Review Article

Amniotic fluid embolism

Kiranpreet Kaur, Mamta Bhardwaj, Prashant Kumar, Suresh Singhal, Tarandeep Singh, Sarla Hooda

Department of Anaesthesiology and Critical Care, Pt. B.D. Sharma PGIMS, Rohtak, Haryana, India

Abstract

Amniotic fluid embolism (AFE) is one of the catastrophic complications of pregnancy in which amniotic fluid, fetal cells, hair, or other debris enters into the maternal pulmonary circulation, causing cardiovascular collapse. Etiology largely remains unknown, but may occur in healthy women during labour, during cesarean section, after abnormal vaginal delivery, or during the second trimester of pregnancy. It may also occur up to 48 hours post-delivery. It can also occur during abortion, after abdominal trauma, and during amnio-infusion. The pathophysiology of AFE is not completely understood. Possible historical cause is that any breach of the barrier between maternal blood and amniotic fluid forces the entry of amniotic fluid into the systemic circulation and results in a physical obstruction of the pulmonary circulation. The presenting signs and symptoms of AFE involve many organ systems. Clinical signs and symptoms are acute dyspnea, cough, hypotension, cyanosis, fetal bradycardia, encephalopathy, acute pulmonary hypertension, coagulopathy etc. Besides basic investigations lung scan, serum tryptase levels, serum levels of C3 and C4 complements, zinc coproporphyrin, serum sialyl Tn etc are helpful in establishing the diagnosis. Treatment is mainly supportive, but exchange transfusion, extracorporeal membrane oxygenation, and uterine artery embolization have been tried from time to time. The maternal prognosis after amniotic fluid embolism is very poor though infant survival rate is around 70%.

Key words: Amniotic fluid/diagnosis, amniotic fluid/ therapy, embolism, maternal mortality

Introduction

Amniotic fluid embolism (AFE) is one of the most catastrophic complications of pregnancy in which it is postulated that amniotic fluid, fetal cells, hair, or other debris enters the maternal pulmonary circulation, causing cardiovascular collapse. It was first reported by Meyer in 1926, and the syndrome was first described by Steiner and Lushbaugh in 1941.[1-4] However, the condition is exceedingly rare, and the exact pathophysiology is still unknown. Recent evidence suggests that the occurrence of AFE is not a consequence of the "simple" mechanical respiratory obstruction, but a humoral effect causing anaphylactoid reactions or complement activation.[2] The process is similar to anaphylaxis than to embolism, so also termed as anaphylactoid syndrome of pregnancy because fetal tissue or amniotic fluid components are not universally found in women who present with signs and symptoms attributable to AFE.[5-8] In some women, AFE may lead to a mild degree of organ dysfunction while in others it may lead to coagulopathy, cardiovascular collapse, and death.[9,10]

Address for correspondence: Dr. Kiranpreet Kaur,
52/9J, Medical Enclave, PGIMS, Rohtak - 124 001, Haryana, India.
E-mail: kiranpreet72@rediffmail.com

Access this article online	
Quick Response Code:	Website: www.joacp.org
	DOI: 10.4103/0970-9185.173356

Incidence and Outcome

Incidence of AFE is estimated to occur between 1 in 8000 and 1 in 80,000 deliveries. The true incidence is unknown because of inaccurate diagnosis and inconsistent reporting of nonfatal cases.[1,5,11] The syndrome typically occurs during labor, soon after vaginal or caesarean delivery, or during second-trimester dilation and evacuation procedures.[9] Previous studies revealed mortality rates as high as 61-86%, but recent estimates suggest a case fatality of 13-26%. This decrease in risk for maternal mortality from AFE may be the result of early diagnosis and better resuscitative care as well as changes in case inclusion criteria. Fetal outcome remains poor if AFE occurs before delivery, with a neonatal mortality rate approximately more than 10%.[3,7,8,12-15]

Causes and Risk Factors

Amniotic fluid embolism is considered an unpredictable and unpreventable event with an unknown cause. AFE may occur in healthy women during labor, during cesarean section, after abnormal vaginal delivery, or during the second trimester of pregnancy. It may also occur up to 48 h postdelivery. It can also occur during abortion, after abdominal trauma, and during amnioinfusion.[5,7] AFE has also been reported following intrauterine injection of hypertonic saline to induce abortion.[7,16]

Identified risk factors include:[3,10,17-19]

- Older maternal age.
- Multiparity.
- Intense contractions during labor.
- Abdominal trauma.
- Cesarean section.
- Induction of labor.
- Placenta previa.
- Eclampsia.
- Multiple pregnancy.
- Tears in the uterus or cervix.
- Early separation of the placenta from the uterus wall.

Fetal factors:

- Fetal distress.
- Fetal death.
- Male baby.

Pathophysiology

The pathophysiology of AFE is not completely understood but various theories have been published. Attwood in 1956 suggested anaphylaxis as a mechanism of AFE.[17] Benson suggested that this hypothesis can be established by testing women acutely ill with AFE for serum tryptase.[17] Tryptase is released by mast cells along with histamine when they degranulate in response to IgE cross-linking on the cell surface in the presence of antigen. Urinary histamine has also been used to diagnose anaphylaxis as a small percentage of histamine is excreted into the urine, unmetabolized. In 1995, Clarke suggested that the syndrome arose from an immune rather than the embolic process.[9,10,15,17]

There are two theories regarding the pathogenesis of AFE. The first historic idea is that a disorderly labor, abnormal placentation, surgical trauma, or any other breach of the barrier between maternal blood and amniotic fluid forces the entry of amniotic fluid into the systemic circulation and results in a physical obstruction of the pulmonary circulation. There must be a pressure gradient that favors transfer of fluid from the uterus into the systemic circulation.[5,7,12,16,20]

The second and increasingly favored hypothesis suggests that entry of amniotic fluid into the maternal circulation activates inflammatory mediators, causing a humoral or immunologic response.[21] Because of which it is named as "anaphylactoid syndrome of pregnancy."[12,17,22,] This theory is supported by the fact that amniotic fluid contains vasoactive and procoagulant products including platelet-activating factor, cytokines, bradykinin, thromboxane, leukotrienes, and arachidonic acid. Concentrations of tissue factor and tissue factor pathway inhibitor, which trigger intravascular coagulation, are higher in amniotic fluid than in maternal serum.[23-26] It is speculated that maternal plasma endothelin concentrations are increased by entry of amniotic fluid into the systemic vasculature. Endothelin acts as a bronchoconstrictor as well as a pulmonary and coronary vasoconstrictor, which may contribute to respiratory and cardiovascular collapse.[1,12,16,27] The direct procoagulant property of amniotic fluid may explain the prevalence of disseminated intravascular clotting (DIC) in AFE.

Few authors suggested that complement activation may have a role to play in the pathophysiology of disease.[17] Complement activation with markedly decreased C3 and C4 concentrations has been shown in patients with AFE. Fetal antigens may react with membrane-bound immunoglobulin E on mast cells, causing the release of histamine and tryptase. Both complement activation and mast cell degranulation support an immunologic mechanism.[12]

The cause of AFE-associated reactions is explained by two hypothesis: The effect of amniotic fluid itself or a host idiosyncrasy ("hypersensitivity" reaction).[2]

The initial respiratory reaction possibly begins with a transient pulmonary vasospasm. Vasospasm may be caused by amniotic microemboli that trigger the release of arachidonic acid metabolites and leads to pulmonary hypertension, intrapulmonary shunting, bronchoconstriction, and severe hypoxia. The second manifestation includes negative inotropism and left ventricular failure resulting in increasing pulmonary edema and hypotension quickly leading to shock. The third manifestation is a neurological response to the respiratory and hemodynamic injury, which may include seizures, confusion, or coma.[9,26]

After thorough literature search we found that few authors have proposed that two clinical forms of AFE exist typical and atypical. Uszynski also documented that symptoms vary in both forms of AFE.[28]

Typical, (classic) with three phases: Phase 1-respiratory and circulatory disorders, Phase 2-coagulation disturbances of maternal hemostasis, Phase 3-acute renal failure and acute respiratory distress syndrome (ARDS), and leading to cardiopulmonary collapse.

Atypical: In contrast to typical embolism, cardiopulmonary collapse does not occur in atypical embolism but the first symptom is life threatening hemorrhage due to DIC. Atypical embolism was observed during caesarean section or immediately after it, in cases of profound rupture of uterine cervix, as well as in the course of placenta abruption and in association with induced midtrimester abortion.[28,29]

The most significant pathologic findings at autopsy are limited to the lungs. Grossly, the lungs show evidence of pulmonary edema (in 70% of the cases). Alveolar hemorrhage and pulmonary embolism of amniotic fluid materials are present; the presence of embolic particles is essential for diagnosis, but on histology they may be missed because of their small size.[7]

Clinical presentation

The symptoms are often sudden. The presenting signs and symptoms of AFE involve many organ systems. Clark proposed a biphasic model of the hemodynamic consequences of AFE. The initial response is acute pulmonary hypertension and vasospasm leading to right ventricular failure, hypoxia, and cardiac arrest.[30] Hankins *et al*. demonstrated in a goat model that injecting 2.5 ml/kg of homologous amniotic fluid IV increased right heart and systemic vascular resistance. They also demonstrated that the presence of meconium was needed to produce left heart failure and hypoxia.[31]

The following signs and symptoms are indicative of possible AFE:[1,6,10,12,19,25]

Acute dyspnea or sudden, agitation, sudden chills, shivering, sweating, coughing and anxiety are common premonitory symptoms. Labored breathing and tachypnea may occur:[9]

- Cough: This is usually a manifestation of dyspnea.
- Altered mental status.
- Rapid decline in pulse oximetry values or sudden absence or decrease in end-tidal carbon dioxide may be apparent.
- Hypotension: Hemodynamic compromise quickly follows these prodromal signs. Hypotension is the most common presenting sign and symptom (100%). Blood pressure may drop significantly with the loss of diastolic measurement. Some researchers postulate that an acute anaphylactoid reaction may play a part in the development of the cardiovascular collapse.[7]
- Cyanosis: Ventilation-perfusion mismatching as a result of pulmonary vascular constriction at the onset of AFE may explain sudden hypoxia and respiratory arrest. As hypoxia/hypoxemia progresses, circumoral and peripheral cyanosis and changes in mucous membranes may manifest.
- Fetal bradycardia: In response to the hypoxic insult, fetal heart rate may drop to <110 bpm. If this drop lasts for 10 min or more, it is a bradycardia. A rate of 60 bpm or less over 3-5 min may indicate a terminal bradycardia.
- Encephalopathy associated with AFE is thought to be secondary to hypoxia and includes a spectrum of symptoms ranging from altered mental state to seizures. Tonic-clonic seizures are seen in 10-50% of patients.
- Uterine atony: Uterine atony usually results in excessive bleeding after delivery.
- Acute pulmonary hypertension and vasospasm results in right ventricular failure, hypoxia, and cardiac arrest. Pulmonary hypertension and right heart strain/failure may be the result of physical amniotic fluid debris in the pulmonary vasculature result from circulating pulmonary vasoconstrictive mediators. Proposed explanations include myocardial failure in response to sudden pulmonary hypertension, a direct myocardial depressant effect of humoral mediators in amniotic fluid, deviation of the intraventricular septum due to right ventricular dilation, and/or ischemic myocardial injury from hypoxemia.[8] If one survives this initial insult, then the pulmonary hypertension is generally not sustained and may be replaced with left ventricular failure and pulmonary edema. Increased pulmonary artery pressure has not been consistently reported probably because this finding may be short-lived. When cardiac pressures are measured early in the process, pulmonary and right ventricular pressures have been found to be elevated.[1,32]
- Coagulopathy or severe hemorrhage: Coagulation disorders are a prominent feature of the amniotic fluid syndrome. DIC is present in more than 83% of patients with AFE. The onset can occur as quickly as 10-30 min from the onset of symptoms or may be delayed by as long as 4 h.[1,33] Whether the coagulopathy is primarily a consumptive process or due to massive fibrinolysis is controversial. Amniotic fluid contains tissue factor that acts as a procoagulant and may account for the coagulopathy. Tissue factor binds with Factor VII and activates the extrinsic coagulation pathway. Alternatively, the coagulopathy may be related to fibrinolysis due to increased levels of plasminogen activation inhibitor 1 in amniotic fluid.[1,12]

Four criteria must be present to make the diagnosis of AFE:[5,32]

1. Acute hypotension or cardiac arrest.
2. Acute hypoxia.
3. Coagulopathy or severe hemorrhage in the absence of other explanations.

4. All of these occurring during labor, cesarean delivery, dilation and evacuation, or within 30 min postpartum with no other explanation of findings.

Diagnosis[6,9,16,25,34]

1. Initial diagnostic evaluation should include continuous pulse oximetry and arterial blood gas (ABG) measurements to determine the degree of hypoxemia.
- ABG levels: Expect changes consistent with hypoxia/hypoxemia.
  - Decreased pH.
  - Decreased PO_2.
  - Increased PCO_2 levels.
  - Base excess increased.
2. Serial complete blood counts and coagulation studies should be sent to follow trends and detect early coagulopathy.
- CBC with platelets.
  - Hemoglobin and hematocrit levels should be within reference ranges.
  - Thrombocytopenia is rare.
- Prothrombin time (PT) and activated partial thromboplastin time (aPTT).
  - PT is prolonged because clotting factors are used up. Values are institution specific, but intervention is indicated when the PT is 1.5 times the control value.
  - aPTT may be within reference range or shortened.
- If available, fibrinogen level should be monitored.
3. Blood type and screen in anticipation of the requirement for a transfusion.
4. Chest radiograph posteroanterior and lateral findings are usually nonspecific. The chief radiographic abnormalities in AFE are diffuse bilateral heterogeneous and homogeneous areas of increased opacity, which are indistinguishable from acute pulmonary edema.
5. A 12-lead electrocardiogram may show tachycardia, ST-segment and T-wave changes, and findings consistent with right ventricle strain.
6. Lung scan may demonstrate some areas of reduced radioactivity in the lung field.[5]
7. Increased serum tryptase, urinary histamine concentrations and significantly lower complement concentrations suggest an anaphylactoid process.[12,17,21,35]

Tryptase is a serine protease with a half-life of several hours. Although the specific function of tryptase in anaphylaxis is unknown, with a half-life measured in hours instead of the minutes of histamine, the protein has proven useful in the diagnosis of anaphylaxis.[36]

8. Decreased serum levels of C3 and C4 complement had sensitivities between 88% and 100% and a specificity of 100%.[16]
9. More studies are also needed to determine the utility of both monoclonal TKH-2 antibodies and zinc coproporphyrin as rapid diagnostic markers.[12,22]
10. Few studies have evaluated the diagnostic accuracy of serum sialyl Tn (STN), a fetal antigen present in meconium and amniotic fluid, detected through the use of TKH-2 monoclonal antibody. TKH-2 reacts with meconium and mucin and stains the lung tissue in those with AFE. For serum levels >50 U/ml, the sensitivities varied between 78% and 100% and the specificities between 97% and 99%.[2,9,16,37]

Few authors reported a significant high serum level of STN antigen in the AFE cases as high as 110.8 ± 48.1 U/ml for AFE versus 17.3 ± 2.6 U/ml for control). In few case reports in the literature reported that intravascular fetal material in the uterus can be used to confirm a diagnosis of AFE in situations where AFE is prevented by ligation of uterine artery.[17,25]

11. Bedside transesophageal echocardiography may aid early diagnosis by showing acute pulmonary vasoconstriction, right ventricular dilation, and a collapsed left ventricle with leftward deviation of the intraventricular septum.[38,39] However, rapid access to transesophageal echocardiography is probably not available in many obstetric units.

Previously, it was believed that the distal port of a pulmonary artery catheter can be used to aspirate the amniotic fluid debris and was pathognomonic of the syndrome. These samples may have been contaminated by maternal squamous cells. This test is more supportive of the diagnosis when squamous cells are found in large numbers, are coated with neutrophils, and/or if they are accompanied by the other fetal debris.[9] There are numerous reports in the literature in which fetal material is found in the maternal circulation of living parturients who do not have AFE. Among the earliest reports are two separate cases in which fetal material was found in the maternal circulation.[17] Supportive therapy as indicated by clinical circumstance is always the most important intervention and should supersede diagnostic studies. Attempts at obtaining blood or fluid samples for unvalidated diagnostic purposes should never interfere with resuscitation. We must rely on clinical symptoms and exclusion of other clinical explanations.[10,12]

The diagnosis of AFE has traditionally been made at autopsy when fetal squamous cells are found in the maternal pulmonary circulation. In a patient who is critically ill,

a sample obtained by aspiration of the distal port of a pulmonary artery catheter that contains fetal squamous cells is considered suggestive of but not diagnostic of AFE syndrome.[40]

Differential Diagnosis

The differential diagnosis of AFE includes obstetric, nonobstetric, and anesthetic etiologies.[9,17]

- Anaphylaxis.
- Aortic dissection.
- Cholesterol embolism.
- Myocardial infarction.
- Pulmonary embolism.
- Septic shock.
- Air embolism.
- Eclamptic convulsions and coma.
- Convulsion from the toxic reaction to local anesthetic drugs.
- Aspiration of gastric contents.
- Hemorrhagic shock in an obstetric patient.

Management

To prevent AFE, trauma to the uterus must be avoided during maneuvers such as insertion of a pressure catheter or rupture of membranes. Incision of the placenta during caesarean delivery should also be avoided if possible. Since, one of the most frequent predisposing factors is considered to be tumultuous labor that may occur naturally, excessively strong and frequent uterine contractions should be controlled by administration of intravenous β-adrenergic drugs or magnesium sulfate. Furthermore, oxytocic drugs, which can precipitate excessive tetanic uterine contractions must be used appropriately and judiciously.[3,9]

The key factors in the management of AFE are early recognition, prompt resuscitation, and delivery of the fetus. Early recognition of AFE is critical to a successful outcome. Management is primarily supportive and resuscitative.

General[1,33,36,40]

- Maintaining vital signs. The initial goal is the rapid correction of maternal hemodynamic instability, which includes a correction of hypoxia and hypotension, for preventing the additional hypoxia and subsequent end-organ failure.[16]
- Oxygenation and Control of the airway with tracheal intubation and administration of 100% O_2 with positive pressure ventilation should be performed as soon as possible.
- Fluid resuscitation is imperative to counteract hypotension and hemodynamic instability. Treatment of hypotension includes optimization of preload, with rapid volume infusion of isotonic crystalloid and colloids solutions. Although both can restore blood volume in ongoing hemorrhage, transfusion of packed red blood cells is necessary to restore oxygen carrying capacity.[34]
- Transthoracic or transesophageal echocardiography may guide fluid therapy with evaluation of left ventricular filling. An arterial line and pulmonary catheter may also help to guide therapy. For refractory hypotension, vasopressor therapy is indicated.[3,9]
- Correcting coagulopathy — Blood and blood products, including fresh frozen plasma (FFP), platelets and cryoprecipitate, must be available and administered early in the resuscitation phase of AFE. If platelets are <20,000/μL, or if bleeding occurs and platelets are 20,000-50,000/μL, transfuse platelets at 1-3 U/10 kg/day.
- Administer FFP to normalize the PT.
- If fibrinogen level is <100 mg/dL, administer cryoprecipitate. Each unit of cryoprecipitate raises the fibrinogen level 10 mg/dL.
- Arterial catheterization should also be considered for accurate arterial blood pressure monitoring and frequent blood sampling.[1]

Pharmacological[1,34,36,41]

Vasopressors and inotropic support are generally needed to varying degrees in AFE. Central venous access should be established for vasopressor infusion and monitoring. Choice of vasopressor drug depends on the clinical scenario.

- Epinephrine may be the first-line agent of choice as it is used in other anaphylactoid reactions, in addition to the α-adrenergic vasoconstrictor effects.
- Phenylephrine, a pure α-1 agonist, is often an excellent choice early in the treatment of AFE because at that time point systemic vasodilation is the most prominent circulatory abnormality.
- Inotropic support like dopamine or noradrenaline may be ideal agents because of the additional β-adrenergic effects, which improve cardiac function.
- Vasopressin may be used as primary therapy or as an adjunct to other inotropic therapies and has the benefit of sparing the pulmonary vasculature from vasoconstriction, especially at low doses. In the face of right heart failure, milrinone or other phosphodiesterase inhibitors should be considered.[1,12]
- Digoxin: acts directly on the cardiac muscle and conduction system. Digoxin causes an increase in force and velocity of systolic contraction, a slowing of the heart rate, and decreased conduction velocity through the AV node.

- Hydrocortisone: Because AFE is more similar to an anaphylactic reaction, steroids that mediate the immune responses are recommended.
- Oxytocin: Most commonly used uterotonic. Decreases inflammation by suppressing migration of polymorphonuclear leukocytes and reversing increased capillary permeability.
- Methylergonovine (Methergine): Acts directly on uterine smooth muscle, causing a sustained tetanic uterotonic effect that reduces uterine bleeding.
- Carboprost tromethamine: Prostaglandin similar to F2-alpha (dinoprost), but has longer duration and produces myometrial contractions that induce hemostasis at placentation site, which reduces postpartum bleeding
- The successful use of recombinant factor VIIa (rfVIIa) has been reported.[42] although it has also been associated with massive intravascular thrombosis.
- Aprotinin has also been effective in reducing hemorrhage with AFE.
- Other antifibrinolytic drugs, such as aminocaproic acid and tranexamic acid, have been described in the management of obstetric hemorrhage and menorrhagia and might also be considered during AFE.[1,12]

Left uterine displacement is crucial in resuscitation efforts if the fetus remains *in utero*. It has been reported that immediate cesarean section will improve neonatal neurologic recovery and overall maternal outcome if performed within 5 min of maternal cardiovascular arrest. Maternal resuscitative efforts are also enhanced by relief of aortocaval compression at delivery.[12]

Other novel approaches for the treatment of AFE have been successfully used which included exchange transfusion, extracorporeal membrane oxygenation (ECMO), cardiopulmonary bypass, a right ventricular assist device, uterine artery embolization, intraaortic balloon pump with ECMO have recently been reported with successful outcomes. Continuous hemofiltration, cell-salvage combined with blood filtration and serum protease inhibitors are few other recommended treatment in literature.[3,4,10,43]

Hysterectomy may be required in patients with persistent uterine hemorrhage to control blood loss. rfVII has also been described as a treatment for hemorrhage occurring with AFE, but should be used with caution because a recent review of case reports has suggested worsened outcomes. Both aerosolized prostacyclin and inhaled nitric oxide (NO) act as direct pulmonary vasodilators, and have been successfully used to treat the acute pulmonary vasoconstriction of AFE.[1,12,43]

Few clinicians have tried heparin for treatment of AFE, but its administration is still controversial. This controversy arises because of the manifestation of both DIC and embolism in patients of AFE.[28] Besides heparin, in few animal studies aspirin have been tried. Heparin prophylaxis maintained platelet count whereas aspirin prophylaxis did not. They concluded that the aspirin is not an effective prophylactic drug.[44]

Prognosis[1,12,16]

Survival after AFE has improved significantly with early recognition of this syndrome and prompt and early resuscitative measures. Previously, it was documented that 50% of patients die within the first hour and about two-third within 5 h of the event with high incidence of severe and permanent neurological damage among survivors.[16] Although mortality rates have declined, morbidity remains high with severe sequelae. Beside neurologic impairment, acute oliguric or nonoliguric renal failure, cardiac failure with left ventricular impairment, cardiogenic pulmonary edema, arrhythmias, myocardial ischemia or infarction have been reported. Respiratory failure with noncardiogenic pulmonary edema and refractory bronchospasm are other reported sequelae:[3,9,10]

- The prognosis after AFE is very poor, and most women do not survive.
- If patient survives the embolism, most survivors have neurologic deficits.
- The infant survival rate is 70%. Neurologic status of the infant is directly related to the time elapsed between maternal arrest and delivery.
- Risk of recurrence is unknown. Successful subsequent pregnancies have been reported.

Despite our lack of understanding of the pathophysiologic processes of AFE, it is very clear that early and aggressive management (including immediate cesarean section) of patients with clinically suspected AFE enhances both fetal and maternal resuscitation and improves survival. It is important to always consider AFE in the differential diagnosis of sudden maternal cardiopulmonary instability and remember that the lack of development of DIC and hemorrhage does not exclude the diagnosis of AFE. More research on serum diagnostic tests, such as zinc coproporphyrin, STN antigen, and C3 and C4 complement is needed. Selective pulmonary vasodilators, such as NO for the treatment of severe pulmonary hypertension during the acute phase of AFE, and rfVIIa for managing severe DIC resistant to conventional treatments are promising.[16]

References

1. Gist RS, Stafford IP, Leibowitz AB, Beilin Y. Amniotic fluid embolism. Anesth Analg 2009;108:1599-602.

2. Tsunemi T, Hidekazu OI, Sado T, Naruse K, Noguchi T, Kobayashi H. An overview of amniotic fluid embolism: Past, present and future directions. Open Womens Health J 2012;6:24-9.
3. Moore J, Baldisseri MR. Amniotic fluid embolism. Crit Care Med 2005;33:S279-85.
4. Steiner PE, Lushbaugh C. Maternal pulmonary embolism by amniotic fluid as a cause of obstetric shock and unexplained death in obstetrics. JAMA 1941;117:1245–54.
5. Clark SL, Hankins GD, Dudley DA, Dildy GA, Porter TF. Amniotic fluid embolism: Analysis of the national registry. Am J Obstet Gynecol 1995;172:1158-67.
6. Dedhia JD, Mushambi MC. Amniotic fluid embolism. Contin Educ Anaesth Crit Care Pain J 2007;7:152-6.
7. Skerman JH, Rajab KE. Amniotic fluid embolism. Kuwait Med J 2003;35:91-7.
8. Yentis S. Amniotic fluid embolism. Can J Anaesth 2001;48:829-30.
9. Rudra A, Chatterjee S, Sengupta S, Nandi B, Mitra J. Amniotic fluid embolism. Indian J Crit Care Med 2009;13:129-35.
10. Toy H. Amniotic fluid embolism. Eur J Gen Med 2009;6:108-15.
11. Tuffnell DJ. United kingdom amniotic fluid embolism register. BJOG 2005;112:1625-9.
12. Laura SD, Raford PR, Russell AH, David DH. Case scenario: Amniotic fluid embolism. Anesthesiology 2012;116:186-92.
13. Gei AF, Vadhera RB, Hankins GD. Embolism during pregnancy: Thrombus, air, and amniotic fluid. Anesthesiol Clin North America 2003;21:165-82.
14. Tuffnell D, Knight M, Plaat F. Amniotic fluid embolism — An update. Anaesthesia 2011;66:3-6.
15. Syed SA, Dearden CH. Amniotic fluid embolism: Emergency management. J Accid Emerg Med 1996;13:285-6.
16. Conde-Agudelo A, Romero R. Amniotic fluid embolism: An evidence-based review. Am J Obstet Gynecol 2009;201:445. e1-13.
17. Benson MD. Current concepts of immunology and diagnosis in amniotic fluid embolism. Clin Dev Immunol 2012;2012:946576.
18. Tan A, McDonnell N. Amniotic fluid embolism ATOTW 196 20/09/2010. 1-7.
19. Dobbenga-Rhodes YA. Responding to amniotic fluid embolism. AORN J 2009;89:1079-88.
20. Knight M, Tuffnell D, Brocklehurst P, Spark P, Kurinczuk JJ, UK Obstetric Surveillance System. Incidence and risk factors for amniotic-fluid embolism. Obstet Gynecol 2010;115:910-7.
21. Benson MD. A hypothesis regarding complement activation and amniotic fluid embolism. Med Hypotheses 2007;68:1019-25.
22. Clark SL. Amniotic fluid embolism. Clin Obstet Gynecol 2010;53:322-8.
23. Tuffnell DJ. Amniotic fluid embolism. Curr Opin Obstet Gynecol 2003;15:119-22.
24. Fineschi V, Gambassi R, Gherardi M, Turillazzi E. The diagnosis of amniotic fluid embolism: An immunohistochemical study for the quantification of pulmonary mast cell tryptase. Int J Legal Med 1998;111:238-43.
25. Tan K, Sim Y, Chiu J, Loo C, Yeo S. Maternal-fetal survival following amniotic fluid embolism: 2 case reports. Internet J Gynecol Obstet 2001;1.
26. Uszyński M, Uszyński W. A New Approach to the pathomechanism of amniotic fluid embolism: Unknown role of amniotic cells in the induction of disseminated intravascular coagulation. Asian Pac J Reprod 2012;1:326-9.
27. Weiner AE, Reid DE. The pathogenesis of amniotic-fluid embolism. III. Coagulant activity of amniotic fluid. N Engl J Med 1950;243:597-8.
28. Uszynski M. Amniotic fluid embolism: The complication of known pathomechanism but without pathogenetic therapy? Thromb Haemost 2009;101:795-6.
29. Uszyński M. Amniotic fluid embolism: Literature review and an integrated concept of pathomechanism. Open J Obstet Gynecol 2011;1:178-83.
30. Clark SL. New concepts of amniotic fluid embolism: A review. Obstet Gynecol Surv 1990;45:360-8.
31. Hankins GD, Snyder RR, Clark SL, Schwartz L, Patterson WR, Butzin CA. Acute hemodynamic and respiratory effects of amniotic fluid embolism in the pregnant goat model. Am J Obstet Gynecol 1993;168:1113-29.
32. O'Shea A, Eappen S. Amniotic fluid embolism. Int Anesthesiol Clin 2007;45:17-28.
33. Malhotra P, Agarwal R, Awasthi A, DAS A, Behera D. Delayed presentation of amniotic fluid embolism: Lessons from a case diagnosed at autopsy. Respirology 2007;12:148-50.
34. Saha R, Maharjan S, Thapa J. Amniotic Fluid Embolism understanding pathophysiology from a successfully managed case. N J Obstet Gynaecol 2006;1:55-8.
35. Leighton BL, Wall MH, Lockhart EM, Phillips LE, Zatta AJ. Use of recombinant factor VIIa in patients with amniotic fluid embolism: A systematic review of case reports. Anesthesiology 2011;115: 1201-8.
36. Thongrong C, Kasemsiri P, Hofmann JP, Bergese SD, Papadimos TJ, Gracias VH, *et al.* Amniotic fluid embolism. Int J Crit Illn Inj Sci 2013;3:51-7.
37. Shechtman M, Ziser A, Markovits R, Rozenberg B. Amniotic fluid embolism: Early findings of transesophageal echocardiography. Anesth Analg 1999;89:1456-8.
38. Stanten RD, Iverson LI, Daugharty TM, Lovett SM, Terry C, Blumenstock E. Amniotic fluid embolism causing catastrophic pulmonary vasoconstriction: Diagnosis by transesophageal echocardiogram and treatment by cardiopulmonary bypass. Obstet Gynecol 2003;102:496-8.
39. Kulshrestha A, Mathur M. Amniotic fluid embolism: A diagnostic dilemma. Anesth Essays Res 2011;5:227-30.
40. Sugunadevan M. Amniotic fluid embolism. Sri Lanka J Anaesthesiol 2009;17:25-7.
41. Wilhite L, Melander S. Amniotic fluid embolism: A case study. Am J Nurs 2008;108:83-5.
42. Prosper SC, Goudge CS, Lupo VR. Recombinant factor VIIa to successfully manage disseminated intravascular coagulation from amniotic fluid embolism. Obstet Gynecol 2007;109:524-5.
43. Mato J. Suspected amniotic fluid embolism following amniotomy: A case report. AANA J 2008;76:53-9.
44. Strickland MA, Bates GW, Whitworth NS, Martin JN. Amniotic fluid embolism: Prophylaxis with heparin and aspirin. South Med J 1985;78:377-9.

How to cite this article: Kaur K, Bhardwaj M, Kumar P, Singhal S, Singh T, Hooda S. Amniotic fluid embolism. J Anaesthesiol Clin Pharmacol 2016;32:153-9.
Source of Support: Nil, **Conflicts of Interest:** None declared.