

Pregnancy-associated Death – Clarifying the Cause of Death and Medico-legal Assessments in Accusations of Malpractice

Schwangerschaftsassozierte Todesfälle – rechtsmedizinische Todesursachenklärung und Begutachtung bei Behandlungsfehler-vorwürfen



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Key words

miscarriage, ectopic pregnancy, HELLP syndrome, pregnancy

Schlüsselwörter

Abort, Eileiterschwangerschaft, HELLP-Syndrom, Schwangerschaft

received 19.7.2017

revised 26.8.2017

accepted 26.9.2017

Bibliography

DOI <https://doi.org/10.1055/s-0043-120446>

Geburtsh Frauenheilk 2018; 78: 153–159 © Georg Thieme Verlag KG Stuttgart · New York | ISSN 0016-5751

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Deutsche Version unter:
<https://doi.org/10.1055/s-0043-120446>

ABSTRACT

Background Pregnancy-associated deaths are extremely rare in Germany. Most deaths are from natural causes, and a range of causes are possible.

Method The deaths of 22 women who died of pregnancy-associated causes and who were autopsied in the Institute of Forensic Medicine of Justus-Liebig University Gießen between 1992 and 2016 were analyzed.

Results The autopsy results and histological examinations for the majority of women who died of pregnancy-associated causes between 1992 and 2016 showed that they had died of natural causes, although complications of pregnancy were a leading cause of death.

Conclusion The death of a pregnant woman should not automatically raise the suspicion of malpractice, although the question does arise in cases of bleeding complications only detected at very late stages. Experts must prove that a real mistake was made during treatment and provide evidence of the causality between malpractice and patient death. Particularly when well-known complications of pregnancy were present, this is only the case if poor monitoring resulted in the complication being detected too late or if treatment was not in accordance with accepted standards of care. The majority of pregnancy-associated deaths are from natural causes and the death of a pregnant woman does not mean that medical malpractice was involved, although this accusation is often levelled in cases where rupture was not immediately diagnosed or in cases of fatal postpartum hemorrhage.

ZUSAMMENFASSUNG

Hintergrund Schwangerschaftsassozierte Todesfälle sind in Deutschland sehr selten. Zu erwarten ist ein differenziertes Todesursachenspektrum, es dominieren natürliche Todesursachen. Keinesfalls bedeutet ein schwangerschaftsassoziierter Todesfall, dass Behandlungsfehler vorwürfe begründet sind.

Methodik Analysiert wurde die in den Jahren 1992 bis 2016 im Institut für Rechtsmedizin der Justus-Liebig-Universität Giessen obduzierten schwangerschaftsassozierten Todesfälle.

Ergebnisse Bei der Mehrzahl der präsentierten 22 Todesfälle aus den Jahren 1992 bis 2016 im Zusammenhang mit einer Schwangerschaft konnten im Wege der Obduktion und nachfolgender insbesondere histologischer Untersuchungen natürliche Todesursachen nachgewiesen werden, auch wenn der Schwangerschaft eine krankheitsauslösende Wirkung zukommt.

Schlussfolgerung Keineswegs muss die Tatsache des Todesertritts automatisch einen Behandlungsfehlerverdacht indu-

zieren, dies ist jedoch vor allem bei aufgetretenen und teilweise relativ spät erkannten Blutungskomplikationen der Fall. Gutachterlich muss dann der Behandlungsfehler als solches ebenso substantiiert dargelegt werden wie dessen Kausalität für den Todeseintritt. Dies ist gerade bei bekannten und nicht ausschließbaren Komplikationen einer Schwangerschaft nur möglich, wenn mangelhafte Kontrolle zu einem verspäteten Erkennen der Komplikation geführt hat oder auf eine Komplikation nicht lege artis reagiert wurde.

Introduction

One definition of pregnancy-associated death is death from any cause during pregnancy and up to one year post partum [10, 20, 23]. However, the WHO defines pregnancy-related death as the death of a woman which occurs between nidation of the fertilized ovum and 42 days after termination of pregnancy [27, 28]. But neither of the definitions require the cause of death to be anatomical changes immediately related to pregnancy. This means that in some cases the pregnancy may be the trigger for the fatal event (e.g., due to hormonal changes and/or increased circulatory volume load) but death may also be caused by events which could not occur outside of pregnancy (e.g., amniotic fluid embolism).

Immediate causes of sudden death during pregnancy and pregnancy-associated causes of death are usually disease, intoxication, accidents [11, 43] or, rarely, suicide [37]. In addition to pulmonary thromboembolism, amniotic fluid embolism, air embolism [3, 4, 26, 30, 31] and ruptured aneurysm [35, 36], other possible causes are:

- acute and chronic undetected cardiovascular disease (acute myocardial infarction, myocarditis, postpartum cardiomyopathy, cardiac valve disease, endocarditis, arrhythmias including Long QT syndrome, etc.)
- acute ruptured tubal or ectopic pregnancy with internal bleeding [1, 6, 45]
- fatal intoxication, primarily for drug-addicted pregnant women [18]
- postpartum bleeding (e.g. postpartum atonic bleeding which was not detected or only detected too late, possibly because of inadequate monitoring) [34]
- undetected uterine rupture with hemorrhage [13, 19]
- fatal outcome in HELLP syndrome [48, 49]
- Sheehan's syndrome [39, 41, 42]

If no macroscopic cause of death can be identified, then histopathological examination can help identify the cause of death. This can be useful in providing evidence for or excluding acute or chronic myocarditis or establishing amniotic fluid embolism as the cause of death. If death was due to massive hemorrhage following uterine rupture, the cause of death can be identified, for example by detecting granulation tissue and scar tissue at the site of rupture in women with previous C-section. Other reported causes of death include postpartum coronary artery thrombosis after the administration of bromocriptine [29]. This wide range of causes of pregnancy-associated deaths has led to pregnancy-related

causes of death being defined more narrowly as death from causes which cannot occur in non-pregnant women. In addition to deaths which clearly had natural causes, some deaths which occur in pregnancy, especially in countries with high-quality medical care, almost always raise the question whether medical malpractice could be the cause of death, particularly when death involved perinatal or postpartum hemorrhagic complications. All of the above shows that the cause of any death which occurs in connection with pregnancy must be carefully differentiated.

Material and Methods

The autopsies listed in the Registry of Autopsies of the Institute of Forensic Medicine of Justus-Liebig University Gießen between 1992 and 2016 (i.e. which occurred over a period of 25 years) were analyzed. A total of 22 autopsies were identified where it was assumed that death occurred in connection with pregnancy in accordance with the above-mentioned definition of the WHO. One death was not included in our study, as it was a homicide in early pregnancy and the pregnancy was merely the reason for the killing. One mortality from amniotic fluid embolism, a very rare cause of death, was processed by the Institute for Forensic Medicine of the University of Münster and added to the Gießen cohort because of the rarity of the findings, meaning that the final evaluation consisted of a total of 22 pregnancy-associated deaths. The extent of data depended on the recorded information, with some cases recorded in their entirety and while the records of other cases were incomplete. However, data on the cause of death were available for evaluation in all cases. In addition to age and the time of death during or after the pregnancy, the diagnosed medical cause of death was recorded in all cases and the manner of death was classified as natural, unnatural or unexplained in all cases. If an accusation of medical malpractice was raised, the available expert opinions were reviewed.

Results

All 22 autopsies were carried out by order of the respective department of public prosecution, sometimes following substantiated accusations of malpractice brought by dependents of the deceased or by the department of public prosecution. The average age of the women who died from pregnancy-associated causes was 31.8 years (22–45 years).

Cause of death was differentiated into natural and unnatural causes. In the majority of cases, death occurred suddenly from

► **Table 1** Pregnancy-associated deaths from natural causes (n = 9): age of the pregnant women, duration of pregnancy and cause of death.

Age	Duration of pregnancy	Cause of death
32	6th month of pregnancy	Fulminant pulmonary embolism in a woman with intact twin pregnancy
23	7th month of pregnancy	Cerebral hemorrhage affecting the right-sided cerebellum in a woman with hypertension
23	GW 40	Fulminant pulmonary embolism 27 days post partum
34	7th month of pregnancy	Cerebral hemorrhage with ventricular rupture in a woman with hypertension
28	GW 23	Aortic rupture, pericardial tamponade in a woman with intact twin pregnancy
25	GW 38	Myocarditis 2 days after C-section in a woman with a history of drug abuse
23	8th month of pregnancy	Fiedler's myocarditis
39	6th month of pregnancy	Asthma attack in a woman known to have bronchial asthma
22	GW 15	Acute H1N1 infection with fulminant course

GW = week of gestation

► **Table 2** Pregnancy-induced natural causes of death (n = 3): age of the pregnant women, duration of pregnancy and cause of death.

Age	Duration of pregnancy	Cause of death
29	GW 9	Ruptured tubal pregnancy; on autopsy approx. 2300 ml blood found in the abdominal cavity (► Fig. 1)
33	GW 40	Fatal puerperal sepsis 24 days post partum; on the day she died, the patient complained at home of experiencing a "shivering fit" but did not consult a doctor
39	GW 41	Fatal amniotic fluid embolism requiring reanimation during C-section (► Fig. 2)

GW = week of gestation

natural causes. Of the 22 deaths, 9 deaths were classified as pregnancy-associated deaths because of the time when death occurred but were considered to be due to natural causes occurring independently of the pregnancy status (► **Table 1**).

The cause of death in 3 other cases was classified as pregnancy-induced fatal disease, i.e., the women presented with syndromes which cannot occur without being pregnant (► **Table 2**).

Pregnancy-related complications or fatal hemorrhage were identified in 7 cases as the cause of death (► **Table 3**). Accusations of medical malpractice, i.e., that the bleeding was detected too late or was not treated in accordance with accepted standards of care, were usually levelled in cases of fatal hemorrhage.

Deaths of autopsied women were classified either as pregnancy-associated natural deaths from causes which can also affect non-pregnant women (► **Table 1**; n = 9) or pregnancy-induced deaths from natural causes (► **Table 2**; n = 3), with fatal hemorrhage induced directly or indirectly by pregnancy considered separately (► **Table 3**; n = 7). In addition to the above-mentioned causes of death, there were 3 further deaths which were also considered separately; in 2 cases the cause of death could not be determined (1 × sudden death 1 day after curettage in the 8th week of gestation; 1 × death 4 weeks after miscarriage), in one case, the cause of death was identified as medical error (administration of the wrong medicine) after the patient had received a very high dose of ropivacaine during delivery with epidural anesthesia (EDA) (► **Table 4**).

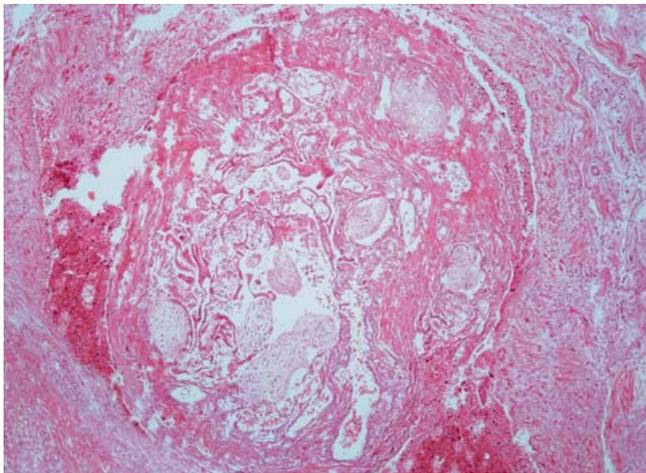
Medical malpractice was found to be an important cause of death, particularly in cases with fatal complications of bleeding where postpartum monitoring was inadequate. The specialist obstetricians and gynecologists were of the opinion that there was a causal relationship between 3 of the 22 deaths discussed in this study and medical malpractice. These cases were: 1 × an excessively high dose of ropivacaine, 2 × inadequate monitoring of the pregnant woman which resulted in fatal bleeding being detected too late.

Discussion

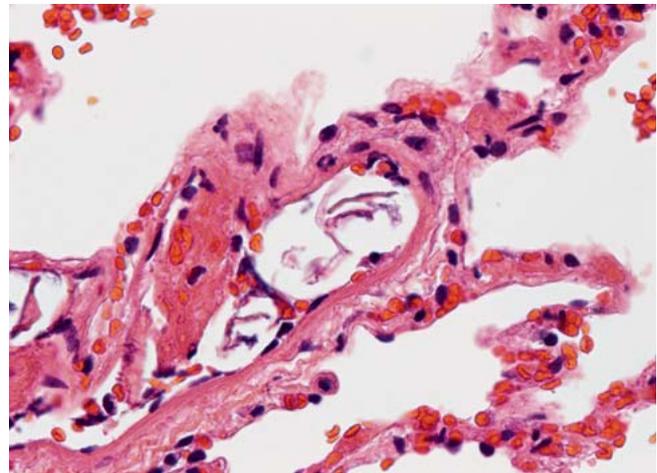
Pregnancy-associated deaths are extremely rare in countries with high-quality medical care. This can mean that in some cases the threshold for reviewing the cause of death may be very low and an initial suspicion of medical malpractice is not dismissed ad hoc and never dismissed without first carrying out an autopsy.

In addition to a number of case histories, there are also studies with larger numbers of maternal deaths [9, 11, 43] and reviews on the processing of, and investigation into, these deaths together with their respective histological findings [14, 20]. Investigations are carried out in both criminal and civil proceedings [10, 12, 27, 28, 38].

Pregnancy-related hormonal effects may facilitate death from natural causes (e.g. fulminant pulmonary embolism, myocarditis, hypertensive intracerebral hemorrhage, aortic rupture, etc.) without it being ultimately possible, in individual cases, to prove this



► **Fig. 1** Necrotic abortive placental villi and circular hemorrhagic lesions in the center part of the isthmus of the fallopian tube in the vicinity of the ruptured ectopic pregnancy (H&E × 40).



► **Fig. 2** Fatal amniotic fluid embolism with numerous non-nucleated keratin lamellae in the peripheral branches of the pulmonary artery and septal capillaries of the pulmonary tissue (H&E × 400).

► **Table 3** Fatal hemorrhages induced directly or indirectly by the pregnancy (n = 7): age of the pregnant women, duration of pregnancy and cause of hemorrhage.

Age	Duration of pregnancy	Cause of hemorrhage
26	GW 39	Para 2, gravida 3; bleeding from initially undetected cervical tear with secondary puerperal sepsis (Group A streptococci) during vaginal delivery with vacuum extraction after discontinued homebirth
35	GW 40	Para 1, gravida 2; postpartum hemorrhage from uterine atony; multiple organ failure (MOF) from hemorrhagic shock despite hysterectomy
40	GW 40	Bleeding from high vaginal tear and hemorrhagic shock from clinically diagnosed uterine atony
33	Early pregnancy	Iatrogenic injury of the right iliac artery during laparoscopy after curettage performed to exclude ectopic pregnancy; cause of death was hemorrhagic shock
31	GW 39	Clinically diagnosed uterine atony with postpartum hemorrhage and death from hemorrhagic shock (exhumation)
36	GW 34	Hemorrhagic shock in a woman with placenta previa, bicornuate uterus and twin pregnancy
38	9th month of pregnancy	Death occurred five days post partum, following initially undetected high vaginal tear following vaginal delivery; cause of death was hemorrhagic shock

GW = week of gestation

► **Table 4** Unusual pregnancy-associated deaths (n = 3): age of the pregnant women, duration of pregnancy and cause of death.

Age	Duration of pregnancy	Cause of death
45	GW 8	s/p curettage carried out one day before death; cause of death unclear
35	s/p miscarriage in early pregnancy	Found lifeless approx. 3–4 weeks after miscarriage, cause of death unclear; toxicological findings were positive for paracetamol + propyphenazone, but not in toxic doses
31	GW 39	Seizures after administration of medication while receiving EDA, then asystole; C-section performed with reanimation; administration of wrong dose of NAROPIN® (= ropivacaine) in clearly toxic amounts, ampoules of ropivacaine 0.75% were administered inadvertently instead of ampoules of ropivacaine 0.25%

EDA = epidural anesthesia; GW = week of gestation; s/p = status post

causal relationship beyond further doubt. Such deaths from natural causes were the most commonly identified deaths. Information on these causes of death is found in the literature, particularly cases of arterial rupture or dissecting arterial aneurysm with fatal hemorrhage during pregnancy or very shortly after delivery [5, 35, 44, 46, 50] and cases of fulminant pulmonary embolism [33]. Causes of death reported in the literature include amniotic fluid embolism [7, 13, 21, 25, 26, 30–32] and – although this is rare – pregnancy-associated air embolism [4]. In some cases, rupture of an ectopic pregnancy, particularly of a tubal pregnancy, can result in fatal hemorrhage [1, 6, 45]. Other causes of death include pregnancy-related complications of bleeding [8, 17, 34], deaths from HELLP syndrome or (pre-)eclampsia [3, 48, 49], and fatal puerperal sepsis with Group A streptococci infection [24].

Other causes of death reported in case histories include spontaneous rupture of an unscarred gravid uterus [19], fatal methadone intoxication of a pregnant woman [18], pregnancy outcomes after traffic accidents [22], spontaneous postpartum liver rupture [47], and acute postpartum coronary artery thrombosis in a woman receiving bromocriptine [29]. Other rare causes of deaths during pregnancy are pregnancy-associated disease, particularly Sheehan's syndrome [39, 40, 42, 43]. Based on the findings of our study, deaths can be differentiated into four groups:

- **Group I:** Deaths from natural causes which could, in principle, also have occurred without the woman being pregnant (e.g., fulminant pulmonary embolism, myocarditis, arterial rupture, etc.).
- **Group II:** Pregnancy-related deaths which were unavoidable but were due to natural causes, such as amniotic fluid embolism, uncontrollable puerperal sepsis despite state-of-the-art care, or late detection of a ruptured tubal pregnancy with fatal hemorrhage.
- **Group III:** Deaths which occurred in the context of fatal pregnancy-related bleeding, such as atonic postpartum bleeding and bleeding from (initially undetected) delivery-related rupture or injury. This also includes deaths from what must be considered medical malpractice (inadequate monitoring).
- **Group IV:** Deaths which coincided with pregnancy but where the cause of death was not clear. This includes death from myocardial disease not diagnosed prior to the time of death (e.g. ionic channel defects or cardiomyopathies where the definitive diagnosis can be extremely time-consuming and difficult).

Of course, every individual death must be carefully reviewed to determine whether treatment was in accordance with accepted standards of medical care. If medical malpractice did occur, the question of whether the cause of death was malpractice must be investigated separately.

Deaths which coincide with pregnancy should generally be investigated by autopsy, although this is currently not a legal requirement. The law on the indications required for terminating pregnancy in the former GDR stipulated that all deaths occurring in connection with a pregnancy required postmortem examination. Autopsies were mandatory for “deceased pregnant women and women who died in childbirth as well as women who died within 6 weeks of giving birth” (Section 8 subsection 1b of the

“Decree Concerning Medical Postmortem Examinations”) [2]. Other countries have similar legal requirements [16].

Autopsy studies in forensic medicine have shown that in the majority of cases, questions about the cause of death are often already answered by the macroscopic findings at autopsy, at the latest after additional histological examination. Moreover, when allegations of medical malpractice were raised, autopsies had an exculpatory effect in the majority of cases, as the autopsy was able to show that death was from natural causes.

Perinatal and postnatal fatal bleeding are adverse events specific to pregnant and postpartum women, as is puerperal sepsis. These causes of death habitually raise the question whether monitoring on the labor ward and post partum was adequate. It is important to note that complications can always occur; any allegation of malpractice must focus on the question whether the bleeding complication or the puerperal sepsis could have been detected and controlled in good time.

Forensic medicine is useful for establishing the status quo at the time of death and for interpreting the autopsy findings but it reaches its limits when events which occurred over a period of time need to be evaluated and it is necessary to determine whether these events could have been diagnosed and treated. The latter two questions require the expert opinion of obstetricians and gynecologists based on the autopsy findings. This approach (i.e., a forensic autopsy report including histological and toxicological examinations and the opinion of an obstetrician or gynecologist on whether medical malpractice was involved) which takes the expertise of the respective specialist into account [15] is standard practice and is accepted in both criminal and civil proceedings.

Particularly in the two cases of fatal complications of bleeding reported in this study, if criminal proceedings are launched, it is the specialist's job to state whether the patient would have almost certainly survived if she had been monitored properly and the bleeding had been detected in time. If this is not possible, then in criminal proceedings the principle of “in dubio pro reo” must apply. But irrespective of any criminal proceedings, it is nevertheless possible to bring a separate civil action for compensation, as this requires a lower standard of proof.

Conclusion

Pregnancy-induced and pregnancy-associated deaths are very rare in Germany and usually require an autopsy to determine the cause of death and, in some cases, additional histological, microbiological, virological and toxicological examinations. The majority of deaths are from natural causes but, particularly if there were complications of bleeding which raised the suspicion of medical malpractice, an expert opinion to identify both the cause and the manner of death is required. The expert opinion must take account of the forensic autopsy report and assess the clinical processes in its obstetrical and gynecological evaluation. The most important aspect is to determine whether the bleeding could have been detected earlier and whether the measures taken to control the bleeding complications complied with the requisite medical standards of care; in the context of criminal proceedings this should serve to answer the question whether the patient

would have almost certainly survived if the bleeding had been detected in good time. Irrespective of any criminal proceedings, it is nevertheless possible to bring a civil action and claim for damages, as the standard of proof with regard to determining causality between malpractice and death is lower in civil actions.

Conflict of Interest

The authors declare that they have no conflict of interest.

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