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Acute kidney injury in patients with HELLP syndrome

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Abstract

Purpose To evaluate the risk factors and renal prognosis of acute kidney injury (AKI) in patients with hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome.

Methods Women with HELLP syndrome over a 15-year period at Peking Union Medical College Hospital, China, were retrospectively studied.

Results A total of 108 patients with HELLP syndrome were included. Fifty-two (48.1%) patients were diagnosed with AKI (median serum creatinine, 139.72 μmol/L; range, 89.00–866.00); 11 (21.2%) required hemodialysis. The AKI group had significantly more multiparity ($p=0.034$), hemorrhage > 400 mL ($p=0.027$), severe systolic hypertension ≥ 160 mmHg ($p=0.005$), infection ($p<0.001$), and low hemoglobin ($p=0.002$) than non-AKI patients. Multivariate logistic regression showed that infection (OR 36.441, 95% CI 3.819–347.732, $p=0.002$), severe systolic hypertension (OR 5.295, 95% CI 1.795–15.620, $p=0.003$), and low hemoglobin (OR 0.960, 95% CI 0.932–0.988, $p=0.006$) were independent risk factors for AKI. Six patients with AKI died (mortality rate: 11.5%); no death occurred among patients without AKI. In addition to infection (OR 16.268, CI 1.334–198.385, $p=0.029$) and eclampsia (OR 69.895, CI 2.834–1723.910, $p=0.009$), elevated serum creatinine (OR 1.006, CI 1.001–1.011, $p=0.031$) was an independent predictor of maternal mortality. Renal function in 43 (82.7%) patients completely recovered. Two (3.8%) patients developed chronic renal dysfunction after 1 to 2 years of follow-up.

Conclusions Elevated creatinine was an independent predictor of maternal mortality in HELLP syndrome. AKI severely affects renal prognosis and mortality in pregnant women. The occurrence of AKI was related to infection, severe hypertension, and renal ischemia.

Keywords HELLP syndrome · Acute kidney injury · Outcome · Pregnancy

Introduction

Hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome is a rare and severe complication of pregnancy. HELLP syndrome develops in 0.1–0.9% of all deliveries, in 10–20% of women with preeclampsia, and in as many as 35.1% of women with eclampsia [1–6]. HELLP syndrome causes a high incidence of maternal and perinatal mortality and morbidity [2, 7, 8].

Acute kidney injury (AKI) is a severe complication of HELLP syndrome. Most previous studies have reported AKI occurrence in 7.7–25% of patients with HELLP syndrome [2, 7–10]; two studies reported AKI occurrence in 54–60% of cases [6, 11]. HELLP syndrome is an important cause of AKI in pregnancy, accounting for 15–65% of cases of pregnancy-related AKI [6, 9, 12–14]. Despite much research on HELLP syndrome, few studies have focused on the effect of AKI on the prognosis of pregnancy and on the risk factors and prognosis of AKI in this population [9, 12]. Therefore, this study aimed to evaluate the effect of AKI on maternal and perinatal outcomes and the risk factors for AKI in

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individuals with HELLP syndrome; patients without AKI were used as controls.

Methods

Patients

This retrospective study was conducted over a 15-year period between January 2002 and March 2017 at Peking Union Medical College Hospital. We included patients who gave birth at our hospital and those who were transferred from other hospitals for intensive postpartum care because of serious complications. Patients with preexisting chronic kidney disease or diabetes mellitus were excluded from this study. The following maternal and fetal variables were recorded: demographics, onset time of HELLP syndrome, symptoms, maternal complications and management, fetal distress, outcome of the newborn during the neonatal period, systolic and diastolic blood pressure, and serum creatinine levels. Specific investigations were performed to exclude rare causes of AKI, including antinuclear antibody, anti-dsDNA antibody, C3, C4, and antiphospholipid antibody. All patients with AKI were followed for at least 1 year postpartum or until death.

Definitions

The diagnosis of HELLP syndrome was made on the basis of the following criteria [8, 15]: (1) microangiopathic hemolytic anemia with an abnormal blood smear and elevated lactate dehydrogenase (LDH) levels > 600 IU/L or bilirubin levels > 20.52 μmol/L; (2) liver dysfunction indicated by aspartate transaminase (AST) levels > 70 IU/L; and (3) a platelet count $< 100 \times 10^9$/L. The following Kidney Disease Outcomes Quality Initiative (KDOQI) criteria were used to diagnose AKI [16]: (1) an increase in serum creatinine of ≥ 0.3 mg/dL (≥ 26.5 μmol/L) within 48 h; (2) an increase in serum creatinine to ≥ 1.5 times baseline within the previous 7 days; or (3) urine volume ≤ 0.5 mL/kg/h for 6 h. AKI was further classified into three stages according to KDOQI criteria as follows: (1) Stage 1, an increase in serum creatinine of 1.5–1.9 times baseline or ≥ 0.3 mg/dL (≥ 26.5 μmol/L), or urine output of < 0.5 mL/kg/h for 6–12 h; (2) Stage 2, an increase in serum creatinine of 2.0–2.9 times baseline, or urine output of < 0.5 mL/kg/h for ≥ 12 h; (3) Stage 3, increase in serum creatinine of 3 times baseline or to ≥ 4.0 mg/dL (≥ 353.6 μmol/L) or initiation of renal replacement therapy, or urine output of < 0.3 mL/kg/h for ≥ 24 h or anuria > 12 h [16].

Preeclampsia was defined as the onset of hypertension (> 140/90 mmHg) and proteinuria > 0.3 g/24 h after 20 weeks of gestation. Eclampsia was defined as occurrence of new-onset seizures in the presence of preeclampsia. In patients with preexisting hypertension, preeclampsia was defined as the development of new proteinuria or terminal organ dysfunction after 20 weeks of gestation. Patients were followed-up till death, complete or partial recovery of renal function, and the duration from AKI occurrence to complete recovery was recorded at five time points (1 week, 1 month, 3 months, 6 months and 1 year). Complete recovery of AKI was determined when serum creatinine levels returned to the normal range. Partial recovery was defined as improved renal function, but with persistently elevated serum creatinine levels in dialysis-independent patients. Infection was diagnosed on the basis of clinical manifestations, positive microbiological evidence, and imaging changes in the lungs, gastrointestinal tract, or urogenital tract.

Statistical analysis

Statistical analysis was performed with SPSS version 21.0 (IBM, Armonk, NY, USA). Continuous variables with a normal distribution were analyzed with the independent-samples *t* test. Data with a non-normal distribution were compared with the Mann–Whitney *U* test. The χ^2 test was used to analyze categorical variables. Univariate and multivariate logistic regression models were constructed with variables that were significantly different between women with versus without AKI to assess their possible association with AKI. Predictive factors of maternal mortality were analyzed with logistic regression in the whole cohort. A two-sided value of $p < 0.05$ was considered statistically significant for all analyses.

Results

Characteristics of patients with AKI and HELLP syndrome

A total of 108 women who were diagnosed with HELLP syndrome were included. AKI developed in 52 (48.1%) patients. Women with AKI had a significantly higher maternal mortality rate than those without AKI (11.5% vs. 0.0%, $p = 0.011$). The AKI group had significantly higher rates of multiparity ($p = 0.034$), bleeding > 400 mL ($p = 0.027$), severe systolic hypertension ≥ 160 mmHg ($p = 0.005$), and lower hemoglobin levels ($p = 0.002$), compared with the non-AKI group (Table 1). Patients with AKI were divided into three groups, according to KDOQI classification. The platelet count and hemoglobin level were significantly lower, and AST was significantly higher among patients with Stage 2 and Stage 3 AKI than among those with Stage 1 (Table 2).

Among all patients with HELLP syndrome, 15 (13.9%) developed infections, including pulmonary infection

Table 1 Characteristics of women with HELLP syndrome with versus without acute kidney injury

Variable	All patients ($n=108$)	Non-AKI ($n=56$)	AKI ($n=52$)	p value
Age (years)	31.25 ± 5.97	31.39 ± 5.62	31.10 ± 6.39	0.798
History of hypertension	11 (10.2%)	4 (7.1%)	7 (13.5%)	0.348
Multipara	54 (50.0%)	22 (39.3%)	32 (61.5%)	0.034
Onset time of HELLP (weeks)	32.29 ± 4.46	32.04 ± 5.01	32.56 ± 3.83	0.542
Premature birth[a]	98/114 (86.0%)	48/58 (82.8%)	50/56 (89.3%)	0.421
Cesarean delivery	101 (93.5%)	50 (89.3%)	51 (98.1%)	0.115
Eclampsia	20 (18.5%)	8 (14.3%)	12 (23.1%)	0.322
Bleeding (> 400 mL)	21 (19.4%)	6 (10.7%)	15 (28.8%)	0.027
Infection	15 (13.9%)	1 (1.8%)	14 (26.9%)	< 0.001
Perinatal death[a]	46/114 (40.4%)	19/58 (32.8%)	27/56 (48.2%)	0.126
Maternal death	6 (5.6%)	0 (0.0%)	6 (11.5%)	0.011
SBP ≥ 160 mmHg	68 (63.0%)	28 (50.0%)	40 (76.9%)	0.005
DBP ≥ 110 mmHg	46 (42.6%)	19 (41.3%)	27 (58.7%)	0.080
Lowest platelet count ($\times 10^9$cell/L)	50.74 ± 23.58	54.09 ± 23.95	47.13 ± 22.86	0.126
Lowest hemoglobin (g/L)	88.53 ± 18.85	93.95 ± 18.20	82.69 ± 17.92	0.002
LDH (U/L)	684 (602, 1031)	650 (426, 980)	704 (638, 1169)	0.064
AST (U/L)	127 (75, 273)	124 (75, 321)	127 (79, 273)	0.794
ALT (U/L)*	136.5 (77, 225.50)	121 (76, 213)	144 (83, 259)	0.517
Total bilirubin (μmol/L)*	15.50 (9.83, 33.95)	11.50 (8.90, 18.50)	25.80 (11.90, 51.64)	< 0.001
Direct bilirubin (μmol/L)*	5.90 (3.44, 12.10)	4.50 (3.00, 7.52)	8.10 (4.70, 14.80)	0.001
Serum creatinine (μmol/L)*	85.00 (69.25, 137.00)	70.00 (62.25, 80.86)	139.72 (103.50, 427.25)	< 0.001*

HELLP hemolysis, elevated liver enzymes, and low platelet count, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *LDH* lactate dehydrogenase, *AST* aspartate transaminase, *ALT* alanine transaminase

*Variables are expressed as median and interquartile range; other unindicated data are shown as mean ± SD or number (%)

[a]The total number of fetuses in each group was used as the denominator for calculation of percentage

($n=10$), uterine cavity infection ($n=2$), and gastrointestinal infection ($n=2$). Fourteen (26.9%) cases of infection occurred in the AKI group, whereas only one (1.8%) occurred in the non-AKI group ($p<0.001$).

In the whole cohort, 82 (75.9%) women had preeclampsia and 20 (18.5%) had eclampsia. Twenty-four (21.1%) intrauterine stillbirths were detected and 22 (19.3%) neonates died in the neonatal period, for a perinatal death rate of 40.4%. None of these variables was significantly different between the AKI and non-AKI groups.

Risk factors for developing AKI in HELLP syndrome

Among the variables shown in Table 1, univariate logistic regression analysis showed that the following five variables were associated with AKI: multiparity ($p=0.022$), bleeding ($p=0.021$), infection ($p=0.004$), severe systolic hypertension ($p=0.005$), and low hemoglobin levels ($p=0.003$). Multiple regression analysis showed that infection ($p=0.002$), severe systolic hypertension ($p=0.003$), and low hemoglobin levels ($p=0.006$) were independently associated with AKI in patients with HELLP syndrome (Table 3).

Predictive factors for maternal death in HELLP syndrome

Six women died within 3 weeks postpartum. The median serum creatinine level ($p=0.003$) and the incidence of AKI ($p=0.011$) were significantly higher in the non-survivor group compared with the survivor group. The non-survivor group also had significantly higher rates of perinatal infant mortality ($p=0.038$), infection ($p=0.034$), and eclampsia ($p=0.010$), and higher total and direct bilirubin levels ($p=0.004$ and 0.012, respectively) than the survivor group (Table 4).

Univariate regression analysis showed that the following variables were significantly associated with maternal mortality: total bilirubin ($p=0.008$), direct bilirubin ($p=0.030$), serum creatinine ($p=0.036$), infection ($p=0.021$), and eclampsia ($p=0.009$). When these five variables were included in a multiple regression model, serum creatinine ($p=0.031$), infection ($p=0.029$), and eclampsia ($p=0.009$)

Table 2 Comparison of patient characteristics according to AKI stage in women with HELLP syndrome

Variable	Stage 1 ($n=27$)	Stage 2 ($n=12$)	Stage 3 ($n=13$)	p value
Age (years)	31.37 ± 6.51	30.08 ± 6.52	31.46 ± 6.41	0.827
History of hypertension	2 (7.4%)	2 (16.7%)	3 (23.1%)	0.370
Onset time of HELLP (weeks)	31.70 ± 3.83	31.92 ± 4.01	33.77 ± 3.32	0.295
Premature birth[b]	25/28 (89.3%)	11/12 (91.7%)	14/16 (87.5%)	0.940
Eclampsia	9 (33.3%)	2 (83.3%)	1 (7.7%)	0.164
Bleeding (> 400 mL)	5 (18.5%)	5 (41.7%)	5 (38.5%)	0.229
Infection	5 (18.5%)	4 (33.3%)	5 (38.5%)	0.350
Perinatal death[b]	15/28 (50.0%)	6/12 (50.0%)	6/16 (43.8%)[a]	0.585
Maternal death	2 (7.4%)	2 (16.7%)	2 (15.4%)	0.622
SBP ≥ 160 mmHg	21 (77.8%)	10 (83.3%)	9 (69.2%)	0.697
DBP ≥ 110 mmHg	15 (55.6%)	7 (58.3%)	5 (38.5%)	0.526
Lowest platelet count ($\times 10^9$cell/L)	57.22 ± 23.32	38.00 ± 19.66[a]	34.62 ± 14.33*,**	0.002
Lowest hemoglobin (g/L)	92.37 ± 16.80	76.42 ± 14.19[a]	68.38 ± 9.85*	< 0.001
LDH (U/L)[a]	695.00 (624.00, 974.50)	902.00 (617.00,1477.00)	801.00 (650.00, 1940.00)	0.521
AST (U/L)[a]	89.00 (74.00, 189.00)	98.00 (81.00, 121.00)	348.35 (228.50, 454.50)*	0.009
Total bilirubin (μmol/L)[a]	17.70 (11.8, 40.2)	33,55 (22.15, 62.02)	35.47 (13.45, 147.60)	0.169

HELLP hemolysis, elevated liver enzymes, and low platelet count, *SBP*, systolic blood pressure, *DBP* diastolic blood pressure, *LDH* lactate dehydrogenase, *AST* aspartate transaminase

[a]Variables are expressed as median and interquartile range; other unindicated data are shown as mean ± SD or number (%)

[b]The total number of fetuses in each group was used as the denominator for calculation of percentage

*$p < 0.01$, compared with Stage 1

**$p < 0.01$, compared with Stage 2

Table 3 Univariate and multivariate logistic regression analyses of factors associated with acute kidney injury

Variable	Univariate analysis		Multivariate analysis	
	Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value
Multipara	2.473 (1.140, 5.364)	0.022		0.468
Bleeding (> 400 mL)	3.378 (1.197, 9.537)	0.021		0.330
Infection	20.263 (2.556, 160.655)	0.004	36.441 (3.819, 347.732)	0.002
SBP ≥ 160 mmHg	3.333 (1.452, 7.652)	0.005	5.295 (1.795, 15.620)	0.003
Lowest hemoglobin (g/L)	0.966 (0.944, 0.988)	0.003	0.960 (0.932, 0.988)	0.006

SBP systolic blood pressure; *CI* confidence interval

remained independent risk factors for maternal death (Table 5).

Outcomes of AKI as a complication of HELLP syndrome

Among 52 patients who developed AKI, 11 (21.2%) required renal replacement therapy. Among these, seven patients had anuria with a duration of 7 to 22 days. Five (9.6%) women had plasma exchange. Twenty-three (44.2%) patients were administered plasma transfusion, and 22 (42.3%) were provided blood transfusion with a total volume of 400 to 4800 mL. Two (3.8%) patients underwent hysterectomy because of persistent uterine bleeding.

Although six non-surviving patients had AKI, renal function improved in five of them before death and none of them died of AKI. One patient was lost to follow up after discharge. Her renal function began to recover after 1 week of hemodialysis, with serum creatinine levels decreasing to 436 μmol/L 2 weeks postpartum. In the other 45 women, renal function completely recovered in 43 (82.7%) patients; 32 (74.4%) of these women recovered within 1 week (Table 6). Two (3.8%) patients had partial recovery, with a serum creatinine level of 195 μmol/L after 1 year in one patient and 127 μmol/L after 2 years in the second patient.

Table 4 Comparison of characteristics between surviving and non-surviving women with HELLP syndrome

Variable	Survivors ($n=102$)	Non-survivors ($n=6$)	p value
Age (years)	31.11 ± 5.91	33.67 ± 7.15	0.310
History of hypertension	10 (9.8%)	1 (16.7%)	0.484
Multipara	49 (48.0%)	5 (83.3%)	0.205
Duration of pregnancy (weeks)	32.31 ± 4.53	31.83 ± 3.31	0.799
Premature birth[b]	92/108 (85.2%)	6/6 (100.0%)	0.593
Perinatal death[b]	41/108 (38.0%)	5/6 (83.3%)	0.038
Prepartum HELLP	98 (96.1%)	6 (100%)	1.000
Infection	12 (11.8%)	3 (50.0%)	0.034
Bleeding, > 400 mL	18 (17.6%)	3 (50.0%)	0.086
Eclampsia	16 (15.7%)	4 (66.7%)	0.010
SBP ≥ 160 mmHg	63 (61.8%)	5 (83.3%)	0.409
DBP ≥ 110 mmHg	43 (42.2%)	3 (50.0%)	0.698
AKI incidence	46 (45.1%)	6 (100.0%)	0.011
Lowest hemoglobin (g/L)	88.81 ± 19.23	83.67 ± 10.39	0.518
Lowest platelet, ($\times 10^9$/L)	51.18 ± 23.93	43.33 ± 16.26	0.431
ALT[a] (U/L)	135.80 (75.00, 224.00)	149.20 (79.00, 605.00)	0.380
AST[a] (U/L)	127.00 (75.00, 273.00)	262.85 (102.00, 423.70)	0.539
LDH[a] (U/L)	682.00 (602.00, 980.00)	1141.00 (632.00, 1477.00)	0.309
Total bilirubin[a] (μmol/L)	14.35 (9.70, 32.30)	47.43 (31.60, 240.30)	0.004
Direct bilirubin[a] (μmol/L)	5.75 (3.30, 11.20)	16.40 (7.60, 42.75)	0.012
Albumin (g/L)	26.38 ± 4.94	25.27 ± 3.49	0.590
Serum creatinine[a] (μmol/L)	85.88 (68.00, 117.00)	174.50 (141.44, 671.80)	0.003

HELLP hemolysis, elevated liver enzymes, and low platelet count, *AKI* acute kidney injury, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *ALT* alanine transaminase, *LDH* lactate dehydrogenase, *AST* aspartate transaminase

[a]Variables are expressed as median and interquartile range; other unindicated values are shown as mean ± SD or number (%)

[b]The total number of fetuses in each group was used as the denominator for calculation of percentage

Table 5 Univariate and multivariate logistic regression analyses for predictive factors of maternal mortality in HELLP syndrome

Variable	Univariate analysis		Multivariate analysis	
	Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value
Total bilirubin (μmol/L)	1.010 (1.003, 1.018)	0.008		0.371
Direct bilirubin (μmol/L)	1.011 (1.001, 1.021)	0.030		0.493
Serum creatinine, (μmol/L)	1.003 (1.000, 1.006)	0.036	1.006 (1.001, 1.011)	0.031
Infection	7.500 (1.357, 41.463)	0.021	16.268 (1.334, 198.385)	0.029
Eclampsia	10.750 (1.814, 63.700)	0.009	69.895 (2.834, 1723.910)	0.009

HELLP hemolysis, elevated liver enzymes, and low platelet count, *CI* confidence interval

Discussion

The incidence of pregnancy-related AKI has significantly declined over the last three decades in developing countries, but it remains an important cause of maternal and fetal morbidity and mortality [1]. HELLP syndrome is a serious disorder in pregnancy, accounting for 15–40% of all cases of pregnancy-related AKI and up to 54–65% of severe cases [6, 9, 12–14]. The incidence of AKI ranges from 7.7 to 60% among patients with HELLP syndrome, based on different definitions of AKI in different studies [2, 6–11, 17]. In the present study, AKI developed in 48.1% of women with HELLP syndrome. This incidence of AKI is similar to that in another Chinese report [11].

HELLP syndrome frequently results in adverse maternal outcomes [18]. The mortality rate varies from 0 to 12% in women with HELLP syndrome [2, 6, 8, 9] and from 12 to 34% in women with AKI and HELLP syndrome [8, 10, 14, 19]. However, few studies have investigated the effect of

Table 6 Outcomes of acute kidney injury in women with HELLP syndrome

Outcome	Number of cases ($n=52$)	Percentage
Death	6	11.5
Lost of follow-up	1	1.9
Complete recovery	43	82.7
Within 1 week	*32*	*74.4* (*74.4*)[a]
Within 1 month	*5*	*11.6* (*86.0*)[a]
Within 3 months	*2*	*4.7* (*90.7*)[a]
Within 6 months	*3*	*7.0* (*97.7*)[a]
Within 1 year	*1*	*2.3* (*100.0*)[a]
Partial recovery	2	3.8

HELLP hemolysis, elevated liver enzymes, and low platelet count

[a]Data are expressed as percentage of recovery, with 43 as the denominator; cumulative percentages are shown in parentheses

AKI on the prognosis of pregnant women with this syndrome. In our study, we compared patients with versus without AKI. All maternal deaths in this study occurred in the AKI group. Multivariate regression analysis showed that serum creatinine levels were an independent risk factor for maternal death after adjustment for confounders. This finding suggests that AKI is an important risk factor for poor outcome in patients with HELLP syndrome. Infection was also an independent predictor of maternal prognosis in HELLP syndrome. Multivariate regression showed infection was independently associated with AKI. Although a causal relationship could not be identified because of the retrospective nature of this study, AKI may combine with infection to aggravate HELLP syndrome and worsen its prognosis. In our study, non-survivors had a higher rate of eclampsia than did survivors. Multivariate logistic regression showed that eclampsia was another independent risk factor for maternal death.

Perinatal morbidity and mortality rates are significantly higher in women with HELLP syndrome than in the general population [2, 9, 19]. The overall perinatal mortality rate is 7–26.1% in HELLP syndrome [2, 9] and 26.1–34% in HELLP syndrome complicated by AKI [9, 19]. Gul et al. found that perinatal mortality was related to the severity of kidney injury in patients with HELLP syndrome and AKI [9]. Perinatal mortality was 11.8% in patients with creatinine levels < 176.8 μmol/L, while it was 37.5% when creatinine levels were > 176.8 μmol/L. Preterm birth and intrauterine growth restriction were the main causes of perinatal death. Preterm delivery occurs in approximately 70–72% of patients with HELLP syndrome [19, 20]. In our study, the preterm delivery rate was 85.2%. Intrauterine stillbirths were detected in 21.1% of patients and 19.3% of neonates died in the neonatal period, with a total perinatal mortality rate of 40.4%. We compared preterm delivery and perinatal mortality rates in patients with versus without AKI and did not find any significant differences between the groups. These results suggest that HELLP syndrome is the main risk factor for perinatal death, with AKI having no further significant effect on perinatal mortality.

Termination of pregnancy is the main effective treatment for HELLP syndrome. Most patients with HELLP syndrome start to improve within the first 24 to 48 h after delivery [21]. Patients who fail to improve after delivery are at major risk of higher morbidity and mortality rates. Postpartum plasma exchange is effective for severe HELLP syndrome [22, 23]. Recently, Simetka et al. recommended that plasma exchange should be considered in all patients who show no significant improvement in AST levels, and especially in platelet levels, within 24 to 48 h of delivery [23]. In our study, only five (9.6%) women received plasma exchange. Dialysis was performed in 21.2% of patients in this study. AKI associated with HELLP syndrome usually has a favorable renal outcome. Most of these patients (93–100%) are discharged without any significant residual renal impairment [8, 9, 12]. Among 52 patients who developed AKI in our study, 74.4% had complete recovery, while 3.8% had partial recovery and 11.5% died. This outcome is much worse than that reported in previous studies [8, 9, 12]. Jacquemyn et al. studied long-term renal function after HELLP syndrome and found that HELLP syndrome was not associated with long-term renal complications after 5 years of follow-up [24]. However, that study included only 10 patients who completed follow-up and included no basic information about renal function at the time of pregnancy termination.

The mechanisms of AKI occurring in HELLP syndrome are not well known. Our study showed that severe anemia, severe systolic hypertension, and infection were independent factors associated with AKI. Hemorrhage is the leading cause of pregnancy-related AKI [25–27]. In patients with HELLP syndrome, postpartum hemorrhage is the second most common cause of AKI, accounting for 26% of all cases [12]. In our study, hemorrhage (> 400 mL) occurred in 19.4% of patients and its occurrence was significantly more common in the AKI group than in the non-AKI group. Although hemorrhage was not associated with AKI in multivariate regression, a reduced hemoglobin level, which was caused by hemorrhage and/or intravascular hemolysis, was related to the severity of kidney injury and was an independent risk factor for AKI. Recently, Ospina-Tascon et al. observed substantial changes in microcirculatory blood flow and capillary density in patients with HELLP syndrome [28]. Microvascular dysfunction may increase the sensitivity of the kidney to ischemia. A previous study reported that patients with HELLP syndrome and AKI had higher LDH and AST levels than HELLP syndrome patients without AKI [9]. Although the AST level was associated with the severity of AKI in the present study, no difference was found in

LDH or AST between patients with versus without AKI. One explanation for this finding may be that the maximum values of LDH and AST were not obtained in our study because these parameters were not monitored as regularly as platelets, hemoglobin, and serum creatinine.

Notably, HELLP syndrome overlaps with hemolytic uremic syndrome (HUS), especially atypical HUS and thrombotic thrombocytopenic purpura (TTP) during the perinatal period. The differential diagnosis is challenging in some cases, particularly when patients present with severe AKI. The diagnosis of HELLP syndrome in this study was based on the relatively specific criteria of the triad of microangiopathic hemolytic anemia, low platelet count, and elevated liver enzymes, including AST greater than 70 IU/L. The levels of ADMADS-13 activity and HUS-related complement system activation and regulation were not measured to exclude the possibility of TTP/HUS because they are not available at our hospital. However, the obvious liver dysfunction and the rapid recovery of AST, ALT, and hemolysis after delivery supported the diagnosis of HELLP syndrome rather than HUS/TTP.

There are several limitations to the present study. First, this was an observational study. We could not determine a causal relationship between AKI and its associated factors. Second, our hospital not only provides medical services for local pregnant women but also admits patients with severe and complicated conditions from throughout the country. Some patients with severe complications of HELLP syndrome were transferred from other hospitals for further intensive therapy. Therefore, the incidence of AKI and maternal and perinatal mortality rates in HELLP syndrome do not represent the true rates in the general population of pregnant women. A large prospective study on AKI development, its renal pathology, and clinical prognosis in women with HELLP syndrome is necessary to confirm the present results.

In summary, AKI is a serious complication of HELLP syndrome during pregnancy and the postpartum period. The present study found that elevated serum creatinine levels were an independent predictive factor of maternal mortality. Development of AKI was associated with severe systolic hypertension, severe anemia, and infection.

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Compliance with ethical standards

Conflict of interest The authors declares that they have no conflict of interest.

Ethical approval All procedures performed in studies were in accordance with the ethical standards of the Ethics Committee at Peking Union Medical College Hospital and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required.

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