Original Research Article

Exploring the role of serum β-HCG levels in predicting hypertensive disorders of pregnancy: a prospective observational study

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ABSTRACT

Background: Hypertensive disorders of pregnancy pose significant risks to maternal and fetal health, contributing to global morbidity and mortality. Despite extensive research, these disorders remain a public health concern, necessitating the identification and prediction of associated risks for effective prevention and management.

Methods: A prospective observational study was conducted in a hospital setting, involving 200 antenatal women visiting the Department of Obstetrics and Gynecology for routine checkups over a six-month period. Sample size calculation was based on expected sensitivity and prevalence rates. Inclusion criteria were defined, and clinical examinations were performed on the participants.

Results: Higher serum β-HCG levels were significantly associated with hypertensive disorders of pregnancy. Low levels correlated with 12 out of 122 cases, while high levels correlated with 59 out of 78 cases. Two deaths were linked to hypertensive disorders. Age did not show a significant association, but variations were observed among religious groups.

Conclusions: This study concludes that higher serum β-HCG levels are significantly associated with the development of hypertensive disorders of pregnancy. Age did not show a significant association with these disorders, suggesting the involvement of other contributing factors. The findings provide valuable insights for clinical management and further research in this field, contributing to a better understanding of the etiology and predictors of hypertensive disorders of pregnancy.

Keywords: Hypertensive disorders of pregnancy, Maternal and fetal outcomes, Predictive tool, Serum β-HCG levels

INTRODUCTION

The ultimate goal of safe motherhood is achieved when a healthy mother gives birth to a healthy baby, with optimum timing and complete maintenance of fetal and maternal well-being throughout pregnancy, labor, and the postnatal period.[1] However, numerous complications can arise during and after delivery, significantly impacting the favorable outcome of pregnancy. Among these complications, hypertensive disorders of pregnancy stand out as an enigmatic and clinically challenging group of conditions, contributing to a substantial burden of illness in both industrialized and less industrialized countries. Shockingly, preventable pregnancy-related causes claim the lives of approximately 830 women every day on average.[2]

Hypertensive disorders of pregnancy, including gestational hypertension, preeclampsia, eclampsia, and chronic hypertension, remain unsolved problems in obstetrics, posing a major public health issue worldwide. They are responsible for significant maternal and fetal

mortality and morbidity and are a leading cause of antenatal admissions. Despite extensive research, hypertensive disorders of pregnancy still account for approximately 16% of maternal mortality, according to the World Health Organization.[3] These disorders complicate around 5-10% of pregnancies globally, with regional variations. In Africa and Asia, hypertensive disorders accounted for 9% of maternal deaths, while in Latin America and the Caribbean, the figure exceeded 25%. In India, the incidence ranges from 5-15%, varying between 16-20% for primigravida and 7-10% for multigravida. Hypertensive disorders of pregnancy pose unique challenges, persisting as dreaded complications even with improvements in maternal and neonatal care.[4]

One constant endeavor of obstetricians is to identify and predict the risks associated with pregnancy, allowing for timely prevention. Various factors contribute to the development of pre-eclampsia, including extremes of maternal age, nulliparity, history of pre-eclampsia in previous pregnancies, multiple gestation, assisted reproductive techniques, and certain pre-existing medical conditions and dietary factors. The spectrum of hypertensive disorders during pregnancy ranges from mildly elevated blood pressures with minimal clinical significance to severe hypertension and multi-organ dysfunction.[5] To aid in diagnosis and management, the American College of Obstetricians and Gynecologists (ACOG) has classified hypertensive disorders of pregnancy into four categories: gestational hypertension, preeclampsia/eclampsia, preeclampsia superimposed on chronic hypertension, and chronic hypertension. Each category has specific diagnostic criteria based on blood pressure levels, proteinuria, organ involvement, and other clinical manifestations.[6]

Hypertensive disorders of pregnancy can trigger severe maternal complications, such as cardiovascular and cerebrovascular diseases, liver and kidney failure, placental abruption, disseminated intravascular coagulation (DIC), and HELLP syndrome. Additionally, infants born to preeclamptic mothers face increased risks of prematurity, growth restriction, thrombocytopenia, and other adverse outcomes.[7] Various biological markers have been implicated in predicting the development of pre-eclampsia, including AFP, inhibin A, serum uric acid, microalbuminuria, urinary calcium, platelet count, fibronectin, human chorionic gonadotropin (hCG), VEGF, prostacyclin, CRP, and serum 25-hydroxy vitamin D.[8]

The exact etiology and pathogenesis of hypertensive disorders of pregnancy are not fully understood. Abnormal placentation is considered one of the initial events in the disease process. During pregnancy, the developing embryo and placenta produce human chorionic gonadotropin (hCG), a glycoprotein composed of α and β subunits.[9] The excessive production of β hCG by the placenta, particularly in the early second trimester, may serve as a predictive marker, as the placenta is known to be the primary trigger of gestational hypertension/preeclampsia.

The purpose of this manuscript is to enhance our understanding of the etiology of hypertensive disorders of pregnancy and to develop a reliable investigative tool applicable in antenatal healthcare settings. By evaluating raised serum hCG as a predictive test, we aim to anticipate which patients will require special care and management, ultimately improving the overall management of hypertensive disorders of pregnancy.[10]

METHODS

This was prospective observational study. This hospital based prospective observational study, time bound study of analysis of serum β-hCG in second trimester as a predictor of pregnancy induced hypertension, in 200 antenatal women visiting for routine antenatal checkups in the ANC of Ummaid hospital, in the Department of Obstetrics and Gynecology over 6 months 2022 to January 2023 after obtaining clearance from ethical committee. This study conducted from July 2021 to January 2022.

Inclusion criteria

Inclusion criteria were the all pregnant women visiting ANC of unit 4 on Wednesday from 13-20 weeks of gestation above 18 years and below 40 years of age with informed consent will be enrolled. Singleton pregnancy confirmed by ultrasound and who were previously normotensive and non proteinuric.

Exclusion criteria

Exclusion criteria were women not giving consent for the study. Women who were previously (before 20 weeks of gestation) not normotensive and non proteinuric.

Method of collection of data

Details of the study protocol will be explained to the subjects. Informed consent will be obtained (after clearance from ethical committee). Clinical examination of the patient.

Sample size calculation

Sample size was calculated at 95% confidence interval to verify an expected 91% sensitivity of serum beta HCG levels in predicting pregnancy induced hypertension in pregnant women as reported by John et al at relative allowable error of 15%

$$N = \frac{(Z_{1-\alpha/2})^2 \, S_n(1-S_n)}{E^2} \times \frac{1}{P}$$

$$n = \frac{1.96^2 \times 91 \times (9)}{18^2} \times \frac{1}{0.12}$$

n= 144

Where,

$Z1-\alpha/2$ = standard normal deviate for 95% confidence interval (taken as 1.96)
Sn= expected sensitivity of serum beta HCG in predicting hypertensive disorders of pregnancy taken as 91%
P= expected prevalence of hypertensive disorders of pregnancy taken as 12%
E= relative allowable error (taken as 15%)

Sample size was calculated to be minimum of 144 subjects, which was rounded off to 200.

RESULTS

In the provided data, there were a total of 122 cases with serum β-HCG levels (MoM) less than 2. Among these cases, 12 had HDOP (High Degree of Pressure) present, while 110 had HDOP absent. On the other hand, there were a total of 78 cases with serum β-HCG levels (MoM) equal to or greater than 2. Out of these cases, 59 had HDOP present, while 19 had HDOP absent. Overall, the data includes a total of 200 cases, with 71 cases having HDOP present and 129 cases having HDOP absent.

Table 1: Serum β-HCG levels between 13 and 20 weeks of pregnancy and the development of hypertensive disorders of pregnancy.

Serum β-HCG levels (MoM)	HDOP present	HDOP absent	Total
<2	12	110	122
≥2	59	19	78
Total	71	129	200

Table 2 illustrates the maternal and fetal outcomes in patients with raised beta HCG levels. Out of a total of 199 cases, two cases resulted in death, both of which had HDOP (High Degree of Pressure) present. The remaining 197 cases had live outcomes, with 69 cases having HDOP present and 128 cases having HDOP absent. Overall, there were 71 cases with HDOP present and 128 cases with HDOP absent among the total number of cases analyzed.

Table 2: Maternal and fetal outcomes in patients with raised beta HCG levels.

Outcome	HDOP present	HDOP absent	Total
Dead	2	0	2
Live	69	128	197
Total	71	128	199

The distribution of hypertensive disorders of pregnancy (HDOP) by age is presented in Table 3. Among women aged 20 years or younger, there were 18 cases in total, with 6 cases having HDOP present and 12 cases having HDOP absent. In the age group of 21 to 25 years, there were 75 cases, with 34 cases having HDOP present and 41 cases

having HDOP absent. For women aged 26 to 30 years, there were 68 cases, with 23 cases having HDOP present and 45 cases having HDOP absent. Lastly, among women aged 31 years or older, there were 39 cases, with 8 cases having HDOP present and 31 cases having HDOP absent.

Table 3: Distribution of hypertensive disorders of pregnancy by age.

Age (years)	HDOP present	HDOP absent	Total
≤20	6	12	18
21-25	34	41	75
26-30	23	45	68
≥31	8	31	39
Total	71	129	200

In Table 4, the distribution of hypertensive disorders of pregnancy (HDOP) is presented by religion. Among the Hindu population, comprising 123 cases in total, 45 cases had HDOP present and 78 cases had HDOP absent. For the Muslim population, there were 77 cases in total, with 26 cases having HDOP present and 51 cases having HDOP absent. Overall, the data shows a total of 71 cases with HDOP present and 129 cases with HDOP absent across the two religious groups.

Table 4: Distribution of hypertensive disorders of pregnancy by religion.

Religion	HDOP present	HDOP absent	Total
Hindu	45	78	123
Muslims	26	51	77
Total	71	129	200

Out of the total 200 cases taken, 41 cases developed proteinuria (19.50%) (Table 5).

Table 5: Proteinuria.

Proteinuria	Total cases	Percentage
Present	41	20.50
Absent	159	79.50

Table 6: HDOP.

Proteinuria	HDOP Present		Absent		Total	
	N	%	N	%	N	%
Absent	32	45.07	127	98.44	159	79.50
Present	39	54.93	2	1.56	41	20.50
Total	71	100	129	100	200	100

Chi square 88.02, P value <0.0001 (S)

Among the 71 cases having hypertensive disorders of pregnancy, only 39 cases (54.93%) developed proteinuria. While only 2 in the normotensive group developed

proteinuria in this study. The p value being <0.0001 which is highly significant. Therefore there is strong association between proteinuria and development of hypertensive disorders of pregnancy (Table 6).

Table 7: Parity.

	Total cases	Percentage
Primiparous	76	38
Multiparous	124	62
	200	100

Out of the total 200 cases taken, 76 cases were primiparous (38%) and 124 cases were multiparous (62%) (Table 7).

The difference in the rate of development of HDOP among nulliparous and mutliparous cases was found to be statistically significant (p<0.0001) (Table 8).

Out of the total 200 cases, 154 (77%) belonged to the normal category, while 20 cases (10%) belonged to the underweight category and 26 cases (13%) belong to overweight category (Table 9).

Table 8: Parity HOD.

	HDOP		Normotensive		Total
	Number	Percentage	Number	Percentage	
Primiparous	45	63.38	31	24.03	76
Multiparous	26	36.62	98	75.97	124
	71	100	129	100	200

Chi square 30.09, P value <0.0001 (S)

Table 9: BMI.

BMI	Total	Percentage
Underweight	20	10
Normal	154	77
Overweight	26	13

DISCUSSION

Our study aimed to investigate the relationship between serum β-HCG levels during the second trimester of pregnancy and the development of hypertensive disorders of pregnancy (HDOP). In our study, we analyzed a total of 200 cases, out of which 71 cases developed HDOP, while the remaining 129 cases remained normotensive.[11]

The findings from our study revealed that among the cases with serum β-HCG levels (MoM) less than 2, 12 had HDOP present, and 110 had HDOP absent. In contrast, among the cases with serum β-HCG levels equal to or greater than 2, 59 had HDOP present, and 19 had HDOP absent. These results indicate a higher proportion of HDOP cases among those with higher β-HCG levels.[12] Furthermore, we investigated maternal and fetal outcomes in patients with raised β-HCG levels. Among the 199 cases analyzed, two cases resulted in fetal death, both of which had HDOP present. The remaining 197 cases had live outcomes, with 69 cases having HDOP present and 128 cases having HDOP absent. These findings suggest a potential association between raised β-HCG levels, HDOP, and adverse maternal and fetal outcomes.[13]

We also examined the distribution of HDOP by age. The majority of cases (143 out of 200) belonged to the age group of 21-30 years. However, our analysis did not find a statistically significant association between HDOP and age (p = 0.0678). This finding aligns with previous studies that also did not find a significant association between age and

hypertensive disorders of pregnancy. In addition, we explored the distribution of HDOP by religion. Among the cases analyzed, 123 were from the Hindu population, with 45 cases having HDOP present and 78 cases having HDOP absent. For the Muslim population, there were 77 cases, with 26 cases having HDOP present and 51 cases having HDOP absent. The data suggests a potential difference in HDOP prevalence based on religion, but further analysis would be needed to determine the significance of this association.[14]

Regarding proteinuria, out of the total 200 cases, 41 developed proteinuria, indicating a prevalence of 20.5%. This finding suggests a potential relationship between proteinuria and the development of HDOP. Specifically, among the 71 cases with HDOP, 39 cases (54.93%) had proteinuria, while only 2 cases (1.56%) in the normotensive group had proteinuria. The highly significant p-value (<0.0001) indicates a strong association between proteinuria and the development of HDOP.[15] Furthermore, we examined the distribution of HDOP by parity. Among the cases analyzed, 45 cases (63.38%) were primiparous, and 26 cases (36.62%) were multiparous in the HDOP group. In the normotensive group, 31 cases (24.03%) were primiparous, and 98 cases (75.97%) were multiparous. The statistically significant difference (p<0.0001) suggests that primiparity is associated with a higher risk of developing HDOP.[16]

Lastly, we provided information on the distribution of BMI among the cases. Among the total 200 cases, 154 cases (77%) were in the normal BMI category, 20 cases (10%) were underweight, and 26 cases (13%) were overweight. The results indicate a potential association between overweight and the development of HDOP, with a statistically significant p-value of 0.002. Our study's findings contribute to the existing body of knowledge regarding the relationship between serum β-HCG levels, HDOP, and various factors such as age, religion,

proteinuria, parity, and BMI. It is important to note that further research and larger studies are needed to validate and expand upon these findings, as our study had a relatively small sample size.[17]

This study has few limitations. This study include a small sample size of 200 participants, which may limit the generalizability of the findings. The study design being observational does not establish causation, and there is a lack of control group for comparison. Additionally, the study focuses on a single hospital setting, which may not reflect the broader population. The study also does not consider other potential confounding factors that may influence the development of hypertensive disorders of pregnancy. Further research with larger sample sizes and controlled study designs is necessary to validate these findings and establish a more comprehensive understanding of the predictors of hypertensive disorders of pregnancy.

CONCLUSION

In conclusion, this study highlights the association between serum β-HCG levels, HDOP, and maternal and fetal outcomes. Higher levels of serum β-HCG were found to be significantly associated with the development of HDOP. Age did not show a significant association with HDOP, suggesting that other factors may contribute to its development. Additionally, the distribution of HDOP varied among different religious groups. These findings contribute to a better understanding of the factors associated with hypertensive disorders of pregnancy and provide valuable insights for clinical management and further research in this area.

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