



DETECTION OF SERUM HOMOCYSTEINE LEVEL AND IT'S CORRELATION WITH MEAN ARTERIAL PRESSURE IN PRE ECLAMPSIA AND ECLAMPSIA

Dr Ramona Perhar	Lecturer, Ex Associate Professor Department Of Obs& Gynae MLN Medical College Prayagraj.
Dr Shilpi Singh*	Junior Resident Department Of Obs & Gynae MLN Medical College Prayagraj. *Corresponding Author
Dr. Nishita Chaudhari	Junior Resident Department Of Obs & Gynae MLN Medical College Prayagraj.

ABSTRACT **OBJECTIVE** :Plasma Homocysteine level and its correlation with Mean Arterial Pressure in Pre eclampsia and eclampsia.

METHOD: The present study was conducted in 150 antenatal women with normotensive and hypertensive pregnancy attending out patient , in **Swaroop Rani Nehru Hospital and Kamla Nehru Memorial Hospital**, Department of Obstetrics and Gynaecology, Prayagraj over a period of 12 month from August 2018 to July 2019. 25(31.25%) cases had MAP in range of 100-120, 55(68.75%) cases had >120, in study group. Mean value in study group 123.54±9.09 compared to mean value in control group was 97.60±7.67 .p<0.001 which is highly significant. Positive correlation was present between serum homocysteine and MEAN ARTERIAL PRESSURE (r=0.45)

RESULT: Women with raised blood pressure are at risk of developing Pre eclampsia and Eclampsia , and it serves as a predictive marker of pre eclampsia. Serum homocysteine was significantly increased in Eclampsia, severe Pre eclampsia and mild Pre eclampsia in comparison to control group.

CONCLUSION: High levels of homocysteine may be considered a precocious marker of vascular damage and may denote a higher risk of pre-eclampsia and elevated level of serum homocysteine may be associated with severity of pre-eclampsia.

KEYWORDS : Mean Arterial Pressure, Homocysteine, Pre Eclampsia, Eclampsia.

INTRODUCTION

Hypertensive disorders of pregnancy including pre-eclampsia complicate up to 2 to 8% of pregnancies world wide, constituting one of the greatest cause of maternal and perinatal morbidity and mortality, approximately 26% of all maternal deaths.

Pre eclampsia complicates 3-5% of first pregnancy and 1-2% of subsequent pregnancies with about 5-10% of severe cases.

Pre eclampsia is a hypertensive disorder of pregnancy, associated with wide spread vascular endothelial malfunction and is clinically defined as a multisystem disorder characterized by development of hypertension to the extent of 140/90 mmHg or more with proteinuria after the 20th week in a previously normotensive without proteinuria .

According to the ACOG diagnostic criteria (2013) for pre eclampsia , the dependence of the diagnosis on proteinuria has been eliminated

Features of severe pre eclampsia include, systolic blood pressure of 160 mmHg or higher ,or diastolic blood pressure of 110mmHg or higher on two occasions atleast 4 hours apart , thrombocytopenia (platelet count <100,000/microlitre) ,impaired liver function as indicated by abnormally elevated blood concentrations of liver enzymes ,severe persistent right upper quadrant or epigastric pain, progressive renal insufficiency, pulmonary oedema ,new onset cerebral or visual disturbances.

Eclampsia is defined as the presence of new onset grandmal seizures in a women with preeclampsia , preceded by a wide range of signs and symptoms, ranging from severe to absent or minimal hypertension , massive to no proteinuria , and prominent to no oedema.

Within the past 10 years, substantial advances in the understanding of pre eclampsia pathophysiology as well as increased efforts to obtain evidences to guide therapy have emerged. There are many theories about the etiology of pre eclampsia, including abnormal trophoblastic invasion of the uterine blood vessels, discordance of the immunologic tolerance between placental and fetal tissues, vascular endothelial cell damage.

Intact endothelium has anticoagulant properties and it blunts the response of vascular smooth muscle to agonists by releasing nitric oxide .Damaged or activated endothelial cells secrete substances that

promote coagulation and increase the sensitivity to vasopressors. The vasucular changes induced by homocysteine are similar to those associated with pre eclampsia and include atherosclerosis and endothelial dysfunction resulting in blunted vasorelaxation mechanism.

HOMOCYSTEINE, a sulfur containing essential amino acid derived from demethylation of dietary methionine, which is required for growth of cells and tissues in human body. elevated circulating homocysteine is a risk factor of endothelial dysfunction and vascular disease such as atherosclerosis and occlusive disorders.

Homocysteine is atherogenic and thrombophilic, elevated homocysteine levels are implicated in coronary, cerebrovascular and peripheral arterial disease, DVT and pre eclampsia

AIMS AND OBJECTIVES

1. To detect the maternal plasma level of homocysteine in all pregnant women.
2. To establish a relationship between homocysteine level with MAP in pre eclampsia and its complications.
3. To find out factors that might influence plasma homocysteine levels in hypertensive disorders of pregnancy

MATERIAL AND METHOD

The present study was conducted in antenatal women with normotensive and hypertensive pregnancy attending out patient, in **Swaroop Rani Nehru Hospital and Kamla Nehru Memorial Hospital**, Department of Obstetrics and Gynaecology, Prayagraj

The study was being carried out in 150 pregnant women attending outpatient and inpatient department over a period of 12 month from August 2018 to July 2019.

70 of these antenatal women were with no complication formed the control group while 80 cases were of hypertensive pregnancy including pre eclampsia and eclampsia.

A written informed consent was obtained from all subjects prior to the performance of any study related procedure.

A Detailed clinical history was taken with special references to age, gravida, parity, habitat, socio economic status, education, booked or unbooked, duration of marriage was taken.

A past and family history was taken regarding diabetes mellitus, thyroid disorder, pregnancy loss, thrombotic disorders and tuberculosis in any site or any operation on or near genital tract, any other previous illness and operations.

A detailed personal history was taken regarding eating habits addiction to tobacco, alcohol, caffeine, any contraception practiced or duration for which contraception has been practiced.

A detailed Obstetric history was taken with special references to history of abortions, congenital anomaly, complications like toxemia, accidental haemorrhages and multiple pregnancies, pre term labour and delivery, IUGR and IUD was taken

General examination was done regarding height, weight, body mass index (weight in kg/height m²), pallor, icterus, edema, pulse rate, temperature, Blood pressure (Mean Arterial Pressure calculated as: MAP=2/3 diastolic blood pressure+1/3systolic blood pressure), presence of rashes, any thyroid enlargement, breast examination. Systemic examination and detailed obstetrical examination was done at the time of antenatal visit and at time of admission.

SELECTION OF CASES-

1. Normal pregnant women
2. Pre eclampsia patients
3. Eclampsia group

INCLUSION CRITERIA-

1. Singleton pregnancies
2. None of the subjects were in active labour
3. No signs of infection.

EXCLUSION CRITERIA-

1. Essential hypertension suggested by history or documentation of hypertension in pre pregnant state or hypertension before weeks of gestation
2. Cardiovascular disease
3. Renal disease
4. Liver disease
5. Multiple pregnancy
6. Diabetes mellitus
7. Inflammatory or infective disorders
8. Coincidental seizures in pregnancy
9. History or documentation of epilepsy in pre pregnant state
10. Space occupying lesion in brain like tuberculoma or brain tumor
11. Trauma to brain
12. Hyperpyrexia
13. On treatment with antifolate drugs such as methotrexate,

Routine investigations like blood group/Rh, haemoglobin, HIV 1 AND 2, HBsAg, HCV, VDRL, Fasting Blood sugar, Post prandial blood sugar was done.

Peripheral venous blood samples were collected for thyroid stimulating hormone assays (T3, T4, TSH), s. urea, s.creatinine, s.bilirubin, SGOT, SGPT, platelet count and urine routine microscopy. Specific investigations include -Serum homocysteine level.5 ml of blood sample was drawn from each subject by venepuncture. samples were then immediately centrifused.

METHOD OF DETERMINING HOMOCYSTEINE

Plasma homocysteine levels were detected by chemiluminescent method using an automatic immunoanalyser (IMMULITE)

OBSERVATION

The present study was carried out on 150 antenatal women, hypertensive pregnancy as well as normotensive pregnancy attending the outpatient and inpatient Department of **Swaroop Rani Nehru Hospital and Kamla Nehru Memorial Hospital**, Department of Obstetrics and Gynaecology, over a period of 12 months from august 2018 to July 2019. Serum homocysteine was measured in normotensive as well as in hypertensive pregnancies.

70 of these antenatal women were with no complication formed the control group while 80 cases were of hypertensive pregnancy including pre eclampsia and eclampsia..

TABLE NO. 1: DEMOGRAPHIC FEATURES

Variables	Control Group		Study Group	
	NO.	Percentage	NO.	Percentage

Age				
18-23	21	30%	30	37.5%
24-29	31	44.28%	39	48.75%
30-35	15	21.4%	9	11.25%
35-40	3	4.28%	2	2.5%
Gravidity				
Gravida 1	34	48.57%	48	60%
Gravida 2	15	21.42%	20	25%
Gravida 3	11	15.71%	9	11.25%
Gravida 4	10	14.28%	3	3.75%
Parity				
P0	26	37.14%	44	55%
Para 1	23	32.85%	18	22.5%
Para 2	16	22.85%	8	10%
Para 3	2	2.85%	6	7.5%
Para 4	3	4.28%	4	5%
Socio Economic Status				
Upper (Class I)	3	4.28%	2	2.5%
Upper Middle (Class II)	9	12.85%	6	7.5%
Lower Middle (Class III)	9	12.85%	12	15%
Upper Lower (Class IV)	17	24.28%	18	22.5%
LOWER (CLASS V)	32	45.71%	42	52.5%
Education				
Illiterate	30	42.85%	34	42.5%
Primary And Middle School	18	25.71%	27	33.75%
High School And Intermediate	15	21.42%	13	16.25%
Graduate And Higher	7	10%	6	9.25%
UNEMPLOYED	49	70%	59	73.75%
Laboureres	14	20%	18	22.5%
Office Work	7	10%	3	3.75%
Rural Area	27	38.5%	44	55%
Urban Area	43	61.42%	36	45%
BMI				
<18.5	2	2.85%	5	6.25%
18.5-24.9	30	42.85%	47	58.75%
25-29.9	21	30%	25	31.25%
30-34.9	12	17.14%	3	3.75%
>35	5	7.14%	0	-

TABLE NO 2: SERUM HOMOCYSTEINE LEVELS

	RANGE µmol/L	MEAN±SD µmol/L	P value<0.001
Normotensive	5.1 – 9.2	6.92± 1.474	
Mild Preeclampsia	6.2 – 12.2	9.60 ±1.35	
Severe Preeclampsia	9.6 – 16.4	12.3± 2.54	
Eclampsia	9.4 – 18.6	14.1± 3.27	

TABLE NO. 3: SYSTOLIC BLOOD PRESSURE AT THE TIME OF ADMISSION

SYSTOLIC BP mmHg	CONTROL GROUP		STUDY GROUP	
	NO.	PERCENTAGE	NO.	PERCENTAGE
<140	70	100%	0	-
>140	0	-	34	42.5%
>160	0	-	46	57.5%
MEAN± SD	116.57±2.74		159.13±3.39	

P VALUE – 0.001

FIGURE NO. 1. SYSTOLIC BLOOD PRESSURE

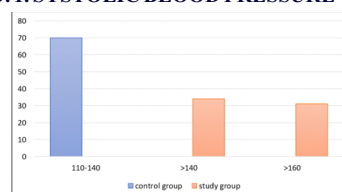


TABLE NO. 4; DIASTOLIC BLOOD PRESSURE AT THE TIME OF ADMISSION

DIASTOLIC BP mmHg	CONTROL GROUP		STUDY GROUP	
	NO.	PERCENTAGE	NO.	PERCENTAGE
<90	70	100%	0	-
>90-100	0	-	44	55%
>100	0	-	36	45%
MEAN± SD	75.78±3.79		96.87±4.64	

P Value- 0.001

FIGURE NO.-2 DIASTOLIC BLOOD PRESSURE

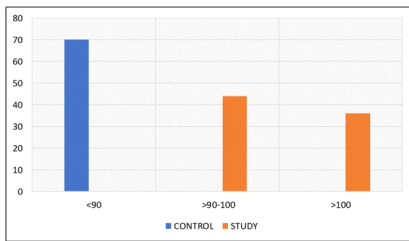


TABLE NO.5; MEAN ARTERIAL PRESSURE AT THE TIME OF ADMISSION

Mean Arterial pressure mmHg	CONTROL GROUP		STUDY GROUP	
	NO.	PERCENTAGE	NO.	PERCENTAGE
70-100	43	61.42%	0	-
100-120	27	38.5%	25	31.25%
>120	0	-	55	68.75%
TOTAL	70	100%	80	100%
MEAN ±SD	97.60±7.67		123.54±9.09	

P VALUE – 0.001

FIGURE NO. 3: MEAN ARTERIAL PRESSURE

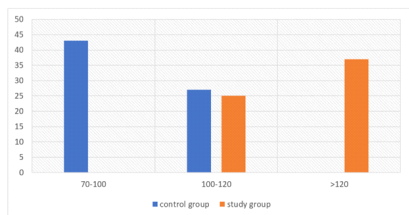
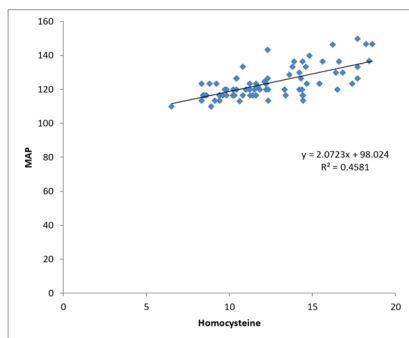


FIGURE NO.4: CORELLATION BETWEEN S. HOMO CYSTEIN AND MAP



DISCUSSION: SYSTOLIC BLOOD PRESSURE-

34 cases (42.5%) presented with Systolic BP>140(mild preeclampsia),

46(57.5%) presented with Systolic BP>160 (severe preeclampsia). In control group, none of them had systolic BP above >140. Mean systolic BP in control group was 116.57±2.74 whereas in study group it was BP is 159±3.39 which was highly significant (p<0.001)

DIASTOLIC BLOOD PRESSURE-

44(55%) cases had diastolic BP >90-100 and 36(45%) presented with >100 in study group. Mean diastolic BP in pre eclampsia group was 96.87±4.67 whereas mean diastolic BP in normotensive pregnancy was 75.78±3.79, which was highly significant(p<0.001).

MEAN ARTERIAL PRESSURE-

25(31.25%) cases had MAP in range of 100-120,55(68.75%) cases had >120, in study group. Mean value in study group 123.54±9.09 compared to mean value in control group was 97.60±7.67 .p<0.001 which is highly significant. Positive correlation was present between serum homocysteine and MAP (r=0.45)

Abudu olalekan et al(2009),found a strong correlation between the homocysteine level and the systolic/diastolic blood pressure in the eclamptic group(r=0.944,p=0.0001;r=0.98;p=0.0001)

Ferdausi M et al(2013) suggested a positive correlation between serum homocysteine and systolic blood pressure(r=0.528,p=,0.001) and between serum homocysteine and diastolic blood pressure (r=0.579,p<0.001)

Shalini et al(2013) ,found a strong positive correlation between serum homocysteine with blood pressure(systolic and diastolic) which is highly significant.

CONCLUSION

1. In this study group, 44(55%) and 27(38.5%) of control groups belonged to rural area, whereas 36(45%) of study group and 43(61.42%) of control group were to urban dwellers.
2. Mean systolic BP was 159±3.39 in the study group whereas it was 116.57±2.74 in the control group with p=0.001 which implies that it is significant. Positive correlation was found between S .homocysteine and systolic blood pressure.
3. Mean diastolic BP was 96.87±4.67 in the study group whereas it was 75.78±3.79 in the control group with p value of 0.001 which proves its significance. Positive correlation was found between S. homocysteine and diastolic blood pressure.
4. MAP in study group was 123.54±9.09 compared to MAP in control group which was 97.60±7.67. The p<0.001 is significant. Positive correlation was found between serum homocysteine and MAP (r=0.45)
5. Thus women with raised blood pressure are at risk of developing Pre eclampsia and Eclampsia , and it serves as a predictive marker of preeclampsia.
6. Serum homocysteine level in eclampsia ranged from 9.4-18.6µmol/L with a mean of 14.1. In severe pre eclampsia it ranged from 9.6-16.4µmol/L with mean of 12.3. And in mild pre eclampsia it ranged from 6.2-12.2µmol/L with mean of 9.6.

Serum homocysteine level in control group ranged from 5.1-9.2µmol/L with mean of 6.92 with P value <0.0001 which is highly significant. Serum homocysteine was significantly increased in Eclampsia, severe Pre eclampsia and mild Pre eclampsia in comparison to control group. Thus high levels of homocysteine may be considered a precocious marker of vascular damage and may denote a higher risk of preeclampsia and elevated level of serum homocysteine may be associated with severity of pre-eclampsia.

REFERENCES

1. American College of Obstetricians and Gynecologists; Task Force on Hypertension in Pregnancy. Hypertension in Pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. Obstet. Gynecol. 2013, 122, 1122–1131.
2. Maru L, Verma M, Jinsiwale N. Homocysteine as Predictive Marker for Pregnancy-Induced Hypertension - A Comparative Study of Homocysteine Levels in Normal Versus Patients of PIH and Its Complications. J Obstet Gynecol India 2016; 66(1): 167-71.
3. Dr. V. Geetha , Dr. P. Thilagavathy et al; Study of Relationship between Plasma Homocysteine Levels and Gestational hypertension IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) e-ISSN: 2279-0853, p-ISSN: 2279-0861. Volume 16, Issue 1 Ver. II (January, 2017), PP01-06
4. Laskowaka M. Analysis of the homocysteine levels in maternal serum in pregnancies complicated by severe preeclampsia Lubin Poland; 2010.
5. Dekker GA, de Vries JI, Doelitzsch PM, Huijgens PC, von Blomberg BM, Jakobs C, van Geijn HP. Underlying disorders associated with severe early-onset preeclampsia. Am J Obstet Gynecol. 1995;173: 1042–1048.
6. Khosrowbeygi A, Ahmad vand H. Circulating level of homocysteine in preeclamptic women, Bangladesh med Res coune Bull 2011., 37: 106109.

7. Rasha Eltayeb Ahmed and Nour Mahmoud Abdelatif Ali Assessment of Maternal Plasma Homocysteine levels among Sudanese Pregnant Ladies with Preeclampsia, International Journal 126|Int. J. of Multidisciplinary and Current research, Vol.6 (Jan/Feb 2018)
8. Faith Sanlikn, Fatma Tufan, Ahmed Gocmen, Ceyda Kabaday Erkan Sengil. References 93 The evaluation of homocysteine level in patients with preeclampsia. Ginekolo Pol. 2015, 86, 287-291.
9. Kanan Avinash Yelikar*, Sonali Satish Deshpande, Manisha Laxmikant Kulkarni, Association of maternal serum homocysteine level with severity of preeclampsia: a case control study, Yelikar KA et al. Int J Reprod Contracept Obstet Gynecol. 2016 Aug;5(8):2713-2717.
10. Alruba Taimoor, Khalid Buland*, Aamir Nazir, Sadaf Anwar Qureshi. comparison of serum homocysteine levels in primigravidas during second and third trimesters of normal pregnancy and preeclampsia. Pak Armed Forces Med J 2019; 69 (2): 302-06
11. Weronika Dymara-Konopka * and Marzena Laskowska , The Role of Nitric Oxide, ADMA, and Homocysteine in The Etiopathogenesis of Preeclampsia— Review: Int. J. Mol. Sci. 2019, 20, 2757
12. Wang J., Trudinger B., Duarte N., Nilchen D. and Wang X.: Elevated circulating homocysteine levels in placental vascular disease and associated preeclampsia. Br. J. Obstet. Gynecol., 107: 935-938, 2000
13. Powers RW, Evans RW, Majors AK et al. Plasma homocysteine concentration is increased in preeclampsia and associated with evidence of endothelial activation. Am J Obstet Gynecol 1998;179:1605-11. 6.
14. Raijmakers, M.; Zusterzeel, P.L.M. ; Steegers, E.A.P. ; Peters, W.H.M. European Journal of Obstetrics & Gynaecology and Reproductive Biology, (2000)
15. Lopez-Quesada E, Vilaseca MA, Lailla JM. Plasma total homocysteine in uncomplicated pregnancy and in preeclampsia. Eur J Obstet Gynecol Reprod Biol 2003; 108(1): 45-9.
16. D Anna .R., Baviera,G., Corrado,F., Ientile,R., Granese, D &Stella,N.C.(2004) Plasma Homocysteine in early and late pregnancies complicated with preeclampsia and isolated intrauterine growth restriction. Acta Obstet .Gynecol.Scand, 83,155-158.
17. Dorothy J. Vanderjagt Rina J. Patel Aliyu U. El Nafaty George S. Melah Michael J. Crossey Robert H. Glew High density lipoprotein and homocysteine levels correlate inversely in preeclamptic women in northern Nigeria 2004
18. Mignini LE, Latthe PM, Villar J, Kilby MD, Carroli G, Khan KS. Mapping the theories of preeclampsia: the role of homocysteine. Obstet Gynecol. 2005; 105(2):411–25
19. Ingec M, Borekci B, Kadanali S. Elevated plasma homocysteine concentrations in severe preeclampsia and eclampsia. Tohoku J Exp Med 2005; 206(3): 225-31. 21.
20. Singh Urmila 1, Gupta HP 2, Singh RK 3, Shukla Manju 4, Mehrotra Seema 5, Prasad Shweta 6, Homocysteine: Association with preeclampsia and normotensive pregnancy, J Obstet Gynecol India Vol. 59, No. 3 : May/June 2009 pg 235-238
21. Amal Mansour ,Hisham Harb and Mohamed Abdelhafeez, Diagnostic Value of Homocysteine and Other Preeclampsia Markers: Relationship with Severity; International Journal of Biological Chemistry 5(4):227-237, 2011
22. Sunita G, Sheela J, Bhavna K Madhur G, Chaitanya S. A study of serum homocysteine levels during normal pregnancy and preeclampsia. Journal of South Asian Federation of Obstetrics and gynecology May-Aug. 2011; 3(2):7174.