



Maternal mortality and severe maternal morbidity from acute fatty liver of pregnancy in the Netherlands

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ABSTRACT

Objective: To assess maternal death and severe maternal morbidity from acute fatty liver of pregnancy (AFLP) in the Netherlands.

Study design: A retrospective study of all cases of maternal mortality in the Netherlands between 1983 and 2006 and all cases of severe maternal morbidity in the Netherlands between 2004 and 2006, in which all 98 maternity units in the Netherlands participated. Maternal mortality ratio (MMR) and incidence of severe maternal morbidity were the main outcome measures.

Results: The MMR from direct maternal mortality from AFLP was 0.13 per 100,000 live births (95% CI 0.05–0.29). The incidence of severe maternal morbidity from AFLP was 3.2 per 100,000 deliveries (95% CI 1.8–5.7).

Conclusions: AFLP is a rare condition which still causes severe maternal morbidity and in some cases mortality. Referral to a tertiary care hospital for treatment of this uncommon disease should be considered.

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1. Introduction

Acute fatty liver of pregnancy (AFLP) is a rare, but potentially fatal condition in the third trimester of pregnancy. AFLP is characterised by fatty microvascular infiltration of hepatocytes with progressive loss of liver function [1]. The incidence is estimated between 6 and 14 per 100,000 pregnancies [2–4]. It is more common in the third trimester of the first ongoing pregnancy and in women with multiple gestation [5–8]. The onset of AFLP is usually between 28 and 40 weeks' gestation with an average of 35 weeks [6,7,9]. Most women present with a one to two week history of anorexia, nausea, vomiting, midepigastria or right upper quadrant pain, headache and jaundice. This can rapidly progress to hepatic failure and encephalopathy [10,11]. AFLP can mimic severe pre-eclampsia (PE) with or without hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome [12,13].

The mortality of AFLP used to be very high, up to 85% [14], but with early recognition and prompt termination of pregnancy the prognosis has improved and the mortality is now estimated to be between 0 and 12.5% [5,6,8]. Nevertheless, a large population-

based cohort study in the United Kingdom demonstrated that severe maternal morbidity from this disease remains high; 37/57 (65%) of women with AFLP were admitted to an intensive care or specialist liver unit, with a case fatality rate of 1.8% [8]. The aim of this retrospective study was to assess maternal death and severe maternal morbidity from AFLP in the Netherlands.

2. Materials and methods

All reported cases of maternal death from AFLP in the period 1983–2006 and cases of severe maternal morbidity from AFLP in the period August 2004 to August 2006 in the Netherlands were included. In the absence of generally accepted criteria for the diagnosis of AFLP, either a clinical diagnosis, supported by compatible laboratory results, was made by the obstetrician, or the diagnosis was made post mortem. A clinical diagnosis of AFLP was considered in women presenting with a sudden onset of nausea, vomiting, midepigastria or right upper quadrant pain, headache and/or jaundice in the third trimester of pregnancy or postpartum.

2.1. Maternal mortality

Nearly all cases of maternal death in the Netherlands are voluntarily reported to the Maternal Mortality Committee (MMC)

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Table 1
Cases of maternal mortality of AFLP.

Patient no.	Parity	Gestational age (weeks)	Mode of delivery	Time of diagnosis	Maternal complication	Fetal outcome
1	1	40.3	None	Post mortem	Cardiac arrest, death	IUFD
2	1	35.7	Vaginal	Antepartum	Parauretral hematoma, vulvar hematoma, encephalopathy, DIC, sepsis, ARDS, renal failure, MOF, death	IUFD
3	1	34.7	CS	Postpartum	Respiratory insufficiency, DIC, abdominal wall hematoma, sepsis, renal failure, liver failure, MOF, death	Two live births
4	1	41.4	CS	Postpartum	Obstetric haemorrhage, DIC, renal failure, liver failure, encephalopathy, death	Live born
5	1	41.6	CS	Post mortem	DIC, death	Death
6	1	35.6	CS	Postpartum	DIC, renal failure, liver failure, cardiac arrest, death	Live born

ARDS, acute respiratory distress syndrome; CS, caesarean section; DIC, disseminated intravascular coagulation; IUFD, intrauterine fetal death; MOF, multi organ failure.

by obstetricians, and in some cases by midwives and general practitioners. Additional cases are collected after a cross-check with Statistics Netherlands (Central Bureau of Statistics, CBS). Maternal death was defined according to the World Health Organization's (WHO) International Classification of Diseases, tenth revision (ICD-10). Maternal mortality ratio (MMR) due to AFLP was defined as the number of deaths from AFLP per 100,000 live births, within 42 days after termination of pregnancy. Late maternal death is defined as death more than 42 days but less than one year after termination of pregnancy [15].

Data for each maternal death were collected on a standard questionnaire that included socio-economic data, data concerning general and obstetric history, and data on the index pregnancy. Any available material such as pregnancy check-lists, laboratory and bacteriological results, pathology and autopsy results and professional correspondence were also analysed. The exact classification and assessment of all cases is previously described in the national enquiries for the periods 1983–1992 and 1993–2005 [16,17].

Substandard care was defined as all care factors which may have resulted in low standards of care and which had a probably negative influence on the chain of events leading directly to death. It could be assigned to any person involved in the care of pregnant women and to the pregnant woman herself. Avoidance of such factors did not necessarily mean that death would have been prevented [17].

2.2. Severe maternal morbidity

Cases of severe maternal morbidity were collected from the Nationwide Enquiry into ethnic determinants of severe maternal morbidity (LEMMoN study), a prospective population-based cohort study in which all 98 maternity units in the Netherlands participated [18]. In the LEMMoN study, cases of severe maternal morbidity were classified in one or more of the following five categories: (1) intensive care admission, (2) uterine rupture, (3) eclampsia/HELLP syndrome with liver hematoma or rupture, (4) major obstetric haemorrhage requiring transfusion of 4 units of red blood cells or more and (5) other cases of severe maternal morbidity in the opinion of the treating obstetrician. Cases of AFLP were included based on either admission to an intensive care unit for that reason (category 1) or on clinical diagnosis in category 5.

3. Results

3.1. Maternal mortality

In the period 1983–2006, 538 cases of maternal death were reported to the MMC, of which 385 were direct maternal deaths (late deaths included). In the period 1983–1992, there was no

direct maternal death from AFLP. In the period 1993–2006, direct maternal death from AFLP occurred in six women. One case took place in 1995, and the other five in 2000–2001. In the period 1983–2006 there were 4,608,253 live births. This corresponds to a MMR from AFLP of 0.13 per 100,000 live births (95% CI 0.05–0.29).

Characteristics of the six women who died directly from AFLP are shown in Table 1. The mean age was 29.7 years (range 25–36 years). All women were in the third trimester of the first ongoing pregnancy and one of them carried a twin pregnancy (17%). The mean gestational age at delivery was 38.2 weeks (range 34.7–41.6 weeks).

One woman was diagnosed with AFLP antepartum, three women were diagnosed postpartum and in two women the diagnosis was not made until post mortem examination. The woman diagnosed in the antepartum period delivered within 24 h of diagnosis. Two of the women diagnosed postpartum were diagnosed within 24 h after delivery. Three women were admitted to an intensive care unit (50%). The length of hospital stay ranged from 1 to 27 days (median 6.5, interquartile range 1–22).

Four women were delivered by caesarean section (66.7%), two because of fetal distress, one for prolonged first stage and one for prolonged second stage. One woman gave birth vaginally to a stillborn infant. Another woman died before she could give birth to her dead fetus. One of the infants delivered by caesarean section died immediately postpartum despite resuscitation by a paediatrician.

None of the cases of maternal mortality had a liver biopsy. Post mortem examination was performed in four of the six women. Microscopic examination of the liver showed histological signs of AFLP in all these cases.

3.2. Severe maternal morbidity

In the period August 2004 to August 2006 there were 371,021 deliveries in the Netherlands. A total of 2552 cases of severe maternal morbidity were included in the Nationwide Enquiry into ethnic determinants of severe maternal morbidity. Of these, 12 cases (0.47%) were caused by AFLP. The incidence of AFLP in this period is 3.2 cases per 100,000 deliveries (95% CI 1.8–5.7). In this period no women died due to AFLP.

Characteristics of the 12 women are shown in Table 2. The mean age was 31.8 years (range 23–40 years). Six women were primiparous (50%) and there were three twin pregnancies (25%). The mean gestational age was 34.5 weeks (range 27.1–39.6).

In five women the diagnosis was made antepartum and in seven postpartum. Of the women who were diagnosed in the antepartum period, three delivered within 24 h after diagnosis (60%), one woman delivered after four days and one after seven days. All women diagnosed in the postpartum period were diagnosed within 24 h from delivery (100%). Six women were admitted to an

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