DOI: https://doi.org/10.53350/pjmhs221610793

ORIGINAL ARTICLE

Predicting the Frequency of Pregnancy Induced Hypertension in Early Pregnancy by Maternal Serum Beta Human Chorionic Gonadotropin Levels

FAKHRA ASHIQUE[1], AMMARA NADEEM[2], NASREEN REHMATULLAH[3], JAVAIRA MUMTAZ[2], ANISA SALEEM[2], RIZWANA GUL[2]
[1]*Senior Registrar Gyae & Obs Department, AJKMC Muzaffarabad*
[2]*Senior Registrar Gyae & Obs Department, HBS Medical and Dental College, Islamabad*
[3]*Consultant Gynaecologist, KRL hospital, Islamabad*
Corresponding author: Fakhra Ashique, Email: drfakhragardezi@gmail.com

ABSTRACT

Background: During early pregnancy raised beta human chorionic gonadotropin (β-HCG) level occurs during placental development. It may be used for identifying the pregnancy induced hypertension. There are certain factors that causes pregnancy induced hypertension and preeclampsia. However, many of the associated factors and specific cause is not known. Some common risk factors for preeclampsia are nulliparity, preeclampsia in a previous pregnancy, family history, history of hypertension, renal disease and antiphospholipid antibody syndrome or thrombophilia. However no single lab investigation can be done cost-effectively to make the early diagnosis of pregnancy induced hypertension. The objective of this study was to determine the frequency of Pregnancy induced hypertension in patients with high maternal serum β-HCG at early pregnancy (13-20 weeks of gestation).

Methodology: A descriptive cross sectional study was conducted on Out Patient Department and in patient wards of the Obstetrics and Gynecology Department of KRL General Hospital, Islamabad. The study was done from 28th December 2018 to 27th June 2019. A total of 75 pregnant women, primary gravida and multi gravida with age range from18-40years with raised β-HCG at 13-20 weeks of gestation were included. All patients were observed during their stay in the hospital for the development of any complications of pregnancy induced hypertension.

Results: Mean age of pregnant females was 32.12 ± 5.29 years. Mean gestational period was 17.31 ± 2.05 weeks. Mean β-HCG levels was 7.63±3.71. Pregnancy induced hypertension (PIH) in patients with high maternal serum β-HCG at 13-20 weeks of gestation was found in 64 (85.33%) patients, however there was no Pregnancy induced hypertension in 11 (14.65%) ladies.

Conclusion: The outcome of this study concluded that frequency of pregnancy induced hypertension in pregnant femal with high maternal serum β-HCG at 13-20 weeks of gestation was high. Early screening of raised β-HCG can be made for the prevention of complications due to pregnancy induced hypertension.

Keywords: Beta Human chorionic gonadotropin, pre-eclampsia, pregnancy induced hypertension.

INTRODUCTION

Pregnancy induced hypertension may lead to poor pregnancy outcome. It can be determined during pregnancy to prevent the complications. It is considered as pregnancy related hypertension and preeclampsia. Pregnancy realted hypertension is defined as: “systolic blood pressure 140 mmHg and a diastolic blood pressure 90 mmHg, in the absence of proteinuria in a previously normotensive pregnant woman at or after 20 weeks of gestation”.(1) Pregnancy related hypertension is common complications of pregnancy. It complicate approximately 12-24% of all pregnancies.(2) It is an important risk factor in pregnant women which is associated with increased maternal morbidity and mortality.

The presentation of pregnancy induced hypertension varies among females. It may be labelled as mild, moderate or severe symptoms. Some females may present with proteinuria, eclampsia, preterm labour. Severe complication may also manifest as haemolysis elevated liver enzymes (HELP) syndrome, fetus death is the another severe outcome.(3)

. There are certain factors that causes pregnancy induced hypertension and preeclampsia. However, many of the associated factors and specific cause is not known. Some common risk factors for preeclampsia are nulliparity, preeclampsia in a previous pregnancy, family history, history of hypertension, renal disease and antiphospholipid antibody syndrome or thrombophilia.

The most common complication of pregnancy with poor maternal and child outcome is with pregnancy induces hypertension. Almost 5 to 10 percent pregnancy complications are related to it.(4) Pregnancy induced hypertension (PIH) is associated with certain conditions like proteinuria and edema. These clinical manifestation usually occurs during late pregnancy and regresses after delivery of fetus. Even with good antenatal care to pregnant female the outcome of PIH is very dreadful. The obstetricians try to predict and identify the risks leading to PIH for controlling the outcome. If diagnosed early, then prevention will be possible naturally. An effective prediction would be possible by surveillance of mothers at high risk of PIH to reduce the risk of complications.(3)

There have been many tests performed to predict early diagnosis of PIH, but due to their less sensitivity they are not commonly used. Only two markers, maternal serum free β-human chorionic gonadotrophin (free β-hCG) and pregnancy associated plasma protein-A (PAPP-A) are widely used due to their more predictive value.(5) In a study it was found that during mid-trimester, immunological changes occur in the trophoblasts. It gives secretory response, which is seen as a rise in the beta HCG levels. Hence high βHCG production in late first and early second trimester where there is placental development taking place, it may be used as an indicator of identifying women at risk for pregnancy induced hypertension.(6) In a study, prevalence of pregnancy induced hypertension was found in 83.33% with raised beta HCG levels >2MOM. Also the sensitivity and specificity of beta HCG in predicting pregnancy induced hypertension was 90.91% and 97.44% respectively. In another study, the sensitivity and specificity of beta HCG in predicting pregnancy induced hypertension was found as 83.3% and 96.9% respectively.(7)

The human beta-hCG is with lipid structure that is present in trophoblast and various malignant tumors as a glycoprotein. The function of Human placenta is that it synthesizes hormones, protein, and glycoprotein hormones throughout gestation. These hormones are required for implantation and maintenance of viability of pregnancy. So it is known that preeclampsia is due to trophoblastic disorder and the diagnosis in early pregnancy can be made by it.(8) Preeclampsia is related to increase beta hcg level at 13-20 weeks gestation. 95% prevalence rate of PIH was found in women having serum beta hCG > 40,000 mIU/ml at second trimester of pregnancy.(9)

The aim of this study was to predict PIH by raised serum beta hCG at 13-20 weeks of gestation so that we can take preventive measures in order to reduce the maternal and neonatal morbidity and mortality, and risk stratify patients and manage them accordingly.

METHODOLOGY

Objective: To determine the frequency of Pregnancy induced hypertension in patients with high maternal serum beta hCG early gestational period.

Operational definitions: Pregnancy induced hypertension (PIH) is defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg in a previously normotensive pregnant woman who is ≥ 20 weeks of gestation at two different occasions.(10)

Serum Beta hCG: Unexplained elevation of beta HCG has been defined with cut-offs varying from > 4.0 MoM.

Study design: Descriptive cross sectional.

Setting: Out Patient Department (OPD) and in patient wards of the Obstetrics and Gynecology Department of KRL General Hospital, Islamabad.

Duration of study: 28th December 2018 to 27th June 2019.

Sample size: By standard Formula for sample size estimation, sample size was 75 patients

With confidence interval = 95%

5% margin of error

95% prevalence rate of PIH in women having raised serum beta hCG .

Sample technique: Convenience sampling.

Sample selection:

A Inclusion Criteria:

- All pregnant women, primary gravida and multi gravida regarding age 18-40yrs with raised beta HCG at 13-20 weeks of gestation (confirmed on USG).

Exclusion Criteria:

- Patients with diseases like chronic hypertension, renal disease, heart disease, diabetes, epilepsy or women with twin pregnancy.

Data collection and analysis: All the information was collected on preformed questionnaire. Institutional ethical committee approval of study was taken before commencement. Verbal informed consent was obtained from all patients. The funding was by researcher and department. Primary gravida and multigravida at 13-20 weeks of gestation with raised beta HCG were enrolled in this study who fulfilled the above mentioned inclusion criteria. All patients were observed during their stay in the hospital for development of any complications that is PIH by the researcher. Follow up was done till delivery. For Follow up address and contact numbers were noted.

The data was entered and analyzed using Statistical Package for Social Sciences version 23. Descriptive statistics like mean (standard deviation) were calculated for age, weight, BP and serum beta hCG levels. Frequency and percentages were measured for PIH, parity, family history of PIH (yes/no), past history PIH (yes/no) and dyslipidemia (yes/no). Chi-square test of significance was applied with P-value <0.05 taken as level of significance.

RESULTS

Age range in this study was reproductive age from 18 to 40 years with mean age of 32.12 ± 5.29 years. Majority of the females 46 (61.33%) were between 30 to 40 years of age.

Mean gestational age was 17.31 ± 2.05 weeks. the frequency distribution according to gestational age is shown in figure 1. Mean weight was 65.33± 7.51 kg. Mean systolic blood pressure was 162.69±11.48 mmHg and diastolic blood pressure was 106.28±9.87 mmHg. Mean β-hCG levels were 7.63±3.71.

Distribution of patients according to parity and family history, past history of PIH and dyslipidemia is shown in table 1.

PIH in patients with high maternal serum beta HCG at 13-20 weeks of gestation was found in 64 (85.33%) females, whereas there was no PIH in 11 (14.65%) females as shown in Figure 2.

When comparison of PIH was done statistically on age groups, it was found that there was no significant difference between different age groups also with respect to gestational age, parity and family history of PIH has shown no significant difference between different groups (table 2).

Table 1: Frequency Distribution of patient's characteristics (n=75).

	No.of patients	Percentage
Parity Primigravida Multigravida	 31 44	 41.3 58.67
Previous history of PIH Yes No	 18 57	 24.0 76.0
Family history of PIH Yes No	 38 37	 50.67 49.33

Table 2: Association of pregnancy induced hypertension with patient's characteristics.

Characteristics of patients	PIH		p-value
	Present	Absent	
Parity Primary gravida Multigravida	28 (90.32%) 36 (81.82%)	03 (9.68%) 08 (18.18%)	0.305
Gestational age 13-17 18-20	29 (87.88%) 35 (83.33%)	04 (12.12%) 07 (16.67%)	0.581
Family history of PIH Yes No	32 (84.21%) 32 (86.49%)	06 (15.79%) 05 (13.51%)	0.781
Dyslipidemia Present Absent	21 (84.0%) 43 (86.0%)	04 (16.0%) 07 (14.0%)	0.817
Beta HCG	64(85.33%)	11(914.65%)	0.000

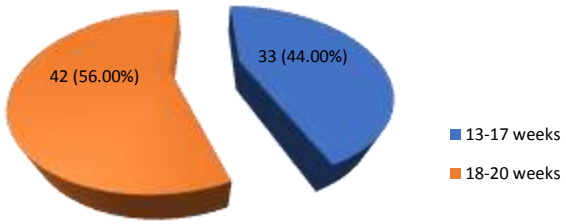

Figure 1: Frequency distribution of patients according to gestational age

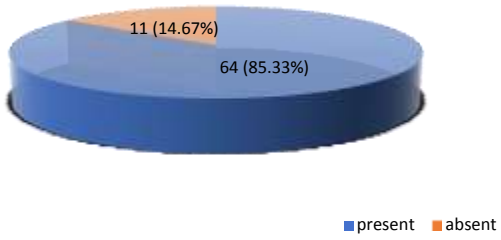

Figure 2: Frequency of pregnancy induced hypertension among patients with raised beta HCG

DISCUSSION

This study was carried out to predict the pregnancy induced hypertension (PIH) during early pregnancy by raised beta HCG level. The findings revealed that raised level of βHCG was significantly related to PIH.

In relation to this a study conducted on Iranian women revealed that high level of βHCG was significantly associated with early detection of preeclampsia. (5)

Majority of the females were in age group between 30 to 40 years. The age of women and gestational age were described as predicting risk factors in causing pre-eclampsia and PIH in previous study.(11) High level of maternal serum beta HCG at 13-20 weeks of gestation was found in majority of women. In another study, prevalence of pregnancy induced hypertension was also more with raised βHCG. There was 97.44% sensitivity and specificity of beta HCG in predicting pregnancy induced hypertension. (12)

In another prospective cohort study, among 190 pregnant women,13.1% developed PIH. Among them who developed gestational hypertension 88% were having β HCG levels >2 MOM ($p<0.001$). Absolute β HCG levels were also raised in them ($p<0.001$). Sensitivity(82.7) specificity(95.9), positive predictive value (80.1) and the negative predictive value (97.4) for β HCG at >2 MOM were determined at 95% CI.(13)

In another study conducted in Japan it was found that human chorionic gonadotropin (β-HCG), and malondialdehyde, a marker of oxidative stress when carried out on 52 primigravidae women and in 48 multigravida women at 15-20 weeks of gestation, the results showed 19 women developed pre- eclampsia and β-hCG levels were significantly ($P<0.001$) elevated in these pregnant females as compared to the females who not developed pre-eclampsia.(14)

A study conducted on 610 pregnant women in China, the multiple of median (MOM) of beta HCG showed that women with raised early pregnancy human chorionic gonadotropin levels are at more risk to develop preeclampsia with odds ratio 6.03 at 95 % confidence interval 1.87 to 16.88).(4) No significant difference was found for maternal serum-free β-HCG concentration at first trimester in normotensive females and those that develop pre-eclampsia.(15). In contrary to our findings another study suggested that the level of β-hCG and inhibin-A at second trimester can be useful in predicting women who were at high risk for adverse pregnancy outcomes and pre-eclampsia.(16)

An association between the PIH and βeta HCG was determined in our study while no other demographic variable showed any association. A study conducted in Iraq also showed same findings with no significant difference with age of women and gestational age but a significant difference with βHCG level ($p < 0.01$).(17) The study concluded that the β-HCG level could be used as a marker in determining PIH.

Another study conducted in Istanbul, compared β-hCG levels in 85 females suffering from mild pregnancy induced hypertension, severe PIH, superimposed hypertension and chronic hypertension with 25 normotensive pregnant females. The results showed that the β-HCG level in females with severe PIH was significantly more than those in others ($p<0.001$).(18)

In another study aimed at assessing the serum level of β-HCG after second trimester of pregnancy, females with elevated β-HCG levels in the second trimester of their pregnancies were found to be at more risk for pre-eclampsia.(19)

The outcome of pregnancy induced hypertension is related to increase in mortality and morbidity of mother and neonate. Early screening is important to prevent the complications of pre-eclampsia. (20) Intension to improve maternal and neonatal outcomes is achieved by universal protocol of early screening as well as preventive and promotive strategies.(21)

CONCLUSION

This study concluded that frequency of pregnancy induced hypertension in pregnant females with raised level of maternal serum beta HCG at early pregnancy (13-20 weeks of gestation) is very high. It is recommend that serum β-HCG levels in early pregnancy should be done as a screening tool in every pregnant females to predict pregnancy induced hypertension in order to reduce the maternal and neonatal morbidity, mortality and poor pregnancy outcome.

REFERENCES

1. Tsakiridis I, Giouleka S, Arvanitaki A, Giannakoulas G, Papazisis G, Mamopoulos A, et al. Gestational Hypertension and Preeclampsia: An Overview of National and International Guidelines. Obstet Gynecol Surv. 2021;76(10):613-33.
2. Mol BWJ, Roberts CT, Thangaratinam S, Magee LA, de Groot CJM, Hofmeyr GJ. Pre-eclampsia. Lancet. 2016;387(10022):999-1011.
3. Xiong Y, Xia HX, Wang YS, Lin XL, Zhu TT, Zhao Y, et al. [High risk factors analysis of stillbirth]. Zhonghua Fu Chan Ke Za Zhi. 2017;52(12):811-7.
4. He M, Sun X, Wang C, Sui Y. Analysis of the risk of complications during pregnancy in pregnant women with assisted reproductive technology: a retrospective study using registry linkage from 2013 to 2018 in Shanghai, China. BMC Pregnancy Childbirth. 2022;22(1):526.
5. Honarjoo M, Kohan S, Zarean E, Tarrahi MJ. Assessment of β-human-derived chorionic gonadotrophic hormone (βhCG) and pregnancy-associated plasma protein A (PAPP-A) levels as predictive factors of preeclampsia in the first trimester among Iranian women: a cohort study. BMC Pregnancy Childbirth. 2019;19(1):464.
6. Long W, Zhou Q, Wang H, Lu B, Chen Y, Zhang B, et al. Second-trimester Maternal Serum Screening Biomarkers in the Risk Assessment for Preeclampsia. Ann Clin Lab Sci. 2018;48(3):308-13.
7. Chen Y, Ning W, Chu X, Chen Y, Gu L, Xie Z, et al. Predicting Hypertensive Disease in the First Trimester of Pregnancy: Risk Models and Analysis of Serum D-dimer Levels Combined with Plasma Pregnancy-Associated Protein A, Free β-Subunit of Human Chorionic Gonadotropin, and Fetal Nuchal Translucency. Biomed Res Int. 2022;2022:8264958.
8. Parry S, Carper BA, Grobman WA, Wapner RJ, Chung JH, Haas DM, et al. Placental protein levels in maternal serum are associated with adverse pregnancy outcomes in nulliparous patients. Am J Obstet Gynecol. 2022;227(3):497.e1-.e13.
9. Svirsky R, Levinsohn-Tavor O, Feldman N, Klog E, Cuckle H, Maymon R. First- and second-trimester maternal serum markers of pre-eclampsia in twin pregnancy. Ultrasound Obstet Gynecol. 2016;47(5):560-4.
10. Chen Y, Chen Y, Wang X, Chu X, Ning W, Gu L, et al. Second trimester maternal serum D-dimer combined with alpha-fetoprotein and free β-subunit of human chorionic gonadotropin predict hypertensive disorders of pregnancy: a systematic review and retrospective case-control study. J Transl Med. 2021;19(1):94.
11. Wright D, Wright A, Nicolaides KH. The competing risk approach for prediction of preeclampsia. Am J Obstet Gynecol. 2020;223(1):12-23.e7.
12. Panwar M, Kumari A, Hp A, Arora R, Singh V, Bansiwal R. Raised neutrophil lymphocyte ratio and serum beta hCG level in early second trimester of pregnancy as predictors for development and severity of preeclampsia. Drug Discov Ther. 2019;13(1):34-7.
13. Zhang X, Huangfu Z, Shi F, Xiao Z. Predictive Performance of Serum β-hCG MoM Levels for Preeclampsia Screening: A Meta-Analysis. Front Endocrinol (Lausanne). 2021;12:619530.
14. Zhang H, He Y, Wang JX, Chen MH, Xu JJ, Jiang MH, et al. miR-30-5p-mediated ferroptosis of trophoblasts is implicated in the pathogenesis of preeclampsia. Redox Biol. 2020;29:101402.
15. Yu N, Cui H, Chen X, Chang Y. First trimester maternal serum analytes and second trimester uterine artery Doppler in the prediction of preeclampsia and fetal growth restriction. Taiwan J Obstet Gynecol. 2017;56(3):358-61.
16. Neuman RI, Alblas van der Meer MM, Nieboer D, Saleh L, Verdonk K, Kalra B, et al. PAPP-A2 and Inhibin A as Novel Predictors for Pregnancy Complications in Women With Suspected or Confirmed Preeclampsia. J Am Heart Assoc. 2020;9(19):e018219.
17. Taher SI, Alalaf SK. Association between serum beta-human chorionic gonadotropin and preeclampsia and its effects on perinatal and maternal outcomes: a case control study. Arch Gynecol Obstet. 2019;299(3):713-8.
18. Asiltas B, Surmen-Gur E, Uncu G. Prediction of first-trimester preeclampsia: Relevance of the oxidative stress marker MDA in a combination model with PP-13, PAPP-A and beta-HCG. Pathophysiology. 2018;25(2):131-5.
19. Bokslag A, van Weissenbruch M, Mol BW, de Groot CJ. Preeclampsia; short and long-term consequences for mother and neonate. Early Hum Dev. 2016;102:47-50.
20. Boutin A, Gasse C, Guerby P, Giguère Y, Tétu A, Bujold E. First-Trimester Preterm Preeclampsia Screening in Nulliparous Women: The Great Obstetrical Syndrome (GOS) Study. J Obstet Gynaecol Can. 2021;43(1):43-9.
21. Agrawal A, Wenger NK. Hypertension During Pregnancy. Curr Hypertens Rep. 2020;22(9):64.