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Incidence and Risk Factors of HELLP Syndrome in Thai Pregnant Women with Severe Pre-eclampsia

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ABSTRACT

Objectives To determine the incidence and risk factors of HELLP syndrome in pregnant Thai women with severe pre-eclampsia and to compare pregnancy outcome.

Design Cross-sectional study.

Subject A total of 255 pregnant women with severe pre-eclampsia, ≥28 weeks of gestation, who delivered at Siriraj Hospital between January 2005 and June 2007.

Materials and Methods The medical records were reviewed to determine the incidence of HELLP syndrome. Characteristics regarding current pregnancy and delivery and maternal and neonatal outcomes were extracted.

Results The incidence of HELLP syndrome was 12.5%. Women with HELLP syndrome were significantly older, more likely to be multiparous and delivered at lower gestational age ($p<0.05$). Placental abruption and birth asphyxia significantly increased among women with HELLP syndrome ($p<0.05$).

Conclusion HELLP syndrome was found in 12.5% of severe pre-eclampsia pregnant women in our institute. Risk factors were old maternal age and preterm gestation.

Keywords: incidence, HELLP syndrome, severe pre-eclampsia, risk factors

Introduction

HELLP syndrome is a severe complication of pregnancy characterized by hemolysis, elevated liver enzymes and low platelet count. The term HELLP syndrome was described by Weinstein in 1982.[1] Some pregnant women develop just one or two of characteristics of this syndrome, which is termed partial HELLP syndrome (PHS).[2] It can be found in second trimester (15%), third trimester (50%), peripartum or postpartum period until 48 hours after delivery.[3] HELLP syndrome is a complication of severe pre-eclampsia that is insidious and progressive disease. If the diagnosis is rapid with prompt treatment, may decrease maternal and fetal morbidity and mortality. Between 4 and 18.9% of patients with pre-eclampsia or eclampsia develop HELLP syndrome.[4,5] Patients whose pregnancies are complicated by HELLP syndrome are at higher

risk for renal failure, consumptive coagulopathy, abruptio placentae, pulmonary and cerebral edema, subcapsular liver hematoma and hypovolumic shock.

Maternal complications were reported about 1.1-24.2%[5,6] and perinatal outcomes such as birth asphyxia, IUGR and fetal death were reported about 7.7-60%[7,8] resulted in preterm delivery. Genetics[9] and other factors such as maternal age, parity, race[10] may affect severity of disease individually.

The definite therapy for severe pre-eclampsia or eclampsia with or without HELLP syndrome is removal of all gestational products from the uterus. The use of antepartum corticosteroids, rescue surfactant, neonatal intensive care unit technology and the maternal transport of premature and immature pregnancies to tertiary care facilities have collectively increased the survivability of the infants.

The purpose of this report was to determine incidence of HELLP syndrome, to assess risk factors of HELLP syndrome in patients with severe pre-clampsia and to compare maternal and perinatal outcomes between women with severe pre-eclampsia and women with HELLP syndrome. The data from this study use to evaluation risk factors of HELLP syndrome for early diagnosis, early management and prevention of the progression of severe pre-eclampsia to HELLP syndrome.

Materials and Methods

A retrospective study was conducted at Siriraj Hospital with the approval of the institutional ethic committee. A total of 255 pregnant women who were diagnosed severe pre-eclampsia, gestational age 28 weeks or more who delivered in this hospital were enrolled.

HELLP syndrome was defined by the presence of all of the three following criteria[11]: hemolysis (characteristic peripheral blood smear, serum lactate dehydrogenase ≥600U/l, total serum bilirubin ≥1.2 mg/ml), elevated liver enzymes (serum aspartate aminotransferase ≥70 U/l) and low platelet count (<100,000 cells/μl).

Medical records and labor records were reviewed, data including baseline characteristics, current and past obstetric history, laboratory investigations such as hematocrit, platelet count, liver function test, creatinine and coagulogram, maternal complications and neonatal outcomes were recorded. Incidence of HELLP syndrome was estimated. Various characteristics were compared between HELLP syndrome and severe pre-eclampsia to determine associated factors for HELLP syndrome. Maternal and neonatal outcomes were also compared between groups.

The patients were divided into two groups: severe pre-eclampsia group (patients with severe pre-eclampsia but without alterations in laboratory tests for HELLP syndrome) and HELLP syndrome group.

Statistical analysis was performed using SPSS for Windows. Univariate analysis was used to compare various characteristics between different diseases. Using student t-test or chi-square test were used as appropriate. A p-value of <0.05 was considered statistically significant.

Results

During January 1st, 2005- June 30th, 2007, a total of 255 women with severe pre-eclampsia, who had gestational age of ≥ 28 weeks and deliverd at Siiriraj Hospital were recruited.

The baseline characteristics of the women with severe pre-eclampsia were as followed: mean maternal age was 28.3 ± 7.1 years and mean gestational age at diagnosis was 35.9 ± 3.9 weeks. Majority of these women were nulliparous (61.2%).

Of these 255 women with severe pre-eclampsia, 32 were diagnosed as HELLP syndrome. Therefore, the incidence of HELLP syndrome in this study was 12.5%.

Table 1 shows comparison of various characteristics between women with HELLP syndrome and severe pre-eclampsia. It was found that maternal age, number of parity, laboratory investigations such as LDH (serum lactate dehydrogenase), uric acid, TB (total bilirubin), DB

(direct bilirubin), AST (serum aspartate transminase, ALT (serum alanine transminase), creatinine and coagulogram were significantly increased in women with HELLP syndrome; however gestational age was significant lower in women with HELLP syndrome in varying degree (all p-values were < 0.05).

Table 2 shows multilogistic regression between women with HELLP syndrome and severe pre-eclampsia. It was found that maternal age more than 30 years and gestational age less than 32 weeks were independent factors of HELLP syndrome also compared with severe pre-eclampsia.

Table 3 shows comparison of maternal and women with HELLP syndrome neonatal outcomes between the two groups. Placental abruption was significantly increased in women with HELLP syndrome compared with women with severe pre-eclampsia (21.9% VS 1.3%, p-value < 0.001) but eclampsia and mode of delivery were not significantly different. Apgar scores at 1 and 5 minutes of <7 were significantly more common among HELLP syndrome.

Table 1. Baseline characteristics of pregnant women with severe preclampsia.

Characteristics	
Mean maternal age(years) ±SD	28.3 ±7.1
Mean gestational age(weeks) ±SD	35.9 ± 3.9
Parity (N %)	
Nullipara	156 (61.2%)
Multipara	99 (38.8%)

Table 2. Comparison of various characteristics.

	Severe pre-eclampsia (N=223)	HELLP syndrome (N=32)	p-value
Mean maternal age (years) ± SD	27.9 ± 7.0	31.7 ± 6.8	0.004
Mean gestational age (weeks) ± SD	36.3 ± 3.7	33.2 ± 4.5	<0.001
Parity (%)			0.011
Nullipara	143 (64.1%)	13 (40.6%)	
Multipara	80 (35.9%)	19 (59.4%)	
Lab.investigations (Mean ± SD)			
Hct (%)	35.48 ± 4.8	33.0 ± 5.9	0.011
Platelet (/μl)	234,452.0 ± 67,742.0	90,709.3 ± 60,900.8	<0.001
LDH (mg/dl)	435.4 ± 182.4	1,474.1 ± 1,450.3	0.005
Uric acid (mg/dl)	6.3 ± 1.7	7.3 ± 1.8	0.005
TB (mg/dl)	0.4 ± 0.5	1.7 ± 2.1	<0.001

DB (mg/dl)	0.1 ± 0.2	0.9 ± 1.9	<0.001
AST (mg/dl)	28.4 ± 29.3	268.2 ± 352	<0.001
ALT (mg/dl)	20.2 ± 33.2	198.5 ± 268.9	<0.001
Creatinine (mg/dl)	0.6 ± 0.3	0.9 ± 0.6	<0.001
PT (seconds)	10.9 ± 1.2	15.8 ± 16.0	<0.001
APTT (seconds)	27.6 ± 5.6	32.3 ± 8.2	<0.001

(Hct : hematocrit, TB : total bilirubin, DB : direct bilirubin, AST : serum aspartate transminase, ALT : serum alanine transminase<, PT : prothrombin time, APTT : activated partial prothombin time)

Table 3. Multilogistic regression between severe pre-eclampsia and HELLP syndrome.

	Adjusted odds ratio	**95% CI**	**p-value**
Age > 30 years	2.7	1.1-6.5	0.02
Gestational age < 32 weeks	5.9	2.3-15.3	0.00
Multipara	1.9	0.8-4.3	0.12

Table 4. Comparison of maternal outcomes and neonatal outcomes.

		Severe preeclampsia (N = 223)	**HELLP (N = 32)**	**p-value**
Placental abruption N(%)		3 (1.3)	7 (21.9)	<0.001
Eclampsia N(%)		1 (0.4)	1 (3.1)	0.108
Mode of delivery N(%)				0.475
	Normal	75 (33.6)	2 (6.3)	
	V/E	10 (4.5)	10 (4.5)	
	C/S	138 (62.4)	20 (62.5)	
Apgar score at 1st minute N(%)				<0.001
	7-10	190 (85.2)	16 (50)	
	4-6	24 (11.0)	6 (18.8)	
	0-3	9 (4.1)	10 (31.3)	
Apgar score at 5th minute N(%)				<0.001
	7-10	215 (96.4)	24 (75.0)	
	4-6	2 (0.9)	0 (0.0)	
	0-3	6 (2.8)	8 (25.0)	

(V/E : vacuum extraction, C/S : cesarean section)

Discussions

Although the term HELLP syndrome was defined by Weinstein[1] but the incidence and the risk factor of HELLP syndrome were not studied in our hospital.

In this study, the incidence of HELLP syndrome was 12.5% among severe pre-eclampsia. The reported rates of HELLP syndrome were different between studies. The retrospective population based cohort study of 558 pregnancies with severe pre-eclampsia showed that 12% had HELLP syndrome.[12] Another report of 615 Indian pregnant women found the incidence of HELLP syndrome was 23.68% among hypertensive disorder during pregnancy.[13] The differences might be due to the differences in patient's characteristics and conditions in each population and the differences in diagnostic criteria. This study used the standardized strict laboratory criteria which were defined by Sibia.[11]

Previous study found that the risk factor of HELLP syndrome was multipara compared with severe pre-eclampsia group[14] and in White and Chinese populations have HELLP syndrome more than East Indian population[15] due to appropriate ANC, early detection of severe pre-eclampsia and good medical records. Smoking in pregnant women was reduced the incidence of severe pre-eclampsia.[16]

Our study found that the possibility of HELLP syndrome increased if the pregnant women were older and preterm gestation. Laboratory findings showed that LDH, uric acid, total bilirubin, direct bilirubin, SGOT, SGPT, creatinine and coagulogram in pregnant were higher than severe pre-eclampsia group, while hematocrit and platelet count were less than severe pre-eclampsia group.

Maternal complications in pregnant women with HELLP syndrome included acute renal failure, disseminated intravascular coagulopathy, pulmonary edema, marked ascites, pleural effusion, adult respiratory distress syndrome and abruption of placenta.[17] This study, we found acute renal failure in 6 cases (0.18%) and disseminated intravascular coagulopathy in 2 cases (0.06%) of total cases of HELLP syndrome. In some study, eclampsia was found more frequently in HELLP syndrome group.[18]

This study demonstrated that maternal placental abruption increased significantly among HELLP syndrome group, but the maternal eclampsia and modes of delivery were not different between two groups. The cesarean section rates in two groups were very high, because when the disease was diagnosed we opted for the termination of pregnancy to avoid worsening complications of severe pre-eclampsia.

Perinatal outcome associated with placental abruption, intrauterine asphyxia and prematurity.[17] Our study demonstrated that neonatal morbidities increased significantly among HELLP syndrome group, including low Apgar scores at 1 and 5 minutes and majorities of such morbidities were due to prematurity.

HELLP syndrome was rapidly progressive with more maternal and perinatal morbidity and mortality, sometimes were not complete criteria of HELLP syndrome but significantly increased rate of cesarean delivery, eclampsia and preterm delivery.[18]

The limitation of this study were small sample size for HELLP syndrome group because we have clinical practice guideline for proper management of severe pre-eclampsia so that patients with severe pre-eclampsia usually did not progress to HELLP syndrome, lost some data from medical records and the last, some pregnant women did not delivery in our hospital because some cases had been refer to other hospitals.

Severe pre-eclampsia and HELLP syndrome must be diagnosed as soon as possible, so as to get the good maternal and perinatal outcomes. So, this is recommended that all pregnant or post-delivery women with slight or severe blood pressure elevation should be investigated in order to make an early diagnosis of severe pre-eclampsia or HELLP syndrome.

In conclusion, the incidence of HELLP syndrome in Siriraj Hospital was 12.5%. The factors that associated with HELLP syndrome included more maternal age, preterm gestational age. Maternal and neonatal morbidities increased among that HELLP syndrome. Therefore, early diagnosis and proper management could be attempted to improve maternal and perinatal outcomes.

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อุบัติการณ์และปัจจัยเสี่ยงของ HELLP syndrome ในสตรีตั้งครรภ์ไทยที่มีภาวะครรภ์เป็นพิษรุนแรง

ราชรัตน์ คำสัตย์, ธันยารัตน์ วงศ์วนานุรักษ์, ดิฐกานต์ บริบูรณ์หิรัญสาร

วัตถุประสงค์ *: เพื่อศึกษาอุบัติการณ์และปัจจัยเสี่ยงของ HELLP syndrome ในสตรีตั้งครรภ์ไทยที่มีภาวะครรภ์เป็นพิษรุนแรง และเปรียบเทียบผลของการตั้งครรภ์*

วิธีการศึกษา *: การศึกษาแบบตัดขวาง*

ประชากรที่ศึกษา *: หญิงตั้งครรภ์ที่ได้รับการวินิจฉัยครรภ์เป็นพิษรุนแรงจำนวน 255 ราย อายุครรภ์ตั้งแต่ 28 สัปดาห์ขึ้นไป และคลอดที่ รพ.ศิริราช*

วัสดุและวิธีการ *: เวชระเบียนผู้ป่วยใน ของผู้ป่วยที่ถูกศึกษา ได้ถูกนำมาเก็บข้อมูลวิเคราะห์เกี่ยวกับอุบัติการณ์ของ HELLP syndrome ลักษณะและปัจจัยต่างๆ ที่เกี่ยวกับการตั้งครรภ์และการคลอด และภาวะแทรกซ้อนของมารดาและทารก*

ผลของการศึกษา *: อุบัติการณ์ของ HELLP syndrome ในกลุ่มที่ทำการศึกษาพบว่ามี 12.5% ผู้หญิงที่มีภาวะ HELLP syndrome มีอายุมากกว่า มีประวัติคลอดมาแล้วหลายครั้ง อายุครรภ์น้อยกว่า มีผลตรวจทางห้องปฏิบัติการที่แตกต่าง ภาวะรกลอกตัวก่อนกำหนดมากกว่า และคะแนน Apgar น้อยกว่ากลุ่มครรภ์เป็นพิษรุนแรงอย่างมีนัยสำคัญ*

สรุป *: จากการศึกษาในสถาบันของเราพบว่า HELLP syndrome พบ 12.5% ของผู้ป่วยที่มีภาวะครรภ์เป็นพิษ ปัจจัยต่างๆ ที่มีผลได้แก่ อายุมารดามากและอายุครรภ์ก่อนกำหนด*