4th Biennial report 2018-2019
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1. Introduction.

In obstetric medicine we know several diseases and complications that can result in so-called near-miss events: severe life-threatening obstetric complications necessitating urgent medical intervention in order to prevent likely death of the mother. Many of these obstetric complications cannot be anticipated by risk factors or tests. Obstetricians will be challenged by these complications at the most a few times along their clinical career, therefore individual expertise is scarce. It is challenging to investigate rare diseases and severe complications to find robust evidence on incidence, risk factors and pathophysiology as basis for evidence-based guidelines on prevention and management.

The United Kingdom was a pioneer when developing the UK Obstetric Surveillance System (UKOSS) in 2006, a nationwide survey to identify and study ‘near-miss’ events and rare diseases of pregnancy. Collaboration of all maternity units nationwide to collect data enables identification of a relatively small number of women. This allows to conduct descriptive epidemiologic studies, case-control and parallel cohort studies (https://www.npeu.ox.ac.uk/ukoss/completed-surveillances). Gathering experience and knowledge on incidence, risk factors, pathophysiology and management, results in better understanding, better patient information and care by practical improvements in prevention and treatment of these uncommon conditions.

Similar surveillance systems have been set up in other countries and the International Network of Obstetric Surveillance Systems (INOSS) was constituted in July 2010. Current member countries of INOSS include Australia, Austria, Belgium, Denmark, Finland, France, Germany, Iceland, Italy, the Netherlands, New Zealand, Norway, Portugal, Slovakia, Spain, Sweden and the United Kingdom. The mission of INOSS is to co-operate, share information and enable cross-national comparisons and analyses (https://www.npeu.ox.ac.uk/inoss).

The Belgian Obstetric Surveillance System was constituted in 2011 supported by the College of physicians for the Mother and Newborn, a consultative body of the Federal Public Service of Health, and started its registration in the whole of Belgium in January 2012. Meanwhile B.OSS has proven to be successful in monitoring severe maternal morbidity. Belgian gynaecologists are willing to participate in order to receive advice based on own data, because practice in Belgium and certainly the organization of medical care differs from neighbouring countries. Whereas Peristat (http://www.europeristat.com) develops valid and reliable indicators that can be used for monitoring and evaluating perinatal health in the EU, the purpose of B.OSS in Belgium and of INOSS internationally is trying to analyse and explain the figures obtained and to establish the best possible treatment to avoid maternal near misses and deaths. The results of the first studies suggest the need to develop nationally adopted guidelines and invite to critically evaluate the current organisation of obstetric health care in Belgium.
2. **Objective.**

The objective of B.OSS is at first, to get an accurate picture of the obstetric complications under investigation in Belgium and secondly, to improve the quality and safety of obstetric care in Belgium by practical recommendations based on the results.

The first objective is achieved through descriptive epidemiological studies on rare obstetric disorders. Based on B.OSS data we are able to define the incidence in Belgium, to identify risk-factors, to describe and evaluate management and compare with international studies and guidelines.

The secondary objective can be achieved by recommendations for prevention: primary prevention (based on risk-factors) and secondary prevention (based on management and substandard care) formulated in national guidelines.

Aim is a high-quality performance of the Belgian Obstetric Surveillance System (B.OSS) to be a respectable partner of INOSS, capable to co-operate and compare with other international obstetric surveillance systems.

3. **Organisation and methods.**

**Institute**

B.OSS is endorsed by the two professional associations for gynaecologists, VVOG and GGOLFB, and by the perinatal registries, SPE and CEpiP. The College of physicians for Mother and Newborn operated as the steering committee of B.OSS until a formal scientific board was constituted in 2017, with representatives of SPE, CEpiP, the Belgian Health Care Knowledge Centre (KCE), the Scientific Institute of Public Health (Sciensano, formally known as WIV-ISP) and the College of Mother and Newborn. Since start in 2012, daily reporting and data collection tasks are carried out by two cooperating teams: one in Flanders coordinated by a research team from the University Hospital Ghent, another in Brussels and Wallonia coordinated by the CepiP research team. The teams cooperate and regularly meet to update on their progress and to discuss difficulties. From January 2020 onward the B.OSS project is supported financially by the Federal Public Service of Health in an 18 months pilot project. Mrs Karolien Benoit was introduced as B.OSS officer and takes up most of the daily reporting and data collection tasks, in close cooperation with CepiP and SPE.

**Ethics approval.**

The B.OSS methodology was approved by the Medical Ethics Committee of Ghent University Hospital (EC UZG 2012/734; B670201215359) and by the Medical Ethics Committee of the Erasme University Hospital, Brussels (EC ULB 2012/111; B406201213660) at the beginning in 2012. The Medical Ethics Committee of the Ghent University Hospital became central Ethics
Committee in 2015 (EC UZG 2015/1470; B670201526875) and Ethics Committees of the participating maternities were informed and included in this multicentre study following approval. Initially, the women eligible for inclusion were informed by their gynaecologists and offered an information letter enabling them to opt-out. Since the General Data Protection Regulation (GDPR) is introduced in May 2018, women are obliged to sign an informed consent. Informed consents are guarded in the proper hospitals by the local B.OSS investigator, so that cases remain anonymous for the B.OSS research team. Person-identifiable information is eliminated from data-analysis. Confidentiality is guaranteed for mother, provider and hospital during data processing, data analysis and disclosure of results.

**Methods.**

B.OSS has adopted the methodology for case reporting of severe obstetric morbidity, developed by the UKOSS. Briefly, an appointed contact person (a gynaecologist, senior-midwife or clerk) in each participating maternity unit is invited by monthly mailing to report a selected number of rare obstetric complications that may have occurred in the preceding month. In the event a case was reported in reply, the contact person is asked to complete an extensive data collection form. In case of incomplete reporting, the appointed contact person is encouraged repeatedly by email and phone to provide missing data.

Initially, data on reported cases were obtained through the use of a standardized form, filled out electronically or on hard copy according to preference of the local responsible. Web-based data-collection was gradually introduced following the launch of the B.OSS website (www.b-oss.be) in August 2013, facilitating monthly reporting and completion of data collection forms online. Monthly emails are generated automatically calling to report for the previous month with reminders for missing reporting forms and incomplete data collection forms. Restricted access to the website is provided to the appointed B.OSS-contact person, who has access to the reporting forms and data collection forms of their maternity unit. Data protection is secured by the use of hash codes, replacing person-identifiable information such as the woman’s name, date of birth or hospital number.

**Registered variables.**

Data collection forms question maternal characteristics, medical history and obstetrical history, details on the index pregnancy, circumstances of the event, the management and the outcome for mother and the foetus or new born.
4. Participation.

**Number of participating maternities:**
At the beginning in 2012, 97.3 % (110/113) of the Belgian maternities formally agreed to participate in B.OSS: 2 centers have refused explicitly and 1 center never replied. The number of Belgian maternities dropped from 113 to 107 in 2018 and to 105 (situation in April 2020) as a result of merging and closure of centers. Meanwhile, all maternities are willing to participate in B.OSS, with the exception of 1 center that refuses explicitly because of the lack of remuneration. Ethical Committee approval for the B.OSS study is confirmed for 87 maternities of the 104 reporting units.

![Figure 1 – Participation of Belgian maternity centers – situation in 2017.](image)

**The overall case reporting response rate:**
96% (1239 of 1288 reporting forms that were sent have been completed and returned) between January and December 2018. There were no ongoing registrations in 2019. Since start in January 2020 more than 52.8% (>277 of 525) reporting forms were returned.

![Figure 2 – Response rate in % of all Belgian maternity centers since start of B.OSS.](image)
5. Studies.


B.OSS completed the following national studies:
- Uterine rupture (2012-2013) (*results reported in B.OSS report 2014-2015*)
- Peripartum hysterectomy and/or arterial embolisation of the uterine arteries (2012-2013) (*results reported in B.OSS report 2014-2015*)
- Eclampsia (2012-2014)
- Antenatal pulmonary embolism (APE) (2015-2018)

B.OSS participated in the INOSS international studies of:
- Anaphylaxis in pregnancy (2016-2018)
- Global Maternal Sepsis Study (GLOSS) (1 week study in 2017)

5.1.1. Eclampsia in Belgium.

**Definition**
Defined according to UKOSS as any woman with convulsion(s) during pregnancy or within the first 10 days after delivery, in combination with at least 2 of the following features within 24 hours of the convulsion(s):
- Hypertension: a maximum diastolic Blood Pressure of $\geq 90$ mmHg and a diastolic increment of $\geq 25$ mmHg (having had a diastolic Blood Pressure $<90$ mmHg at the first antenatal visit)
- Proteinuria: at least $+$ protein in a random urine sample or $\geq 0.3$ g of proteins in a 24-hour collection
- Thrombocytopenia: platelet count $< 100000$ /ml
- Raised transaminase levels: ALT of $\geq 42$ IU/l or AST of $\geq 42$ IU/l

**Surveillance period**
January 2012 – December 2015

**Results**
Results were published in November 2019 in the national Journal Gunaïkea (vol. 24 nr 4). Full-text can be found through this link:
In summary:

B.OSS registered 74 women with an eclamptic insult between January 2012 and December 2014, of whom 59 women could be included in the analysis of results. Consequently the estimated incidence of eclampsia in Belgium is 1,6 (95%-BI: 1,2-2,1) per 10,000 deliveries. This number is low compared to the Netherlands (5,4 per 10,000 deliveries) and the United Kingdom (2,7 per 10,000 deliveries). A likely explanation is the organisation of antenatal care in Belgium, where family doctor, midwife and gynaecologist are easily accessible and where gynaecologists are the main care providers for most pregnancies whatever the risk stratification of the women. This guarantees a good continuity of care.

The eclamptic insult occurred in the hospital in 39 women (66%), at home in 18 women (31%); ante-partum, intra-partum and post-partum in respectively 36, 7 and 16 women. In the end 54 women (91,5%) were administered magnesiumsulphate, of whom 6 women profylactically before the insult. Thirty-four women (58%) received anticonvulsive treatment (mostly diazepam), this was started as first choice in 15 women on the moment of the insult. Fifty-one women (86%) received antihypertensive treatment, of whom 12 women before the insult. Forty-three women (73%) were admitted to an Intensive Care Unit, nineteen suffered severe morbidity besides the eclampsia. One mother died (case fatality rate: 1,7%). There were four fetal demises and one neonatal death (perinatal fatality rate: 8,5%).

Most likely the prevention and management of this rare complication in Belgium can further be improved by an increase in the administration of aspirin starting from the first trimester, and by improving the timely administration of antihypertensive drugs and prophylactic magnesiumsulphate. Therefore we should increase awareness of family-doctors and emergency room doctors and inform them on the use of magnesiumsulphate as first choice drug to manage an eclamptic insult. This could be enhanced through the development of a Belgian guideline on eclampsia.

**5.1.2. Spontaneous hemoperitoneum in pregnancy (SHiP).**

The study was initiated by Prof. Jens Langhoff-Roos, University of Copenhagen, Denmark, and supported by the International Network of Obstetric Survey Systems (INOSS). Besides Denmark and Belgium, SHiP was registered in the United Kingdom, the Netherlands and Italy.

**Definition**

SHiP is the occurrence of sudden hemorrhage intra-abdominally in pregnancy - unrelated to trauma or rupture of the uterus. SHiP has been associated with endometriosis, rupture of uterine artery or varicose veins and aneurysms of the splenic artery.

Inclusion: any pregnancy after 22 weeks with sudden intra-abdominal hemorrhage requiring surgery (CS, laparotomy, laparoscopy) - without preceding trauma.

Exclusion: cases of uterine rupture, cases of hemoperitoneum following trauma.
Surveillance period
September 2015 – December 2017

Results
In Belgium 18 cases of SHiP were reported, only 10 cases could be included in the analysis of the study. Consequently the incidence of SHiP in Belgium is estimated at 0.28 per 10,000 deliveries. The mean maternal age was 31.9 (±4.3) years. Five women with SHiP were known with endometriosis in their history. Nine women presented with acute abdominal pain, four of them had an abnormal foetal heart rate at presentation. The bleeding was located mainly in the left pelvic region. Eight women underwent caesarean section, two women had a laparotomy because of SHiP post-delivery. The median estimated blood loss was 2000 (1275-2800) ml. The median birth weight was 2275 (1223 – 2774) gram at a median gestational age of 32.5 (28 – 37.5) weeks.
There were no maternal deaths. One foetus died in utero, there was 1 neonatal death and 5 neonates with severe morbidity.
In conclusion, SHiP is a rare and challenging obstetric urgency. Increased awareness for this severe complication is warranted, notably for women known with endometriosis.

International analysis
Belgian cases will be included in an INOSS multi-country study of this rare condition. We will keep you informed when results are published.

5.1.3. Anaphylaxis in pregnancy.

B.OSS participated in this INOSS international collaborative study, together with France, the Netherlands, the United Kingdom and Finland. Principal investigators were Stephen Mc Call and Professor Marian Knight, National Perinatal Epidemiology Unit, University of Oxford, UK.

Definition
Anaphylaxis is defined as a severe, life-threatening generalised or systemic hypersensitivity reaction. The following two criteria must be met for a diagnosis of anaphylaxis to be made:

1. A life-threatening airway problem and/or breathing problem and/or circulatory problem
2. Sudden onset and rapid progression of symptoms

A life-threatening airway problem is taken to include:

- Laryngeal or pharyngeal oedema
- Hoarse voice
- Stridor

A life-threatening breathing problem is taken to include:

- Shortness of breath and raised respiratory rate
- Wheeze
- Decreased oxygen saturations
- Confusion secondary to hypoxia
- Cyanosis
- Respiratory exhaustion or respiratory arrest

A life-threatening circulatory problem is taken to include:
- Signs of shock such as faintness, pallor or clammy skin
- Tachycardia >100bpm
- Systolic BP <90mmHg
- Decreasing level of consciousness
- Signs of ischaemia on ECG
- Cardiac arrest

**Surveillance period**

September 2016 – January 2018

**Results**

The results were published in the open access journal Anaesthesia in May 2020.
The full-text is available via this link: https://onlinelibrary.wiley.com/doi/10.1111/anae.15069

In summary:
Anaphylaxis in pregnancy is a rare but severe complication for both mother and infant. Population-based data on anaphylaxis in pregnancy are lacking from mainland European countries. This multinational study presents the incidence, causative agents, management and maternal and infant outcomes of anaphylaxis in pregnancy. This descriptive multinational study used a combination of retrospective (Finnish medical registries) and prospective population-based studies (UK, France, Belgium and the Netherlands) to identify cases of anaphylaxis. Sixty-five cases were identified among 4,446,120 maternities (1.5 per 100,000 maternities; 95%CI 1.1–1.9). The incidence did not vary between countries. Approximately three-quarters of reactions occurred at the time of delivery. The most common causes were antibiotics in 27 women (43%), and anaesthetic agents in 11 women (17%; including neuromuscular blocking drugs, 7), which varied between countries. Anaphylaxis had very poor outcomes for one in seven mothers and one in seven babies; the maternal case fatality rate was 3.2% (95%CI 0.4–11.0) and the neonatal encephalopathy rate was 14.3% (95%CI 4.8–30.3). Across Europe, anaphylaxis related to pregnancy is rare despite having a multitude of causative agents and different antibiotic prophylaxis protocols.
5.1.4. GLOSS

The Global Maternal Sepsis Study is a WHO study, which aimed to assess the frequency of maternal infections in health facilities, according to maternal characteristics and outcomes, and coverage of core practices for early identification and management. Maternal infections are an important cause of maternal mortality and severe maternal morbidity. B.OSS participated to this study via the INOSS.

**Definition**
The cases were all pregnant or recently pregnant women (up to 42 days after the end of pregnancy) hospitalised with suspected or confirmed infection.

**Surveillance period**
28 November – 4 December 2017

**Results**
The results of the WHO Global Maternal Sepsis Study were published in the Lancet in May 2020. The full-text can be consulted via this link: [https://doi.org/10.1016/S2214-109X(20)30109-1](https://doi.org/10.1016/S2214-109X(20)30109-1)

In summary:

**Background**
Maternal infections are an important cause of maternal mortality and severe maternal morbidity. We report the main findings of the WHO Global Maternal Sepsis Study, which aimed to assess the frequency of maternal infections in health facilities, according to maternal characteristics and outcomes, and coverage of core practices for early identification and management.

**Methods**
We did a facility-based, prospective, 1-week inception cohort study in 713 health facilities providing obstetric, midwifery, or abortion care, or where women could be admitted because of complications of pregnancy, childbirth, post-partum, or post-abortion, in 52 low-income and middle-income countries (LMICs) and high-income countries (HICs). We obtained data from hospital records for all pregnant or recently pregnant women hospitalised with suspected or confirmed infection. We calculated ratios of infection and infection-related severe maternal outcomes (i.e., death or near-miss) per 1000 livebirths and the proportion of intrahospital fatalities across country income groups, as well as the distribution of demographic, obstetric, clinical characteristics and outcomes, and coverage of a set of core practices for identification and management across infection severity groups.

**Findings**
Between Nov 28, 2017, and Dec 4, 2017, of 2965 women assessed for eligibility, 2850 pregnant or recently pregnant women with suspected or confirmed infection were included. 70.4 (95%
10,9 (9,8–12,0) women per 1.000 livebirths presented with infection-related (underlying or contributing cause) severe maternal outcomes. Highest ratios were observed in LMICs and the lowest in HICs. The proportion of intrahospital fatalities was 6,8% among women with severe maternal outcomes, with the highest proportion in low-income countries. Infection-related maternal deaths represented more than half of the intrahospital deaths. Around two-thirds (63,9%, n=1821) of the women had a complete set of vital signs recorded, or received antimicrobials the day of suspicion or diagnosis of the infection (70,2%, n=1875), without marked differences across severity groups.

**Interpretation**
The frequency of maternal infections requiring management in health facilities is high. Our results suggest that contribution of direct (obstetric) and indirect (non-obstetric) infections to overall maternal deaths is greater than previously thought. Improvement of early identification is urgently needed, as well as prompt management of women with infections in health facilities by implementing effective evidence-based practices.

### 5.1.5. Antenatal Pulmonary Embolism (APE)

**Definition**
1. EITHER PE should be confirmed by using suitable imaging techniques (such as angiography, computed tomography, echocardiography, magnetic resonance imaging or ventilation-perfusion scan showing a high probability of PE
2. OR PE is confirmed at surgery or post-mortem
3. OR a clinician has made a diagnosis of PE with signs and symptoms consistent with PE present, and the patient has accordingly received a course of anticoagulation therapy (>1 week duration)

**Surveillance period**
January 2015 – December 2018

**Results**
Thirty-two cases of antenatal pulmonary embolism (APE) were reported of which 29 cases could be included in the analysis of the study. This is translated in an estimated incidence of 0,65 per 10.000 deliveries in Belgium. The median gestational age at the moment of diagnosis was 30 weeks (range 5 weeks 1 day – 38 weeks 2 days). 72% of women had at least one identifiable risk-factor for the development of a venous thrombo-embolism (VTE). The majority of the women was managed at first with low-molecular-weight-heparin (86%). One mother died, 3 women were resuscitated and a total of 8 women was admitted to an Intensive Care Unit. Three patients were on thromboprophylaxis during pregnancy, but the dose appeared to low in two of them. A further three women should have received thromboprophylaxis in pregnancy according to international guidelines.
In conclusion, this study demonstrates that antenatal pulmonary embolism is a rare, but serious complication in Belgium. We observed a great heterogeneity in the management and particularly in the prevention of VTE. Women eligible did not always receive thromboprophylaxis or did not receive the appropriate dose of thromboprophylaxis. We should aim for more uniformity in the care of pregnant women which could be achieved by the development of (national) evidence-based guidelines.


5.2.1. Intrahepatic cholestasis of pregnancy.

**Definition**
Every pregnant woman identified as having Intermediate (bile acids 40-99micmol/L) or Severe (bile acids ≥ 100micmol/L) Intrahepatic Cholestasis of Pregnancy (ICP).

Defined as:
- Pruritus without rash associated with elevated serum bile acid levels ≥ 40 micmol/L
- At any stage of the pregnancy,
- Not explained by other pathologies,
- Disappearing after the delivery.

Exclusion criteria:
- Serum bile acid levels less than 40 micmol/L
- Other hepatic/infectious/dermatologic/pregnancy disease, which could explain the symptoms

**Surveillance period**
January 2020 – December 2021

**Interim results**
During the first 4 months, 27 cases of intrahepatic cholestasis of pregnancy (ICP) were reported. We received 15 completed data collection forms.

5.2.2. COVID-19.

**Definition**
Any pregnant woman or postpartum up till 42 days after the end of pregnancy with diagnosis of COVID-19 infection, admitted to hospital.

**Surveillance period**
March 2020 – March 2021
Interim results
With support of the College of physicians for the Mother and Newborn B.OSS initiated the registration of COVID-19 in pregnancy to identify the impact of COVID-19 on the pregnant population in Belgium. B.OSS participates in the INOSS international project. All 105 maternities in Belgium participate. From 1 March 2020 until 23 June 2020, 264 cases were reported. We received 121 complete data collection forms so far. There were no cases of maternal deaths. Symptoms of COVID-19 were present in 62 of these 121 patients. Seven of 102 neonates born were tested positive on COVID-19. Three stillbirths occurred (1 between 34-36 weeks, the neonate was not tested / and a twin between 24-28 weeks, placenta tested positive) and 2 miscarriages (1 miscarriage without information / 1 spontaneous miscarriage at gestational age of 16w1d).

5.3. Future studies.

5.3.1. Surgical complications of bariatric surgery in pregnancy.

Definition
Every pregnant woman known with bariatric surgery prior to conception presenting with a surgical complication (Internal herniation, Intussusception, Volvulus, Gastric ulcer, Staple line stricture(s), Erosion of the gastric band, Migration of the gastric band).

Surveillance period
January 2021 – December 2022

5.3.2. Maternal mortality.

The interest of the Federal Public Service in a Belgian enhanced system for Maternal Mortality registration and analysis, resulted in their financing for a pilot project during 18 months. (See 3. Organisation and methods). Thereby, our officer Karolien Benoit can work full-time on B.OSS and on the development of the Belgian Analysis system for Maternal Mortality (BAMM).

Since 2018 the working group (Caroline Daelemans, Julie Belhomme, Hilde Logghe, Griet Vandenberghe, Elena Costa, Sarah Michel, Annick Bogaerts, Fabienne Roelants, Marc Coppens, Michel Willems, Gisèle Vandervelpen) developed a Belgian adopted system in 7 brainstorm sessions, with the support of the B.OSS scientific committee, the College of Physicians of Mother and Newborn and the FPS supervisory committee. The aim of the BAMM system is to accurately determine the Belgian Maternal Mortality ratio. But more importantly the aim of BAMM is to take lessons of the rare dramatic cases of maternal death in Belgium, by formulating recommendations that can be extrapolated from the hospital in case to the organization of (obstetric) care in Belgium.
The methodology of BAMM represented in the timeline in Figure 3 can be summarised in 5 core-ideas. 1) Cases of maternal mortality will be reported using the existing platform of B.OSS, 2) cases of maternal death will be analysed in 2 levels: at first locally in the hospital by the care givers involved supported by the quality coordinator and BAMM officer, secondly on a national level by a multidisciplinary team of experts, 3) consensus will be sought during the national analysis by using the Delphi methodology, 4) a sensitisation campaign is needed to inform family doctors, psychiatrists, intensive care specialists, besides gynaecologists and midwives, 5) a system of triangulation (linkage) of 3 existing federal databases will be developed parallel to the BAMM system, to capture all late and less-evident maternal deaths and to control for missing cases.

6. B.OSS within INOSS.

The International Network of Obstetric Survey Systems (INOSS) is a multi-country collaboration which was formed to promote and facilitate studies of uncommon and severe complications in pregnancy and childbirth.

B.OSS was represented at the annual meetings of the INOSS in France (Paris) in 2012, in Germany (Munich) in 2013, in Sweden (Finnhamn) in 2014, in Canada (Vancouver) in 2015, in Italy (Rome) in 2016, in Copenhagen (Denmark) in 2017, in Belgium in 2018, and in Bratislava in 2019.

B.OSS participated in three INOSS studies, as discussed in Chapter 5. Spontaneous Hemoperitoneum of Pregnancy (SHiP), Anaphylaxis in Pregnancy and the GLOSS study.
B.OSS was the main investigator of the International Study of uterine rupture, an international comparative analysis of cases of uterine rupture. B.OSS participated in the International Study of Peripartum hysterectomy.

More information on INOSS, aims and members can be found on https://www.npeu.ox.ac.uk/inoss.

7. Publications.

A nationwide population-based cohort study of uterine rupture in Belgium: results from the Belgian Obstetric Surveillance system.
G. Vandenberghe, M De Blaere, V Van Leeuw, K Roelens, Y Englert, M Hanssens, H Verstraelen
BMJ Open 2016;6:5 e010415; DOI: 10.1136/bmjopen-2015-010415

A nationwide population-based cohort study of peripartum hysterectomy and arterial embolisation in Belgium: results from the Belgian Obstetric Surveillance System.
G. Vandenberghe, M. Guisset, I. Janssens, V Van Leeuw, K Roelens, M Hanssens, E Russo, J Van Keirsbick, Y Englert, H Verstraelen
BMJ Open Nov 2017, 7 (11) e016208; DOI: 10.1136/bmjopen-2017-016208

The Belgian Obstetric Surveillance System to monitor severe maternal morbidity.
Vandenberghe G, Roelens K, Van Leeuw V, Englert Y, Hanssens M, Verstraelen H.


B.OSS onderzoekt ernstige maternale morbiditeit
Le B.OSS étudie la morbidité maternelle sévère en Belgique
Gunaïkeia 2018 Maart; vol. 23 nr 2

Eclampsie in België: resultaten van het Belgian Obstetric Surveillance System
L’éclampsie en Belgique: résultats du Belgian Obstetric Surveillance System
Gunaïkeia 2019 Juni; vol. 24 nr 4
Uterusruptuur in België: resultaten van de Belgian Obstetric Surveillance System
Rupture utérine en Belgique: résultats du Belgian Obstetric Surveillance System
Gynaïkeia 2019 Sept; vol. 24 nr 5

Frequency and management of maternal infection in health facilities in 52 countries (GLOSS): a 1-week inception cohort study.
The Lancet Global Health 2020 May; Volume 8, Issue 5, Pages e661-e671

Anaphylaxis in pregnancy: a population-based multinational European study.
Anaesthesia 2020 May, doi: 10.1111/anae.15069

Epidemiological analysis of peripartum hysterectomy across nine European countries.
Athanasios F. Kallianidis, Alice Maraschini, Jakub Danis, Lotte B. Colmorn, Catherine Deneux-Tharaux, Serena Donati, Mika Gissler, Maija Jakobsson, Marian Knight, Alexandra Kristufkova, Pelle G. Lindqvist, Griet Vandenberghe, homas Van Den Akker, on behalf of INOSS (the International Network of Obstetric Survey Systems)


The development of a Belgian guideline on the ‘Delivery with a scarred uterus’ is finalised. An AGREE assessment of existing international guidelines, a literature research of topics that were under discussion, and an expert opinion review using a Delphi methodology were used to come to the result, that will be published later this year. An online tool to support patients and gynaecologists in their decision-making process is under construction.

9. Acknowledgements.

Eight years since we started, B.OSS still stands firm and has become a competent registration system.
We are aware that this success is essentially thanks to the contribution of all clinicians reporting to B.OSS, who persevere in notifying cases and completing data collection forms, who never complain of website breakdowns or lengthy questionnaires.
We would like to thank all B.OSS contact persons, all gynaecologists, registrars, midwives, secretaries throughout Belgium who have contributed in one or another way to B.OSS, without whom this work would not have been possible.
10. Funding.

We wish to thank the College of Physicians for the Mother and the Newborn, section Mother, who supported the establishment of the Belgian Obstetric Surveillance System, and has continued funding the registration and evaluation of serious obstetric complications in Belgium until 2020.

We are very grateful that further financing is now possible directly through the FPS of health, thanks to the efforts and support of Mieke Walraevens, Margareta Haelterman and Isabelle Van Den Brempt. We wish to thank them sincerely for their believe in the B.OSS and BAMM projects.

11. Future.

B.OSS continues the registration and evaluation of rare obstetric complications in Belgium in 2020 with current studies (intrahepatic cholestasis of pregnancy and COVID-19 during pregnancy) and new studies (surgical complications of bariatric surgery in pregnancy and Maternal Deaths). We rely on your further enthusiasm and participation and hope that the few maternities that have dropped out will be motivated or remotivated by the reported results and first publications.

ANNEX

2. Epidemiological analysis of peripartum hysterectomy across nine European countries.
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Original Article

Anaphylaxis in pregnancy: a population-based multinational European study*

S. J. McCall, 1,2 M.-P. Bonnet, 3,4,5 O. Ayras, 6 G. Vandenbergh, 7 M. Gissler, 8,9 W.-H. Zhang, 10,11 V. Van Leeuw, 12 C. Deneux-Tharaux, 13 J. J. Kurinczuk, 14 and M. Knight, 15 on behalf of the INOSS collaboration

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Summary
Anaphylaxis in pregnancy is a rare but severe complication for both mother and infant. Population-based data on anaphylaxis in pregnancy are lacking from mainland European countries. This multinational study presents the incidence, causative agents, management and maternal and infant outcomes of anaphylaxis in pregnancy. This descriptive multinational study used a combination of retrospective (Finnish medical registries) and prospective population-based studies (UK, France, Belgium and the Netherlands) to identify cases of anaphylaxis. Sixty-five cases were identified among 4,446,120 maternities (1.5 per 100,000 maternities; 95% CI 1.1–1.9). The incidence did not vary between countries. Approximately three-quarters of reactions occurred at the time of delivery. The most common causes were antibiotics in 27 women (43%), and anaesthetic agents in 11 women (17%; including neuromuscular blocking drugs, 7), which varied between countries. Anaphylaxis had very poor outcomes for one in seven mothers and one in seven babies; the maternal case fatality rate was 3.2% (95% CI 0.4–11.0) and the neonatal encephalopathy rate was 14.3% (95% CI 4.8–30.3). Across Europe, anaphylaxis related to pregnancy is rare despite having a multitude of causative agents and different antibiotic prophylaxis protocols.

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Introduction

Anaphylaxis is a severe immune hypersensitivity disorder that is rapid in onset and occurs without premonitory signs. It often involves compromise to the cardiovascular, respiratory, cutaneous and gastro-intestinal systems, and in pregnancy can result in severe morbidity and mortality for both mother and infant [1].

The majority of the literature on anaphylaxis in pregnancy consists of case series and case reports, with limited high quality studies [1, 2]. To date, only two population-based studies have described anaphylaxis in pregnancy; a UK study showed an incidence of 1.6 per 100,000 maternities [3], while a national hospital database study in the USA identified an incidence of 3.8 per 100,000 pregnancy-related hospitalisations [4]. There are no population-based studies examining anaphylaxis in pregnancy in continental European countries.

As anaphylaxis in pregnancy is very rare, national studies from small populations may not accrue sufficient cases unless they are conducted for long periods; on the other hand, multinational studies are able to provide larger numbers that enable more precise estimates of incidence [5]. This study aimed to estimate the incidence, causative agents, management and outcomes of anaphylaxis in pregnancy across Europe using both prospective and retrospective data collection methods.

Methods

Anaphylaxis is defined as a severe, life-threatening generalised or systemic hypersensitivity reaction [6]. It is diagnosed by the presence of at least one of the following criteria: a life-threatening airway problem; life-threatening breathing problem; life-threatening circulatory problem (Fig. 1); in addition, there is sudden onset and rapid progression of symptoms. For inclusion in this study, such a reaction must have occurred at any point during pregnancy or up to 48 h after delivery. In addition, women were not included if the senior attending obstetrician or anaesthetist did not consider the case to be anaphylaxis on clinical grounds.

Women that had anaphylaxis during pregnancy were prospectively identified at a national level in the UK, Netherlands, France and Belgium. The UK data were collected using the UK Obstetric Surveillance System [7]; this study has been published previously [3]. In Belgium and the Netherlands, cases were notified through the respective Belgian Obstetric Surveillance System (B.OSS) and Netherlands Obstetric Surveillance System (NethOSS) [8, 9]. Women in Finland were retrospectively identified in the Finnish Medical Birth Registry linked to the Hospital Discharge Register [10]. A detailed description of data collection is presented in Table S1, and the methodology in each country is presented in Table S2.

The online data collection form used in France, Belgium, Finland and the Netherlands was a modified version of the UKOSS data collection form, with the majority of variables being the same. Identification of the study population is shown in Figure S1. Anonymised information on maternal characteristics, previous medical history, suspected causes and management of anaphylaxis, and maternal and perinatal outcomes of notified cases were entered. The online data collection used the OpenClinica system [11].

The incidence is presented as rate per 100,000 maternities, with the 95% CI estimated using the binomial distribution. Initially, the characteristics of women, management, causative agents and outcomes between the countries were checked to assess comparability. The Chi-squared test was used to assess statistical difference between categorical variables and countries; if there were no statistically significant differences between the countries, they are presented as a combined cohort. Management was different between the UK and mainland Europe, and as a consequence the results are presented separately. Women were categorised according to when the anaphylactic reaction occurred in relation to delivery. These groups included: antenatal (not in delivery suite or theatre); intrapartum (immediately before delivery); and post-delivery (up to 48 h after delivery). Women were categorised using the time of anaphylaxis and time of delivery, suspected causative agent and additional information included in the case notes. It is possible that management and causative agents may have changed over a 10-year period, so a sensitivity analysis was carried out in Finnish women who had anaphylaxis before 2012 to assess any difference in the management and causative agents. Analyses were completed using Stata version 13 (StataCorp LLC, College Station, TX, USA).

Results

There were 65 confirmed cases of anaphylaxis in 4,446,120 maternities, giving an estimated incidence of 1.5 per 100,000 maternities (95% CI 1.1–1.9; Table 1). The Netherlands was unable to collect data for its two reported cases due to changes in the General Data Protection Regulation guidance given to obstetricians in the Netherlands. Results are presented for the remaining 63 cases.

The characteristics of the women are given in Table 2. The majority of reactions, 35 (56%), occurred before delivery, with 16 (25%) reactions occurring in the antenatal...
period (not related to delivery), and 19 (30%) occurring immediately before delivery. Reactions immediately after delivery made up over a third of all reactions (Fig. 2). The timing of reactions according to country and mode of delivery is presented in Table S3. Three out of fourteen women who had a known penicillin allergy were given a penicillin-based antibiotic resulting in an anaphylactic reaction; two women with a known penicillin allergy had a reaction to a cephalosporin.

The majority of the reactions that occurred immediately before delivery, 18 (95%) occurred in women having a caesarean section. Four reactions occurred after administration of anaesthetic agents, three followed suxamethonium and one followed administration of spinal anaesthesia. Figure S2 and Table S4 show that there was only one reaction caused by prophylactic antibiotics before a caesarean section in France and Belgium, and there were no cases in Finland. Two of the three reactions that were the result of antibiotics given for the prophylaxis of Group B streptococcus occurred in France. In those who had reactions after delivery, 12 (43%) women had a reaction to an agent given for the management of a postpartum haemorrhage.

Reactions related to anaesthesia occurred in 11 (17%) women (Fig. 2). The suspected agents were: suxamethonium; suxamethonium or thiopental; lidocaine; sugammadex; unspecified agent but temporally related to anaesthesia.

IgE testing was completed in 9 (32%) women in mainland Europe (this question was not asked in the UK). Seven of nine women had a specified antigen identified; four had an anaesthetic agent confirmed (suxamethonium; sugammadex) and three had a penicillin-based agent

Table 1 Incidence of anaphylaxis in pregnancy across countries.

<table>
<thead>
<tr>
<th>Country</th>
<th>Anaphylaxis in pregnancy</th>
<th>Maternities</th>
<th>Rate per 100,000 (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK</td>
<td>35</td>
<td>2,324,522</td>
<td>1.5 (1.1–2.1)</td>
</tr>
<tr>
<td>France</td>
<td>17</td>
<td>1,125,495</td>
<td>1.5 (0.9–2.4)</td>
</tr>
<tr>
<td>Finland</td>
<td>9</td>
<td>642,430</td>
<td>1.4 (0.6–2.7)</td>
</tr>
<tr>
<td>Netherlands</td>
<td>2</td>
<td>173,013</td>
<td>1.2 (0.1–4.2)</td>
</tr>
<tr>
<td>Belgium</td>
<td>2</td>
<td>180,660</td>
<td>1.1 (0.1–4.0)</td>
</tr>
<tr>
<td>Combined</td>
<td>65</td>
<td>4,446,120</td>
<td>1.5 (1.1–1.9)</td>
</tr>
</tbody>
</table>

*aExcluded from further analysis – see text.
confirmed. Peri-operative anaphylaxis occurred in 36 (57%) women. The suspected causative agents for these women were as follows: 20 (56%) women had a reaction to an antibiotic; anaesthetic agents caused 11 (31%) reactions; and five (14%) reactions were the result of other agents. No anaesthetic-related reaction was associated with epidural analgesia during labour.

The UK and mainland European countries had similar proportions of women receiving oxygen and intravenous fluid to manage the reaction (Table 3). There was a difference in the proportion of women receiving adrenaline, 19 (67.9%) in Finland, Belgium and France combined vs. 27 (93%; p = 0.016) in the UK. A sensitivity analysis was performed without including the women from Finland who had a reaction before 2012. In this restricted cohort, 44 (85%) women received adrenaline, while 45 (88%) received corticosteroid and 29 (67%) received antihistamine.

Two women died giving a case fatality rate of 3.2% (95% CI 0.4–11.0), one from suxamethonium and one from amoxicillin combined with clavulanic acid (Co-amoxiclav; Table 4). There were no perinatal deaths or stillbirths to mothers who had anaphylaxis before delivery. The proportion affected by neonatal encephalopathy was 14.3% (95%CI: 4.8–30.3; Table 5).

Table 3 Management of anaphylaxis in pregnancy in UK compared with European nations. Values are number (proportion of those with information).

<table>
<thead>
<tr>
<th></th>
<th>France, Belgium and Finland (n = 28)</th>
<th>UK (n = 35)</th>
<th>Combined (n = 63)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High flow oxygen</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>22 (88.0%)</td>
<td>27 (79.4%)</td>
<td>49 (83.1%)</td>
</tr>
<tr>
<td>No</td>
<td>3 (12.0%)</td>
<td>7 (20.6%)</td>
<td>10 (16.9%)</td>
</tr>
<tr>
<td><strong>Intravenous fluid</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>25 (92.6%)</td>
<td>30 (85.7%)</td>
<td>55 (88.7%)</td>
</tr>
<tr>
<td>No</td>
<td>2 (7.4%)</td>
<td>5 (14.3%)</td>
<td>7 (11.3%)</td>
</tr>
<tr>
<td><strong>Epinephrine</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>19 (67.9%)</td>
<td>27 (93.1%)</td>
<td>46 (80.7%)</td>
</tr>
<tr>
<td>No</td>
<td>9 (32.1%)</td>
<td>2 (6.9%)</td>
<td>11 (19.3%)</td>
</tr>
<tr>
<td><strong>Antihistamine</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>3 (20.0%)</td>
<td>26 (86.7%)</td>
<td>29 (44.4%)</td>
</tr>
<tr>
<td>No</td>
<td>12 (80.0%)</td>
<td>4 (13.3%)</td>
<td>16 (25.6%)</td>
</tr>
<tr>
<td><strong>Corticosteroid</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>17 (77.3%)</td>
<td>32 (97.0%)</td>
<td>49 (89.1%)</td>
</tr>
<tr>
<td>No</td>
<td>5 (22.7%)</td>
<td>1 (3.0%)</td>
<td>6 (10.9%)</td>
</tr>
</tbody>
</table>

Figure 2 Timing of anaphylaxis in the INOSS study and suspected causative agents. * multiple agents including latex, penicillin, prostaglandin and temazepam. CS, caesarean section; GBS, Group B streptococcus; NSAID, non steroidal anti-inflammatory drug.
Table 4 Severe maternal outcomes in 63 women with anaphylaxis. Values are number (proportion).

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number</th>
<th>Proportion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>2</td>
<td>(3.2%)</td>
</tr>
<tr>
<td>Severe morbidity including death</td>
<td>9</td>
<td>(14.3%)</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>3</td>
<td>(4.8%)</td>
</tr>
<tr>
<td>Thrombotic event</td>
<td>2</td>
<td>(3.2%)</td>
</tr>
<tr>
<td>Othera</td>
<td>4</td>
<td>(6.3%)</td>
</tr>
<tr>
<td>ICU admissionb</td>
<td>28</td>
<td>(45.2%)</td>
</tr>
<tr>
<td>Intubation requiredc</td>
<td>13</td>
<td>(48.1%)</td>
</tr>
</tbody>
</table>

aOne each of: acute renal injury, acute cardiac failure and thrombocytopenia; respiratory distress or failure; stress cardiomyopathy; hypoxic brain injury.

b\(n = 62\).
cOnly collected in France, Belgium and Finland \(n = 27\).

Table 5 Perinatal outcome information available from 35 infants of women who had an anaphylactic reaction before delivery. Values are number (proportion).

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number</th>
<th>Proportion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perinatal deatha</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>Neonatal ICU admissionb</td>
<td>12</td>
<td>(35.3%)</td>
</tr>
<tr>
<td>Neonatal encephalopathy</td>
<td>5</td>
<td>(14.3%)</td>
</tr>
<tr>
<td>Baby cooled</td>
<td>4</td>
<td>(11.4%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>1</td>
<td>(2.9%)</td>
</tr>
<tr>
<td>Apgar ≤ 6@ 5 minc</td>
<td>5</td>
<td>(16.1%)</td>
</tr>
</tbody>
</table>

N.B. four infants were included from two multiple pregnancies.

a\(n = 33\).
b\(n = 34\).
c\(n = 31\).

Discussion

There appears to be a similar incidence of anaphylaxis in pregnancy across five European countries, affecting 1.5 per 100,000 women among almost 4.5 million births. Most reactions occurred at or around the time women gave birth. There was variation in the diagnosis and management of anaphylaxis between the UK and mainland Europe.

The main causative agents for anaphylaxis were antibiotics and anaesthetic agents, in particular neuromuscular blocking drugs [1, 2]. Similar to previous studies, the most commonly suspected causative agent was an antibiotic [2, 12], given either prophylactically for Group B streptococcus [12–14] or for surgical prophylaxis [2]. Three women had anaphylaxis following antibiotic administered for Group B streptococcus, including two in France and one in the UK. Over a fifth of reactions were found to be the direct result of prophylactic use of antibiotics at the time of caesarean section [15, 16]. Half of these reactions occurred once the caesarean section had been carried out. Importantly, had the antibiotics been administered before surgery, the burden of infant morbidity may have been higher. In Finland and France, prophylactic antibiotics were given at induction (before skin incision). The majority of women who had a peri-operative reaction did not receive an IgE specific test to confirm the causative agent involved, which would have important implications for future surgical procedures.

The findings from this study are similar to that of the 6th National Audit Project (NAP6); in particular, antibiotics and neuromuscular blocking drugs were the primary suspected causative agents [17]. It is interesting to note that suxamethonium was the only neuromuscular blocking agent used in this study, whereas rocuronium was the most common agent in NAP6 [17]. This may be explained by preferential use of suxamethonium during induction of general anaesthesia at caesarean section [18]. Furthermore, a previous study in France reported that neuromuscular blocking drugs were the main causes of maternal death from anaphylaxis [19]. It is important that allergy to neuromuscular blocking drugs is identified to guide management of future general anaesthesia.

Three women who had known penicillin allergies were administered the drug resulting in an anaphylactic reaction. This highlights that these cases were preventable, and indicates that a detailed drug allergy history must be taken at booking and immediately before administration of any antibiotics. Human factors have been demonstrated to play a role in medication errors [20]. The World Health Organization surgical checklist should be undertaken before caesarean section to reduce the risk of medical error [21], and we suggest that this concept might be extended to women having vaginal delivery.

The study findings show that an even lower proportion of women received adrenaline in mainland Europe compared with the UK. The NAP6 project stated that there was a low mortality rate from anaphylaxis, which was likely to be a consequence of the early detection and management of reactions [17]. Current guidelines recommend adrenaline as first line management of anaphylaxis, and timely use will prevent hypoxia and mortality [22–24]. In order to improve management, the anaphylaxis algorithm should be immediately available in operating theatres and delivery suites [6, 25].

This study has shown poor outcomes for women who have anaphylaxis, with a 3.5% case fatality rate and 11% of women suffering additional severe morbidity. The Confidential Enquiries into Maternal Deaths in the UK and France report a similar case fatality for anaphylaxis related to pregnancy [19, 26]. Furthermore, there were severe outcomes for infants, with a third of...
infants admitted to neonatal ICU, one in six infants with abnormal Apgar scores, and one in seven with neonatal encephalopathy that required therapeutic cooling. This is consistent with previous case series and literature reviews [1, 2].

This multinational study, which included three countries with obstetric surveillance systems and two other countries using similar methodologies, has provided a large-scale study of a very rare complication of pregnancy. The prospective study design has the added advantage of being able to use a uniform case definition across nations. For the Finnish registry data, the method of case ascertainment allowed routinely identified cases of anaphylaxis to be validated against hospital records. This prevented false positives from being included in the study dataset.

Prospective studies have the same limitations as national surveillance systems, as they rely on reporters to identify cases within each maternity unit and are susceptible to under-ascertainment. In the case of the Netherlands, we had no reported cases entered into the data entry system; as a result, they were only included in the estimate of incidence. For the Finnish registry data, case notification relied on ICD-10 codes for the identification of cases with anaphylaxis. Consequently, the sample was still vulnerable to false negatives, and was reliant on the accuracy of the coding of clinical data for the identification of women with anaphylaxis. The validation of cases resulted in the removal of over half of the women identified using ICD-10 codes. In addition, as the sample was retrospective, it is possible that the management of anaphylaxis was historically different to that during the period of the prospective data collection for the rest of the study.

In conclusion, across five European countries, anaphylaxis related to pregnancy is similarly rare, despite having a multitude of causative agents and different prophylaxis protocols. It is imperative that current international management protocols are followed, which include immediate administration of adrenaline. Against the background of increased medicalisation of childbirth, an accurate drug allergy history and a visible signal of an allergy, for example, a coloured wristband, may prevent a medical error from causing a potentially fatal reaction.

Acknowledgements

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References


Supporting Information

Additional supporting information may be found online via the journal website.


Figure S2. Suspected causes of anaphylaxis in pregnancy in Belgium, France and Finland. *indicates Finnish case **includes one Finnish case.

Table S1. Summary of the case identification from each country.
Table S2. Summary of data collection from each country.
Table S3. Timing of anaphylaxis by country and mode of delivery.
Table S4. Suspected cause of anaphylaxis by country.
Original Research Article

Epidemiological analysis of peripartum hysterectomy across nine European countries

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Abstract

Introduction: Peripartum hysterectomy is a surgical procedure performed for severe obstetric complications such as major obstetric hemorrhage. The prevalence of peripartum hysterectomy in high-resource settings is relatively low. Hence, international comparisons and studying indications and associations with mode of birth rely on the use of national obstetric survey data. Objectives were to calculate the prevalence and indications of peripartum hysterectomy and its association with national cesarean section rates and mode of birth in nine European countries.

Material and methods: We performed a descriptive, multinational, population-based study among women who underwent peripartum hysterectomy. Data were collected from national or multiregional databases from nine countries participating in the International Network of Obstetric Survey Systems. We included hysterectomies performed from 22 gestational weeks up to 48 hours postpartum for obstetric hemorrhage, as this was the most restrictive, overlapping case definition between all countries. Main outcomes were prevalence and indications of peripartum hysterectomy. Additionally, we compared prevalence of peripartum hysterectomy between women giving birth vaginally and by cesarean section, and between women giving birth with and without previous cesarean section. Finally, we calculated correlation between prevalence of peripartum hysterectomy and national cesarean section rates, as well as national rates of women giving birth after a previous cesarean section.

Results: A total of 1302 peripartum hysterectomies were performed in 2 498 013 births, leading to a prevalence of 5.2 per 10000 births ranging from 2.6 in Denmark to 10.7 in Italy. Main indications were uterine atony (35.3%) and abnormally invasive placenta (34.8%). Relative risk of hysterectomy after cesarean section compared with
1 | INTRODUCTION

Peripartum hysterectomy refers to surgical removal of the uterus during pregnancy or postpartum.1 It is usually performed for severe obstetric complications such as major obstetric hemorrhage, abnormally invasive placenta, uterine rupture, or sepsis. Peripartum hysterectomy is defined by the World Health Organization as a maternal near-miss criterion and used as a proxy for severe postpartum hemorrhage and therefore frequently used as an outcome of interest in obstetric surveillance.2

The association between peripartum hysterectomy and cesarean section has previously been described, with relative risk for women giving birth by cesarean section ranging from 8.5 to 18.3.3–8 In addition, pregnancy in a woman who gave birth by cesarean section previously is a risk factor for abnormally invasive placenta, which may in turn lead to hysterectomy. This risk is known to increase for every additional previous cesarean section.9 Such associations are of particular interest in light of the rising cesarean section rates worldwide because these could potentially lead to increasing rates of peripartum hysterectomies as well.

Prevalence of peripartum hysterectomy in high-resource settings is relatively low.10 Hence, indications and outcomes are often studied retrospectively, or through national obstetric survey systems.11–15 Multinational comparisons of prevalence and outcomes to optimize management strategies may be facilitated by international collaborations combining national data.1,16

The main aim of this study was to compare the prevalence of peripartum hysterectomy between high-income countries, as part of the International Network of Obstetric Survey Systems (INOSS). Secondary aims were to describe the indications for hysterectomy, and perform analyses of prevalence of peripartum hysterectomy stratified by mode of birth and previous cesarean section. In addition, we examined the correlation between national rates of peripartum hysterectomy and national cesarean section rates, and the rate of women giving birth after previous cesarean section.

vaginal birth was 9.1 (95% CI 8.0–10.4). Relative risk for hysterectomy for birth after previous cesarean section compared with birth without previous cesarean section was 10.6 (95% CI 9.4–12.1). A strong correlation was observed between national cesarean section rate and prevalence of peripartum hysterectomy (ρ = 0.67, P < .05).

Conclusions: Prevalence of peripartum hysterectomy may vary considerably between high-income countries. Uterine atony and abnormally invasive placenta are the commonest indications for hysterectomy. Birth by cesarean section and birth after previous cesarean section are associated with nine-fold increased risk of peripartum hysterectomy.

**KEYWORDS**

cesarean section, maternal morbidity, mode of birth, obstetric hemorrhage, peripartum hysterectomy

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**Key message**

Peripartum hysterectomy rates vary considerably between high-income countries and are associated with national cesarean section rates.

2 | MATERIAL AND METHODS

This was a descriptive, multinational, population-based study. We used data from nine countries participating in INOSS that had previously conducted studies on peripartum hysterectomy. Most of these countries, except France and Slovakia, have previously published outcomes of peripartum hysterectomy surveillance.11–15,17–20 INOSS is an international collaboration of national obstetric survey systems, aiming to increase knowledge of management of uncommon obstetric complications.16 Participating in this study were: Slovak Obstetric Survey System (SOSS) in Slovakia, Italian Obstetric Surveillance System (ItOSS) in Italy, Belgian Obstetric Surveillance System (B.OSS) in Belgium, Épidémiologie de la Morbidité Maternelle Sévère (EPIMOMS) in France, Nordic Obstetric Surveillance System (NOSS) with data from Denmark, Finland and Sweden, Landelijke studie naar Ethische determinanten van Maternale Morbiditeit (LEMMOn) in the Netherlands, and United Kingdom Obstetric Surveillance System (UKOSS) in the UK. All were nationwide studies except for EPIMOMS in France, which included six regions (Alsace, Auvergne, Basse-Normandie, Île-de-France, Lorraine, and Rhône-Alpes) covering 20% of national births and ItOSS, which encompassed six regions (Piedmont, Emilia-Romagna, Tuscany, Lazio, Campania, and Sicily) representing 49% of births in Italy.

Methods of data collection were described previously.20–25 In brief, all countries performed national or multiregional survey studies in which women who underwent peripartum hysterectomy were identified. Identification of cases was performed in most countries.
by monthly communication (electronic database, mailing or paper) to appointed clinicians in each maternity unit. When a case was reported, further details were requested through a data collection form. To ensure completeness of data, regular reminders were sent and a ‘nothing to report’ response was requested. All data were collected prospectively, except for the data from Slovakia, which were collected retrospectively. Studies were performed during different periods, from August 2004 to August 2016. Validation and identification of additional cases were performed after cross-checking health registers and hospital databases for the Nordic countries (Hospital Discharge Register, Medical Birth Register and delivery logbooks). Each country managed and cleaned their own database after which all anonymized databases were merged in Leiden, The Netherlands (see Supplementary material, Table S1).

In order to overcome differences in case selection between studies we applied a uniform case definition. Definitions used in the different survey studies were specified for inclusion criteria such as minimum gestational age, postpartum follow up, inclusion of non-obstetric indications (such as malignancy), or other specific inclusion or exclusion criteria if present (such as including only cases of obstetric hemorrhage in Italy). To arrive at a uniform definition, the most restrictive definition was chosen to account for differences. We opted not to exclude hysterectomies in case of missing information regarding indication or gestational age, as it was postulated that the very few women who would have had an indication other than obstetric hemorrhage or a peripartum hysterectomy before 22 weeks of gestation would be greatly outnumbered by those with hemorrhage or hysterectomy ≥22 weeks. The most restrictive definition was defined as hysterectomies performed from the 22nd week of gestation up to 48 hours postpartum for obstetric hemorrhage (see Supplementary material, Table S2).

All countries provided background data on number of births during the study period. Background data differed between countries on the lower limit of gestational age, ranging from ≥22 weeks to 25 weeks (see Supplementary material, Table S1). For countries registering births ≥24 weeks, calculation of births ≥22 weeks was not possible. In a previous INOSS study, correction of background data resulted in minimal non-significant differences because the proportion of births at those gestational ages was very low in all countries, so we decided not to perform such a correction. Additionally, all countries provided aggregate data on national cesarean section rates, and numbers of cesarean sections and vaginal births. When actual numbers of cesarean section and vaginal births were unknown, these were estimated by multiplying the total number of births by the cesarean section rate. Numbers of women giving birth with and without previous cesarean section were calculated accordingly.

There were differences between studies in coding indications of hysterectomy. Some countries reported only one indication per hysterectomy whereas others coded all indications that arose during the process leading to hysterectomy. Therefore, we included the most important indication of those registered by applying a hierarchical system. From the indications listed, the one highest in rank was used. The hierarchy of indications, which was determined after reaching consensus among researchers of participating countries, in order of importance, was as follows: abnormally invasive placenta, placenta previa, uterine rupture, placental abruption, uterine atony, infection, cervical laceration, fibroids, unspecified hemorrhage, diffuse intravascular coagulation, and other.

Main outcomes were overall prevalence and indications of peripartum hysterectomy. Secondary outcomes were prevalence of peripartum hysterectomy for women giving birth vaginally and women who underwent cesarean section, and for women giving birth with and without previous cesarean section, with calculations of relative risk. Additionally, correlations between prevalence of peripartum hysterectomy and national cesarean section rates and national proportion of women giving birth after previous cesarean section were recorded.

### 2.1 Statistical analyses

Prevalence was calculated per 10,000 births with 95% CI or per 10,000 cesarean sections or vaginal births where appropriate. For calculation of relative risk, individual data were used from women with hysterectomy, but only aggregate data were available for women without hysterectomy. To adjust for weighting and clustering, calculation of total proportions and relative risks was done using a fixed-effects model. Descriptive data are presented with mean (95% CI) or median (interquartile range) whenever appropriate. Proportions were calculated after subtracting the missing data from the totals, as they cannot be classified in either category of binary variables. Correlation between prevalence of peripartum hysterectomy and mode of birth and previous cesarean section rates per country were calculated using nonparametric Spearman rank order correlations (ρ). Results were considered statistically significant when \( P < .05 \). All analyses were performed using IBM SPSS Statistics version 18.0 (IBM Corp.), R version 6.3.6 (cran.r-project.org) and Office Excel 2019 (Microsoft Corp.).

### 2.2 ETHICAL APPROVAL

Due to the nature of this study, ethical approval was not required. Each study, from which data were used, was approved by their national or local ethics committee.

### 3 RESULTS

A total of 1393 peripartum hysterectomies were reported in the nine participating countries. During the study period, 2,498,013 births were registered. A total of 91 hysterectomies were excluded: 17 because the hysterectomy was performed at gestational age <22 weeks, 72 because of postpartum interval >48 hours, two hysterectomies because of indication other than
obstetric hemorrhage (one gynecological malignancy and one necrotic uterus after uterine artery embolization). Using the uniform definition for all data sets, 1302 hysterectomies were included leading to a prevalence of 5.2 (95% CI 4.9-5.5) per 10 000 births. Prevalence was highest in Italy with 10.7 (95% CI 9.8-11.6) hysterectomies per 10 000 births and lowest in Denmark with 2.6 (CI 2.0-3.5) hysterectomies per 10 000 births (Table 1, Figure 1). As the result of differences in the time period in which studies were performed, we compared countries that included cases before 2012 (The Netherlands, Denmark, the UK, Finland, Sweden) with countries that included cases starting in 2012 (Italy, France, Belgium, Slovakia). The prevalence was 3.7 (3.4-4.0) versus 7.3 (6.8-7.9) per 10 000 births, respectively.

Overall, background characteristics such as maternal age, parity, and body mass index were comparable between countries (Table 2). A total of 996/1292 (77.1%) women gave birth by cesarean section and 452/770 (58.7%) were planned. Moreover, 586/1177 (49.8%) women had given birth by cesarean section in a previous pregnancy.

### TABLE 1 Prevalence of peripartum hysterectomy using national definitions and after use of uniform definition

<table>
<thead>
<tr>
<th>Countries (study)</th>
<th>PRH (n)</th>
<th>Births (n)</th>
<th>Prevalence per 10 000 births (95% CI)</th>
<th>PRH uniform definition (n)</th>
<th>Prevalence -uniform definition per 10 000 births (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Denmark (NOSS) Apr 2009-Dec 2011</td>
<td>50</td>
<td>168 170</td>
<td>3.0 (2.3-3.9)</td>
<td>44</td>
<td>2.6 (2.0-3.5)</td>
</tr>
<tr>
<td>Netherlands (LEMMon)</td>
<td>110</td>
<td>358 874</td>
<td>3.1 (2.5-3.7)</td>
<td>95</td>
<td>2.7 (2.2-3.2)</td>
</tr>
<tr>
<td>Belgium (BOSS) Jan 2012-Dec 2013</td>
<td>84</td>
<td>252 272</td>
<td>3.3 (2.7-4.1)</td>
<td>73</td>
<td>2.9 (2.3-3.6)</td>
</tr>
<tr>
<td>Sweden (NOSS) Sep 2009-Aug 2011</td>
<td>52</td>
<td>175 575</td>
<td>3.0 (2.3-3.9)</td>
<td>52</td>
<td>3.0 (2.3-3.9)</td>
</tr>
<tr>
<td>UK (UKOSS) Feb 2005-Feb 2006</td>
<td>315</td>
<td>609 300</td>
<td>5.2 (4.6-5.8)</td>
<td>276</td>
<td>4.5 (4.0-5.0)</td>
</tr>
<tr>
<td>Finland (NOSS) Apr 2009-Aug 2011</td>
<td>74</td>
<td>145 546</td>
<td>5.1 (4.1-6.4)</td>
<td>72</td>
<td>5.0 (3.9-6.2)</td>
</tr>
<tr>
<td>France (EPIMOMS) May 2012-Nov 2013</td>
<td>104</td>
<td>182 309</td>
<td>5.7 (4.7-6.9)</td>
<td>98</td>
<td>5.4 (4.4-6.6)</td>
</tr>
<tr>
<td>Slovakia (SOSS) Jan 2012-Dec 2014</td>
<td>104</td>
<td>146 972</td>
<td>7.1 (5.8-8.6)</td>
<td>103</td>
<td>7.0 (5.8-8.5)</td>
</tr>
<tr>
<td>Italy (ITOSS) Sep 2014-Aug 2016</td>
<td>500</td>
<td>458 995</td>
<td>10.9 (10.0-11.9)</td>
<td>489</td>
<td>10.7 (9.8-11.6)</td>
</tr>
<tr>
<td>Total</td>
<td>1 393</td>
<td>2 498 013</td>
<td>1 302</td>
<td>5.2 (4.9-5.5)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; PRH, peripartum hysterectomy.
### TABLE 2  Maternal and pregnancy characteristics at time of peripartum hysterectomy

<table>
<thead>
<tr>
<th>Women's characteristics</th>
<th>Belgium (n = 73)</th>
<th>Denmark (n = 44)</th>
<th>Finland (n = 72)</th>
<th>France (n = 98)</th>
<th>UK (n = 276)</th>
<th>Italy (n = 489)</th>
<th>Netherlands (n = 95)</th>
<th>Slovakia (n = 103)</th>
<th>Sweden (n = 52)</th>
<th>TOTAL (n = 1302)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age, years</td>
<td>34.6 ± 4.4</td>
<td>33.7 ± 5.2</td>
<td>34.2 ± 5.1</td>
<td>34.4 ± 6.0</td>
<td>34.0 ± 5.4</td>
<td>35.6 ± 5.7</td>
<td>34.3 ± 4.3</td>
<td>31.7 ± 5.5</td>
<td>34.2 ± 4.9</td>
<td>34.5 ± 5.5</td>
</tr>
<tr>
<td>Missing, n (%)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>5 (1.0)</td>
<td>0 (0.0)</td>
<td>3 (2.9)</td>
<td>0 (0.0)</td>
<td>8 (0.6)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>24.6 ± 4.5</td>
<td>26.1 ± 5.5</td>
<td>24.9 ± 5.5</td>
<td>24.9 ± 5.4</td>
<td>26.7 ± 5.7</td>
<td>24.9 ± 4.5</td>
<td>24.9 ± 6.1</td>
<td>27.1 ± 3.8</td>
<td>28.0 ± 5.9</td>
<td>25.6 ± 5.2</td>
</tr>
<tr>
<td>Missing, n (%)</td>
<td>14 (19.2)</td>
<td>2 (4.5)</td>
<td>2 (2.8)</td>
<td>8 (8.2)</td>
<td>36 (13.0)</td>
<td>71 (14.7)</td>
<td>31 (32.6)</td>
<td>8 (7.8)</td>
<td>7 (13.5)</td>
<td>180 (13.8)</td>
</tr>
<tr>
<td>Parity, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primiparous</td>
<td>10 (13.7)</td>
<td>12 (27.3)</td>
<td>19 (26.4)</td>
<td>25 (26.0)</td>
<td>33 (12.0)</td>
<td>145 (31.5)</td>
<td>16 (16.8)</td>
<td>18 (18.0)</td>
<td>10 (19.2)</td>
<td>288/1269 (22.7)</td>
</tr>
<tr>
<td>Multiparous</td>
<td>63 (86.3)</td>
<td>32 (72.7)</td>
<td>53 (73.6)</td>
<td>71 (74.0)</td>
<td>243 (88.0)</td>
<td>316 (68.5)</td>
<td>79 (83.2)</td>
<td>82 (82.0)</td>
<td>42 (80.8)</td>
<td>981/1269 (77.3)</td>
</tr>
<tr>
<td>Missing, n (%)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>2 (2.0)</td>
<td>0 (0.0)</td>
<td>28 (5.7)</td>
<td>0 (0.0)</td>
<td>3 (2.9)</td>
<td>0 (0.0)</td>
<td>33 (2.5)</td>
</tr>
<tr>
<td>Mode of birth, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cesarean section</td>
<td>49 (68.1)</td>
<td>36 (81.8)</td>
<td>52 (72.2)</td>
<td>67 (68.4)</td>
<td>226 (81.9)</td>
<td>410 (84.5)</td>
<td>59 (62.1)</td>
<td>51 (52.0)</td>
<td>46 (88.5)</td>
<td>996/1202 (77.1)</td>
</tr>
<tr>
<td>Vaginal birth</td>
<td>23 (31.9)</td>
<td>8 (18.2)</td>
<td>20 (27.8)</td>
<td>31 (31.6)</td>
<td>50 (18.1)</td>
<td>75 (15.5)</td>
<td>36 (37.9)</td>
<td>47 (48)</td>
<td>6 (11.5)</td>
<td>296/1202 (22.9)</td>
</tr>
<tr>
<td>Missing</td>
<td>1 (1.4)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>4 (0.8)</td>
<td>0 (0.0)</td>
<td>5 (4.9)</td>
<td>0 (0.0)</td>
<td>10 (0.8)</td>
</tr>
<tr>
<td>Planned cesarean section, n (%)³</td>
<td>13 (26.5)</td>
<td>15 (41.7)</td>
<td>28 (53.8)</td>
<td>43 (64.2)</td>
<td>N/A</td>
<td>285 (69.5)</td>
<td>11 (18.6)</td>
<td>26 (51.0)</td>
<td>31 (67.4)</td>
<td>452/907 (58.7)</td>
</tr>
<tr>
<td>Missing</td>
<td>1 (1.4)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>N/A</td>
<td>88 (18.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>89 (6.8)</td>
</tr>
<tr>
<td>Gestational age, weeks, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>22⁰-23⁰-6⁰</td>
<td>1 (1.4)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (1.0)</td>
<td>0 (0.0)</td>
<td>2 (0.4)</td>
<td>1 (1.1)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>5/992 (0.4)</td>
</tr>
<tr>
<td>24⁰-31⁰-6⁰</td>
<td>9 (12.3)</td>
<td>2 (4.5)</td>
<td>4 (5.6)</td>
<td>6 (6.1)</td>
<td>24 (8.9)</td>
<td>31 (6.8)</td>
<td>5 (5.3)</td>
<td>11 (11.1)</td>
<td>3 (5.8)</td>
<td>95/992 (7.5)</td>
</tr>
<tr>
<td>32⁰-36⁰-6⁰</td>
<td>23 (31.5)</td>
<td>13 (29.5)</td>
<td>20 (27.8)</td>
<td>22 (22.4)</td>
<td>80 (29.5)</td>
<td>166 (36.2)</td>
<td>16 (16.8)</td>
<td>26 (25.7)</td>
<td>21 (40.4)</td>
<td>387/992 (30.7)</td>
</tr>
<tr>
<td>≥37⁰⁰</td>
<td>40 (54.8)</td>
<td>29 (65.9)</td>
<td>48 (66.7)</td>
<td>69 (70.4)</td>
<td>167 (61.6)</td>
<td>259 (56.6)</td>
<td>73 (76.8)</td>
<td>62 (61.4)</td>
<td>28 (53.8)</td>
<td>775/992 (61.4)</td>
</tr>
<tr>
<td>Missing</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>5 (1.8)</td>
<td>31 (6.3)</td>
<td>0 (0.0)</td>
<td>4 (3.9)</td>
<td>0 (0.0)</td>
<td>40 (3.1)</td>
</tr>
<tr>
<td>Previous cesarean section, n (%)</td>
<td>36 (50.0)</td>
<td>25 (56.8)</td>
<td>24 (33.3)</td>
<td>36 (37.9)</td>
<td>149 (54.0)</td>
<td>228 (51.0)</td>
<td>40 (42.1)</td>
<td>20 (83.3)</td>
<td>28 (53.8)</td>
<td>586/1177 (49.8)</td>
</tr>
<tr>
<td>Missing</td>
<td>1 (1.4)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>3 (3.1)</td>
<td>0 (0.0)</td>
<td>42 (8.6)</td>
<td>0 (0.0)</td>
<td>79 (76.7)</td>
<td>0 (0.0)</td>
<td>125 (9.6)</td>
</tr>
</tbody>
</table>

Note: All data are presented as n (%) or mean ± standard deviation unless otherwise specified. Percentages are calculated after subtracting missing data.

³Presented as percentage of number of cesarean sections.
In 670 women multiple indications were coded before use of the hierarchical system. Commonest indication was uterine atony for 459 women (35.3%) followed by abnormally invasive placenta for 453 women (34.8%), and uterine rupture in 98 women (7.5%). Observed frequencies for abnormally invasive placenta indication varied from 14/73 (19.2%) in Belgium up to 26/52 (50%) in Sweden. Hysterectomy in case of placenta previa only was not performed at all in Belgium and Denmark whereas this was the indication in 41/276 (14.9%) of women in the UK. Hemorrhage due to cervical lacerations was notably higher in Denmark (6/44) compared with other countries (Table 3).

Prevalence of peripartum hysterectomy after cesarean section was highest in Italy with 23.2 per 10 000 cesarean sections (95% CI 21.1-25.6) and lowest in Belgium with 9.0 per 10 000 cesarean sections (95% CI 6.8-11.9). Following vaginal birth, prevalence was highest in Slovakia with 4.6 per 10 000 births (95% CI 3.5-6.1) and lowest in Sweden with 0.4 per 10 000 births (95% CI 0.2-0.9). Overall relative risk for hysterectomy after cesarean section compared with vaginal birth was 9.1 (95% CI 8.0-10.4) (Table 4). Relative risk ranged from 2.5 (95% CI 1.7-3.7) in Slovakia to 38.2 (95% CI 16.3-89.5) in Sweden, in the latter country this being due to a very low incidence after vaginal birth. Because of the unknown number of planned cesarean hysterectomies in case of suspected abnormally invasive placenta, calculations were repeated after excluding women with hysterectomy for abnormally invasive placenta. Relative risk of peripartum hysterectomy in women who gave birth by cesarean section versus those who gave birth vaginally was 6.8 (95% CI 5.9-8.0) per 10 000 births (see Supplementary material, Table S3). There was a strong, positive correlation between national cesarean section rate and prevalence of peripartum hysterectomy ($\rho = 0.67, n = 9, P < .05$) (Figure 2).

Prevalence of peripartum hysterectomy in women with previous cesarean section varied from 10.7 per 10 000 births (95% CI 7.9-14.6) in the Netherlands to 36.7 (95% CI 31.3-43.1) in the UK. In women without previous cesarean section, prevalence varied considerably less, ranging from 1.3 per 10 000 births (95% CI 0.8-2.0) in Denmark to 3.7 per 10 000 births in Finland and France. Overall relative risk for peripartum hysterectomy in women who had given birth by cesarean section in a previous pregnancy compared with women without a previous cesarean section this was 10.6 (95% CI 9.4-12.1) (Table 5). After excluding women with hysterectomy for abnormally invasive placenta this relative risk was still 6.4 (95% CI 5.5-7.6) per 10 000 births (see Supplementary material, Table S4). A statistically non-significant weak correlation was observed between national proportions of women giving birth with a previous cesarean section and national prevalence of pregnancy-related hysterectomy ($\rho = 0.26, n = 8, P = .5$) (Figure 3).

4 | DISCUSSION

The prevalence of peripartum hysterectomy varied significantly in nine European countries. Prevalence was considerably higher in

| Table 3: Most important indication for peripartum hysterectomy presented as n (%) |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Indications of hysterectomy | Belgium (n = 97) | Denmark (n = 44) | Finland (n = 11) | France (n = 72) | Germany (n = 44) | Italy (n = 278) | Netherlands (n = 49) | Slovakia (n = 103) | Sweden (n = 52) | Total (n = 1302) |
| Uterine atony | 29 (29.7%) | 12 (27.3%) | 17 (22.6%) | 19 (25.6%) | 23 (32.5%) | 14 (22.2%) | 14 (28.5%) | 10 (19.4%) | 199 (40.7%) | 459 (35.3%) |
| Abnormally invasive placenta | 14 (14.3%) | 17 (38.6%) | 16 (20.2%) | 23 (32.1%) | 103 (73.3%) | 188 (38.4%) | 36 (72.5%) | 36 (35.2%) | 453 (34.8%) | 453 (34.8%) |
| Uterine rupture | 10 (10.3%) | 9 (20.5%) | 17 (23.6%) | 9 (12.5%) | 30 (21.1%) | 24 (50%) | 30 (61.2%) | 16 (15.5%) | 98 (7.5%) | 98 (7.5%) |
| Unspecified hemorrhage | 5 (5.2%) | 0 | 11 (15.3%) | 2 (2.2%) | 14 (14.3%) | 14 (22.2%) | 14 (28.5%) | 10 (19.4%) | 93 (7.1%) | 44 (3.4%) |
| Placenta previa | 0 | 0 | 9 (12.5%) | 0 | 9 (12.5%) | 11 (21.1%) | 11 (22.4%) | 10 (19.4%) | 7 (13.5%) | 7 (13.5%) |
| Placental abruption | 0 | 2 (4.5%) | 0 | 6 (6.1%) | 0 | 20 (41.3%) | 0 | 2 (3.8%) | 0 | 2 (3.8%) |
| Cervical laceration | 0 | 6 (13.6%) | 0 | 6 (6.1%) | 0 | 20 (41.3%) | 0 | 2 (3.8%) | 0 | 2 (3.8%) |
| Fibroids | 0 | 2 (4.5%) | 0 | 6 (6.1%) | 0 | 20 (41.3%) | 0 | 2 (3.8%) | 0 | 2 (3.8%) |
| DIC | 0 | 1 (2.2%) | 0 | 1 (2.2%) | 0 | 20 (41.3%) | 0 | 2 (3.8%) | 0 | 2 (3.8%) |
| Infection | 0 | 1 (2.2%) | 0 | 1 (2.2%) | 0 | 20 (41.3%) | 0 | 2 (3.8%) | 0 | 2 (3.8%) |
| Other | 0 | 3 (6.8%) | 0 | 7 (7.1%) | 0 | 20 (41.3%) | 0 | 2 (3.8%) | 0 | 2 (3.8%) |
| Missing | 13 (13.7%) | 0 | 0 | 3 (1.1%) | 0 | 7 (1.1%) | 0 | 23 (4.6%) | 0 | 23 (1.8%) |

Abbreviations: DIC, disseminated intravascular coagulopathy.
women giving birth by cesarean section and in women who had
given birth by cesarean section in a previous pregnancy. Additionally,
indications for hysterectomy also varied notably between countries
and considerable variance was observed for all reported indications.
Such differences may result from differences in women’s character-
istics, national cesarean section rates, and national rates of preg-
nant women with scarred uteri. Such differences may also reflect
differences in clinical management of major obstetric hemorrhage
between participating countries.

Compared with a systematic review and meta-analysis where
weighted prevalence for upper- and high-income countries was cal-
culated at 7 per 10 000 births, our study demonstrated lower prev-
ance for all countries except Italy. Another study on emergency
peripartum hysterectomy in high-income countries, reported prev-
ance for most European countries <10 per 10 000 births, in line
with our results.8

We found a nine-fold higher risk of hysterectomy after cesarean
section. However, 77% of women undergoing hysterectomy were
delivered by cesarean section and more than half of these were
planned. Reason for this may be antenatal diagnosis of placenta
previa with or without abnormally invasive placenta, in which case
vaginal birth is not an option and risk of hysterectomy is very high.27
The number of planned cesarean hysterectomies was not known.
Therefore, we repeated calculations after excluding women who
had hysterectomy for abnormally invasive placenta, which was the
second most frequent indication among all hysterectomies. In these
women, it is the indication for the cesarean section that places them
at increased risk of hysterectomy rather than the indication itself.
Some of these hysterectomies might in fact have been planned be-
fore birth. However, even following exclusion of women with ab-
normally invasive placenta, the prevalence of hysterectomy after
cesarean section and in birth following a previous cesarean section
both remained significantly higher. Our results are in line with liter-
ature, where cesarean section is a strong risk factor for emergency
peripartum hysterectomy.8 Increased risk of hysterectomy after
previous cesarean section has been shown before and was demon-
strated to be independent of the intended mode of birth.8,28 As such,
the variance of prevalence between countries might, to a consid-
erable extent, be explained by the difference in national cesarean
section rates.

The strength of this study is its unique multinational charac-
ter including data from nine nationwide or multiregional studies.
Collaboration between national and multiregional obstetric survey
systems previously led to insights into prevalence and management
of uterine rupture.26 The INOSS collaboration enables the collection
of considerably robust data regarding rare obstetric diseases.

Main limitations arise from the fact that included studies were
performed in different time intervals, over 2 or 3 consecutive years
with little or no overlap. Obstetric practice and risk factors such as
cesarean section rates might have changed over time.8,13,29 Data
stratified by year would reflect differences between studies rather
than being indicative of changes in practice over time. However,
pooling data from recent and older studies showed a marked differ-
ence in prevalence of hysterectomy which, in light of other evidence,
may be the result of rising cesarean section rates. Furthermore, there
were 40 registered hysterectomies with missing information on ges-
tational age. Given the fact that only 1% of all hysterectomies in the
database were excluded because of a gestational age <22 weeks, we
opted that excluding these cases would lead to exclusion of actu-
ally valid cases, which would lead to underestimation of prevalence.
Also, a previous cesarean section is strongly associated with birth by
cesarean in the index pregnancy. In the calculation of the correla-
tion between prevalence of hysterectomy and mode of birth, pre-
vious cesarean section should be taken into consideration. As such,
calculation of adjusted relative risks for each exposure would have
led to better estimation of the independent role of each of them.
However, for the background data we only had aggregate numbers
for mode of birth and for previous cesarean section and could not

| TABLE 4 Relative risk of peripartum hysterectomy for cesarean section compared with vaginal birth |
|-----------------------------------------------|-----------------------------------------------|
| Country          | Cesarean section rate (%) | Cesarean section | Vaginal birth |
|                  | Number of PRH | Number of CS | Prevalence<sup>a</sup> (95% CI) | Number of PRH | Number of vaginal births | Prevalence<sup>a</sup> (95% CI) | Relative risk |
| Belgium          | 21.5 | 49 | 54,369 | 9.0 (6.8-11.9) | 23 | 197,903 | 1.2 (0.7-1.7) | 7.8 (4.7-12.7) |
| Denmark          | 21.3 | 36 | 35,821 | 10.1 (7.3-13.9) | 8 | 132,349 | 0.6 (0.3-1.2) | 16.6 (7.7-35.8) |
| Finland          | 16.2 | 52 | 23,542 | 22.1 (16.9-29.0) | 20 | 122,004 | 1.6 (1.1-2.6) | 13.5 (8.0-22.6) |
| France           | 21.5 | 67 | 39,194 | 17.1 (13.5-21.7) | 31 | 143,115 | 2.2 (1.5-3.1) | 7.9 (5.2-12.1) |
| Italy            | 38.5 | 410 | 176,713 | 23.2 (21.1-25.6) | 75 | 282,282 | 2.6 (2.1-3.3) | 8.8 (6.8-11.2) |
| The Netherlands  | 15.0 | 59 | 53,762 | 11.0 (8.5-14.2) | 36 | 305,112 | 1.2 (0.9-1.6) | 9.3 (6.1-14.1) |
| Slovakia         | 30.5 | 51 | 44,826 | 11.4 (8.7-15.0) | 47 | 102,146 | 4.6 (3.5-6.1) | 2.5 (1.7-3.7) |
| Sweden           | 16.7 | 46 | 29,327 | 15.7 (11.8-20.9) | 6 | 146,248 | 0.4 (0.2-0.9) | 38.2 (16.3-89.5) |
| United Kingdom   | 23.5 | 226 | 143,185 | 15.8 (13.9-18.0) | 50 | 466,115 | 1.1 (0.8-1.4) | 14.7 (10.8-20.0) |
| Total            | 24.0 | 996 | 600,739 | 296 | 1,897,274 | 9.1 (8.0-10.4) |

Abbreviations: CI, confidence Interval; CS, cesarean sections; PRH, peripartum hysterectomy.
<sup>a</sup>Prevalence per 10 000 births or cesarean sections.
perform such analysis. Accordingly, in the correlation of prevalence of peripartum hysterectomy with previous cesarean section, taking parity into account would lead to more valid results. Also, the number of previous cesarean sections adds up to the risk of hysterectomy and other serious morbidity with every additional operation, as previously described. Unfortunately, in our database we only had access to binary information on presence of a previous cesarean section. Therefore, the effect of number of previous cesareans was not measured. Another limitation is the fact that case identification and study objectives differed between countries. Seven of nine studies were designed specifically to report peripartum hysterectomy whereas the studies from the Netherlands and France included women with severe maternal morbidity. In Slovakia, data were collected retrospectively, which may have led to some underreporting.
Nonetheless, their numbers still gave them the second highest prevalence; actual prevalence may have been even higher.

For enhanced comparability of national survey studies, collectively designed surveillance studies using uniform criteria are required and INOSS may provide an important platform to perform such studies. In addition, use of a uniform definition for upcoming studies is important. Therefore, INOSS proposed a definition of ‘pregnancy-related hysterectomy’ using a Delphi process: “Surgical removal of the uterus during pregnancy or up to 42 days postpartum”. This definition is wide enough to include all indications and pregnancy intervals. As our specific study includes only a subset of women who had a hysterectomy around the time of birth, we decided to apply the common terminology “peripartum hysterectomy” in this paper. Streamlining multiple national surveys is necessary to overcome problems related to different study intervals.

5 | CONCLUSION

Prevalence of peripartum hysterectomy varied widely between countries and was higher in countries with higher cesarean section rates. Commonest indications were uterine atony and abnormally invasive placenta. Rate of peripartum hysterectomy was considerably higher in women who gave birth by cesarean section as well as in women with a previous cesarean section. Further investigation is necessary to fully understand the underlying factors that contribute to these differences. Further work is needed to determine optimal management strategies and comparison of those strategies between countries.

ACKNOWLEDGMENTS

We thank Ms Bente Elgersma for her contribution to building the database. The Netherlands: NethOSS board Kitty Bloemenkamp (also INOSS chair), Jos van Rooysen, Timme Schaap, Thomas van den Akker, Joost Zwart. We would like to acknowledge all clinicians reporting data to the LEMMoN study between 2004 and 2006. Italy: We would like to acknowledge all clinicians reporting data to the ItOSS study. Finland: Kati Ojala (Oulu University Hospital); Maija-Riitta Ordén (Kuopio University Hospital), Nanneli Pallasmaa (Turku University Hospital and Outi Palomäki (Tampere University Hospital), Anna-Majia Tapper (UCH Hylvinkää Hospital), Outi Äyräs (Helsinki University Hospital). Sweden: Karin Källén, Karin Gottvall and all clinicians reporting to the NOSS study between 2009 and 2011. France: Epimeoms study, all clinicians and research staff who contributed to case identification and data collection. We also want to thank all clinicians who contributed to case identification and data collection in the UK, Denmark, Slovakia and Belgium. Permission has been obtained from all named persons.

CONFLICTS OF INTEREST

None.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

Frequency and management of maternal infection in health facilities in 52 countries (GLOSS): a 1-week inception cohort study

The WHO Global Maternal Sepsis Study (GLOSS) Research Group*

Summary

Background Maternal infections are an important cause of maternal mortality and severe maternal morbidity. We report the main findings of the WHO Global Maternal Sepsis Study, which aimed to assess the frequency of maternal infections in health facilities, according to maternal characteristics and outcomes, and coverage of core practices for early identification and management.

Methods We did a facility-based, prospective, 1-week inception cohort study in 713 health facilities providing obstetric, midwifery, or abortion care, or where women could be admitted because of complications of pregnancy, childbirth, post-partum, or post-abortion, in 52 low-income and middle-income countries (LMICs) and high-income countries (HICs). We obtained data from hospital records for all pregnant or recently pregnant women hospitalised with suspected or confirmed infection. We calculated ratios of infection and infection-related severe maternal outcomes (ie, death or near-miss) per 1000 livebirths and the proportion of intrahospital fatalities across country income groups, as well as the distribution of demographic, obstetric, clinical characteristics and outcomes, and coverage of a set of core practices for identification and management across infection severity groups.

Findings Between Nov 28, 2017, and Dec 4, 2017, of 2965 women assessed for eligibility, 2850 pregnant or recently pregnant women with suspected or confirmed infection were included. 70·4 (95% CI 67·7–73·1) hospitalised women per 1000 livebirths had a maternal infection, and 10·9 (9·8–12·0) women per 1000 livebirths presented with infection-related (underlying or contributing cause) severe maternal outcomes. Highest ratios were observed in LMICs and the lowest in HICs. The proportion of intrahospital fatalities was 6·8% among women with severe maternal outcomes, with the highest proportion in low-income countries. Infection-related maternal deaths represented more than half of the intrahospital deaths. Around two-thirds (63·9%, n=1821) of the women had a complete set of vital signs recorded, or received antimicrobials the day of suspicion or diagnosis of the infection (70·2%, n=1875), without marked differences across severity groups.

Interpretation The frequency of maternal infections requiring management in health facilities is high. Our results suggest that contribution of direct (obstetric) and indirect (non-obstetric) infections to overall maternal deaths is greater than previously thought. Improvement of early identification is urgently needed, as well as prompt management of women with infections in health facilities by implementing effective evidence-based practices.


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Introduction Maternal infections are an important cause of maternal mortality and severe maternal morbidity.23 Global estimates suggest that direct (obstetric) infections are the third most common cause of maternal mortality, representing about 10·7% of maternal deaths, with the largest toll estimated in low-income and middle-income countries (LMICs) at 10·7% compared with high-income countries (HICs) at 4·7%.5 The contribution of infections to maternal deaths could be larger, as these figures do not include deaths due to abortion-related infections or indirect (non-obstetric) infections, which are not a result of, but aggravated by, pregnancy. Maternal deaths due to infection occur mainly through maternal sepsis, “a life-threatening condition defined as organ dysfunction resulting from infection during pregnancy, childbirth, post-abortion, or post-partum period”.6 This definition aligns with the recent Sepsis-3 definition for adults7 and includes both direct and indirect infections.8,9 Accurate assessment of the burden of maternal infections and its complications, including sepsis,
Maternal and neonatal sepsis are key factors for reducing related morbidity and mortality, as reflected in the 2017 World Health Assembly sepsis resolution. 

Evidence before this study
We identified primary studies and systematic reviews on frequency and management of maternal infections and sepsis using results of a previous systematic review by us, including searches in PubMed, MEDLINE, and Embase from Jan 1, 2010, to Feb 15, 2016, with no language restrictions (updated in September, 2019). We also identified WHO publications on the topic, and checked reference lists to identify additional studies. Globally, direct (obstetric) maternal infections are the third most common cause of maternal mortality, representing about 10·7% of all maternal deaths. Infections are also an important cause of indirect (non-obstetric) maternal deaths (eg, malaria, HIV, and influenza-like illness, among others). Globally, in 2017, there were approximately 5·7 million women presenting with maternal disorders complicated with sepsis. The reported incidence of maternal sepsis varies across settings from 0·1 to 2·0 cases per 1000 livebirths. However, the true burden of maternal sepsis and its complications is uncertain given the absence of standard definitions, identification criteria, and measurement tools, as well as variations in populations and sources of infections studied. It is globally recognised that prevention, early diagnosis, and prompt management of infections and sepsis are key factors for reducing related morbidity and mortality, as reflected in the 2017 World Health Assembly sepsis resolution.

Added value of this study
To the best of our knowledge, this is the first study to provide global data for the frequency and intrahospital management of maternal infections and its complications in 713 health facilities in 52 countries, across the continuum of pregnancy and post-pregnancy timelines. This study provides insights on frequency of maternal infections, according to demographic, obstetric, clinical characteristics and outcomes, and coverage of core practices for the prevention, early identification, and management of maternal infections.

Implications of all the available evidence
Maternal direct and indirect infections are an important underlying and contributing cause of maternal mortality and severe morbidity. Improved understanding of epidemiological and clinical characteristics of maternal infections is key for sustaining the reduction of preventable maternal morbidity and mortality. To do so, further efforts are required for the development and implementation of comprehensive approaches for effective prevention, improved identification, monitoring, and management of maternal infections and sepsis in health facilities.

Methods
Study design and participants
We did a facility-based, prospective, 1-week inception cohort study in selected health facilities in 52 LMICs and HICs (figure 1). We identified all women with suspected or confirmed infection, during any stage of pregnancy and up to the 42nd day after end of pregnancy, admitted to or already hospitalised for at least 12 h in participating health facilities between Nov 28, and Dec 4, 2017, in purposively selected countries and geographical areas, based on prespecified criteria.

Women who had a clinical suspicion or diagnosis of infection, a request for culture of any body fluid, or who...
were receiving antimicrobial treatment were eligible for inclusion (appendix p 1). All maternal deaths that occurred during the identification week, regardless of the cause, were also included. Women who presented with non-severe, localised, uncomplicated infection; uncomplicated chronic infection; bacterial colonisation; non-infectious hypothermia or hyperthermia; or who received prophylactic antibiotics were not eligible as defined in the appendix (p 1). Women were followed up for up to 6 weeks or until hospital discharge, transfer to a health facility outside the study area, or death, whichever occurred first and regardless of pregnancy outcome. Nine women remained hospitalised at the end of the follow-up period, and their outcomes were collected at the time of discharge. Infants born to women included in the study were followed up for 7 days after birth or until hospital discharge, transfer outside the participating area, or death, whichever occurred first.

All health facilities providing obstetric, midwifery, or post-abortion care; or facilities with an emergency room, adult ward, intensive care unit or high dependency care; or any other setting where pregnant or recently pregnant women could be admitted because of pregnancy-related complications located within the selected geographical areas were eligible and invited to participate.

Ethical approvals were obtained from the WHO ethics review committee and as required by national or local entities. Women were informed about the study using posters placed in visible areas of the participating health facilities. In addition, study teams informed all eligible women about the study and the need to review their medical records for this purpose, as well as those of their neonates. Written informed consent or a waiver of written consent (opt-out) was obtained as required by local or national committees.

Details of the study protocol, including selection of countries, geographical areas, and facilities, have been published elsewhere. An awareness campaign targeting health providers accompanied the study.

Procedures

Data were collected at the area, facility, and individual level using standardised paper forms specially designed for the study. These forms were based on tools used in previous multi-country surveys and existing facility assessment tools, and were customised and piloted for this study. Forms were translated from English into French, Portuguese, Russian, and Spanish, as well as additional official country languages by professional translators as needed. Data collection was standardised wherever possible and defined in the manual of operations designed for this study. A customised data entry and monitoring system was developed for the study.
A single geographical area questionnaire was completed by country teams to collect information on the main characteristics of the area, including estimated population size and number of births (or deliveries) in 2016. In each facility, a one-off facility questionnaire collected information on structural characteristics of each of the participating facilities: type of administration, location, level of specialisation, number of births in 2016 and during the week of identification, and availability of maternity services and adult intensive care unit or high dependency care.

The individual data form collected information on demographic, obstetric, and clinical characteristics of the woman; characteristics of infections and management during stay in the health facility; and pregnancy, childbirth, or post-partum or post-abortion period. Infections could be confirmed using clinical examination alone, or complemented by radiological, laboratory, or microbiological findings. Suspicions or confirmation of infection was undertaken as part of standard routine care in health facilities, and the study did not require additional collection of any laboratory, diagnostic, or other investigations. Abortion included any abortive outcome (induced abortion, miscarriage, ectopic, and molar pregnancy) as defined locally. Near-miss criteria (defined as a woman who nearly died but survived a life-threatening condition during pregnancy, childbirth, or post-partum or post-abortion periods) were not collected in six European countries (Belgium, Denmark, Italy, Spain, the Netherlands, the UK) as they implemented an adapted protocol using existing systems of surveillance of maternal morbidity. Inclusions were checked against hospital records, admissions to intensive care units or high dependency care, and for all maternal deaths during the identification week. Data quality assurance processes, including checks for accuracy and completeness of data, were put in place during data collection, data entry, and analysis.

**Statistical analysis**

A sample size of 2800 women was estimated to ensure at least 100 cases of severe maternal outcomes (ie, death or near-miss), based on a global birth rate of 19·6 livebirths per 1000 population per year, and assuming a 7% frequency of infections requiring hospital admission. Approximately 50 geographical areas with 20 000 000 inhabitants would have to be included to cover about 40 000 births in 1 week.

Women with infection were assigned to three groups according to the severity of the infection during hospital stay: (1) infection-related severe maternal outcomes included women presenting with WHO near-miss criteria to define organ system dysfunction or maternal death, and corresponds to the prespecified primary outcome of the study; (2) infections with complications included women with an invasive procedure to treat the source of infection (vacuum aspiration, dilatation and curettage, wound debridement, drainage [incision, percutaneous, culdotomy], laparotomy and lavage, other surgery), admission to intensive care unit or high dependency unit, or transfer to another facility. Maternal death or near-miss: At least one WHO near-miss criteria. Includes seven deaths due to direct (obstetric) cause, five due to abortion, six due to indirect (non-obstetric) cause (respiratory infection, meningitis, gastrointestinal). Includes two deaths due to obstetric haemorrhage, one hypertensive disorder, one other direct cause, two indirect cause, two with unknown cause.

For UN data see http://data.un.org

For the World Bank classification see https://databank.worldbank.org/data/
infection, early initiation of therapeutic antibiotics or other antimicrobials (initiated the same day of suspicion or diagnosis, or day after if suspicion or diagnosis was after 1800 h), drawing of any samples for culture before initiation of antibiotic therapy, and identification and control of the source of infection.

Maternal deaths without infections that occurred during the identification week were excluded from this analysis (n=20). Missing values were less than 10% for all sociodemographic variables, except schooling (54% of values missing), and less than 5% for all obstetric and other clinical characteristics and outcomes, except anaemia during pregnancy (33% missing), and neonatal status at end of follow-up (12%). Therefore, no additional analyses were undertaken to account for missing data. Two separate manuscripts are being developed to report on additional predefined primary and secondary outcomes, including identification criteria of severe maternal infection and sepsis, and the full set of neonatal outcomes.

Categorical variables are presented as proportions and continuous variables as medians and IQRs. 95% CIs for ratios were calculated using normal approximation. Comparisons between infection severity groups were obtained using ordinal multinomial mixed models for percentages and linear models for medians, adjusting for clustering at the country level. Statistical analyses were done using SAS version 9.4.

Role of the funding source

The funders of the study had no role in data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data for the study and had final responsibility for the decision to submit for publication.

Results

Of 2965 women assessed for eligibility, 2850 women were included in this analysis who were admitted for or already hospitalised with a suspected or confirmed infection (figure 2) in 713 facilities in 52 countries (408 facilities in 43 LMICs and 305 facilities in nine HICs). Participating facilities were mainly public, in urban locations, and tertiary or secondary level (appendix p 2). One participating low-income country was excluded from the study because we were unable to complete the prespecified data quality assurance process (six health facilities, 76 women). Six facilities in LMICs and 16 in HICs in the predefined geographical areas refused to participate. 19 eligible women refused to participate.

The ratio of intrahospital maternal infections (suspected or confirmed) was 70.4 (95% CI 67.7–73.1) women per 1000 livebirths (table 1) and 10.9 (9.8–12.0) of 1000 livebirths presented with infection-related severe maternal outcomes. The highest ratio was observed in upper-middle-income countries (106.4, 95% CI 98.1–114.7) and the lowest in HICs (38.6, 34.1–43.1; table 1). Differences across LMICs were less marked for infection-related severe maternal outcomes.

Intrahospital case fatalities among women with infection-related severe maternal outcomes was 7% (26 of 381 women with severe maternal outcomes; figure 2). Higher case fatalities were found in low-income (12 [15%] of 81) and lower-middle-income (13 [7%] of 179) than in upper-middle-income (one [1%] of 91) countries. No maternal deaths were reported in HICs. Infection was the underlying cause—including direct and indirect infections—or contributing cause in more than half of the intrahospital deaths that occurred in participating facilities during the identification week (19 of 39 maternal deaths; appendix p 3). Additional details of the distribution of organ dysfunction by system, causes of maternal deaths, and contribution of infections to maternal deaths are described in the appendix (pp 3–4).

Table 2 shows demographic, obstetric, and clinical characteristics of all women, and by infection severity groups. At eligibility, more than half of the women were...
post-partum or post-abortion and were identified at admission to the facility from home. Around a third were identified during pregnancy, not in labour, or were already hospitalised. Sociodemographic characteristics did not vary across the infection severity groups. Number of previous births, identification at post-partum or post-abortion, and anaemia during pregnancy increased with severity of the infection.

At least one source of infection was identified for 79.7% of women (table 3). The most common sources of maternal infections were of the genital (endometritis and chorioamnionitis) or urinary tract, skin or soft tissues, respiratory tract, and abortion-related. The most common source of infection leading to complications or severe maternal outcomes were endometritis, skin or soft tissue, and abortion-related.

Regarding the use of core practices for early identification and management of maternal infections, close to two-thirds of women had a complete set of vital signs recorded, and 70.2% received antibiotics or other antimicrobials the day of suspicion or diagnosis of the infection (table 3). Less than half of the women had samples drawn for
Articles

Data are n (%), n/N (%), or median (IQR) unless specified. *Includes women who had an invasive procedure to treat the source of infection (vacuum aspiration, dilatation and curettage, wound debridement, drainage [incision, percutaneous, culdotomy] laparotomy and lavage, other surgery), admission to intensive care or high dependency unit, or transfer to another facility. †Maternal death or near-miss. Geographical areas in six western European countries (Belgium, Denmark, Italy, Spain, the Netherlands, the UK) did not collect data on WHO near-miss criteria. ‡Multinomial mixed models for percentages and linear model for logarithm (length of stay) adjusting for clustering at country level. §More than one source possible. ¶Women who had an abortion, ectopic, or molar pregnancy. ||Same day or previous day after 1800 h. **Includes culture drawn at entry in study or any time during stay in the facility. ††Includes culture of any body fluid, microscopy, or specific test (e.g., malaria, tuberculosis, HIV). ‡‡Includes all organisms identified in women without inferring causation (when organism identified). Each woman could have more than one type of microorganism identified. §§More than one intervention possible.

Table 3: Characteristics of maternal infections and management by severity group

<table>
<thead>
<tr>
<th>Primary source of infection identified§</th>
<th>All women (n=2850)</th>
<th>Less severe infections (n=1835)</th>
<th>Infections with complications* (n=634)</th>
<th>Infection-related severe maternal outcome† (n=381)</th>
<th>p value‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary tract</td>
<td>652 (27·9 %)</td>
<td>504 (36·8 %)</td>
<td>69 (12·0 %)</td>
<td>59 (18·2 %)</td>
<td>...</td>
</tr>
<tr>
<td>Endometritis</td>
<td>343 (15·1 %)</td>
<td>178 (13·0 %)</td>
<td>88 (15·3 %)</td>
<td>77 (22·8 %)</td>
<td>...</td>
</tr>
<tr>
<td>Chorioamnionitis</td>
<td>338 (14·9 %)</td>
<td>236 (17·4 %)</td>
<td>66 (11·5 %)</td>
<td>34 (10·5 %)</td>
<td>...</td>
</tr>
<tr>
<td>Skin or soft tissue</td>
<td>336 (14·8 %)</td>
<td>106 (7·7 %)</td>
<td>188 (32·2 %)</td>
<td>46 (14·2 %)</td>
<td>...</td>
</tr>
<tr>
<td>Respiratory</td>
<td>204 (9·0 %)</td>
<td>116 (8·5 %)</td>
<td>21 (3·7 %)</td>
<td>67 (20·7 %)</td>
<td>...</td>
</tr>
<tr>
<td>Abortion-related¶</td>
<td>193 (8·5 %)</td>
<td>33 (2·4 %)</td>
<td>115 (19·9 %)</td>
<td>45 (13·9 %)</td>
<td>...</td>
</tr>
<tr>
<td>Bloodstream</td>
<td>115 (5·1 %)</td>
<td>97 (7·1 %)</td>
<td>7 (1·2 %)</td>
<td>11 (3·4 %)</td>
<td>...</td>
</tr>
<tr>
<td>Peritonitis or abdominal cavity</td>
<td>69 (3·0 %)</td>
<td>4 (0·3 %)</td>
<td>27 (4·7 %)</td>
<td>38 (11·7 %)</td>
<td>...</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>63 (2·8 %)</td>
<td>39 (2·9 %)</td>
<td>11 (1·9 %)</td>
<td>13 (4·0 %)</td>
<td>...</td>
</tr>
<tr>
<td>Breast</td>
<td>30 (1·3 %)</td>
<td>22 (1·6 %)</td>
<td>5 (0·9 %)</td>
<td>3 (0·9 %)</td>
<td>...</td>
</tr>
<tr>
<td>CNS</td>
<td>10 (0·4 %)</td>
<td>3 (0·2 %)</td>
<td>0 (0·2 %)</td>
<td>6 (1·9 %)</td>
<td>...</td>
</tr>
<tr>
<td>Other</td>
<td>197 (9·2 %)</td>
<td>132 (10·6 %)</td>
<td>42 (8·0 %)</td>
<td>23 (7·1 %)</td>
<td>...</td>
</tr>
<tr>
<td>Method of identification of the infection if source identified</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical examination alone</td>
<td>910 (40·1 %)</td>
<td>526 (38·5 %)</td>
<td>282 (48·7 %)</td>
<td>102 (31·5 %)</td>
<td>...</td>
</tr>
<tr>
<td>Clinical examination and laboratory test</td>
<td>890 (39·2 %)</td>
<td>648 (47·4 %)</td>
<td>159 (27·5 %)</td>
<td>83 (25·6 %)</td>
<td>...</td>
</tr>
<tr>
<td>Clinical examination and imaging</td>
<td>201 (8·8 %)</td>
<td>85 (6·3 %)</td>
<td>49 (8·5 %)</td>
<td>67 (20·6 %)</td>
<td>...</td>
</tr>
<tr>
<td>Clinical examination, laboratory, test, and imaging</td>
<td>267 (11·7 %)</td>
<td>107 (7·8 %)</td>
<td>88 (15·2 %)</td>
<td>72 (22·2 %)</td>
<td>...</td>
</tr>
<tr>
<td>Complete set of vital signs recorded on day infection was suspected or confirmed</td>
<td>1821 (63·9 %)</td>
<td>1100 (59·9 %)</td>
<td>435 (68·6 %)</td>
<td>286 (75·1 %)</td>
<td>0·0093</td>
</tr>
<tr>
<td>Antimicrobials started the day of suspicion or diagnosis of infection</td>
<td></td>
<td></td>
<td>1875 (70·2 %)</td>
<td>1198 (70·6 %)</td>
<td>435 (68·6 %)</td>
</tr>
<tr>
<td>Antibiotics started the day of suspicion or diagnosis of infection</td>
<td></td>
<td></td>
<td>1843 (70·2 %)</td>
<td>1165 (70·5 %)</td>
<td>435 (68·6 %)</td>
</tr>
<tr>
<td>Sample for culture drawn at any time**</td>
<td>1269 (46·6 %)</td>
<td>788 (46·0 %)</td>
<td>280 (44·7 %)</td>
<td>201 (52·8 %)</td>
<td>0·19</td>
</tr>
<tr>
<td>Sample for culture drawn before administration of antibiotics</td>
<td>760/1177 (64·6 %)</td>
<td>496/745 (66·6 %)</td>
<td>165/254 (65·0 %)</td>
<td>99/178 (55·6 %)</td>
<td>0·044</td>
</tr>
<tr>
<td>Any microorganism identified by any method††</td>
<td>590 (21·2 %)</td>
<td>360 (20·0 %)</td>
<td>147 (25·6 %)</td>
<td>101 (31·2 %)</td>
<td>0·0017</td>
</tr>
<tr>
<td>Any positive culture of any body fluid**</td>
<td>579 (25·6 %)</td>
<td>331 (24·2 %)</td>
<td>133 (21·6 %)</td>
<td>97 (26·1 %)</td>
<td>0·011</td>
</tr>
<tr>
<td>All microorganisms identified by any methods¶¶</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bacteria</td>
<td>455 (77·1 %)</td>
<td>257 (71·4 %)</td>
<td>116 (87·2 %)</td>
<td>82 (84·5 %)</td>
<td>...</td>
</tr>
<tr>
<td>Fungi</td>
<td>47 (8·0 %)</td>
<td>30 (8·3 %)</td>
<td>6 (4·5 %)</td>
<td>11 (11·3 %)</td>
<td>...</td>
</tr>
<tr>
<td>Parasite</td>
<td>94 (15·0 %)</td>
<td>79 (21·9 %)</td>
<td>7 (5·3 %)</td>
<td>8 (8·2 %)</td>
<td>...</td>
</tr>
<tr>
<td>Virus</td>
<td>21 (3·6 %)</td>
<td>13 (3·6 %)</td>
<td>3 (2·3 %)</td>
<td>5 (5·1 %)</td>
<td>...</td>
</tr>
<tr>
<td>Median length of stay in health facility, days (IQR)</td>
<td>5 (3–9)</td>
<td>5 (3–7)</td>
<td>7 (4–11)</td>
<td>9 (5–17)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Admission to intensive or high dependency care</td>
<td>355 (13·8 %)</td>
<td>167 (27·8 %)</td>
<td>188 (49·3 %)</td>
<td>188 (49·3 %)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

culture at suspicion or confirmation of infection, and two-thirds of the samples were taken before the administration of antibiotics. Microorganisms were reported in 21·2% of the samples, bacteria being the most frequent (77·1%); they are reported here without inferring direct causality. There were no marked differences in use of this core set
of practices for early identification and management of maternal infections across severity groups. Table 4 shows pregnancy, maternal, and neonatal outcomes by pregnancy status at entry in the study and severity group. Most women were discharged alive and had a live neonate who was discharged alive. Adverse pregnancy and neonatal outcomes increased with infection severity.

### Discussion

This is the first study, to our knowledge, to provide data for frequency and management of maternal infections requiring hospital management in a large number of LMICs and HICs, and across the continuum of pregnancy and post-pregnancy periods up to 42 days. The observed frequency of suspected or confirmed maternal infections was of 70-4 pregnant or recently pregnant women per 1000 live births. The burden of intrahospital severe outcomes related to maternal infections is high, with more than a third of women who had an infection developing severe maternal outcomes or requiring invasive procedures to treat the source of infection, admission to intensive care unit or high dependency care, or transfer to another facility. Lack of adequate assessment of vital signs and delays in antimicrobial therapy were frequent.

Our results suggest that there are marked differences in frequency of infections and outcomes of maternal infections between LMICs and HICs. The burden of infections between LMICs and HICs. The burden of intrahospital severe outcomes related to maternal infections is lower in HICs compared with LMICs, as previously described. Although we found rates of infection-related severe maternal outcomes in HICs similar to those previously reported, rates in LMICs are much higher in our report.}

### Table 4: Pregnancy, maternal, and neonatal outcomes by pregnancy status at entry in the study and severity group

This is the first study, to our knowledge, to provide data for frequency and management of maternal infections requiring hospital management in a large number of LMICs and HICs, and across the continuum of pregnancy and post-pregnancy periods up to 42 days. The observed frequency of suspected or confirmed maternal infections was of 70-4 pregnant or recently pregnant women per 1000 live births. The burden of intrahospital severe outcomes related to maternal infections is high, with more than a third of women who had an infection developing severe maternal outcomes or requiring invasive procedures to treat the source of infection, admission to intensive care unit or high dependency care, or transfer to another facility. Lack of adequate assessment of vital signs and delays in antimicrobial therapy were frequent.

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sample, particularly in upper-middle-income countries. The observed variation across countries could be related to use of different admission criteria or resources available to identify severe conditions or to manage in-patient women with infections across facilities, geographical areas, and countries. This difference in identification and management of women with infection could partly explain the higher burden of infectious morbidities in upper-middle-income countries than lower-middle-income countries, where facilities might have lower thresholds for admission of women with maternal infection or more resources to identify or treat complications compared with facilities in low-income countries.

Infections were the underlying cause of most intrahospital deaths attributed to other direct (eg, abortion-related) and indirect (eg, respiratory infection, meningitis) causes. Infections were also present in about a third of deaths attributed to other causes, in concurrence with previous findings in obstetric, and general populations. These results suggest that the role of infections as an underlying or contributing cause of maternal deaths, across the continuum from pregnancy to post-partum or post-abortion, is higher than previously thought. As previously suggested, the inclusion of non-obstetric wards in our study might have led to an increase in identification of maternal deaths and near-miss cases related to indirect infections. This finding could also reflect a trend towards an increasing proportion of indirect causes of maternal deaths, although the contribution of infections as a direct cause of severe maternal outcomes remains high. It is worth noting that the distribution of causes of intrahospital maternal deaths is close to the most recent estimates of causes of maternal mortality.

The most common infections identified in this study were urinary tract infections, endometritis, chorio-amnionitis, abortion-related infections, and skin and soft tissue, in line with previous studies. Several of the obstetric infections identified in our sample and associated with severe maternal outcomes, namely skin and soft tissue and abortion-related infections, are highly preventable. Good infection control measures are key for the prevention of infections after caesarean section, epistaxis, or other invasive procedures. In addition, prophylactic antibiotics are recommended to reduce infections due to caesarean section. However, data for coverage of prophylactic antibiotics for caesarean section suggest that its use is suboptimal across the world, with wide variations across health facilities. Post-abortion infections are preventable through access to safe abortion, and prompt appropriate management of abortion-related complications.

This study highlights important gaps regarding early identification and management of maternal infections in health facilities. A complete set of vital signs on the day of suspicion or diagnosis of infection was not reported for a third of women. Although most women received antimicrobials around the time of suspicion or diagnosis of the infection, about a third did not, and fewer than half had samples drawn for cultures before administration of antibiotics. In general, women with severe maternal outcomes had fewer invasive procedures to control the source of infection. Previous studies have also reported inadequate recognition and management of women with infection and sepsis in LMICs and HICs, including incomplete monitoring and delayed initiation of antibiotics. A substantial opportunity exists for improvement in early identification and prompt management of women with infections in health facilities, requiring more than just raising awareness. The use of quality improvement initiatives, including bundles, protocols, and checklists contribute to improving practices and outcomes. The use of trigger tools has shown an increase in the recording of vital signs and improved management. Timely completion of bundles of care (1 h and 3 h bundles) has also been associated with a reduction in adult mortality. These strategies should also contribute to better antimicrobial stewardship and strengthen efforts to minimise antimicrobial resistance.

Our study is one of the few to report data for maternal infections in the continuum of pregnancy, childbirth, and the post-partum or post-abortion period, and across different severity groups. We sought to identify women with maternal infections by ensuring a good coverage of facilities within geographical areas, including participation of non-obstetric wards. The awareness campaign might have contributed to better identification of eligible cases. However, generalisability of results is limited to intrahospital outcomes and geographical areas similar to those included in the study. Comparisons with other studies reporting on the burden of infections and sepsis are limited by differences in case definitions, sources of infections considered, or stage of pregnancy included. Temporality of organ dysfunction and infection was difficult to assess in our study, which might result in overestimating sepsis cases. However, as discussed in previous studies, diagnosing infection and attributing organ dysfunction to infection are often subjective. Reverse causality might also complicate this association in cases of multiple maternal complications—eg, infection and post-partum haemorrhage. A detailed description of strategies put in place to address potential sources of selection and measurement bias in our study is presented in the published protocol. We expected a minimal effect of geographical or seasonal clusters of infectious morbidities given the large number of countries distributed between the northern and southern hemispheres and that most of the cases would be genitourinary tract infections not subjected to seasonality. Our study did not evaluate infections not requiring hospital management and was not designed to cover maternal infection-related deaths in the community. Inclusion in the study was based on standard routine...
care in participating health facilities, including admission and diagnosis criteria, as well as collection of any laboratory, diagnostic, or other investigations. However, in women with complications or severe maternal outcomes, we would not have expected differing admission thresholds. This group is likely to have needed in-hospital management regardless of the admission criteria or resources available, in particular for women with infection-related near-miss who otherwise would have died if not treated in the facility. We did not collect the time of initiation of antimicrobials and therefore were not able to determine compliance with 3 h and 6 h sepsis bundles. The study design did not enable us to evaluate the long-term effects of maternal infections, including for example readmission or death after discharge, or infertility.7,8

The frequency of infections among pregnant or recently pregnant women requiring management in health facilities is high. Our results suggest that contribution of direct and indirect infections to overall maternal deaths is greater than previously thought. There is a substantial opportunity to improve the prevention, early identification, and prompt management of women with infections in health facilities by implementing effective evidence-based practices.

Contributors
JPS, MB, and AMG conceptualised the study and developed the study protocol with inputs from the research group. MB, VB, EA, CC, BF, MK, SK, PL, AN, AMG, and JPS contributed to statistical analysis, interpretation of findings, and provided substantial input to the manuscript. CC did statistical analysis. AB, MC, BK, MK, SK, PL, AN, AMG, and JPS contributed to statistical analysis, interpreted findings, and commented on previous versions of the manuscript. All members of the research group approved the final manuscript.

WHO Global Maternal Sepsis Study Research Group


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**Articles**
Eclampsie in België: resultaten van het Belgian Obstetric Surveillance System

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Tussen januari 2012 en december 2014 registreerde B.OSS 74 vrouwen die een eclamptisch insult doormaakten, waarvan 59 in de analyse konden worden geïncludeerd. De daaruit afgeleide frequentie van eclampsie in België, 1,6 (95%-BI: 1,2-2,1) per 10.000 bevallingen, is laag ten opzichte van Nederland (5,4 per 10.000 bevallingen) en het Verenigd Koninkrijk (2,7 per 10.000 bevallingen). Mogelijk kunnen we dit verklaren door de organisatie van de antenatale zorg in België, waarbij toegang tot antenatale zorg bij huisarts, vroedvrouw of gynaecoloog zeer laagdrempelig is en zwangere vrouwen, ongeacht hun risicostratifie, door een gynaecoloog worden gevolgd, waardoor continuïteit van zorg is verzekerd.

Het insult gebeurde in het ziekenhuis bij 39 vrouwen (66%) en thuis bij 18 vrouwen (31%); ante partum, intra partum en post partum bij respectievelijk 36, 7 en 16 vrouwen. Uiteindelijk kregen 54 vrouwen (91,5%) magnesiumsulfaat toegediend, waarvan 6 vrouwen dit reeds profylactisch kregen. Vierendertig vrouwen (58%) kregen ook een anticonvulsivum (meestal diazepam) toegediend, bij 15 vrouwen werd dit als eerste keuze gestart op moment van het insult. Eenvijftig vrouwen (86%) kregen antihypertensiva, waarvan 12 vrouwen reeds voor het insult. Drieëvenveertig vrouwen (73%) werden opgenomen op intensieve care, bij 19 vrouwen was er behoudens het eclamptische insult sprake van ernstige comorbiditeit. Er was één maternaal overlijden (case fatality rate: 1,7%). Er waren vier foetale sterfgevallen en één neonataal sterfgeval (perinatal fatality rate: 8,5%).

Mogelijk kunnen de preventie en aanpak van deze zeldzame complicatie in België nog worden verbeterd door een toename in gebruik van acetylsalicylzuur vanaf het eerste trimester en door het tijdiger toedienen van antihypertensiva en profylactisch magnesiumsulfaat. Ook huisartsen en urgentieartsen zouden gesensibiliseerd moeten worden over het gebruik van magnesiumsulfaat als eerste keuze bij een eclampstisch insult. Een Belgische richtlijn zou hierin een positieve rol kunnen spelen.

Eclampsie doet zich voor bij 2-3% van de zwangere vrouwen met ernstige pre-eclampsie zonder gebruik van magnesiumsulfaat (1, 2). Onder meer dankzij de introductie van magnesiumsulfaat is het voorkomen van eclampsie in hoge-inkomenslanden sterk gedaald, en daarmee ook de maternele mortaliteit en morbiditeit (3, 4).

Het registreren en analyseren van gevallen van ernstige maternale morbiditeit (SMM) en maternale near-miss (MNM), gedefinieerd als een levensbedreigende obstetrische complica-

INLEIDING

Eclampsie is een zeldzame obstetrische complicatie die geassocieerd is met een hoge maternale en perinatale morbiditeit en mortaliteit. De zwangere of pas bevallen vrouw ontwikkelt geassocieerde convulsies, vaak voorafgaan door een stadium van ernstige pre-eclampsie. Ernstige gevolgen bij moeder zijn onder meer intracerebrale bloedingen, hypoxie en organfalen; voor de neonaat zijn peripartale asfyxie en doodgeboorte geen uitzondering.

Het doel van deze studie was het in kaart brengen van de frequentie, de risicofactoren, de aanpak en de uitkomst van de ernstige complicatie eclampsie in België. Vergelijken met gegevens van gelijkaardige studies in Nederland en het Verenigd Koninkrijk maakt het mogelijk om de kwaliteit en veiligheid van de obstetrische zorg in België te evalueren.


De gegevens van de achtergrondpopulatie werden gehaald uit de perinatale registratie in Vlaanderen, het Studiecentrum voor Perinatale Epidemiologie (SPE) (6-8) en in Wallonië en Brussel, het Centre d’Épidémiologie Périnatale (CEpiP) (9-13). Statistische analyse gebeurde aan de hand van IBM SPSS, versie 23 (14), de statistische software van MEDCALC® (15) en EpiTools (16).

Sociodemografische en obstetrische karakteristieken werden afgetoetst aan deze van de achtergrondpopulatie door middel van odds ratios en 95%-betrouwbaarheidsintervallen (95%-BI). P-waarden < 0,05 werden significant bevonden. De B.OSS-methodologie en deze studie werden goed-gekeurd door de ethische commissies van het Universitair Ziekenhuis Erasmus Brussel (EC ULB 2012/111; B406201213660), het Universitair Ziekenhuis Gent (EC UZG 2012/734; B670201215359 en EC UZG 2015/1470; B670201526875) en het Universitair Ziekenhuis Leuven (mp08950-S58924).

RESULTATEN

> INCIDENTIE
Rapportering gebeurde vanuit 97% (112/115) van alle Belgische materniteiten, verantwoordelijk voor 98,6% van het aantal bevallingen van de studieperiode. Er werden in totaal 74 vrouwen met eclampsie aangemeld. In 9 gevallen werd geen vragenlijst teruggestuurd. Eén casus werd geëxcludeerd wegens een voorgeschiedenis van epilepsie. Vijf casussen voldeden niet aan de inclusiecriteria. Uiteindelijk werden 59 casussen geïncludeerd over 371.170 bevallingen, dit is het totale aantal bevallingen in België voor de duur van de studieperiode gecorrigeerd voor de niet-deelnemende materniteiten. De frequentie van eclampsie in België bedraagt daarmee 1,59 per 10.000 bevallingen (95%-BI: 1,23-2,05/10.000).

Tabel 1: Definitie van eclampsie.

<table>
<thead>
<tr>
<th>Symptoom</th>
<th>Condities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Convulsies tijdens de zwangerschap of binnen de 10 dagen na de bevalling, samen met minstens twee van volgende klinische tekenen binnen de 24 uur na de convulsies:</td>
<td></td>
</tr>
<tr>
<td>- hypertensie: maximale diastolische bloeddruk ≥ 90mmHg én een diastolische stijging van ≥ 25mmHg (bij een diastolische bloeddruk &lt; 90mmHg bij de eerste antenatale controle);</td>
<td></td>
</tr>
<tr>
<td>- proteïnurie: tenminste 1+ proteïnurie in een random urinestaal of ≥ 0,3g proteïnurie in een 24-uurs-urinecollectie;</td>
<td></td>
</tr>
<tr>
<td>- trombocytopenie: bloedplaatjes &lt; 100.000/mm³;</td>
<td></td>
</tr>
<tr>
<td>- gestegen transaminasen: ALT ≥ 42 IU/L of AST ≥ 42 IU/L.</td>
<td></td>
</tr>
</tbody>
</table>

Figuur 1: Klinische tekenen en symptomen voor het eclamptische insult.
> **RISICOFACTOREN**

Sociodemografische en obstetrische kenmerken van de vrouwen die eclampsie doormaken, worden weergegeven in tabel 2. Nullipariteit en tienerzwangerschap (< 20 jaar) zijn significante risicofactoren.

> **KLINIEK VOORAFGAAND AAN EN VOLGEND OP HET ECLAMPTISCHE INSULT**


Bij 39 vrouwen gebeurde het insult tijdens een ziekenhuisopname: anteparaal (n = 17), durante partus (n = 7), postparataal (n = 15). Gegevens van het laatste controlemoment voor het insult zijn bekend voor 24 vrouwen: bij 21 vrouwen waren alarmerende tekenen of symptomen aanwezig (Figuur 1). Bij 2 vrouwen was dit niet duidelijk waar het insult plaatsvond en 18 vrouwen (32%; n = 56) hadden meer dan één insult.

De aanwezigheid van hypertensie, proteïnurie en klinische klachten kort na het moment van de eclamptische aanval staan samengevat in figuur 2. Trombopenie en gestegen transaminasen binnen de 24u na eclampsie traden bij respectievelijk 14 (24,6%; n = 57) en 35 (61,4%; n = 57) vrouwen op.

> **OMSTANDIGHEDEN VAN HET ECLAMPTISCHE INSULT EN DE BEVALLING**

De gemiddelde zwangerschapsduur bij de bevalling bedroeg 34 weken + 1 dag: 7 vrouwen (12%) bevielen extreem preterm (< 28 weken), 10 vrouwen (17%) vroeg-preterm (≥ 28 ≤ 32 weken) en 22 vrouwen (37%) laat-preterm (≥ 32 ≤ 37 weken). De gemiddelde zwangerschapsduur was 31 weken + 5 dagen (range: 23 weken-38 weken + 5 dagen) bij de insulten thuis versus 33 weken + 4 dagen (range: 24 weken + 5 dagen-39 weken + 6 dagen) bij de antenatale insulten in het ziekenhuis. De omstandigheden van de partus staan opgesomd in tabel 3.

> **BELEID**

Magnesiumsulfaat werd aan 54 vrouwen toegediend (91,5%), 6 vrouwen kregen dit reeds profylactisch, bij 23 vrouwen was magnesiumsulfaat de eerstekeuzebehandeling op het moment van het insult. Drieëntwintig vrouwen kregen een bolus van 4 gram magnesiumsulfaat gevolgd door een onderhoudsdosis van 1 gram per uur, bij 21 vrouwen werd van deze dosering afgezwakt. Voor 10 vrouwen werd de dosering niet gerapporteerd. Bij 15 vrouwen werd in de behandeling van het eclamptische insult gestart met een anticonvulsivum. In totaal kregen 34 vrouwen een anticonvulsivum toegediend waarbij diazepam het vaakst werd gebruikt (n = 25). Voor 5 vrouwen werd het al dan niet gebruik van anticonvulsiva niet gerapporteerd. Antihypertensiva werden gestart bij 51 vrouwen, 3 vrouwen kregen dit niet, bij 5 vrouwen werd het gebruik van antihypertensiva niet gerapporteerd. Twaalf vrouwen kregen antihypertensiva reeds vóór de eclamptische aanval. Het type antihypertensiva waren β-blokkers bij 71% van de vrouwen, verder calciumantagonisten (51%), centraalwerkende antihypertensiva (29%), vasodilatatoren (12%) en ACE-inhibitoren (4%). Bij 30 vrouwen werden meerdere antihypertensiva gebruikt.

---

**Tabel 2: Sociodemografische en obstetrische kenmerken van de vrouwen die eclampsie doormaken.**

| Klasseificatie | Aantal
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Nullipariteit</td>
<td>18</td>
</tr>
<tr>
<td>Intollerantie</td>
<td>12</td>
</tr>
</tbody>
</table>

---

**Figuur 2: Klinische tekenen en symptomen net na het eclamptische insult.**

- **Hypertensie**
- **Proteïnurie**
- **Geen alarmsgymptomen**

---

**Tabel 3: Omstandigheden van de partus.**

| Klasseificatie | Aantal
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Anteparaal</td>
<td>17</td>
</tr>
<tr>
<td>Durante partus</td>
<td>7</td>
</tr>
<tr>
<td>Postparataal</td>
<td>15</td>
</tr>
</tbody>
</table>
Drieënveertig vrouwen (48%) werden opgenomen op een afdeling intensive care gedurende 3 dagen gemiddeld (range: 1-14 dagen). Bij 19 vrouwen was er naast eclampsie ook sprake van andere ernstige morbiditeit (pulmonair, cardiaal, posterior reversible encephalopathy syndrome). Eén moeder overleed, wat overeenkomt met een case fatality rate van 1,7%. Zij was een primigravida van Afrikaanse origine die op 33 weken een sectio onderging wegens ernstige vroege pre-eclampsie gepaard met intra-uteriene groeirestrictie. Vijf dagen postpartaal kreeg zij een eclamptisch insult, waarvoor opname op de afdeling intensive care en behandeling met antihypertensiva. Ze stierf vier dagen later aan een combinatie van hersenoedeem, longoedeem en hartfalen.

Foetale sterfte trad op bij 4 foetussen op een amenorroeduur van 23 weken + 1 dag, 24 weken + 5 dagen, 25 weken, 36 weken + 3 dagen, alle vóór het optreden van een eclamptisch insult. Er was één neonataal overlijden door de gevolgen van asfyxie 16 dagen na een premature partus op 32 weken + 1 dag. Dit brengt de perinatal fatality rate op 8,5%. De neonatale uitkomst wordt in detail weergegeven in tabel 4.

**UITKOMST**

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**INTERNATIONALE VERGELIJKING**

In tabel 5 vergelijken we de Belgische gegevens met de gelijkaardige studies van Nederland (Landelijke studie naar Ernstige Maternale Morbiditeit in Nederland – LEMMoN) en het Verenigd Koninkrijk (UKOSS) (4, 17, 18). Gegevens uit Nederland zijn aangepast aan de striktere UKOSS-definitie, die we ook in deze studie hebben gebruikt.

Gelet op de zwangerschapsduur bij optreden van eclampsie, zijn vrouwen zowel in Nederland als in het Verenigd Koninkrijk gemiddeld à terme. In België daarentegen lijkt eclampsie vaker vroeger te optreden, gemiddeld rond 32 weken. Het gebruik van magnesiumsulfaat in België lijkt lager en het gebruik van antihypertensiva hoger, ten opzichte van onze buurlanden.

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**Tabel 2: Risicofactoren voor eclampsie.**

<table>
<thead>
<tr>
<th>Sociodemografische factoren</th>
<th>Eclampsie (n = 59)</th>
<th>Achtergrond-populatie (n = 376.471)</th>
<th>OR (95%-BI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tienerzwangerschap</td>
<td>5 (8%)</td>
<td>7.566 (2%)</td>
<td>4,52* (1,81-11,29)</td>
</tr>
<tr>
<td>&gt; 35 jaar</td>
<td>8 (14%)</td>
<td>65.665 (17%)</td>
<td>0,74 (0,35-1,56)</td>
</tr>
<tr>
<td>BMI &gt; 30kg/m²</td>
<td>8 (14%)</td>
<td>45.286 (12%)</td>
<td>1,15 (0,54-2,42)</td>
</tr>
<tr>
<td>Zwarte etniciteit</td>
<td>15 (25%)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Roken**</td>
<td>6 (10%)</td>
<td>11.184 (3%)</td>
<td>1,21 (0,52-2,81)</td>
</tr>
</tbody>
</table>

**Medische factoren**

| Pre-existente hypertensie           | 2 (3%)             | 17.415 (5%)                         | 0,72 (0,18-2,96)  |
| Diabetes, vooraf bestaan           | 1 (2%)             | 20.521 (6%)                         | 0,30 (0,04-2,16)  |

**Obstetrische factoren**

| Geassisteerde fertilité             | 3 (5%)             | 20.600 (6%)                         | 0,93 (0,29-2,96)  |
| Nullipariteit                       | 41 (70%)           | 164.495 (44%)                       | 2,94* (1,69-5,11) |
| PE/HELLP/… in anamnese             | 6 (10%)            | -                                   | -             |

* Significant resultaat (p-waarde < 0,05)
** Op basis van resultaten SPE Vlaanderen: 119.420 bevallingen
We zien in deze studie dat slechts een kwart van de vrouwen behandeld werd met antihypertensiva vóór het eclamptische insult, wat opleef tot meer dan 85% op het moment van het eclamptische insult. Magnesiumsulfaat werd profylactisch toegepast bij 10% van de vrouwen in deze studie, hoewel bij ruim 70% van de in het ziekenhuis opgenomen vrouwen minstens twee alarmsymptomen (hypertensie, proteïneurie of klinische klachten) werden gerapporteerd. Mogelijk waren eclamptische insulin bij voorkeur geweest omdat de eerder opstarten profylactisch magnesiumsulfaat, vooral in geval van de in het ziekenhuis opgenomen vrouw.
### Tabel 4: Neonatale uitkomst bij moeders met eclampsie in relatie tot de zwangerschapsduur bij geboorte.

<table>
<thead>
<tr>
<th></th>
<th>Ante partum (n = 36)</th>
<th>Intra partum (n = 7)</th>
<th>Post partum (n = 16)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Preterm</td>
<td>A terme</td>
<td>Preterm</td>
</tr>
<tr>
<td>Foetale sterfte</td>
<td>3</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Dysmatuur</td>
<td>5</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Opname N*</td>
<td>9</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>NIC</td>
<td>22</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Respiratoire ondersteuning</td>
<td>22</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

### Tabel 5: Internationale vergelijking van eclampsie in België, Nederland en het Verenigd Koninkrijk.

<table>
<thead>
<tr>
<th></th>
<th>België</th>
<th>Nederland</th>
<th>Verenigd Koninkrijk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bevallingen tijdens studieperiode</td>
<td>371.170</td>
<td>358.874</td>
<td>775.186</td>
</tr>
<tr>
<td>Eclampsie</td>
<td>59 (1,6/10.000)</td>
<td>192 (5,4/10.000)</td>
<td>214 (2,7/10.000)</td>
</tr>
<tr>
<td>Gemiddelde AD in ante-partumgroep</td>
<td>31w5d</td>
<td>37w5d</td>
<td>38w0d</td>
</tr>
<tr>
<td>Tijdsinterval eclampsie-partus (ante partum)</td>
<td>186min</td>
<td>420min</td>
<td>160min</td>
</tr>
<tr>
<td>Sectio</td>
<td>122min</td>
<td>240min</td>
<td>127min</td>
</tr>
<tr>
<td>Magnesiumsulfaat</td>
<td>54 (91,5%)</td>
<td>181 (94,3%)</td>
<td>211 (98,6%)</td>
</tr>
<tr>
<td>Profylactisch</td>
<td>6 (10,2%)</td>
<td>19 (9,8%)</td>
<td>12 (5,6%)</td>
</tr>
<tr>
<td>Anthypertensiva</td>
<td>51 (86,4%)</td>
<td>31 (16,1%)</td>
<td>151 (70,8%)</td>
</tr>
<tr>
<td>Maternale sterfte</td>
<td>3 (1,7%)</td>
<td>3 (1,6%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Perinatale sterfte</td>
<td>5 (8,5%)</td>
<td>9 (5%)</td>
<td>5 (2%)</td>
</tr>
</tbody>
</table>

AD: amenoroeduur; w: weken; d: dagen; min: minuten
deling van eclampsie. Hieruit bleek dat magnesiumsulfaat voor een betere controle zorgt van het eclamptische insult en de kans op herhaalde epileptische werkingen (number needed to treat = 7), waardoor ook het risico op mater nale sterfte verlaagt. Bovendien wordt bij magnesiumsulfaat een neuroprotective effect gezien bij de moeder én bij de neonaat (21) en zal de combinatie van magnesiumsulfaat met een anticonvulsivum het risico op ademhal ingedepressie versterken. Huisartsen en urgentieartsen zijn vaak de eerst aanwezige artsen in geval van een eclamptisch insult en minder onder drrict in het gebruik van magnesiumsulfaat dan gynaecologen en vroedvrouwen.

De grote sterkte van deze studie is de deelname van meer dan 98% van de mater niteiten in de registratie van deze zeldzame ob strettische complicatie, alsook de grote response rate van deze groep. Desondanks kunnen we geen zekerheid bieden over de inclusie van alle eclampsiacasussen in België, aangezien B.OSS steunt op vrijwillige rapportering van drukbezette clinici. Het vervolledigen van de vragenlijsten eclampsie verliep moeizaam als gevolg van de uitgebreidheid en een aantal onduidelijkheden in de vragenlijst zelf. Wel licht konden enkele klinisch evidentie casus sen hierdoor niet geïncludeerd worden.

Om in de toekomst internationale vergelijkingen en samenwerkende studies te verbeteren, werd door het International Net work of Obstetric Survey System (INOSS) (22) voor verschillende obstrettische complicaties een eenduidige definitie opgesteld. In deze INOSS-consensus wordt eclampsie gedefini eerd als convulsies tijdens de zwangerschap of binnen tien dagen na de bevalling, samen met slechts één klinisch teken (hyperten sie, proteinurie, gestegen transaminasen of trombopenie). Indien toegepast op de Bel gische cohorte, kunnen er vijf casussen extra geïncludeerd worden en wordt de Belgische frequentie 1,72 (95%-BI: 1,35-2,20) per 10.000 bevallingen.

CONCLUSIE

De frequentie van eclampsie in België is zeer laag. Mogelijk kunnen de preventie en aanpak van deze zeldzame complicatie in

België nog worden verbeterd door het tijdig herkennen van subjectieve alarmsymptomen en het tijdig profylactisch toedienen van magnesiumsulfaat en antihypertensiva. Ook huisartsen en urgentieartsen zouden gesensibiliseerd moeten worden over het gebruik van magnesiumsulfaat als eerste keuze bij een eclamptisch insult. Een Belgische richtlijn zou hierin een positieve rol kunnen spelen.

Dankwoord

We willen graag onze dank uitdrukken aan alle Belgische materi teiten, en met name aan alle B.OSS-contactpersonen. De resultaten die B.OSS boekt, zijn enkel mogelijk doordat deze mensen vrijwillig tijd en moeite nemen om te registreren.

Financiering


Referenties

9. De frequentie van eclampsie in België is zeer laag. Mogelijk kunnen de preventie en aanpak van deze zeldzame complicatie in
**INTRODUCTION**

L’éclampsie est une complication obstétricale rare associée à une morbidité et à une mortalité maternelles et périnatales élevées. La femme enceinte ou venant d’accoucher développe des convulsions généralisées, souvent précédées d’un stade de pré-éclampsie sévère. Les conséquences graves pour la mère incluent notamment des hémorragies intracrâniennes, une hypoxie et une défaillance d’organes; chez le nouveau-né, l’asphyxie perpartum et la mort à la naissance ne sont pas rares.

L’éclampsie touche 2 à 3% des femmes enceintes victimes d’une pré-éclampsie sévère n’ayant pas reçu de sulfate de magnésium (1, 2). Grâce à l’introduction du sulfate de magnésium, entre autres, la fréquence de l’éclampsie et, par conséquent, les taux de mortalité et de morbidité maternelles ont fortement diminué dans les pays à haut revenu (3, 4).

Le recensement et l’analyse des cas de morbidité maternelle sévère et de « near miss » maternel (MNM pour maternal near miss), défini comme une complication obstétricale potentiellement mortelle qui entraînerait la mort de la mère en l’absence d’intervention médicale immédiate (5), peuvent contribuer à une optimisation des soins périnatals.

L’objectif de l’étude présentée dans cet article était de cartographier la fréquence, les conséquences et la prise en charge des cas de morbidité maternelle sévère et de « near miss » maternel (MNM) en Belgique, à savoir la mortalité maternelle et la morbidité maternelle sévères, de la péripartum à la postpartum.

Entre janvier 2012 et décembre 2014, le Belgian Obstetric Surveillance System a recensé 74 femmes victimes d’une crise d’éclampsie, dont 59 ont pu être incluses dans l’analyse. Sur cette base, la fréquence de l’éclampsie en Belgique, à savoir 1,6 cas (IC 95%: 1,2-2,1) pour 10.000 accouchements, est faible en comparaison avec celle observée aux Pays-Bas (5,4 cas pour 10.000 accouchements) et au Royaume-Uni (2,7 cas pour 10.000 accouchements). Cette différence peut probablement s’expliquer par l’organisation de la prise en charge pré-natale en Belgique, où les soins prénatals chez le généraliste, la sage-femme ou le gynécologue sont très accessibles et où les femmes enceintes, quelle que soit la stratification du risque, sont suivies par un gynécologue, ce qui permet d’assurer la continuité des soins. La crise est survenue en milieu hospitalier pour 39 femmes (66%) et à domicile pour 18 (31%), et ce au cours de la période ante partum, per partum et post partum chez respectivement 36, 7 et 16 femmes. Du sulfate de magnésium a finalement été administré à 54 patientes (91,5%), dont 6 qui en avaient déjà reçu au préalable en guise de prophylaxie. 34 femmes (58%) ont également reçu un anticonvulsivant (dans la plupart des cas, du diazépam); chez 15 d’entre elles, il s’agit du traitement qui a été entamé en première intention au moment de la crise. 51 femmes (86%) ont reçu des antihypertenseurs; parmi celles-ci, 12 prenaient déjà ce type de médicaments avant la crise. 43 patientes (73%) ont été admises aux soins intensifs; chez 19 d’entre elles, il était question, en plus de la crise éclamptique, d’une comorbidité sévère. Un décès maternel (taux de létalité: 1,7%), ainsi que 4 cas de mort fœtale et 1 cas de mort néonatale (taux de mortalité périnatale: 8,5%) ont été recensés. En Belgique, la prévention et la prise en charge de cette complication rare pourraient probablement encore être améliorées en utilisant davantage l’acide acétylsalicylique à partir du 1er trimestre et en administrant des antihypertenseurs et du sulfate de magnésium à visée prophylactique en temps plus opportun. Les généralistes et les médecins urgentistes devraient également être sensibilisés à l’emploi du sulfate de magnésium en première intention en cas de crise d’éclampsie. Une directive belge pourrait avoir un effet positif à cet égard.

**L’éclampsie en Belgique: résultats du Belgian Obstetric Surveillance System**

Ann Langedock, Griet Vandenberghe, Virginie Van Leeuw, Charlotte Leroy, Yvon Englert, Frédéric Debiève, Myriam Hanssens, Kristel Van Calsteren, Kristien Roelens

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2. Département d’Obstétrique, UZ Gent
3. Centre d’Épidémiologie Périnatale (CEpiP); Faculté de Médecine, ULB, Bruxelles
4. Centre d’Épidémiologie Périnatale (CEpiP); Département d’Obstétrique, Clin. Univ. St Luc, Bruxelles
facteurs de risque, la prise en charge et l’issue de l’éclampsie en Belgique. La comparaison avec les données d’études similaires réalisées aux Pays-Bas et au Royaume-Uni permet d’évaluer la qualité et l’innocuité des soins obstétriques en Belgique.

**MÉTHODE**


La définition de l’éclampsie a été établie par analogie avec celle du *United Kingdom Obstetric Surveillance System* (UKOSS) (Tableau 1). Une enquête a également été réalisée sur les manifestations cliniques suivantes: troubles de la vision, céphalées, douleurs épi-gastriques, difficultés à respirer, oligurie et hyperréflexie.

Les données de la population de référence ont été obtenues, en Flandre, auprès du registre périnatal et du *Studiecentrum voor Perinatale Epidemiologie* (SPE) (6-8) et, en Wallonie et à Bruxelles, auprès du Centre d’Épidémiologie Périnatale (CÉpiP) (9-13). L’analyse statistique a été réalisée au moyen d’IBM SPSS version 23 (14), du logiciel de statistiques de MedCalc® (15) et d’EpiTools (16). Les caractéristiques socio-démographiques et obstétriques ont été examinées en comparaison avec celles de la population de référence en se basant sur les rapports de cotes et les intervalles de confiance à 95% (IC 95%). Les valeurs p < 0,05 étaient jugées significatives. La méthodologie du B.OSS et cette étude ont été approuvées par les comités d’éthique de l’Hôpital Érasme - Cliniques universitaires de Bruxelles (EC ULB 2012/111; B406201213660), de l’UZ Gent (EC UZG 2012/734; B670201215359 et EC UZG 2015/1470; B670201526875) et de l’UZ Leuven (mp08950-558924).

**RÉSULTATS**

**> INCIDENCE**

Le recensement a été réalisé par 97% (112/115) de l’ensemble des maternités belges, lesquelles ont pris en charge 98,6% des accouchements survenus au cours de la période d’étude. Au total, 74 femmes victimes d’une éclampsie ont été signalées. Dans 9 cas, aucun questionnaire n’a été renvoyé. Un cas

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### Tableau 1: Définition de l’éclampsie

- **Convulsions survenant pendant la grossesse ou dans les 10 jours suivant l’accouchement, avec présence d’au moins 2 des signes cliniques suivants dans les 24 heures suivant les convulsions:**

  - **hypertension:** tension artérielle diastolique maximale ≥ 90mmHg et élévation de la tension diastolique ≥ 25mmHg (en cas de tension diastolique < 90mmHg lors du premier contrôle prénatal);

  - **protéinurie:** au moins 1+ dans un échantillon d’urine aléatoire ou ≥ 0,3g dans une collecte des urines pendant 24 heures;

  - **thrombocytopénie:** plaquettes < 100.000/mm²;

  - **élévation des transaminases:** ALT ≥ 42UI/l ou AST ≥ 42UI/l.

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**Figure 1:** Signes et symptômes cliniques précédant la crise d’éclampsie.

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**PATIENTE AMBULATOIRE (N = 16)**

- **SYMPTÔMES**
  - HYPERTENSION: 2
  - PROTÉINURIE: 1

**PATIENTE HOSPITALISÉE (N = 24)**

- **SYMPTÔMES**
  - HYPERTENSION: 4
  - PROTÉINURIE: 9

**AUCUN SYMPTÔME D’ALERTE (N = 10)**

**AUCUN SYMPTÔME D’ALERTE (N = 3)**
a été exclu en raison d’antécédents d’épilepsie. Cinq cas ne remplissaient pas les critères d’inclusion. Finalement, 59 cas ont été inclus sur 371 170 accouchements, soit le nombre total d’accouchements en Belgique durant la période d’étude corrigé pour les maternités non participantes. Sur cette base, la fréquence de l’éclampsie en Belgique s’élève à 1,59 cas pour 10 000 accouchements (IC 95%: 1,23-2,05/10 000).

> FACTEURS DE RISQUE

Les caractéristiques socio-démographiques et obstétricales des femmes ayant été victimes d’une éclampsie sont reprises dans le tableau 2. La nulliparité et la grossesse à l’adolescence (< 20 ans) sont des facteurs de risque significatifs.

> SIGNES CLINIQUES PRÉCÉDANT ET SUIVANT LA CRISE ÉCLAMPTIQUE

Chez 18 femmes, la crise s’est produite à domicile. Les données du dernier contrôle étaient connues pour 16 femmes. Un des cas concernait une éclampsie postpartum survenue 5 jours après l’accouchement. L’intervalle entre le dernier contrôle et l’éclampsie était en moyenne de 11 jours (médiane: 7; intervalle: 2-36 jours; n = 16). Chez 6 femmes, des signes ou symptômes d’alerte (hypertension, protéinurie ou manifestations cliniques) avaient été décelés lors de ce dernier contrôle (Figure 1).

Chez 39 femmes, la crise s’est produite alors qu’elles étaient hospitalisées: ante partum (n = 17), per partum (n = 7), post partum (n = 15). Les données du dernier contrôle avant la survenue de la crise étaient connues pour 24 femmes: 21 d’entre elles présentaient des signes ou des symptômes d’alerte (Figure 1). Pour 2 femmes, l’endroit où la crise était survenue n’était pas clair, et 18 femmes (32%; n = 56) avaient été victimes de plusieurs crises.

La présence d’une hypertension, d’une protéinurie et de symptômes cliniques peu après la survenue de la crise d’éclampsie est illustrée dans la figure 2. Une thrombopénie et une élévation des transaminases ont été observées dans les 24 heures suivant l’éclampsie chez respectivement 14 (24,6%; n = 57) et 35 (61,4%; n = 57) femmes.

> CIRCONSTANCES DE LA CRISE D’ÉCLAMPSIE ET DE L’ACCOUCHEMENT

La durée de grossesse moyenne au moment de l’accouchement s’élevait à 34 semaines + 1 jour. 7 femmes (12%) ont accouché de très grands prématurés (< 28 semaines), 10 (17%) de grands prématurés (> 28 ≤ 32 semaines) et 22 (37%) de prématurés moyens (> 32 ≤ 37 semaines). La durée de grossesse moyenne était de 31 semaines + 5 jours (intervalle: 23 semaines-38 semaines + 5 jours) dans le cas des crises survenues à domicile, contre 33 semaines + 4 jours (intervalle: 24 semaines + 5 jours-39 semaines + 6 jours) pour les crises prénatales en milieu hospitalier. Les circonstances de l’accouchement sont résumées dans le tableau 3.

> STRATÉGIE

Du sulfate de magnésium a été administré à 54 femmes (91,5%), 6 patientes en avaient déjà reçu en guise de prophylaxie, et il a constitué le traitement de première intention au moment de la crise pour 23 femmes. Vingt-trois patientes ont reçu un bolus de 4g de sulfate de magnésium, suivi d’une dose d’entretien de 1g par heure; 21 femmes ont reçu un dosage différent. Pour 10 patientes, le dosage n’a pas été rapporté. Chez 15 femmes, le traitement de la crise d’éclampsie a commencé par un anticonvulsivant. Au total, 34 femmes ont reçu un anticonvulsivant, du diazépam dans la plupart des cas (n = 25). Pour 5 patientes, l’utilisation éventuelle d’anticonvulsivants n’a pas été rapportée. Des antihypertenseurs ont été administrés à 51 femmes; 3 patientes n’en ont pas pris.
Quant aux 5 dernières, on ne sait pas si elles en ont reçu ou non. Douze femmes avaient déjà pris des antihypertenseurs avant la survenue de la crise éclamptique. Les principaux antihypertenseurs administrés étaient les bêta-bloquants (71% des femmes), suivi des inhibiteurs calciques (51%), des antihypertenseurs centraux (29%), des vasodilatateurs (12%) et des inhibiteurs de l’enzyme de conversion de l’angiotensine (4%). Trente femmes ont reçu plusieurs types d’antihypertenseurs.

> ISSUE

Quarante-trois femmes (48%) ont été admises dans un service de soins intensifs pendant en moyenne 3 jours (intervalle: 1-14 jours). Chez 19 d’entre elles, il était question, en plus de l’éclampsie, d’une autre comorbidité sévère (pulmonaire, cardiaque, syndrome d’encéphalopathie postérieure réversible). Une mère est décédée, ce qui équivaut à un taux de létalité de 1,7%. Il s’agissait d’une primigeste d’origine africaine qui avait subi une césarienne à 33 semaines de grossesse en raison d’une pré-éclampsie précoce sévère combinée à un retard de croissance intra-utérin. Cinq jours après avoir accouché, elle a été victime d’une crise éclamptique, à la suite de quoi elle a été admise au service des soins intensifs et traitée au moyen d’antihypertenseurs. Elle est décédée 4 jours plus tard d’une combinaison d’œdème cérébral, d’œdème pulmonaire et d’insuffisance cardiaque.

Quatre cas de mort fœtale (à 23 semaines + 1 jour, 24 semaines + 5 jours, 25 semaines et 36 semaines + 3 jours d’aménorrhée) ont été recensés; tous sont survenus avant une crise éclamptique. Un nouveau-né est également décédé des suites d’une asphyxie 16 jours après un accouchement prématuré à 32 semaines + 1 jour, ce qui porte le taux de mortalité perinatale à 8,5%. L’issue néonatale est détaillée dans le tableau 4.

> COMPARAISON INTERNATIONALE

Dans le tableau 5, nous comparons les données belges avec celles d’études similaires réalisées aux Pays-Bas (Landelijke studie naar Ernstige Maternale Morbiditeit in Nederland)

### Tableau 2: Facteurs de risque d’éclampsie

<table>
<thead>
<tr>
<th>Facteurs socio-démographiques</th>
<th>Éclampsie (n = 59)</th>
<th>Population de référence (n = 376.471)</th>
<th>RC (IC 95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grossesse à l’adolescence</td>
<td>5 (8%)</td>
<td>7.566 (2%)</td>
<td>4,52* (1,81-11,29)</td>
</tr>
<tr>
<td>&gt; 35 ans</td>
<td>8 (14%)</td>
<td>65.685 (17%)</td>
<td>0,74 (0,35-1,56)</td>
</tr>
<tr>
<td>IMC &gt; 30kg/m²</td>
<td>8 (14%)</td>
<td>45.286 (12%)</td>
<td>1,15 (0,54-2,42)</td>
</tr>
<tr>
<td>Ethnicité noire</td>
<td>15 (25%)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Tabagisme**</td>
<td>6 (10%)</td>
<td>11.184 (3%)</td>
<td>1,21 (0,52-2,81)</td>
</tr>
</tbody>
</table>

| Facteurs médicaux              |                    |                                     |            |
| Hypertension préexistante      | 2 (3%)             | 17.415 (5%)                         | 0,72 (0,18-2,96) |
| Diabète préexistant            | 1 (2%)             | 20.521 (6%)                         | 0,30 (0,04-2,16) |

| Facteurs obstétricaux          |                    |                                     |            |
| Procréation assistée           | 3 (5%)             | 20.600 (6%)                         | 0,93 (0,29-2,96) |
| Nulliparité                   | 41 (70%)           | 164.495 (44%)                       | 2,94* (1,69-5,11) |

| PE/HELLP/… à l’anamnèse       | 6 (10%)            | -                                  | -          |

* Résultat significatif (p < 0,05)
** Sur base des résultats du SPE Flandre: 119.420 accouchements
– LEMMoN) et au Royaume-Uni (UKOSS) (4, 17, 18). Les données néerlandaises ont été adaptées en fonction de la définition plus stricte de l’étude UKOSS, que nous avons également utilisée dans notre étude.

En ce qui concerne la durée de la grossesse au moment de la survenue d’une éclampsie, les femmes aux Pays-Bas et au Royaume-Uni sont en moyenne à terme. En revanche, en Belgique, les cas d’éclampsie semblent plus souvent se produire plus tôt, aux alentours de 32 semaines. En comparaison avec les pays voisins, nous semblons avoir moins recours au sulfate de magnésium et utiliser davantage d’antihypertenseurs.

**COMMENTAIRE**

La fréquence de l’éclampsie en Belgique sur la base de cette étude (1,59 cas pour 10.000 accouchements) est inférieure à celle observée dans les pays voisins. Par ailleurs, en Belgique, les cas d’éclampsie se produisent en moyenne à un moment plus précoce de la grossesse. Cela peut s’expliquer par la continuité des soins dans notre pays, où chaque femme enceinte, indépendamment de la stratification du risque, est suivie dès le début de la grossesse par un (même) médecin, la plupart du temps un gynécologue. Aux Pays-Bas et au Royaume-Uni, les femmes présentant une grossesse à faible risque sont d’abord suivies par une sage-femme et ne sont renvoyées vers un gynécologue qu’en cas de problèmes. En Belgique, grâce à la continuité et à l’accessibilité des soins prénatals, les cas de pré-éclampsie (sévère) sont probablement détectés à un stade plus précoce et peuvent être pris en charge plus rapidement. Toutefois, même un suivi prénatal rigoureux ne permet pas d’exclure totalement la survenue d’une éclampsie, puisque notre étude révèle que plus de la moitié des femmes ne présentaient aucun symptôme d’alerte lors du dernier contrôle prénatal. Certains cas d’éclampsie resteront donc inéluctables, dans la mesure où il s’agit d’une détérioration clinique rapide.

Une bonne stratification du risque de chaque femme enceinte sur base de son anamnèse médicale et obstétricale demeure indispensable. En présence d’un risque accru de pré-éclampsie, une dose préventive d’acide acétylsalicylique à partir de 12 semaines de grossesse permet de réduire le risque de développement d’une (pré-)éclampsie (*number needed to treat* [NNT]: 42, IC: 26-200) (19). Le recours plus systématique à ce traitement pendant la grossesse pourrait permettre de faire baisser encore davantage le nombre de cas d’éclampsie.

Notre étude révèle que seulement un quart des femmes prenaient des antihypertenseurs avant la survenue de la crise éclamptique, un pourcentage qui a grimpé à plus de 85% au moment de la crise. Du sulfate de

---

**Tableau 3:**

Circonstances de l’accouchement chez les femmes victimes d’une éclampsie.

<table>
<thead>
<tr>
<th></th>
<th>Ante partum (n = 36)</th>
<th>Per partum (n = 7)</th>
<th>Post partum (n = 16)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Durée de grossesse (moyenne, intervalle)</strong></td>
<td>32s6j (23s1j - 38s5j)</td>
<td>38s2j (24s5j - 38s2j)</td>
<td>39s5j (31s5j - 40s6j)</td>
</tr>
<tr>
<td><strong>Intervalle éclampsie-accouchement</strong></td>
<td>72min (14min – 24h)</td>
<td>45min (5min – 25h)</td>
<td>39h (103min – 7h)</td>
</tr>
<tr>
<td><strong>Mode d’accouchement</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spontané, par voie basse</td>
<td>2</td>
<td></td>
<td>8</td>
</tr>
<tr>
<td>Provocation</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Césarienne</td>
<td>34</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td><strong>Induction du travail</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surmaturité</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pré-éclampsie</td>
<td>3</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Mort in utero</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

s: semaines; j: jours; min: minutes; h: heures
### Tableau 4: Issue néonatale pour les mères avec éclampsie en rapport avec la durée de grossesse à la naissance.

<table>
<thead>
<tr>
<th></th>
<th>Ante partum (n = 36)</th>
<th>Per partum (n = 7)</th>
<th>Post partum (n = 16)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Avant terme</td>
<td>À terme</td>
<td>Avant terme</td>
</tr>
<tr>
<td>Mort fœtale</td>
<td>3</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Dysmaturité</td>
<td>5</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Hospitalisation</td>
<td><strong>N</strong></td>
<td>9</td>
<td><strong>1</strong></td>
</tr>
<tr>
<td>N° Soins intensifs néonatals</td>
<td>22</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Assistance respiratoire</td>
<td>22</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

### Tableau 5: Comparaison internationale de l’éclampsie en Belgique, aux Pays-Bas et au Royaume-Uni.

<table>
<thead>
<tr>
<th></th>
<th>Belgique</th>
<th>Pays-Bas</th>
<th>Royaume-Uni</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accouchements pendant la période d’étude</td>
<td>371.170</td>
<td>358.874</td>
<td>775.186</td>
</tr>
<tr>
<td>Éclampsie</td>
<td>59 (1,6/10.000)</td>
<td>192 (5,4/10.000)</td>
<td>214 (2,7/10.000)</td>
</tr>
<tr>
<td>DA moyenne dans le groupe ante partum</td>
<td>31s5j</td>
<td>37s5j</td>
<td>38s0j</td>
</tr>
<tr>
<td>Intervalle éclampsie-accouchement (ante partum)</td>
<td>186min</td>
<td>420min</td>
<td>160min</td>
</tr>
<tr>
<td>Césarienne</td>
<td>122min</td>
<td>240min</td>
<td>127min</td>
</tr>
<tr>
<td>Sulfate de magnésium</td>
<td>54 (91,5%)</td>
<td>181 (94,3%)</td>
<td>211 (98,6%)</td>
</tr>
<tr>
<td>Prophylaxie</td>
<td>6 (10,2%)</td>
<td>19 (9,8%)</td>
<td>12 (5,6%)</td>
</tr>
<tr>
<td>Antihypertenseurs</td>
<td>51 (86,4%)</td>
<td>31 (16,1%)</td>
<td>151 (70,6%)</td>
</tr>
<tr>
<td>Mortalité maternelle</td>
<td>3 (1,7%)</td>
<td>3 (1,6%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Mortalité périnatale</td>
<td>5 (8,5%)</td>
<td>9 (5%)</td>
<td>5 (2%)</td>
</tr>
</tbody>
</table>

DA: durée d’aménorrhée; s: semaines; j: jours; min: minutes
magnésium a été administré en prophylaxie à 10% des femmes incluses dans cette étude, alors qu’un peu plus de 70% des femmes hospitalisées présentaient au moins 2 symptômes d’alerte (hypertension, protéinurie ou manifestations cliniques). Des crises éclamptiques auraient peut-être pu être évitées si du sulfate de magnésium prophylactique avait été administré plus tôt, en particulier dans le cas du groupe hospitalisé.


Les gros points forts de cette étude réside dans la participation de plus de 98% des maternités au recensement de cette complication obstétricale rare, ainsi que dans le grand taux de réponse de ce groupe. Malgré cela, nous ne pouvons pas garantir que tous les cas d’éclampsie en Belgique ont été inclus, puisque le B.OSS repose sur le rapport volontaire de cliniciens débordés. Le remplissage des questionnaires a été compliqué en raison de leur ampleur, mais aussi de certaines imprécisions qu’ils comportaient. De ce fait, quelques cas cliniquement évidents n’ont peut-être pas été inclus.

Pour améliorer les comparaisons internationales et les études collaboratives à l’avenir, l’INOSS (International Network of Obstetric Survey Systems) (22) a élaboré une définition univoque pour plusieurs complications obstétricales. Dans ce consensus, l’éclampsie est définie comme la survenue de convulsions pendant la grossesse ou dans les 10 jours suivant l’accouchement, en combination avec un seul signe clinique (hypertension, protéinurie, élévation des transaminases ou thrombopénie). Si on applique cette définition à la cohorte belge, 5 cas supplémentaires peuvent être inclus, et la fréquence de l’éclampsie en Belgique passe à 1,72 cas (IC 95% : 1,35-2,20) pour 10.000 accouchements.

CONCLUSION