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Amniotic fluid embolism: A rare and destructive obstetric complication

Efthymia Thanasa [1], Anna Thanasa [1], Ektoras-Evangelos Gerokostas [2], Evangelos Kamaretsos [2], Gerasimos Kontogeorgis [2] and Ioannis Thanasas [2,*]

[1] *Department of Health Sciences, Medical School, Aristotle University of Thessaloniki, Thessaloniki, Greece.*
[2] *Department of Obstetrics and Gynecology, General Hospital of Trikala, Trikala, Greece.*

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Abstract

Amniotic fluid embolism is a rare, unpredictable and often catastrophic obstetric complication that usually occurs during labor or caesarean section. The pathogenetic mechanism has not been fully elucidated to date. Amniotic fluid embolism is believed to happen due to an anaphylactic reaction to embryonic antigens that enter the mother's circulation and trigger a variety of immune processes that produce an anaphylactic-like response. The diagnosis remains clinical. The disease manifests abruptly with cardiovascular shock, encephalopathy, fetal discomfort and disseminated intravascular coagulation. There is no special treatment. The treatment is supportive and focuses on rapid stabilization of the cardiopulmonary system, adequate oxygenation of the vital organs and correction of coagulation, ensuring the best possible perinatal outcome. In this article, based on current data, a literature review of this rare obstetric complication is attempted, particularly with regard to diagnosis and the basic treatment principles, the timely and correct application of which can provide the best possible outcome for the mother and the newborn.

Keywords: Amniotic fluid embolism; Diagnosis; Management; Prognosis

1. Introduction

Placental and amniotic fluid emergencies during pregnancy can occur in any trimester and endanger the life of the mother, as well as the life of the fetus and newborn. Premature rupture of fetal membranes and premature birth, umbilical cord prolapse, uterine atony, chorioamnionitis, diffuse intravascular coagulation and amniotic fluid embolism are serious pathologies associated with dysfunction and dysfunction.

Amniotic fluid embolism is a rare and often disastrous obstetric complication that can occur during pregnancy, usually during a normal birth or caesarean section, but also after delivery in the first days of pregnancy in about onethird of cases [1]. It is a multifactorial syndrome that affects all organs and is characterized by sudden cardiovascular shock, change in the mental level of the mother and diffuse intravascular coagulation.The severity of the disease varies from mild dysfunction to cardiovascular collapse and maternal death.In most cases amniotic fluid embolism results in a double tragedy with devastating consequences, both for the pregnant woman and for the fetus and the newborn [2].

1.1. Historical background – epidemiological information

Amniotic fluid embolism was first described by Ricardo Meyer in 1926. Meyer first reported the finding of fetal elements in the pulmonary circulation of a mother with sudden death [3]. In 1941 amniotic fluid embolism was recognized as a syndrome by Steiner and Lushbaugh, who described the clinical and histopathological findings of 42 women who died suddenly during or shortly after giving birth [4]. In 1949 Shotton and Taylor published a case of pulmonary embolism

*Corresponding author; Ioannis Thanasas
Department of Obstetrics and Gynecology, General Hospital of Trikala, Trikala, Greece.

from amniotic fluid, describing the then modern symptoms of sudden and severe shock, shortness of breath, cyanosis and pulmonary edema [5]. Nevertheless, Eastman's commentary from 1948 remains very apt, pointing out that the diagnosis of amniotic fluid embolism should not be a waste basket for all cases of unexplained death during childbirth [6]. Later in 1995, Clarke and his colleagues proposed renaming the disease into anaphylaxis of pregnancy, due to the humoral and immune factors that are blamed for its release [7].

Amniotic fluid embolism is uncommon.The results of a recent systematic review and meta-analysis, the population of which was studied in many different countries showed that the estimated incidence of amniotic fluid embolism ranges from 0.8 to 1.8 cases per 100,000 pregnancies and the percentage of women who died or had permanent neurologicalranged from 30% - 41%[8]. Amniotic fluid embolism in 70% of cases occurs during childbirth and uterine cramps.After vaginal delivery it concerns, 11% of the cases, while after cesarean section and the exit of the fetus it concerns 19% of the total cases.The association between amniotic fluid embolism and the sex of the fetus is significant, with the disease occurring more frequently in mothers who are pregnant with male fetuses [7].

Also, a recent systematic literature review of studies that used a similar methodology highlights the significant differences recorded in the incidence of the syndrome from country to country and from continent to continent. The incidence of amniotic fluid embolism is more than three times higher in North America than in Europe. Also, of the 1.9 cases per 100,000 pregnancies estimated to be in the United Kingdom, in Australia the incidence of the disease is much higher at 6.1 cases per 100,000 pregnancies [9].Similarly, in a recent study from Australia and New Zealand, the incidence of amniotic fluid embolism is estimated to be high in European countries at 5.4 cases per 100,000 pregnancies [10].

1.2. Pathogenesis

The pathogenetic mechanism of amniotic fluid embolism to date has not been elucidated with absolute accuracy.Obtaining reliable information on risk factors is difficult due to the rarity of the syndrome combined with the fact that the clinical diagnosis is based mainly on the exclusion of pathological conditions with similar symptoms, and not on the availability and application of diagnostic criteria for the disease [11]. A necessary condition for the onset of the syndrome is considered to be the disturbance of the anatomical relationship between the placenta, the myometrium, the cervical vessels and the placental aloe [12].

Many conditions and procedures related to pregnancy or prenatal or postnatal pregnancy are associated with a significantly higher risk of developing amniotic fluid embolism syndrome (Table 1). More specifically, the black race is estimated to be twice as likely to develop the syndrome as the white race. Also, the incidence of amniotic fluid embolism increases significantly with the age of the mother, and especially after the age of 39 years. The pathological individual memory of the pregnant woman is associated with the occurrence of amniotic fluid embolism: heart disease increases by about 70 times the risk of developing the syndrome, while cerebral and vascular disorders are associated with an increased risk of amniotic fluid embolism by almost 25 times [13].

Table 1 Risk factors associated with amniotic fluid embolism

Sr.No.	Related factors with mother	Related factors with pregnancy
1.	Race	Multiple pregnancy
2.	Age	Polyhydramnios
3.	Multiparous pregnant	Hypertensive disease of pregnancy
4.	Smoking	Preeclampsia – eclampsia
5.	Diabetes	Placenta previa
6.	Heart disease	Placental abruption
7.	Kidney disease	Uterine rupture
8.	Brain disorders	Cesarean section
9.	Vascular disorders	Stimulation of Labor

Similarly, many studies have found that multiple pregnancies and polyhydramnios, gestational hypertension, preeclampsia and eclampsia, precursor placenta, placental abruption, uterine rupture, and caesarean section after labor significantly increase the risk of amniotic fluid embolism. It is estimated that preeclampsia, placenta previa andpolyhydramnios are 7 to 13 times more likely to develop the syndrome than pregnant women who do not have a pathology in pregnancy [13,14,15]. The challenges of childbirth, especially when they involve long – term use of oxytocin or a combination of oxytocin and prostaglandins, increase the risk of amniotic fluid embolism [16]. Recently, Indraccolo and colleagues, analyzing the results of a systematic review of amniotic fluid embolism cases from 1990 to 2015 showed that only the injection of oxytocin during the course of labor statistically significantly increases the risk of developing the syndrome [17].

1.3. Pathophysiology

In amniotic fluid embolism, amniotic fluid and fetal elements enter the systemic circulation of the pregnant woman, which was initially attributed to the collapse of the physiological barrier between mother and fetus.Based on this view the pathophysiological mechanism of the syndrome was considered to be mechanical and due to the incoming volume of amniotic fluid which results in respiratory failure, bronchospasm and shock [18]. Subsequent studies attributed the underlying mechanism to an anaphylactoid reaction to fetal antigens entering the maternal circulation accompanied by a variety of reactions in the maternal organism.Fetal antigens trigger a variety of immune processes that produce a reaction similar to anaphylaxis [19].

More recently, Tamura and colleagues have shown that amniotic fluid embolism is recognized as a type of syndrome characterized by the sudden onset of hypoxia, hypotension, seizures, or diffuse intravascular coagulation. Diffuse intravascular coagulation is due to the entry of the maternal circulation of thrombogenic components of amniotic fluid that activate the exogenous pathway of the coagulation cataract. The time of thrombus formation is reduced, the adhesion of platelets is induced, probably as a result of activation of the complement resulting in the creation of a hypercoagulable state of the organism, the consumption of coagulation factors and the increase of fibrinolytic activity. This often results in uncontrolled bleeding from the uterus, but also bleeding from other parts and positions of the body [20,21].

1.4. Diagnostic approach

The diagnosis of amniotic fluid embolism remains clinical.No specific diagnostic laboratory tests to date are able to rule out or confirm the definitive diagnosis of the disease [22]. The definitive diagnosis of amniotic fluid embolism is made mainly at necropsy by confirming the presence of fetal material in the pulmonary circulation or in a surviving patient in bronchial lavage with special Nile stains, according to Wright or Papanikolaou [23]. The varied clinical symptoms and the difficult clinical diagnosis make the amniotic fluid embolism a challenge in the obstetric clinical practice, the correct and effective management of which requires the smooth and close cooperation of doctors of various specialties.An experienced medical team of obstetricians - gynecologists, surgeons, anesthesiologists, neonatologists, hematologists, vascular surgeons and intensivists is considered necessary to ensure the best possible outcome for the mother and the newborn [10].

The onset of the disease may occur in otherwise healthy pregnant women without any symptoms or may be due to non-specific precursor symptoms a few hours before its clinical onset, such as agitation, cold, dizziness, anxiety, nausea, vomiting and acupuncture on the fingers. Predominant clinical manifestations of amniotic fluid embolism occur in 30% - 40% of cases. Acute dyspnea and cyanosis affect about 50% - 80% of patients and are the main symptoms. A sharp drop in blood pressure occurs in 56% to 100%, heart failure in 30% - 87% and fetal discomfort with an increased risk of sudden and unexplained deterioration of fetal heart rate is observed in 20% to 36% of all cases with amniotic fluid embolism. Seizures and loss of consciousness - coma affects 15% to 50% of patients [24,25].

A recent retrospective multicenter study lasting ten years (2005-2015) showed that the most common initial symptom of amniotic fluid embolism was a sudden loss of consciousness which was observed in 66.7% of cases, followed by fetal bradycardia (50%) and dyspnea (55%). Typically in 55% of cases a post-mortem caesarean section was performed in the operating room, except for one case, in which the caesarean section was performed at the place of receipt of interest[26]. According to other studies in up to 12% of cases the initial symptom is severe bleeding from a blood clotting disorder which is life threatening to the pregnant woman [27,28]. Later, after the initial phase, acute heart failure occurs with consequent pulmonary edema in 51% to 100% of cases with hypovolemia and myocardial ischemia [29,30].

In general, the diagnosis of amniotic fluid embolism should be considered in any case of sudden cardiovascular collapse or maternal death during childbirth or in the first hours after childbirth with unexplained etiology. Maternal death is

due to sudden cardiac arrest, heavy bleeding due to a coagulation disorder, the development of acute respiratory distress, and multiple organ failure. To date, there are no specific laboratory tests to diagnose the syndrome. Diagnostic criteria for amniotic fluid embolism used in the international literature are the criteria of UKOSS (UK Obstetric Surveillance System) [16] and the Benson criteria[31], as listed in the table below (Table 2).

Table 2 Diagnostic criteria for amniotic fluid embolism

Criteria UKOSS (2010)	**Benson Criteria (2007)**
Acute heart failure without other clear cause with one or more than:	Pregnant up to 48 hours after delivery with one or more of:
Heart attack	Hypotension and/or cardiac arrest
Cardiac arrhythmia	Breathing difficulty
Hypotension	Diffuse intravascular coagulation
Maternal bleeding	Coma and/or seizures
Precursor symptoms	K No other medical explanation
Epileptic seizures	
Shortness of breath of abrupt onset	

Table 3 Pathological conditions that require differential diagnosis from amniotic fluid embolism

1.	Massive pulmonary embolism
2.	Air embolism
3.	Acute myocardial infarction
4.	Pulmonary edema
5.	Septic shock
6.	Anaphylactic shock
7.	Automatic pneumothorax
8.	Uterine rupture
9.	Uterine atony
10.	Placental abruption
11.	Eclampsia
12.	Epilepsy
13.	Hypoxemia
14.	Hypoglycemia
15.	Stroke

The blood test, which may show an increase in white blood cells, thrombocytopenia, prolongation of clotting times, decreased fibrinogen levels, increased di – dimmers and increased cardiac enzymes does not help much in the diagnosis of amniotic fluid embolism. Also, tachycardia, right ventricular strain, and non-specific ST and T lesions imaging on electrocardiography are not pathognomonic findings of the disease. Similarly, a chest x – ray which may show dilatation of the right atrium, dilatation of the right ventricle and pulmonary artery, and pulmonary edema is not indicative of the diagnosis of the disease. Special tests, such as esophageal ultrasound and rotational thrombocytopenia, help not only to confirm the diagnosis, but also to monitor the progression of the amniotic fluid embolism being treated [32,33].

Measurement of the STN (sialyl TN antigen) in peripheral blood or by right catheterization is currently estimated to be of significant help in the diagnosis of amniotic fluid embolism [34,35]. In contrast, pulmonary angiography is not widely used clinically and should be performed in cases of persistent hypotension to rule out the diagnosis of pulmonary embolism [34]. Promising biochemical diagnostic markers, such as zinc coproporphyrin, tryptase, and complement factors C3, C4, have not been established in clinical practice as pathognomonic markers for the diagnosis of amniotic fluid embolism [35,36]. Even the presence of embryonic cells in the pulmonary vessels is not a reliable diagnostic criterion for amniotic fluid embolism, as embryonic cells can be detected in 21% to 100% of pregnant women who do not have the disease [24].

Table 4 Basic principles of treatment of pregnant women with amniotic fluid embolism

1.	**Breathing support**
	endotracheal intubation
	oxygenation
2.	**Traffic support**
	administration of crystalline solutions
	administration of dopamine
	administration of inotropic substances
	administration of sodium bicarbonate
3.	**Treatment of diffuse intravascular coagulation**
	red blood cell transfusion
	plasma transfusion
	platelet transfusion
	administration of anticoagulant therapy
	administration of rivaroxaban?
4.	**Treatment of uterine atony**
	administration of contraceptive drugs
	uterine closure
	obstetric hysterectomy
5.	**Pregnancy management**
	fetal monitoring
	cesarean section
	post-mortem caesarean section

The absence of specific diagnostic indicators and the need for diagnosis based on clinical criteria pose a serious differential diagnostic problem of amniotic fluid embolism from many other pathological conditions of similar symptomatology. The most common condition that must first be differentiated from amniotic fluid embolism is massive pulmonary embolism. The latter is very different from amniotic fluid embolism in terms of typical risk factors, chest pain, rarer hypotension and usually the absence of blood coagulation disorders. Similarly, air embolism, acute myocardial infarction, septic shock, pulmonary edema, uterine rupture, uterine atony, eclampsia, epilepsy and other pathological conditions (Table 3) should be included in the diagnostic amniotic fluid embolism[18,30,34].

1.5. Treatment

Treatment of amniotic fluid embolism, due to its urgency and high mortality rate, should initially be supportive and focus on rapid stabilization of the mother's cardiorespiratory system and adequate oxygenation of vital organs (Table

4).There is no special treatment.The key to treatment is immediate recognition of the syndrome and a high rate of clinical suspicion [37,38]. In the past, the first actions were limited to the use of morphine, atropine and oxygen. Current management focuses on oxygenation, maintenance of cardiac output, control of bleeding and correction of coagulation. Providing airway and mechanical respiratory support with 100% oxygen and positive expiratory pressure (PEEP) to the extent permitted by the hemodynamic status is usually necessary to improve the patient's oxygenation. In case of failure of the manipulations, the extracorporeal membrane oxygenation and the continuous venous hemodialysis can be valuable treatments[3,39].

At the same time, the administration of crystalline solutions should be started immediately to treat hypotension and hemodynamic instability.The non-reduction of hypotension requires the administration of vasoconstrictor treatment.Intravenous administration of dopamine and inotropic substances is indicated based on hemodynamic parameters, in order to maintain systolic blood pressure at levels greater than 90mmHg [40]. Recent promising treatments include selective pulmonary vasodilators and recombinant activated factor VIIa.In patients who do not respond to support measures and there is a deficiency of the right ventricle and pulmonary hypertension, the choice of sodium bicarbonate should be seriously considered, the use of which can lead to an immediate normalization of cardiac parameters [3,41].

Anticoagulant therapy is the most important strategy for inhibiting excessive coagulation cataract activation in patients with amniotic fluid embolism and diffuse intravascular coagulation. Oral therapy with rivaroxaban, a novel anticoagulant and selective direct inhibitor of factor Xa, has not yet been established in the treatment of these patients. Isolated published cases in the literature have shown good therapeutic efficacy of the drug in the treatment of patients with amniotic fluid embolism and diffuse intravascular coagulation. Based on these and the positive results of major trials and strong guidelines, rivaroxaban should be considered as the first preferred anticoagulant therapy for the majority of patients [42,43].

Diffuse intravascular coagulation associated with bleeding is treated depending on the degree of bleeding. Transfusion with red blood cells and platelets, for those cases that have thrombocytopenia is considered necessary. Continued uterine bleeding (uterine atony) that does not respond to uterine contractions may require obstetric hysterectomy. Disruption of the coagulation mechanism in embolism by amniotic fluid, which is established in an extremely short period of time, is not directly proportional to bleeding. In any case of suspected amniotic fluid embolism, immediate determination of the fibrinogen level is required in order to assess the degree of coagulation disorder. Immediate treatment of coagulation is estimated to help reduce maternal mortality from amniotic fluid embolism[44].

Trying to complete the birth in the safest way for the mother and always taking into account the condition of the fetus should be a priority in the treatment of pregnant women with amniotic fluid embolism. Although the primary responsibility of the physician is to ensure the health and life of the mother, intervention to save the fetus is considered appropriate in some cases. Continuous monitoring of the fetus is mandatory in pregnancies longer than 24 weeks. In cases of maternal heart failure, immediate caesarean section is recommended [45]. Given that brain damage begins in 5 minutes of anoxia and therefore the post-mortem cesarean section should be completed within 4 minutes (the 4-minute rule) in order to improve the perinatal outcome and possibly the outcome of maternal health [46], the publication of the results of a twenty-year study (1985-2004) is far from proving that postmortem caesarean section within 4 minutes of maternal cardiac arrest in the third trimester of pregnancy improves maternal and neonatal outcome [47]. According to current guidelines, the post-mortem caesarean section should be included in the pregnant woman after 5 minutes of unsuccessful cardiopulmonary resuscitation and if completed in time it is estimated that it could possibly help save the fetus and its critical non-resuscitation [48].

1.6. Prognosis

The prognosis for amniotic fluid embolism is not good, with most women ending up.Total maternal mortality is currently estimated at 11% to 44%, with the best available data supporting an overall mortality rate of 20.4%[49]. It is estimated that half of patients die within the first hour of the onset of the syndrome and that about two-thirds end up in the first five hours.If the pregnant woman survives, in most cases she has serious neurological problems.If a patient with amniotic fluid embolism develops cardiac arrest, the chances of surviving without neurological deficits are negligible [24]. The survival rate of newborns is estimated to reach 70%.The neurological condition of the infant is directly related to the time interval between the clinical manifestation of the syndrome and the completion of labor [50].

Although mortality rates are estimated to have declined in recent years, morbidity remains high. In addition to permanent neurological damage in most cases, acute renal failure, heart failure with left ventricular failure, cardiogenic pulmonary edema, arrhythmias, myocardial ischemia or acute myocardial infarction have been reported. Respiratory

failure as well as non-cardiogenic pulmonary edema should be among the possible subsequent complications of women surviving amniotic fluid embolism [18,24,50,25]. The risk of recurrence in future pregnancies is unknown.Although it cannot be accurately estimated, successful subsequent pregnancies reported in the literature support the attempt to achieve future pregnancies in women who have survived amniotic fluid embolism.The risk of recurrence in future pregnancies is unknown[51,52,53].

1.7. Prevention

Improving the management of obstetric bleeding is considered important for the prevention of amniotic fluid embolism. Avoiding injuries to the cervix and body of the uterus during medical procedures and avoiding injuries to the placenta during caesarean section could significantly help prevent the syndrome with all the devastating complications it can have for mother and newborn. Similarly, labor and uterine tetanus contractions should be treated with appropriate treatment, while the use of oxytocin should be done with great caution [54]. Also, the care for the early recognition of the precursor symptoms and signs of amniotic fluid embolism by health professionals seems to be crucial.Reports from the patient, such as shortness of breath, chest pain, cold, anxiety, panic, nausea and vomiting, should in any case be taken seriously and evaluated accurately in order to achieveearly diagnosis of the disease and the most effective treatment [55,1].

2. Conclusion

Amniotic fluid embolism is a double tragedy, as it can lead to disastrous results for both the pregnant woman and the fetus and the newborn. An accurate understanding of the etiology and pathophysiology of the syndrome remains incomplete to this day. Similarly, diagnostic criteria are controversial and cannot lead to an early and correct diagnosis of the disease. The continuation of the research effort in the future is expected to shed light on important and crucial aspects of this serious obstetric problem and to significantly improve perinatal and maternal mortality. It is expected that limiting research on amniotic fluid embolism to women who meet the criteria of the classic trinity will enhance the validity of published data and help identify risk factors and potentially useful biomarkers for early diagnosis and effective treatment.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare that they have no conflict of interest regarding the publication of article review.

References

[1] Sundin CS, Mazac LB. Amniotic Fluid Embolism. MCN Am J Matern Child Nurs. 2017, 42(1): 29 – 35.

[2] Sultan P, Seligman K, Carvalho B. Amniotic fluid embolism: update and review. Curr Opin Anaesthesiol. 2016, 29(3): 288 – 296.

[3] West M. Amniotic fluid embolism: a historical perspective in diagnosis and management. BJOG. 2016, 123(1): 110.

[4] Steiner PE, Lushbaugh CC. Landmark article, Oct. 1941: Maternal pulmonary embolism by amniotic fluid as a cause of obstetric shock and unexpected deaths in obstetrics. By Paul E. Steiner and C. C. Lushbaugh. JAMA. 1986, 255(16): 2187 – 2203.

[5] Shotton DM, Taylor CW. Pulmonary embolism by amniotic fluid; a report of a fatal case, together with a review of the literature. J Obstet Gynaecol Br Emp.1949, 56(1): 46 – 53.

[6] Eastman NJ. Editorial comment. Obstet Gynecol Surv. 1948; 3: 35 – 36.

[7] Clark SL, Hankins GD, Dudley DA, Dildy GA, Porter TF. Amniotic fluid embolism: analysis of the national registry. Am J Obstet Gynecol.1995, 172(4 Pt 1): 1158 – 1167; discussion 1167 – 1169.

[8] Fitzpatrick KE, van den Akker T, Bloemenkamp KWM, Deneux – Tharaux C, Kristufkova A, Li Z, Schaap TP, Sullivan EA, Tuffnell D, Knight M. Risk factors, management, and outcomes of amniotic fluid embolism: A multicountry, population – based cohort and nested case – control study. PLoS Med. 2019, 16(11): e1002962.

[9] Knight M, Berg C, Brocklehurst P, Kramer M, Lewis G, Oats J, Roberts CL, Spong C, Sullivan E, van Roosmalen J, Zwart J. Amniotic fluid embolism incidence, risk factors and outcomes: a review and recommendations. BMC Pregnancy Childbirth. 2012, 12: 7.

[10] McDonnell N, Knight M, Peek MJ, Ellwood D, Homer CS, McLintock C, Vaughan G, Pollock W, Li Z, Javid N, Sullivan E; the Australasian Maternity Outcomes Surveillance System (AMOSS). Amniotic fluid embolism: an Australian – New Zealand population – based study. BMC Pregnancy Childbirth. 2015, 15: 352.

[11] Fitzpatrick KE, Tuffnell D, Kurinczuk JJ, Knight M. Incidence, risk factors, management and outcomes of amniotic – fluid embolism: a population – based cohort and nested case – control study. BJOG. 2016, 123(1): 100 – 109.

[12] Tamura N, Nagai H, Maeda H, Kuroda RH, Nakajima M, Igarashi A, Kanayama N, Yoshida K. Amniotic fluid embolism induces uterine anaphylaxis and atony following cervical laceration. Gynecol Obstet Invest.2014, 78(1): 65 – 68.

[13] Fong A, Chau CT, Pan D, Ogunyemi DA. Amniotic fluid embolism: antepartum, intrapartum and demographic factors. J Matern Fetal Neonatal Med.2015, 28(7): 793 – 798.

[14] Cristina Rossi A, Mullin P. The etiology of maternal mortality in developed countries: a systematic review of literature. Arch Gynecol Obstet. 2012, 285(6): 1499 – 1503.

[15] Rath WH, Hoferr S, Sinicina I. Amniotic fluid embolism: an interdisciplinary challenge: epidemiology, diagnosis and treatment. Dtsch Arztebl Int. 2014, 111(8): 126 – 132.

[16] 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(5): 910 – 917.

[17] Indraccolo U, Battistoni C, Mastrantonio I, Di Iorio R, Greco P, Indraccolo SR. Risk factors for fatality in amniotic fluid embolism: a systematic review and analysis of a data pool. J Matern Fetal Neonatal Med. 2018, 31(5): 661 – 665.

[18] Gist RS, Stafford IP, Leibowitz AB, Beilin Y. Amniotic fluid embolism. Anesth Analg.2009, 108(5): 1599 – 1602.

[19] Chen KB, Chang SS, Tseng YL, Chiu TH, Liao CC, Ho M, Huang GS, Li CY. Amniotic fluid induces platelet – neutrophil aggregation and neutrophil activation. Am J Obstet Gynecol.2013, 208(4): 318.e1-7.

[20] Kanayama N, Tamura N. Amniotic fluid embolism: pathophysiology and new strategies for management. J Obstet Gynaecol Res. 2014, 40(6): 1507 – 1517.

[21] Tamura N, Farhana M, Oda T, Itoh H, Kanayama N. Amniotic fluid embolism: Pathophysiology from the perspective of pathology. J Obstet Gynaecol Res.2017, 43(4): 627 – 632.

[22] Society for Maternal – Fetal Medicine (SMFM). Electronic address: pubs@smfm.org, Pacheco LD, Saade G, Hankins GD, Clark SL. Amniotic fluid embolism: diagnosis and management. Am J Obstet Gynecol.2016, 215(2): B16 – 24.

[23] Sisodia SM, Bendale KA, Khan WA. Amniotic fluid embolism: a cause of sudden maternal death and police inquest. Am J Forensic Med Pathol. 2012, 33(4): 330 – 334.

[24] Conde – Agudelo A, Romero R. Amniotic fluid embolism: an evidence – based review. Am J Obstet Gynecol. 2009, 201(5): 445. e1-13.

[25] Dean LS, Rogers RP 3rd, Harley RA, Hood DD. Case scenario: amniotic fluid embolism. Anesthesiology. 2012, 116(1): 186 – 192.

[26] Skolnik S, Ioscovich A, Eidelman LA, Davis A, Shmueli A, Aviram A, Orbach – Zinger S. Anesthetic management of amniotic fluid embolism -- a multi – center, retrospective, cohort study. J Matern Fetal Neonatal Med. 2019, 32(8): 1262 – 1266.

[27] Davies S. Amniotic fluid embolus: a review of the literature. Can J Anaesth. 2001, 48(1): 88 – 98.

[28] Stolk KH, Zwart JJ, Schutte J, VAN Roosmalen J. Severe maternal morbidity and mortality from amniotic fluid embolism in the Netherlands. Acta Obstet Gynecol Scand. 2012, 91(8): 991 – 995.

[29] O'Shea A, Eappen S. Amniotic fluid embolism. Int Anesthesiol Clin. 2007, 45(1): 17 – 28.

[30] Clark SL. Amniotic fluid embolism. Clin Obstet Gynecol. 2010, 53(2): 322 – 328.

[31] Benson MD. A hypothesis regarding complement activation and amniotic fluid embolism. Med Hypotheses. 2007, 68(5): 1019 – 1025.

[32] Loughran JA, Kitchen TL, Sindhakar S, Ashraf M, Awad M, Kealaher EJ. Rotational thromboelastometry (ROTEM®) – guided diagnosis and management of amniotic fluid embolism. Int J Obstet Anesth. 2019, 38: 127 – 130.

[33] Pujolle E, Mercier FJ, Le Gouez A. Rotational thromboelastometry as a tool in the diagnosis and management of amniotic fluid embolism. Int J Obstet Anesth. 2019, 38: 146 – 147.

[34] Brennan MC, Moore LE. Pulmonary embolism and amniotic fluid embolism in pregnancy. Obstet Gynecol Clin North Am.2013, 40(1): 27 – 35.

[35] Busardò FP, Frati P, Zaami S, Fineschi V. Amniotic fluid embolism pathophysiology suggests the new diagnostic armamentarium: β – tryptase and complement fractions C3 – C4 are the indispensable working tools. Int J Mol Sci.2015, 16(3): 6557 – 6570.

[36] Toy H. Amniotic fluid embolism. Eur J Gen Med. 2009,6: 108 – 115.

[37] McBride AM. Clinical Presentation and Treatment of Amniotic Fluid Embolism. AACN Adv Crit Care. 2018, 29(3): 336 – 342.

[38] Nawaz N, Buksh AR. Amniotic Fluid Embolism. J Coll Physicians Surg Pak. 2018, 28(6): S107 – S109.

[39] Wise EM, Harika R, Zahir F. Successful recovery after amniotic fluid embolism in a patient undergoing vacuum – assisted vaginal delivery. J Clin Anesth. 2016, 34: 557 – 561.

[40] McDonnell NJ, Chan BO, Frengley RW. Rapid reversal of critical haemodynamic compromise with nitric oxide in a parturient with amniotic fluid embolism. Int J Obstet Anesth.2007, 16(3): 269 – 273.

[41] Evans S, Brown B, Mathieson M, Tay S. Survival after an amniotic fluid embolism following the use of sodium bicarbonate. BMJ Case Rep. 2014, 2014. pii: bcr2014204672.

[42] EINSTEIN–PE Investigators, Büller HR, Prins MH, Lensin AW, Decousus H, Jacobson BF, Minar E, Chlumsky J, Verhamme P, Wells P, Agnelli G, Cohen A, Berkowitz SD, Bounameaux H, Davidson BL, Misselwitz F, Gallus AS, Raskob GE, Schellong S, Segers A. Oral rivaroxaban for the treatment of symptomatic pulmonary embolism. N Engl J Med.2012, 366(14): 1287 – 1297.

[43] Wu HD, Song ZK, Cao HY, Xu XY, Tang ML, Yang S, Liu Y, Qin L. Successful treatment of amniotic fluid embolism complicated by disseminated intravascular coagulation with rivaroxaban: A case report. Medicine (Baltimore). 2020, 99(4): e18951.

[44] Tanaka H, Katsuragi S, Osato K, Hasegawa J, Nakata M, Murakoshi T, Yoshimatsu J, Sekizawa A, Kanayama N, Ishiwata I, Ikeda T. Value of fibrinogen in cases of maternal death related to amniotic fluid embolism. J Matern Fetal Neonatal Med. 2017, 30(24): 2940 – 2943.

[45] Soskin PN, Yu J. Resuscitation of the Pregnant Patient. Emerg Med Clin North Am. 2019, 37(2): 351 – 363.

[46] Katz VL. Perimortemcesarean delivery: its role in maternal mortality. Semin Perinatol. 2012, 36(1): 68 – 72.

[47] Katz V, Balderston K, DeFreest M. Perimortemcesarean delivery: were our assumptions correct? Am J Obstet Gynecol.2005, 192(6): 1916 – 1920; discussion 1920 – 1921.

[48] Drukker L, Hants Y, Sharon E, Sela HY, Grisaru – Granovsky S. Perimortemcesarean section for maternal and fetal salvage: concise review and protocol. Acta Obstet Gynecol Scand. 2014, 93(10): 965 – 972.

[49] Benson MD. Amniotic fluid embolism mortality rate. J Obstet Gynaecol Res.2017, 43(11): 1714 – 1718.

[50] Kaur K, Bhardwaj M, Kumar P, Singhal S, Singh T, Hooda S. Amniotic fluid embolism. J Anaesthesiol Clin Pharmacol. 2016, 32(2): 153 – 159.

[51] Demianczuk CE, Corbett TF. Successful pregnancy after amniotic fluid embolism: a case report. J Obstet Gynaecol Can. 2005; 27(7): 699 – 701.

[52] Abecassis P, Benhamou D. Is amniotic fluid embolism likely to recur in a subsequent pregnancy? Int J Obstet Anesth. 2006, 15(1): 90.

[53] Caeiro AFC, Ramilo IDTM, Santos AP, Ferreira E, Batalha IS. Amniotic Fluid Embolism. Is a New Pregnancy Possible? Case Report. Rev Bras Ginecol Obstet. 2017, 39(7): 369 – 372.

[54] Bonnet MP, Zlotnik D, Saucedo M, Chassard D, Bouvier – Colle MH, Deneux – Tharaux C; French National Experts Committee on Maternal Mortality. Maternal Death Due to Amniotic Fluid Embolism: A National Study in France. Anesth Analg. 2018, 126(1): 175 – 182.

[55] Shen F, Wang L, Yang W, Chen Y. From appearance to essence: 10 years review of atypical amniotic fluid embolism. Arch Gynecol Obstet. 2016, 293(2): 329 – 334.