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βHCG FOR SCREENING OF GESTATIONAL HYPERTENSION : A PROSPECTIVE OBSERVATIONAL STUDY IN NORTH INDIAN POPULATION

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ABSTRACT
To measure maternal serum beta human chorionic gonadotropin during 13-24 weeks of pregnancy and compare the same between those who develop pregnancy induced hypertension with those who do not. In a prospective study βhCG levels were estimated in 75 antenatal women in the second trimester (12-24 weeks) by ELISA technique. Results were noted in terms of development of preeclampsia, mean serum levels of the marker, mode of delivery and complications. During the course of study, a total of 8 (10.7%) patients developed hypertension. Thus incidence of pregnancy induced hypertension was 10.7%. A significant rise of mean serum βhCG level (32022MIU/ml, mean)was present in those who developed preeclampsia.The marker can prove an important role in early recognition of a pregnancy related complication and provides the obstetrician ample opportunity to guide the management during pregnancy.

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INTRODUCTION
Hypertensive disorders are one of the most common and probably the most widely studied disorders of pregnancy. Hypertension has been estimated to complicate 5% of all pregnancies and 11% of first pregnancies (1). Among hypertensive disorders of pregnancy, gestational hypertension comprises a major subset that complicates nearly 5-8% of pregnancies and is also associated with increased risks of perinatal morbidity and mortality and maternal morbidity (2,3). Since it is postulated that pre-eclampsia is a trophoblastic disorder, there might be a link between concentration of βhcg which is exclusively secreted by placenta (4).

The human chorionic gonadotropin (hCG) is a glycoprotein with lipid structure. Its best known biologic function is the maintenance of the corpus luteum of pregnancy (5). Twin pregnancies and molar pregnancies produce higher levels of hCG and they are associated with a higher incidence of pre-eclampsia than uncomplicated singleton pregnancies (4). The leutinizing hormone-hCG receptors are found in myometrium and in uterine vascular tissue. Low serum concentration of hyperglycosylated hCG-h have been found to be associated with early pregnancy loss. Various studies have been done which show association of decreased PAPP A with pre eclampsia. But there are clear conflicts. On one hand there are studies which show clear association of βhCG and gestational hypertension (6-8)there are studies show no association between βhcg and poor pregnancy outcomes (9,10).

The present study aims to fill up this void in literature. The aim is to prospectively evaluate relationship between concentration of βhcg and subsequent development of hypertension.

AIM
To evaluate the relationship between concentration of serum βhCG and risk of gestational hypertension

MATERIALAND METHODS
Study Area: Department of Obstetrics, Era's Lucknow Medical College & Hospital, Lucknow.
Study duration: 18 months (Jan. 2015-Sep. 2016)
Study Population: Pregnant women attending the O.P.D. and I.P.D. of Era's Lucknow Medical College & Hospital, Lucknow.
Sample Size: 75
Study Design: Prospective observational study.

Inclusion Criteria
- Pregnant women in second trimester of their pregnancy (13-24 weeks).
- Singleton pregnancy
- Booked for delivery

Exclusion Criteria
- Patients having

1. Pre existing hypertension,
2. Twin or multiple pregnancy
3. Molar pregnancy
4. Known medical conditions like-heart disease, diabetes mellitus, severe anemia
5. Pregnancies with fetal chromosomal or structural abnormalities.

Study Interventions:
A total of 75 pregnant women in second trimester (13-24 weeks) of pregnancy falling in sampling frame (fulfilling the conditions of inclusion and exclusion criteria) were enrolled in the study. Informed consent was taken from all participants and patient information sheet distributed. Ethical clearance was obtained from institute`s ethical committee
At the time of enrolment, demographic details were noted, detailed obstetric and medical history was taken. All the subjects underwent thorough clinical and routine obstetric examination. Blood pressure was recorded. Routine antenatal tests were performed as required and indicated.
At the time of enrolment 1 ml of blood sample was obtained from the women and was collected in plain vial for analysis of serum levels of β-human chorionic gonadotropin, using ELISA technique. All the pregnancies were followed up regularly till delivery. Primary outcome measure was development of gestational hypertension and its relation with free βhcg value of second trimester. Secondary outcome measures were mode of delivery and other maternal complications in hypertensive cases.

Method of Measurement of Outcome of Interest:
a) Serum β human chorionic gonadotropin level using ELISA technique.
b) Incidence of Pregnancy induced hypertension.
c) Maternal complication and mode of delivery.

Statistical analysis
The data was analyzed using Statistical Package for Social Sciences version 15.0 or above. Chi-square test was used for comparing categorical results. For evaluation of quantitative outcomes, for ordinal parameters Mann-Whitney test was used whereas for continuous parameters 't'-test was used. A 'p' value less than 0.05 was considered to indicate statistically significant association.

RESULTS
Majority of women included in the study were aged 20-25 years 41 (54.7%) There were 26 (34.7%) women in age group 26-30 years and 8 (10.7%) in age group >30 years (Table 1). Mean age of patients was 26.27±3.9 years. Statistically, this difference between two groups was not significant (p=0.159). Majority of women (50.7%) were primigravida and 37 were (49.3%) multigravida (Table 2). Significantly higher proportion of hypertensive women 7 (87.5%) as compared to normotensive women 31 (46.3%) were primigravida (p=0.027) (Table 3). Nearly half of the women 37 (49.3%) were enrolled in the study at gestational age 12-18 weeks. Remaining 38 (50.7%) women were enrolled in study at gestational age

SN	Age Group (Years)	Total (n=75)	
		No.	%
1.	20 -25 Yrs	41	54.7
2.	26 -30 Yrs	26	34.7
3.	>30 Yrs	8	10.7
Mean Age±SD (Range) in years		26.27±3.86 (20-38)	

Table 1: Age profile of patients

SN	Parity	Total (n=75)	
		No.	%
1.	Primigravida	38	50.7
2.	Multigravida	37	49.3

Table 2: Distribution of subjects according to obstetric history

SN	PIH Status	Total (n=75)	
		No.	%
1.	Normotensive	67	89.3
2.	Hypertensive	8	10.7

Table 3: Showing distribution of women according to PIH status

18w1d-24 weeks.
The cohort of patients was then followed up till delivery. Women with pregnancy induced hypertension were identified. During the course of study, a total of 8 (10.7%) patients developed hypertension. Thus incidence of pregnancy induced hypertension was 10.7%.
-βhCG levels were above the cut-off value of 30,000 mIU/ml in 7.5% of normotensive women as compared

SN	Number of cases	β-HCG levels			
		Normal		Elevated	
		No.	%	No.	%
1.	Normotensive (n=67)	62	92.5	5	7.5
2.	Hypertensive (n=8)	1	12.5	7	87.5

Table 4: Comparison of β-hHCG levels in patients who developed gestational hypertension and among patients who remained Normotensive (n=75)*

SN	Variable	PIH (n=8)		Normotensive (n=67)		Statistical significance	
		Mean	SD	Mean	SD	't'	'p'
1.	β-hCG (mIU/ml)	32022	2890	15057	13936	3.415	0.001

Table 5: Comparison of βhCG level between two groups

Among maternal complications identified only 1 patient developed abruption. No other complication apart from PIH was noted in this cohort of 75 patients

SN	Variable	PIH (n=8)		Normotensive (n=67)	
		No.	%	No.	%
1.	Vaginal delivery	1	12.5	55	82.1
2.	LSCS delivery	7	87.5	12	17.9

Table 6: Comparison of two groups for mode of delivery

to 87.5% of hypertensive women. On evaluating the difference between two groups, the difference was found to be significant statistically (p<0.001) (Table 4). Mean value of βhCG in women who developed gestational hypertension was 32022mIU/ml and that in normotensive women was 15057mIU/ml (Table 5).

In hypertensive group, mode of delivery was Lower Segment Caesarean Section(LSCS) in 7 out of 8 (87.5%) women. In 6 out of these 7 hypertensive LSCS cases, the indication for LSCS was fetal distress. In normotensive group, LSCS cases were 12 (17.9%) (Table 6). Statistically, there was a significant difference between two groups with respect to mode of delivery (p<0.001).

DISCUSSION

Main findings

In this prospective observational study of 75 pregnant women a statistically significant association was found between serum beta hcg in second trimester of pregnancy and subsequent development of gestational hypertension in later pregnancy. Another secondary outcome was LSCS which was found more significantly associated with hypertensive patients.

Strengths and weaknesses of study.

The major strength of this trial was 100% short term follow up rate. This high follow up was related to the fact that despite being a private hospital our hospital offers all services free of cost. The trial population was homogenous as all high risk medical conditions that could be source of bias were excluded.

Some limitations of study may apply. We had a small sample size but a strong correlation was found between elevated serum beta hcg and hypertensive cases. Hence large observational studies will be of value in this field to get a broader picture of this correlation.

In present study, except for abruptio placentae in one case, in none of the cases any significant complication apart from PIH could be diagnosed and hence the predictive efficacy of this marker for different complications could not be gauged. Thus further studies for predictive value of this marker for other complications need to be done. Another limitation of current study is women were not followed post partum which may have led to diagnosis of more hypertensive cases.

Interpretation

In order to apply results to other populations and settings several factors have to be considered. Overall the study population was young in age group 20-25 years (54.6%) and were primiparous (50.7%). Subjects were healthy women with no medical condition or high risk factors.

Comparing the parity of patients with gestational hypertension our study found primiparity to be significantly associated with gestational hypertension. Incidence of pre eclampsia in multi parous women has been found to be lower then primiparous women (11) but higher if pregnancy occurs with a new partner (12) highlighting the role of not only nulliparity but primipaternity in the origin of disease.

We found increased beta hcg to be significantly associated with gestational hypertension. Malick et al (13) in a similar prospective study of 100patients found second trimester beta hcg and dyslipidaemia to

be significantly associated with pre-eclampsia. Wright et al(14) measured serum beta hcg and PAAP A in 94,989 patients in all three trimesters and found positive correlation between first and second trimester beta hcg and development of gestational hyprertension. Kumar et al(15) found patient BMI, mean arterial pressure, PAPP-A and pulstality index to be effective predictors of hypertension during pregnancy. In a study in Tunisia (16) beta hcg was found to be highly predictive for adverse pregnancy outcome. Paredes et al(17) also found correlation of higher beta hcg with near term severe pre eclampsia. Kiekella et al(6) concluded beta hcg if used along with PAPP A as a marker of early onset pre eclampsia will have high detection rates.

In contrast Spencer demonstrated serum beta hcg in patients who subsequently developed pre eclampsia was reduced or similar to uncomplicated pregnancies(18). Also Dugoff (19) found evidence of association between low serum beta hcg and development of pre eclampsia. This difference could be attributed to the difference in subject profiles and sample size.Our study also found LSCS rates are more in hypertensive patients. This could be correlated to the fact that hypertensive patients are subjected to more close patient monitoring and surgery decided at earliest evidence of distress.Our results suggest that measuring serum β hcg levels in second trimester of pregnancy could be made a part of routine tests done for antenatal women. Being a primary preventive measure it would play a major role in decreasing maternal morbidity and mortality due to pre eclampsia.

CONCLUSION

The present study showed that β hCG has a high predictive efficacy in detection of PIH. The predictive value of the marker could be gauged from the fact that even in a small sample size, the predictive value was nearly 90% for the marker. Thus β hCG could have an important role in early recognition of a pregnancy-related complication and provide the obstetrician ample opportunity to guide the management of parturient during pregnancy and to make appropriate arrangements for any consequential emergency.

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None

Conflicts of Interest

The authors declare that there is no conflict of interest related to this manuscript.

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