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The clinical course of patients with septic abortion admitted to an intensive care unit

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Abstract *Objective:* The purpose of this study was to describe the clinical course, complications, and outcome of patients with septic abortion admitted to the intensive care unit (ICU). *Design, setting, and patients:* In this retrospective study, the records of 63 patients with septic abortion admitted to the ICU of a university hospital in Argentina between 1985 and 1995 were reviewed. *Results:* The mean age of the patients was 28.5 years, and 33% had had previous abortions. The mean gestational age was 10.5 weeks. The first ICU day Acute Physiology and Chronic Health Evaluation (APACHE) II mean score was 13.9. Acute renal failure developed in 73% (46 of 63) of the patients, disseminated intravascular coagulation (DIC) in 31% (15 of 49), and septic shock in 32% (20 of 63). Blood cultures were positive in 24% (15 of 62). Twelve patients died (19%). Eight of the deaths occurred during the first 48 h of the ICU admission. Compared with survivors, non-survivors had higher median number of organ failures (1.0 vs 4.0, $p<0.0001$), mean first ICU day SOFA scores (6.6 vs 10.0, $p=0.0059$), and mean APACHE II scores (12.7 vs 20.2, $p=0.0003$), and were more likely to have septic shock (18 vs 92%, $p<0.0001$), and receive dopamine (37 vs 83%, $p=0.0040$), mechanical ventilation (8 vs 83%, $p<0.0001$), and pulmonary artery catheter (8 vs 41%, $p=0.0026$). *Conclusions:* Although it is an avoidable complication, septic abortion requiring admission to the ICU is associated with high morbidity and mortality.

Keywords Abortion · Septic abortion · APACHE · Female · Pregnancy · Sepsis

Introduction

Unsafe abortion, abortion characterized by the lack or inadequate skills of health care providers, hazardous techniques, and unsanitary facilities is one of the neglected health care problems in developing countries [1]. Abortion remains a common cause of maternal death in the developing world, and deaths from abortion result primarily from sepsis [1, 2].

Morbidity and mortality from septic abortion are widespread in countries where abortion is illegal or inaccessible [2]. The reported mortality rate from septic abortion has ranged from 0 to 34% [3, 4, 5, 6, 7, 8, 9, 10]. Complications occur frequently following septic abortion. These complications include peritonitis, hemorrhage requiring transfusion, uterine perforation, renal failure, coagulopathy, liver dysfunction, and lower genitourinary tract injury [5, 6, 10]. In countries where abortion is legal, mortality due to abortion is infrequent, and septic abortion has become a rare condition. In the United States (where abortion is legal), the Centers for Disease Control and Prevention identified nine deaths among 884,273 legally induced abortions reported in 1998 and none died as a result of illegally induced abortion [11]. In a recent study of 74 obstetric patients admitted consecutively to an intensive care unit (ICU)

from January 1991 to December 1998, only one had septic abortion [12].

In Argentina, abortion is illegal and the estimated proportion of maternal deaths due to abortion has remained around 30% [1, 13]. Since hemodialysis was started at Instituto de Investigaciones Médicas "Alfredo Lanari" (IDIM) in 1958 [14], the IDIM has become a referral center for critically ill patients with septic abortion [10, 15]. Since 1968 the management of these patients consisted of antibiotics, early hemodialysis, and a conservative approach regarding hysterectomy (only in the presence of uterine gangrene or perforation) [4, 8, 10, 15, 16].

Despite being a widespread problem worldwide, data addressing the clinical course and outcome of patients admitted to the ICU for septic abortion are scarce and old [8, 9]. This study describes the clinical course, and outcome of patients treated from 1985 through 1995, in an ICU of a university hospital in Argentina for septic abortion.

Materials and methods

In this retrospective, cohort study, we reviewed the medical records of patients consecutively admitted to the ICU of the IDIM, Facultad de Medicina, Universidad de Buenos Aires, Argentina, from January 1985 to December 1995 for septic abortion. The authors (J.D.F., F.D.D.F., and P.G.H.) saw most of the patients during their training years. The study was approved by the Ethics Committee of the IDIM, and was therefore performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

The IDIM is 70-bed, tertiary-care, adult, university hospital. Patients were admitted directly by the staff of the hospital, or by referral. The ICU at the IDIM was a 4-bed unit that provided care to critically ill medical, surgical, and non-trauma neurosurgical patients. A team of internists, pulmonologists or intensivists, along with house staff, treats all the patients admitted to the ICU. The attendings were available in the ICU for most of the day, and resident house staffs were available 24 h each day.

The data collected included demographics, initial symptoms, time from onset of symptoms to seeking medical care, gestational age, type of abortion (provoked or spontaneous) as stated by the patient, presence of premorbid medical conditions, laboratory values, utilization of and recordings from central lines and pulmonary artery catheters, presence and length of oliguria, number and length of dialysis treatments, microbiology results, antibiotics used, time from abortion to beginning of antibiotics, use of dopamine (the only vasopressor agent used during the study period), use of mechanical ventilation, surgical interventions, development of organ failure, ICU and hospital length of stay (LOS), year of admission, mortality and cause of death.

Renal failure was defined as serum creatinine $\geq$2.0 mg per dl or need for hemodialysis. Oliguria was defined as urine output of less than 400 ml in 24 h. Cardiovascular, respiratory, hematologic, and neurology failures were defined according to Knaus et al. [17]. Liver failure was defined as a bilirubin >6 mg per dl and a prothrombin time $\leq$60%. Gastrointestinal (GI) failures was defined as GI bleeding, intestinal obstruction, or pancreatitis preventing enteral feeding for at least 24 h or until death. Multiple organ failure was defined as failure of two or more organs. In addition, the first ICU day Sequential Organ Failure Assessment (SOFA) score was calculated as described in the literature [18]. Disseminated intravascular coagulation (DIC) was defined as the presence of three of the next criteria: platelets <100,000; prothrombin time <60%; and positive fibrin degradation products or positive D-dimmer, antithrombin <80% [19, 20]. A predisposing condition was not included in the definition since all the patients had sepsis, known to be associated with DIC [19, 20]. Acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) were defined as in the American–European Consensus Conference [21]. The APACHE II scores and predicted mortality rates were calculated as described in the literature [22]. Sepsis was defined according to the ACCP-SCCM consensus conference [23]. The standardized mortality ratio (SMR) was defined as the ratio of actual mortality to predicted mortality.

StatView 5.0 computer software (SAS Institute, Cary, N.C.) was used for statistical analyses. Descriptive data are summarized as mean (standard deviation), median (range), or percentages. Comparisons between the groups were made using Student's *t*, Mann-Whitney U, chi-square, and Fischer's exact tests. The 95% confidence interval (CI) was calculated when needed. A p value <0.05 was considered statistically significant.

Results

During the study period, 67 patients were referred to the ICU of the IDIM for septic abortion. Four patients were excluded from the study because their admission was found not to be related to septic abortion: two had dead fetus syndrome, one had thrombotic thrombocytopenic purpura, and another one tricuspid valve bacterial endocarditis. The remaining 63 patients were included in this study.

The baseline characteristics of the patients are shown in Table 1. No premorbid medical condition was present in any patient. Their initial symptoms are shown in Table 2. The median time from the onset of symptoms to seeking medical care was 48 h (range 3–720 h). Sepsis was present in 17% (11 of 63) of the patients, severe sepsis in 51% (32 of 63), and septic shock in 32% (20 of 63). Acute renal failure developed in 73% (46 of 63) of the patients, DIC in 31% in (15 of 49), ALI in 3 patients,

Table 1 Characteristics of patients with septic abortion

Age (years)		28.5±6.5
Marital status[a]		
	Married	30 of 56 (54%)
	Single	24 of 56 (43%)
	Divorced	2 of 56 (4%)
Previous abortions		17 of 51 (33%)[b]
No. of previous pregnancies (median with range)		4 (1–11)
No. of previous deliveries (median with range)		2 (0–10)
Type of abortion		
	Provoked	39 of 63 (62%)
	Spontaneous	5 of 63 (8%)
	Not stated	19 of 63 (30%)
Gestational age (weeks)		10.5±4.9

[a] In some patients, information regarding the marital status was not available

[b] Of these 17 patients, 15 had one previous abortion, 1 had three, and 1 had five

Table 2 Initial symptoms and signs in the 63 patients with septic abortion

Symptoms/signs	Number
Vaginal bleeding	52 (84)
Fever	35 (57)
Abdominal pain	32 (52)
Chills	29 (47)
Oliguria	26 (42)
Jaundice	19 (32)
Putrid discharge	16 (26)
Vomiting	15 (24)
Malaise	14 (23)
Myalgias	9 (14)
Nausea	9 (14)
Confusion	6 (10)
Diarrhea	6 (10)
Choluria	5 (8)
Hematuria	3 (5)
Other symptoms[a]	

Numbers in parentheses are percentages
[a] Dyspnea in 3 patients, pallor in 2, headache in 2, productive cough in 1, and polyarthralgia in 1

and ARDS in 5 patients. A central line was inserted in 79% (50 of 63) of the patients on the day of admission. The median central venous pressure was 4 mm Hg (range 0–20 mm Hg). The central venous pressure was less than 5 mm Hg in 22 patients (55%). A pulmonary artery catheter was inserted in 9 patients; the pulmonary capillary wedge pressure was 8.4±4.4 mm Hg. We did not find statistically significant differences in the central venous and pulmonary capillary wedge pressures between survivors and non-survivors. Ninety percent (51 of 57) of the patients were resuscitated with intravenous fluid. Patients received an average of 4.3±2.6 l of intravenous fluid in the first 24 h. Of the 63 patients, 41 (66%) were transfused with 4.0±3.3 units of packed red blood cells. Platelets were transfused in 3 patients who had DIC.

After 24 h in our institution, 39% (23 of 59) of the patients remained oliguric. In the survivors, oliguria lasted for a median of 12 days (range 1–27 days). Hemodialysis was performed intermittently in 35 patients (76% of the patients in acute renal failure); 30 patients were dialyzed in the first 24 h of admission and it was not clear in 4 patients whether the treatments were started on the first or second day of hospital stay. The patients received a median of 4 (range 1–16) hemodialysis treatments for a median of 5 days (range 1–42 days). In all the survivors, hemodialysis was discontinued before discharge from the hospital.

Blood cultures were obtained in 62 patients upon admission to the ICU and 15 were positive (24%). The pathogens isolated from the blood were *Escherichia coli* (n=9), *Clostridium perfringens* (n=4), *Proteus mirabilis* (n=1), *Proteus vulgaris* (n=1) *Acinetobacter spp.* (n=1), *Bacteroides spp.* (n=1), *Enterobacter cloacae* (n=1), *and Enterococcus faecalis* (n=1). A single organism was isolated in 12 cases, and 2 organisms in 3 cases. Cultures from the uterine cavity were obtained in 9 of the 15 patients with positive blood culture and all 9 grew the same pathogens as the ones grown from the blood. Three of the 15 patients with positive blood cultures (all had *Clostridium perfringens*) died compared with 9 of the 47 patients with negative blood cultures (p value was non-significant).

The time from the onset of symptoms to the beginning of antibiotic treatment was known in 46 patients, and the median delay was 48 h (range 12–720 h). Only 37% (23 of 62) of the patients received antibiotics before transfer. Upon admission to our ICU, empiric antibiotic treatment was begun in 62 patients. The most commonly used antibiotic regimen, used in 52 patients, was a combination of ß-lactam, aminoglycoside, and Chloramphenicol, Clindamycin, Metronidazole or Ornidazole. After 72 h of empiric antibiotic treatment, the antibiotic regimen was changed in 4 of 54 patients, who were still alive, because of culture findings.

Of the 63 patients, 38 (60%) had uterine curettage, 3 (5%) had hysterectomy, 5 (8%) had both, and 17 (27%) had no surgery. Twelve patients underwent abdominal surgeries; 7 patients underwent hysterectomy (pre-transfer to our institution), and 5 patients had exploratory laparotomy. Among the 5 patients who underwent exploratory laparotomy, purulent peritonitis was found in two, hemoperitoneum in two, and a hysterectomy was performed in one for uterine perforation. Three of the 12 patients who underwent surgery died.

The mean APACHE II score was 13.9±6.2. Twelve patients died (19%). None of the patients with an APACHE II score <15 died. Excluding two patients whose APACHE II score could not be calculated because they died in less than 12 h of ICU admission, the observed mortality rate was 16.4%, the mean APACHE II predicted mortality rate was 23.6%, and the SMR 0.7 (95% CI: 0.3–1.1). The median hospital LOS was18 days (range 5–71 days) for survivors compared with 1.5 days (range 1–13 days) for non-survivors (p<0.0001). The survivors' median ICU LOS was 5 days (range 2–19 days) compared with 1.5 days (range 1–8 days) for non-survivors (p=0.0038). Compared with survivors, non-survivors had higher mean APACHE II scores and were more likely to have septic shock, ARF, DIC, and receive dopamine, mechanical ventilation and pulmonary artery catheter (Table 3).

Six of the 12 deaths occurred during the first 24 h after transfer. Another 2 patients died by the end of the second day of admission. The mortality rate was 24% (9 of 38) for patients admitted before 1990 compared with 12% (3 of 25) for patients admitted at the later period (p=0.3337). Multiple organ failure developed in 37% (19 of 51) of the survivors compared with 92% (11 of 12) of the non-survivors (p=0.0001); the median number of organ failure was 1 (range 0–4) for survivors compared with 4 (range 2–6) for non-survivors (p<0.0001). The first ICU day

Table 3 Comparison of survivors and non-survivors in 63 patients with septic abortion. *ARF* acute renal failure, *DIC* disseminated intravascular coagulation, *PAC* pulmonary artery catheter

	Survivors		Non-survivors		
	Number		Number		*P*
APACHE II[a]	51	12.7±5.8	10	20.2±3.9	0.0003
Onset symptoms consult[b]	38	48	9	72	0.6555
ARF	51	34 (67)	12	12 (100)	0.0193
DIC	44	11 (25)	5	4 (80)	0.0115
Positive blood culture	50	12 (24)	12	3 (25)	0.9421
Hemodialysis	51	29 (57)	12	6 (50)	0.6669
Fluid resuscitation	46	41 (89)	11	10 (91)	0.8629
PAC	51	4 (8)	12	5 (41)	0.0026
Dopamine	51	19 (37)	12	10 (83)	0.0040
Mechanical ventilation	51	4 (8)	12	10 (83)	<0.0001
Sepsis severity					<0.0001
Sepsis	51	11 (22)	12	0 (0)	–
Severe sepsis	51	31 (61)	12	1 (8)	–
Septic shock	51	9 (18)	12	11 (92)	–

Numbers in parentheses are percentages
Comparisons between survivors and non-survivors were done using the unpaired *t* test for APACHE II, Mann-Whitney U test for onset of symptoms to consult, and chi-square or Fischer's exact tests for the other variables
[a] The median APACHE II score was 13 (range 1–27) for survivors and 21.5 (range 15–26) for non-survivors
[b] Results are medians, and the unit is hours

Table 4 Differences in the type of organ failure between survivors and non-survivors

Organ failure	Survivors	Non-survivors	*P*
	(*n*=51)	(*n*=12)	
Renal	34 (67)	12 (100)	0.0193
Hematologic	15 (29)	7 (58)	0.0586
Cardiovascular	4 (8)	7 (58)	<0.0001
Liver failure	5 (10)	5 (42)	<0.0001
Gastrointestinal	4 (8)	5 (42)	0.0026
Respiratory	3 (6)	5 (42)	0.0008
Neurology	0	0	–

Numbers in parentheses are percentages

SOFA scores for survivors and non-survivors were 6.6±3.8 vs 10.0±3.4 (p=0.0059). The type of organ failure for survivors and non-survivors is presented in Table 4. The cause of death was multiorgan failure in 7 patients, bleeding in two, pulmonary embolism or myocardial infarction in two, and septic embolism during emergency surgery for tricuspid endocarditis in another one.

Discussion

This retrospective study describes the clinical course and outcome of 63 patients referred to an ICU of a university hospital with septic abortion. Severe sepsis, septic shock, acute renal failure, DIC, and hemolysis were frequent complications in these patients. Hospital mortality was about 20%, most of the deaths occurring in the first 48 h of admission. Compared with survivors, non-survivors had higher number of organ failures, SOFA scores, and APACHE II scores. Septic shock and the use of dopamine, mechanical ventilation, and pulmonary artery catheter were more common in non-survivors.

The patients studied in this paper were young healthy women, suffering from a critical condition, as a consequence of termination of an unwanted pregnancy (by self, doctor, or other), in a hostile environment because of the illegal nature of the procedure, and in a region of the world where some treatment modalities might not be on hand and the known epidemiological sepsis data may not apply.

Early and adequate antibiotics [24, 25], and early fluid resuscitation [26], have been shown to improve outcome in septic patients; however, in our cohort there was a considerable delay in seeking medical attention (median of 2 days), and only 37% of the patients received antibiotics pre-transfer. Additionally, most of the patients had low filling pressures and required aggressive fluid resuscitation in the first 24 h in our institution, suggesting inadequately pre-transfer resuscitation in these otherwise healthy population. The delay in seeking medical care can be attributed to women's reluctance to admit their condition in a country where abortion is illegal [1, 27]. The inappropriate pre-transfer care could be explained by the inability to recognize the symptoms of septic abortion, or by the lack of resources. We believe, like others [2, 8, 16] that the antibiotic regimen used in the study was adequate empirical therapy for septic abortion patients (in only 4 cases this regimen needed adjustment due to culture findings). Antibiotic coverage of *Clostridium* is important since it has been isolated from the vagina and cervix in 19–29% of women in the postabortion interval, and sepsis due to this organism carries high morbidity and mortality [16, 28, 29].

Measurements of illness severity is important in describing and comparing patient outcome [22, 24]; and the APACHE II is the prognostic system most widely cited to predict mortality of critically ill patients admitted to ICUs. We are not aware of any studies addressing the role of APACHE II in predicting mortality of patients treated in the ICU for septic abortion. The APACHE system has been used to assess the severity of illness and to predict mortality in critically obstetric patients with conflicting results [12, 30, 31, 32, 33]. Our study was too small to elaborate any conclusion, and the APACHE II predicted mortality was higher than the observed mortality, but the 95% CI of the SMR (0.3–1.1) suggests good estimation of mortality. It is possible that some of the physiologic changes associated with pregnancy, such as higher respiratory and heart rates, and a lower hematocrit, could lead to higher APACHE II scores, causing falsely elevated predicted mortality rates. Also it is unlikely that

the original database used to develop the APACHE II prognostic system had included enough obstetric patients.

Organ failure in critically ill patients is associated with increased mortality [17, 34]. In our study, multiple organ failure developed in 48% (30 of 63) of the patients. Acute renal failure was the most common organ failure. The etiology of the renal failure was probably due to acute tubular necrosis. In a previous study, 43 of 45 autopsies performed at our institution in patients with septic abortion between 1958 and 1967 had shown acute tubular necrosis [10]. Early and frequent hemodialysis has been the practice in the IDIM since 1968 when a more aggressive dialysis strategy was instituted because survival rates from septic abortion improved from 66% in the period 1958–1967 to 85% in the period 1968–1971 [10].

Current mortality and morbidity data from septic abortion in the ICU is unknown. To our knowledge, only one study has looked at patients with septic abortion in the ICU [9]. This study included 21 patients in 1975; renal dysfunction was present in 16 (76%), shock in 15 (71%), DIC in 7 (33%); and 5 (23%) patients died [9]. A good comparison between the two studies cannot be performed because no classification of the severity of the condition was available in 1975, the definitions used were different, and both studies were small and two decades apart. Nonetheless, mortality rates as well as the incidence of renal failure and DIC were similar between Cane et al.'s [9] and our study. In the current study, we expected advances in treatment strategies, technology, and knowledge to lead to better outcome during the later period of our study; however, because of our small sample size, we were not able to find statistically significant differences in survival between the early and later periods.

Our study had several limitations: the data were collected retrospectively, the sample size was small, there was a clear selection bias (the sickest patients were transferred to our institution and some of them might have died before the transfer took place), and no information was available after survivors were dismissed from the hospital. Because our study took place in an inner-city tertiary medical center in Argentina, our findings may not apply to other patient populations. Despite these limitations, our study provides important information about critically ill women with septic abortion.

Serious complications and deaths from septic abortion are preventable [2]. Unfortunately, the prevention of death from abortion remains more of a political than a medical problem in some countries [2]. Meanwhile, women should be educated on family planning and encouraged to seek medical care early. Physicians should be trained to recognize the signs and symptoms of abortion and sepsis, and to implement therapy early including aggressive fluid resuscitation and appropriate empiric antibiotic therapy (including antibiotics against *Clostridium*). Finally, since in this study abortion took place during the course of the patients' fifth pregnancy, and the fact that a third had had previously induced abortions, this procedure was used as a birth control method. This implies that all these deaths could have being potentially avoided with adequate reproductive health programs [2, 35, 36].

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