Journal of Research in Medical and Dental Science
Volume 5, Issue 6, Page No: 6-13

Available Online at: www.jrmds.in
eISSN No. 2347-2367: pISSN No. 2347-2545

Prevalence of Persistent Hypertension Following Delivery Complicated by Hypertensive Disorders and Related Obstetric and Laboratory Risk Factors

Tahereh Ashraf Ganjoei[1], Sara Defaee[1]*, Eznollah Azargashb[2], Sahar Defaee[1]

[1]Preventative Gynecology Research center (PGRC), Ground Floor, Emam Hossein Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[2]Department of health and social medicine, School of medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

DOI: 10.24896/jrmds.2017562

ABSTRACT

This study examined prevalence of persistent hypertension following delivery complicated by hypertensive disorders and related obstetric and laboratory risk factors. This prospective cohort study was conducted in a teaching medical center on 270 women with more than 20 weeks of gestation who were admitted for examination and management of high blood pressure. The patients were followed up for blood pressure in two visits at 6 and 12 weeks postpartum. After 12 weeks, women were assigned to three groups of healthy, pre-hypertension and persistent hypertension. Background information was reviewed to find independent factors associated with persistency of blood pressure using statistical t-test and logistic regression. In bivariate analysis, relative risk of persistent hypertension was estimated at 95% confidence interval. Of 270 patients (46.2%), 110 patients developed persistent hypertension. Among risk factors, high BMI, delivery in less than 34 weeks of pregnancy, history of preeclampsia, history of diabetes, severe preeclampsia and drug control for PIH were independently associated with persistent hypertension. Abnormal laboratory findings included thrombocytopenia, increased serum uric acid and serum creatinine and severe proteinuria associated with this disorder (P <0.05). Almost one in every two pregnant women with hypertensive disorders was prone to postpartum persistent hypertension. This risk particularly increased in maternal obesity, preterm birth due to preeclampsia and abnormal laboratory findings indicating severe preeclampsia. Therefore, more detailed follow-up of high-risk patients is recommended in puerperal visits for diagnosis and timely treatment.

Keywords: Preeclampsia, Parturition, Pregnancy-Induced Hypertension

HOW TO CITE THIS ARTICLE: Tahereh Ashraf Ganjoei, Sara Defaee, Eznollah Azargashb, Sahar Defaee, Prevalence of Persistent Hypertension Following Delivery Complicated by Hypertensive Disorders and Related Obstetric and Laboratory Risk Factors, J Res Med Dent Sci, 2017, 5 (6): 6-13, DOI: 10.24896/jrmds.2017562

Corresponding author: Sara Defaee
e-mail✉ *sara.defaee@chmail.ir*
Received: 15/06/2017
Accepted: 20/09/2017

INTRODUCTION

Hypertensive disorders are one of the most controversial problems in the field of obstetrics. These disorders generally occur in 5-10% of all pregnancies. With a global study of maternal mortality by 2006, the World Health Organization (WHO) concluded that hypertensive disorders accounted for 16% of maternal death. The ratio is higher than three other main causes, i.e. hemorrhage (13%), abortion (8%) and sepsis (2%). According to studies, more than half of the deaths associated with hypertensive disorders were preventable. In the past 20 years, the obtained evidence shows that pregnancy-induced hypertensive (PIH) disorders suggest next incidence of cardiovascular mortality. Pregnant women who develop these disorders, particularly preeclampsia, should be followed-up regularly

during the first few months postpartum for prevention, early diagnosis and treatment. PIH disorders complicate 5 to 10% of pregnancies. In addition to infection and obstetric hemorrhage, PIH is an important factor in increasing the rate of maternal mortality, particularly in developed countries. According to WHO systematic review of maternal deaths in 2006, PIH accounted for more than 16% of maternal deaths in developing countries. This ratio is higher than other factors such as obstetric hemorrhage (13%), abortion (8%) and infections (2%) [1]. PIH is prevalent in 6-8% of pregnancies, involving a spectrum of symptoms associated with high blood pressure. According to a new updated classification based on ACOG 2013, disorders are divided into 4 groups [2]:

1. Gestational hypertension
2. Eclampsia and preeclampsia syndromes
3. Chronic hypertension of any previous etiology
4. Preeclampsia syndrome superimposed on chronic hypertension

One of the important features of this classification is differentiation of preeclampsia syndrome from other hypertensive disorders. Preeclampsia syndrome is potentially more dangerous and is considerably different from other groups in terms of etiology, pathogenesis and treatment of clinical disorders [3]. Preeclampsia is an idiopathic, multi-member disorder which occurs in pregnancy and accounts for 3.9% of complications. In addition to obstetric complications such as placental abruption, uteroplacental disorders and IUGR, preeclampsia is the most effective factor in causing chronic hypertension and its postpartum complications. Preeclampsia primarily infects primiparous and young women (3-10%), while older pregnant women mostly develop preeclampsia superimposed on chronic hypertension [3]. Genetic, racial, environmental, socio-economic and even seasonal factors are effective on incidence of preeclampsia [4]. Some other risk factors of preeclampsia include obesity, multiple pregnancies, nulliparity, maternal age (over 40 years and less than 20 years) [5], hyperhomocysteinemia, diabetes and metabolic syndrome [6,7]. Paradoxically, smoking has been reported as a protective factor against high blood pressure in pregnancy [3]; however, it certainly plays an important role in long-term vascular complications leading to hypertensive disorders. Reducing role of smoking seems to be related to increase in hypoxia-induced placental Adrenomedullin gene expression due to smoking and ultimately increased trophoblast invasion and better conservation of vascular homeostasis [4,8]. There is a progressive relationship between PIH and maternal BMI. By maternal weight gain in BMI>35, approximately 13% prevalence of PIH has been reported versus 2% disorders in women with normal weight [3]. By definition, PIH returns to normal usually after 12 weeks postpartum. Postpartum hypertension can be classified as persistent blood pressure following preeclampsia, persistent chronic hypertension before pregnancy or new incidence of hypertension after uncomplicated pregnancies (primary and secondary) [3]. There is conflicting data about certain time of normal blood pressure after delivery. The reason for this may be due to differences in the populations studied, intensity of the factors causing hypertension (severe preeclampsia and related syndromes or severe chronic hypertension during pregnancy), duration and frequency of follow-up and the criteria used to determine persistent postpartum hypertension. In most women with gestational HTN, blood pressure usually returns to normal within a week postpartum [9]. This is different in patients with preeclampsia, because the body needs more time in recovery phase of preeclampsia to compensate the damage on systemic and renal vascular endothelium; this time has been estimated at 2 weeks for patients with preeclampsia. In all patients with PIH, blood pressure should return to normal by 12 weeks postpartum [3]. Due to the increased risk of persistent blood pressure following preeclampsia compared with normotensive women, these patients need to be followed up after delivery [3,10]. In particular, recent studies showed that patients with some risk factors for preeclampsia developed chronic hypertension in the postpartum follow-up sooner than other patients. Some of these factors included preterm preeclampsia (less than 34 weeks), maternal age, persistent proteinuria, abnormal levels of renal function parameters (creatinine and uric acid) [5]. Using puerperal follow-up visits, these complications can be prevented in many cases even without medical treatment by early diagnosis and preventive cares, lifestyle changes such as weight loss and diet, medication and more stringent follow-up in patients with underlying risk factors [11]. In fact, diagnosis and management of postpartum hypertensive disorders requires a multi-disciplinary approach

relying on risk factors before pregnancy, time of incidence, associated symptoms and paraclinical examinations. The limited studies conducted on acute or chronic postpartum hypertension are generally related to patients with a sharp rise in blood pressure in 2-6 days postpartum or those readmitted due to new incidence of preeclampsia, eclampsia, HELLP syndrome or acute complications related to high blood pressure. In general, prevalence of hypertension de novo with or without puerperal preeclampsia has been reported at 0.3-27.5% [12,13]. Several studies confirmed that the incidence of PIH indicates the increased risk of morbidity and mortality and long-term cardiovascular consequences are greater in all cases than normotensive mothers [6]. Unfortunately, these patients are not diagnosed and treated for a long time (at least until the next pregnancy) due to lack of regular visits and lack of follow-up; this will lead to long-term cardiovascular complications. In recent decades, many studies have been conducted on incidence, risk factors, pathogenesis, predictive factors, prevention and treatment of preeclampsia. However, little is known about diagnosis of persistent postpartum hypertension. The limited studies conducted in this field are primarily based on prenatal care, prepartum care or patients hospitalized due to acute complications of postpartum hypertension. To prevent long-term cardiovascular, brain and renal complications, it is essential to consider follow-up, early diagnosis and treatment of persistent postpartum hypertension. This study examines prevalence of persistent hypertension following delivery complicated by hypertensive disorders and related obstetric and laboratory risk factors. In addition, this study evaluates the effect of hypertensive disorders in pregnancy, maternal age, parity and high BMI on incidence of persistent postpartum hypertension.

MATERIALS AND METHODS

This project was conducted in the form of a prospective cohort study in Imam Hussein Teaching Medical Center affiliated to Shahid Beheshti University of Medical Sciences and Health Services in 2013-2014. At least 70% sensitivity was expected for prediction of people with regard to previous studies. Since about 18% prevalence of postpartum hypertensive disorders was reported in these patients, about 18% of cases were expected to be positive. Thus, the required sample size was estimated at 260 cases. Therefore, 260 women with more than 20 weeks of pregnancy diagnosed with PIH (with or without preeclampsia) and admitted to maternity ward of Imam Hussein Hospital in 2013-2014 enrolled in the study. Inclusion criteria included diagnosis of a hypertensive disorder including preeclampsia, eclampsia, HELLP and PIH. Exclusion criteria included previous diagnosis of essential or chronic HTN, history of hypertension in the first trimester, history of known renal or cardiac disease. After obtaining informed consent, demographic and obstetric information, medical history and risk factors of preeclampsia were recorded in a questionnaire. In cases of uncertain information, prenatal care records were used to complete the questionnaire. Laboratory findings (biochemistry, CBC, urinary protein) were recorded on admission. Course of blood pressure during hospital stay, need for medication to control blood pressure and blood pressure at discharge were recorded. In diagnosis of PIH and the need for immediate termination of pregnancy due to hypertensive disorder, its type and severity were recorded by the definition provided. Phone calls were made for follow-up once at the end of the sixth week and the other after the end of the twelfth week postpartum. Unfortunately, some subjects were excluded because of not responding (26), change of residence (3), obstetric causes (4) and maternal death due to hypertensive disorder (1 TTP). In addition to usual postpartum cares, blood pressure of patients was recorded by a manual manometer in seating position and twice within 30 minutes after rest for half an hour. The patients were referred to the cardiologist for antihypertensive therapy in both visits in case of BP ≥160.90 or ≥140.90 or at least two cardiovascular risk factors (obesity, smoking, dyslipidemia, personal or family history). According to the reference cardiovascular standard, postpartum hypertension was classified as follows (Table 1):

After the second visit, the patients with persistent BP>120.80 were assigned to healthy, pre-hypertension and persistent hypertension groups. The patients with persistent hypertension were referred to cardiologist. According to the prenatal information recorded in the questionnaire, risk factors of preeclampsia, its severity and initial laboratory parameters were compared between these two groups. Mean ± standard deviation and frequency (%) were used to describe data. Chi-

square test (or exact Fisher's test, if necessary) was used to examine the relationship between nominal variables. Ordinal variables were compared between different groups by Mann-Whitney test. T-test was used to compare normally distributed variables. Multiple logistic regression was used to find a scoring method for predicting persistent hypertension (P-value<0.05).

RESULTS

Of 270 pregnant women eligible for the study, 238 patients received two follow-up visits at 6 and 12 weeks postpartum. Prevalence of persistent postpartum hypertension was estimated at 46.2%. Figure 1 shows frequency of different PIH disorders and Figure 2 shows Severity of prenatal PIH in the studied mothers also Figure 3 shows frequency of PIH types in three BP groups at week 12 postpartum and Figure 4 shows Severity of hypertension at week 12 postpartum.

A significant relationship was observed between increased PIH and persistent hypertension. For example, PIH BP>180mmHg significantly increased the risk of persistent hypertension 9 times (Table 2).

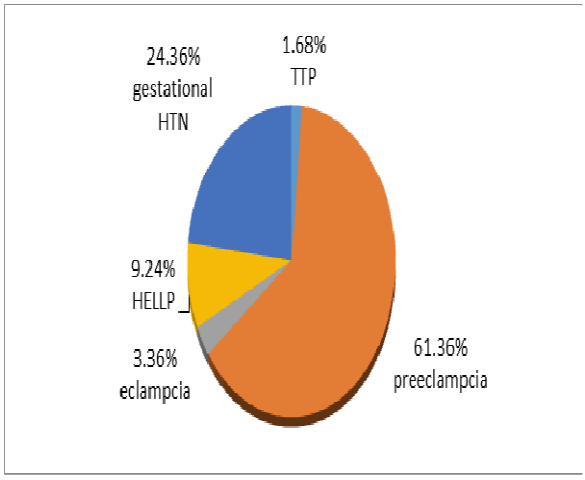

Figure 1: Frequency of prenatal PIH disorders in the studied population

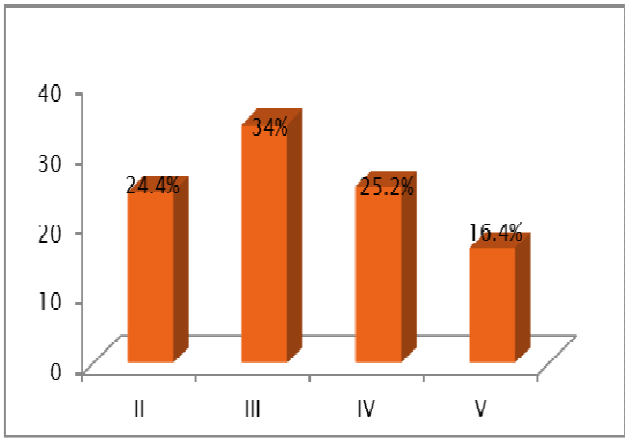

Figure 2: Severity of prenatal PIH in the studied mothers

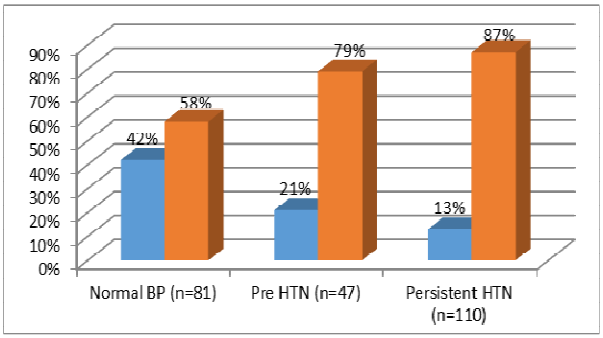

Figure 3: Frequency of PIH types in three BP groups at week 12 postpartum (blue: gestational HTN; red: preeclampsia)

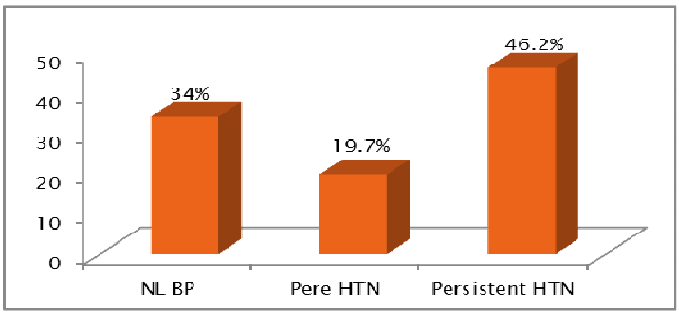

Figure 4: Severity of hypertension at week 12 postpartum

The studied patients aged 14-45 years (mean 29.58); 12% of mothers were younger than 20 and 18% were older than 40 years. Mean maternal BMI was 28.43 and 30.2% of mothers had BMI>35. In comparison of above demographic parameters in three groups, age and parity were not significantly different, while BMI>35 (P=0.051) and gestational age <34 weeks (P=0.001) were significantly higher in patients with persistent HTN (Table 3). In examining the relationships between PIH risk factors and persistent postpartum hypertension, gestational hypertension, preeclampsia, severe preeclampsia symptoms, history of gestational diabetes and the need for blood pressure control during pregnancy had significant relationships (Table 3). In comparison of abnormal laboratory parameters, platelet count <105, severe proteinuria (+3 or +4), serum uric acid ≥ 3/6 and serum creatinine ≥1 were significantly related to incidence of persistent postpartum hypertension (Table 3).

Table 1: Grading severity of PIH

Blood pressure	Degree
BP≤120.80	1 (normal)
140.90≥BP>120.80	2 (PreHTN)
160.100≥BP>140.90	3 (Mild HTN)
180.110≥BP>160.100	4 (Mod. HTN)
BP>180.110	5 (Severe HTN)

Table 2: Relationship between PIH and persistent postpartum hypertension

BP before pregnancy	Persistent hypertension after pregnancy		OR	$CI_{95\%}$		P-value
	Yes n (%)	No n (%)		lower	Upper	
12-14	44 (75.9)	14 (24.1)	Reference	-	-	
14-16	48 (59.3)	33 (40.7)	2.161	1.024	4.561	0.043
16-18	26 (43.3)	345 (56.7)	4.110	1.867	9.046	0.000
>18	10 (25.6)	29 (74.4)	9.114	3.570	23.267	0.000

Table 3: Comparison of demographic ad obstetric parameters in three BP groups 12 weeks postpartum

OBS & historical characteristics	Normal lBP 6Wpostpart	Pre HTN 6W postpartum	Persistent HTN 6Wpostpartu	P value
Gestational HTN Yes No	19(21.8%) 62(41.1%)	17(19.5%) 30(19.9%)	51(58.65%) 59(31.1%)	0.005
Preeclampsia Yes No	46(25.6%) 35(60.3%)	35(19.4%) 12(20.7%)	99(55%) 11(19%)	0.002
Severity sign Yes No	26(24%) 55(42.3%)	22(20.3%) 25(19.2%)	60(66.7%) 50(38.4%)	0.021
Diabetes Hx Yes No	19(22.6%) 62(40.3%)	21(25%) 26(16.9%)	44(52.4%) 66(42.9%)	0.021
Family Hx of HTN Yes No	22(17.7%) 32(28%)	52(41.9%) 48(42.1%)	50(40.3%) 34(29.9%)	0.214
Anti HTN drugs Yes No	5(11.6%) 76(39%)	7(16.4%) 40(20.5%)	31(72%) 79(40.5%)	0.001
Laboratory data	**Normal BP 6Wpostpartum**	**Pre HTN 6W postpartum**	**Persistent HTN**	**P value**
Proteinuria Neg 1 2 3 4	41(41%) 10(41.7%) 22(41.5%) 5(17.2%) 3(9.4%)	17(17%) 7(29.2%) 14(26.4%) 2(6.9%) 7(21.9%)	42(42%) 7(29.2%) 17(36.1%) 22(75.2%) 22(68.8%)	0.23 0.52 0.19 0.002 0.001
PLT ≤100000 100000<	6(9.2%) 75 (48.4%)	12(18.5%) 35(20.2%)	47(72.3%) 63(36.4%)	0.001
Uric acid <6.3 ≥6.3	75(42.1%) 6(10%)	42(23.6%) 5(8.3%)	61(34.3%) 49(81,7%)	0.002
Cr <1 1≤	67(45%) 14(16.1%)	29(19.5%) 17(19.5%)	53(35.6%) 56(64.4%)	0.001

CONCLUSION

This study determined prevalence of persistent postpartum hypertension and related risk factors in women with PIH. According to the results, prevalence of persistent postpartum hypertension was estimated at 46.2% (110 of 270 patients), which is clearly higher than similar studies. Ndayambagye estimated the prevalence of this disorder at 27.7% [5], while Bagga reported it at 18.6% [14]. This difference may be due to a higher frequency of women with preeclampsia (54%) than other PIH disorders in the current study; preeclampsia is known as one of the effective factors on persistent hypertension [5], which is proven in this study. By definition, persistence of high blood pressure after 12 weeks of gestation is considered as hypertension. According to available studies, high blood pressure is expected to return to normal within 9-16 days [13]; however, it may persist for 6 months postpartum [4]. Bagga considered hypertension after 6 weeks as the baseline [14]. According to the newest systematic review of Chocrane in 2013, examination and follow-up of women with PIH has been recommended from 6 weeks postpartum [15]. In this study, the first follow-up was 6 weeks and the next was 12 weeks postpartum. In most women with gestational HTN, blood pressure usually returns to normal within a week postpartum [15]. This is different in patients with preeclampsia, because the body needs more time in recovery phase of preeclampsia to compensate the damage on systemic and renal vascular endothelium; this time has been estimated at 2 weeks for patients with preeclampsia [14, 15]. In all patients with PIH, blood pressure should return to normal by 12 weeks postpartum [3]. In this study, likelihood of persistent hypertension increased by 1.8 times in patients older than 40 years and 1.3 times in patients younger than 20 years; however, this increase was not significant. This is inconsistent with Ndayambagye in which age was significantly effective [5]. Moreover, PIH incidence had no significant effect on these disorders in preterm gestational ages. According to Eldow [10], preeclampsia-induced preterm labor was associated with 18-fold increase in persistent hypertension. Maternal BMI>35 significantly increased the risk of persistent hypertension by 1.5 times, which is consistent with Hwang [16]. In the current study, both

preeclampsia and its higher severity (severe feature) increased the risk of persistent hypertension. In addition to preeclampsia, gestational HTN significantly increased the risk of persistent hypertension, which indicates the need for proper postpartum follow-up in all mothers with recent history of PIH as well as preeclamptic mothers. In addition, the need for blood pressure control with medicine pre- or postpartum which indicates severity of the disease had a significant effect on prevalence of persistent hypertension. This suggests that patients discharged with antihypertensive drug during pregnancy or postpartum require more detailed follow-up. Hwang claimed that dose of drug administered for postpartum hypertension was involved in high blood pressure after six weeks postpartum [16]. Platelet count $<10^5$, severe proteinuria (+3 or +4), serum uric acid ≥ 6.3 mg/dl and serum creatinine ≥1 mg/dl had a significant role in increased incidence of persistent postpartum hypertension. Ndayambagye also found a significant relationship between increased creatinine and proteinuria [5]. In fact, the increased serum uric acid and serum creatinine is similar to urine protein excretion, reflecting renal dysfunction following PIH, particularly pre-eclampsia. In a normal pregnancy, serum creatinine and uric acid decrease slightly following physiological increase in blood volume and renal clearance [3]. The exact cause of renal dysfunction during PIH is still not clearly understood; however, it may develop as a result of damaged neurons by endothelin. Significant effect of thrombocytopenia and severe proteinuria may explain the direct relationship between severity of preeclampsia and incidence of persistent postpartum hypertension. Due to the lack of postpartum care clinics at medical centers and inability to track patients in scheduled clinical visits, it was not possible to visit all patients directly. Considering the significant role of proper follow-up and early treatment, it is recommended to follow the instructions related to follow-up of high-risk patients (women with risk factors mentioned) in terms of persistent postpartum hypertension in obstetric clinics.

REFERENCES

1. Khan KS, Wojdyla D, Say L, Gülmezoglu AM, Van Look PF. WHO analysis of causes of maternal death: a systematic review. The lancet. 2006;367(9516):1066-1074.
2. American College of Obstetricians and Gynecologists. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in pregnancy. Obstet Gynecol 2013b; 122(1):1121-1122
3. Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS. Obstetricia de Williams. McGraw Hill Brasil; 2016 .
4. Kraus D, Fent L, Heine RP. Smoking and preeclampsia protection: cigarette smoke increases placental adrenomedullin expression and improves trophoblast invasion via the adrenomedullin pathway. Abstract No. 43, Am J Obstet Gynecol.2013; 208(1): S25-S26.
5. Ndayambagye EB, Nakalembe M, Kaye DK. Factors associated with persistent hypertension after puerperium among women with pre-eclampsia/eclampsia in Mulago hospital, Uganda. BMC pregnancy and childbirth.2010; 10(1):1-2.
6. Conde-Agudelo A, Belizan JM. Risk factors for pre-eclampsia in a large cohort of Latin American and Caribbean women. Br J Obstet Gynaecol.2000; 107(2):74-75.
7. Bainbridge SA, Sidle EH, Smith GN. Direct placental effects of cigarette smoke protect women from pre-eclampsia: the specific roles of carbon monoxide and antioxidant systems in the placenta. Med Hypotheses.2005; 64(3):16-17.
8. Clark AB. Plasma endothelin levels in Pre-eclampsia: elevation and correlation with uric acid levels and renal impairment. Am J Obstet Gynecol. 1992; 166(3):962-968.
9. Ferrazzani S, De Carolis S, Pomini F, Testa AC, Mastromarino C, Caruso A. The duration of hypertension in the puerperium of preeclamptic women: relationship with renal impairment and week of delivery. Am J Obstet Gynecol. 1994;171(2):506-12.
10. Edlow AG, Srinivas SK, Elovitz MA. Investigating the risk of hypertension shortly after pregnancies complicated by preeclampsia.2009 ;200(5):e60-e62
11. Visser VS, Hermes W, Franx A, Koopmans CM, van Pampus MG, Moil BW, de Groot CJ. High blood pressure six weeks postpartum after hypertensive pregnancy disorders at term is associated with chronic hypertension. Pregnancy Hypertens. 2013;3(4):242-247.
12. Piver MS, Corson SL, Bolognese RJ. Hypertension 6 weeks' postpartum in

apparently normal women: a reappraisal and challenge. Am. J Obstet Gynecol. 1967; 30:238-41.
13. Podymow T, Aujgust P. Postpartum course of gestational hypertension and preeclampsia. Hypertens Pregnancy .2010;29:294-300
14. Bagga A,Sinha A, Saha A, Kumar M, Sharma S, Afzal K, Mehta A, Kalaivani M, Hari P. Extending initial prednisolone treatment in a randomized control trial from 3 to 6 months did not significantly influence the course of illness in children with steroid-sensitive nephrotic syndrome. Kidney international.2015;87(1):217-224.
15. Reiter L. Hypertension in pregnancy: The incidence of underlying renal disease and essential hypertension. Am J Kidney Dis 1994, 24(3):883-887.
16. Hwang JW, Park SJ, Oh SY, Chang SA, Lee SC, Park SW, Kim DK. The Risk Factors That Predict Chronic Hypertension after Delivery in Women With a History of Hypertensive Disorders of Pregnancy. Medicine (Baltimore) 2015; 94(42):17-47.