay.

RESULTS: There were no statistically significant differences in gravidity and parity in patient profiles between groups. Systolic and diastolic blood pressures were significantly higher in the study group in comparison with the control group. Pregnant women with severe preeclampsia had higher maternal serum homocysteine levels than the normotensive controls. The mean values of maternal homocysteine were 10.386 +/- 3.459 $\mu\text{mol/L}$ in group Pre compared with 7.615 +/- 2.764 $\mu\text{mol/L}$ in the control group respectively.

CONCLUSIONS: Our results presented in this study suggest that normal homocysteine concentrations are crucial for normal course of pregnancy and that hypehomocysteinemia may be one of the important factors responsible for endothelial cell dysfunction in pregnancies complicated by preeclampsia.

Further studies are needed to explain these aspects and evaluate the role of homocysteine in preeclampsia in order to improve the management and therapeutic strategies for this pregnancy complication.

Keywords: severe preeclampsia, homocysteine