Serum β HCG as a Predictor and Potent Marker for Pregnancy Induced Hypertension in Salah Aldeen General Hospital

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Abstract

Aim: This study was conducted to predict gestational hypertension by using serum beta HCG and thereby to follow up the risk patients and to reduce both maternal and perinatal morbidity and mortality.

Patients and Methods: A prospective study was carried out in Tikrit city from the beginning of October 2020 to May 20201 and included 150 women, 25 were lost to follow-up. The rest 125 patients followed up in their second trimester (13-20) weeks, attending Salah Aldeen General Hospital. Routine antenatal investigations were done. All patients underwent thorough clinical and routine obstetrical examination. Venous blood sample was collected for determination of serum β HCG level.

Results: The study showed no significant difference between women with pregnancy induced hypertension (PIH) and Normal mothers regarding their age at the time of booking(P>0.05). The mean age of PIH women was 32.2±5.9 year and normal women was 32.2±6.2 year. Although 26.67% of PIH women were below 20 year of age compared with 12.73% of Normal women. The relationship between β−hCG (absolute) levels and PIH and the association between mean β−hCG level of PIH patients and Normotensives was statistically significant ($p< 0.001$) and as the level of β−HCG increases the PIH also increases. The study showed that, 66.67% of PIH women have severe elevation in hypertension and majority of women with severe PIH (90%) have Beta hCG level above 80000 mIU/ml and only 10% have level ≤80000 mIU/ml while 60% of women with mile PIH have level ≤80000 mIU/ml. The mean increase of SBP of PIH mothers was 40.1 mm/Hg.

Keywords: *pregnancy, Serum β HCG, hypertension, Salah Aldeen General Hospital*

Introduction

Hypertensive disorders of pregnancy complicate 5 - 10% of pregnancies worldwide and constitute one of the greatest causes of maternal morbidity and mortality and perinatal morbidity and mortality [(1)]. In developed countries 16% of maternal deaths are attributed to hypertensive disorders. Hypertensive disorders are a frequently encountered complication of pregnancy and remain a major cause of maternal and perinatal morbidity and mortality [(2)]. The Confidential Enquiry into Stillbirths and Deaths in Infancy report cites one in six stillbirths as occurring in pregnancies complicated by maternal hypertension. Hypertensive disorders vary from mild gestational hypertension to severe preeclampsia and have a number of possible etiologies[(3)]. Several tests have been proposed but none has been accepted widely due to their low predictive value [(4)]. The abnormal placentation has been considered as one of the initial events in the disease process hypothesized that during mid-trimester, immunological changes occur in the trophoblasts, resulting in a secretory response, which is seen as a rise in the beta Human chorionic gonadotropin (HCG) levels [(5)]. Hypertensive disorders are also responsible for perinatal mortality and morbidity. Pre-eclampsia is a risk factor for stillbirth, Intrauterine growth restriction (IUGR), Low birth weight (LBW), Preterm delivery, Respiratory distress syndrome, and admission in the neonatal intensive care unit. Hypertensive disorders account for 8-10%

of all preterm births. A variety of biochemical and biophysical markers have been proposed for predicting the development of preeclampsia in pregnancy[6]. Pregnancy Induced Hypertension, Gestational Hypertension or Transient Hypertension of pregnancy are terms used to describe new hypertension which appears after mid-term (20 weeks) and resolves within 10 days postpartum without other symptoms of pre-eclampsia in a previously normotensive woman[7]. In pregnancy, the placenta forms especially large quantities of Human Chorionic Gonadotropin which is essential to a normal pregnancy and more so in Pregnancy Induced Hypertension. Elevated serum β-hCG in the second trimester has repeatedly been shown to be significantly associated with later PIH. The patients with abnormal β-hCG levels and in very few reports, the free β-subunit (free β-hCG) were reported as possible predictors of pre-eclampsia, pregnancy-induced hypertension, spontaneous miscarriage, low birth weight,preterm delivery and intra uterine growth retardation (IUGR) [8]. This study was conducted to predict gestational hypertension by using serum beta HCG and thereby to follow up the risk patients and to reduce both maternal and perinatal morbidity and mortality.

Patients and Methods

A prospective study was carried out in Tikrit city from the beginning of October 2020 to May 20201. The study conducted to determine the role of β HCG in pregnant women, the included 150 women, 25 were lost to follow-up. The rest 125 patients followed up in their second trimester (13-20) weeks, attending Salah Aldeen General Hospital. Routine antenatal investigations were done.

Inclusion criteria

Pregnant women with:

- Nonproteinuric.
- Normotensive.
- Primi/Multi gravida.
- Singleton
- Gestational age 13-20 weeks as determined by last menstrual period or ultrasound scan.

Exclusion criteria

- Chronic hypertension.
- Molar Pregnancy.
- Diabetes mellitus.
- Anomalous foetus.
- Multiple pregnancies.

All patients were informed about the study and informed written consent was taken before they were enrolled in the study. At the time of enrollment, demographic details were noted, detailed obstetric and medical history was taken. Gestational age was calculated from reliable menstrual history dates and/or Ist trimester ultrasonographical measurement of fetal crown rump length. All patients underwent thorough clinical and routine obstetrical examination. Baseline blood pressure (average of 3 readings) using a sphygmomanometer was recorded using the auscultatory method. Routine antenatal tests were performed as required and indicated.

A routine antenatal investigation was done. 5 ml of venous blood sample was collected and tests were carried out. Estimation of serum β HCG level was done by immunofluorescence immunoassay as manufacture instructions. The cases were followed up in antenatal clinic and were examined 4 weekly till 28 weeks, fortnightly up to 34 weeks and thereafter weekly till delivery. At every visit. Serum β HCG as a predictor and potent marker for pregnancy induced hypertension. Blood pressure was recorded and urine was examined for albumin. PIH included gestational hypertension and preeclampsia. Gestational hypertension was defined as blood pressure 140/90 mmHg on two occasions at least 6 hours apart after 20 weeks of gestation. Preeclampsia was defined as gestational hypertension and proteinuria of at least 1

+ on the dipstick.

Severity of PIH

The severity of PIH is assessed by the extent of symptoms. Both blood pressure and proteinuria are dependable indicators of severity[1].

v **Mild PIH:** Blood pressure is ≥140/90 mmHg but <160/110 mmHg after 20 weeks gestation, and proteinuria is ≥300 mg/24 hours without exceeding 2.0 g/24 hours or 3+ dipstick

v **Severe PIH:** Blood pressure is ≥160/110 mmHg, and proteinuria exceeds 2.0 g/24 hours or 3+ dipstick.

Data collection form

A structured format was prepared for collecting the demographic details, personal, obstetric and medical history, data related to all ANC visits, outcomes of serum β-hCG assessment, perinatal events and outcomes.

Results

In this study, 150 women completed the study, 25 were lost to follow-up. The rest 125 patients followed, 15 women developed PIH constituting 12% of the study population. Thus, the incidence of PIH was 12% in our study (Figure 1). When further subdivided, the incidence of preeclampsia was 20% of the PIH (*n* = 3). Of these 3 preeclamptic patients, 2 women had early-onset preeclampsia (onset before 34 weeks), whereas the rest 1 had late-onset disease. Most of the patients (83.33%) had late-onset PIH (after 34 weeks), whereas the incidence of early-onset PIH (before 34 weeks) was only 16.67% (Table 2).

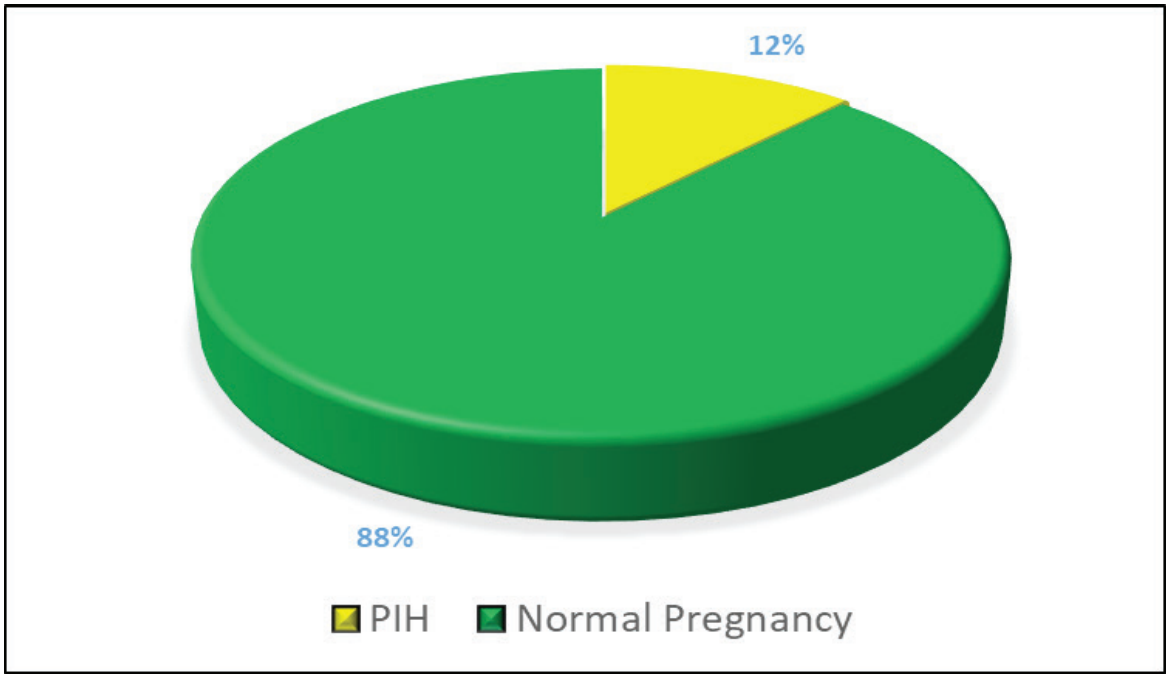

Figure 1: Incidence of PIH

Table 1: Distribution of pregnancy-induced hypertension into pregnancy-induced hypertension and preeclampsia

PIH women	PIH		early-onset (before 34 weeks)		Late Onset (>34 weeks)	
	No.	%				
	No.	%	No.	%	No.	%
Pre-eclampsia	3	20	2	66.67	1	33.33
Continue PIH	12	80%	2	16.67	10	83.33

The study showed no significant difference between women with pregnancy induced hypertension (PIH) and Normal mothers regarding their age at the time of booking(P>0.05). The mean age of PIH women was 32.2±5.9 year and normal women was 32.2±6.2 year. Although 26.67% of PIH women were below 20 year of age compared with 12.73% of Normal women, Table 2.

Table 2: Comparison between pregnant women with induced hypertension and normal pregnant women regarding age

Age (years)	Pregnancy Induced Hypertension		Normal women	
	No.	%	No.	%
15-20	4	26.67	14	12.73
21-30	3	20.00	40	36.36
31-40	4	26.67	44	40.00
>40	4	26.67	12	10.91
Total	15	100	110	100
Mean ± SD	32.2±5.9		32.2±6.2	

P>0.05 (non-significant)

Table 3 shows the relationship between β−hCG (absolute) levels and PIH and the association between mean β−hCG level of PIH patients and Normotensives was statistically significant ($p< 0.001$) and as the level of β−HCG increases the PIH also increases.

Table 3: Comparison between PIH and normal pregnant women regarding the level of serum hCG level

Beta hCG level (mIU/ml)	PIH		Normal women		P. value
	No.	%	No.	%	
<30,000	0	0.0	12	9.60	<0.001
30,000-40,000	0	0.0	40	32.00	
40,001-50,000	1	6.7	41	32.80	
50,001-60,000	2	13.3	23	18.40	
60,001-70,000	1	6.7	5	4.00	
70,001-80,000	0	0.0	4	3.20	
80,001-90,000	4	26.7	0	0.00	
90,001-1,00,000	3	20.0	0	0.00	
>1,00,000	4	26.7	0	0.00	
Total	15	100.0	125	100	
Mean ± SD	96325.3±39757.5		41343.6±24737.5		<0.001

The study showed that, 10 of 15 (66.67%) of PIH women have severe elevation in hypertension (Figure 2). The study also showed that, majority of women with severe PIH (90%) have Beta hCG level above 80000 mIU/ml and only 10% have level ≤80000 mIU/ml while 60% of women with mile PIH have level ≤80000 mIU/ml , Table 4.

Figure 2: Rate of Severity of PIH

Table 4: Relation of beta hCG level with severity of PIH

Beta hCG level (mIU/ml)	PIH women (n:15)				Total	
	Mild		Severe			
	No.	%	No.	%	No.	%
≤80000	3	60.0	1	10.0	4	27
>80000	2	40.0	9	90.0	11	73
Total	5	100	10	100	15	100

P<0.05

The mean increase of SBP of PIH mothers was 40.1 mm/Hg. The mean increase of SBP of Normal mothers was 9.3mm/Hg. The difference between them was statistically very highly significant (P<0.001). Similarly, the DBP mean increase of PIH mothers was 24.3 mm/Hg. The mean increase of DBP of Normal mothers was 3.2 mm/Hg. The difference between them was statistically highly significant (P<0.001) Figure 4.2.

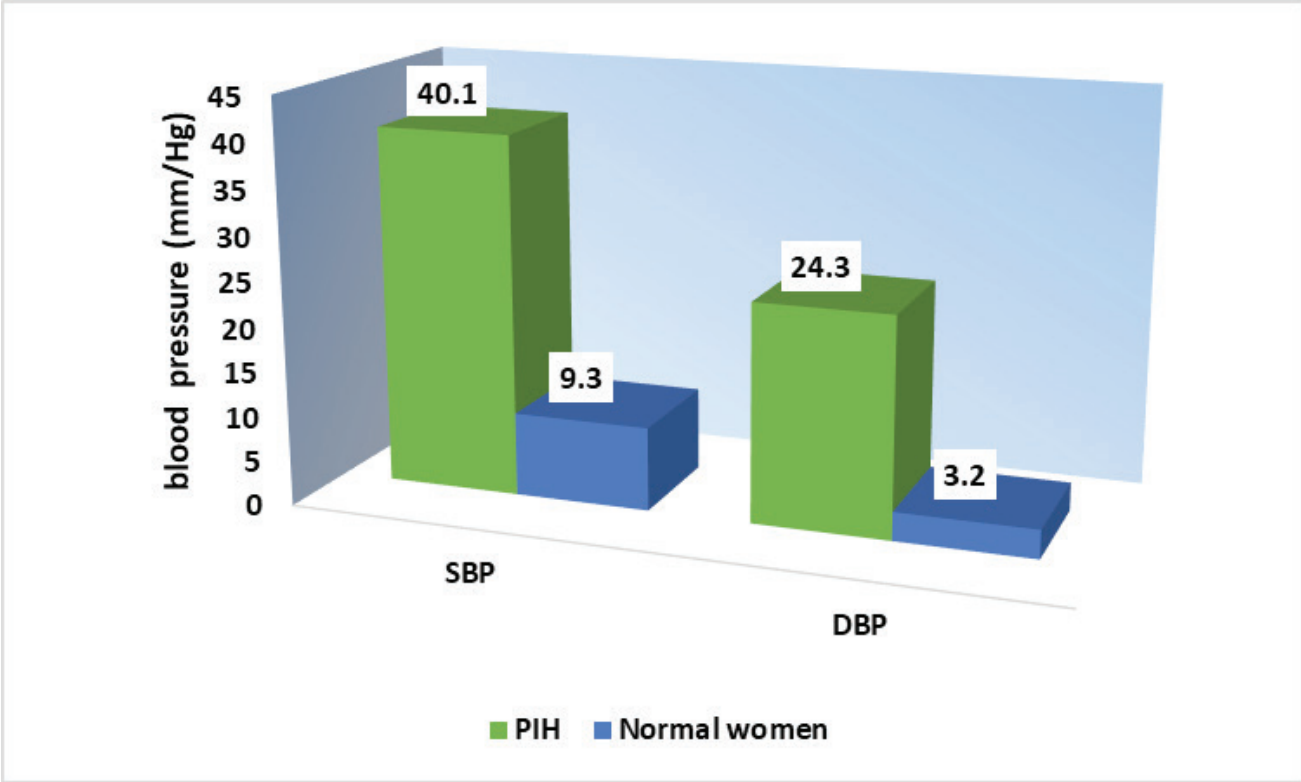

Figure 2: Comparison of increased SBP and DBP between PIH and normal mothers.

Table 5 shows the mode of delivery of the studied patients where cesarean was in majority of the cases (80%) where as in normotensive patients cesarean was in 48.18% and the association was found to be statistically significant between hypertensive and normotensive patients (p< 0.05).

Table 5: Mode of Delivery in the studied groups

Mode of delivery	PIH		Normal women	
	No.	%	No.	%
Vaginal	3	20	53	48.18
LSCS	12	80	57	51.82
Total	15	100	110	100

P. value: 0.039

Discussion

Hypertension and proteinuria are important complications of pregnancy. Abnormal placentation is one of the important pathologies for the development of GHT. Because of abnormal placentation, there may be an increased synthesis of beta HCG [1]. There may be deregulation of lipoprotein lipase in GHT prone women, that causes elevated plasma lipid and lipoprotein levels, may induce endothelial dysfunction is the prominent pathology, usually occurs in early trimester (8-18 weeks) but signs and symptoms occur in a late trimester [1]. In this study serum beta HCG estimated in the early second trimester, women with elevated levels, categorized under the high-risk group. So it is easy to identify the high-risk women and kept under regular follow up. It helps in preventing the development of complication in GHT. Since the year 1950 HCG is reported to be elevated in toxemic pregnancy [2,3]. Like in present study, Mazhari and Varun [9], Soundararanjan *et al* [10] Muthulakshmi *et al* [11], Kulkarni *et al* [12] and Rajesh *et al* [35] also use hCG production level as a measurement tool for the prediction of pregnancy induced hypertension. In the present study the prevalence of PIH was observed to be in 12% which was comparable to the studies performed by Mazhari and Varun [9] who found that the prevalence of PIH was 13.33% and Pawar *et al* [14] (11.53) which were in agreement with our finding Table 2 shows the relationship between β−hCG (absolute) levels and PIH and the association between mean β−hCG level of PIH patients and Normotensives was statistically significant ($p< 0.001$) and as the level of β−HCG increases the PIH also increases. Elevated serum β-hCG in second trimester has repeatedly been shown to be significantly associated with PIH [41]. It has been reported that women with markedly elevated maternal serum β-hCG levels has significantly increased risks of having spontaneous miscarriage, preterm delivery and IUGR [15].The estimation of serum β-hCG levels may be helpful in both the early detection of PIH and to initiate necessary treatment to avoid associated complications [16]. This will perhaps bring down the maternal and foetal morbidity and mortality [17,18] reported from their study that all those who developed PIH had higher levels of serum β-hCG confirmed 100% correlation between high serum β-hCG levels and development of PIH which in turn significantly increased risks of having poor/adverse pregnancy outcomes (Spontaneous miscarriage, Intra Uterine Growth Retardation (IUGR) and Preterm delivery), where the magnitude of risk correlates with the levels of β-hCG. The present study results indicate that β-hCG determination may have value in the prediction of PIH[19]. It is evident from the different studies that, the serum β-hCG levels were significantly higher and significantly correlated with increased risk of PIH in women with increased β-hCG levels in the hypertensive group as compared to those in the normotensive group; which indicates the strong correlation between higher serum β-hCG levels and development of PIH later on during pregnancy [20,21]. It seems reasonable to presume from the results of the present experimental study that the increased synthesis and secretion of free β-hCG is associated with immunosuppressive activity of hCG which helps to initiate early treatment so as to minimize and/or avoid adverse effects of PIH[22,23]. The study showed that, 10 of 15 (66.67%) of PIH women have severe elevation in hypertension, The study also showed that, majority of women with severe PIH (90%) have Beta hCG level above 80000 mIU/ml and only 10% have level ≤75000 mIU/ml while 60% of women with mile PIH have level ≤80000 mIU/ml. Our study is in accordance to the study performed by Chowdhary *et al* [24] who reported 60% with severe hypertension and 40.0% with mild hypertension.

Conclusion

The study showed that measuring second trimester beta HCG levels is useful in clinical practice to identify women who will develop PIH in the same pregnancy.

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: "All experimental protocols were approved under the Al-Anbar Health directorate and carried out in accordance with approved guidelines".

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