

Kramer MS, Rouleau J, Baskett TF, Joseph KS, for the Maternal Health Study Group of the Canadian Perinatal Surveillance System. Amniotic fluid embolism and medical induction of labour: a retrospective, population-based cohort study. *Lancet*. 2006;368:1444-1448.

Q Does inducing labor raise the risk of amniotic fluid embolism?

A Yes. In this retrospective, population-based study involving more than 3 million hospital deliveries in Canada over 12 years, medical induction of labor was strongly associated with fatal amniotic fluid embolism (AFE) and a near doubling of the risk of overall AFE. Maternal age (≥ 35), grand multiparity, cesarean and instrumental vaginal delivery, polyhydramnios, cervical laceration or uterine rupture, placenta previa or abruption, eclampsia, and fetal distress were also associated with an increased risk of AFE.

EXPERT COMMENTARY

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Although earlier studies suggested an association between AFE and medical induction of labor, as well as an association between AFE and the risk factors listed above, no controlled trials had confirmed or refuted this assumption until now. A population-based study by Gilbert in 1999¹ looked at pregnancy complications and mortality associated with AFE, rather than risk factors per se.

Incidence of AFE is hard to define

Worldwide, the incidence of AFE is estimated to range from 1 in 8,000 to 1 in 83,000 live births.^{2,3} In the United States, the estimate is 1 in 20,000 to 1 in 30,000 live births.^{4,5} In the study by Kramer and colleagues, the incidence of AFE was approximately 1 case per 17,000 singleton pregnancies, or 6 cases per 100,000—slightly higher than the 4.8 cases per 100,000 reported by Gilbert.¹

The fatality rate varies, too

Overall, the reported mortality rate of AFE ranges from 26% to 90%.^{2,6} AFE is the fifth most common cause of maternal death in the world.^{7,8} In Canada, maternal deaths from AFE rank third behind cerebrovascular and hypertensive disorders.

Kramer and colleagues found a comparatively low mortality rate of only 13%. They reasoned that higher mortality rates in earlier uncontrolled case series may have been caused by a bias arising from selective reporting of more severe cases of AFE, such as fatal cases. They also postulated that the relatively constant annual rate of fatal AFE in their population argues against significant misdiagnosis.

AFE is linked to risk factors

The association between AFE and specific risk factors such as labor induction, cesarean section, and operative vaginal delivery was strengthened considerably when Kramer and colleagues restricted their analysis to fatal cases. The authors acknowledged that the link between AFE and cesarean section, instrumental delivery, and the presence of fetal distress may reflect the difficult labors that led to operative delivery—that is, reverse causality. If that is the case, it would substantiate the current belief that AFE is propagated by the tearing and shearing of fetal membranes and uterine vessels, which occurs more frequently in difficult and augmented labors with strong contractions. This theory is consistent with the authors' finding that dystocia (probably associated with weaker contractions and early rupture of membranes) resulted in a significant reduction in the risk of AFE.

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FAST TRACK

Medical induction of labor is strongly associated with fatal amniotic fluid embolism

Nonfatal cases were hard to identify

The identification and analysis of nonfatal AFE cases were more problematic. Kramer and colleagues pointed out that the lower mortality rate found in their study may be secondary to some degree of overdiagnosis of nonfatal AFE, which can be difficult to identify. The lack of an absolute gold standard and the lack of specificity of the signs and symptoms of AFE may contribute to both overreporting and underreporting of this syndrome.

Compounding the dilemma is the fact that many signs and symptoms associated with AFE are also clinical syndromes that can occur in its absence, such as anaphylactic shock, left ventricular failure, sepsis, adult respiratory distress syndrome, and diffuse intravascular coagulation. Most commonly, AFE is a diagnosis of exclusion, made during pregnancy or the immediate postpartum period. However, even this temporal association lends little support to the diagnosis of AFE, because any and all of these other clinical syndromes can and do occur in isolation during and after pregnancy.

References

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The constellation of many of the clinical sequelae, rather than isolated signs and symptoms, is what many recognize as the sine qua non of AFE. However, this hypothesis is also slightly problematic because not all cases of AFE—especially nonfatal cases—present with multiorgan disease involving cardiac, respiratory, renal, neurologic, and hematologic failure.

Choose elective induction wisely

Despite the relative rarity of AFE, the phenomenon is worthy of attention because the incidence of elective labor induction has been increasing steadily. The absolute increase in the risk of AFE among women who undergo medical induction is very small: 4 or 5 cases of AFE and 1 or 2 cases of fatal AFE for every 100,000 labors induced. However, with nearly 4 million births annually and induction rates of 20% in the United States, the incidence of AFE could escalate to 30 to 40 cases a year and 10 to 15 deaths. This statistic is alarming, especially given the increasing use of elective medical induction. Extra caution in choosing elective induction is therefore justified.

FAST TRACK

Extra caution is justified in choosing elective induction because of its link to AFE

Q Should all obese women be screened for PCOS?

A Probably. In this evaluation of 113 consecutive premenopausal women referred to a university hospital in Madrid for treatment of overweight or obesity, 32 (28.3%) were diagnosed as having PCOS according to the Na-

tional Institutes of Health criteria of unexplained hyperandrogenic chronic anovulation. This is a marked increase over the 5.5% incidence of PCOS found in lean women in Spain in an earlier study by the same researchers.¹

Álvarez-Blasco F, Botella-Carretero JI, San Millán JL, Escobar-Morreale HF. Prevalence and characteristics of the polycystic ovary syndrome in overweight and obese women. *Arch Intern Med.* 2006;166:2081-2086.

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EXPERT COMMENTARY

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Polycystic ovary syndrome (PCOS) is often accompanied by obesity, and the obesity epidemic appears to have been accompanied by a PCOS epidemic. Rather than focus on obesity's effects on PCOS, Álvarez-Blasco and colleagues looked for stigmata of PCOS in an unselected obese population.

Findings in line with earlier studies

This study adds credence to other investigations that have found women with a metabolic abnormality more likely than an unselected sample of the same population to have PCOS. Another study found a similar prevalence of PCOS—26.7%—among premenopausal women with type 2 diabetes.²

Obesity per se is associated with metabolic abnormalities, and the investigators showed an increasing prevalence of the metabolic syndrome and its components with increasing obesity among the study cohort. The components of metabolic syndrome are:

- waist circumference >88 cm
- triglyceride level >150 mg/dL
- HDL cholesterol ≤50 mg/dL
- blood pressure ≥130/85 mm Hg
- fasting glucose ≥100 mg/dL

Interestingly, the incidence of PCOS did not increase as the degree of obesity increased. Among women with a body mass index (BMI) of 25 to 29, the incidence of PCOS was 40%, but it was 23% among those with a BMI of 30 to 34, and 27% among women with a BMI of 35 to 39. These findings suggest that factors other than obesity are associated with PCOS stigmata, or perhaps that increasing metabolic morbidity may mask or suppress PCOS symptoms.

Strengths and weaknesses

The prospective design, size of the cohort, and full phenotyping performed on

all subjects are strengths of this study.

The major weakness is the referral bias of a university-based endocrine clinic that is likely to attract women who are obese and also have endocrine abnormalities such as PCOS. (Endocrinology and nutrition are a single medical specialty in Spain.)

The best prevalence study of PCOS in the US general population involved asymptomatic women applying for employment at a university medical center.³ A similar study design and findings would strengthen the investigators' recommendations to routinely screen for PCOS in an obese population.

This study did not use the revised Rotterdam criteria, which incorporate ultrasonographic size and morphology of the ovaries into the diagnosis. Preliminary studies show that these revised criteria tend to increase the prevalence of PCOS by about 50% among women with oligomenorrhea,⁴ so Álvarez-Blasco and colleagues likely underdetected PCOS by these criteria.

Bottom line: Screen obese patients for PCOS and metabolic syndrome

This study adds evidence of obesity's adverse effects on reproduction, and suggests that routine screening of obese women for both PCOS and the metabolic syndrome is a high-yield procedure (25–30% for both). ■

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FAST TRACK

In obese women, the prevalence of PCOS exceeds 28%