EARLY PREDICTION OF GESTATIONAL HYPERTENSION USING B-HCG LEVELS: A CROSS-SECTIONAL STUDY IN A TERTIARY HOSPITAL DHAKA, BANGLADESH

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KEYWORDS

Gestational hypertension, β-HCG, pregnancy complications, biomarker, maternal health

ABSTRACT:

Background: Gestational hypertension (GH) is a common pregnancy complication that poses significant risks to maternal and fetal health. Early detection is crucial for effective management and improved outcomes. Beta-human chorionic gonadotropin (β-HCG) has been investigated as a potential biomarker for predicting GH, yet its clinical utility remains underexplored. **Aim of the study:** This study aims to assess the association between β-HCG levels and the early detection of gestational hypertension in pregnant women in a tertiary hospital in Dhaka, Bangladesh. **Methods:** A cross-sectional observational study was conducted on 110 pregnant women between 14 and 19 weeks of gestation. Serum β-HCG levels were measured using a chemiluminescence-based assay, and blood pressure was monitored throughout pregnancy. Participants were classified into hypertensive and normotensive groups, and statistical analysis was performed to determine the correlation between β-HCG levels and GH. **Result:** The study found a significant association between elevated β-HCG levels and gestational hypertension ($p < 0.001$). Women with β-HCG levels above 80,000 mIU/ml had a higher likelihood of developing GH, with severe hypertension occurring in 75% of cases in this group. No cases of GH were observed among participants with β- HCG levels below 30,000 mIU/ml. The findings suggest a dose-dependent relationship between β-HCG levels and GH severity. **Conclusion:** Elevated β- HCG levels in the second trimester may serve as a useful biomarker for predicting gestational hypertension. These findings support the potential for β-HCG screening as a non-invasive tool for early GH detection, enabling timely interventions and better pregnancy outcomes.

INTRODUCTION

Gestational hypertension (GH), a common pregnancy complication characterized by elevated blood pressure after the 20th week of gestation, presents significant risks to both maternal and fetal health [1]. It is a precursor to more severe hypertensive disorders such as preeclampsia and eclampsia, which are major contributors to maternal and neonatal morbidity and mortality worldwide [2]. Hypertensive disorders are responsible for approximately 14% of global maternal deaths, with nearly 95% of these

fatalities occurring in low- and middle-income countries [2]. In Bangladesh, the situation is critical, as studies have indicated that hypertensive disorders are a leading cause of maternal mortality, accounting for a significant proportion of maternal deaths [3]. Early detection and intervention are essential to mitigate these risks, and thus, identifying reliable biomarkers for the early prediction of gestational hypertension (GH) could improve clinical outcomes [4]. β-human chorionic gonadotropin (β-hCG), a glycoprotein hormone primarily secreted by the syncytiotrophoblast cells of placenta, has been identified as a potential early biomarker for various pregnancy complications, including hypertensive disorders [5]. During early pregnancy, β-hCG supports the corpus luteum and promotes the production of progesterone, essential for maintaining the uterine lining and supporting fetal growth [6]. Traditionally, β-hCG is used as a marker for pregnancy detection and monitoring, with its levels rising during the first trimester before plateauing and declining toward the end of pregnancy [7]. However, emerging studies have suggested that elevated β-hCG levels, particularly beyond the expected plateau period, may be linked to the development of gestational hypertension and preeclampsia [8]. This is thought to occur through the influence of β-hCG on the angiogenesis process, where it can disturb the balance between pro-angiogenic and anti-angiogenic factors, potentially impairing placental development and contributing to vascular dysfunction [9]. The prevalence of hypertensive disorders in pregnancy in Bangladesh is a serious concern, with estimates suggesting that approximately 5–10% of pregnancies are affected by gestational hypertension [10]. This is compounded by the challenges faced in rural and urban hospitals, where early diagnosis and management may be hindered by limited resources and a lack of screening mechanisms. Given the increasing burden of gestational hypertension, finding cost-effective and accessible screening methods, such as monitoring β-hCG levels, could be an effective solution to improve maternal health outcomes [11]. Although previous research has demonstrated an association between elevated β-hCG levels and the onset of hypertensive disorders, limited studies have investigated the correlation between β-hCG levels and the severity of gestational hypertension specifically in the context of Bangladesh [12]. Understanding whether β-hCG could serve as an early indicator of GH severity could significantly improve risk stratification and guide clinical management [13]. This study, aims to explore the potential of β-hCG levels as an early predictor of gestational hypertension, examining whether it could serve as a reliable biomarker for early identification of at-risk pregnancies.

METHODOLOGY & MATERIALS

A cross-sectional observational study was undertaken at the Department of Obstetrics and Gynecology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh from June 2021 to July 2022, with complete follow-up of all participants. The 110 pregnant women were included in this study.

Hypertensive (n=16): Patients with hypertension
Normotensive (n=94): Patients without hypertension

All of the patients were carefully observed to meet the research objectives and provide valuable insights within the specified timeframe.

Inclusion Criteria:

- Singleton pregnancies.
- Gestational age between 14 and 19 weeks.
- Random selection from women attending antenatal clinics.
- Included regardless of parity.

Exclusion Criteria:

- Multiple pregnancies.
- Known fetal congenital anomalies.
- Pre-existing (essential) hypertension.
- Diabetes mellitus.
- Molar pregnancy.
- History of Down syndrome in previous pregnancies.

Ethical Considerations
Ethical considerations were integral to the study design and execution. The study adhered to ethical principles of confidentiality and privacy, ensuring that all patient data were anonymized and securely stored. Informed consent was obtained where applicable, and the research protocol was reviewed and approved by the relevant institutional ethics committee, ensuring compliance with ethical standards in human subject research.

Data Collection Procedure
Eligible participants underwent a detailed clinical evaluation, including medical history and physical examination. Blood pressure was measured using the auscultatory method. For beta-HCG analysis, 3 ml of venous blood was collected in clot-activator tubes. After clotting, samples were centrifuged at 3000 rpm for 5 minutes to obtain serum, which was stored in 1.5 ml microfuge tubes at -20°C until further analysis. Serum β-HCG levels were quantified using a chemiluminescence-based assay.

Follow-Up and Outcome Measurement
Participants were monitored throughout pregnancy up to 40 weeks of gestation or until delivery. The primary outcome was the development of gestational hypertension. estational hypertension was diagnosed when a systolic blood pressure of ≥140 mmHg or a diastolic pressure of ≥90 mmHg was observed on two separate occasions at least six hours apart after 20 weeks of gestation, without the presence of proteinuria. Preeclampsia was classified based on severity: mild preeclampsia was defined as blood pressure ≥140/90 mmHg accompanied by proteinuria of ≥300 mg in 24 hours or ≥1+ on dipstick, while severe preeclampsia was defined as blood pressure ≥160/110 mmHg with proteinuria ≥5 g in 24 hours or ≥3+ on dipstick.

Statistical Analysis
Descriptive statistics were used for summarizing continuous variables, while categorical variables were presented as frequencies and percentages. Associations between variables were evaluated using chi-square or Fisher's exact test, as appropriate. A p-value <0.05 was considered statistically significant. All statistical analyses were conducted using SPSS software version 26.0.

RESULT
The study included pregnant women, primarily aged between 21 and 30 years, with 38.18% in the 21–25 age group and 36.36% in the 26–30 age group. Most participants were unemployed (63.64%) and belonged to the middle socio-economic class (48.18%). Regarding gestational age, 52.73% were at 18 weeks and the least representation was at 16 weeks (1.82%) (Table 1). Among all, 16 were hypertensive and 94 were normotensive. In the hypertensive group, most of the women (56.7%) were nulliparous (P0), followed by women with one previous birth (P1) at 30.6%, and those with two or more births (≥P2) at 12.7%. In contrast, a higher proportion of normotensive women were nulliparous (76.60%), while 13.83% were P1 and 9.57% were ≥P2 (Table 2). The study observed a significant association between β-HCG levels and gestational hypertension ($p < 0.001$). Among women with β-HCG levels below 30,000 mIU/ml, all were normotensive. Hypertensive cases increased with rising β-HCG levels, notably with 100% of cases being hypertensive in the 80,000–90,000, 90,000–100,000, and >100,000 mIU/ml groups. Conversely, the majority of women with β-HCG levels between 30,000–70,000 mIU/ml were normotensive, though the proportion of hypertensive cases was higher in the 50,000–70,000 range (25%) (Table 3). Table 4 shows that a significant relationship was found between β-HCG levels and the severity of gestational hypertension ($p < 0.001$). Among hypertensive women with β-HCG levels ≤80,000 mIU/ml, all had mild hypertension. In contrast, among those with levels >80,000 mIU/ml, 75% had severe hypertension, while only 25% had mild hypertension.

Table 1: Baseline characteristics of the study population (n=110)

Variable	Frequency (n)	Percentage (%)
Age Group (years)		
21-25	42	38.18

26-30	40	36.36
31-35	25	22.73
36-38	3	2.73
Occupation		
Unemployed	70	63.64
Employed	40	36.36
Socio-Economic Status		
Lower Class	43	39.09
Middle Class	53	48.18
Upper Class	14	12.73
Gestational Age (weeks)		
14	23	20.91
15	9	8.18
16	2	1.82
17	11	10.00
18	58	52.73
19	7	6.36

Table 2: Parity among women (n=110)

Parity	Hypertensive (n=16)		Normotensive (n=94)	
	n	%	n	%
P0	9	56.7	72	76.60
P1	5	30.6	13	13.83
≥P2	2	12.7	9	9.57

Table 3: Relationship between beta HCG (absolute) levels and gestational hypertension

Beta HCG levels (MIU/ml)	No of cases	Hypertensive (n=16)		Normotensive (n=94)		P-value
		n	%	n	%	
<30,000	6	0	0.00	6	100.00	< 0.001
30,000-40,000	42	3	7.14	39	92.86	
40,000-50,000	40	2	5.00	38	95.00	
50,000-60,000	8	2	25.00	6	75.00	
60,000-70,000	4	1	25.00	3	75.00	
70,000-80,000	2	0	0.00	2	100.00	
80,000-90,0’00	2	2	100.00	0	0.00	
90,000-1,00,000	3	3	100.00	0	0.00	
>1,00,000	3	3	100.00	0	0.00	

Table 4: Beta HCG values (absolute) and severity of gestational hypertension

Beta HCG level (mIU/ml)	Mild hypertension		Severe hypertension		P-value
	n	%	n	%	
≤80000 (n=8)	8	100.0	0	0.00	< 0.001
>80000 (n=8)	2	25.0	6	75.0	

DISCUSSION

Gestational hypertension (GH) is a significant pregnancy-related complication associated with increased maternal and fetal morbidity, particularly in low-resource settings. Early identification of

women at risk is crucial for timely intervention and improved outcomes. Beta-human chorionic gonadotropin (β-HCG), a placental hormone, has been proposed as a potential biomarker for predicting hypertensive disorders in pregnancy. This study aims to assess the relationship between β-HCG levels and the early detection of GH among pregnant women in a tertiary hospital in Dhaka, Bangladesh. The study population predominantly comprised women aged 21–30 years, accounting for 74.54% of the cohort. Most participants were unemployed (63.64%) and belonged to the middle socio-economic class (48.18%). In other study, 20-29 years was the most predominant age group [14]. The majority were in their 18th gestational week (52.73%), aligning with the inclusion of women in the second trimester. Primigravida women (P0) constituted the largest subgroup among both hypertensive (56.7%) and normotensive (76.60%) participants. However, the proportion of hypertensive cases was relatively higher among multiparous women (≥P1), suggesting that parity may influence GH risk. Our results are consistent with observations of Yadav et al in which, 93% of women in normotensive group (control) and 73.3% in hypertensive group (cases) were primigravida [15]. Kour et al in their study found no significant association between parity and PIH but occurrence of PIH was more among primiparas [16]. A significant association was observed between elevated β-HCG levels and gestational hypertension ($p < 0.001$). Feng et al also concluded that there was a positive correlation between the absolute beta-HCG levels and the severity of pregnancy induced hypertension ($p<0.001$) [17]. No hypertensive cases occurred below 30,000 mIU/ml, while all women with levels above 80,000 mIU/ml were hypertensive, indicating a strong predictive value. This suggests a dose-dependent relationship, where rising β-HCG may reflect placental dysfunction, contributing to hypertension. Moderate levels (30,000–70,000 mIU/ml) were mostly linked to normotensive cases, but GH risk increased sharply beyond 80,000 mIU/ml. These findings highlight β-HCG's potential as an early, non-invasive marker for GH, warranting further research to confirm its predictive utility. Our findings were also in conformity with the findings of Gurbuz et al and Choudhury et al. [18,19]. We found that β-HCG levels exceeding 80,000 mIU/ml were associated not only with a higher likelihood of developing gestational hypertension but also with increased disease severity ($p < 0.001$). Among those who developed GH, 8 patients had β-HCG levels above 80,000 mIU/ml, and 6 patients (75.0%) with severe hypertension fell into this high β-HCG category. Similar results have been reported by Zhonghua et al. and Basirat Z et al. [18,19].

Limitations of the study:

- The sample size was relatively small, which may limit the generalizability of the findings to a broader population.
- The study duration was limited, preventing long-term follow-up on pregnancy outcomes beyond gestational hypertension.
- Potential confounding factors such as genetic predisposition, dietary habits, and socio-economic status were not extensively analyzed.

CONCLUSION

This study provides compelling evidence that elevated β-HCG levels in the second trimester are significantly associated with the onset and severity of gestational hypertension. The findings highlight the potential role of β-HCG as an early predictive biomarker, which could aid in the timely identification and management of at-risk pregnancies. The results emphasize the need for further large-scale studies to validate these observations and to explore the integration of β-HCG screening into routine antenatal care protocols. Implementing such screening measures could improve maternal and fetal outcomes, particularly in resource-limited settings where GH poses a significant health burden.

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REFERENCES

1. Antza C, Cifkova R, Kotsis V. Hypertensive complications of pregnancy: a clinical overview. Metabolism. 2018 Sep 1; 86:102-11.
2. Phipps E, Prasanna D, Brima W, Jim B. Preeclampsia: updates in pathogenesis, definitions, and guidelines. Clinical Journal of the American Society of Nephrology. 2016 Jun 1;11(6):1102-13.
3. Duley L. The global impact of pre-eclampsia and eclampsia. InSeminars in perinatology 2009 Jun 1 (Vol. 33, No. 3, pp. 130-137). WB Saunders.
4. Lorenzo-Almorós A, Hang T, Peiró C, Soriano-Guillén L, Egido J, Tuñón J, Lorenzo Ó. Predictive and diagnostic biomarkers for gestational diabetes and its associated metabolic and cardiovascular diseases. Cardiovascular diabetology. 2019 Dec; 18:1-6.
5. Gridelet V, Perrier d'Hauterive S, Polese B, Foidart JM, Nisolle M, Geenen V. Human chorionic gonadotrophin: new pleiotropic functions for an "old" hormone during pregnancy. Frontiers in immunology. 2020 Mar 13; 11:343.
6. Devoto L, Fuentes A, Kohen P, Céspedes P, Palomino A, Pommer R, Munoz A, Strauss III JF. The human corpus luteum: life cycle and function in natural cycles. Fertility and sterility. 2009 Sep 1;92(3):1067-79.
7. Chetty M. Novel biochemical markers in the diagnosis and management of early pregnancy problem (Doctoral dissertation, Newcastle University).
8. Korevaar TI, Steegers EA, de Rijke YB, Schalekamp-Timmermans S, Visser WE, Hofman A, Jaddoe VW, Tiemeier H, Visser TJ, Medici M, Peeters RP. Reference ranges and determinants of total hCG levels during pregnancy: the Generation R Study. European journal of epidemiology. 2015 Sep; 30:1057-66.
9. Benton SJ. Angiogenic factors in placentally-mediated pregnancy complications (Doctoral dissertation, University of British Columbia).
10. Hossain SM, Sultana K, Rouf S, Akter R, Roy S, Anwar S, Kirk K, Warren CE. Hypertensive disorders in pregnancy: Assessing postnatal quality of care and outcomes for women and their infants in Bangladesh.
11. Austin K, Wilson K, Saha S. Hyperemesis gravidarum. Nutrition in Clinical Practice. 2019 Apr;34(2):226-41.
12. PRIYA KV. The Efficacy of Second-Trimester Serum Beta Hcg Levels In The Prediction Of Pregnancy Induced Hypertension: A Prospective Study.
13. Nwabuobi C, Arlier S, Schatz F, Guzeloglu-Kayisli O, Lockwood CJ, Kayisli UA. hCG: biological functions and clinical applications. International journal of molecular sciences. 2017 Sep 22;18(10):2037.
14. 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 Mar;6(3):1040-44.
15. YADAV S, GUPTA S. Correlation of Elevated Levels of Maternal Serum β-hCG in Pregnancy Induced Hypertension and Pregpancy Outcomes in These Patients. Indian Journal of Pathology and Microbiology. 1997 Jul 1;40(3):345-9.
16. Kaur G, Jain V, Mehta S, Himani S. Prediction of PIH by maternal serum beta HCG levels in the second trimester (13–20 weeks) of pregnancy. The Journal of Obstetrics and Gynecology of India. 2012 Feb; 62:32-4.
17. Feng Q, Cui S, Yang W. Clinical significance of beta-hCG and human placental lactogen in serum of normal pregnancies and patients with pregnancy induced hypertension. Zhonghua fu Chan ke za zhi. 2000 Nov 1;35(11):648-50.
18. Gurbuz A, Karateke A, Mengulluoglu M, Gedikbasi A, Ozturkmen M, Kabaca C, Sahinoglu Z. Can serum HCG values be used in the differential diagnosis of pregnancy complicated by hypertension? Hypertension in pregnancy. 2004 Jan 1;23(1):1-2.
19. Choudhury KM, Das M, Ghosh S, Bhattacharya D, Ghosh TK. Value of Serum beta-hCG in Pathogenesis of Pre-Eclampsia. Journal of Clinical Gynecology and Obstetrics. 2012 Oct 23;1(4-5):71-5.