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Impact of Elevated Serum Beta hCG in the Second Trimester on the Incidence of Induced Hypertension in Pregnant Women

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ABSTRACT

Objective: To determine the frequency of pregnancy-induced hypertension (PIH) in pregnant women with raised serum beta HCG in the second trimester. This descriptive study was conducted at the Department of Obstetrics & Gynaecology, Ziauddin University Hospital, Karachi, Pakistan, six months after the approval of the synopsis from April 19 to October 18, 2019. **Materials and Methods:** All patients who fulfilled the inclusion criteria and visited Ziauddin University Hospital, Karachi, were included in the study. Informed consent was obtained after the procedure, and the risks and benefits of the study were explained. In our research, detailed history was taken from each patient, and BHCG was done using the CLIA method. Those patients with raised BHCG were included in this study, and blood pressure and proteinuria were examined. Estimation of mid-trimester beta HCG can be used to predict the early development of PIH. All the collected data were entered into the proforma attached at the end and used electronically for research. **Results:** Mean ± SD of Age was 27.9±5.3 years. Gestational Age was 17.3±4.2 weeks, and serum beta HCG levels were 53,469.3±235.2 mlU/mL. Pregnancy-induced hypertension (PIH) was observed in 56 (77.8%) patients. **Conclusion:** It is to be concluded that pregnancy-induced hypertension is found to be significantly high among pregnant women in our population. PIH is associated with maternal Age and perinatal outcomes. The results suggest that pregnant women and members of their families should be urgently educated to understand the importance of antenatal care.

Keywords: Pregnancy Induced Hypertension, Pregnancy Serum beta HCG, Trimester

INTRODUCTION

Hypertensive disorders complicating pregnancy are common and are one among triad along with haemorrhage and infections, which results in much maternal morbidity and mortality related to pregnancy [1]. Pregnancy-induced hypertension is a unique disease characterized by increased blood pressure in pregnancy and seen only in pregnancy, affecting 12% to 15% of all pregnant women [2]. Hence, PIH is considered one of the leading public health issues worldwide and a significant cause of mortality in both the mother and fetus [3]. Abnormal placentation has been considered one of the initial events in the disease process. It is

hypothesized that during the mid-trimester, immunological changes occur in the trophoblast, resulting in a secretory response, seen in the rise in beta HCG levels [4].

American College of Obstetricians and Gynecologists (ACOG) has classified pregnancy-induced hypertension (PIH) into four groups of disorders: gestational hypertension, where resting BP is 140/90 mmHg or higher after 20 weeks of gestation.; Chronic Hypertension that exists before pregnancy or begins in the first 20 weeks of gestation; preeclampsia (raised BP and oedema or proteinuria)/eclampsia (preeclampsia and seizures); and preeclampsia superimposed on chronic hypertension [5].

Several studies demonstrated that women with PIH are at greater risk of other medical conditions such as hypertension, cardiovascular diseases, diabetes mellitus and kidney diseases in later life [6]. Despite improvement and development in maternal and neonatal care, PIH is still considered a dreaded complication of pregnancy. Several tests have been proposed for predicting PIH in the antenatal period before the development of complications, but none have been accepted wisely due to their low predictive value. Human beta HCG is a glycoprotein with a lipid structure expressed in trophoblasts and various malignant tumors. Human placentas synthesize steroids, protein, and glycoprotein hormones throughout gestation [7]. Placental function changes in the form of increased serum beta HCG have been documented and several prospective studies indicate changes in the hormones that may be present before the clinical diagnosis of preeclampsia. Human chorionic gonadotropin has been acknowledged as a hormone for years. Recent studies have revealed its immunological face, so many of the newer applications of HCG are now confined to the immunological phase rather than the endocrinal phase [8]. Hence, serum beta HCG estimation at mid-trimester (13–20 weeks) is a good predictor of PIH, and high levels of beta HCG are associated with increased severity of PIH [9].

A study conducted at the Department of Obstetrics and Gynaecology, Lalla Ded Hospital, Srinagar, from April 2013 to September 2014 focused on maternal mid-trimester beta HCG Levels as a marker of subsequent pregnancy-induced hypertension development. In a study, 500 cases were initially enrolled. However, only 447 patients, 89.4%, could be evaluated for the final results. The 53 cases that were left out were due to missed abortions 08, spontaneous abortions 33, congenital malformations 12 and 10 were lost to follow-up. The mid-trimester period (13-20 weeks) was chosen for the current study as a time for estimating the Beta HCG Levels [10].

A total of 447 cases were finally evaluated; 387 patients (86.57%) had beta HCG levels < 02 MOM, whereas 60 cases (13.43%) had values > 02 MOM. The multiple of the median and Beta HCG values for that particular gestational age group were calculated. Of 387 cases with Beta HCG level <02MOM, only 06 cases (1.5%) developed PIH. In the remaining cases, 381 (98.5%) were normotensive, and out of 60 cases with beta HCG values > 02 MOM, 49 cases (81.66%) developed PIH, and only 11 cases (18.33%) were normotensive [11].

RATIONALE OF STUDY

In this study, I tried to find out whether the abnormal rise in beta HCG can predict the development of PIH. Our study focused on the role of maternal mid-trimester beta HCG levels as a marker of subsequent pregnancy-induced hypertension. If we found a high frequency of PIH in patients with raised Beta HCG in the second trimester, we closely monitored those females who had raised serum beta HCG for that period of gestation for early development of PIH and prescribed treatment to avoid complications.

OBJECTIVE

To determine the frequency of PIH in pregnant women with raised serum beta HCG in the second trimester

MATERIAL & METHODS

Study Design: Descriptive Study.

Study Setting: Department of Obstetrics & Gynaecology, Ziauddin University Hospital, Karachi.

Duration of Study: Six months after the approval of synopsis from April 19, 2019, to October 18, 2019.

Sample Size: Sample size was calculated using the WHO calculator by taking statistics for Prevalence P=81.66%, Margin of Error d=9%, and Confidence interval Cl=95% [2]. The estimated sample size was 72.

Sampling Technique: Non-Probability, Consecutive Sampling

SAMPLE SELECTION

Inclusion Criteria

- Pregnant women at 13 - 20 weeks of gestation calculated by date of last menstrual period with raised beta HCG or from dating scan at
- 12th week for confirmation of gestational stage.
- Women aged between 18-35 years.
- Women with singleton pregnancy confirmed with ultrasound.
- All primiparous and multiparous were included in the study.

Exclusion Criteria

- Patient with a history of chronic hypertension.
- Patient with a family history of Down's syndrome or previous child affected with Down's syndrome.
- Patients with a history of renal cardiovascular disease were excluded as they may contribute to hypertension.
- Patient with gestational trophoblastic diseases confirmed on ultrasound.

DATA ANALYSIS

All the collected data was entered into SPSS version 10. Quantitative variables, i.e. Age, gestational Age, gravida, and parity, were presented by Mean±SD (Standard Deviation). Qualitative variables, i.e. frequency of patients with PIH, were calculated. Stratification was done on Age, gestational age, gravida, parity, and serum beta HCG levels by applying a chi square test. P-value <0.05 was considered as significant.

In this study, 72 patients were included to evaluate pregnancy-induced hypertension (PIH) in pregnant women with raised serum beta HCG in the second trimester, and the results were analyzed as follows:

The mean ± SD of Age was 27.9±5.3 with C.I (26.65…….29.14) years, gestational Age was 17.3±4.2 with C.I (16.31…….18.28) weeks, gravida was 2.77±1.4 with C.I (2.77…….3.42), parity was 2.4±1.1 with C.I (2.14…….2.65) and serum beta HCG levels were 53,469.3±235.2 with C.I (53414…….53524.6) mIU/mL as shown in Table 01.

Table 01: Descriptive Statistics n=72

Descriptive Statistics n=72					
	Age	Gestational Age	Gravida	Parity	Serum β-HCG Levels
Mean	27.9 (Years)	17.3 (Weeks)	3.1	2.4	53469.3 (mIU/mL)
Standard deviation	5.3	4.2	1.4	1.1	235.2
95% confidence interval	26.65…….29.14	16.31…….18.28	2.77…….3.42	2.14…….2.65	53414…….53524.6
Minimum	18	13	0	1	26,300
Maximum	35	20	6	5	150,700
Range	17	7	6	4	124,400

The pregnancy-induced hypertension was observed in 56 (77.8%) women (Figure 1).

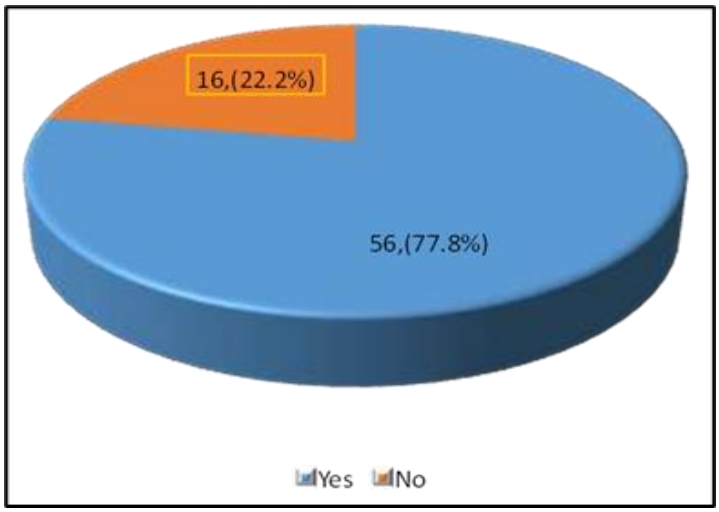

Figure 01: Frequency of Pregnancy Induced Hypertension n=72

Stratification of age group, gestational Age, gravida, parity, and serum beta HCG levels was done concerning pregnancy induced hypertension to assess significant differences (Table 2).

Table 2. Stratification of parameters with pregnancy-induced hypertension n=72

Age group [years]	Yes	No	P-value
18 – 25	22 (30.6%)	5 (6.9%)	0.390
>25	34 (47.2%)	11 (15.3%)	
Gestational Age [weeks]	**Yes**	**No**	**P-value**
13 – 16	42 (58.3%)	9 (12.5%)	0.146
>16	14 (19.4%)	7 (9.7%)	
Gravida	**Yes**	**No**	**P-value**
0 – 2	25 (34.7%)	13 (18.1%)	
>2	31 (43.1%)	3 (4.2%)	0.010
Parity	**Yes**	**No**	**P-value**
1 – 2	29 (40.3%)	12 (16.7%)	
>2	27 (37.5%)	4 (5.6%)	0.090
Serum β-HCG Levels	**Yes**	**No**	**P-value**
26,300 – 30,000	24 (33.3%)	11 (15.3%)	0.068
>30,000	32 (44.4%)	5 (6.9%)	

Applied Fisher's Exact test

DISCUSSION:

Hypertension and proteinuria are significant complications of pregnancy. Abnormal placentation is one of the essential pathologies for the development of GHT. Because of abnormal placentation, there may be an increased synthesis of beta HCG [12]. There may be deregulation of lipoprotein lipase in GHT-prone women, which causes elevated plasma lipid and lipoprotein levels and may induce endothelial dysfunction. The prominent pathology usually occurs in the early trimester (8-18 weeks), but signs and symptoms occur in the late trimester [13]. This study estimated serum beta HCG in the early second trimester; women with elevated levels were categorized under the high-risk group. So, it is easy to identify the high-risk women and keep them under regular follow-up. It helps in preventing the development of complications in GHT.

Hypertensive disorders of pregnancy are one of the most common complications of pregnancy and affect up to 8% of all gestation [14]. Pregnancy-induced hypertension, haemorrhage, and infection form a deadly triad contributing significantly to maternal morbidity and mortality rates. The exact mechanism of pregnancy-induced hypertension is unknown, no standards for prediction exist, and most facets of management are unclear, so management of pregnancy-induced hypertension remains challenging and

controversial. Reduction of maternal and perinatal mortality and morbidity due to pregnancy-induced hypertension is a high priority in the international community, and it is one of the millennium developmental goals [15].

The placenta is the known primary trigger of pregnancy-induced hypertension. Pathophysiological placental abnormalities are seen consistently to be associated with pregnancy-induced hypertension. Women with pregnancy-induced hypertension have hyper-paracentesis or abnormal placentation [16]. Hypoxic placental damage caused by hypertensive disorders results in relative hyperplasia of cytotrophoblastic cells and increased hormone β-hCG. Over the last decade, there has been enhanced awareness of predictors. Despite many predictors, the search is still for an ideal predictor due to the lack of more extensive randomized trials. Since the etiology is obscure, controversies in management prevail, leaving the clinician in a quandary.

The mean Age of the cases for the present study was 27.9±5.3 years. However, there was no statistically significant correlation found between Age and the occurrence of pregnancy-induced hypertension, which was in concordant with the results of a study conducted by AyselKabuku et al., who observed that there was no statistically significant difference between study and control groups concerning the maternal Age. Sharma V et al. [1] reported the mean Age as 24.66 years, while Rajesh A et al. [17] noted 27.08 years. The mean gestational Age was 17.3±4.2 weeks. The mean gravida was 2.77±1.4, and the mean parity was 2.4±1.1. In our study, the parity status of the mother was significantly associated with the occurrence of pregnancy-induced hypertension; the incidence was higher in the primigravidas as compared to the multiparas.

In a study conducted by some researchers, no significant correlation was found between parity and pregnancy-induced hypertension. The mean serum beta HCG levels was 53,469.3±235.2 mlU/mL.Similar results have been shown by Zhong et al., in which the author concluded a positive correlation between the absolute Beta-HCG levels and the severity of pregnancy-induced hypertension (p-value <0.05). The serum level of Beta-HCG in the mild pregnancy-induced hypertension group was 42,190±17,720 [18]. Rajesh A et al. [17] noted the serum level of Beta-HCG as 69808.66. In our study, pregnancy-induced hypertension was observed in 56 (77.8%) patients. Sharma V, et al [2] reported PIH in 387 (86.57%) cases. Moreover, 88.88% of patients had PIH in Murmu S et al. [20], whereas 72.8% in Rajesh A et al. [17]. In this study, stratification of confounders/effect modifiers concerning pregnancy-induced hypertension, the insignificant difference was noted in age group (P=0.390), gestational Age (P=0.146), gravida (P=0.010), parity (P=0.090) and serum beta HCG level (P=0.068). Pregnancy-induced hypertension is still a little-understood entity despite the enormous impact of its complications on maternal and fetal outcomes [21].

High serum β-hCG levels are a high-risk factor which helps us in the prediction of pregnancy-induced hypertension. Women with high serum β-hCG levels estimated at 12 to 24 weeks of gestation have a 1.67 times risk of developing pregnancy-induced hypertension [22]. The maternal and perinatal outcome was directly proportional to levels of serum β-hCG. Hypertensive disorders in pregnancy and their sequelae are a dreaded complication of pregnancy. There has been a constant attempt to identify the risk involved in pregnancy and its prediction. Prevention will follow if prediction is possible [23].

CONCLUSION

It is to be concluded that pregnancy-induced hypertension is found to be significantly high among pregnant women in our population. PIH is associated with maternal Age and perinatal outcomes. The results suggest that pregnant women and members of their families should be urgently educated to understand the importance of antenatal care. Additional studies are needed to confirm our findings probably with a larger sample size and with more parameters in multiple study centers in Pakistan to validate the results of the present study.

REFERENCES

1. Sharma V, Sharma P, Firdous N. Beta HCG in mid-trimester as a predictor of pregnancy induced hypertension. Int J Sci Res. 2016;5:303-5
2. Mitka M. Any hypertension during pregnancy raises risk for several chronic diseases. JAMA. 2013;309(10):971-2.
3. Mannisto T, Mendola P, Vaarasmaki M, Jarvelin MR, Hartikainen AL, Pouta A, et al. Elevated blood pressure in pregnancy and subsequent chronic disease risk. Circulation. 2013;127(6):681-90
4. Say L, Chou D, Gemmill A, Tunçalp Ö, Moller AB, Daniels J, et al. Global causes of maternal death: A WHO systematic analysis. Lancet Glob Health. 2014;2:e323–33
5. ACOG practice bulletin no. 203: chronic hypertension in pregnancy. Obstet Gynecol 2019;133:e26–50.

6. Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J, Blomström-Lundqvist C, Cifkova R, De Bonis M, et al. 2018 ESC guidelines for the management of cardiovascular diseases during pregnancy: the task force for the management of cardiovascular diseases during pregnancy of the European Society of Cardiology (ESC). Eur Heart J. 2018;39(34):3165241.
7. Magee LA, Pels A, Helewa M. Diagnosis, evaluation, and management of the hypertensive disorders of pregnancy: executive summary. J Obstet Gynaecol Can 2014; 36:416–41
8. Meah VL, Cockcroft JR, Backx K, Shave R, Stöhr EJ. Cardiac output and related haemodynamics during pregnancy: a series of meta-analyses. Heart 2016;102(7):518– 26.
9. Ngene NC, Moodley J. Role of angiogenic factors in the pathogenesis and management of preeclampsia. Int J Gynaecol Obstet 2018;141(1):5–13
10. Webster LM, Conti-Ramsden F, Seed PT, Webb AJ, Nelson-Piercy C, Chappell LC. Impact of antihypertensive treatment on maternal and perinatal outcomes in pregnancy complicated by chronic hypertension: a systematic review and meta-analysis. J Am Heart Assoc. 2017;6(5):e005526
11. Tucker KL, Bankhead C, Hodgkinson J, Roberts N, Stevens R, Heneghan C, et al. How do home and clinic blood pressure readings compare in pregnancy. Hypertension. 2018;72(3):686-94.
12. Tremonti C, Beddoe J, Brown MA. Reliability of home blood pressure monitoring devices in pregnancy. Pregnancy Hypertens. 2017;8:9–14.
13. Shekhar S, Gupta N, Kirubakaran R, Pareek P. Oral nifedipine versus intravenous labetalol for severe hypertension during pregnancy: a systematic review and metaanalysis.BJOG 2016;123(1):40–7.
14. Rolnik DL, Wright D, Poon LC, O'Gorman N, Syngelaki A, de Paco Matallana C, et al. Aspirin versus placebo in pregnancies at high risk for preterm preeclampsia. N Engl J Med 2017;377:613–22
15. . Stott D, Bolten M, Salman M, Paraschiv D, Douiri A, Kametas NA. A prediction model for the response to oral labetalol for the treatment of antenatal hypertension. J Hum Hypertens. 2017;31(2):126–31.
16. Bateman BT, Heide-Jørgensen U, Einarsdóttir K, Engeland A, Furu K, Gissler M, et al. βblocker use in pregnancy and the risk for congenital malformations: an international cohort study. Ann Intern Med 2018; 169(10):665–73
17. Rajesh A, Muralidharan V. Serum beta hCG in early second trimester as a predictor of gestational hypertension. Int J Reprod Contracept Obstet Gynecol. 2018;;7(6):2356
18. Zhong Y, Zhu F, Ding Y. Serum screening in first trimester to predict preeclampsia, small for gestational Age and preterm delivery: systematic review and meta-analysis. BMC Pregnancy Childbirth. 2015;15:191
19. 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 Appl Basic Med Res. 2020; 10(1):49.
20. Bateman BT, Patorno E, Desai RJ, Seely EW, Mogun H, Maeda A, et al. Late pregnancy beta blocker exposure and risks of neonatal hypoglycemia and bradycardia. Pediatrics. 2016;138(3):e20160731.
21. Eriksen NB, Damm P, Mathiesen ER, Ringholm L. The prevalence of congenital malformations is still higher in pregnant women with pregestational diabetes despite near-normal HbA1c: a literature review. J Matern Fetal Neonat Med. 2019;32(8):1225-9
22. Riccetti L, Yvinec R, Klett D, Gallay N, Combarnous Y, Reiter E, et al. Human luteinizing hormone and chorionic gonadotropin display biased agonism at the LH and LH/CG receptors. Sci Rep. 2017;7(1):1-1.
23. Koistinen H., Hautala L., Koli K., Stenman UH Absence of TGF-β receptor activation by highly purified hCG preparations. Mol Endocrinol. 2015;29:1787–91