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Assessment of Umbilical Cord Plasma Homocysteine Concentration in Parturient Women with Preeclampsia in Comparing with Normal Healthy Parturient Women

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Abstract
Background: Preeclampsia is a syndrome which is common in obstetrics practice and considered one of the most causes that lead to maternal and fetal morbidity and mortality. Preeclampsia is multi-system disorder happened in pregnancy by new onset hypertension and proteinuria after 20 weeks of gestation. Homocysteine is homologue of amino acid cysteine which is found elevated in preedampsia, mechanisms of disease linking homocysteine to preeclampsia are complex and still incompletely understood. To date, vascular endothelial cell dysfunction that is provoked by an elevated level of homocysteine is suggested to be the most important connection.
Aim: To estimate the level of umbilical cord plasma homocysteine concentration in parturient women with preeclampsia in comparison with those who carried normal healthy pregnancy and to look any fetal compromise because of homocysteine level**.**
Patients and methods: A case control (comparative) study, the study carried out in Al Zahraa Maternity and Pediatric Teaching Hospital at Al- Najaf City. Umbilical cord plasma homocysteine was estimated in 96 pregnant women divided into 2 groups. Group I (study group) consist of 48 pregnant women with preeclampsia. Group II (control group) consist of 48 normal healthy pregnant women in labor their gestational age was from 24 to 40 weeks of gestation and an age from 16 – 42 years.
Results: Umbilical cord homocysteine level is seen higher in preeclamptic patients than normal healthy parturient women. The homocysteine level of preeclamptic group was found to be with of (mean $\pm$SD=8.11 $\pm$ 3.5) which was higher than control group (mean $\pm$SD= 1.66 $\pm$0.11); p. value < 0.001 statistically significant.
Conclusions: Umbilical cord plasma homocysteine is significantly elevated in preeclamptic pregnant parturient women in comparison to normally healthy pregnant women.
Keywords: Preeclampsia, Homocysteine, Healthy pregnant women

Introduction

Elevated concentrations of total homocysteine or reduced homocysteine are associated with an increased risk for vascular disease and the development of thrombosis [1]. Many

studies have suggested that total homocysteine may be altered in pregnancy. In healthy pregnant women, plasma total homocysteine levels are low [2]. However, elevated levels of total homocysteine are observed in several pathological pregnancy conditions, such as situations involving women who previously had infants with neural tube defects, those who experienced placental abruption or placental infarction, or unexplained recurrent early pregnancy loss, or those who had preeclampsia at the time of delivery [3].

Hyperhomocysteinaemia can result from a variety of genetic and environmental factors, such as cystathioninehβ -synthase or methylenetetrahydrofolate reductase deficiency, and vitamin B12, folate or vitamin B6 deficiency [4].Elevated homocysteine levels are caused by four major factors, including genetic deficiencies in enzymes involved in homocysteine metabolisms such as cystathionine β synthase (CBS), nutritional deficiency in vitamins (B6, B12 and folate); renal failure for effective amino acid clearance; drug interactions such as nitric oxide, methotrexate and phenytoin that interfere with homocysteine metabolisms [5]. There are inborn errors that affect the efficiency by which homocysteine can be metabolized.

The mechanisms by which elevated homocysteine impairs vascular function are not completely understood. However, it has been found in oxidative stress and endothelial dysfunction in hyperhomocysteinaemia, inflammatory response and hyperhomocysteinaemia and atherothrombosis and hyperhomocysteinaemia. The association of hyperhomocysteinemia and preeclampsia has initially been suggested by Decker et al. [6], and all authors have not confirmed it. However, the majority of evidence suggests a positive correlation.

Aim of the study

To estimate the level of umbilical cord plasma homocysteine concentration in parturient women with preeclampsia in comparing to normal healthy parturient women and to look for any fetal compromise because of high homocysteine level.

Patients and methods

Patient's selection

In this study 96 of women who attend labor room either they had labor or for control their blood pressure after obtaining oral informed consent from all patient who were followed and observed critically by me in our department during the period of this study.

The inclusion criteria

Women who attend labour room with singleton pregnancy, gestational age 24-40wk, and patient with diagnosis of preeclampsia.

The exclusion criteria

Women with multiple pregnancies, chronic hypertension, renal diseases, liver diseases, diabetic mellitus, bleeding disorders, smoking, and drug intake eg. epileptic drug.

The women included in the study were divided into the following groups:

First group I (study group):- Consist of 48 pregnant women with preeclampsia subdivided to; 38 pregnant women with mild preeclampsia (blood pressure $\geq$ 140/90 mmHg).10 pregnant women with sever preeclampsia (blood pressure $\geq$ 160/110 mmHg).

Second group II (control group):- Consist of 48 pregnant women with normal healthy pregnancy. The data of each patient in this study was gathered and recorded in the predesigned questionnaire form; which name, age, antenatal care (no or one visit, poor visit 2-4, good antenatal care $\geq$5, BMI (is defined as the body weight divided by square of the body height) calculated for each patient then the blood pressure had measured in semi recumbent position with a left lateral, in the right arm by sphygmomanometer, laboratory investigation included blood group and RH ,complete blood picture and general urine examination(simplifier albumin in urine by dipstick method) .

The preeclamptic patients subdivided to mild preeclampsia where blood pressure ≥ 140/90 mmHg. On two occasions 6 hours apart and ≥2+ albumin on dipstick in two urine sample 6 hours apart and without evidence of any organ damage. Sever preeclampsia is defined as preeclampsia with presence of one or more of the following symptoms or sign, systolic (blood pressure of 160 mmHg.), or higher diastolic (blood pressure of 110 mmHg) or higher on two occasion at least 6 hours apart.

- ✓ Pulmonary edema or cyanosis
- ✓ Persistent headaches
- ✓ Thrombocytopenia
- ✓ Oliguria (<400ml in 24 hours)
- ✓ Epigastric pain or impaired liver function impaired liver enzymes.
- ✓ Oligohydraminas (low amniotic fluid level) with signs of fetal growth restriction.

Method

From each candidate 5 ml. of blood were taken from umbilical cord after baby delivery and before clumping of umbilical cord. The specimen was centrifuged at 2000 RPM for ten minutes and the plasma separated and stored at -70 C^0 until testing homocysteine.
The antenatal care: no visits (0-1).
Poor antenatal care: (2-4) visits.
Good antenatal care: ≥ 5 visits.

Materials

Human Homocysteine ELISA Kit (Enzyme – Linked Immunosorbent Assay (ELISA). The plate had been pre –coated with human Hcy antibody. The test performed according to manufacturer instructions.

Statistical Analysis

The data of patients were analyzed by application of Microsoft excel program and statistical package for social sciences (SPSS) version 23. Outcomes of analysis were arranged in scales variables (mean &standard deviation) and in categorical variables. Chi square test and Fishers exact tests were used for categorical variables comparison. Independent sample t-test was used to compare between two means. ROC curve was used to assess the appropriate value of Homocysteine in prediction of preeclampsia with an appropriate validity. P value less than and equal to 0.05 was regarded as significant.

Results

This study included 48 pregnant women with preeclampsia and 48 healthy pregnant women as control. Table 1 show that there was a highly significant difference between study groups regarding age ($p<0.001$); pregnant women with preeclampsia were significantly older in age. Table 2 show that a highly significant association was observed between BMI of pregnant women and preeclampsia ($p<0.001$). There was a significant difference between pregnant women from two study groups regarding social class ($p=0.001$); pregnant women with low social class were significantly related to preeclampsia. No significant differences were observed between study groups pregnant women regarding antenatal care history ($p=0.3$).

A highly significant association was observed between increased gravidity of pregnant women and preeclampsia ($p<0.001$). There was a highly significant difference between pregnant women from two study groups regarding parity ($p=0.001$); pregnant women with increased parity were significantly related to preeclampsia. No significant differences were observed between study groups pregnant women regarding history of abortion ($p=0.1$). There

was a highly significant association between preterm gestational age of pregnant women and preeclampsia (p<0.001), Table 3.

Table 1: **Distribution of pregnant woman's age according to study groups.**

Variable	Study groups				P
	Preeclampsia		Controls		
	No.	%	No.	%	
Age groups					**<0.001***
<20 years	**13**	**27.1**	**19**	**39.6**	***Highly significant***
20-29 years	**12**	**25.0**	**29**	**60.4**	
30-39 years	**22**	**45.8**	**0**	**-**	
40-42 years	**1**	**2.1**	**0**	**-**	

***Fishers exact test.**

Table 2: **Distribution of BMI and social characteristics according to study groups.**

Variable	Study groups				P
	Preeclampsia		Controls		
	No.	%	No.	%	
BMI					**<0.001***
Normal (20-24.9%)	**0**	**-**	**25**	**52.1**	***Highly***
Overweight (25-29.9%)	**7**	**14.6**	**15**	**31.2**	
Obese≥30%	**41**	**85.4**	**8**	**16.7**	***significant***
Social class					**0.001***
Low (illiterate & primary school)	**35**	**72.9**	**30**	**62.5**	***Significant***
Moderate (secondary school)	**13**	**27.1**	**7**	**14.6**	
High (university)	**0**	**-**	**11**	**22.9**	
Antenatal care					**0.3***
No (0-1)	**17**	**35.4**	**18**	**37.5**	***Not***
Poor (2-4)	**17**	**35.4**	**11**	**22.9**	
Good (≥ 5)	**14**	**29.2**	**19**	**39.6**	

***Chi-square test.**

Table 3: Distribution of gestational characteristics according to study groups.

Variable	Study groups				P
	Preeclampsia		Controls		
	No.	%	No.	%	
Gravidity					**<0.001*** ***Highly significant***
Primigravida	**7**	**14.6**	**27**	**56.3**	
1-4 gravida	**24**	**50.0**	**19**	**39.6**	
≥5 gravida	**17**	**35.4**	**2**	**4.1**	
Parity					**<0.001**** ***Highly significant***
Nulliparous	**7**	**14.6**	**27**	**56.2**	
1-4 children	**36**	**75.0**	**21**	**43.8**	
≥5 children	**5**	**10.4**	**0**	**-**	
Abortion					**0.1**** ***Not significant***
No	**42**	**87.5**	**46**	**95.8**	
Yes	**6**	**12.5**	**2**	**4.2**	
Gestational age					**<0.001*** ***Highly significant***
Preterm	**17**	**35.4**	**0**	**-**	
Term	**31**	**64.6**	**48**	**100.0**	

***Chi-square test, **Fishers exact test.**

Table 4 show that there was a highly significant association between high blood pressure of pregnant women and preeclampsia with P value of ($p<0.001$). A highly significant association was observed between increased albumin in urine of pregnant women and preeclampsia with P value of ($p<0.001$).

Table 5 show that no significant differences were observed among the studied groups regarding mode of delivery with P value of ($p=0.4$). A highly significant association was observed between low neonatal apgar score at 1 minute and pregnant women with preeclampsia with P value of ($p<0.001$). There was a significant difference between neonates of pregnant women from the two studied groups regarding birth weight with P value of ($p=0.006$); neonates of pregnant women with preeclampsia were significantly related to low birth weight. There was a highly significant association between neonatal NICU admission and preeclampsia with P value of ($p<0.001$).

As shown in Table 6 and figure 4 that, the umbilical cord plasma homocysteine level was significantly higher among pregnant women with preeclampsia in comparison to the controls with P value of ($p<0.001$). Table 7 shows that There was a significant association between increased age of pregnant women and severe preeclampsia with P value of ($p=0.03$). Table 8 show that No significant differences were observed between pregnant women with different severity of preeclampsia regarding BMI with P value of ($p=0.6$) and social class

with P value of (p=0.1). There was a highly significant association between pregnant women with severe preeclampsia and those who had no antenatal care with P value of (p<0.001).

Table 4: Distribution of clinical characteristics according to study groups.

Variable	Study groups				P
	Preeclampsia		Controls		
	No.	%	No.	%	
Blood pressure					**<0.001*** ***Highly significant***
Normal	**5**	**10.4**	**48**	**100.0**	
High	**43**	**89.6**	**0**	**-**	
Albumin in urine					**<0.001*** ***Highly significant***
No	**0**	**-**	**48**	**100.0**	
+	**15**	**31.3**	**0**	**-**	
++	**18**	**37.4**	**0**	**-**	
+++	**15**	**31.3**	**0**	**-**	

***Chi-square test.**

Table 5: Distribution of maternal and neonatal outcomes according to study groups.

Variable	Study groups				P
	Preeclampsia		Controls		
	No.	%	No.	%	
Mode of Delivery					0.4* ***Not significant***
Normal vaginal delivery	35	72.9	38	79.2	
Cesarean section	13	27.1	10	20.8	
Neonatal apgar score at 1 minute					**<0.001*** ***Highly significant***
Normal (7-10)	33	68.7	48	100.0	
Low (< 7)	15	31.3	0	-	
Neonatal birth weight					**0.006**** ***Significant***
Normal	41	85.4	48	100.0	
Low	7	14.6	0	-	
NICU admission					**<0.001*** ***Highly significant***
Yes	15	31.3	0	-	
No	33	68.7	48	100.0	

***Chi-square test, **Fishers exact test.**

Table 9 show that A significant association was observed between increased gravidity of pregnant women with preeclampsia and severe preeclampsia with P value of ($p<0.001$). No significant differences were observed between pregnant women with different severity of preeclampsia regarding parity with P value of ($p=0.2$). A highly significant association was observed between pregnant women with history of abortion and severe preeclampsia with P value of ($p<0.001$). There was a significant association between preterm gestational age of pregnant women with preeclampsia and severe preeclampsia with P value of ($p=0.001$).

Table 10 show that No significant differences were observed between pregnant women with different severity of preeclampsia regarding blood pressure with P value of ($p=0.2$). There was a significant difference between pregnant women with different severity of preeclampsia regarding albumin in urine with P value of ($p=0.006$); pregnant women with increased albumin in urine were significantly related to severe preeclampsia.

Table 11 show that There was a significant association between pregnant women with severe preeclampsia and cesarean section delivery with P value of ($p=0.008$). A significant association was observed between low neonatal Apgar score at 1 minute and pregnant women with severe preeclampsia with P value of ($p=0.003$). There was a highly significant difference between neonates of pregnant women with different severity of preeclampsia regarding birth weight with P value of ($p<0.001$); neonates of pregnant women with severe preeclampsia were significantly related to low birth weight. There was a highly significant association between neonatal NICU admission and severe preeclampsia with P value of ($p=0.003$).

Table 6: Distribution of umbilical cord plasma homocysteine level according to study groups.

Variable	Preeclampsia Mean ± SD	Controls Mean ± SD	P
Homocysteine level (nmol/ml)	**8.11±3.5**	**1.66±0.11**	**<0.001*** ***Highly significant***

**Independent sample t-test.*

Table 7: Distribution of pregnant woman's age according to preeclampsia severity.

Variable	Preeclampsia severity				P
	Mild		Severe		
	No.	%	No.	%	
Age groups					**0.03*** ***Significant***
<20 years	**13**	**34.2**	**0**	**-**	
20-29 years	**10**	**26.3**	**2**	**20.0**	
30-39 years	**15**	**39.5**	**7**	**70.0**	
40-42 years	**0**	**-**	**1**	**10.0**	

***Fishers exact test.**

Table 8: Distribution of BMI and social characteristics according to preeclampsia severity.

Variable	Preeclampsia severity				P
	Mild		Severe		
	No.	%	No.	%	
BMI					0.6* *Not significant*
Overweight	6	15.8	1	10.0	
Obese	32	84.2	9	90.0	
Social class					0.1* *Not significant*
Low	26	68.4	9	90.0	
Moderate	12	31.6	1	10.0	
Antenatal care					**<0.001*** *Highly significant*
No	8	21.1	9	90.0	
Poor	12	31.6	1	10.0	
Good	18	47.3	0	-	

***Fishers exact test.**

Table 9: Distribution of gestational characteristics according to preeclampsia severity.

Variable	Preeclampsia severity				P
	Mild		Severe		
	No.	%	No.	%	
Gravidity					**0.004*** *Significant*
Primigravida	7	18.4	0	-	
1-4 gravida	22	57.9	2	20.0	
≥5 gravida	9	23.7	8	80.0	
Parity					0.2* *Not significant*
Nulliparous	7	18.4	0	-	
1-4 children	28	73.7	8	80.0	
≥5 children	3	7.9	2	20.0	
Abortion					**<0.001*** *Highly significant*
No	38	100.0	4	40.0	
Yes	0	-	6	60.0	
Gestational age					**0.001*** *Significant*
Preterm	9	23.7	8	80.0	
Term	29	76.3	2	20.0	

***Fishers exact test.**

Table 10: Distribution of clinical characteristics according to preeclampsia severity.

Variable	Preeclampsia severity				P
	Mild		Severe		
	No.	%	No.	%	
Blood pressure					0.2* *Not significant*
Normal	5	13.2	0	-	
High	33	86.8	10	100.0	
Albumin in urine					**0.006*** *Significant*
+	15	39.5	0	-	
++	15	39.5	3	30.0	
+++	8	21.0	7	70.0	

***Fishers exact test.**

Table 11: Distribution of maternal and neonatal outcomes according to preeclampsia severity.

Variable	Preeclampsia severity				P
	Mild		Severe		
	No.	%	No.	%	
Delivery mode					**0.008**** *Significant*
Normal vaginal delivery	31	81.6	4	40.0	
Cesarean section	7	18.4	6	60.0	
Neonatal apgar score at 1 minute					**0.003*** *Significant*
Normal	30	78.9	3	30.0	
Low	8	21.1	7	70.0	
Neonatal birth weight					**<0.001**** *Highly significant*
Normal	38	100.0	3	30.0	
Low	0	-	7	70.0	
NICU admission					**0.003*** *Significant*
Yes	8	21.1	7	70.0	
No	30	78.9	3	30.0	

***Fishers exact test.**

As shown in table 12 and figure 5, those the umbilical cord plasma homocysteine level was significantly higher among pregnant women with severe preeclampsia in comparison to pregnant women with mild preeclampsia with P value of ($p<0.001$).

Table 12: Distribution of umbilical cord plasma homocysteine level according to preeclampsia severity.

Variable	Mild Mean ± SD	Severe Mean ± SD	P
Homocysteine level (nmol/ml)	**6.65±1.86**	**13.64±2.68**	**<0.001* *Highly significant***

Independent sample t-test.

As shown in Table 13 and Figure 1; the acceptable cut off points and the corresponding validity values for umbilical cord plasma homocysteine in prediction of preeclampsia was shown in table 13 and figure 5; cutoff plasma homocysteine level of 3.1 nmol/L had acceptable validity results (100% sensitivity, 100% specificity, 100%PPV, 100% NPV and accuracy. 100%).

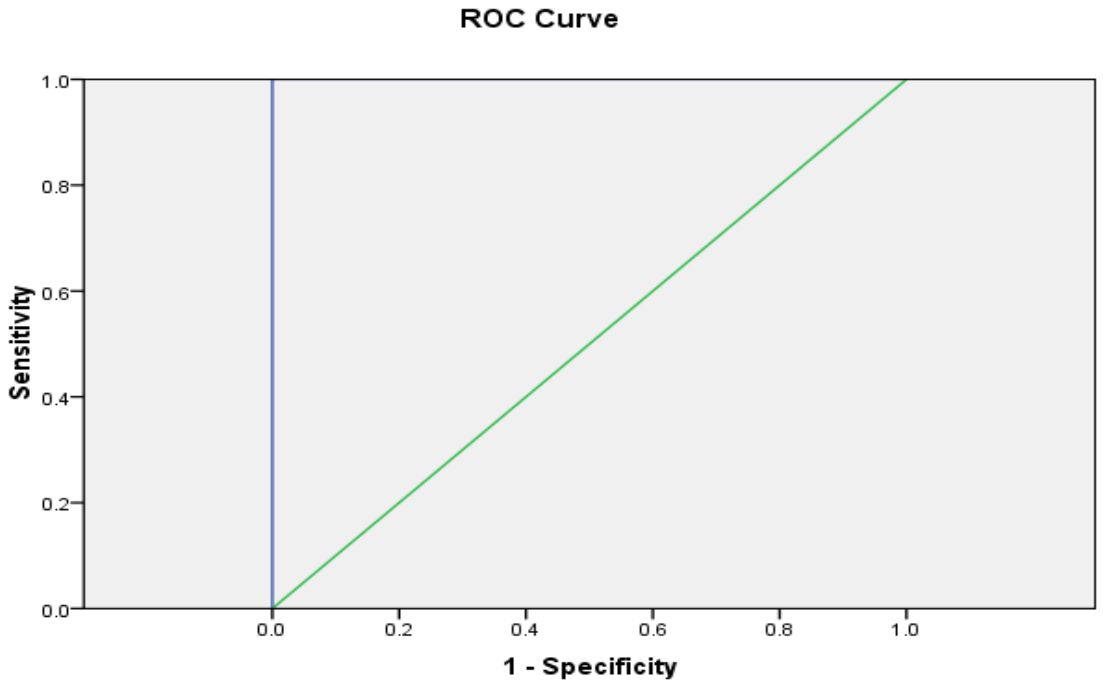

Figure 1: ROC for homocysteine prediction of preeclampsia (AUC=1.0).

Table 13: ROC coordinates for prediction of preeclampsia by plasma homocysteine.

Cutoff point	Sensitivity	Specificity	PPV	NPV	Accuracy
1.9 nmol/ml	**100%**	**58%**	**86%**	**54%**	**62%**
3.1 nmol/ml	**100%**	**100%**	**100%**	**100%**	**100%**
4.3 nmol/ml	**93.8%**	**100%**	**85%**	**100%**	**94%**

Discussion

The preeclampsia is regarded as common cause of morbidity and mortality in all hypertension diseases with higher incidence reaching to approximately3-10% of all pregnancies. HHcy, leading to accumulation of ADMA, may contribute to eNOS blockade and NO deficiency in the presence of general appropriate concentration of its synthase. The reduced release of NO by endothelial cells in HHcy was observed, suggesting the impairment of the NO pathway by DDAH inhibition [7].

The hypothesized mechanisms of disease linking homocysteine to preeclampsia are complex and still incompletely understood. To date, vascular endothelial cell dysfunction that is provoked by an elevated level of homocysteine (Hcy) is suggested to be the most important connection. However, some authors questioned whether mild Hcy observed in PE, with Hcy values that are similar to those found in normotensive non-pregnant women, can provoke damage of the vascular endothelium. They postulate that this damage can be mediated rather by oxidative stress, as endothelium of pregnant women might be more vulnerable to oxidative injury [8]. Hyperhomocysteinemia is also associated with lesions in endothelial cells, due to vascular fibrosis, which results in alterations in coagulation system, enhanced platelet activation, and thrombogenesis—changes that are noted in preeclampsia [9]. On the other hand, metabolism in the kidney is the major route by which homocysteine is cleared from plasma. The association between Hcy and glomerular filtration rate (GFR) seems linear and it is present, even in the hyperfiltrating range [9]. Thus, this route of elimination may be affected by the already established preeclamptic changes in the kidney and secondarily lead to increased Hcy concentrations in plasma [10,11].

Preeclampsia is one of tenth diseases causing death of both mothers and fetuses in developing countries [12]. Early diagnosis of preeclampsia is vital for preventing complications. Pathogenesis of preeclampsia and hyperhomocysteinemia is similar as both of them causing endothelial dysfunction [13].

The present study showed that umbilical cord plasma homocysteine level was significantly higher among pregnant women with preeclampsia in comparison to the controls ($p<0.001$). This finding is consistent with many literatures such as Ali study in Iraq [14] and Napolitano et al [15] study in USA which all revealed a higher level of umbilical cord plasma homocysteine in pregnant women complicated with preeclampsia. It was suggested that chronic placental hypoperfusion inducing production and release of certain agents like homocysteine which are responsible for endothelial activation and injury [16]. However, Bobić et al [17] study in Croatia on 55 pregnant women with mild to moderate preeclampsia and 50 healthy pregnant women found a higher level of homocysteine by (0.74 mmol/L) in pregnant women with preeclampsia in comparison to controls, but this higher level of homocysteine was reduced by (0.87 mmol/L) 6 months after delivery. Another study carried out in Iran by Khosrowbeygi et al [18] found that higher level of homocysteine in pregnant women with preeclampsia is related to stress and not related to leptin. The maternal plasma homocysteine level is found to be related to many pregnancy complications [19]. This finding is attributed to important role of homocysteine in endothelial dysfunction and its contributing effect for cardiovascular disease, in addition to higher homocysteine level is might play a significant role in placenta-mediated pregnancy complications such as preeclampsia, placental abruption, intrauterine growth restriction and pregnancy loss [20,21]. These diseases are sharing same abnormal placental vasculature, placental pathophysiology and higher recurrence risk [22]. Studying the relationship between higher levels of umbilical cord plasma homocysteine in pregnant women with preeclampsia is beneficial in diagnosis of preeclampsia. This finding is similar to results of Mansour et al [23] study in Egypt which

reported that higher homocysteine level that is related to TNF-α and TGF-β1 is important in diagnosis of preeclampsia.

In the present study, the umbilical cord plasma homocysteine level was significantly higher among pregnant women with severe preeclampsia in comparison to pregnant women with mild preeclampsia with P value of ($p<0.001$). This finding is consistent with results of Acilmis et al [24] study in Turkey which found that maternal and fetal serum homocysteine level were significantly higher among pregnant women with severe preeclampsia in comparison to pregnant women with mild preeclampsia and controls. Another case control study conducted in India by Yelikar et al [25] on 120 pregnant women (40 preeclampsia, 40 eclampsia and 40 normotensive) found that homocysteine level was increased with increased severity of preeclampsia. The present study showed that best cutoff plasma homocysteine level of 3.1 nmol/L in prediction of preeclampsia with validity results (100% sensitivity, 100% specificity and 100% accuracy). These findings are close to results of Erdemoğlu et al [26] study in Turkey which reported that homocysteine levels of more than 3 nmol/L had good validity results in prediction of preeclampsia.

Current study showed a highly significant association between older age pregnant women and preeclampsia ($p<0.001$). Similarly, Sheen et al [27] study in USA documented that highest risk of preeclampsia was found among pregnant women with extremes of age. However, Dietl et al [28] found that although pregnant women over 40 years were more vulnerable for chronic diseases and pregnancy complications such as preeclampsia, but the pregnancy outcomes were not varying between them and younger age pregnant women. Our study showed a highly significant association between obesity of pregnant women and preeclampsia ($p<0.001$). This finding coincides with reports of Roberts et al [29] study in USA which stated that obesity play an important role in development of preeclampsia. Additionally, the obesity is considered as risk factor for severity of preeclampsia [30]. In present study, there was a significant association between pregnant women with low social class and preeclampsia ($p=0.001$). This finding is consistent with results of Silva et al [31] study in Netherlands which reported that low maternal socioeconomic class is a strong risk factor for preeclampsia. Pregnant women with preeclampsia in current study were significantly related with increased gravidity and parity ($p<0.001$). This finding is in agreement with results of Sulastri et al [32] study in Indonesia and Singh et al [33] study in Nigeria which all documented that increased gravidity and parity history is commonly regarded as risk factor for preeclampsia. In our study, pregnant with preeclampsia were significantly accompanied by higher blood pressure and albumin in urine as compared to controls ($p<0.001$). Consistently, many guidelines and studies confirmed the significant role of blood pressure and albumin in urine for screening and diagnosis of preeclampsia among pregnant women [34,35]. Our study also showed a highly significant association between preterm gestational age of pregnant women and preeclampsia ($p<0.001$). This finding is similar to results of Shen et al [36] study in Canada which reported that preterm birth is common outcome of pregnant women with preeclampsia. Indeed, current study revealed a significant relationship between pregnant women with preeclampsia and neonatal low Apgar score, low birth weight and NICU admission. These findings are in agreement with results of Masoura et al [37] study in Greece which reported an increase in neonatal adverse outcomes in late preterm infants of preeclamptic pregnant women.

Current study revealed a significant association between increased age of pregnant women and severe preeclampsia ($p=0.03$). This finding coincides with the results of Lamminpää et al [38] study in Finland which stated that preeclampsia is more prevalent among advanced maternal age with more complication and severity of preeclampsia. Our study found a highly significant association between pregnant women with severe

preeclampsia and lack of antenatal care (p<0.001).This finding is similar to results of Liu et al [39] study in Taiwan. In present study, higher gravidity history and history of abortion were significantly related to severe preeclampsia. These findings are consistent with results of Bej et al [40] study in India. Our study showed that pregnant women with increased albumin in urine were significantly related to severe preeclampsia. Similarly, Risberg et al [41] study in Sweden found that albumin in urine was higher among pregnant women with preeclampsia as compared to mild preeclampsia. Our study found that pregnant women with severe preeclampsia were significantly related to adverse maternal and neonatal outcomes like preterm gestational age, cesarean section delivery, low neonatal Apgar score, low neonatal birth weight and neonatal admission to NICU. These findings are in agreement with results of many literatures such as Thanh et al [42] study in Thailand, Mengistu et al [43] study in Ethiopia and Caviello et al [44,45] study in USA which all referred to significant relationship between severe preeclampsia and adverse maternal and neonatal outcomes.
In conclusion, umbilical cord plasma homocysteine is significantly elevated in preeclamptic pregnant parturient women in comparison to normally healthy pregnant women.

ETHICAL APPROVAL: Basrah University College of Medicine [BUCOM] Ethical Committee
CONSENT TO PARTICIPATE: Informed consent was taken from each subject before their enrolment in the study.
HUMAN AND ANIMAL RIGHTS: The study conducted in adherence with Helsinki Ethical standards.
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