Pregnancy outcome of patients with septic shock complicating pregnancy: a retrospective study

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Research article

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Abstract

Background: To detect the maternal and neonatal outcomes of late pregnant patients complicated with sepsis shock.

Methods: The medical records of all late pregnant patients (≥ 28 weeks) complicated with septic shock from January 2011 through November 2018 in Peking Union Medical College Hospital were retrospectively reviewed. Pertinent literature was identified by searching PubMed and EMBASE.

Results: A total 9 patients with an average age of 26.11 ± 6.9 years were included in this study. And the mean gestational age at diagnosis of septic shock was 33 weeks plus 1 day. 87.5% of patients accepted emergency delivery, in which cesarean section was the main delivery mode. 7 patients underwent emergency delivery (including 3 cases of fetal death) and 3 cases of live births (including 1 case of mild neonatal asphyxia). The total maternal mortality rate was 33.3%, and neonatal death rate was 55.6%. Only 1 patient continued pregnancy after disease recovery. 15 published case reports were reviewed. The reported maternal and perinatal death rates were 20% and 46.7% respectively. 2 patients could continue pregnancy after treatment. Group A streptococcus was considered as the main pathogenic bacteria.

Conclusions: Late pregnancy complicated with septic shock was associated with high maternal and fetal mortality. Emergency delivery was advised in most of patients. And cesarean section was the main mode of delivery.

Background

Sepsis during pregnancy have been proven to be the third leading cause of maternal mortality, accounting for 10.7% deaths in 2014[1]. The overall incidence of maternal sepsis was 29.4 per 100000 births and the Maternal mortality due to severe sepsis was about 4.7/10,000 maternities. 19.5% women developed septic shock, 1.4% died. Genital tract infection (31%) and the *Escherichia coli* (21%) were the main causes in the statistic data of UK between 2011-2012

[2]. And Group A streptococcal (GAS) infection is the most common pathogen, resulting

in 25% of maternal deaths from sepsis in Australia. However, the incidence of severe sepsis complicated with pregnancy might be underestimated because of out-of-hospital delivery [3].

The first vision of septic shock's definition was standardized in 1991 by the American College of Chest Physicians (ACCP) and the Society of Critical Care Medicine (SCCM) [4]. Septic shock is now clinically determined by a vasopressor requirement to maintain a MAP (MAP, mean arterial pressure) of 65mmHg or greater and serum lactate level greater than 2 mmol/L ($>18\text{mg/dL}$) in the absence of hypovolemia [5, 6]. However, because of the special physiology during pregnancy, there is still not an accurate standard applied for it. In some country, there are some changes in the assessment system called omeqSOFA

(omeqSOFA, obstetrically modified sequential organ failure assessment). In our study, septic shock was diagnosed according to the general criteria.

Because of the low incidence, it is difficult for obstetricians to benefit from little clinical experience. The appropriate time to termination is still unknown. In this work, maternal and fetus outcomes were analyzed based on our hospital clinical data and published literature.

Methods

Pregnant patients complicated with septic shock admitted to Peking Union Medical College Hospital (PUMCH) from Jan 2011 to Nov 2018 were included, which was approved by the PUMCH Ethics Committee. The inclusion criteria were as followed: (1) pregnancy; (2) diagnosis of septic shock according to the aforementioned ACCP and SCCM criteria, no matter what the infected organ or pathogenic bacteria was; (3) maternal and infant outcomes could be followed up. And the external criterial were:(1)non-pregnancy;(2) not reach the diagnosis of septic shock, such as sepsis. Clinical details were collected, including age, gestational age, pregnancy status, infection information, laboratory examination, treatments, and prognosis. The maternal and fetus outcomes were described and analyzed.

PubMed and EMBASE were searched using the term "septic shock" or "sepsis" or "systemic inflammatory response syndrome" and "pregnancy". Case reports or case series describing septic shock patients during late pregnancy with detailed description of maternal and fetus outcome were included. Finally 15 case reports were retrieved.

Descriptive statistics are reported as means with standard deviation and medians with range and frequency.

Results

Clinical characteristics of 9 septic shock patients during pregnancy

All patients were diagnosed with septic shock in their late pregnancy, with an average age of 26.11 ± 6.9 years, ranging from 18 to 39 years. And the mean gestational age was 33 weeks plus 1 day (Table 1). 78% of patients were from rural area. Two patients were diagnosed as GDM (GDM, gestational diabetes mellitus) and severe preeclampsia during pregnancy respectively. And one patient was complicated with chronic hypertension. Fever was common initial symptom, accompanied by some other symptom, such as lymph node enlargement, gastrointestinal symptom, dyspnea, fatigue and mental symptom. All patients suffered from multiple organ failure. Respiration and circulation were main affected organs (9/9,100%), followed by coagulation (4/9,44.4%), renal function (4/9,44.4%) and liver function (2/9,22.2%). Because of the individual difference, the difference in the period of advanced life support was significant, ranging from 1 to 22 days (Table 1).

The exact location of infection and pathogen was difficult to identify in a short time. More than half of patients (5 in 9 patients) did not be identified the source of infection. The other four patients were respectively infected by *Listeria*, influenza A virus, *Baumanii* and *Legionella*. In the patients whose pathogen were certain, 3/4(75%) had a good prognosis, and only 1/4(25%) progressed rapidly to death, even though the use of ECMO(ECMO, extracorporeal membrane oxygenation)(Table 1).

Pregnancy and fetus outcomes

All patients received advanced life support and were treated with empirical antibiotic until exact pathogenic bacteria was identified. One patient died as soon as admission to hospital due to delayed medical treatments. As shown in Table 2, among the remaining 8 patients, 1 patient continued pregnancy after recovery and the other 7 patients (87.5%) accepted emergency delivery after multidisciplinary discussion. Most of patients underwent cesarean section (5 out of 7 patients, 71.4%, Table 2). After many efforts, 2 women died in childbirth, 1 of whom was infected with influenza A virus, and 5 mothers recovered. The total maternal mortality was 33.3% (3 out of 9 patients). Of the 8 patients, 3 patients (37.5%) had IUFD (IUFD, intrauterine fetal death). After emergency delivery, 2 patients recovered and 1 died. Except for 3 cases of IUFD, the rate of live birth was 75% (3 in 4 patients, Table 2), and 1 newborn died from severe asphyxia. The total mortality rate among the 9 patients, including IUFD, was 55.6%. About the time from admission in hospital to termination, there were three patients terminating at around 6 hours (from 4 hours to 8 hours) and four patients beyond 24 hours (range from 25 hours to 168 hours). The maternal was all survived in the early-termination group and 50% survived in the late-termination group.

Maternal and neonatal outcome reported in published literature

As shown in Table 3, due to the rare disease, only 15 case reports were retrieved and reviewed. After diagnosed with septic shock, 12 of the 15 patients (80%) received emergency delivery, including 1 patient died shortly and 2 patients were able to continue pregnancy after recovery. The rate of cesarean section was 83.3%. Among 12 patients who chose to deliver, 2 mothers died and 10 mothers recovered after treatment. However, the overall maternal mortality rate was 20%. Most of patients could recover after delivery. The incidence of IUFD was 20%. In 15 patients, the neonatal survival rate was 53.3% (Table 3). Group A streptococcus was considered as the main pathogenic bacteria.

Discussion

Septic shock in late pregnancy is rare and the outcome of maternal and perinatal outcome are poor. Although the diagnostic criteria and treatment for septic shock are reported, the clinical experience for septic shock complicating pregnancy is too little to guide our clinical work as a young obstetrician.

PUMCH is a comprehensive tertiary hospital in China, mainly responsible for high-risk pregnant women. In this work, we retrospectively analyzed 9 clinical cases of late pregnant women diagnosed with septic shock in the department of obstetrics and gynecology, PUMCH from 2011 to 2018, and 15 case reports

retrieved from PubMed and EMBASE. Most patients (over 80%) accepted emergency delivery after the septic shock was diagnosed. There was little chance for them to continue pregnancy. Cesarean section was a good choice for patients to improve the rate of live birth. The total maternal and perinatal mortality in PUMCH are both close to data published. Nearly 20 to 30 percent of patients died. But half of them died because of delayed medical treatments. Many women could survive after emergency delivery and appropriate treatment. IUFD occurs in 20 to 37.5 percent of patients due to maternal poor condition. Half of fetus also could survive although they were preterm birth and may suffered from asphyxia at birth.

The Royal of college of obstetricians and gynaecologists (RCOG) recommended that for sepsis patient during pregnancy, excepting intrauterine infection, attempting delivery in the setting of maternal instability can increase the maternal and fetal mortality rates [7]. John R et al also published an clinical expert series on severe sepsis and septic shock in pregnant women and advised immediate delivery if the condition of mother and fetus deteriorated continuously [8]. In terms of the delivery mode, based on our experience and published cases, caesarean section seems to be preferable because of short second stage of labor during which the conditions of mother and fetus were easier to monitor.

Among the 9 PUMCH patients, over 50% of patients had unknown pathogens. The exact reason was difficult to elucidate in individual studies. Based on the results of 15 published cases, GAS(GAS, group A streptococcus) might be the main pathogen, but this varied in different cohort. Effective treatment for specific pathogen can significantly improve the prognosis of mother and fetus.

Conclusions

In conclusion, pregnancy complicated with septic shock is serious. Little experience could be referred. Early diagnosis of disease, timely delivery, and effective treatment for pathogens can improve outcomes of both mother and fetus.

For the limitation of a retrospective study with small sample, there is still a lot of clinical questions unknown, such as, what are the high risk factors for septic shock during pregnancy, what kind of patients are fit for continuous pregnancy, and what is the most popular pathogen. It is necessary for us to accumulate clinical experience continuously.

Abbreviations

ECMO: extracorporeal membrane oxygenation; ICU: intensive care unit; IUFD: intrauterine fetal death; MODS: multiple organ dysfunction syndrome; NA: not applicable; WHO: world health organization; ACCP: the American college of chest physicians; SCCM: society of critical care medicine; SOFA: sequential organ failure assessment; omeqSOFA: obstetrically modified sequential organ failure assessment; GDM: gestational diabetes mellitus; GAS: group A streptococcus; UK: unknown; MOF: multiple organ failure; VD: vaginal delivery; CS: cesarean section

Declarations

Ethics approval and consent to participate

The study protocol was approved by the ethics committee of Peking Union Medical College Hospital. And written informed consents to participate and publish were obtained from patients or their family members.

Consent for publication

Both authors agree to public our article and data.

Availability of data and materials

All data generated or analysed during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests in this section.

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Authors' contributions

ML, Project development, data collection, and manuscript writing; JY, Project development and manuscript editing. Both authors read and approved the final manuscript.

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Tables

Table 1 Clinical characteristics of 9 Patients

Patients	age (years)	parity	GA (weeks + days)	infected organ	pathogenic bacteria	ICU (days)	mechanical ventilation (Days)	MOF
21		0	31+6	UK	UK	5	3	Y
23		0	39+0	UK	Listeria	4	2	Y
21		0	28+6	UK	UK	3	3	Y
22		0	36+4	Lung	influenza A virus	22	22	Y
32		1	34+4	UK	UK	10	9	Y
35		0	32+2	UK	UK	1	1	Y
39		1	31+5	Abdomen	Baumanii	25	13	Y
24		0	29+1	Lung	Legionella	6	5	Y
18		0	34+1	UK	UK	1	1	Y

GA: gestational age; NA: not applicable; UK: unknown; MOF: multiple organ failure; ICU: intensive care unit

Table 2. Maternal and neonatal outcomes of 9 patients

patients	emergency delivery	delivery mode	maternal outcome	neonatal outcome
1	no	NA	alive	continue pregnancy → term live birth
2	yes	CS	alive	IUFD
3	yes	VD	dead	IUFD
4	yes	CS	dead	mild asphyxia → alive
5	yes	CS	alive	alive
6	yes	CS	alive	alive
7	yes	CS	alive	IUFD
8	yes	VD	alive	severe asphyxia → dead
9	NA	NA	dead	IUFD

NA: not applicable; CS: caesarean section; VD: vaginal delivery; IUFD: intrauterine fetal death

Table 3. Maternal and neonatal outcomes in 15 published case reports

case No.	age (years)	GA (weeks)	pathogenic bacteria	emergency delivery	delivery mode	maternal outcome	Neonatal outcome
1	38	34	GAS	yes	VD	dead	IUFD
2	36	35	GAS	yes	VD	alive	IUFD
3	35	37	GAS	yes	CS	alive	alive
4	29	36	GAS	yes	CS	alive	severe asphyxia → dead
5	30	28	legionella	no	NA	alive	mild asphyxia → alive
6	21	35	legionella	yes	CS	alive	severe asphyxia → alive
7	28	36	S. salivarius	yes	CS	alive	alive
8	35	34	GAS	no	NA	alive	alive
9	18	32	HSV	yes	CS	dead	dead
10	30	36	S. pneumoniae	yes	CS	alive	alive
11	38	38	GAS	yes	CS	alive	dead
12	24	32	S. pyogenes	yes	CS	alive	alive
13	16	37	GAS	NA	NA	dead	IUFD
14	-	32	GAS	yes	CS	alive	alive
15	31	34	GAS	yes	CS	alive	dead

GA: gestational age; HSV: herpes simplex virus; NA: not applicable; CS: caesarean section; VD: vaginal delivery; IUFD: intrauterine fetal death;
GAS: group A streptococcus

Table 4 The conditions of 9 patients

Patients	1	2	3	4	5	6	7	8	9
Age(years)	21	23	21	22	32	35	39	24	18
Gravidity	2	2	3	1	2	2	4	1	1
Parity	0	0	0	0	1(VD)	0	1(CS)	0	0
GA (weeks + days)	31+6	39+0	28+6	36+4	34+4	32+2	31+5	29+1	34+1
MAP(mmHg)	44	72	59	85(preeclampsia)	80	66	93	75	119(hypertention)
Heart rate (bpm)	144	130	97	100	140	120	119	130	164
Lactate max(mmol/L)	2.4	16.4	5.8	1.1	2.6	2.1	4	3.3	4.4
WBC $\times 10^9/L$	19.44	5.84	8.83	8.22	37.37	15.28	19.31	7.34	22.87
NET%	86.6	60.3	93.3	89.2	96.3	93.6	77.8	93.9	87.7
Platelets $\times 10^9/L$	226	15	55	127	183	204	129	118	370
Billrubin $\mu mol/L$	5.8	147.4	139.2	7.5	9.1	47.8	12.9	8.8	4.1
Creatinine $\mu mol/L$	82	316	261	133	89	48	239	44	275
Gastrointestinal ulcer	N	N	N	Y	N	N	Y	N	N
Respiratory failure	Y	Y	Y	Y	Y	Y	Y	Y	Y
NT-proBNP (pg/ml)	3825	NA	NA	NA	4931	NA	NA	NA	20527
APTT(s)	NA	59.9	69.8	NA	NA	NA	52.9	NA	NA
EF%	60%	45%	NA	63%	49%	NA	NA	NA	20%

GA: gestational age; NA: not applicable; MAP: mean arterial pressure; WBC: white blood cell; NT-proBNP: amino-terminal pro-brain natriuretic peptide; APTT: amino-terminal pro-brain natriuretic peptide; EF%:ejection fraction