ORIGINAL ARTICLE

Maternal Complications and Perinatal Outcomes Associated with Gestational Hypertension and Severe Preeclampsia in Taiwanese Women

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Background/Purpose: The role of proteinuria in disease severity of preeclampsia and gestational hypertension has not been determined. The objective of this study was to compare the effects of disease severity on maternal complications and pregnancy outcome between women with severe preeclampsia and women with gestational hypertension.

Methods: A retrospective case-control study using daily records from the birth registry for the years 1994 to 2003 was conducted. Cases ($n = 364$) were defined as women with severe preeclampsia. Controls ($n = 249$) were selected from women with gestational hypertension. The outcome measures were maternal complications and perinatal-related factors.

Results: Women with severe preeclampsia had an increased risk of intrauterine growth restriction (adjusted odds ratio [aOR], 2.16; 95% confidence interval [CI], 1.10–4.24; $p = 0.026$). Risk factors associated with severe preeclampsia patients were lack of prenatal care (aOR, 2.95; 95% CI, 1.45–5.99), systolic blood pressure ≥ 180 mmHg (aOR, 14.3; 95% CI, 1.69–121.0), and diastolic blood pressure ≥ 105 mmHg (aOR, 21.2; 95% CI, 6.99–64.3) compared with women with gestational hypertension in Model I. When we added proteinuria as a variable, two significant risk factors, diastolic blood pressure ≥ 105 mmHg (aOR, 18.2; 95% CI, 4.85–68.3) and significant proteinuria (aOR, 1.01; 95% CI, 1.006–1.014), were associated with severe preeclampsia patients in Model II. A subgroup of women with gestational hypertension and proteinuria had an increased risk of placental abruption (unadjusted OR, 4.36; 95% CI, 1.05–18.1) and disseminated intravascular coagulation (unadjusted OR, 6.46; 95% CI, 1.05–39.8). Finally, maternal complications (aOR, 2.59; 95% CI, 1.34–5.04) became the single significant factor associated with gestational hypertension and proteinuria.

Conclusion: Proteinuria may play a role in the progression of gestational hypertension to severe forms of preeclampsia associated with subsequent maternal complications and extremely-low-birth-weight babies. [*J Formos Med Assoc* 2008;107(2):129–138]

Key Words: gestational hypertension, maternal complications, pregnancy outcome, proteinuria, severe preeclampsia

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Preeclampsia is a disease of multiple organ systems that is unique to pregnancy and is often associated with significant maternal and neonatal morbidity and mortality, especially when it is severe and occurs well before term.[1–4] Because the only cure for severe preeclampsia is delivery, there is universal consensus to deliver patients if the disease develops after 34 weeks of gestation or if there is evidence of maternal complications and fetal distress before that time.[3] Despite the severity of disease of both preeclampsia and gestational hypertension, differences in risk factors between severe preeclampsia and gestational hypertension may increase controversies over expectant versus aggressive treatment, and there is insufficient literature on Asian women with preeclampsia and gestational hypertension regarding the issue of maternal complications. As there is a discrepancy between the definition of mild to moderate preeclampsia and gestational hypertension in terms of proteinuria, the less than 300 mg/24 hours of slight proteinuria may not belong to the preeclampsia group. We might raise a question, "Is gestational hypertension an early sign of preeclampsia?"[5] We then tested the hypothesis that the presence of significant proteinuria may have an impact on pregnancy outcome. In addition, the subgroup of gestational hypertension with slight proteinuria (< 150 mg/24 hours) might have more adverse perinatal outcome than the subgroup without proteinuria. The main purpose of this study was to identify differences in the effect of hypertension and its management between two entities of hypertension—severe preeclampsia and gestational hypertension—with regard to maternal complications and perinatal outcome in Taiwanese women with hypertensive disorders. Another purpose was to investigate whether the presence of proteinuria in women with gestational hypertension may have an impact on pregnancy outcome.

Methods

This study was a retrospective cohort analysis of pregnant women with preeclampsia from January 1994 through 2003 at a single tertiary care and academic center. Data were obtained from daily records of a birth registry and medical chart review. A database containing clinical information on pregnant women who received outpatient services and inpatient services for delivery was created. We used the American College of Obstetricians and Gynecologists (ACOG) criteria for the definitions of gestational hypertension and severe preeclampsia.[6–8]

Severe preeclampsia was defined as the presence of one or more of the following criteria: (a) blood pressure (BP) of 160 mmHg or higher systolic or 110 mmHg or higher diastolic on two occasions at least 6 hours apart while the patient is on bed rest; (b) proteinuria of 5 g or higher in a 24-hour urine specimen or 3 + or greater on two random urine samples collected at least 4 hours apart; (c) oliguria of less than 500 mL in 24 hours; (d) cerebral or visual disturbances; (e) pulmonary edema or cyanosis; (f) epigastric or right upper-quadrant pain; (g) impaired liver function; (h) thrombocytopenia; and (i) fetal growth restriction. Eclampsia was defined as seizures occurring in a woman with preeclampsia that cannot be attributed to another cause but may complicate severe preeclampsia.

The definition of gestational hypertension was a systolic BP of at least 140 mmHg and/or a diastolic BP of at least 90 mmHg on at least two occasions at least 6 hours apart after the 20th week of gestation in women known to be normotensive before pregnancy and before 20 weeks of gestation. The BP recordings used to establish the diagnosis should be made no more than 7 days apart. Women with gestational hypertension and less than 1+ to 2+ proteinuria were included in our study cohort. Proteinuria was defined as the urinary excretion of ≥ 0.3 g of protein in a 24-hour specimen. This will usually correlate with ≥ 30 mg/dL (≥ 1 + reading on dipstick).[7] Significant proteinuria is demonstrated when there is more than 500 mg of protein as above.

Women who met the above criteria included women with severe preeclampsia (case) ($n = 364$) and women with gestational hypertension

(control) ($n=249$) who did or did not have their prenatal care at the study hospital but did deliver their babies at the study hospital. The exclusion criteria for this study were missing or unavailable data from clinical visit or delivery and no available record in our obstetric daily logbook. Based on our criteria, we excluded patients with chronic hypertension ($n=39$) and patients with chronic hypertension superimposed preeclampsia ($n=7$). Although the complex features of the disease entity accurately reflected the disease patterns in a tertiary center, we believe that it may not be necessary to exclude all women with the following preexisting or concurrent medical diseases during their pregnancies. These patients encompassed a wide range of preexisting or concurrent diseases including: uterine myoma ($n=7$); gestational diabetes mellitus, insulin-dependent diabetes mellitus and glucose intolerance ($n=6$); nephropathy, uremia, acute renal failure, and glomerulonephritis ($n=9$); hepatitis ($n=1$); recurrent pituitary tumor ($n=1$); tuberculosis and pleural effusion ($n=1$); hyperthyroidism and thyroiditis ($n=4$); hypoparathyroidism ($n=1$); adrenal cortical adenoma ($n=1$); thrombotic thrombocytopenic purpura ($n=1$); immune thrombocytopenic purpura ($n=1$); angina and coronary heart disease ($n=2$); cerebral infarction and intracerebral hemorrhage ($n=2$); L3-4 dislocation ($n=1$); systemic lupus erythematosus ($n=3$); mastitis ($n=1$); urinary tract infection; and acute pyelonephritis ($n=2$). Some patients may have had more than one of the listed preexisting medical diseases during their pregnancies.

All patients were admitted to the labor and delivery area and carefully evaluated. They were counseled about maternal and perinatal risks with regard to severe preeclampsia. Initial drug therapy consisted primarily of intravenous magnesium sulfate to prevent convulsions and bolus injections of hydralazine or labetalol to maintain diastolic blood pressure (DBP) below 100 mmHg. Intravenous fluids and urinary output were carefully monitored during the observation period. Oral antihypertensive medications were then given to maintain the diastolic pressure between 90 and 100 mmHg. The antihypertensive drugs used initially were methyldopa, hydralazine and labetalol; nifedipine was used after patients delivered their babies. Corticosteroids were used routinely to accelerate fetal lung maturity in all cases when the gestational age was more than 25 weeks. Absent fetal movement was evaluated by a non-stress test and biophysical profile and was then managed according to the findings of the tests.

Patients with HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome were also recruited for this investigation. Before 34 weeks of gestation, patients received 12.5 mg of dexamethasone intramuscularly over 12 hours in three doses for a total of 37.5 mg. The exclusion criterion was clinical evidence of chorioamnionitis at delivery. In our unit, magnesium sulfate was started in women as a prophylactic measure when there was concern about seizure. We did not routinely use high-dose dexamethasone or corticosteroids for *rescue therapy* for maternal HELLP. However, whether or not to use antepartum corticosteroids for fetal indications of lung maturity was often decided by the physician in-charge. We defined *aggressive* management based on criteria used for immediate delivery within 48 hours including a non-reassuring fetal heart rate tracing, evidence of HELLP syndrome, eclampsia, preterm labor, preterm rupture of membranes, and uncontrolled hypertension. *Expectant management* included assessment of the woman's condition, bed rest, antihypertensive agents, chronic parenteral magnesium sulfate, plasma volume expanders (crystalloids, albumin, fresh frozen plasma), and steroids (dexamethasone or betamethasone). The decision of whether to use aggressive or expectant management was made based on physician preference.

The study was approved by the institutional review board of Chang Gung Memorial Hospital, Taoyuan, Taiwan (No. 96-1094B).

Statistical analysis

Statistical comparison of clinical and demographic factors between patients with severe preeclampsia and patients with gestational hypertension who

delivered babies was carried out using Pearson's χ^2 test and Student's t test. Univariate analysis was carried out and multiple logistic regression analysis was performed to control for potential confounding variables. Statistical procedures were performed with SPSS version 11.0 (SPSS Inc., Chicago, IL, USA). Data are presented as means ± standard deviation. A p value of less than 0.05 was considered statistically significant.

Results

There were a total of 55,763 deliveries during the study period. The 661 patients who met the inclusion criteria during pregnancy and who were treated at Chang Gung Memorial Hospital were recruited and included in the analysis. In our study cohort, 199 (32.5%) patients were noted to have maternal complications. Of the 661 women with preeclampsia and gestational hypertension, 48 had mild to moderate preeclampsia and 364 had severe preeclampsia, including 34 with HELLP syndrome and 34 with eclampsia. There were 249 patients who had gestational hypertension. The mean age of the patients was 30.6 ± 5.3 years (range, 13–48 years). There were 210 (34.3%) patients who were nulliparous. The majority of patients, 398 (60.7%), were non-referral patients. There were 38 (6.2%) women with multiple pregnancies. With regard to HELLP cases, the correlation between cesarean delivery and the two treatment strategies (aggressive and expectant) was not significant ($r = 0.09$, $p = 0.53$). However, the correlation between maternal multiple organ dysfunction syndrome and the two modes of intervention was significant ($r = 0.349$, $p = 0.012$).

Various maternal characteristics are summarized in Table 1. There were no significant differences in the clinical manifestations of disease with respect to maternal age, the diagnosis of hypertension with regard to gestational age, gravida, or multiple pregnancies.

Table 2 shows factors associated with the development of severe preeclampsia. The maternal factors that were significantly associated with severe preeclampsia included: age ≥ 40 years; presence of proteinuria; referral (no prenatal care) versus non-referral (prenatal care) status; and whether or not there were associated medical diseases such as HELLP syndrome. As for neonatal outcomes, the rate of cesarean delivery was significantly higher in the group with severe preeclampsia (87.3%); this mode of delivery was usually for fetal indications.[9] Furthermore, relative growth restriction revealed that a greater proportion of women with severe preeclampsia had preterm deliveries (78%), low-birth-weight (LBW) babies

Table 1. Characteristics of the study population

	Severe preeclampsia (n = 364)	Gestational hypertension (n = 249)	p*
Maternal age (yr)	30.9 ± 5.4	30.1 ± 5.4	0.049
Systolic BP (mmHg)	179.5 ± 19.7	147.9 ± 8.1	< 0.001
Diastolic BP (mmHg)	108.7 ± 16.5	87.8 ± 10.2	< 0.001
Gravida	2.6 ± 1.7	2.4 ± 1.7	0.219
Parity	1.8 ± 1.1	1.6 ± 1.0	0.023
Multiple pregnancies (%)	22 (6.0)	16 (6.4)	0.866
Gestational age at diagnosis (wk)	29.3 ± 7.9	29.2 ± 8.2	0.813
Gestational age at delivery (wk)	33.7 ± 4.0	35.7 ± 3.4	< 0.001
Cesarean delivery (%)	315 (87.3)	192 (77.4)	0.001
Mean birth weight (g)	1957.0 ± 896.1	2459.7 ± 794.6	< 0.001
Preterm labor (%)	278 (77.7)	128 (52.2)	< 0.001
Maternal complications (%)	137 (37.6)	62 (24.9)	0.001

**Student's t test and χ^2 analysis. BP = blood pressure.*

(74.3%), very-low-birth-weight (VLBW) babies (33.6%), and extremely low-birth-weight (ELBW) babies (17.2%) compared to the control group.

Table 3 presents the results of univariate analysis with regard to maternal complications and pregnancy outcome in patients with severe preeclampsia. The significant factors regarding maternal complications that were present in the severe preeclampsia group included HELLP, hypertensive retinopathy, referral status and associated concurrent medical complications or complex diseases. Patients with severe preeclampsia were

Table 2. Factors associated with the development of severe preeclampsia

	Severe preeclampsia ($n = 364$)	Gestational hypertension ($n = 249$)	p
Maternal age ≥ 34 yr (n/N)	103 (28.3)	57 (22.9)	0.160
Nulliparity (n/N)	118 (32.5)	92 (37.1)	0.260
Parity ≥ 3 (n/N)	80/361 (22.2)	52/296 (17.6)	0.171
Gestational age at diagnosis (wk)			
≤ 24 (n/N)	72/361 (19.9)	60/245 (24.5)	0.193
25–28 (n/N)	40/361 (11.1)	25/245 (10.2)	0.790
29–32 (n/N)	93/361 (25.8)	52/245 (21.2)	0.209
33–36 (n/N)	114/361 (31.6)	70/246 (28.5)	0.420
≥ 37 (n/N)	41/360 (11.4)	39/245 (15.9)	0.113
SBP ≥ 180 mmHg (n/N)	149 (40.9)	1 (0.40)	< 0.001
DBP ≥ 105 mmHg (n/N)	210 (58.0)	10 (4.02)	< 0.001
Factors related to maternal complications			
Age ≥ 40 yr (n/N)	33 (9.1)	10 (4.02)	0.016
34 ≤ age < 40 yr (n/N)	78 (21.4)	47 (18.9)	0.476
Age < 34 yr (n/N)	253 (69.5)	192 (77.1)	0.043
Proteinuria (n/N)	118/196 (60.2)*	0/86 (0)	< 0.001
HELLP syndrome (n/N)	34 (9.34)	11 (4.42)	0.026
Eclampsia (n/N)	34 (9.37)	14 (5.62)	0.095
Abruptio placentae (n/N)	18 (4.96)	8 (3.21)	0.317
Referral *vs.* non-referral† (n/N)	156/232 (67.2)	28/107 (26.2)	< 0.001
Associated medical diseases (n/N)	137 (37.6)	62 (24.9)	0.001
Maternal mortality (n/N)	3 (0.82)	2 (0.80)	1.00
Fetal conditions and pregnancy outcome			
Delivery at < 37 wk (n/N)	278 (77.7)	128 (52.2)	< 0.001
Delivery at < 27 wk (n/N)	18/353 (5.10)	5/244 (2.05)	0.082
27 wk ≤ delivery < 30 wk (n/N)	34/353 (9.63)	6/244 (2.46)	0.001
Delivery at ≥ 30 wk (n/N)	301/353 (85.3)	233/244 (95.5)	< 0.001
Birth weight < 2500 g (n/N)	266/358 (74.3)	111/244 (45.5)	< 0.001
Birth weight < 1500 g (n/N)	121/360 (33.6)	34/245 (13.9)	< 0.001
Birth weight < 1000 g (n/N)	62/360 (17.2)	12/245 (4.90)	< 0.001
Neonatal death (n/N)	32/363 (8.82)	9/247 (3.64)	0.013

**Significant proteinuria ≥ 500 mg/24 hours; †no prenatal care vs. care. SBP = systolic blood pressure; DBP = diastolic blood pressure; HELLP = hemolysis, elevated liver enzymes, low platelets.*

Table 3. Univariate analysis of factors associated with severe preeclampsia

	OR	95% CI	*p*
Maternal complications			
DIC	1.38	0.47–4.08	0.562
Sepsis	1.56	0.47–5.11	0.466
Eclampsia	1.73	0.91–3.30	0.094
HELLP	2.23	1.11–4.49	0.025
Abruptio placentae	1.57	0.67–3.67	0.297
Pulmonary edema	2.38	0.87–6.53	0.092
Acute renal failure	1.23	0.53–2.82	0.632
Intracerebral hemorrhage	4.83	0.59–39.5	0.142
Hypertensive retinopathy	2.99	1.21–7.39	0.018
Associated medical complications	1.82	1.27–2.60	0.001
Proteinuria	1.01	1.007–1.014	0.001
Prenatal non-care *vs.* care	5.79	3.47–9.65	<0.001
Maternal mortality	1.03	0.17–6.19	0.977
Pregnancy outcome			
Preterm labor	3.18	2.23–4.52	<0.001
LBW (<2500 g)	3.46	2.45–4.90	<0.001
VLBW (<1500 g)	3.14	2.06–4.80	<0.001
ELBW (<1000 g)	4.04	2.13–7.67	<0.001
1-min Apgar score <5	2.95	1.82–4.79	<0.001
5-min Apgar score <7	2.96	1.71–5.11	<0.001
IUGR	1.53	1.50–10.4	0.005
Date of delivery <27 wk	3.94	0.21–14.1	0.615
27 wk <date of delivery <30 wk	4.23	1.75–10.2	0.001
Date of delivery >30 wk	0.27	0.14–0.54	<0.001
IUFD and neonatal death	2.56	1.20–5.46	0.015

OR = odds ratio; CI = confidence interval; DIC = disseminated intravascular coagulation; HELLP = hemolysis, elevated liver enzymes, low platelets; LBW = low birth weight; VLBW = very low birth weight; ELBW = extremely low birth weight; IUGR = intrauterine growth restriction; IUFD = intrauterine fetal demise.

more likely to have preterm labor and preterm delivery between 27 and 30 weeks of gestation (odds ratio [OR], 4.23; 95% confidence interval [CI], 1.75–10.2; $p=0.001$), LBW babies, VLBW babies, ELBW babies, intrauterine fetal demise (IUFD), and poor Apgar score. The associated significant factors with the highest ORs (which included maternal medical complications, preterm labor, and prenatal care status, together with LBW, VLBW and ELBW babies) were also found to be relatively cumulative.

Table 4 shows the results of multiple logistic regression analyses in the absence of proteinuria as a variable as in Model I. Because significant proteinuria may play a major role in these two entities in terms of disease severity, the associated factors without considering the proteinuria variable that were identified to be significantly correlated with increased risk of severe preeclampsia included patients not receiving prenatal care versus receiving prenatal care (adjusted OR, 2.95; 95% CI, 1.45–5.99; $p=0.003$), systolic blood pressure (SBP) ≥180 mmHg (adjusted OR, 14.3; 95% CI, 1.69–121.0; $p=0.015$), DBP ≥105 mmHg (adjusted OR, 21.2; 95% CI, 6.99–64.3; $p<0.001$), and intrauterine growth restriction (IUGR) (adjusted OR, 2.16; 95% CI, 1.09–4.24; $p=0.026$). With respect to HELLP, women with severe preeclampsia seemed to have a marginally protective effect (adjusted OR, 0.327; 95% CI, 0.10–1.08; $p=0.066$).

Table 4. Multiple logistic regression analysis between patients with severe preeclampsia and gestational hypertension for significant associated factors during pregnancy (Model 1)*

Study factors	Adjusted OR	95% CI	*p*
No prenatal care *vs.* care	2.95	1.45–5.99	0.003
SBP ≥ 180 mmHg	14.3	1.69–121.0	0.015
DBP ≥ 105 mmHg	21.2	6.99–64.3	< 0.001
HELLP syndrome	0.327	0.10–1.08	0.066
ELBW	2.86	0.91–8.99	0.072
IUGR	2.16	1.10–4.24	0.026

**Model I: without considering the proteinuria variable. OR = odds ratio; CI = confidence interval; SBP = systolic blood pressure; DBP = diastolic blood pressure; HELLP = hemolysis, elevated liver enzymes, low platelets; ELBW = extremely low birth weight; IUGR = intrauterine growth restriction.*

Table 5. Multiple logistic regression analysis between patients with severe preeclampsia and gestational hypertension for significant associated factors during pregnancy (Model II)*

Study factors	Adjusted OR	95% CI	*p*
Significant proteinuria	1.01	1.006–1.014	< 0.001
DBP ≥ 105 mmHg	18.21	4.85–68.29	< 0.001

**Model II: with the addition of the proteinuria variable. OR = odds ratio; CI = confidence interval; DBP = diastolic blood pressure.*

Table 6. Maternal complications and pregnancy outcome in women with gestational hypertension for significant factors associated with proteinuria

	Unadjusted OR	95% CI	*p*	Adjusted OR (95% CI)	*p*
Maternal complications	2.59	1.34–5.04	0.005*	2.59 (1.34–5.04)	0.005*
Eclampsia	0.67	0.14–3.08	0.60		
DIC	6.46	1.05–39.8	0.04*		
HELLP	1.57	0.40–6.13	0.52		
MODS	1.88	0.55–6.37	0.31		
Placental abruption	4.36	1.05–18.1	0.04*		
Pulmonary edema	2.79	0.45–17.2	0.27		
Pregnancy outcome					
Preterm labor	0.94	0.50–1.76	0.85		
LBW (< 2500 g)	0.82	0.43–1.54	0.53		
VLBW (< 1500 g)	0.83	0.33–2.14	0.70		
ELBW (< 1000 g)	2.16	0.62–7.49	0.23		
IUGR	0.64	0.32–1.29	0.21		
IUFD	1.19	0.24–5.93	0.83		
1-min Apgar score < 5	1.43	0.53–3.82	0.48		
5-min Apgar score < 7	0.81	0.23–2.93	0.75		

**Statistical significance. OR = odds ratio; CI = confidence interval; DIC = disseminated intravascular coagulation; HELLP = hemolysis, elevated liver enzymes, low platelets; MODS = multiple organ dysfunction syndrome; LBW = low birth weight; VLBW = very low birth weight; ELBW = extremely low birth weight; IUGR = intrauterine growth restriction; IUFD = intrauterine fetal demise.*

Table 5 presents the risk factors associated with severe preeclampsia after considering the presence of significant proteinuria as in Model II. DBP ≥ 105 mmHg became a significant risk factor (adjusted OR, 18.21; 95% CI, 4.85–68.3; $p < 0.001$) for patients with severe preeclampsia.

Table 6 shows that the presence of proteinuria, even when not significant (< 1+ to 2+,

< 100 mg/dL), in women with gestational hypertension may increase the risk of maternal complications such as disseminated intravascular coagulation (unadjusted OR, 6.46; 95% CI, 1.05–39.8; $p = 0.04$) and placental abruption (unadjusted OR, 4.36; 95% CI, 1.05–18.1; $p = 0.04$) by four- to six-fold, as well as maternal complications (adjusted OR, 2.23; 95% CI, 1.29–3.88; $p = 0.04$). After multiple logistic regression analysis, the risk of maternal complications was almost three-fold greater (adjusted OR, 2.59; 95% CI, 1.34–5.04; $p = 0.005$) than in women with gestational hypertension without proteinuria.

Discussion

There are three main findings from our study that are related to women with severe preeclampsia. First, patients with severe preeclampsia were more likely to be found in the referral (no prenatal care) group; similarly, those patients often had another medical disease or pregnancy complications. Second, in terms of neonatal outcomes, LBW, VLBW and ELBW babies were found more often in the severe preeclampsia group, which may be a result of the fetal indications that were refractory to control of maternal hypertension. This finding was consistent with the occurrence of preterm delivery. The relative strength of risk compatible with dose-response is shown as a 3.46-fold, 3.14-fold and 4.04-fold increased risk of preterm delivery with LBW, VLBW and ELBW babies. There was also a 2.56-fold increased risk of IUFD in the severe preeclampsia group. Finally, we should not neglect any slight proteinuria that occurs early on or is noted after their prenatal care visits. Slight proteinuria could be an early sign in gestational hypertension patients because they may progress to preeclampsia and be associated with maternal and medical complications.

Maternal complications

The optimal management of pregnancies complicated by severe preeclampsia remains a controversial issue in obstetrics. One important issue concerns the decision of whether to initiate expectant management or immediate delivery.[10] Expectant management allows for prolongation of pregnancy which potentially can improve neonatal outcome. However, expectant management poses a significant risk with regard to maternal complications and neonatal adverse outcome. Our results emphasize that in referral patients who received no prenatal care, SBP > 180 mmHg and DBP > 105 mmHg and preterm delivery between 27 and 30 weeks of gestation are the key features of women with severe preeclampsia and they are more likely to have LBW and IUGR babies.

Maternal complications generally correlated with the severity of preeclampsia, and we also demonstrated with a relatively high OR that no prenatal care and an Apgar score < 5 at 1 minute were associated with poor fetal outcome.[11] These results suggest multiorgan involvement in severe preeclampsia.[12] Maternal complications are those related to the effect of severe preeclampsia on multiple organ systems, together with those associated with medical complications during pregnancy and the course of labor.[13] Pregnant women of advanced age of more than 40 years could be a new population in Taiwan, and our findings provide evidence for a high-risk pregnancy of severe preeclampsia in this group. These findings were different from those of Eskenazi et al's study[14] but consistent with Knuist et al's results that advanced maternal age was a significant predictor of preeclampsia.[15] The increased risk of hypertensive retinopathy in univariate analysis may suggest that routine ophthalmology consultation should be recommended for women with severe preeclampsia. However, they do not appear after multiple regression model calculations.

There are many factors that contribute to the prognosis of gestational hypertension. A well-established BP control protocol may prolong the pregnancy, and gestational hypertension without proteinuria may indicate relatively fair prognosis. However, one should pay heed to severe gestational hypertension patients, especially when they have slight proteinuria at prenatal visits during their pregnancy. In addition, some obstetric events

unrelated to BP may predispose to immediate delivery. Nonetheless, the ultimate treatment goal in severe preeclampsia is delivery, which seems like a final resolution with regard to BP control that is refractory to pharmacologic therapy and other factors such as placental abruption and acute or chronic fetal distress. Furthermore, because of the features of a retrospective study, an outcome-oriented risk-assessment approach should be discussed and emphasized.

Pregnancy outcome

Gestational age is the variable that is the strongest predictor of fetal mortality and morbidity, especially at less than 30 weeks of gestation.[16] In univariate analysis, delivery between 27 and 30 weeks of gestation was a significant risk factor for women with severe preeclampsia (OR, 4.23; 95% CI, 1.75–10.2; $p=0.001$). However, in multivariate analysis, this variable disappeared. Comparison with the result of IUFD revealed that women with severe preeclampsia had an increased risk (OR, 2.56; 95% CI, 1.20–5.46; $p=0.015$). This may be consistent with a previous study which showed that neonatal morbidity and mortality were related to gestational age of onset with expectant management.[17] In addition, the presence of IUGR appears to be detrimental rather than protective for neonatal survival and severe preeclampsia and limits expectant management. Our series indicated that women with severe preeclampsia may have a statistically increased risk of IUGR (OR, 2.16; 95% CI, 1.10–4.24; $p=0.026$), which is consistent with Witlin et al's findings which suggested that IUGR was associated with decreased survival in univariate analysis (OR, 5.88; 95% CI, 1.81–19.26; $p=0.001$).[18] Interestingly, our results revealed that the marginally protective effect of HELLP was also implicated that to those of such disease may not only demonstrate in severe preeclampsia patients alone. For fear of the maternal complications in severe preeclampsia patients, precautionary strategies, well-prepared protocol and timely diagnosis could prevent the impending adverse events in suspected HELLP patients. The relatively high OR in terms of the risk of IUGR babies in the severe preeclampsia group was comparable to that of Chammas et al[19] who reported that immediate delivery may be beneficial for LBW and IUGR babies of severe preeclampsia patients.

The problems associated with delivery between 27 and 30 weeks of gestation could be attributable to refractory hypertension control in women with severe preeclampsia. Not only was there a high cesarean section rate but it was also noted that there was a prospect of neurodevelopmental disability in these extremely preterm newborns which really presents a clinical challenge.[20]

The strengths of our study were that it focused on Asian women (Taiwanese and Chinese); used clinical data from daily practice; was aware of the validity and reliability of data recording, coding, and keying in data accurately; delineated a whole spectrum of disease severity for preeclampsia; dealt with the effect of slight or little proteinuria in a subgroup of gestational hypertension patients and their progression later on and added some policy issue concerns regarding prenatal care versus no prenatal care,[21] which has a significant impact on public health affecting both mothers and their infants alike whether they are Taiwanese or Chinese.

Our study still had some limitations: it was hospital-based and unicenter-oriented; having a retrospective design, it did not have complete socioeconomic data or enough family history; the sample size was small; it did not entirely exclude preexisting medical conditions; some "key" lab data that could be used to diagnose some specific diseases were lacking; a model was not proposed in advance; clinical data were not used to monitor the progression from gestational hypertension to preeclampsia; it may not be easy to distinguish whether lack of BP control or disease *per se* alone affected pregnancy outcome; there was no standardized physicians' practice style or set well-established research protocol; and it was only performed from the perspective of hospital-oriented health care and medical center-based, and did not integrate or incorporate community health care services as a health care system model.

We suggested that women with severe preeclampsia have a greater chance to develop maternal complications and have a poor neonatal outcome, especially if they had not received prenatal care. The risk factor in women with gestational hypertension associated with maternal complications and poor pregnancy outcome was slight proteinuria that may lead to a greater likelihood of DIC and placental abruption. Risk factors associated with severe preeclampsia were prenatal care status, advanced maternal age, SBP and DBP, and significant proteinuria. In addition, with regard to the effect of gestational hypertension in patients with mild proteinuria, maternal complications became the only significant factor that contributed to pregnancy outcome. Although significant proteinuria was the main diagnostic criteria of severe preeclampsia, the importance of severe gestational hypertension without proteinuria or mild gestational hypertension with slight proteinuria cannot be overemphasized. We believe that these associated factors should be described to appropriately counseled patients. In our view, the important benefits of successful consultation and prenatal care may outweigh the risks encountered in women with hypertensive disorders in further describing to these patients the risks and possible outcomes before their pregnancy and delivery.

In conclusion, severe preeclampsia in women was significantly associated with maternal complications and preterm delivery, as well as LBW babies. Proteinuria may play some role in the progression of gestational hypertension to severe forms of preeclampsia associated with subsequent maternal complications and ELBW babies.

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