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Original Article

Pregnancy Induced Hypertension

Pak Armed Forces Med J 2020; 70 (6): 1712-16

ASSOCIATION OF HUMAN CHORIONIC GONADOTROPHIN WITH PREGNANCY INDUCED HYPERTENSION

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ABSTRACT

Objective: To determine the positive predictive value of beta Human Chorionic Gonadotrophin in early second trimester for predicting pregnancy induced hypertension.

Study Design: Cross-sectional study.

Place and Duration of Study: Department of Obstetrics and Gynaecology Combined Military Hospital, Lahore, from Jun 2017 to Nov 2017.

Methodology: A total of 214 female pregnant patients met the criteria for inclusion in this study. Patients with beta human chorionic gonadotrophin (βHcg) levels ≥2 MoM were followed at 22, 26, 30 and 34 weeks of gestation. Blood pressure was monitored. Pregnancy induced hypertension (PIH) was labelled after 20 weeks (as per dating scan) of gestation in patients who did not have proteinuria (≥300 mg 24 hour urine sample) and had a systolic blood pressure ≥140 mmHg and/or a diastolic blood pressure ≥90 mmHg (blood pressure readings taken at two separate points in time four hours apart).

Results: Patients ranged between 18-35 years of age, with the mean age being 27.3 ± 4.3 years. Mean gestational age was observed to be 15.6 ± 1.8 weeks. Mean BMI was 23.8 ± 3.2 kg/m^2. Out of 214 patients, 30 patients (14%) had beta human chorionic gonadotrophin level >2 MoM. Out of these 30 patients, 25 patients (83.3%) developed PIH. There were 100 primigravida (46.7%) and 114 multigravidas (53.3%). Beta human chorionic gonadotrophin in predicting pregnancy induced hypertension showed sensi-tivity of 96.1%, a specificity of 97.3%, with a PPV 83.3%, a NPV 99.4% and diagnostic accuracy of 97.2%.

Conclusion: Pregnant women with beta human chorionic gonadotrophin levels >2 MoM at 13-18 weeks gestation were at an increased risk of developing pregnancy induced hypertension.

Keywords: Beta human chorionic gonadotropin (β-HCG), Positive predictive value, pregnancy induced hypertension.

INTRODUCTION

Pregnancy induced hypertension (PIH) is a major global medical condition affecting both the pregnant women and the fetus[1,2]. The incidence of this disorder varies geographically from 6-8% to as high as 12-15% of all pregnant women especially in developing countries[3]. As the name implies, pregnancy induced hypertension is exclusively encountered in pregnancy, and is a major contributor to maternal and perinatal morbidity[4]. Although adequate prenatal care combined with diligent surveillance for signs of pre-eclampsia and prompt intervention has reduced the number of poor outcomes, maternal and fetal morbidity still occurs[5]. The National High Blood Pressure Education Program Working group in pregnancy categorizes hypertension in pregnancy into four categories, chronic hypertension, gestational hypertension, pre-eclampsia, and pre-eclampsia super imposed on chronic hypertension[6].

Maternal age, familial aggregation, race, smoking, history of hypertension in parents, family history of diabetes, socioeconomic level, diet, BMI and climate are identified risk factors of PIH[7,8,9].

The pathogenesis of the disease remains poorly understood. Abnormal placentation in the second trimester has been suggested as the initial culprit[10]. Hypothetically it is proposed that immunological changes in the trophoblast causes a secretory response with elevation of beta Human

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Received: 31 Oct 2019; revised received: 08 Dec 2019; accepted: 10 Dec 2019

Chorionic Gonadotrophin levels. Furthermore it is suggested that blood vessel damage in the placenta in pre-eclamptic patients leads to decreased oxygen perfusion, which ultimately causes an increase in β-HCG production by syncytiotrophoblasts. Levels of serum β-HCG can act as a predictor for PIH, and can aid in stratifying patients that are destined to encounter PIH in the very same pregnancy[1].

We conducted our study to determine the positive predictive value of beta HCG in early prediction of high risk patients for PIH, to use this for vigilant monitoring and timely management of the disease, as well as curtailing the maternal mortality and morbidity and fetal complications associated with PIH.

METHODOLOGY

Our cross-sectional study was conducted atthe Department of Obstetrics and Gynaecology, Combined Military Hospital, Lahore and ran for a duration of six months in total (June 2017 to November 2017).

A sample size of 214 was calculated with 95% confidence level and 5% margin of error while taking expected positive predictive value of beta HCG in predicting PIH to be 83.33%[11]. The technique used for sampling was non-probability consecutive sampling. Patients included in the study were gravid females (13-18 weeks of gestation as per dating scan) having ≥2 MoM (multiple of median for gestational age) beta HCG levels were suspected to have PIH as they were having significantly raised levels of beta HCG.

Patients with twin pregnancy or fetal anomaly on ultrasound were excluded from the study. Patient with diabetes women already on antihypertensive medication, patients with liver disorder (bilirubin >1.2 mg/dl) or renal disorder (serum creatinine > 1.2 mg/dl) were also excluded.

After having been approved by the ethical review committee (435/ERC/CMHLMC) of the hospital, data was collected for 214 gravid females who presented in the outpatient department of Combined Military Hospital, Lahore and fulfilled the outlined criteria above were counselled and explained the details of the study. Written informed consent and detailed history was taken from each patient.

Gravid females after 20 weeks of gestation (as per dating scan) having a systolic blood pressure (SBP) equal to or more than 140 mmHg, and/or those with a diastolic blood pressure (DBP) ≥90 mmHg (at two separate points in time four hours apart) without proteinurea (≥300 mg 24 hours urine sample) were followed up on 22, 26, 30 and 36 weeks. Blood pressure was taken using mercury sphyg-momanometer. All the data were noted and recorded on a proforma along with demographic details of the patient. All the lab tests were carried out in the same lab (CMH Lab) and all the blood pressure recordings were done on the same blood pressure apparatus to eliminate bias, confounding variables were controlled by exclusion. All of the aforementioned data was compiled and analysed in SPSS version 20.0. Numerical variables i.e. age and gestational age at the time of presentation were presented by mean ± SD.

Categorical variables i.e Parity and positive predictive value (PPV) n of beta HCG were presented as frequency and percentage. Post stratification chi-square test was applied taking value of ≤0.05 as statistically significant.

RESULTS

A total of 214 patients were included in the study and demographic features are shown in table-I. Out of 214 patients 30 patients (14%) had beta HCG level >2MoM. Out of these 30 patients in 25 patients (83.3%), developed PIH.

Table-II shows sensitivity, specificity, positive predictive value and negative predictive value (NPV) of beta HCG in the prediction of gestational hypertension with a diagnostic accuracy 97.2%.

Stratification for gestational age and beta HCG value in predicting pregnancy induced hypertension are shown in table-III with diagnostic accuracy of 98.6%, 98.1% and 95.4% in

patients between the gestational age of 13-14 weeks, 15-16 weeks and 17-18 weeks of gestation.

Table-I: Demographic variables.

Characteristics	Number	Percentage (%)
Age (years)		
18- 25	82	38.3
26-35	132	61.7
Mean ± SD	27.3 ± 4.3	
Gestational Age (Week)		
13-14	74	64.6
15-16	53	24.8
17-18	87	40.7
Mean ± SD	15.6 ± 1.8	
BMI (kg/m²)		
≤ 25	147	68.7
≥ 25	67	31.3
Mean ± SD	23.8 ± 3.2	
Parity		
Primigravida	100	46.7
Multigravida	114	53.3
Beta HCG level		
>2 MOM	30	14
<2MOM	184	86
Pregnancy induced hypertension (PIH) among cases having beta HCG >2MOM level n=30		
PIH	**Number**	**Percentage (%)**
Yes	25	83.3
No	5	16.7

DISCUSSION

Numerous haematological, biochemical and biophysical markers have been used to screen the antenatal population topredict pregnancy induced hypertension over the past 60 years but none has been universally accepted due to low predictive values. Early trimester colour Doppler ultrasonography has an excellent role to play as a predictor of pregnancy induced hypertensionbut its accessibility in day to day practice is limited[11]. Our study was conducted to determine the possibility of using beta HCG which is readily available to predict pregnancy induced hypertension.

In our study the mean age of patients was 27.3 ± 4.3 which was similar to a study conducted by Kabukcu *et al*[12], suggesting PIH to be common in women in their twenties. In the mid 1900 it was reported that HCG levels were elevated in toxemia of pregnancy. Patients in this study who had higher levels of serum beta HCG (>2MoM) during their second trimester were more likely to encounter PIH further down the line in their own pregnancy, (*p*-value <0.001). Of 83.3% of patients with elevated serum levels of beta HCG went on the develop PIH (sensitivity 96.1%, specificity

Table-II: Stratification for gestational hypertention and beta HCG value.

Gestational hypertension	HCG>2 MOM	HCG <2MOM	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	*p*-value	Chi Square
Yes	TP=25	FP=5	96.1%	97.3%	83.3%	99.4%	<0.001	165.64
No	FN=1	TN=183						

TP=True Positive, FN= False Negative, FP=False Positive, TN= True Negative

Table-III: Stratification for gestational age and beta HCG value.

	Gestational Hyper-tension	HCG>2 MOM	HCG<2 MOM	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	*p*-value	Chi square
GA 13-14 Weeks n=74	Yes	TP=10	FP=0	90.1%	100%	100%	98.4%	<0.001	66.222
	No	FN=1	TN= 63						
GA 15-16 Weeks n=53	Yes	TP=4	FP=1	100%	97.8%	80%	100%	<0.001	41.535
	No	FN=0	TN=48						
GA 17-18 Weeks n=87	Yes	TP=11	FP=4	100%	94.7%	73.3%	100%	<0.001	60.442
	no	FN=0	TN=72						

97.3%, PPV 83.3%, NPV 99.4% and diagnostic accuracy 97.2%). Our results are comparable with the study of Kaur *et al*[11], with *p*-value of <0.01 and positive predictive value of 83.3% which is the same as our study.

As pointed out by Rajesh *et al*[13], prevention of PIH will follow if early prediction is possible. In that study serum beta HCG was estimated between 14-20 weeks of gestation in 90 women with singleton pregnancy. A total of (14.8%) cases developed gestational hypertension. Levels of serum β-HCG were higher in subjects that developed gestational hypertension. Serum beta HCG (median >32726 mIU/ml) had a sensitivity of 75%, specificity of 72.5%, a PPV of 32.1% and an accuracy of 72.8%.

Jindal also found a correlation between elevated serum beta HCG levels and PIH[14]. Kaur *et al*[15] and colleagues observed that higher levels of beta HCG are associated with increased severity of PIH (*p*-value <0.01). The sensitivity was 90.91%, specificity was 97.44% and positive predictive value was 83.33%. Thisfurther supports our finding that beta HCG has a valuable role in predicting PIH.

PIH seldom develops after the second trimester, and the pathogenesis starts early in pregnancy[16], as shown by stratification of gestational age and beta HCG levels in pregnant patients between 13-18 weeks of gestation (*p*-value <0.001; significant). Similar results have been shown by Feng *et al*, who displayed the positive correlation between absolute levels of serum beta-HCG and the severity of pregnancy induced hypertension (*p*-value ≤0.05)[17]. To focus on high risk women and to identify them in time, screening has a pivotal role[18].

CONCLUSION

An increased risk of gestational hypertension in gravid patients with high levels of beta HCG levels >2MoM at 13-18 weeks gestation was found. Beta HCG has shown to be a practical, reliable and readily available test for the prediction of PIH and should be used as a screening tool in pregnant women.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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