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Comparing maternal and perinatal outcomes in pregnancies complicated by preeclampsia superimposed chronic hypertension and preeclampsia alone

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Summary

Aim: The study was to determine whether preeclampsia with superimposed chronic hypertension results in worse maternal and perinatal outcomes than preeclampsia alone. *Materials and Methods:* A retrospective study involving 850 pregnant women was conducted and divided into two groups: preeclampsia superimposed on chronic hypertension (group A, n= 84) and preeclampsia alone (group B, n= 766). The maternal and fetal outcomes of all subjects were collected and analyzed. *Results:* There were no significant differences between the two groups in baseline information. However, the systolic and diastolic blood pressures in group A were significantly higher than those in group B ($p < 0.05$). The average interval between the onset of preeclampsia and the termination of pregnancy was significantly longer in group A as compared to group B. The incidence of serious maternal complications showed no differences between the two groups ($p > 0.05$). It showed a higher rate of neonatal respiratory distress syndrome and intracranial hemorrhage in group A than in group B ($p < 0.05$). *Conclusions:* Women in group A had higher risks of maternal and perinatal outcomes as compared to women in group B.

Key words: Chronic hypertension; Pre-eclampsia; Pregnancy outcome.

Introduction

Hypertensive disorders in pregnancy compose approximately 10% of pregnancies and are the leading causes of maternal, fetal and neonatal morbidity, and mortality worldwide [1, 2]. In the USA, hypertensive disorders in pregnancy affect 12%-22% of all pregnancies and 17.6% of maternal deaths can be attributed directly to hypertension [3]. Among the hypertensive disorders of pregnancy, chronic hypertension complicates 5% and because the recent increase in obesity and gestational age among pregnant women, the rates with chronic hypertension are expected gradually increased as well [4]. Several studies have demonstrated a higher risk of preterm birth, fetal death, and placental abruption among women with chronic hypertension who developed superimposed preeclampsia compared with women who had preeclampsia alone [5-7]. It has been speculated that the underlying vascular abnormalities in women with chronic hypertension cause an escalation of complications when preeclampsia develops [8].

Although several studies have evaluated perinatal outcomes among women with chronic hypertension in combination with or without superimposed preeclampsia [7, 9], there are no large-scale, randomized, controlled trials comparing the outcomes of pregnancy between women with preeclampsia superimposed on chronic hypertension and those with preeclampsia alone. In the current study, maternal and neonatal outcomes between women with preeclampsia superimposed on chronic hypertension and those with preeclampsia alone were compared. The authors, therefore, carried out a population-based study to determine whether preeclampsia superimposed on chronic hypertension was associated with increased adverse maternal and perinatal outcomes. They anticipate that the results of our study will provide a theoretical basis in the counseling and treatment of pregnancies in women with preeclampsia superimposed on chronic hypertension.

Materials and Methods

Between July 1, 2008 and June 30, 2012, 52,685 gravidas were delivered at the Obstetrics and Gynecology Hospital of the Zhejiang University School of Medicine. Among them, 850 (1.619%) had preeclampsia. The women were separated into two groups such that 84 women with preeclampsia superimposed on chronic hypertension (0.167% of the total number of women and 9.88% of women with preeclampsia) constituted group A and group B included 766 women with preeclampsia alone (1.45% of the total number of women and 90.12% of women with preeclampsia). The diagnosis of hypertension was made in accordance with international standards used to determine hypertensive disorders in pregnancy [10].

Women with mild preeclampsia attended regular prenatal visits where monitoring of symptoms and daily blood pressure and body weight checks were conducted. Urine protein was checked every two to three days. Fetal growth and development, as well as placental functioning, were monitored regularly. Commencing at 34 weeks

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Table 1. — *Clinical data of the two groups.*

	Preeclampsia superimposed on chronic hypertension (Group A)	Preeclampsia (Group B)	*p* value
Case number	84	766	
Age (years)	33.3	29.9	<0.001
BMI (kg/m^2)	28.91	28.45	0.526
Blood pressure (mmHg)			
Systolic blood pressure	167.9	156.6	0.001
Diastolic blood pressure	107.6	100.4	0.001
Onset of illness (weeks)	31.5	33.6	0.008
≤ 34 weeks gestation (case number)	48	336	
> 35 weeks gestation (case number)	36	430	0.020
Termination of pregnancy (weeks)	34.8	35.7	0.118
≤ 34 weeks (case number)	33	231	
> 35 weeks (case number)	51	535	0.086
Interval between onset of preeclampsia and termination of pregnancy (weeks)	3.34	2.10	<0.001

Table 2. — *Comparison of pregnancy outcomes between the two groups.*

	Preeclampsia superimposed on chronic hypertension (Group A)	Preeclampsia (Group B)	*p* value
Severe preeclampsia (percentage)	66 (78.57%)	574 (74.93%)	0.463
Early severe preeclampsia (percentage)	48 (57.14%)	336 (43.86%)	0.020
Operative delivery rate (percentage)	82 (97.62%)	689 (89.95%)	0.022
Diabetes	4 (4.76%)	53 (6.92%)	0.453
Maternal complications and co-morbidities (percentage)	26 (30.95%)	220 (28.72%)	0.669
HELLP	2	7	0.212
Eclampsia	0	4	0.507
Abruption	7	33	0.08
Postpartum hemorrhage	2	9	0.353
Oligohydramnios	2	53	0.108
ICP	9	70	0.637
Renal diseases	2	11	0.503
Heart diseases	0	22	0.116
Other	2	11	0.503
Total	26	220	0.340

of gestation, the fetal heart rate was monitored on a weekly basis. The treatment plan focused on additional rest, a low-salt diet, and antihypertensive therapy. For those women with blood pressure levels ≥ 160/110 mmHg, antihypertensive medications were administered. Ideal systolic and diastolic blood pressures were considered to be 140 ~ 155 mmHg and 90 ~ 105 mmHg, respectively. Blood pressure levels were checked to ensure that they did not decline sharply or drop significantly below ideal pressure levels. Labetalol (50 ~ 100 mg, two to three times per day) was the preferred anti-hypertensive therapy. If the condition was stable, the women could expect a full-term pregnancy. If the women had a higher risk of serious maternal complications, such as placental abruption, HELLP syndrome and eclampsia, the pregnancy was terminated immediately.

Hospitalization was preferred for women with severe preeclampsia. Magnesium anti-spasmodics and sedatives were prescribed along with anti-hypertensive treatment, supplemented with diuretic therapy if necessary. If the fetus was mature, women were treated for 24 to 48 hours, followed by termination of the pregnancy. In cases where the fetus was immature, women were given glucocorticoids to promote fetal lung maturation. For those showing an improvement in their condition, pregnancy was continued and monitored closely; however, if no improvement was noted after 48 hours of active treatment, fetal lung maturity was promoted followed by termination of the pregnancy at 28 weeks of gestation.

All statistical analyses were conducted using SPSS16.0. A *p*-value of < 0.05 was considered to represent a statistically significant difference between the groups.

Results

Comparisons of clinical data between the two groups

Pregnancy clinical characteristics for women are shown in Table 1. A total of 898 women were found to have preeclampsia between July 1, 2008 and June 30, 2012. Of the 898 women with preeclampsia, 84 (9.4%) women in group A had chronic hypertension with superimposed preeclampsia, 850 (94.6%) women in group B had preeclampsia alone. Women in group A were older than those in group B (33.3 years *vs* 29.9 years, $p < 0.001$). While two groups had a similar body mass indexes ($p = 0.526$). Women in group A had higher systolic and diastolic blood pressures than those in group B ($p = 0.001$). Although the average gestational age in group A was lower than the average gestational age in group B ($p = 0.008$), the average gestational ages at which pregnancies were terminated were similar between the two groups ($p = 0.118$). The average interval between the onset of preeclampsia and the termination of pregnancy was 3.34 weeks in group A and 2.1 weeks in group B ($p < 0.001$).

Comparison of pregnancy outcomes

Table 2 displays risk estimates of adverse maternal and neonatal outcomes between the two groups. The ratio of women with severe preeclampsia was not significantly different ($p = 0.463$); however, the ratio of women with severe preeclampsia having early onset was significantly higher in group A ($p = 0.020$). There were only two natural deliveries in group A. The remaining 82 gravidas underwent cesarean sections (operative delivery rate = 97.62%). In group B, 77 women had natural deliveries, seven gravidas had cesarean sections, and 682 gravidas had lower uterine segment cesarean sections (operative delivery rate = 89.95%). Thus, the operative delivery rate in group A was significantly higher than the rate in group B ($p = 0.022$). There were not signifi-

Table 3. — *Neonatal outcomes between the two groups.*

	Preeclampsia superimposed on chronic hypertension (Group A)	Preeclampsia (Group B)	*p* value
Total	84	766	
FGR (percentage)	15 (17.86%)	156 (20.37%)	0.002
Gestational age (weeks)			
< 28	0	18 (2.35%)	
28~32	24 (28.51%)	121 (15.80%)	
33~34	9 (10.71%)	92 (12.01%)	
35~36	22 (26.19%)	137 (17.89%)	
≥ 37	29 (34.52%)	398 (51.56%)	0.002
Perinatal death			
Stillbirth	0	9	
Induction	0	20	
Neonatal death	2 (2.38%)	2 (0.26%)	0.007
Neonatal complications	33 (39.29%)	103 (13.45%)	<0.001
Hypoxic-ischemic encephalopathy	0	2 (0.26%)	0.639
Intracranial hemorrhage	18 (21.43%)	44 (5.74%)	0.001
Respiratory distress syndrome	11 (13.10%)	55 (7.18%)	0.054
Retinopathy	2 (2.38%)	2 (0.26%)	0.007
Necrotizing enterocolitis	2	0	<0.001
Transfer to NICU	35 (41.67%)	282 (36.81%)	0.383
NICU stay	20.8	17.7	0.522

cantly different in overall maternal complications or co-morbidities such as HELLP syndrome, eclampsia, placental abruption, postpartum hemorrhage, oligohydramnios, intrahepatic cholestasis of pregnancy (ICP), kidney disease, and heart disease between the two groups. However, women in group A were more likely to suffer serious complications such as HELLP, eclampsia, placental abruption, and postpartum hemorrhage, than those in group B (13.10% *vs* 6.92%; $p = 0.001$).

Comparison of neonatal outcomes

Table 3 displays a comparison of neonatal outcomes between the two groups. In group A, there were 15 cases of neonates with fetal growth restriction (FGR), all occurring in pregnancies with early-onset severe preeclampsia. In group B, there were 156 neonates with FGR, which occurred in pregnancies with early-onset severe, late-onset severe or mild preeclampsia. The women in group A had the lower incidence incidence of FGR than those in group B (17.8% *vs* 18.3%, $p = 0.002$). Gestational age was directly related to the prognosis of newborns, as the composition of the two groups differed ($p = 0.002$). In the current study, women in group A delivered after 28 weeks of gestation. In group B, 18 women delivered before 28 weeks of gestation, including nine gravidas who underwent labor induction. The percentage of neonates delivered before 32 weeks of gestation was higher in group A than in group B and this difference was associated with an increase in adverse neonatal outcomes. There were no stillbirths in group A, whereas there were nine stillbirths in group B. Of 20 gravidas in group B who underwent labor induction, nine were induced before 28 weeks of gestation and 11 had umbilical blood flow after 28 weeks of gestation with absent diastolic flow. Two neonatal deaths were reported in both groups (the neonates died after family withdrew treatment) and the incidence between the two groups was significant ($p = 0.007$). The neonates of women in group A were more likely to suffer adverse outcomes predominantly neonatal respiratory distress syndrome and intracranial hemorrhage, than those in group B. There were no differences in neonatal transfer rates to the neonatal intensive care unit (NICU) or the average length of NICU stay between the two groups ($p = 0.383$ and 0.522, respectively).

Discussion

The percentage of adults with chronic hypertension in developed countries is between 25% and 30%. In the past two decades, the incidence of chronic hypertension has also increased in China. In the current study, the incidence of preeclampsia superimposed on chronic hypertension was significantly lower than the previously reported rate [11] and there are several possibilities to explain this observation. First, incidences lower than those reported in the US and Europe may have been attributable to differences in geography, ethnicity, or reproductive ages. Second, the records from the Chinese health care system may have been incomplete due to the mobility of the Chinese population. Therefore, hospital-based statistics may not be entirely representative or generalizable.

Several studies have evaluated that pregnancies in women with preeclampsia superimposed chronic hypertension are at an increased risk of adverse perinatal outcomes that include fetal growth, restriction, preterm birth, placental abruption, and intrauterine growth [12-15]. Placental insufficiency is recognized as the most common cause of fetal growth restriction among clinically healthy [16]. Ferrazzani *et al.* indicated an association between chronic hypertension and SGA only when superimposed with preeclampsia [17]. In the current study, the authors evaluated maternal and neonatal outcomes in women with preeclampsia with or without chronic hypertension and the data from the current study indicated that pregnancies complicated by preeclampsia superimposed on chronic hypertension represented a serious threat to maternal and neonatal health and survival.

In the current study, the operative delivery rate was significantly higher in group A than in group B and may have been associated with oligohydramnios, ICP, or other complications. Oligohydramnios may be caused by poor placental erosion closely associated with gestational hypertension and small vessel disease. Whether or not small vessel disease is more severe in women with preeclampsia superimposed on chronic hypertension than in women with preeclampsia alone remains

to be confirmed. There were no maternal deaths or differences in overall maternal complications and co-morbidities between the two groups; however, serious complications such as HELLP, eclampsia, placental abruption, and postpartum hemorrhage, were higher in group A than in group B.

Results from the current study showed that women with preeclampsia superimposed on chronic hypertension had a significantly lower rate of FGR, suggesting chronic hypertension itself does not increase the incidence of FGR. Indeed, preeclampsia induces systemic small artery spasm and ischemia resulting in decreased uteroplacental perfusion and may be a key factor in the triggering of FGR. Moreover, preeclampsia also induces various adverse outcomes, including an infiltration barrier, shallow placental implantation, endothelial dysfunction, immune imbalance, placental vascular acute atherosclerosis, placental dysfunction, and drastically reduced blood flow. As a result, the fetus develops chronic hypoxia and the incidence of FGR is dramatically increased, further suggesting that preeclampsia is a major risk factor for FGR.

The women in the current study were able to reach 35 weeks of gestation after active treatment and the majority of neonatal outcomes were good; however, in comparing neonatal complications, group A had higher incidences than group B. Group A had a relatively earlier onset of preeclampsia and the proportion of births before 32 weeks of gestation was higher than in group B. The neonatal mortality and growth rates in group A were associated with existing social factors and the economic status of the parents.

As compared to preeclampsia alone, preeclampsia superimposed on chronic hypertension triggered early onset of severe preeclampsia, early onset of severe illness, and high blood pressure among women; however, there were no significant differences in gestational ages between the two groups. Results from the current study suggested that even in women with preeclampsia superimposed on chronic hypertension, systematic treatment, proper expectations, and close monitoring of mother-infant conditions could improve the prognosis. All women in the current study delivered after 28 weeks of gestation, with significant improvements observed in newborn prognosis. Therefore, a profound healthcare system with proper prenatal care for pregnant women, along with active treatment plans and strict control on the termination of pregnancy, could ensure safety and improve maternal neonatal outcomes for women with preeclampsia superimposed on chronic hypertension.

In conclusion, the present data indicate that women with chronic hypertension who developed superimposed preeclampsia had a longer average interval between the onset of preeclampsia and the termination of pregnancy, high systolic and diastolic blood pressures, and severe maternal complications than women with superimposed preeclampsia alone and also have a significantly increased risk of several adverse neonatal outcomes. Women with preeclampsia superimposed with hypertension have elevated risks of intervention-related events compared with women with preeclampsia alone. This may be the result of earlier disease onset, so consideration of expectant management of early onset preeclampsia superimposed chronic hypertension is reasonable in the absence of contraindications.

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References

[1] de Swiet M.: "Maternal mortality: confidential enquiries into maternal deaths in the United Kingdom". *Am. J. Obstet. Gynecol*., 2000, *182*, 760.
[2] Waterstone M., Bewley S., Wolfe C.: "Incidence and predictors of severe obstetric morbidity: case-control study". *BMJ.,* 2001, *322*, 1089.
[3] Walker J.J.: "Preeclampsia". *Lancet.,* 2000, *356*, 1260.
[4] Chappell L.C., Enye S., Seed P., Briley A.L., Poston L., Shennan A.H.: "Adverse perinatal outcomes and risk factors for preeclampsia in women with chronic hypertension: a prospective study". *Hypertension,* 2008, *51*, 1002.
[5] Rey E., Couturier A.: "The prognosis of pregnancy in women with chronic hypertension". *Am. J. Obstet. Gynecol*., 1994, *171*, 410.
[6] Vanek M., Sheiner E., Levy A., Mazor M.: "Chronic hypertension and the risk for adverse pregnancy outcome after superimposed preeclampsia". *Int. J. Gynaecol. Obstet.,* 2004, *86*, 7.
[7] McCowan L.M., Buist R.J., North R.A., Gamble G.: "Perinatal morbidity in chronic hypertension". *BJOG.,* 1996, *103*, 123.
[8] Creasy R.K., Resnik R., Iams J.D., Lockwood C.J., Moore T.R.: "Creasy & Resnik's maternal-fetal medicine: principles and practice" *Philadelphia: Saunders*, 2009, 651.
[9] Sibai B.M., Abdella T.N., Anderson G.D.: "Pregnancy outcome in 211 women with mild chronic hypertension". *Obstet Gynecol.,* 1983, *61*, 571.
[10] Cunningham F.G., Leveno K.J., Bloom S.L.: "Williams Obstetrics, 22nd ed". New York: McGraw-Hill, 2005, 761.
[11] Tuuli M.G., Rampersad R., Stamilio D.: "Perinatal outcomes in women with preeclampsia and superimposed preeclampsia: do they differ?" *Am. J. Obstet. Gynecol*., 2011, *204*, 1.
[12] Vanek M., Sheiner E., Levy A., Mazor M.: "Chronic hypertension and the risk for adverse pregnancy outcome after superimposed preeclampsia". *Int. J. Gynecol. Obstet.,* 2004, *86*, 7.
[13] Marik P. E.: "Hypertensive disorders of pregnancy". *Postgrad. Med.,* 2009, *121*, 69.
[14] Ferrer R.L., Sibai B.M., Mulrow C.D., Chiquette E., Stevens K.R., Cornell J.: "Management of mild chronic hypertension during pregnancy: a review". *Obstet. Gynecol.,* 2000, *96*, 849.
[15] Chappell L. C., Enye S., Seed P., Briley A.,L., Poston L. Shennan A. H.: "Adverse perinatal outcomes and risk factors for Preeclampsia in women with chronic hypertension - A prospective study". *Hypertension*, 2008, *51*, 1002.
[16] Baschat A. A., Hecher K.: "Fetal growth restriction due to placental disease". *Semin. Perinatol.*, 2004, *28*, 67.
[17] Ferrazzani S., Caruso A., Decarolis S., Martino I. V., Mancuso S., "Proteinuria and Outcome of 444 Pregnancies Complicated by Hypertension". *Am. J. Obstet. Gynecol*., 1990, *162*, 366.

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