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Frequency Of Pregnancy-Induced Hypertension and Its Association With Elevated Serum Beta Human Chorionic Gonadotropin Levels During Mid-Trimester Of Pregnancy

Saman Habib[1], Aqsa Ikram-ul-haq[2], Shama Bashir[3], Nadia Sadiq[4], Noreen Majeed[5], Nabeela Waheed[6]

Abstract

Objective: To determine the frequency of PIH amongst elevated beta-hCG levels and non-elevated beta-hCG in the mid-trimester of pregnancy.

Materials and Methods: It was Descriptive case series conducted for six months (02-12-2019 to 02-06-2020) in OPD of Gynae Unit-II, Holy Family Hospital, Rawalpindi. A total of one hundred and twenty-two (n=122) normotensive pregnant females at 13-20 weeks gestational age and 18-35 years of maternal age were selected in this study after informed consent from every patient. The frequency of PIH in patients with elevated serum beta-hCG was measured. Data were analyzed using SPSS version 20. Effect modifiers were controlled by stratification. A p-value of ≤ 0.05 was considered significant.

Results: Mean beta-hCG levels in the total study population were found to be 7305.09±3900.64 IU/mL. Median b-hCG levels in our study population were noted as 6936.15 IU/mL. Pregnancy-induced hypertension was found positive in 16 (13.1%) patients. Raised beta-hCG levels were present in 10 (8.2%) patients. The frequency of PIH in raised beta-HCG levels was found in 7/10 (70%) of patients. We found a statistically significant (p-value ≤ 0.05) difference in the frequency of PIH among patients with elevated and not-elevated beta-hCG levels.

Conclusion: It is evident from my study that patients with raised levels of serum β-hCG during mid-trimester pregnancy are at increased risk to develop hypertensive disorders of pregnancy. We further elaborated that there is a statistically significant difference in various effect modifiers such as maternal age, gestational age, residential status, and BMI for developing PIH among patients with elevated and non-elevated beta-hCG levels.

Keywords: mid-trimester, pregnancy-induced hypertension, gestational age, beta human chorionic gonadotrophin.

[1] Postgraduate trainee, Holy Family Hospital, Rawalpindi; [2] Assistant Professor, Rawalpindi Medical University [3] Assistant Professor, Rawalpindi Medical University, Rawalpindi; [4] Women Medical Officer, Rawalpindi Medical University; [5] Associate Professor Gynae/Obs, Wah Medical College; [6] Professor Gynae/Obs, Rawalpindi Medical University, Rawalpindi. **Correspondence:** Dr Aqsa Ikram Ul Haq, Assistant Professor, Rawalpindi Medical University, Rawalpindi. **Email:** dr.aqsa81@gmail.com

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1. Introduction

Pregnancy-induced hypertension (PIH) is the most significant and intriguing unsolved problem in obstetrical practice, especially in low- and middle-income countries like India and Pakistan. The global prevalence of hypertension in pregnancy is between 5 to 11% constituting among the greatest causes of maternal morbidity and mortality. [1,2] Its prevalence in Pakistan has been reported about 6.5%. PIH is associated with major complications of pregnancy such as preterm delivery, IUGR, placental abruption, low birth weight fetus, and intra-uterine death, etc. [3] The proposed pathogenesis of PIH is decreased uteroplacental blood flow due to abnormal invasion of cytotrophoblast cells by spiral arterioles.[4] Decreased blood flow causes placental ischemia and it leads to activation of maternal vascular endothelium and which results in increased production of beta Human chorionic gonadotrophin (βhCG) by syncytiotrophoblast cells. In pregnancy, serum βhCG level increases slowly and reaches a peak at 8 to 10 weeks of gestation and then falls to a plateau at 18th - 20th weeks of gestation. [5,6] Numerous clinical, biophysical, and biochemical tests have been proposed during the past two decades for the early detection of PIH, but no test has been accepted widely because of their less predictive value.[7] Sharma V and colleagues in their study highlight the relationship between serum βHCG levels in 2nd trimester (13-20 weeks) and complications of pregnancy by PIH and they found that 387 cases (86.57%), had βHCG levels, <2MOM out of which only 6 cases (1.56%) developed PIH, and 13.48% (60cases) had values >2 MOM, out of which 49 (81.67%) cases developed pregnancy-induced hypertension (p-value <.001).[8,9] In a recent study, Chowdhary H et al found out the frequency of

PIH in non-hypertensive patients with gestational age 13-20 weeks and further evaluated if β HCG levels determined between this period could be used as a predictive tool for PIH. Their study results showed that total of 190 patients, out of them (25 patients) 13.1% had PIH.[10] Of those who suffered from PIH, (22 patients) 88% had β HCG level >2 MOM while 12% (3 patients) had β HCG level ≤2 MOM ($p<0.001$) and absolute β HCG levels i-e, Mean±SD were also profoundly higher (54907±295 vs 41095±191 mIU/ml; $p<0.001$ in patients those develop PIH later on. [10,11]

Diagnosis of PIH in early pregnancy is vital, so the management plan for high-risk pregnancies can be made earlier to reduce its effect on maternal, fetal, and neonatal morbidity and mortality.[12] Recently, few internationally published studies reported that the elevated serum βhCG levels in the mid-trimester of pregnancy are a strong predictor of PIH, but results vary with geographic, ethnic, and other study variables. [13] According to my knowledge based upon available data, no study has been done on our local population on this topic. The present study is planned to determine the frequency of PIH and its association with elevated serum βhCG levels in our local population. If study results showed a significant association of PIH with raised serum βhCG levels, we would recommend routine screening of these biomarkers in pregnant females to predict the future risk of PIH. Early identification and prevention of PIH will help obstetricians to reduce associated morbidity and mortality in our local population.[14]

2. Materials & Methods

It was Descriptive case series conducted for six months (02-12-2019 to 02-06-2020) in OPD of Gynecology Unit-II, Holy Family Hospital, Rawalpindi. The sample size was calculated by using the WHO sample size calculator. The sample size calculated comes out to be n=122. The sampling technique was Non-probability Consecutive sampling. The study was conducted after permission and approval of the hospital's ethical review committee for conducting research. Pregnant females in their 2nd trimester of pregnancy who were normotensive were enrolled on the OPD. Gestational age was determined by the last menstrual period and was confirmed by performing obstetric ultrasound. Written informed consent was taken from all the patients who were to be enrolled in the study. A comprehensive clinical history was taken, and a physical examination was performed. After enrollment in the study, 5 ml of blood using an aseptic technique was drawn into the vacutainer tubes and centrifuged for serum separation. Estimation of serum β HCG level was done by ELISA method using an automated analyzer from the hospital laboratory. The cases were followed up and examined 4 weekly till 32 weeks, and then fortnightly till delivery. During every visit, blood pressure and other necessary examinations were performed. Pregnancy-induced hypertension was diagnosed as an increase in blood pressure after 20 weeks of pregnancy. All the data collected was recorded in the especially designed proforma.

Data was entered and analyzed on SPSS version 20. Quantitative variables like the patient`s age, gestational age, and serum beta HCG were measured as mean ±SD. Qualitative variables like residential status. Beta HCG levels and PIH were expressed as frequency and percentages. PIH in patients with elevated and non-elevated beta HCG were compared by applying a chi-square test and a p-value <0.05 was considered significant. Effect modifiers like patient`s age, gestational age, residential status, and BMI were controlled by stratification. Post-stratification chi-square test was applied. p-value less than equal to 0.05 is considered as significant.

3. Results

A total of one hundred and twenty-two (n=122) normotensive pregnant females at 13-20 weeks gestational age and 18-35 years of maternal age were selected in this study after informed consent from every patient. Exclusion criteria were strictly followed. After enrollment demographic profiles of the patients were recorded. The cases were examined and followed monthly till 32 weeks, and then fortnightly till delivery. Pregnancy-induced hypertension will be diagnosed as per our operational definition. ELISA measurement was done for beta-hCG levels. The mean age of the patient was found to be 27.44±3.76 years while the mean gestational age was noted as 16.34±2.35 weeks. Other demographic variables like BMI and residential status are described in the table. Maternal and gestational age of patients were further divided into two different groups and the frequency of these groups is discussed separately in figure 1 and 2. Mean beta-hCG

levels in the total study population were found to be 7305.09±3900.64 IU/mL. Median b-hCG levels in our study population were noted as 6936.15 IU/mL. Pregnancy-induced hypertension was found positive in 16 (13.1%) patients. Elevated beta-hCG levels were found in 10 (8.2%) patients. Cross tabulation was done for PIH and elevated beta-HCG levels and we found a statistically significant (p-value ≤ 0.05) difference in it. Stratification was done for effect modifiers like maternal age, gestational age, BMI, and residential status. We noticed that a statistically significant (p-value ≤ 0.05) difference was noted for all the effect modifiers. Results are presented in the table.

Table: Frequency of pregnancy-induced hypertension in patients with elevated and non-elevated beta-hCG levels in the study sample (gestational age-based stratification)

GESTATIONAL AGE GROUPS	β-hCG STATUS	PREGNANCY-INDUCED HYPERTENSION		TOTAL	P-VALUE CHI-SQUARE
		POSITIVE	NEGATIVE		
≤16 WEEKS	NOT-ELEVATED	5	56	61	0.000
		62.5%	98.2%	93.8%	
	ELEVATED	3	1	4	
		37.5%	1.8%	6.2%	
	TOTAL	8	57	65	
		100.0%	100.0%	100.0 %	
>16 WEEKS	NOT-ELEVATED	4	47	51	0.000
		50.0%	95.9%	89.5%	
	ELEVATED	4	2	6	
		50.0%	4.1%	10.5%	
	TOTAL	8	49	57	
		100.0%	100.0%	100.0 %	

5. Discussion

In recent evidence compared to developed countries, developing countries have a much higher percentage of maternal mortalities secondary to hypertensive disorders and its complications in pregnancy so finding a marker for early prediction of this disorder will be helpful. Few other studies have also worked at specific hCG subunits.[15,16] Romero et al. also highlighted the significance of incomplete remodeling of a spiral artery leading to IUGR, pre-eclampsia, placental abruption, and preterm labor.[17]

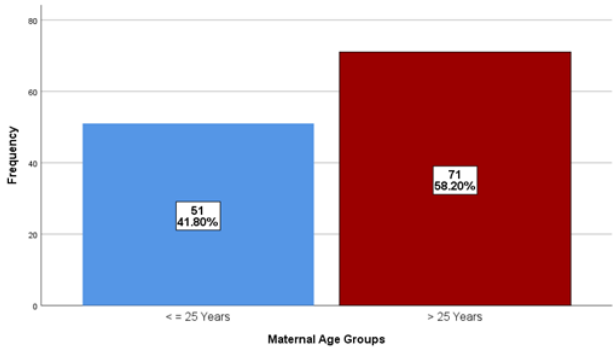

Figure-1 Distribution of study population in different maternal age groups (n=122)

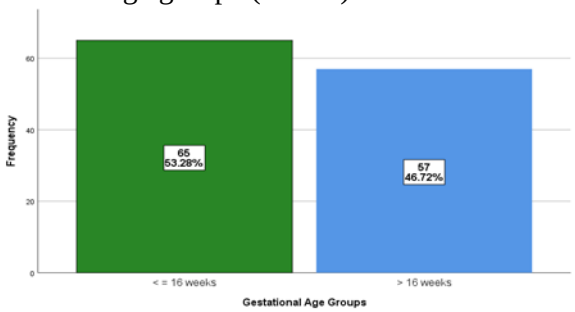

Figure-2 Distribution of the study population in different gestational age groups (n=122)

Remzi Gokdeniz et al. found a close connection between severe pre-eclampsia and increased β-hCG levels. Their results are comparable with the results of our study which showed 10 cases out of 112 with b-hCG values > 2MoM, 705 cases developed PIH and 30% were normotensive. [18] Other studies done by Pankaj Desai et al, Ashour et al, and Zhonghua et al, also showed a positive correlation between increased levels of b-hCG in 2nd trimester and hypertensive disorders of pregnancy.[19,20]

Recently Vanitha V et al conducted a study in the tertiary care center and checked the role of serum b-hCG in the prediction of pre-eclampsia from 13-20 weeks of gestation. According to this study women having b-hCG >71220mIU/ml in mid-trimester develop hypertensive disorders, so this can be used as a marker in pregnancy.[21,22]Similarly, a prospective observational cohort study was conducted by Chowdhary H and colleagues, Dayal M and colleagues, Choudhury KM et

al. and Mallika A et al, also supports our findings. On the other hand, contrary to our study Stamilio et al, and Munirah M found no association between increased 2nd-trimester b-hCG levels and hypertensive disorders of pregnancy.[23,24]

Based on the results of our and all these studies, a conclusion made was that increased levels of b-hCG in mid-pregnancy have a significant role in the development of pre-eclampsia. In turn, the more would be maternal and neonatal complications, the b-hCG levels must be used as a marker for early diagnosis of pre-eclampsia in high-risk pregnancies.[25]

To summarize our results and previously published studies strongly endorsed that high b-hCG levels in the second trimester of pregnancy are strongly associated with pre-eclampsia or hypertensive disorder in pregnancy. The strength of our study is that previously no similar study has been done on our local population. So, this study could be used as a reference study for future research. However, our study also has a few limitations. We have not determined the association of severity of preeclampsia or included association with co-morbid like diabetes. We also have not analyzed the association of gravidity and parity in our study sample. Furthermore, our study had a limited sample size and the study population belonged to a similar ethnic group due to technical boundaries. Our study was limited by the fact that we considered only a single b- hCG level available for each woman made us unable to examine inter-individual differences in hCG variation during pregnancy. Further studies are required to assess whether b-hCG trajectory has a role in pre-eclampsia. We suggest a larger-scale study on the same topic to overcome all the limitations of the study.

5. Conclusion

It is evident from our study that patients with increased levels of serum β-hCG during mid-trimester pregnancy are at increased risk of having hypertensive disorders during pregnancy.

CONFLICTS OF INTEREST- None

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Potential competing interests: None to report

Contributions:

S.H, A.I - Conception of study
S.H, A.I, S.B - Experimentation/Study conduction
S.H -Analysis/Interpretation/Discussion
A.I, S.B, N.S - Manuscript Writing
A.I, N.S, N.W N.S - Critical Review
N.S, N.W, N.S - Facilitation and Material analysis

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