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## **Maternal morbidity and mortality in the Netherlands and their association with obstetric interventions**

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# Maternal mortality after caesarean section in the Netherlands

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On behalf of the Dutch Audit Committee Maternal Mortality and Morbidity

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## ABSTRACT

**Objectives:** Maternal mortality is rare in high-resource settings. This hampers studies of the association between maternal mortality and mode of birth, although this topic remains of importance, given the changing patterns in mode of birth with increasing caesarean section rates in most countries. Purpose of this study was to examine incidence of caesarean section-related maternal mortality in the Netherlands and association of surgery with the chain of morbid events leading to death.

**Study Design:** We performed a retrospective cohort study using the Confidential Enquiry into Maternal Deaths, including all 2,684,946 maternities in the Netherlands between January 1st, 1999, and December 31st, 2013, registered in the Dutch Perinatal Registry. All available medical records of cases reported to the Dutch Maternal Mortality and Severe Morbidity Audit Committee were assessed by two researchers, and one or two additional experts in case of contradicting opinions, based on a set of pre-identified clinical criteria. Main outcome measures were (1) incidence and relative risk of maternal death following caesarean section and vaginal birth and (2) incidence of death directly related to caesarean section and death in which caesarean section was one of the contributing factors.

**Results:** Risk of death after caesarean section was 21.9 per 100,000 caesarean sections (86/393,443) versus 3.8 deaths per 100,000 vaginal births (88/2,291,503): Relative Risk (RR) 5.7 (95% Confidence Interval [CI] 4.2–7.7). Death directly related to complications of caesarean section occurred in 8/86 women: 2 per 100,000 caesarean sections. With addition of 43 women in which caesarean section did not initiate, but contributed to the chain of events leading to mortality, risk of death increased to 13 per 100,000 caesarean sections (51/393,443; RR 3.4; 95%CI 2.4–4.8). At the start of caesarean section, pre-existing morbidity was present in 70/86 women (81.4%).

**Conclusions:** Compared to vaginal birth, maternal mortality after caesarean section was three times higher following exclusion of deaths that had no association with surgery. In approximately one in ten deaths after caesarean section, surgery did in fact initiate the chain of morbid events.

## INTRODUCTION

Caesarean section rates have increased worldwide, despite several recommendations by the World Health Organization (WHO) to curb this increase.<sup>1,2</sup> A WHO ecological study found that rates above 10% are not associated with reduction of maternal and perinatal mortality.<sup>3,4</sup> Caesarean sections carry short- and long-term risks for index and subsequent births.<sup>5-8</sup>

Death of a woman during pregnancy, childbirth or puerperium has become a rare event in high-resource settings.<sup>9,10</sup> This makes examining the association between maternal mortality and mode of birth difficult. Previous facility-based studies comparing maternal mortality after caesarean and vaginal birth have shown inconsistent results. Comparisons are hampered by indication bias, limited power and absence of uniform categorization of caesarean sections. Only few studies have assessed caesarean section-related mortality on a nationwide scale.<sup>11-16</sup>

The Netherlands have seen an increase in caesarean section rate from 10.8% in 1999 to 16.6% in 2015, although still lower than in almost any other high-income country at that time.<sup>10,17</sup> Confidential Enquiries into Maternal Deaths revealed that the maternal mortality ratio (MMR) rose from 9.7 to 12.1 per 100,000 live births between the time frames 1983-1992 and 1992-2005. This rise was attributed to a changing risk profile, since advanced maternal age, pre-existing medical conditions and non-resident status increased among pregnant women.<sup>18,19</sup> In 1983-1992, maternal mortality was found to be seven times higher following caesarean section compared to vaginal birth.<sup>14</sup>

Aim of this study was to investigate risk of maternal mortality following caesarean section and vaginal birth in the Netherlands in more recent times, and assess to what extent surgery contributed to the chain of events that ultimately leading to maternal death.

## MATERIALS AND METHODS

This was a nationwide retrospective cohort study, including all maternal deaths reported to the Dutch Maternal Mortality and Severe Morbidity Audit Committee (MMSMAC) between January 1st, 1999, and December 31st, 2013.

In the Netherlands, all maternal deaths are voluntarily reported to the MMSMAC by specialists, general practitioners and midwives. The MMSMAC consists of eleven obstetricians and one obstetric anesthetist. All members are employed at either non-university teaching hospitals or university hospitals. Deaths were cross-checked with maternal mortality data from Statistics Netherlands (CBS) up to 31st December 2011. Thereafter, cross-check did not happen due to very small numbers of maternal deaths that CBS feared individual cases could have become recognizable, putting confidentiality at risk.<sup>20</sup>

After a case is reported, all medical records are requested to be sent to the MMSMAC. These include antenatal charts, microbiology and laboratory results, theatre records, autopsy reports and local maternal death reviews. The MMSMAC classifies underlying causes of death, mode of death and audits substandard care factors. All patient records are anonymised and kept in a secured database that can only be accessed after approval by MMSMAC.

Records for all maternal deaths following caesarean section were accessed and information about maternal history and current pregnancy extracted. Maternal death was defined according to the WHO's International Classification of Diseases, tenth revision (ICD- 10).<sup>21</sup> Late maternal deaths – occurring longer than 42 days but within one year after delivery - and deaths unrelated to pregnancy, e.g. traffic deaths were excluded from calculations and analysis. After in-depth examination of case files, deaths were categorised according to relation with mode of delivery as directly related, associated and not associated with caesarean section. A pre-specified set of criteria was used to categorise deaths according to relation with surgery. Death was defined to be directly related to surgery if the chain of events leading to death started during or within 24 h after surgery and the cause or mode of death were the direct result of surgical or anesthetic complications. In addition, a death was also categorised as directly related to surgery, if the chain of morbid events started with uterine scar rupture resulting from previous caesarean section. Deaths were categorised to be associated with surgery, if caesarean section was assessed to have contributed to the chain of morbid events that had already started prior to surgery. Such deaths 'associated with caesarean section' occurred in women with already complicated pregnancies or labor, but in whom surgery or anesthesia was deemed to have contributed to the fatal outcome, as assessed by the audit panel. Deaths were categorised as not associated with caesarean section, if surgery had not contributed. These deaths included women who had given birth by perimortem caesarean section during cardiopulmonary resuscitation and women with advanced stages of obstetric or non-obstetric illness, in whom caesarean section was done to save the life of the fetus with poor chances of a woman's survival. Categorization was done by two investigators (AK and TA) in the following manner: in a first round both investigators independently examined and categorised all maternal deaths according to the above definition. AK is a registrar who had no previous knowledge of the cases. TA is a consultant obstetrician who has been a member of the MMSMAC for seven years and was involved in obstetric audit in other settings even before that time.<sup>22-24</sup> For deaths in which there was discrepancy between these two investigators, a second round was conducted after additional inquiry into the woman's medical records. In this round, a third (JR, previous chair of the MMSMAC with ample experience in audit<sup>25,26</sup>) and/or fourth investigator (prof. K. Bloemenkamp, current chair of the MMSMAC) were consulted and consensus was needed for eventual categorization.

We calculated the overall MMR for the study period and risk of death following caesarean section and vaginal birth before and after excluding cases with no association between surgery and mortality. MMR was defined as the number of maternal deaths per 100,000 live births. Caesarean sections were classified into 'primary or elective' in cases where vaginal birth had never been intended even if the woman presented in labor, and 'secondary' when decision for caesarean section was made during labor. This classification is not meant to reflect sense of emergency surrounding the procedure and is based on the intention to treat principle. Pre-existing morbidity was defined as any medical or obstetric condition, or any pregnancy-related complication present before birth, which had a significant impact on the pathophysiological pathway leading to death. Often, these complications were the indication for caesarean section. Obesity was defined as a body mass index of 30 kg/m<sup>2</sup> or more, or when body mass index was unknown, when obesity was explicitly stated in the maternal charts.

The total number of live births, for calculation of MMR, was extracted from Statistics Netherlands.<sup>20</sup> National numbers for caesarean sections and vaginal births were collected from the Dutch Perinatal Registry, in which approximately 95.5% of all births with gestational age of at least 22 weeks were recorded before 2011, and since that year more than 99%.<sup>17</sup>

Statistical analyses were performed using IBM SPSS for Windows version 21 (SPSS Inc., Chicago, IL, USA). A two-sided  $p < 0.05$  was considered statistically significant.

The MMSMAC is authorised and mandated by the Netherlands Society of Obstetrics and Gynaecology for collection and analysis of maternal mortality in the Netherlands. Members are appointed by the Society. Confidential Enquiry into Maternal Deaths involves the assessment of anonymised reported data. In the Netherlands, ethical approval is not required for confidential enquiry.

No funding was received for this study.

## RESULTS

Over the fifteen-year study period, 269 deaths (excluding deaths unrelated to pregnancy) were reported to the MMSMAC. Of these 269 deaths, 32 were late deaths and therefore excluded, leaving 237 maternal deaths for further analysis. Eighty-six women (36.3%) died following caesarean section, 88 (37.1%) following vaginal birth, 55 (23.2%) undelivered and eight (3.4%) following complications of abortion, miscarriage or ectopic pregnancy. Overall MMR was 8.3 per 100,000 live births (237/2,841,663). Risk of maternal mortality following caesarean section was 21.9 per 100,000 caesarean sections (86/393,443) versus 3.8 per 100,000 vaginal births (88/2,291,503) (Relative Risk [RR] 5.7; 95% Confidence Interval [CI] 4.2–7.7).

In the categorization of deaths according to the relation with surgery the two investigators agreed in 76/86 cases (kappa for agreement 0.8), a second round was needed in ten cases and a third round in only one. In eight women (9.3%), death was categorised as directly related to caesarean section, giving a case fatality rate of 2 per 100,000 caesarean sections (Box 1). In addition, in 43 women (50%), death was categorised to be associated with caesarean section. This gives a combined case fatality rate of 13 per 100,000 caesarean sections (51/393,443) and a RR for caesarean section of 3.4 (95%CI 2.4–4.8) compared to vaginal birth. There was no association between caesarean section and death in 34 women (39.5%). One maternal death could not be categorised due to missing medical records.

Women who died after caesarean section had a mean age of 31.9 years (standard deviation 5.6). The majority ( $n = 59$ ; 68.6%) had preterm births. Twenty-four women (27.9%) were of non-Dutch origin. Eleven (12.8%) had a caesarean section in a previous pregnancy. At their initial antenatal visit, 50 women (58.1%) were booked as 'high-risk' for obstetric care, while 36 (41.9%) started as 'low-risk' in primary midwifery care and were referred during pregnancy or labor (Table 1). At the time of surgery, 70 women (81.4%) had one or more pre-existing morbidities: 32 (37.6%) hypertensive disorders of pregnancy, 11 (12.8%) cerebrovascular disorders (meningitis, encephalitis, epilepsy, neurological tumor, intracranial haemorrhage), ten (11.6%) cardiovascular disorders (severe hypertension, dilated aorta, aortic dissection, cardiomyopathy or mechanical heart valve), ten (11.6%) sepsis and ten (11.6%) other obstetric and non-obstetric conditions (liver cirrhosis, psychiatric conditions, morbid obesity, abnormally invasive placenta, history of severe thromboembolism, acute fatty liver of pregnancy).

Of all caesarean sections, 58 (67.4%) were 'primary or elective' and 28 (32.6%) 'secondary'. Most frequent indications for caesarean section were hypertensive disorders in 30 women (34.9%), followed by 'severe non-obstetric medical condition' in 22 (25.6%) and fetal distress in 12 (14%) (Table 2). Commonest underlying causes of death were hypertensive disorders ( $n = 25$ ; 29%), cardiovascular disease ( $n = 11$ ; 128%) and cerebrovascular disease ( $n = 10$ ; 116%) (Table 3).

Compared to 1983–1992, combined risk of maternal mortality directly due to or associated with caesarean section decreased from 28 to 13 per 100,000 operations (RR 0.47; 95%CI 0.3–0.74).<sup>14</sup> Risk of maternal mortality directly related to surgery or anesthesia decreased considerably from 13 to 2 per 100,000 (RR 0.16; 95%CI 0.07–0.38). Deaths due to anesthesiology-related complications decreased from 3.7 to 0.3 per 100,000 surgeries (RR 0.07; 95% CI 0.008–0.62) (Table 4).



**Table 1.** Maternal characteristics of women who died after caesarean section

<b>Maternal characteristics</b>	
	N (%)
<b>Ethnicity</b>	
Dutch native	62 (72.1%)
Black African	12 (14%)
Surinam/Dutch Antilles	6 (7%)
Asian	3 (3.5%)
Turkish	1 (1.2%)
Missing	2 (2.3%)
<b>Age (years)</b>	
<20	2 (2.3%)
20-24	10 (11.6%)
25-29	18 (20.9%)
30-34	28 (32.6%)
35-39	20 (23.3%)
≥ 40	7 (8.1%)
Missing	1 (1.2%)
<b>Parity (n)</b>	
0	48 (55.8%)
≥ 1	38 (44.2%)
<b>Gestational age (weeks <sup>+days</sup>)</b>	
Term (≥37)	27 (31.4%)
32 - 36 <sup>+6</sup>	41 (47.7%)
24 - 31 <sup>+6</sup>	18 (20.9%)
<b>Multiple gestation</b>	
Singleton	78 (90.7%)
Multiple	8 (9.3%)
<b>Previous caesarean section</b>	11 (12.8%)
<b>Pre-existing morbidity</b>	70 (81,4%)

**Table 2.** Indications of Caesarean Section

	<b>Primary N=58 (67.4%)</b>	<b>Secondary N=28 (32.6%)</b>	<b>Total N=86</b>
Hypertensive disorder	24 (41.4%)	6 (21.4%)	30 (34.9%)
Preeclampsia	18 (26,3 %)	6 (21.4%)	24 (27.9%)
HELLP	4 (6.9 %)	0	4 (4.7%)
Eclampsia	2 (3.4 %)	0	2 (2.3%)
Non-obstetric medical condition <sup>a</sup>	20 (34.5%)	2 (7.1%)	22 (25.6%)
Fetal distress	1 (1.7%)	11 (39.3%)	12 (14%)
Prolonged labor	0	8 (28.6%)	8 (9.3%)
Perimortem	5 (8.6 %)	1 (3.6%)	6 (7%)
Non-vertex presentation	4 (6.9 %)	0	4 (4.7%)
Previous caesarean section	2 (3.4 %)	0	2 (2.3%)
Other <sup>b</sup>	2 (3.4 %)	0	2 (2.3%)

<sup>a</sup> Six cases of deteriorating heart disease, eight cases of non-obstetrical sepsis, five cases of cerebrovascular haemorrhage, two cases of respiratory failure due to pneumonia and one due to cystic fibrosis.

<sup>b</sup> One case of uterine leiomyoma and one with previous uterine surgery.

**Table 3.** Underlying causes of maternal mortality according to association with caesarean section.

	<b>Direct (n=8)</b>	<b>Association (n=43)</b>	<b>No association (n=34)</b>	<b>Total (n=86)<sup>a</sup></b>
<b>Obstetric causes</b>				
Hypertensive disorders	0	17	7	25 (29%) <sup>a</sup>
Preeclampsia	0	10	2	12 (14%)
Eclampsia	0	3	3	6 (7%)
HELLP	0	4	2	7 (8.1%) <sup>a</sup>
Obstetric sepsis	2	5	0	7 (8.1%)
Obstetric haemorrhage	5	2	0	7 (8.1%)
Thromboembolism	0	5	0	5 (5.8%)
Acute Fatty Liver of Pregnancy	0	3	0	3 (3.5%)
Amniotic Fluid Embolism	0	2	0	2 (2.3%)
Anesthesiological complication	1	0	0	1 (1.2%)
Unknown	0	4	1	5 (5.8%)
<b>Non obstetric causes</b>				
Cardiovascular disease	0	3	8	11 (12.8%)
Cerebrovascular disease	0	0	10	10 (11.6%)
Non-obstetric sepsis	0	0	5	5 (5.8%)
Mental disorders	0	0	2	2 (2.3%)
Other	0	2	1	3 (3.5%)

<sup>a</sup> One case of maternal death due to HELLP could not be categorised due to missing information but was taken into account for totals of underlying cause of death.

**Table 4.** Women with hypertensive disorders of pregnancy, by primary or secondary caesarean section.

	<b>Primary 27 (81.8%)</b>	<b>Secondary 6 (18.2%)</b>	<b>Total (N=33)</b>
Pregnancy induced hypertension <sup>a</sup>	1 (100%)	0	1
Pre-eclampsia <sup>b</sup>	12 (70.6%)	5 (29.4%)	17
Eclampsia <sup>c</sup>	6 (85.7%)	1 (14.3%)	7
HELLP-syndrome <sup>d</sup>	8 (100%)	0	8

<sup>a</sup> Mode of death: epilepsy.

<sup>b</sup> Mode of death: Hypovolemic shock (5), Intracerebral haemorrhage (3), Multiorgan failure (2), Acute Respiratory Distress Syndrome/respiratory failure (3), Sepsis (2), Thromboembolism (1), Suicide (1).

<sup>c</sup> Mode of death: Intracerebral haemorrhage (4), post anoxic encephalopathy (2), respiratory failure (1).

<sup>d</sup> Mode of death: Intracerebral haemorrhage (5), Multi-organ failure (2), Unknown

## DISCUSSION

Caesarean section in the Netherlands was associated with a three-fold increase in risk of maternal death compared to vaginal birth, which is in line with literature from other settings.<sup>11-13</sup> Impact of surgery on the chain of events varied, and in most women pre-existing morbidity was present at the start of surgery, hampering differentiation between contribution of surgery and other morbid factors. In approximately one in ten deaths, caesarean section initiated the chain of events, and in half of deaths the operation contributed. At the same time, our findings indicate that the risk of caesarean section has decreased significantly in this period compared to the previous period of investigation.<sup>14</sup>

The decrease in anesthesiology-related deaths is in line with results from the United Kingdom and may be due to improved care and procedures for women before, during and after surgery.<sup>27</sup> Hypertensive disorders remain the predominant underlying cause of death in our study.<sup>14,18</sup> This underlines the fact that preeclampsia poses women at increased risk of haemorrhage and that caesarean section may contribute to this risk.<sup>28</sup> Finally, even though the percentage of women with a non-native background is comparable to the general population during the study period (19.5% in 2006 increasing to 25.7% in 2013), this does not apply to women from sub-Saharan Africa and Suriname or the Dutch Antilles, who were over-represented.<sup>29</sup> This supports previous literature that non-native background or immigrant status is a risk factor for maternal mortality and morbidity and that risk factors differ importantly between different non-native groups.<sup>18,30,31</sup>

Comparison with previous studies from France and Brazil is hampered by variations in study design and setting.<sup>13,32</sup> Maternal deaths with obstetric or non-

obstetric morbidity present before birth and multiple gestations were excluded in those studies in order to correct for indication bias. We purposely did not exclude women with pre-existing maternal morbidity or multiple gestation because also in these women, mode of birth may contribute to the chain of events leading to death. Only by including these cases can the actual incidence of surgery-related death be calculated. Accuracy of comparisons of underlying causes of death between different countries has been questioned, since classification is not uniform.<sup>22</sup>

Major strength of our study is its nationwide coverage. Categorization of association of caesarean section with maternal death was performed by two independent investigators, and in multiple rounds in case of discrepancy in order to minimise interpretation bias. We excluded cases in which caesarean section did not contribute to death, avoiding overestimation. Completeness of case files was exceptionally high for a retrospective study covering 15 years and allowed categorization in all but one woman.

Reporting maternal deaths in the Netherlands is based on voluntary reporting and cross-check with Statistics Netherlands took place up to December 2011, leaving 22 cases in our cohort that could not be cross-checked. Guidelines of the Netherlands Society of Obstetrics and Gynaecology describe failure of reporting maternal deaths as substandard care. For the period 1993–2005, we found that cross-checking revealed an additional 11% of unreported maternal deaths.<sup>18</sup>

Main limitations are inherent to the retrospective design. Indication bias is unavoidable, since women with severe morbidity before birth are at higher risk of caesarean section. A threefold higher risk, however, does not differ from previous studies in the Netherlands and other settings.<sup>8,12,13</sup> Since we had to rely on case notes, we were also confronted with variations in quality of documentation. A significant time frame was necessary to achieve sufficient numbers of deaths, but obstetric practice will have changed over time. Perimortem caesarean sections are performed more frequently since the introduction of the “Managing Obstetric Emergencies and Trauma” course in 2004 and hypertensive disorders are treated more aggressively.<sup>33,34</sup>

Finally, considering rising rates of caesarean section, obstetric caregivers should realise that risk of maternal death following caesarean section in high-income countries, even though small, remains threefold higher than after vaginal birth. Especially in women with severe non-obstetric morbidity and hypertensive complications of pregnancy, vaginal birth should be considered, maternal and fetal condition permitting. Ensuring that caesarean sections are performed when medically necessary remains an important cornerstone to avoid unnecessary maternal deaths.

**Box 1.** Cases in which maternal mortality was a direct consequence of caesarean section or anesthesia.

**Case 1:** G1P0, 25 years, previously healthy, breech presentation, failed external cephalic version, elective caesarean section at term, fever post-partum, antibiotics given, paralytic bowel obstruction, septic shock, re-laparotomy with no abnormalities, progressive septic shock, maternal death six days post-partum due to obstetric sepsis.<sup>35</sup>

**Case 2:** G4P2, 29 years, previously healthy, twin gestation, elective caesarean section due to breech lie of first child at term, first postoperative day cardiac arrest and death. Postmortem: severe intra-peritoneal haemorrhage.

**Case 3:** G2P1, 39 years, Asian, history of caesarean section and pre-existing hypertension; current pregnancy: placenta praevia, mild pre-eclampsia and intrauterine growth restriction. Elective caesarean section at 35+1 weeks, due to suspicion of fetal distress. Perioperative: covered uterine rupture and profound difficulty of placental removal. Post-operative postpartum haemorrhage, re-laparotomy and emergency peripartum hysterectomy, second and third re-laparotomy due to intra-peritoneal bleeding, maternal death 19 days after delivery due to Acute Respiratory Distress Syndrome and pneumonia.

**Case 4:** G2P1, 33 years, sub-Saharan African, with history of sickle cell trait and chronic hepatitis B infection, prolonged labor at term, emergency caesarean section complicated by laceration of left uterine artery. First day postpartum cardiopulmonary resuscitation due to hypovolemic shock, emergency re-laparotomy, bleeding from uterotomy, Acute Respiratory Distress Syndrome, multi-organ failure, maternal death due to obstetric sepsis 22 days post-partum.

**Case 5:** G1P0, 22 years, sub-Saharan African, previously healthy, induced at 42 weeks, emergency caesarean section due to prolonged labor, complete spinal block, cardiac arrest, maternal death.

**Case 6:** G1P0, 28 years, previously healthy, induced at 42 weeks, uncomplicated emergency caesarean section due to fetal distress, massive postpartum haemorrhage immediately after surgery, uterotonics, maternal death five days postpartum due to disseminated intravascular coagulation and multi-organ failure.

**Case 7:** G4P0, 23 years, previously healthy, Surinamese; current pregnancy: HELLP syndrome, breech lie. Emergency caesarean section at 36 weeks, due to fetal distress, post-operative intra-peritoneal bleeding treated with multiple blood transfusion because re-laparotomy was deemed too hazardous, cardiac arrest, Cardiopulmonary resuscitation, re-laparotomy due to abdominal compartment syndrome, maternal death three days postpartum due to multi-organ failure.

**Case 8:** G2P1, 40 years, obstetric history: eclampsia and caesarean section. Current: pre-eclampsia, preterm labor at 33+5 weeks, emergency caesarean section due to fetal distress, no signs of clotting disorder, complicated by excessive blood loss, postoperative hypovolemic shock, re-laparotomy: emergency peripartum hysterectomy, maternal death one day post-partum due to ischemic complications.

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