Scholars Academic Journal of Biosciences (SAJB) **ISSN 2321-6883**
Sch. Acad. J. Biosci., 2013; 1(3):85-89

(An International Publisher for Academic and Scientific Resources)
www.saspublisher.com

Research Article

Review of 24 cases of Maternal Deaths from Amniotic-Fluid Embolism: in Correlation with Clinical and Histopathological Findings

Ambika Prasad Patra*[1], Kusa Kumar Shaha[2], Anand P. Rayamane[3]
[1]Senior Resident, Dept. of Forensic Medicine & Toxicology, JIPMER (Govt. of India), Puducherry
[2]Assistant Professor, Dept. of Forensic Medicine & Toxicology, JIPMER (Govt of India), Puducherry
[3]Assistant Professor, Dept. of Forensic Medicine, Mysore Medical College & Research Institute, Mysore

Corresponding author
Ambika Prasad Patra
Email: dr.ambika@yahoo.co.in

Abstract: The present study demonstrates the significance of autopsy in cases of maternal deaths in elucidating the cause of death due to Amniotic fluid embolism; and to corroborate the pathological, microscopic and clinical features of such deaths. A retrospective five year cross-sectional study on 24 fatal cases of amniotic fluid embolism, confirmed by autopsy findings, clinical features and post-mortem histopathological reports; and, was conducted at our department of Forensic Medicine and Toxicology during the period 2007-2012. It showed that the majority (88%) of cases died due to amniotic fluid embolism were married, multiparous women; and had 1-3 uneventful past-pregnancies each. Eighteen cases had normal antenatal histories. In all cases, the clinical onset was sudden and unexpected, having occurred during the first stage of labour in 12 cases, and being associated with convulsions in eight. Seventeen cases showed features of coagulopathy, with 14 cases of disseminated intravascular coagulation (DIC). Overall foetal survival rate was poor. Seven cases were associated with induction of labour, while another 6 occurred after augmentation. Emergency caesarean sections were performed in 9 cases. Autopsy demonstrated moderate to severe pulmonary edema in 22 cases, accompanied by pulmonary hemorrhage in 16 cases. Coronary atheroma was seen in 15 cases, with 6 cases showing subendocardial hemorrhage. Significant utero-cervical injuries were found in 9 cases. The median survival time is 6 hours. Microscopic observation demonstrated the presence of squamous epithelial cell emboli within the pulmonary vasculature in all cases; seven cases showed fibrin microthrombi (DIC), alveolar and pulmonary interstitial inflammation, focal myocardial and hepatocellular necrosis, and myocardial interstitial inflammation. It can be concluded that amniotic fluid embolism is a sudden, unexpected, of course relatively rare cause of maternal death. Multiparous mothers in third decade of their life are vulnerable of developing it during labour, but may have post-partum presentation too; and, the mortality rate is relatively rapid, usually within 12 hour..
Keywords: amniotic; fluid; embolism; maternal death

INTRODUCTION

Amniotic fluid embolism usually present as sudden, unexpected maternal death that may occur during labour or, less frequently, in the early post-partum period [1]. The occurrence of amniotic fluid embolism is relatively rare with a varying incidence rate of 1in 8,000 to 1 in 80,000 pregnancies; however, the mortality rate is high i.e. 80% or more [2]. The precise pathogenesis of amniotic fluid embolism has been remained somewhat obscure. The recent evidence points towards a combination of a severe haemodynamic disturbance followed by secondary coagulopathy in about 40% of patients who survive the initial event [3]. Leucotrienes, prostaglandins and other vasoactive substances contained in amniotic fluid are postulated to play a fundamental role in its pathogenesis. Amniotic fluid is also thought to possess thromboplastin-like properties [4.] As with other causes of maternal death, a thorough medico-legal autopsy is warranted. The significance of maternal deaths from amniotic fluid embolism in a medico-legal perspective, resides in three important facts. Firstly, its presentation in the form of sudden, unexpected peripartum death in an otherwise healthy women who often have an uneventful antenatal obstetric history; secondly, clinical diagnosis is inconclusive in a dead case of amniotic fluid embolism and it is dependent on autopsy and post-mortem histopathology findings; and thirdly, the very real possibility that allegations of medical negligence may be made against the medical staff in attendance. In addition, such deaths fall within the general ambit of maternal mortality which warrants a thorough investigation, both as to their causation and the adequacy of obstetric care. The purpose of the present study is to determine the medico-legal aspects of death due to amniotic fluid embolism in Pondicherry area, in the light of the proposed theories of its aetio-pathogenesis.

MATERIALS AND METHOD

It is a retrospective five year cross-sectional study. We have reviewed the available case records of the period from January 2007 to December 2012 at our department to pick up the cases for study. From a total 66 number of unnatural maternal deaths registered as medico-legal case (MLC) by the police and brought for autopsy to our department, 24 cases of death from amniotic fluid embolism (with confirmed opinion) were

extracted for further study. Clinical and pathological correlations were established; this being facilitated by access to copies of the clinical case records, histopathology reports and copies of relevant case files submitted by the investigating police officer at the time autopsy. Those maternal death cases with incomplete or equivocal opinion of death from amniotic fluid embolism, maternal deaths of other causes, and cases with pending chemical and/or histopathological reports, were excluded from the study.

OBSERVATION

Age: the age range of 24 subjects was from 17 to 36 years; and, 25.8 years being the mean age, while 27 years is the median age.

Marital status: out of 24 cases, all were married women except one unmarried mother of 20 year old.

Post-mortem Findings

a. **Lungs:** twenty-two subjects showed pulmonary edema, this being severe in twenty cases. The combined weights of the lungs ranged from 596-1550 gm, the average weight being 979 gm. In 16 cases, there was evidence of pulmonary hemorrhage, of which 9 were in the form of sub-pleural petechiae, the remaining 7 presenting as focal intra-parenchymal hemorrhage. Pulmonary collapse was noted in 5 cases, while severe bronchopneumonia was found in 3 subjects who survived for over 4 days after the initial event.
b. **Heart:** seven cases had no gross cardiac pathology. However, 15 subjects showed evidence of thin atheromatous plaques in coronaries, although the coronary arteries were patent. Six cases showed features of systemic shock (subendocardial hemorrhages), while three cases presented with pericardiaI petecheal hemorrhages.
c. **Liver:** in 16 cases, the liver showed hepatic congestion, fatty changes, or both.
d. **Reproductive tract:** utero-cervical injury was found in 9 subjects, comprising 5 cases of right postero-lateral cervical laceration, three right lateral utero-cervical rupture, and a case of severe bilateral utero-cervical lacerations.
e. Rest all organs showed no significant gross pathology.
f. **Microscopic findings:** in all 24 cases, squamous epithelial cell emboli were detected in the pulmonary vasculature, and five of these showed presence of mucin too. Seven cases showed squamous epithelial cells in the renal vasculature, while in four cases, they were also found in the blood vessels of the myometrial interstitium and at the edge of an utero-cervical laceration. Nine cases showed mixed inflammatory infiltrates within the alveolar spaces, while in another four; there was evidence of similar pulmonary interstitial, perivascular and peri-bronchiolar inflammation. Focal myocardial necrosis was present in five cases, while another two cases showed evidence of interstitial mononuclear inflammatory infiltrates within the myocardium. Hepatocellular necrosis was found in one case. In 7 cases, features consistent with disseminated intravascular coagulation (fibrin microthrombi) were found within the pulmonary vasculature.

Clinical presentation: in 12 subjects (50%), the clinical onset occurred during the first stage of labour, with each of the remaining cases occurred during the second and third stages respectively. Sixteen cases (67%) presented with dyspnoea (2 without cyanosis), and hypotension of sudden onset during labour, these being preceded by chest pain in 3 cases. The remaining 8 (33%) cases presented with generalized convulsions, in the absence of any pre-existing pregnancy-related hypertensive disorder. In all of these cases, the sudden clinical deterioration was quite unexpected.

Coagulopathy & DIC at admission: seventeen (71%) subjects showed clinical evidence of coagulopathy, comprising 14 cases (82%) of disseminated intravascular coagulation (DIC), while the rest 3 cases presented with prolonged clotting time. Out of 14 cases of DIC, 11cases (79%) were corroborated by post-mortem histological examination.

Events during pregnancy: eighteen subjects had uneventful antenatal history with respect to the pregnancies associated with amniotic fluid embolism. Each of the remaining 6 cases, 5 were presented with premature rupture of the gestational membrane, and the other with pre-eclampsia, diminished foetal movements, and pyrexia respectively.

Parity: twenty-one subjects (88%) were multiparous women, who had 1to 3 previous pregnancies each (Para: 1-3). Of these, 12 cases (57%) had 3 previous pregnancies and two subjects (10%) were primiparous.

Past obstetric history: of the 21 multiparous subjects, 14 (67%) had uneventful past-pregnancies, with 5 (21%) having had between1 to 2 terminations previously; and, the remaining subjects had 2 (10%) previous intra-uterine deaths, each on a separate occasion.

Obstetric procedures adopted: labour was induced in 7 (29%) subjects, while another 6 (25%) had augmentation of labour (artificial rupture of membranes, with or without intravenous oxytocin). Five cases (21%) had forceps-assisted delivery and 9 (38%) underwent emergency caesarean sections following

clinical onset of amniotic fluid embolism. In 8 (34%) subjects, post-partum total hysterectomy was performed for uterine atony and non-stop hemorrhage.

Gestational outcome: the gestational period ranged from 36 to 40 weeks of amenorrhoea, the average gestation being 37.5 weeks. All cases involved singleton pregnancies except 2 (8%), which were twin pregnancies. There were 14 male and 10 female foetuses, of which 22 were full-term and apparently normal, while 2 were delivered at 36 and 38 weeks. Eighteen were delivered, either vaginally or by means of caesarean section, of which 12 were live-births, comprising 4 males and 8 females; while 7 were still births, comprising 4 males and 3 female.

Sources of obtaining obstetric care: fourteen cases delivered at government hospital, five cases were done at private nursing homes, four cases attended by traditional birth attendants (TBA), and a single case, an unmarried mother took help of a village quack for delivery.

Survival period: the minimum and the maximum survival time period recorded were 2 hour and 14 hours respectively; and the median duration being 5 hours.

DISCUSSION

With the progress of age and parity, it appears that the chance of amniotic fluid embolism is also increased; an observation which is consistent with the results of present study [5]. It may be due to the fact that, both these conditions predispose to the spontaneous rupture of the gestational membranes, which tend to be weaker in elderly and multiparous women [6].

Fatal amniotic fluid embolism can only be conclusively established at autopsy; which depends on the microscopic demonstration of intra-vascular foetal debris, especially, within the pulmonary vasculature. Epithelial squames may be demonstrated by the routine hematoxylin and eosin (H&E) staining and confirmed with phloxine-tartrazine which confers a bright red colour upon keratin squames. Other stains such as Alcian-Blue for mucin and Sudan Black or Oil Red-O for vernix caseosa may also be employed [7,8]. Immunoperoxidase staining method is also an alternate confirmatory method, which detects foetal isoantigens and human keratin of maternal tissues. Manier's Scarlet Blue or Phosphotungistic acid-haematoxylin (PTAH) are some staining methods which demonstrates the presence of intra-vasculature fibrin micro-thrombi to establish the diagnosis of disseminated intravascular coagulation [9,10]. The intravascular epithelial squames are usually sparingly found, and per se, the particulate nature of amniotic fluid ensues only in the last months of pregnancy; thus, extensive tissue sampling, particularly of the lungs, is required for its successful demonstration [11]. However, there is possible cropping up of false positive results, as there is postulation of occurrence of small-scale, asymptomatic embolisation of foetal squamous cells in maternal blood; and this being akin to the established observation of trophoblastic cells in maternal venous circulation without producing any adverse effects thereof [12-15]. Therefore, it is recommended that, the presence of foetal elements in the pulmonary vasculature must be corroborated with the clinical features, as illustrated by the present study. The final diagnosis of amniotic fluid embolism should be differentiated with the other possibilities e.g. septic shock, aspiration pneumonitis, acute myocardial infarction, pulmonary thromboembolism and abruptio-placenta [3].

It is postulated that, the acute effects of amniotic fluid embolism is obstructive in nature [4]. Thence, the occlusion of the pulmonary vasculature by foetal debris was thought to cause pulmonary hypertension and consequent acute right ventricular failure [16,17,4]. Epithelial squames from the foetal skin, lanugo hair, vernix caseosa, mucin from the foetal respiratory and gastrointestinal tracts and, bile from meconium contamination of the amniotic fluid, enter the maternal circulation and may be found in the patient's pulmonary microcirculation on post-mortem examination, a feature that was found in all 24 cases studied [3, 18-20]. However, there is no satisfactory correlation between the amount of amniotic fluid debris found within the vessels and the rapidity of the fatal course, as is established by repeated post-mortem examinations and studies [21,22,3]. Furthermore, the conventional hemodynamic alterations theory of entry of amniotic fluid debris into the pulmonary vasculature to produce fatal effects, are the results produced experimentally in animals models and subsequently extrapolated to human beings; when in fact, left ventricular failure is the only hemodynamic abnormality consistently observed in humans [21,22,3].

Some authors postulated a hypothesis of biphasic pathophysiological response, beginning with an initial phase of acute pulmonary vasospasm kindled by the amniotic fluid contents, resulting in pulmonary hypertension and hypoxia thereof; and, probably this transient initial phase may be responsible for about 50% deaths during the first hour, which is in accordance with the rapidity with which death occurred in 24 cases reviewed by us [23,3] .The subsequent development of acute left ventricular failure may be attributed either to profound hypoxia or to a direct myocardial-depressant effects of the amniotic fluid contents [24]. Nevertheless, experimental evidence indicates that the coronary perfusion may be compromised in amniotic fluid embolism [25,26]. The pulmonary edema is observed in up to 92% of cases. However, part of it is non-cardiogenic in origin and is thought to be related to increased permeability of the damaged alveolar-capillary membrane [27,28]. A theory of anaphylactic response to the contents of amniotic fluid is also

postulated, which involves release of mediators of immediate hypersensitivity reactions like leuctorienes, prostaglandins, histamine, serotonin, and proteolytic enzymes etc.[12,18]. Moreover, during labour, it is seen that the concentrations of leuctorienes and prostaglandins are raised in the amniotic fluid [28]. The contents of the amniotic fluid has been shown to shorten the whole blood clotting time, display thromboplastic-properties, induce platelet aggregation, promote the release of platelet factor III and activate Factor X, as well as the complement cascade, and thus, contribute substantially to the development of disseminated intravascular coagulation; which was observed among 29% of the cases reviewed here [29,30,4].

The tear in the placental membranes and rupture of the uterine, placental or cervical veins of the female genital tract engenders the entry of amniotic fluid into the maternal circulation. This could be related to a vaginal or cervical laceration, a uterine rupture, a caesarean section wound, following placental abruption, or even following the normal placenta separation. It is the most plausible postulation of abnormal amniotic fluid infusion into the maternal circulation; as the introduction of normal amniotic fluid into the maternal circulation is usually harmless [31].

Acute onset of dyspnoea, shock, cyanosis with rapid circulatory collapse and severe acute pulmonary oedema during labour, occurring usually, though not exclusively, in an elderly, multiparous woman is pathognomonic of amniotic fluid embolism. These symptoms tend to occur during vigorous labour with hypertonic uterine contractions, although this is not a pre-requisite [2, 3]. Further, grand mal convulsions may complicate the clinical picture. The present study clearly demonstrates these features, together with poor foetal survival.

Apart from labour and delivery, the condition may also occur without warning in the immediate post-partum stage [4, 3]. Other situations in which it may arise include first and second trimester abortion, including hysterotomy and prostaglandin and saline-induced abortions; uncomplicated second trimester pregnancy; blunt abdominal trauma; amniocentesis and even castor oil induced of labour.[32,33,34,35,36,37,39,40] Occasionally, it may also occur during a caesarean operation. The role of oxytocic agents in the pathogenesis of amniotic fluid embolism is somewhat controversial [41].

CONCLUSION

Maternal deaths from amniotic fluid embolism is an issue of tremendous medico-legal concern to the medical and nursing staffs, due to it sudden, unexpected occurrence without warning; which causes considerable distress to the victims' relatives, and may kindle charges of negligence thereof. Here, the forensic pathologist plays a crucial role, to establish the exact cause and manner of death. The success of such medico-legal investigation depends to a large extent on the accuracy and completeness of the autopsy, histopathological and other laboratory reports. It constitutes an important matter for a thorough elucidation of the cause of death. In such situations, the forensic pathologist must remain impartial and objective in assessing his findings; and, due confidentiality must be observed. And, the autopsy findings have a direct bearing on any subsequent civil action which may be undertaken against the treating staff by the aggrieved relatives in cases where there are sufficient grounds to warrant a charge of medical negligence.

REFERENCES

1. Meyer JR; Embolia pulmonar amnio-caseosa. Brasil Medico.,.1926; 2: 301-303.
2. Morgan M; Amniotic fluid embolism. Anaesthesia, 1979; 34: 20-32.
3. Clark SL; New concepts of amniotic fluid embolism: A review. Obstet. Gynecol. Surv., 1990; 45: 360-368.
4. Chatelain SM and Quirk JG; Amniotic and thromboembolism. Clin Obstet Gynecol., 1990; 33: 473-481.
5. Peterson EP and Taylor HB; Amniotic fluid embolism. Obstet. Gynecol., 1970; 35: 787-793.
6. Gillibrand PN; Premature rupture of the membranes and prematurity. J Obstet Gynaecol Br Cwlth., 1967; 74: 678-682.
7. Attwood HD; The histological diagnosis of amniotic fluid embolism. J. Path. Bact. 1958; 76: 211-215.
8. Attwood HD and Delprado WJ. Amniotic fluid embolism: fatal case confirmed at autopsy five weeks after delivery. Pathology, 1988; 20: 381-382.
9. Garland IWC and Thompson WD. Diagnosis of amniotic fluid embolism using an antiserum of human keratin. J Clin Pathol., 1983; 36: 625-627.
10. Ishiyama I, Mukaida M. Komuro E and Keil W; Analysis of a case of generalised amniotic fluid embolism by demonstrating the fetal isoantigen (A blood type) in maternal tissues of B blood type, using immunoperoxidase staining. Am J Clin Pathol., 1986; 85: 239-241.
11. Westbrook OC and Thomas JR; Amniotic fluid embolism complicating late abortion. Am J Obstet Gynecol., 1956; 71: 447-8.
12. Plauche WC. Amniotic fluid embolism (letter). Am J Obstet Gynecol., 1983; 147: 982.
13. Clark SL, Pavlova Z, Greenspoon J, Horenstein J and Phelan JP. Squamous cells in the maternal pulmonary circulation. Am J Obstet Gynecol 1986; 154: 104-106.

14. Lee W, Ginsburg KA, Cotton DB and Kaufman RH. Squamous and trophoblastic cells in the maternal pulmonary circulations identified by invasive hemodynamic monitoring during the peri-partum period. Am J Obstet Gynecol., 1986; 155: 999-1001.
15. Thompson WB and Budd JWL; Erroneous diagnosis of amniotic fluid embolism. Am J Obstet Gynecol., l965; 91:606-616.
16. Attwood HD and Downing SE; Experimental amniotic fluid embolism. Surg Gynecol Obstet., 1965; 120: 255-262.
17. Reis RL, Pierce WS and Behrendt DM; Hemodynamic effects of amniotic fluid embolism, Surg Obstet Gynecol., 1969; 129: 45-48.
18. Steiner PE and Lushbaugh CC; Maternal plumonary embolism by amniotic fluid, as a cause of obstetric shock and unexpected deaths in obstetrics. JAMA, 1941; 117: 1245-54, 1341-5.
19. Dolynuik M, Orfei E, Vania H, Karlman R and Tomich P; Rapid diagnosis of amniotic fluid embolism. Obstet Gynecol., 1983; 61: 28S-30S.
20. Duff P, Engelsjerd B, Zingery LW, Huff RW and Montiel MM; Haemodynamic observations in a patient with intrapartum amniotic fluid embolism. Am J Obstet Gynecol., 1983; 146: 112-115.
21. Clark SL, Montz FJ, Phelan JP. Haemodynamic alterations associated with amniotic fluid embolism: A reappraisal. Am J Obstet Gynecol., 1985; 151: 617-621.
22. MacMillan D; Experimental amniotic fluid infusion. J Obstet Gynaecol Br Cwlth., 1968; 75: 849-852.
23. Clark SL, Cotton DB, Gonik B, Greenspoon J and Phelan JP; Central haemodynarnic alterations in amniotic fluid embolism. Am J Obstet Gynecol., 1988; 158: 1124-1126.
24. Courtney LD. Amniotic fluid embolism. Obstet Gynecol Surv., 1974; 29: 169-177.
25. Spencer MR and Mason KG. Experimental amniotic fluid embolism in rabbits. Am J Obstet Gynecol., 1974;119:1073-8.
26. Richards DS, Carter LS, Corke B, Spielman F and Cefalo RC. The effect of human amniotic Fluid on the isolated perfused rat heart. Am J Obstet Gynecol., 1988; 158: 210-214.
27. Girard P, Hal HM, Laine JF and Petitpretz P; Left heart failure in amniotic fluid embolism. Anesthesiology 1986; 64:262-5.
28. Karim SMM, Devlin J. Prostaglandin content of amniotic fluid during pregnancy and labour. J Obstet Gynaecol Br Cwlth., 1967; 74: 230-246.
29. Ratnoff OD and Vosburgh GJ; Observations of the clotting defect in amniotic fluid embolism. N Engl J Med., 1952;247: 970-3.
30. Courtney LD, Allington LM; Effect of amniotic fluid on blood coagulation. Br J Haematol., 1972; 22: 353-355.
31. Paterson WG, Grant KA, Grant JM and McLean N; The pathogenesis of amniotic fluid embolism, with particular reference to transabdominal amniocentesis. Europ J Obstet Gynaecol: Reprod Biol., 1977; 7:319-24.
32. Guidotti RJ, Grimes DA and Cates W; Fatal amniotic fluid embolism during legally induced abortion in the United States, 1972-1978. Am J Obstet Gynecol., 1981; 141: 257-261.
33. Cromey MG, Taylor PJ and Cummings DC; Probable amniotic fluid embolism after first trimester pregnancy termination. J Reprod Med., 1983; 28: 209-211.
34. Turnbull AC and Anderson ABM; Changes in uterine contractibility following intra-amniotic injection of hypertonic saline to induce therapeutic abortion. J Obstet Gynaecol Br Cwlth., 1965; 72: 755-762.
35. Schiffer MA, Pakter J and Clahr J; Mortality associated with hypertonic saline abortion. Obsret Gynecol., 1973; 42: 759-764.
36. Mirchandani HG, Mirchandani IH and Parikh SR; Hypernatremia due to amniotic fluid embolism during a saline-induced abortion. Am J Foren Med Pathol., 1988; 9: 48-50.
37. Ballas S, Michowitz M and Lessing JB; Amniotic fluid embolism and disseminated intravascular coagulation complicating hypertonic saline-induced abortion. Postgrad Med J., 1983; 59: 127-129.
38. Meier PR and Bowes WA; Amniotic fluid embolus-like syndrome presenting in the second trimester of pregnancy. Obstet Gynccol., 1983; 61:3IS-34S.
39. Olcott CO, Robinson AJ and Maxwell TM; Amniotic fluid embolism and disseminated intravascular coagulation after blunt maternal trauma. J Trauma, 1973; 13: 37-40.
40. Steingrub JS, Lopez T, Teres D and Steingart R; Amniotic fluid embolism associated with castor oil ingestion. Crit Care Med., 1988; 16: 642-643.
41. Shah K, Karlman R and Heller J; Ventricular tachycardia and hypotension with amniotic fluid embolism during caesarean section. Anesth Analg., 1986; 65: 533-55.