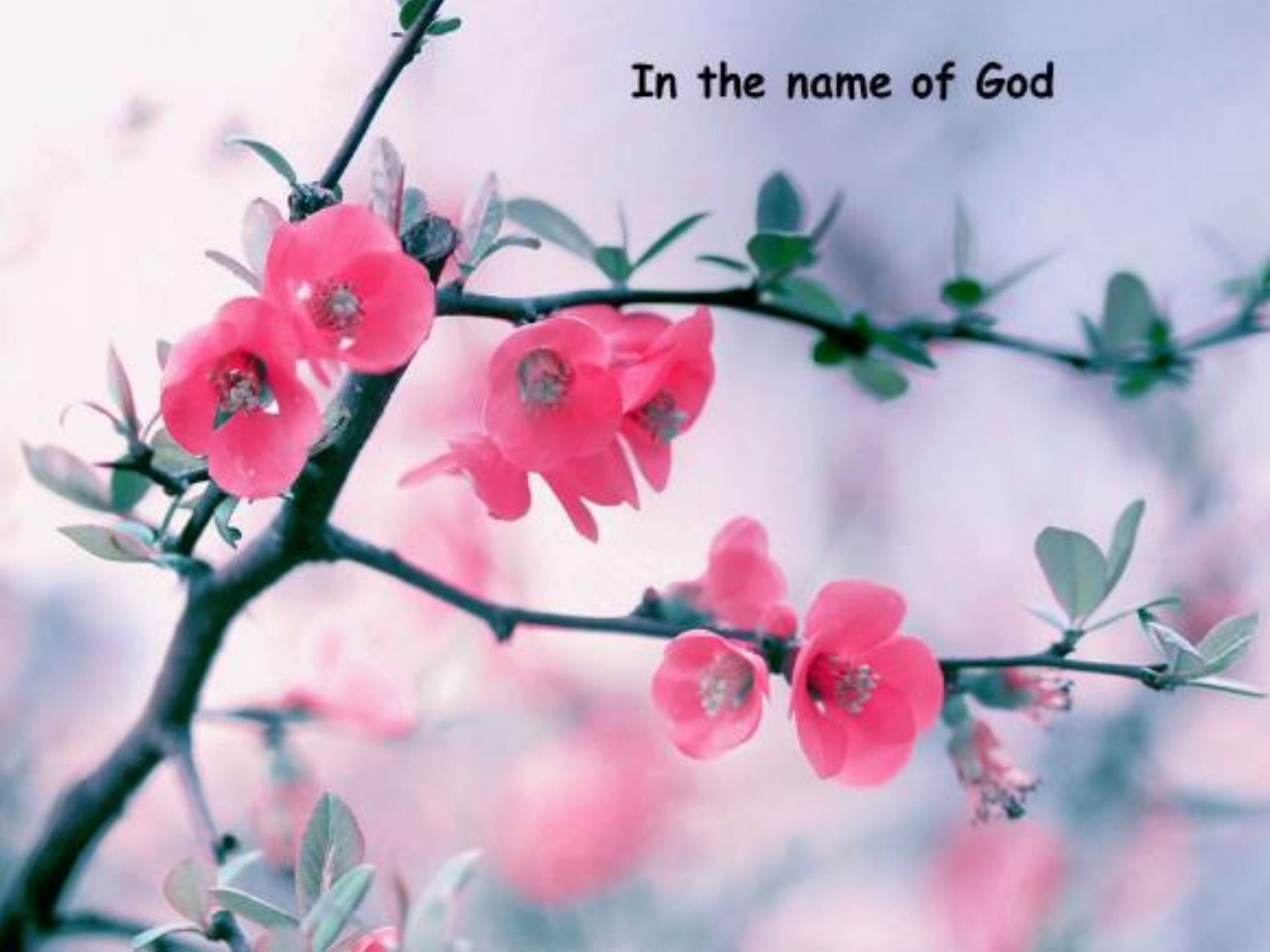
In the name of God

Amniotic fluid embolism

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INTRODUCTION:

Amniotic fluid embolism (AFE) is a rare and typically catastrophic condition that occurs when amniotic fluid enters the maternal circulation .Prompt recognition facilitates rapid initiation of life-saving therapies.

AFE is a catastrophic condition that typically occurs during labor or within 30 minutes postpartum. It is rare (1 to 12 cases per 100,000 deliveries)

DIAGNOSIS:

AFE is a clinical diagnosis based upon the presence of the characteristic clinical findings and exclusion of other potential causes of these findings. The diagnosis should be suspected in pregnant or recently postpartum women who experience sudden cardiovascular collapse, severe respiratory difficulty and hypoxia, and/or seizures, particularly when followed by disseminated intravascular coagulopathy (DIC).

DIAGNOSIS:

The condition generally arises during labor or soon after delivery, in the absence of other explanations for these findings. In many cases, the diagnosis is made retrospectively, after all investigative data, including autopsy data, have been collected.

DIAGNOSIS:

Atypical cases, representing approximately one-fourth of all cases of AFE, may present with only acute respiratory failure and hypotension. Uncommonly, DIC may be the initial presenting feature or may be absent

DIAGNOSIS:

Contrary to popular belief, the identification of amniotic fluid debris (squamous cells, trophoblastic cells, mucin, and lanugo) in blood drawn from the distal end of a pulmonary artery catheter or on histopathology of lung tissue is not diagnostic of AFE since these findings can be found in the maternal circulation and lungs of women without AFE. Furthermore, many women who have classic signs and symptoms of AFE and meet the diagnostic criteria described below do not show any histologic evidence of amniotic material on autopsy

Criteria for AFE (all must be present):

Sudden onset of cardiorespiratory arrest OR hypotension (systolic blood pressure <90 mmHg) with evidence of respiratory compromise (eg, dyspnea, cyanosis, or peripheral oxygen saturation <90 percent).

Documentation of overt DIC

Platelet count >100,000/mL = 0 points, <100,000 = 1 point, <50,000 = 2 points

•Prolonged prothrombin time or international normalized ratio <25 percent increase = 0 points, 25 to 50 percent increase = 1 point, >50 percent increase = 2 points

•Fibrinogen level >200 mg/L = 0 points, <200 mg/L = 1 point

Documentation of overt DIC

A score ≥3 is compatible with overt DIC. Coagulopathy must be detected before hemorrhage itself can account for dilutional or shock-related consumptive coagulopathy.

- Clinical onset during labor or within 30 minutes of placental delivery.
- Absence of fever (≥38°C) during labor.

INCIDENCE

AFE is rare, ranging from 1.9 to 6.1 cases per 100,000 deliveries in a review of reports from Australia, Canada, the Netherlands, the United Kingdom, and the United States that used various criteria for diagnosis

PATHOGENESIS

The pathogenesis of AFE is not clear. It is hypothesized that entry of amniotic fluid (which contains fetal cells and other antigenic material) into the maternal systemic circulation via a breach in maternal/fetal interface leads to abnormal activation of humoral and immunological processes and release of vasoactive and procoagulant substances, similar to the systemic inflammatory response syndrome

PATHOGENESIS

As a result, pulmonary pressures usually become acutely elevated, the right ventricle (RV) pressure increases, and the RV begins to fail. Mechanical obstruction of pulmonary arteries from cellular components of and debris in amniotic fluid plays no role in this RV failure .RV failure may subsequently lead to left ventricle (LV) failure and systemic hypotension. LV failure may also be a direct effect of hypoxic injury to the left ventricle, release of maternal inflammatory mediators, or a direct depressant effect of amniotic fluid on the myocardium.

PATHOGENESIS

Acute pulmonary hypertension also results in severe ventilation/perfusion mismatching, cardiogenic pulmonary edema, and hypoxemic respiratory failure .Later, noncardiogenic pulmonary edema can occur in some patients. The likelihood of damage to the endothelial-alveolar membrane and a capillary leak syndrome is supported by observations of high protein concentrations in edema fluid and amniotic fluid debris in the sputum and alveolar spaces of these patients

PATHOGENESIS

Activation of factor VII and platelets and release of inflammatory mediators likely activates the coagulation cascade, resulting in disseminated intravascular coagulopathy (DIC) and, in turn, ischemic distal organ dysfunction and multi-organ failure. Hemorrhage from DIC further contributes to hemodynamic instability.

RISK FACTORS

the most frequently cited risk factors for AFE appear to be cesarean delivery, instrumental vaginal delivery, placental abnormalities (previa, abruption, accreta), and preeclampsia/eclampsia ,no clinical or demographic risk factor is sufficiently predictable of AFE to alter standard obstetric practice or conclude that AFE would not have occurred in a particular patient in the absence of that risk factor

CLINICAL FINDINGS

Timing for onset of symptoms

AFE occurs during labor and delivery, or within 30 minutes postpartum. In one national registry, 70 percent of cases occurred during labor, 11 percent after vaginal delivery, and 19 percent during cesarean delivery

Timing for onset of symptoms

AFE can also occur following a first or second trimester abortion (medical or surgical), miscarriage, amniocentesis, or abdominal/uterine trauma, but this is rare, and typically only described in case reports

Signs and symptoms

In most patients (90 percent) the clinical presentation of AFE is abrupt, catastrophic, and rapidly progressive .Classically, patients present with cardiorespiratory compromise or sudden hypoxia and hypotension, often accompanied or followed by noncardiogenic pulmonary edema and hemorrhage due to disseminated intravascular coagulopathy.

Clinical manifestations include

- Aura – Up to one-third of patients may experience a sense of sudden doom, chills, nausea and vomiting, agitation, anxiety, or change in mental status immediately preceding the event.

- Sudden cardiorespiratory failure and/or arrest.

- Cardiac arrest

- Hemorrhage

- Tonic-clonic seizures(rare initial manifestations and uncommon complications of AFE)

Hemorrhage – DIC

DIC causes hemorrhage in over 80 percent of patients with AFE .It typically occurs shortly after the development of cardiorespiratory compromise but cases of AFE presenting with hemorrhage in the absence of antecedent cardiopulmonary compromise have been described .In patients who have not delivered, prolonged bleeding from sites of invasive interventions such as intravascular lines are the most common manifestations of DIC. However, after vaginal and cesarean delivery, bleeding is more likely to originate from the uterus and incision/laceration sites. Spontaneous bleeding may also occur in the urinary and/or gastrointestinal tract.

Laboratory and imaging
Coagulation

DIC is the key laboratory abnormality: Elevated D-dimer, low fibrinogen [especially <200 g/L], and thrombocytopenia occur in most patients typically within 30 minutes after the onset of cardiopulmonary compromise. Uncommonly, laboratory abnormalities occur in the absence of cardiorespiratory compromise or are delayed (up to 48 hours after initial presentation)

CBC

are nonspecific and include anemia secondary to hemorrhage and, occasionally, an elevated white blood cell (WBC) count; however, a WBC up to 20,000 cells/microL can be a normal finding in laboring and postpartum women

ABG

reveals hypoxemia, which is often profound, and rarely hypercapnia. Metabolic acidosis occurs in those who have prolonged hypotension or cardiac arrest.

Chest radiograph

Chest imaging is often normal early in the course of the disease, but dense bilateral infiltrates consistent with pulmonary edema, acute respiratory distress syndrome, or hemorrhage may be seen as AFE evolves.

ECG

Electrocardiography typically reveals sinus tachycardia but may also reveal arrhythmias typical of those seen in cardiac arrest

Echocardiography

Echocardiography reveals a rise in pulmonary pressures (usually lasting 15 to 30 minutes), followed by left ventricular failure.

Fetal heart rate pattern

absent baseline fetal heart rate [FHR] variability and late decelerations or terminal bradycardia

INITIAL EMERGENCY MANAGEMENT FOR UNSTABLE PATIENTS

A multidisciplinary, team-based approach involving maternal-fetal medicine, anesthesia, critical care, respiratory, and nursing is desirable to increase the chances of stabilization and avoid further deterioration

The initial set of goals

Initial emergency management of suspected amniotic fluid embolism (AFE)

Begin basic and advanced cardiac life support maneuvers	▪ Manual chest percussions, emergency airway management with 100% oxygen and intubation, and the establishment of intravenous (IV) access. Pregnancy-specific issues include manual uterine displacement to avoid aortocaval compression, intravenous access above the diaphragm, avoidance of alkalosis, lower than usual ventilation volumes, high fractions of inspired oxygen. ECMO may be considered for refractory hypoxemia during CPR.
Provide hemodynamic support	▪ Rapid administration of crystalloid (eg, normal saline or lactated Ringer's solution) for non-hemorrhagic shock or blood for hemorrhagic shock. The response should be acutely followed by the assessment of vital signs, and bedside ultrasound monitoring of the inferior cava, if available. Discontinue fluids when intravascular volume has been replenished or pulmonary edema becomes apparent. ▪ Administer vasopressor therapy for refractory shock. Norepinephrine is typically first choice. Consider addition of dobutamine or other inotrope for cardiogenic shock. Alternatives are epinephrine (preferred in anaphylaxis), ephedrine (post anesthesia hypotension), or phenylephrine (if tacharrythmia is an issue). Many experts avoid vasopressin (increased uterine contractions) and dopamine (possible increase risk in death in sepsis patients).
Management of hemorrhage and coagulopathy*	▪ Prolonged PT, aPTT, fibrinogen <100 mg/dL → FFP and croprecipitate → Goal is normalization of INR and fibrinogen >100 mg/dL. ▪ Platelet count <50,000/microL-one to two units of random donor platelets per 10 kg of body weight. ▪ Consider other agents for cases refractory to standard DIC treatment measures.¶
Delivery of fetus	▪ Determine uterine size and estimate gestational age. Delivery is considered in most cases for pregnancies ≥20 weeks of gestation/uterine size at or above the umbilicus to relieve aortocaval compression and facilitate return of spontaneous circulation, regardless of fetal status (alive or demised). ▪ Consider cesarean delivery if spontaneous circulation has not returned within 4 minutes of maternal cardiorespiratory collapse and delivery of the fetus should be completed within 5 minutes (known as the "4-minute rule" or "the 5-minute rule").Δ ▪ Perimortem operative vaginal delivery with forceps or vacuum is appropriate if it can be achieved within this timeframe. ▪ Delivery is preferably at the location of the arrest (often not an operating room).
Preliminary testing	▪ Complete blood count, chemistries including metabolic profile, PT, aPTT, INR, troponin, brain natriuretic peptide, type and screen, complement 3 and 4, serum tryptase and histamine. Arterial blood gas, chest radiograph, electrocardiography, bedside ultrasonography (if available; this may include thoracic, cardiac, abdominal, and/or lower extremity ultrasonography).

A multidisciplinary, team-based approach involving critical care, maternal-fetal medicine, respiratory care, nursing, and anesthesia specialists is preferred to increase the chances of stabilization and avoid further deterioration. In general, initial resuscitative efforts are simultaneous with diagnostic evaluation in an attempt to elucidate the etiology of cardiorespiratory compromise.

ECMO: extracorporeal membrane oxygenation; CPR: cardiopulmonary resuscitation; PT: prothrombin time; aPTT: activated partial thromboplastin time; FFP: fresh frozen plasma; INR: international normalized ratio; DIC: disseminated intravascular coagulation.

* Applies mostly to patients with active bleeding. However, in the absence of bleeding, treatment may be justified if the risk of bleeding is considered high (eg, surgery is anticipated). In addition, consider activating obstetric massive transfusion protocol, if available.

¶ Case reports suggest success with lyophilized concentrated fibrinogen (eg, RIAstat). C1 esterase inhibitor concentrate, fibrinolytic agents such as aprotinin, aminocaproic acid, and tranexamic acid[1] and a combination of atropine, ondansetron, and ketorolac (A-OK) are investigational but have been used successfully in case reports only. Factor VIIa use in patients with AFE should be reserved as a last resort and only for those with hemorrhage refractory to medical and/or surgical intervention.

Δ Pragmatically, this time frame is difficult to achieve.

Reference:

1. *Shakur H, Beaumont D, Pavord S, et al. Antifibrinolytic drugs for treating primary postpartum haemorrhage. Cochrane Database Syst Rev 2018; 2.*

Perform cardiopulmonary resuscitation (CPR)

"high quality CPR" (eg, rapid [100/minute] forceful [2 inch depth] chest compressions with time for adequate recoil and with minimal [no more than 5 to 10 seconds] interruption) .When real CPR events are videotaped and reviewed, many times clinicians perform "low quality CPR.

Control hemorrhage and reverse coagulopathy

We recommend administering tranexamic acid (TXA) and activating a massive transfusion protocol. (See "Massive blood transfusion".)

●Confirm the presumptive diagnosis of AFE by excluding other diagnoses.

●Deliver the fetus if the fetus is alive or if delivery will aid in maternal resuscitation

Basic and advanced cardiac life support

This typically involves manual chest percussions, emergency airway management with supplemental oxygen and intubation, and the establishment of intravenous (IV) access, if not already in place for fluid resuscitation and arrhythmia management. In general, time should not be wasted or resuscitation withheld while obtaining central IV access. in general, central venous access and monitoring catheters can be placed once the patient stabilizes.

Hemodynamic support (fluids and vasopressors)

In the absence of hemorrhage, crystalloids are generally used (eg, normal saline or lactated Ringer's solution); there does not appear to be any robust mortality benefit to the administration of colloids in most cases of non-hemorrhagic shock (eg, albumin). However, in those with evidence of hemorrhage, blood is preferred but fluids should be administered until blood is available for transfusion.

Hemodynamic support (fluids and vasopressors)

Fluids should be administered as rapid boluses (eg, 500 mL boluses) or infusions with frequent assessment of the response. The response should be acutely followed by the assessment of vital signs; novel tools for assessing the hemodynamic response to fluids have not been validated in pregnant women. Once the intravascular volume has been replenished or pulmonary edema becomes apparent, fluids should be discontinued.

For patients who remain hypotensive after adequate resuscitation

initiation of vasopressor therapy, typically norepinephrine, is appropriate.

dobutamine, may be appropriate for those who have cardiogenic shock. Alternatives to norepinephrine are epinephrine (preferred in anaphylaxis), ephedrine (preferred for post anesthesia hypotension), or phenylephrine (preferred if tachyarrhythmia is an issue). Many experts avoid vasopressin if the fetus has not been delivered since it is thought to increase uterine contractions, and they avoid dopamine because in patients with septic shock it is associated with a possible increased risk in death

Respiratory support

The management of respiratory failure is supportive and includes the administration of supplemental oxygen, and, in most cases, intubation and mechanical ventilation.

Extracorporeal membrane oxygenation (ECMO)

should not be routinely used. Since anticoagulation is required for ECMO, the risk of bleeding is increased in the patients with AFE, who commonly have DIC

Management of hemorrhage and coagulopathy

For patients with a platelet count <50,000/microL, we typically give one to two units of random donor platelets per 10 kg of body weight, or one single donor apheresis unit daily. The increase in platelet count may be less than expected due to ongoing platelet consumption

Management of hemorrhage and coagulopathy

For patients with a prolonged prothrombin time (PT) or activated partial thromboplastin time (aPTT), FFP should be administered with the goal of reducing the international normalized ratio (INR).

Management of hemorrhage and coagulopathy

For patients in whom the fibrinogen level is <200 mg/dL, cryoprecipitate and FFP should be administered. Each unit of cryoprecipitate usually raises the level of fibrinogen by 10 mg/dL (goal >100mg/dL).

FFP is administered to patients with an initial fibrinogen level <50 mg/dL because FFP is often immediately available and provided in the massive transfusion cooler while cryoprecipitate usually needs to be thawed and can take time to arrive at the patient's bedside.

There is no evidence

to support prophylactic anticoagulation for DIC in the absence of thrombus. Further details regarding the management of DIC in pregnancy and complications of massive blood product transfusion are discussed separately.

Recombinant human factor VIIa (rVIIa)

has been used in patients with severe coagulopathy and bleeding.

We believe that factor VIIa use in patients with AFE should be reserved as a last resort and only for those with hemorrhage refractory to medical and/or surgical intervention

Delivery of the fetus

When AFE presents before delivery of a pregnancy >22 to 23 weeks of gestation, the need for immediate delivery must be determined.

urgent delivery include

category III fetal heart rate tracing (ie, preterminal) in a fetus at or above the limit of viability (22 to 23 weeks of gestation), and/or rapid and progressive deterioration of the mother's condition since delivery of a fetus at or beyond this gestational age early in the resuscitation process theoretically may improve the chance of successful maternal resuscitation.

American Heart Association guidelines for cardiopulmonary arrest in pregnancy

recommend beginning perimortem cesarean (resuscitative hysterotomy) at four minutes and completing delivery of the newborn by five minutes following cardiac arrest. In practice, such rapid delivery must be seen as an ideal goal, and is not always possible

Major maternal morbidity or death

is a significant risk when a cesarean delivery is performed in the presence of coagulopathy. If a cesarean delivery has to be performed urgently, blood, FFP, platelets, and cryoprecipitate should be available in the operating room and should be administered if there is any clinical evidence of impaired coagulation (eg, persistent bleeding without clotting from incision or needle sites).

ASSESSMENT AND TREATMENT OF POTENTIAL ETIOLOGIES

We perform the following tests:

- Complete blood count with platelets
- Serum electrolytes, blood urea nitrogen, creatinine, calcium, magnesium, phosphate
- Liver function tests
- Troponin-I
- Brain natriuretic peptide
- INR, activated partial thromboplastin time, fibrinogen
- Blood type and antibody screening (if not done at admission)
- Arterial blood gas
- Bedside chest radiograph
- Electrocardiography
- Bedside ultrasonography (if available), including lower extremity, lung, and abdominopelvic ultrasonography, transthoracic echocardiography; rarely, transesophageal echocardiography

Disorders that mimic the signs and symptoms of AFE

1)hemorrhage secondary to uterine atony lower genital tract and uterine lacerations, and retained placenta.

2) Before delivery, however, placental abruption can cause DIC

3) Medical disorders that can mimic AFE include pulmonary thromboembolism, anesthetic accident, myocardial infarction, and septic shock.

4) Acute pulmonary embolism (PE; obstructive shock)

5) Anaphylactic shock (distributive shock)

6) Septic shock (distributive shock)

7) Cardiogenic shock

8) Anesthetic shock

9) Air embolism

10) Aortic dissection

The following A through H mnemonic was devised by the American Heart Association to help providers remember causes of cardiac arrest that should be considered in pregnant women

- A: Anesthetic complications, Accident/trauma
- B: Bleeding
- C: Cardiac
- D: Drugs
- E: Embolic causes
- F: Fever
- G: General including hypoxia, electrolyte disturbances
- H: Hypertension

PROGNOSIS

AFE is one of the leading causes of maternal mortality and is reported to cause 10 percent of all maternal deaths in developed countries

Maternal mortality rates are high and prognosis in those who survive is poor.

The maternal mortality rate has been reported to range from 10 to 90 percent.

newer data report rates less than 50 percent, with an overall mortality of about 20 percent

Hypoxemia

Those who survive typically have a poor outcome, with as many as 85 percent suffering significant neurologic injury due to cerebral hypoxia although patients with milder presentations likely have better outcomes

Recurrence risk

While case reports suggest successful pregnancy following AFE, the risk of recurrence is unknown since no case of recurrent AFE has been reported

Thank you for your attention

Any Question ?