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Analysis of Risk Factors Affecting the Outcome of Critically Ill Pregnant and Postpartum Women

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Abstract

The mortality of critically ill pregnant women is an important global health concern. Therefore, we evaluated the risk factors affecting the mortality of critically ill pregnant women admitted to the intensive care unit. All critically ill pregnant patients >18 year from the second affiliated hospital of Wenzhou Medical University. Finally, a total of 100 adult pregnant women were admitted to the intensive care unit. 69 pregnant women were survivor (28.29 ± 4.70 year) with gestational age of 33.33 ± 6.13 week; while 31 pregnant women non-survivor (29.50 ± 5.37 year) with gestational age of 33.21 ± 3.44 week. Multivariable logistic regression analysis showed that PT(OR:6.409; 95% CI, 1.855-22.140; p=0.003), total bilirubin (OR:3.125; 95% CI, 1.013-9.644; p=0.037) and APACHE III score (OR:4.750; 95% CI, 1.488-15.167; p=0.009) were associated with maternal mortality. Considering these promising results, PT, total bilirubin and APACHE III score significantly affect the outcomes of pregnant women admitted to the ICU. Critically ill pregnant patients with liver problems should be carefully monitored.

Keywords Pregnancy; Mortality; Intensive Care unit

Introduction

Maternal mortality is unacceptably high. About 800 women die from pregnancy or childbirth-related complications around the world every day. An estimated 287 000 maternal deaths occurred worldwide in 2010, most of which were in low-income and middle-income countries and were avoidable [1]. Critical illness during pregnancy and postpartum is considered to be a serious event. Maternal mortality is monitored and examined as a key indicator of obstetric care. The United Nations considers it to be one of the eight global development goals in the new millennium [2]. Particular emphasis has been placed in the literature on maternal outcomes, which has shown that maternal mortality is a rare complication in developed countries [3,4]. However, there are still significant disparities in developing countries, 99% of all maternal deaths occur in developing countries [5].

Studies from other developed and developing countries have reviewed the care of critically ill obstetric patients. But up-to-date data on these patients in China are limited. The purpose of this study was to determine the risk factors affecting the mortality of critically ill pregnant and postpartum women admitted to our ICU in China.

Methods

This study was retrospective and single-centre and conducted on all pregnant and postpartum women (within 6 weeks) admitted over a 3-year period, from January 2013 to December 2015 to the ICU and emergency intensive care unit (EICU) at the second affiliated hospital of Wenzhou Medical University, China which is a tertiary referral centre have 54 beds in ICU. Written informed consent was obtained from all patients. The second affiliated hospital of Wenzhou Medical University Human Research Ethics Committee approval was obtained for the use of all samples by using a protocol that conforms to the provisions of the Declaration of Helsinki (as revised in Seoul, 2008). Our study was reviewed by their ethics committee and omits all the Declaration of Helsinki stuff it's over kill.

Inclusion criteria: Pregnancy was confirmed by a positive qualitative serum human chorionic gonadotropin test; all pregnant women were >18 yrs; pregnant women were admitted to the ICU or EICU in the antepartum or postpartum period due to different diseases, which are summarized in Tables 1 and 2.

Data worst result within first 24 hours following admission was obtained from the institutional paper and electronic medical records. Numerous characteristics of the patients were collected, including age, hospital stays, ICU stays, gestational weeks, delivery mode, mechanical ventilation, continuous renal replacement therapy (CRRT), primary reason for admission to ICU, and obstetric complications. And there were only ICU data included.

Gem Premier 3000 (USA) was used for blood gas analysis, GE Solar 8000M (USA) was used for monitoring of physiological parameters. The APACHE III scores [6], and laboratory results from the first 24 hr after ICU admission are shown in Table 3. The main maternal outcome was all-cause hospital mortality.

Statistical analysis

Continuous variables in this study followed a normal distribution. Therefore, all continuous data are summarized as (X ± s), and categorical data as percentages. Difference in medians between the two groups was compared with the two-sample t-test. Differences in proportions were compared using the chi-square test or the Fisher's exact test, as appropriate. P<0.05 was considered to be statistically significant. To determine the association of predictors with the main outcome, the variables were considered for multivariable logistic

regression models, had P values <0.05 in the uni-variate analysis, and were biologically plausible. Odds ratio (OR) and 95% confidence intervals (CI) were calculated. SPSS 15.0 was used for data analyses.

Results

During the study period, a total of 100 adult pregnant women (>18 yr) were admitted to the ICU, of whom 69 were survivor (28.29 ± 4.70 yr) with gestational age of 33.33 ± 6.13 week, while 31 non-survivor (29.50 ± 5.37 yr) in antepartum or postpartum period with gestational age of 33.21 ± 3.44 week.

The general characteristics of the women admitted to the ICU during the study period are summarized in Table 1. Most women were postpartum check-in (97%), primipara (58%), had cesarean delivery (68%) and needed mechanical ventilation (65%), while some needed CRRT (39%).

Variable	
AgeY	28.76 ± 5.03
Hospital stayD	20.88 ± 1 7.80
ICU stayD	6.07 ± 5.86
Gestational weekw	34 ± 5.3
<28 w	12 (12%)
28-37 w	56 (56%)
≥ 37 w	32 (32%)
survivor	69(69%)
non-survivor	31(31%)
Prenatal check-in	3 (3%)
Postpartum check-in	97 (97%)
Multipara	42 (42%)
Primipara	58 (58%)
Vaginal delivery	32 (32%)
Cesarean delivery	68 (68%)
Mechanical ventilation	65 (65%)
CRRT	39 (39%)
CRRT timeh	35.90 ± 25.27

Table 1: General characteristics of the admitted women.

The admitted patients were further analyzed to determine the cause of admission (Table 2). Most admissions were due to obstetric causes (61%). Acute fatty liver of pregnancy, postpartum hemorrhage and gestational hypertension syndrome were the most common obstetric causes, while cardiac insufficiency, hepatic insufficiency and pneumonia were the most common non-obstetric causes.

The following risk factors were significantly associated with the outcome of pregnant women by univariate analysis: APACHE III score, higher lactic acid levels, blood count especially Hb level, blood coagulation function including PT level, liver function including ALT, total bilirubin and ALB levels (Table 3).

	Number%
Obstetric	61 (61%)
Acute fatty liver of pregnancy Postpartum hemorrhage	21 (21%) 15 (15%)
Gestational hypertension syndrome	14 (14%)
Pre-eclampsia/eclampsia	12 (12%)
Amniotic fluid embolism HELLP syndrome	7 (7%) 2 (2%)
Others	4 (4%)
Non-obstetric	39 (39%)
Cardiac insufficiency Hepatic insufficiency Pneumonia Sepsis	16 (16%) 11 (11%) 6 (6%) 4 (4%)
SLE	4 (4%)
ITP Central nervous system diseases	2 (2%) 1 (1%)
Pulmonary embolism	1 (1%)
ARDS	1 (1%)
Others	1 (1%)

Table 2: Reasons for ICU admission; HELLP syndrome: Hemolysis, Elevated Liver Enzymes, Low Platelet syndrome; SLE: Systemic Lupus Erythematosus; ITP: Idiopathic Thrombocytopenic Purpura; ARDS: Acute Respiratory Distress Syndrome.

Multivariable logistic regression analysis identified the following independent risk factors associated with maternal mortality: PT, OR 6.409 (95% CI: 1.855-22.140, p=0.003); total bilirubin, OR 3.125 (95% CI: 1.013-9.644, p=0.037); and APACHE score, OR 4.750 (95% CI: 1.488-15.167, p=0.009) (Table 4).

Discussion

Only 0.1-0.9% of pregnant women is admitted to the ICU (7). Several studies have reported the causes of ICU admissions of pregnant women in various centers across the world [3,8,9]. Their care presents specific and exceptional challenges for the doctors [10,11].

The most common causes of ICU admissions of critically ill pregnant women include pregnancy-related complications and severe diseases [12]. Maternal mortality is the measure of a country's comprehensive development index. The cause of maternal mortality varies among different countries and regions, most women die from preeclampsia and obstetric hemorrhage, but multiple organ dysfunction syndrome remains the leading cause in the ICU worldwide [13].

	Pregnant women survivorn=69	Pregnant women non-survivorn=31	t	P
AgeY	28.29 ± 4.70	29.50 ± 5.37	-0.903	0.369
Gestational weeksw	33.33 ± 6.13	33.21 ± 3.44	0.066	0.947
APACHE	54.21 ± 19.07	66.37 ± 27.22	-2.094	0.039
Oxygenation index (mmHg)	311.37 ± 121.68	296.97 ± 120.96	0.410	0.683
MAP(mmHg)	93.58 ± 17.88	93.50 ± 16.82	0.017	0.986
A-aDO2 (mmHg)	163.29 ± 97.67	200.21 ± 100.10	-0.1.081	0.283
Lactic acid (mmol/L)	2.93 ± 0.74	4.80 ± 1.87	-2.301	0.024
White Blood Cell ($\times 10^9$/L)	17.39 ± 7.89	20.34 ± 6.41	-1.138	0.259
Hemoglobin (g/L)	103.20 ± 26.64	90.36 ± 20.6	-2.119	0.037
Blood Platelet ($\times 10^9$/L)	126.55 ± 82.30	101.50 ± 48.60	1.038	0.302
Prothrombin Time (s)	14.25 ± 4.44	23.03 ± 12.13	-4.832	0.000
Total bilirubin (umol/L)	64.20 ± 37.47	157.05 ± 87.04	-3.656	0.000
Alanine Transaminase (U/L)	56.62 ± 33.52	256.12 ± 73.52	-3.749	0.000
Albumin (g/L)	22.90 ± 5.11	27.75 ± 8.81	-2.934	0.004
Pro-ALB(g/L)	172.34 ± 92.18	202.10 ± 115.30	0.426	0.275
Creatinine (umol/L)	173.83 ± 89.48	207.66 ± 96.83	0.217	0.505
Blood Glucose (mmol/L)	7.11 ± 3.53	6.58 ± 3.46	0.616	0.589
Na (mmol/L)	138.31 ± 5.28	137.85 ± 7.62	0.046	0.772
K (mmol/L)	4.13 ± 0.70	4.26 ± 0.84	0.362	0.504

Table 3: Risk factors associated with the outcome of pregnant women; MAP: mean arterial pressure; A-aDO2:alveoli-arterial oxygen difference.

	β	S	Wald	P	OR	95% CI
Prothrombin Time	1.858	0.633	8.626	0.003	6.409	1.855-22.140
Total bilirubin	1.390	0.575	3.928	0.037	3.125	1.013-9.644
APACHE	1.558	0.592	6.919	0.009	4.750	1.488-15.167

Table 4: Multivariable logistic regression analysis.

Our study describes 100 obstetric admissions to the ICU at the second affiliated hospital of Wenzhou Medical University from January 2013 to December 2015. Consistent with international epidemiology reports over several decades, obstetric patients were most commonly admitted to ICU in association with hypertensive diseases of pregnancy or in the context of obstetric haemorrhage [14-17]. But, our study finds that acute fatty liver of pregnancy was the main reason for ICU admission. The predictors of outcomes in pregnant women showed that PT, total bilirubin, and APACHE scores increased the risk of maternal death in perinatal period. Previous studies examining the predictive value of critical care scoring systems such as APACHE or the simplified acute physiologic score in critically ill pregnant women have yielded conflicting data, which makes the applicability of these scores in pregnant patients controversial [9,18-20]. Hazelgrove et al. [21] showed that the predicted mortality of simplified acute physiologic score, and APACHE II and III scores in 210 obstetric ICU patients overestimated the actual mortality. In contrast, Bhagwanjee et al. [22] found that APACHE II score was a good predictor of mortality in critically ill women with eclampsia. We found that APACHE score is critical for predicting outcomes of pregnant women.

The PT and total bilirubin levels indicate liver problems. Abnormalities of liver function are six times more common in a normal pregnancy than non-pregnancy [23,24]. Increase in serum bilirubin suggests either exacerbation of underlying pre-existing liver disease, liver disease related to pregnancy or liver disease unrelated to pregnancy. Liver diseases associated with pregnancy include abnormalities associated with hyperemesis gravidarum, acute fatty liver disease, pre-eclampsia, and HELLP syndrome. Prompt

investigation and diagnosis is important for a successful maternal outcome. Acute fatty liver of pregnancy (AFLP) is a rare, potentially life-threatening, pregnancy-related disease, which occurs more commonly in primi-gravidas, multiple pregnancies, and pregnancies carrying a male fetus (3:1 ratio) [25]. A study with 21 (21%) AFLP pregnant women showed a maternal mortality rate of 18% and a fetal mortality rate of 23% [26]. Some women experience moderate coagulopathy. Severe liver dysfunction with prolonged clotting time is usually present. Hyper bilirubinemia is usually <10 mg/dl with modestly elevated serum transaminase levels. Infants born to mothers with AFLP should be screened for defects of fatty acid oxidation, and recurrence in children is 25% [26].

Liver disease during pregnancy can be divided into three categories: (1) Liver disease due to pregnancy, such as hyperemesis gravidarum, intrahepatic cholestasis during pregnancy, HELLP syndrome; (2) Liver diseases aggravated by pregnancy, such as acute intermittent porphyrin disease, bile duct cystic disease, hepatic adenoma; (3) Severe liver disease affecting pregnancy, such as chronic liver disease, liver cirrhosis, liver transplantation, in which termination of pregnancy is recommended [27]. Artificial liver support system includes non-bioartificial liver and bioartificial liver. Some recent reports have suggested that artificial liver support system can improve the neurological symptoms of patients with liver failure, thereby improving survival [28,29].

The limitations of this study are the result of its retrospective observational design, and the associated inherent biases (6). Our center manages a small volume of obstetric patients. In addition, we do not follow up the pregnant women after discharge, and were not able to assess their cognitive development. Finally, this is a single-center study.

Conclusion

In conclusion, our study reveal clinical evidence that PT, total bilirubin, and APACHE scores may affect the outcomes of pregnant women admitted to the ICU. Further evaluation of critically ill pregnant women is needed to better define their medical risks, and improve critical therapies.

Ethical Approval

This article does not contain any studies with human participants or animals performed by any of the authors.

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