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To Study Role of Homocysteine as a Biochemical Marker in Various Obstetrical Complications

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Abstract--Low plasma homocysteine level during an uncomplicated pregnancy was first demonstrated by Kang et al almost 20 years ago, & this has subsequently been confirmed by numerous investigators. Plasma homocysteine concentrations are 30-60% lower in pregnant women than in non-pregnant women & the lowest levels are observed in the second trimester. Hyperhomocysteinaemia is associated with adverse pregnancy outcome, such as spontaneous early abortion, placental vasculopathy and birth defects. It is not only neural tube defects (NTDs) but also cardiac malformations and cleft lip and/or palate etc. Objective of study is to observe role of Homocysteine as a biochemical marker in various obstetrical complications and to evaluate Homocysteine as a risk factor in obstetrical complications. ADVIA- Centaur equipment is used and method is Chemiluminescence. It has been found that Pre-eclampsia cases have got higher Probabilities of having raised Homocysteine as compared to non-Pre-eclamptic cases, on the other hand Recurrent abortions has been found to be associated with high Homocysteine, indicating adverse effect of Hyperhomocystenemia.

Keywords---abruptio placentae, eclampsia, hyperhomocystenemia, IUGR, NTD.

Introduction

An association between elevated homocysteine levels and human disease was first suggested in 1962 by Carson and Neil, who found high homocysteine concentrations in the urine of some children with mental retardation. The elevated homocysteine levels in these patients were caused by severe enzyme

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defects blocking the homocysteine metabolism ([Selhub, 1999](#); [Holford, 2009](#)). This condition, homocystinuria, was later found to be associated with premature occlusive cardiovascular disease, even in childhood, and about 25% of patients died as a result of cardiovascular events before the age of 30. In addition, hyperhomocysteinaemia is associated with adverse pregnancy outcome, such as spontaneous early abortion, placental vasculopathy and birth defects. It is not only neural tube defects (NTDs) but also cardiac malformations and cleft lip and/or palate, which are associated with higher homocysteine levels than in controls ([Steegers-Theunissen et al., 1997](#); [Kalhan & Iben, 2000](#)).

During pregnancy there are hemostatic changes that result in a hypercoagulable state & can have thrombotic consequences. This condition can be aggravated in women who are carriers of congenital thrombophilic factors. This thrombotic tendency can manifest as thrombotic lesions in the placenta with compromise in utero-placental circulation, which are common characteristics present in obstetric complications, such as pre-eclampsia, IUGR, recurrent abortions, placental abruption ([Stampfer & Malinow, 1995](#); [Mosharov et al., 2000](#)).

Objective

To study role of Homocysteine as a biochemical marker in various obstetrical complications and to evaluate Homocysteine as a risk factor in obstetrical complications ([American Heart Association, 1999](#)).

Material and Method

The study is a hospital based prospective study & is carried out in the department of Pathology, N.S.C.B. Medical college and hospital, Jabalpur MP in 2011. Homocysteine Tests are conducted at PATH CARE LABS, SECUNDERABAD.

Inclusion criteria

- All pregnant females developing hypertension & Oedema.
- All pregnant females with previous history of miscarriages/recurrent abortions.
- All pregnant females having history of NTD in previous pregnancy.
- All pregnant females complaining of bleeding p/v, in second & third trimester.
- All postpartum females giving birth to Low Birth Weight babies.
- Pregnant females showing no fetal movements on examination.

Exclusion criteria

- Pregnant females coming for routine ANC visits, no complications.
- Females with previously done MTP because of some ailment/or medically indicated

Procedure

Sample for testing homocysteine levels is collected and processed by an overnight fasting blood sample either plain or in EDTA/Lithium Heparinized, taking all aseptic precautions by venepuncture (Boers, 1994; Chait et al., 1999). Haemolysed samples should not be used. ADVIA- Centaur equipment is used and method is Chemiluminescence. HYC Calibrator, Ready pack primary reagent pack containing Advia Centaur HYC Lite reagent & Solid phase, Advia Centaur iPTH master curve card, HYC Diluent are required material. The Advia Centaur Homocysteine assay is a competitive immunoassay using direct chemiluminometric technology (Wald et al., 2002; Miner et al., 1997). The different forms of Homocysteine in the patient sample are reduced to free HCY by the reducing reagent. Free HCY is then converted to S-adenosylhomocysteine (SAH) by the enzyme reagent. Converted SAH from the patient sample competes with SAH covalently coupled to paramagnetic particles in the Solid Phase for a limited amount of acridinium ester-labelled anti-SAH in the Lite Reagent. After loading the samples the system automatically performs the following steps:

- Dispenses 20 μ L of sample into a cuvette.
- Dispenses 50 μ L of Reducing reagent & incubates for 3 minutes at 37 $^{\circ}$ C.
- Dispenses 50 μ L of Enzyme reagent & incubates for 2.5 minutes at 37 $^{\circ}$ C.
- Dispenses 50 μ L of Solid Phase & incubates for 2.5 minutes at 37 $^{\circ}$ C.
- Separates, aspirates & washes the cuvettes with reagent water.
- Dispenses 300 μ L each of Acid Reagent & Base Reagent to initiate the chemiluminescent reaction.

Results reported according to the selected option, as described in the system operating instructions. An inverse relationship exists between the amount of HCY present in the sample & the amount of relative light units (RLUs) detected by the system. Assay range is 0.50–65.0 μ mol/L (Puri et al., 2003; Jacques et al., 2001).

Observation

Present study was carried out in N.S.C.B Medical College Jabalpur. 100 pregnant females were included to study the effects of raised Homocysteine on pregnancy (Chait et al., 1999; Selhub, 1999).

Table 1
Age wise distribution of cases

Age	Frequency	Percentage
< 20	3	3.0
20 – 29	69	69.0
30 – 39	26	26.0
40 – 49	2	2.0
Total	100	100.0

As it can be seen in above table that out of 100 cases, maximum patients that is 69%, belong to the age group between 20 – 29yrs which constitutes the peak

reproductive period. 26% patients belong to 30- 39yrs group, & only 3% & 2% belong to <20 yrs & 40 – 49yrs respectively (Neki & Arora, 2001; Prasad, 1999).

Table 2
Distribution of cases according to clinically diagnosed complication

Clinical diagnosis	Frequency	Percentage
Abruptio placentae	17	17.0
Pre eclampsia/eclampsia	30	30.0
IUFD	14	14.0
IUGR	15	15.0
NTD	1	1.0
Recurrent Abortion	23	23.0
Total	100	100.0

Out of 100 patients, based on their clinical diagnosis, maximum no. of cases were of Pre-eclampsia / eclampsia making upto 30%. After that Recurrent Abortions makes about 23% cases. 17% cases belong to Abruptio placentae. IUFD & IUGR includes 14% & 15% cases respectively. NTD being rare included only one case making to 1%.

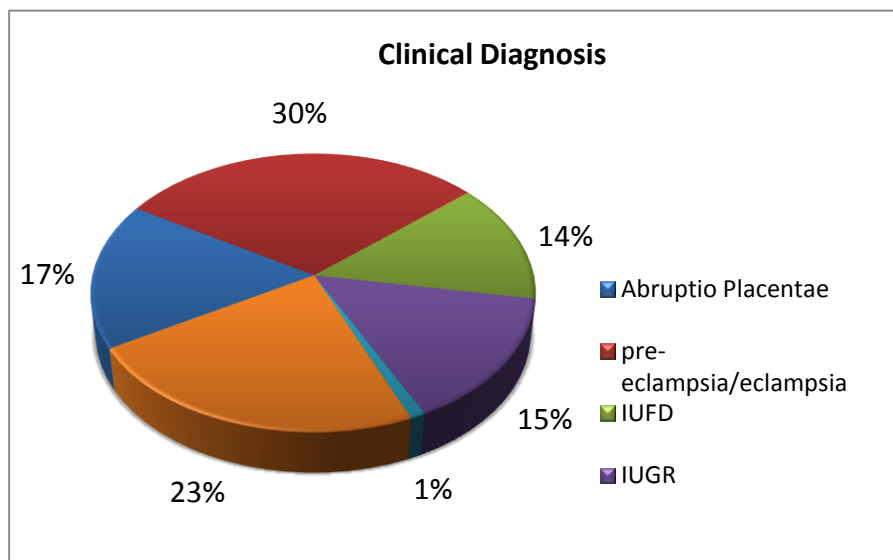


Figure 1. Clinical diagnosis

Table 3
Clinically diagnosed complication v/s Serum HCY cross tabulation

<i>Clinical diagnosis</i>	<i>Serum Homocysteine</i>		<i>Total</i>	<i>Significance</i>
	<i>Normal</i>	<i>Abnormal</i>		
Abruptio Placentae Abru	15 88.2%	2 11.8%	17 100.0 %	$c^2=2.95$ $p>0.05$
Pre-eclampsia / eclampsia	23 76.6%	7 23.3%	30 100.0 %	$c^2=0.66$ $p>0.05$
IUFD	13 92.9%	1 7.1%	14 100.0 %	$c^2=3.78$ $p>0.05$
IUGR	10 66.7%	5 33.3%	15 100.0 %	$c^2=0.16$ $p>0.05$
NTD	0 0.0%	1 100.0%	1 100.0 %	$c^2=2.47$ $p>0.05$
Recurrent Abortion	10 43.5%	13 56.5%	23 100.0 %	$c^2=10.99$ $p<0.001$
<i>Total</i>	<i>71</i> <i>71.0%</i>	<i>29</i> <i>29.0%</i>	<i>100</i> <i>100.0</i> <i>%</i>	-

Above table shows that out of 17 cases of Placental Abruption, 11.8% cases had elevated Homocysteine levels & rest 88.2% were normal. Out of 30 cases included in Pre-eclampsia/eclampsia, 23.3% had raised Homocysteine levels & 76.6% had normal levels. In 14 cases of IUFD, 7.1% had raised Homocysteine & 92.9% were normal. In 15 cases of IUGR, 33.3% had elevated Homocysteine levels & 66.7% were normal. Out of 23 cases of Recurrent Abortions, 56.5% had raised Homocysteine levels & 43.5% were normal. There was only 1 case of NTD & that had raised Homocystein level, making 100%.

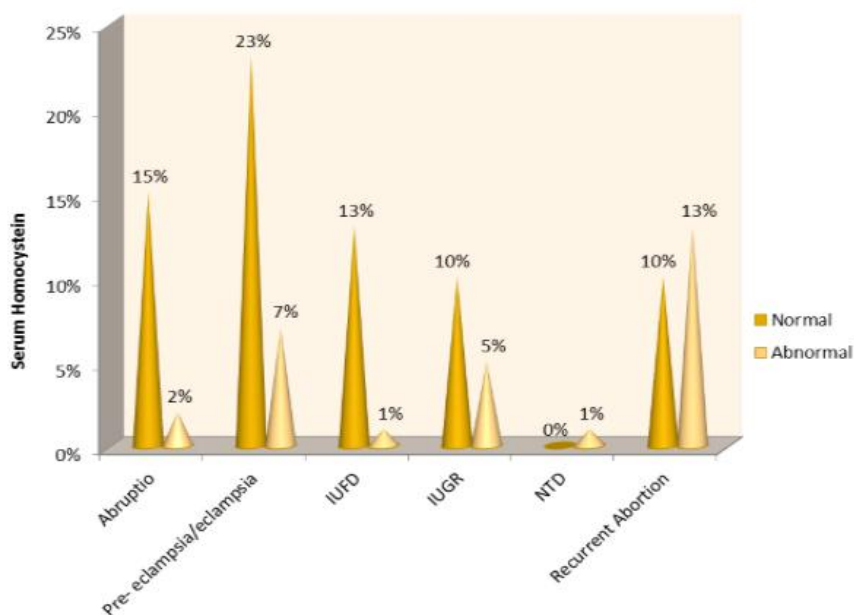


Figure 2. Clinically diagnosed complication v/s Serum Homocysteine

Discussion

Hyperhomocysteinemia belongs among the congenital hypercoagulable states & is a long known vascular disease risk factor. Hyperhomocysteinemia has been suggested as a possible risk factor in women suffering from recurrent abortions, eclampsia, pre-eclampsia, placental abruption, IUGR, NTD's, thromboembolic events etc. The present study demonstrated the usefulness of serum Homocysteine in above mentioned obstetrical complications. In this study maximum patients that is 69%, belong to the age group 20 – 29 yrs which constitutes the peak reproductive period. It shows that maximum females in India conceive in this peak reproductive period (Mudd et al., 1964; Graham et al., 1997).

In present study the majority (30%) of pregnant females were having Pre-eclampsia/ eclampsia as a complication. This shows that Pre-eclampsia is the most common complication occurring during pregnancy. This is comparable to the study by Muthayya S et al, *Eur. J. Clin Nutr.* 2006 June in which Pre-eclampsia forms 44.44% in India. Next bulk of cases were having Recurrent Abortions (23%) as complication. However, association of Pre-eclampsia with high Homocysteine level could not be established in this study, but it has been found that the cases with Pre-eclampsia have higher probabilities of having raised Hcy by 1.92% more compared with Non Pre-eclamptic cases (Graham et al., 1997; Ubbink et al., 1994).

Conclusion

- It is observed that Pre-eclampsia/eclampsia is more common as maximum (30%) pregnant females were having pre-eclampsia. However, its association with raised Homocysteine could not be established.
- It has been found that Pre-eclampsia cases have got higher Probabilities of having raised Homocysteine as compared to non Pre-eclamptic cases.
- On the other hand Recurrent abortions has been found to be associated with high Homocysteine, indicating adverse effect of Hyperhomocystenemia.

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