Dr. Nabnita Patnaik
Associate Professor,
Department of Obstetrics &
Gynaecology, SVS Medical
College and Hospital,
Mahbubnagar, Telangana,
India

Dr. Chapay Soren
Professor and Head,
Department of Paediatrics,
SVS Medical College and
Hospital, Mahbubnagar,
Telangana, India

Dr. Ranjith Kumar C
Associate Professor,
Department of Biochemistry,
SVS Medical College and
Hospital, Mahbubnagar,
Telangana, India

Dr. RL Tejaswi Tirumala
Assistant Professor,
Department of Obstetrics &
Gynaecology, SVS Medical
College and Hospital,
Mahbubnagar, Telangana,
India

Dr. C Venkatrami Reddy
Professor, Department of
Obstetrics & Gynaecology,
SVS Medical College and
Hospital, Mahbubnagar,
Telangana, India

Dr. Mandepudi Geethika
Assistant professor,
Department of Radiodiagnosis,
SVS Medical College and
Hospital, Mahbubnagar,
Telangana, India

Corresponding Author:
Dr. Nabnita Patnaik
Associate Professor,
Department of Obstetrics &
Gynaecology, SVS Medical
College and Hospital,
Mahbubnagar, Telangana,
India

To measure and compare the serum levels of homocysteine in Pre-eclamptic and normotensive pregnancies in a tertiary care hospital

Dr. Nabnita Patnaik, Dr. Chapay Soren, Dr. Ranjith Kumar C, Dr. RL Tejaswi Tirumala, Dr. C Venkatrami Reddy and Dr. Mandepudi Geethika

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Abstract
Aim: To measure and compare the serum levels of homocysteine in Pre-eclamptic and normotensive pregnancies.
Materials and Methods: The present prospective case control study was conducted in the Department of Obstetrics and Gynecology, SVS Medical College and Hospital, MBNR. Pregnant women with preeclampsia were considered as cases and women without any medical or other obstetric and fetal complications were selected as controls. Serum homocysteine was estimated on 2 ml of serum by competitive chemiluminescent enzyme immunoassay method.
Results: The study population comprised of 30 cases and equal number of controls. Around 26.0% of the cases had severe preeclampsia. The mean serum homocysteine values among cases was 12.65±4.24 µmol/L (p <0.001).
Conclusions: Maternal serum levels of total homocysteine were found to be significantly higher among preeclamptic women when compared to normotensive women.

Keywords: Homocysteine, Pre-eclampsia, Pregnant women

Introduction
Homocysteine is an intermediate product in the metabolism of the essential amino acid methionine. The vitamins folate and cobalamin are involved in the remethylation of homocysteine into methionine, and vitamin B6 as pyridoxal 5-phosphate is a cofactor in the transsulfuration of homocysteine by way of cystathionine to cysteine. A shortage of these vitamins, increased age, gender, and polymorphisms in related enzymes lead to elevated homocysteine plasma concentrations [1, 2].

Hyperhomocysteinemia is a risk factor for both cardiovascular disease and vasculopathy. A quantitative meta-analysis of mainly retrospective case-control studies demonstrated a positive association between Hcy and cerebrovascular disease [3]. Furthermore, animal studies suggest that hyperhomocysteinemia affects the walls of blood vessels, causing endothelial changes and smooth muscle proliferation. Several studies have demonstrated that serum homocysteine levels are elevated in preeclampsia at the time of symptoms compared to gestational age–matched normotensive pregnancies, but these elevations do not appear to predate the disease [4, 5].

The studies reported in the previous literature have been primarily retrospective, reviews, and large birth registries. Also, these assessments have been primarily undertaken in European and U.S. populations with very limited data that was evaluated in the Indian phenotype. Hence the present study was undertaken to measure and compare the serum levels of homocystiene in Pre-eclamptic and normotensive pregnancies in a tertiary care setting.

Materials and method
The present prospective case control study was conducted in the Department of Obstetrics and Gynecology, SVS Medical College and Hospital, MBNR.

Inclusion criteria
- Pregnant women, who presented with Pre-Eclampsia
- Period of gestation more than or equal to 20 weeks
- Pregnant women, who gave informed consent

Exclusion criteria
- Women with chronic diseases before pregnancy, such as chronic hypertension, diabetes mellitus, kidney and liver diseases
- Gestational age less than 28 weeks
- Not willing to participate

Ethical approval and Informed consent
The study protocol was reviewed by the Ethical Committee of the Hospital and granted ethical clearance. After explaining the purpose and details of the study, a written informed consent was obtained.

Sample selection
The sample size was calculated using a prior type of power analysis by G* Power Software Version 3.0.1.0 (Franz Faul, Universitat Kiel, Germany). The minimum sample size was calculated, following these input conditions: power of 0.80 and $P \leq 0.05$ and sample size arrived were 24 participants in each group. The final sample achieved was 30 per group.

Grouping
Case Group: Pre-eclamptic women presenting beyond 20 weeks of gestation with blood pressure more than or equal to 140/90mmhg.

Control Group: Age and gestational age matched Normotensive women

Methodology
A comprehensive general physical examination, systemic and obstetric examination was conducted. BP was measured using a Mercury Sphygmomanometer in the right arm, sitting position.
The BP measurement was repeated after 6 hours and the highest reading of the two was entered in the performa. The participant was asked to submit a random midstream urine sample and proteinuria was estimated using a spot urine dipstick method, using visual reagent strips, considered as a quick, portable, and easy to do method for analysis of proteinuria.
Serum homocysteine was estimated on 2 ml of serum by competitive chemiluminescent enzyme immunoassay method and the specimen was transported to the laboratory within 30 minutes of collection.

Statistical analysis
The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2010) and then exported to data editor page of SPSS version 20 (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics included computation of percentages, means and standard deviations were calculated. Statistical test applied for the analysis were student t-test and chi-square test. Level of significance was set at p≤0.05.

Results

Table 1: Demographic and clinical profile

Variables	Groups	Mean	Std. Deviation	p-value
Age (Years)	Case	26.30	2.38	0.732 (NS)
	Control	26.47	2.62	
Gestational Age weeks	Case	32.36	3.18	0.664 (NS)
	Control	33.31	3.09	
BMI	Case	20.69	1.64	0.813 (NS)
	Control	20.56	1.41	

Test applied: student t-test

Table 2: distribution as per parity

Groups	Parity				Total	p-value
	0	1	2	3		
Cases	18	5	5	2	30	0.135 (NS)
	30.0%	8.3%	8.3%	3.3%	50.0%	
Controls	17	11	2	0	30	
	28.3%	18.3%	3.3%	.0%	50.0%	
Total	35	16	7	2	60	
	58.3%	26.7%	11.7%	3.3%	100.0%	

Test applied: chi-square test

Table 3: mode of delivery

Variables	Mode of Delivery		Total	p-value
Groups	NVD	LSCS		
Cases	13	17	30	0.793 (NS)
	21.7%	28.3%	50.0%	
Controls	12	18	30	
	20.0%	30.0%	50.0%	
Total	25	35	60	
	41.7%	58.3%	100.0%	

Test applied: chi-square test

<div style="text-align:center">**Table 4:** mean serum Homocysteine levels</div>

Variables	Group	Mean	Std. Deviation	p-value
Serum Homocysteine	Cases	12.65	4.24	0.010*
	Controls	7.13	3.71	

Discussion

Homocysteine is an amino acid which has gained prominence in the recent years. The mean homocysteine levels normally decrease with gestation either due to physiological response to the pregnancy, increase in estrogen, hemodilution from increased plasma volume or increased demand for methionine by both the mother and fetus [6]. However, it is known to be an offending factor in the vascular pathology causing PE [7]. Stoĭkova V *et al.,* have reported that homocysteinemia is an important independent cardiovascular risk factor, which might induce the endothelial dysfunction observed in preeclampsia [8].

The present study compared the serum levels of total homocysteine in preeclamptic and normotensive pregnant women. The present study included 30 preeclamptic women fulfilling the inclusion criteria as cases and 30 age and gestational age matched normotensive women as controls. It was observed that the mean serum homocysteine levels were found to be significantly higher among the preeclamptic women when compared to the normotensive women (p<0.001).

In the present study, a significant difference was found between the mean serum homocysteine levels of preeclamptic women and normotensive women (p<0.001). This finding was also similar to the result of a study carried out by Sangeetha N *et al.,* in New Delhi and Sanlikan F *et al.,* in Poland [6, 9]. On the contrary, D' Anna R *et al.,* who conducted a study in a cohort of 1874 pregnant women, didn't report a statistically significant difference in the mean homocysteine levels, among women with PE and normotensive controls [10].

Conclusion

Present study concludes that preeclamptic women have a significantly higher serum homocysteine when compared to normotensive women. Thus, estimation of serum homocysteine levels among preeclamptic women may serve as a biomarker for identifying those at risk for complications.

The limitation of the present investigation was potential confounders, such as smoking status and family history of hypertension, that were not studied. The studies with larger sample size and longitudinal study design are required to generalize the results.

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