DOI: 10.7860/JCDR/2023/63954.18140

Original Article

Obstetrics and Gynaecology Section

Efficacy of Mid-Second-Trimester Serum β-HCG Levels as a Predictor of Hypertensive Disorders of Pregnancy: A Longitudinal Cohort Study

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ABSTRACT

Introduction: Hypertensive Disorders of Pregnancy (HDP) affect up to 10% of pregnancies worldwide, despite improvements in maternal and neonatal care. HDP and its sequelae are a dreaded complication of pregnancy. If prediction becomes possible, prevention will follow naturally.

Aim: To study the efficacy of mid-second trimester serum β-hCG levels in the prediction of HDP.

Materials and Methods: This was a longitudinal cohort study conducted in the Department of Obstetrics and Gynaecology at Shri BM Patil Medical College Hospital and Research Centre, Vijayapura, Karnataka, India, between December 2020 and June 2022. All women with gestational age between 16-20 weeks were screened, and 163 pregnant women were enrolled in the study. Serum β-hCG levels were measured at enrollment, and values were followed-up until delivery. The development of HDP was evaluated using statistical analysis, including Chi-square, Independent t-test, Receiver Operating Curve/Area under the ROC Curve (ROC/AUC), sensitivity, and specificity. A p-value of <0.05 was considered significant.

Results: Of the 163 pregnant women enrolled, 49 (30.1%) developed HDP, while 114 (69.9%) remained normotensive. The mean age of the study population was 24±4 years. The mean serum β-hCG level in the normotensive group was 55666 mIU/mL, while in the HDP group, it was 100124 mIU/mL, with a statistically significant p-value of 0.001. A cut-off value of 77817 mIU/mL showed 83.7% sensitivity and 92.1% specificity.

Conclusion: This study suggests that serum β-hCG levels between 16-20 weeks can be used as a non-invasive predictor of HDP. It is a good predictor of HDP and could potentially improve prevention strategies.

Keywords: Hypertensive, Normotensive, Pregnancy, Sensitivity

INTRODUCTION

The health of the mother and the unborn child must be given the highest consideration during pregnancy. Unfavourable situations might endanger both the mother and the unborn child's lives. Gestational diabetes, obesity, and pregnancy-induced hypertension are just a few of the illnesses and side effects related to pregnancy [1-4].

According to National Health Portal, approximately 10% of pregnant women worldwide experience HDP, 3-5% of pregnancies is affected by preeclampsia [5]. In addition to preeclampsia, gestational hypertension, eclampsia, and chronic hypertension are all illnesses that fall under the category of HDP. Nearly 10% of all maternal fatalities in Asia and Africa are linked to hypertensive disorders during pregnancy [5]. Pregnancy-related hypertensive diseases are among the world's top causes of maternal and perinatal death. Preeclampsia is a condition that affects pregnant women and is characterised by newly developed hypertension. It often develops after 20 weeks of pregnancy and commonly close to term [6].

According to American College of Obstetricians and Gynaecologists (ACOG) [7], after 20 weeks of pregnancy, a woman with previously normal blood pressure is said to have gestational hypertension if her systolic blood pressure is 140 mmHg or higher, her diastolic blood pressure is 90 mmHg or higher, or both [6]. The prevalence of many infections and disorders has significantly decreased due to recent improvements in maternal and newborn health, but HDP is still a deadly condition in many areas of the world [8,9]. A few testing options like uterine artery doppler Mean Arterial Pressure (MAP), Placental Growth Factor (PlGF), maternal serum Pregnancy-Associated Plasma Protein-A (PAPP-A) at 11-13 weeks of gestation have been provided for the prediction of Pregnancy-Induced Hypertension (PIH) based on maternal characteristics, medical history, since these tests can identify a high proportion of pregnancies which are at high-risk for early onset PIH [10]. Unfortunately, a lot of these tests have a poor predictive value and don't seem to be very important in the early detection of HDP [10]. Drawbacks of the above-mentioned tests include improper family history, unable to produce the data on the measurements of blood pressure, unable to record repeated measurements, false negative results [10]. According to studies, immunological variations in trophoblasts during pregnancy might cause secretory responses, which further increase β-hCG levels [11,12]. The present study is the only study from the south zonal area of Karnataka. Hence, ethnic group, race, and religion variations also affect hormones and genetics. The aim was to study the efficacy of mid-second trimester serum β-hCG levels in the prediction of HDP.

MATERIALS AND METHODS

This was a longitudinal cohort study was carried out in the Department of Obstetrics and Gynaecology at Shri B M Patil Medical College Hospital and Research Centre, Vijayapura, Karnataka, India, from December 2020 to June 2022 with approval from the Institutional Ethics Commitee (IEC/No-09/2021). All women with gestational age between 16-20 weeks were screened and 163 pregnant women were taken consecutively and were enrolled in the study after taking informed consent, considering the inclusion and exclusion criteria. Serum β-hCG level was measured at the time of enrolment. Routine antenatal investigations were done. Estimation of serum β-hCG level was done by enzyme-linked fluorescence immunoassay. Laboratory values were noted. These were followed-up until delivery. Woman were evaluated for the development of HDP.

Inclusion criteria: Primigravidae/multigravida with a singleton pregnancy with a gestational age of 16 to 20 weeks as determined by the last menstrual period or by ultrasonography who were previously normotensive were included.

Exclusion criteria: Patients with gestational age of <16 weeks or >20 weeks, chronic hypertension, diabetes mellitus, multifoetal pregnancies,

antenatal women with congenital anomalies/Down's syndrome and gestational trophoblastic diseases in a current or previous pregnancy and those who were not willing to participate were excluded.

Women were interviewed to obtain a detailed medical history, and systemic examination including blood pressure measurement was performed in a sitting position. The gestational age was determined using the last menstrual cycle history and dating scan. Venous blood was collected to estimate the serum β-hCG level. Routine antenatal investigations were conducted, and patients were followed-up in the antenatal clinic every fourth week until 28 weeks, fortnightly until 34 weeks, and after that weekly thereafter until delivery. Blood pressure was recorded at every visit, and patients who developed hypertension were monitored more frequently depending on severity and tested for proteinuria. Liver Function Tests (LFT) and Renal Function Tests (RFT) were performed, and patients were admitted as required.

STATISTICAL ANALYSIS

Data were entered in MS-Excel 2007 and analysed using IBM Statistical Package for the Social Sciences (SPSS) software trial version 22.0. Continuous data were expressed as mean and standard deviation. Appropriate statistical tests were applied (Chi-square, t-test, ROC/AUC, sensitivity, and specificity), and p-values less than 0.05 were considered significant.

RESULTS

Most of the participants in the current study were between the ages of 21 and 25 years comprising about 52.8% (mean age of 24 years) [Table/Fig-1].

Age categories (years)	N	N %
18 to 20	25	15.3%
21 to 25	86	52.8%
26 to 30	41	25.2%
31 to 35	10	6.1%
36 and above	1	0.6%
Total	163	100.0%
Mean age in years	24±4	

[Table/Fig-1]: Distribution of cases according to age.

Out of 163 women, 114 (69.9%) were multigravida and 49 (30.1%) were primigravida. Among primigravida 17 (34.7%) developed HDP, whereas only 32 (28.1%) in multigravida [Table/Fig-2]. The mean BMI of the study population was 23.7±2.6 [Table/Fig-3] [13]. The mean values of serum β-hCG at 16-20 weeks were significantly higher in patients who developed HDP [Table/Fig-4]. Based on the ROC curve, the best cut-off value of serum β-hCG at 16-20 weeks for prediction of development of HDP was 77,817 IU/mL with AUC as 0.924, sensitivity and specificity being 83.7% and 92.1% [Table/Fig-5,6].

	HDP			
	Not present		Present	
Parity	N	%	N	%
Multigravida	82	71.9%	32	28.1%
Primigravida	32	65.3%	17	34.7%
Total	114	69.9%	49	30.1%

[Table/Fig-2]: Cases according to parity and development of HDP.
Chi-square value 0.7 p-value=0.3

BMI [13]		N	N %
Non obese	Normal	73	44.80%
	Overweight	43	26.40%
Obese		47	28.80%
Total		163	100.00%
Mean		23.7±2.6	

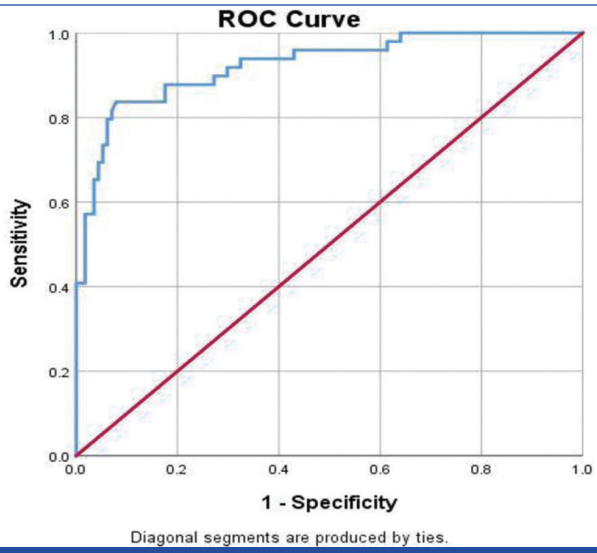
[Table/Fig-3]: Body mass index [13].

β-hCG		N	Mean	SD	SEM	t-value	p-value
HDP	Not present	114	55666.54	19034.302	1782.726	-11.6	0.001
	Present	49	100124.98	28760.994	4108.713		

[Table/Fig-4]: Pregnancy induced hypertension vs β-hCG.
Independent t-test was applied, a p-value <0.05 considered significant

Variable	AUC	95% Confidence Interval (CI)	Cut-off	Sensitivity	Specificity
β-hCG	0.924	0.878 to 0.970	>77817	83.7	92.1

[Table/Fig-5]: Receiver operating characteristic curve in detecting HDP with β-hCG levels.



[Table/Fig-6]: ROC curve.

DISCUSSION

The World Health Organisation (WHO) estimates that preeclampsia affects anywhere between 2% and 10% of pregnancies globally. While the rate is 0.4% in developed countries, about 1.8-16.7% of incidences are documented in developing countries [6]. Although the indications and symptoms of this ailment are widely understood, the aetiology is still a mystery, making disease prevention impossible [6].

In the present study, the majority of the participants were between the ages of 21 and 25 comprising about 52.8% (mean age of 24 years). Murmu S and Dwivedi J, also showed that about 54.34% of the research population were between the ages of 20 and 25 years [14]. According to the latest statistics, the majority of Indian women have a mean age of getting pregnant between 21 and 25 years, which supports the present study [15].

In the present study, most of the study population belonged to multigravida (69.9%). Among primigravida, 34.7% had PIH, whereas only 28.1% in Multigravida. According to studies by Hernández-Daz S et al., preeclampsia in one pregnancy is a reliable predictor of recurrence in subsequent pregnancies but a poor predictor of succeeding pregnancies [16].

Vidyabati RK et al., conducted a study in which 29 cases, out of 135 cases developed PE who had significant raise in β-hCG [17]. The present study is in accordance with this study. Despite associations with Preterm Delivery (PTD) for preeclampsia with MShCG 3.0 MoM or greater {Odds Ratio (OR) 5.9, Confidence Interval (CI) 1.5-23.2} and PTD for foetal indications with MShCG 4.0 MoM or greater (OR 45.5, CI 4.1-509), a different study by Towner D et al., on 309 women found no overall increase in adverse outcomes [18]. With MShCG 3.0-3.9 Multiple of the Median (MoM) (OR 2.5, CI 1.0-5.8), there was an increase in Large of Gestational Age (LGA) children, and a poor pregnancy outcome was linked. Therefore, a rise in this number has a negative impact on pregnancy, and this study, therefore, lends credence to the current study.

Another study, conducted by Taché V et al., noticed that severe preeclampsia was related with elevated levels of human gonadotropin (hCG), Alpha Feto-Protein (AFP), inhibin (INH) {Multiple of the Median (MoM) more than or equal to 95th percentile}, and reduced levels of estriol (uE3) (MoM less than 5th percentile) and early-onset severe preeclampsia was more accurately predicted by these biomarkers [19]. Therefore, this study and ours was comparable. hCG levels were considerably higher in women who later had preeclampsia, according to a study done by Davidson EJ et al., [20].

In the current study, the non PIH group included most people with non obesity, whereas half of the PIH category had obesity. According to Walsh SW study, obese women may have a higher chance of having preeclampsia when they get pregnant and are subject to the additional stresses of pregnancy if their vasculature is inflamed [21].

In the present study, β-hCG cut-off value of 77817 showed 83.7% of sensitivity and 92.1% of specificity. Revankar VM and Narmada L, showed almost similar sensitivity and specificity at a cut-off value at >71142 mIU/mL [22]. Murmu S and Dwivedi J, showed almost lesser sensitivity but almost equal specificity at a lesser cut-off value at >67750 mIU/mL [14].

Limitation(s)

1. Small sample size: The small sample size for this study makes it necessary to conduct additional, extensive research when considering the significance of hCG in HDP prediction.
2. Element of bias: Subjective bias, machinery errors in measuring β-hCG levels.
3. The fact that the study was limited to a particular location (single center) may have caused some statistical bias.
4. The present study was not able to find an association between BMI and PIH as the study population was less.
5. Lipid profile and β-hCG should be done for better foeto-maternal outcomes.

CONCLUSION(S)

Raised second-trimester serum β-hCG can be considered a predictor of PIH. It is a potentially cost-effective technique for identifying women at risk for preeclampsia. A screening scheme like this would enable closer monitoring and can provide early intervention.

REFERENCES

[1] Mammaro A, Carrara S, Cavaliere A, Ermito S, Dinatale A, Pappalardo EM, et al. Hypertensive disorders of pregnancy. J Prenat Med. 2019;3(1):01-05.
[2] Magee LA, Pels A, Helewa M, Rey E, von Dadelszen P, Canadian hypertensive disorders of pregnancy working group. Diagnosis, evaluation, and management of the hypertensive disorders of pregnancy: Executive summary. J Obstet Gynaecol Can. 2014;36(5):416-41.
[3] Von Dadelszen P, Magee LA. Preventing deaths due to the hypertensive disorders of pregnancy. Clin Obstet Gynaecol. 2016;36:83-102.
[4] Sober S, Reiman M, Kika T, Rul lK, Inno R, Vaas P, et al. Extensive shift in placental transcriptase profile in preeclampsia and placental origin of adverse pregnancy outcomes. Sci Rep. 2015;5:13336.
[5] Preeclampsia [Internet]. Gov.in. [cited 2022 Oct 25]. Available from: https://www.nhp.gov.in/disease/gynaecology-and-obstetrics/preeclampsia.
[6] Khan B, Yar RA, Khakwani AK, Karim S, Ali HA. Preeclampsia incidence and its maternal and neonatal outcomes with associated risk factors. Cureus. 2022;14(11):e31143.
[7] Report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy. Am J Obstet Gynecol 2000;183:S1-22.
[8] Poon LC, Nicolaides KH. Early prediction of preeclampsia. Obstet Gynecol Int. 2014;2014:297397.
[9] Soundararajan P, Muthuramu P, Veerapandi M, Mariyappan R. Serum beta human chorionic gonadotropin and lipid profile in early second trimester (14-20 weeks) is a predictor of pregnancy-induced hypertension. Int J Reprod Contracept Obstet Gynecol. 2016;5(9):3011-16.
[10] Begum Z, Ara I, Tanira S, Keya KA. The association between serum betahuman chorionic gonadotropin and preeclampsia. J Dhaka Med Coll. 2014;23(1):89-93.
[11] Chowdhary H, Khurshid R, Parveen S, Yousuf S, Tali SH, Shah ZA. Utility of second trimester beta HCG levels in prediction of gestational hypertension: A prospective cohort study. Int J Reprod Contracept Obstet Gynecol. 2017;6:1040-44.
[12] Martin JN Jr, Thigpen BD, Moore RC, Rose CH, Cushman J, May W. Stroke and severepre eclampsia and eclampsia: A paradigm shift focusing on systolic blood pressure. Obstet Gynecol. 2005;105:246-54.
[13] Lim JU, Lee JH, Kim JS, Hwang YI, Kim TH, Lim SY, et al. Comparison of World Health Organization and Asia-Pacific body mass index classifications in COPD patients. Int J Chron Obstruct Pulmon Dis. 2017;12:2465-75. Published 2017 Aug 21. Doi: 10.2147/COPD.S141295.
[14] Murmu S, Dwivedi J. Second-trimester maternal serum beta-human chorionic gonadotropin and lipid profile as a predictor of gestational hypertension, preeclampsia, and eclampsia: A prospective observational study. Int J App Basic Med Res. 2020;10:49-53.
[15] Ashour AMN, Lieberman ES, Haug LEW, Repke JT. The value of elevated second-trimester β-human chorionic gonadotropin in predicting development of preeclampsia. Am J Obstet Gynecol [Internet]. 1997;176(2):438-42. Available from: http://dx.doi.org/10.1016/s0002-9378(97)70512-x.
[16] Hernández-Díaz S, Toh S, Cnattingius S. Risk of pre-eclampsia in first and subsequent pregnancies: Prospective cohort study. BMJ [Internet]. 2009;338(Jun 18 1):b2255. Available from: http://dx.doi.org/10.1136/bmj.b2255.
[17] Vidyabati RK, Hijam D, Singh NK, Singh WG. Serum beta hCG and lipid profile in early second trimester as predictors of pregnancy induced hypertension. J Obstet Gynecol India. 2014;60:44-50.
[18] Towner D, Gandhi S, El Kady D. Obstetric outcomes in women with elevated maternal serum human chorionic gonadotropin. Am J Obstet Gynecol. 2006;194:1676-81.
[19] Taché V, Baer RJ, Currier RJ, Li CS, Towner D, Waetjen LE, et al. Population-based biomarker screening and the development of severe preeclampsia in california. Am J Obstet Gynecol. 2014;211:377e1-8.
[20] Davidson EJ, Riley SC, Roberts SA, Shearing CH, Groome NP, Martin CW. Maternal serum activin, inhibin, human chorionic gonadotrophin and alpha-fetoprotein as second trimester predictors of preeclampsia. BJOG. 2003;110:46-52.
[21] Walsh SW. Obesity: A risk factor for preeclampsia. Trends Endocrinol Metab [Internet]. 2007;18(10):365-70. Available from: http://dx.doi.org/10.1016/j.tem.2007.09.003.
[22] Revankar VM, Narmada L. Assessment of serum β-hCG and lipid profile in early second trimester as predictors of hypertensive disorders of pregnancy. Int J Gynaecol Obstet [Internet]. 2017;138(3):331-34. Available from: http://dx.doi.org/10.1002/ijgo.12225.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Mar 15, 2023
- Manual Googling: May 16, 2023
- iThenticate Software: Jun 06, 2023 (10%)

ETYMOLOGY: Author Origin

EMENDATIONS: 8

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Mar 08, 2023**
Date of Peer Review: **Apr 28, 2023**
Date of Acceptance: **Jun 10, 2023**
Date of Publishing: **Jul 01, 2023**