ejpmr, 2018,5(7), 189-192

SJIF Impact Factor 4.897

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

AMNIOTIC FLUID EMBOLISM

Mishra Archana*, Arya Priyanka and Arora Renu

India.

***Corresponding Author: Dr. Mishra Archana**

India.

Article Received on 07/05/2018 **Article Revised on 27/05/2018** **Article Accepted on 17/06/2018**

Amniotic fluid embolism is an enigma, a true obstetrician nightmare because of its sudden occurrence, rapid progression causing maternal collapse and high fetomaternal mortality. It's a rare event but a catastrophic emergency that is unique to pregnancy. Etiopathogenesis of AFE is not well understood and diagnostic criterias are controversial. It occurs when amniotic fluid, fetal cells, hair, or other debris enter the maternal circulation causing shortness of breath, altered mental sensorium and cardiovascular collapse. Despite advances in critical care management across the globe, there is no definitive management for AFE, treatment is supportive and not much improvement in the survival or long-term outcome of women with AFE has been achieved yet.

Epidemiology

The true incidence is not known because of inadequate maternal deaths reporting and the fact that AFE is difficult to identify and remains a diagnosis of exclusion; reported incidence being 1:8000 to 1:80000.[1] In 1926, Ricordo Meyer was the first to describe the syndrome of AFE.[2] Later in 1941, Steiner and Lushbaugh published a maternal mortality case series of eight women who had squamous cells and mucin, presumably of fetal origin, within their pulmonary vasculature at postmortem.[3] They described that these histological findings formed the basis of a clinical syndrome characterized by sudden peripartum shock resulting in maternal death.

Owing to advances in critical care and multidisciplinary approach, number of maternal deaths due to AFE has fallen significantly over the last 20 yr. In 1979, the suggested maternal mortality rate was 86%[4]; now decreased to around 61%. Majority of patients with AFE die within the first hour of onset of symptoms and about 85% of those who survive have permanent hypoxia-induced neurological impairment.

Fetal mortality rate is about 21% and half of the surviving neonates experience permanent neurological damage.[5]

Risk factors

There are no proven risk factors, however following conditions have been found to be more frequently associated with risk of AFE:

Advanced maternal age Multiparity Macrosomia Polyhydramnios Intrauterine fetal death Intense uterine contractions Medical induction of labour Caesarean section	Meconium stained liquor Instrumental vaginal delivery Placental abruption Uterine rupture Trauma to abdomen High cervical tears Saline amnioinfusion Male fetus

Pathophysiology

The pathophysiology of AFE syndrome is unclear. A factor that is consistently related to the occurrence of AFE is a tear in the fetal membranes and entry of fetal cells/amniotic fluid into maternal vasculature causing transient pulmonary vasospasm, pulmonary arterial hypertension, cardiac failure, hypoxaemia, and death.

In 1995, Clark suggested that the syndrome resembles an anaphylactic reaction to fetal antigens in the amniotic fluid rather than embolic process and they propose the term "anaphylactoid syndrome of pregnancy" instead of AFE.[6]

Progression of events

Phase 1

Exposure of pulmonary vasculature to both soluble (leukotrienes, surfactant, thromboxane A2, endothelin) and insoluble components (squames, vernix, hair, mucin) of the amniotic fluid induces capillary leak, negative inotropism, and bronchospasm. This results in sudden onset of respiratory distress and cyanosis.

Within minutes, negative inotropic effect becomes prevalent (due to myocardial ischemia). Pulmonary venous pressure (congestion) increases and cardiac output decreases, manifested by pulmonary edema and

hypotension resulting into shock. Phase 1 may last up to 30 min.

Phase2
Amniotic fluid contains activated coagulation factors II, VII, and X. It also has a direct factor X activating property, induces platelet aggregation, releases platelet factor III, and has a thromboplastin-like effect, causing a consumptive coagulopathy in a large proportion of the first-phase survivors. This disseminated intravascular coagulation often results in uterine atony and massive haemorrhage.

Clinical features
AFE classically presents as sudden, profound and unexplained dyspnea, respiratory failure, hypotension followed by cardiovascular collapse, disseminated intravascular coagulation and death.[3]

Most cases of AFE (70%) occur during labour; mainly after rupture of membranes (two third cases occur after artificial rupture of membrane, one third after spontaneous membrane rupture), 19% during Caesarean section and 11% following vaginal delivery.[6] Cases have been reported during early gestation, second trimester abortions, during amniocentesis, or following closed abdominal injury.

There are 3 phases of AFE in humans
Phase 1 includes

- Respiratory distress and cyanosis,
- Pulmonary edema
- Neurologic- confusion and coma
- Fetal distress (late decelerations, bradycardia) and fetal demise

These manifestations can either occur in combination or separately and in different magnitudes.

If patients survive the initial cardiorespiratory insult, then comes phase 2, which is characterized by coagulopathy, hemorrhage, shock and patient is in left sided heart failure.

In phase 3, acute symptoms have passed and there is established injury to brain, lungs and renal systems. Phase 3 may last for weeks and patients may die as a result of severe brain and lung injury, infection and multiple organ system failure.[7]

Diagnosis
There is still no pathognomic marker of AFE, it is poorly understood and diagnosed largely by exclusion. The presence of fetal squamous cells in maternal pulmonary vasculature was once considered diagnostic, but it is now considered to be neither sensitive nor specific.

Differential diagnosis of amniotic fluid embolism	
OBSTETRICS Placental abruption Eclampsia Peripartum cardiomyopathy Hemorrhage	NON OBSTETRICS Pulmonary thromboembolism Air embolism Transfusion reaction Anaphylaxis Myocardial infarction Septic shock Anesthetic complications Aspiration of gastric contents Systemic inflammatory response syndrome

Diagnosis is aided by non-specific and specific diagnostic tests.

Non-specific tests includes

1. A full blood count showing low haemoglobin
2. Coagulation screen to demonstrate abnormal coagulation
3. Arterial blood gases and pulse oxymetry may show hypoxaemia.[8]
4. Chest X-ray does not often show any abnormality in the early stages before ARDS develops
5. ECG may demonstrate tachycardia and right ventricular strain pattern in the early stage.[8]
6. Echocardiography is useful to demonstrate either right or left ventricular dysfunction and low ejection fraction

Specific tests include

1. Cytological analysis of central venous blood and broncho-alveolar fluid showing presence of squamous cells coated with neutrophils and presence of fetal debris
2. Sialyl Tn antigen test - Sialyl is a mucin type glycoprotein that originates in fetal and adult intestinal and respiratory tracts and forms a major component in meconium (10% by weight) and clear amniotic fluid. Using a sensitive anti-mucin antibody TKH-2, it was found that the antigen concentrations were significantly elevated in patients with AFE.[9,10]
3. Zinc coproporphyrin concentration – a characteristic component of meconium and its plasma concentration has been found to be greater in patients with suspected AFE.[9,10]
4. Serum tryptase concentrations – found higher (>10ng/ml) in suspected AFE.[11]

Management
Treatment is only supportive and focuses initially on rapid maternal cardiopulmonary stabilization. It requires multidisciplinary care (anaesthetists, obstetricians, haematologists intensivists). Majority of patients requires intensive care unit admission after initial

stabilization.[12] Main aim is to prevent additional hypoxia and subsequent end-organ failure.

Oxygenation
Target is to achieve arterial oxygen tension of more than 60 mmHg by administering oxygen via a face mask to or tracheal intubation and mechanical ventilation using 100% oxygen in cases of refractory hypoxemia or comatose patients.

Haemodynamic stability
Rapid intravenous filling, direct acting vasopressors and inotropes may be necessary to improve cardiac output. To support BP; dopamine is used, although in severe shock epinephrine or norepinephrine may be ideal agents. During cardiopulmonary resuscitation, left uterine displacement must be maintained in a pregnant woman to relieve aortocaval compression and improve cardiac output.[13]

Other treatment modalities which are beneficial for severe pulmonary hypertension include nitric oxide, as a selective pulmonary vasodilator, prostacyclin and sildenafil.[1,14]

Management of DIC
In less than 4 h, nearly half of the patients who survive the initial phase go on to develop DIC, with massive haemorrhage. Therefore, blood products should be ready ahead of time, and replacement with typed and crossed packed red blood cells, or with O-negative blood, is essential. Other blood products like platelets, cryoprecipitate and fresh frozen plasma should be administered as guided by laboratory assessment of the prothrombin time/ partial thromboplastin time, fibrinogen and fibrin degradation products.

Uterine atony should be managed using uterotonics (oxytocin, ergometrine and prostaglandins such as carboprost and misoprostol). Bimanual uterine massage and uterine packing may also help to reduce blood loss. Surgical management includes hysterectomy and uterine artery embolization.[15]

Administration of recombinant activated factor VII (rVIIa) has been described to treat uncontrollable massive obstetric haemorrhage.[16] However, in patients with disseminated intravascular coagulation and elevated levels of tissue factor (as occurs in amniotic fluid embolism), rVIIa could lead to excessive diffuse thrombosis and multiorgan failure. It should be considered as a last resort in cases in which hemorrhage cannot be stopped with massive blood component replacement and surgical interventions.

Delivery of baby
Severe fetal academia often develops with maternal collapse, and early delivery may improve the neonatal prognosis. If the mother is undergoing cardiopulmonary resuscitation, surgical delivery should be performed within 4 min for improved maternal outcome. Therefore, perimortem cesarean delivery or resuscitative hysterotomy is recommended in pregnant women with AFE and cardiac arrest.[17]

Newer stratergies
It includes Intra-aortic balloon counterpulsation, Extracorporeal membrane oxygenation, Cardiopulmonary bypass, Plasma exchange transfusions , Continuous hemofiltration, Serum protease inhibitors, use of sidenafil, inhaled nitric oxide and prostacyclins and high-dose corticosteroids.[1,14]

CONCLUSION
Most cases of AFE are associated with poor maternal outcomes and fetal outcomes regardless of the quality of care rendered. Most massive PPH cases of unknown etiology accompanied by atonic uterus and DIC have been considered pathognomonic for clinical AFE. Improvement in understanding of the molecular pathophysiology of AFE have lead to the development of preventive measures and more effective and specific treatment.

REFERENCES
1. Davies S. Amniotic fluid embolism: a review of literature. *Can J Anaesth*, 2001; 48: 88– 98 3.
2. Meyer JR. Embolia pulmonary amnio caseosa. Bras Med, 1926; 2: 301-3.
3. Steiner PE, Lushbaugh CC. Landmark article, 1941: Maternal pulmonary embolism by amniotic fluid as a cause of obstetric shock and unexpected deaths in obstetrics. JAMA, 1986; 255: 2187-203.
4. Masson RG. Amniotic fluid embolism. Clin Chest Med, 1992; 13: 657–665.
5. Perozzi KJ, Englert NC. Amniotic Fluid embolism: An obstetric emergency. *Crit Care Nurse*, 2004; 24: 54-61.
6. Clark SL, Hankins GD, Dudley DA, Dildy GA, Porter TF. Amniotic fluid embolism: analysis of the national registry. *Am J Obstet Gynecol*, 1995; 172: 1158–1167.
7. Gilmore DA, Wakim J Secrets J, Rawson R. Anaphylactoid syndrome of preganacy: A review of the literature with latest management and outcome data. AANA J, 2003; 71: 120-6.
8. O'Shea A, Eappen S. Amniotic fluid embolism. *Int Anesthesiol Clin.*, 2007; 45: 17-28.
9. Harboe T, Benson MD, Oi H, Softeland E, Bjorge L, Guttormsen AB. Cardiopulmonary distress during obstetrical anaesthesia: Attempts to diagnose amniotic fluid embolism in a case series of suspected allergic anaphylaxis. *Acta Anaesthesiol Scand*, 2006; 50: 324-30.
10. Oi H, Kobayashi H, Hirashima Y, et al. Serological and immunohistochemical diagnosis of amniotic fluid embolism. *Semin Thromb Hemost*, 1998; 24: 479-84.
11. Tuffnell DJ, Johnson H. Amniotic fluid embolism. *Curr Opin Obstet Gynecol*, 2003; 15: 119–22.

12. Gilbert WM, Danielsen B. Amniotic fluid embolism: decreased mortality in a population-based study. *Obstet Gynecol*, 1999; 93: 973-7.
13. Moore J, Baldisseri MR. Amniotic fluid embolism. *Crit Care Med*, 2005; 33(10 Suppl): 279-85.
14. 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.
15. Goldazmidt E, Davies S. Two cases of hemorrhage secondary to amniotic fluid embolus managed with uterine artery embolisation. Can J Anaesth, 2003; 50: 917-21.
16. 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.
17. Katz VJ, Dotters DJ, Droegemueller W. Perimortem cesarean delivery. *Obstet Gynecol*, 1986; 68: 571-6.