Termination of pregnancy for maternal indications at the limits of fetal viability, an inventory in all Dutch tertiary care centres

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Eerden L van\textsuperscript{a}, Zeeman GG\textsuperscript{j}, Page-Christiaens GCM\textsuperscript{c}, Vandenbussche F\textsuperscript{d}, Oei G\textsuperscript{e}, Scheepers HCJ\textsuperscript{i}, Eyck J van\textsuperscript{g}, Middeldorp JM\textsuperscript{h}, Pajkrt E\textsuperscript{i}, Duvekot JJ\textsuperscript{b}, Groot CJM\textsuperscript{a} de and Bolte AC\textsuperscript{a}

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Abstract

Objective: Maternal morbidity, either pregnancy-related or pre-existent can become life-threatening and of such severity to warrant termination of pregnancy (TOP). In this situation chances of fetal survival are usually poor, either because of low gestational age, and/or because of the fetal effects of the maternal condition. Examples include severe growth restriction in pre-eclampsia and intra-uterine infection due to very early preterm prelabour rupture of membranes. There are nearly no reports on the prevalence of termination of pregnancy for maternal indication at the limits of fetal viability. We investigated the prevalence and indications for TOP on maternal indication in the Netherlands during the past decade.

Study design: we conducted a retrospective review of the medical records of all women who underwent TOP for maternal indications between 22 to 27 completed weeks of gestation in all 10 tertiary care centres in the Netherlands from 2000 to 2009.

Results: During the study period there were 1,929,470 deliveries of which 163,052 (8.4%) took place in tertiary care centres of which 177 pregnancies were terminated for severe maternal disease, 131 for hypertensive disorders, 29 for intra-uterine infection and 17 for other reasons. The mean gestational age at TOP was 171 days (24\textsuperscript{3/7} weeks) ± 10 days. No maternal deaths were recorded. The overall perinatal mortality was 99.4%.

Conclusion: Over a ten year period TOP for maternal indications occurred in 0.1% of deliveries in the 10 Dutch perinatal centres. Hypertensive disorders comprised three quarters of cases.
Article summary

Strengths and limitations of the study:

- This study is the first to estimate the incidence of termination of pregnancy for maternal indications at the limits of fetal viability. The international literature lacks reports on this subject.
- The results of this study raise several questions concerning policy and approach of severely sick mothers at the limits of fetal viability. This might stimulate multidisciplinary discussion as well as more uniform decision making.
- This study is a retrospective study which could introduce bias.
- During the study period there have been changes in protocols concerning active perinatal management at the limits of fetal viability in The Netherlands. This might have had an impact on the approach of severely sick mothers.
Introduction
Maternal morbidity during pregnancy can become life-threatening and severe enough to warrant termination of pregnancy (TOP). Under Dutch legislation termination of pregnancy is possible up to the gestational age where a newborn can survive outside the womb. This is currently considered 24\textsuperscript{0/7} weeks for adequately grown fetuses without lethal disorders and a sufficient amount of amniotic fluid for lung development\textsuperscript{1}. In case of lethal fetal disorders such as trisomy 18, 13 or triploidy termination is also allowed beyond 24 weeks, provided a number of criteria are fulfilled \textsuperscript{2}. These cases are audited by a committee of the Dutch Society of Obstetrics and Gynecology. Termination for severe fetal disorders in case of dismal, but not necessarily lethal, prognosis for the fetus may be excepted from legal prosecution provided adherence to stringent criteria and after assessment by an expert committee appointed by the ministries of Health and Justice consisting of an obstetrician, a paediatrician and an ethicist, and chaired by a lawyer\textsuperscript{2}. This committee reports directly to the Attorney General, the highest legal authority in The Netherlands. Termination of pregnancy beyond 24 weeks’ gestation for life-threatening maternal conditions in combination with dismal fetal prospects (e.g. due to severe growth restriction or anhydramnios) are generally not reported, since termination of pregnancy in such cases is considered inevitable and the only justifiable management option to prevent deteriorating maternal morbidity or even mortality. According to the Guideline on Late Termination of Pregnancy of the Dutch Society of Obstetrics and Gynecology maternal indications that could warrant TOP are, not limitative: hypertensive disorders with organ dysfunction, sepsis, severe exacerbation of auto-immune disorder, severely deteriorating cardiac function, transplant rejection, rapidly progressing malignancies as well as life-threatening
major obstetric haemorrhage. In these situations the fetus is also compromised, either because of the gestational age, and/or because of the low estimated fetal weight. Termination of pregnancy beyond 24 weeks’ gestation for these indications is considered to be extremely rare and is, as such, limited to perinatal tertiary care centres. It is only performed after extensive multidisciplinary consultation.

The literature lacks reports on the prevalence of termination of pregnancy for maternal indication at the limits of fetal viability. The gestational age and estimated fetal weight to consider “active perinatal management” directed towards survival has recently been lowered to 24 weeks and 500 grams in many countries. In the Netherlands such protocols for perinatal and neonatal management at the limits of viability have been revised in 2010. This inevitably will have an impact on the approach of severely sick mothers. We aimed to investigate the prevalence of and indications for TOP in severely sick mothers, at the limits of fetal viability in the Netherlands between 2000 and 2009.

Methods
We conducted a retrospective review of the medical records of all women who underwent TOP for maternal indications between 22 and 27 completed weeks of gestation in all 10 perinatal tertiary care centres in the Netherlands. Cases were identified by using local delivery databases. In all cases the fetus was judged to be non-viable, either because of the gestational age or because of the impact of maternal disease on the prospects for the fetus, e.g. severe growth restriction. The inclusion and exclusion criteria are listed in table 1. Data extraction was performed by the first author in all cases. Data on the total number of deliveries in the 10-year period were extracted from The Netherlands Perinatal Registry (PRN foundation).
Cases of TOP for maternal indication at the limits of fetal viability are not separately registered in this registry.

The study was reviewed by the medical ethics committee of the VU Medical Center in Amsterdam. An ethics approval was not required.

Results
In the ten year study period there were 1,929,470 deliveries in the Netherlands of which 163,052 (8.4%) took place in the 10 tertiary perinatal care centres. Of those 11474 deliveries occurred between 22\(\text{0/7}\) and 27\(\text{6/7}\) weeks of gestation. A total of 177 (1.5%) fulfilled the inclusion criteria, 172 singleton and 5 twin pregnancies. TOP was performed for hypertensive disorders and preterm prelabour rupture of membranes (PPROM) with intra-uterine infection in 131 (74%) and 29 (16%) cases, respectively.
In 17 cases (9%) there was another motive to terminate the pregnancy (figure 1). The mean gestational age at TOP was 171 days (24\(\text{3/7}\)) weeks \(\pm\) 10 days. In the hypertension group the mean gestational age was 173 days (24\(\text{5/7}\)) \(\pm\) 9.7 days as compared to 167 days (23\(\text{6/7}\)) \(\pm\) 10.1 days in the infection group and 162 days (23\(\text{1/7}\)) \(\pm\) 7.0 days for the other indications. The gestational age at termination is significantly less in the infection group compared to the hypertension group (p= 0.0055). This also applies to the hypertension group compared to the other indications (p<0.001), or infections compared to the other indications (p<0.5).
There were no cases of maternal mortality. A total of 182 neonates were born. There was one unexpected survivor born at GA 25\(\text{4/5}\) weeks’ gestation with a birth weight of 600 grams. This pregnancy was terminated without fetal heart rate monitoring for severe HELLP syndrome using intravenous sulprostone. The child is now four years old and has a normal development so far.
The number of pregnancies terminated beyond the limit of 24 weeks’ gestation was 113 (64%). In 94 of these cases (83%) pregnancy was terminated for a severe hypertensive disorder. Fifteen pregnancies (13%) were terminated for overt intrauterine infection in the setting of PPROM and four pregnancies (3.5%) for other indications (table 2).

In 2006 a national guideline on active perinatal and neonatal management was introduced. Before 2006, active management was generally started at 26 weeks’ gestation, whereas this was lowered to 25 weeks’ gestation in the guideline. The introduction of this guideline has had no major effect on the number of TOP for maternal indications. Figure 2 shows the number of TOP per year.

The incidence of TOP varied substantially between different centres (table 3). Decisions to recommend termination of pregnancy were always taken following extensive discussions by a multidisciplinary team. In all cases at least one obstetrician and one neonatologist were involved. Other specialists, such as surgeons, cardiologists, oncologists and intensive care specialists were involved when indicated.

Two exemplary cases:

Case 1: a nulliparous woman, with an unremarkable history, developed severe pre-eclampsia with progressive HELLP syndrome at a gestational age of 23 weeks and 2 days. She was admitted and was treated with multiple intravenous antihypertensive drugs and magnesium sulphate. Ultrasound showed an estimated fetal weight of 480 grams. She was counselled for termination of pregnancy due to the early gestational age and the progressive course of the disease and delivered a stillborn girl of 470 grams (<p10) at 24 weeks’ gestation. The delivery took place on the intensive care unit due to refractory hypertension and pulmonary oedema.
Case 2: a woman in her fourth pregnancy was admitted at a gestational age of 22 weeks’. Her obstetric history revealed dilated peripartum cardiomyopathy. Pre-conceptionally, she was strongly advised not to conceive again. She was admitted to the ICU because of severely deteriorating cardiac function. After extensive counselling by a multidisciplinary team consisting of obstetricians, cardiologists and neonatologists the pregnancy was terminated at 22 weeks and 4 days’ gestation. She delivered a stillborn son.

Comment

In the period 2000-2009 we identified 177 cases of TOP for life-threatening maternal morbidity in the ten tertiary perinatal centres in the Netherlands. We found that there was a difference in incidence of TOP between the tertiary care centres. This may, amongst others, be caused by different local views on active neonatal management at the limits of viability in a period where thresholds for active management were subject to gradual change (see table 3). It is also possible that centres choose to continue the pregnancy anticipating an intra-uterine fetal demise within days.

Whether or not a fetus is considered viable, in the absence of congenital anomalies, mainly depends on the gestational age as well as the estimated fetal weight. Dutch guidelines are in place to recommend whether or not to start active neonatal management by a neonatologist in cases with spontaneous preterm labour and an expected weight appropriate for gestational age. These guidelines are periodically revised based on current (inter)national practice standards. Prior to 2006 the general limit for active obstetric and neonatal management was 26 weeks’ of gestation. After 2006 the recommended limit was 25 weeks’ gestation, with an estimated fetal weight of at least 500 grams7. In the latest guideline dating September 2010, the
recommended limit is 24 weeks' gestation for intubation and ventilation and 25 weeks
for cardiac resuscitation. Estimated fetal weight is no longer included². Protocols
have not been simultaneously introduced in all centres (figure 2). This possibly
explains the differences between centres in the current study. Nevertheless the
prospects of children born at 24-25 weeks are poor, even with active management. A
recent report showed that infants who received active perinatal and neonatal
management survived in 43% of cases at 24 weeks’ and in 61% of cases at 25
weeks’. Severe short term neonatal morbidity was registered in 70-80% of surviving
children⁹. In case of severe maternal morbidity in pregnancy, the prospects for an
intact survival for the fetus are considered to be even worse due to the combination
of a low gestational age and, in most cases, severe growth restriction or fetal
inflammatory response syndrome, as well as the deleterious effects of the underlying
maternal condition, such as chronic fetal hypoxia. In case it becomes inevitable for
the mother’s sake to terminate the pregnancy at the limits of fetal viability, this
expected extremely poor outcome of the child does not support an active
fetal/neonatal management. A caesarean section puts the mother at even higher
short term and long term risks. Therefore, termination via induction of vaginal delivery
with prostaglandins and without fetal monitoring will often be the safest policy.
Hypertensive disease comprised three quarters of the cases. Overall in 64% of the
cases termination was performed after 24 weeks’ of gestation. In 83% of these cases
the indication for the termination was a hypertensive disorder. Experts in the field as
well as the WHO guideline and NICE guideline on hypertensive disorders in
pregnancy, recommend that women who develop severe pre-eclampsia at less than
23 weeks should be counselled towards termination of pregnancy¹⁰,¹¹,¹². Gaugler et
al describe 26 pregnancies, complicated by pre-eclampsia with an onset before 24
weeks’ gestation and managed expectantly. The overall perinatal mortality was 82%, with major maternal morbidity in 65% of the women\textsuperscript{13}.

In 16% of overall cases and 13% of cases beyond 24 weeks, the indication for terminating pregnancy was intra-uterine infection with overt or threatening maternal sepsis. Septic shock and maternal death have been reported in pregnancies managed conservatively\textsuperscript{14,15,16}. Therefore, termination of pregnancy is recommended in case of serious clinical infection\textsuperscript{15}.

In 9% of overall cases and 3.5% of cases beyond 24 weeks pregnancy was terminated for other reasons. In the international literature papers on other reasons for pregnancy termination for maternal indications are scarce\textsuperscript{17}. One Australian study mentions psychiatric disorders, malignancies and cardiac disorders as the most common maternal indications for termination between 5 – 23 weeks’ gestation\textsuperscript{17}.

What can we learn from our observations? First, there are conditions where maternal health and life are compromised to such a degree, while chances for healthy fetal survival so dismal, that termination of pregnancy is inevitable. This entails pregnancy-induced conditions such as pre-eclampsia and HELLP syndrome, intra-uterine infection and obstetric haemorrhage, but also pre-existing or coincidental conditions such as cardiac failure or malignancies. Second, counselling towards termination of pregnancy in these situations should be the result of a multidisciplinary perinatal team discussion involving neonatologists, and a shared decision with the mother and her partner. Third, any delay or hesitation to take such decisions, however difficult they may be, can endanger the health and life of the mother. For this reason termination of pregnancy for maternal reasons should be subject to medical peer-group auditing only.
Conclusion

(Inter)national literature on termination of pregnancy for maternal indication at the limits of fetal viability is virtually non-existent. In this retrospective cohort we found a prevalence of 0.1 % in the ten tertiary care centres in The Netherlands between 2000-2009.

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: The VUmc university medical center Amsterdam has received a research grant from the Dutch Society of Obstetrics and Gynecology for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; H Scheepers reports receiving a research grant from CSE Behring for a study on clotting factors during the previous 36 months; no other relationships or activities that could appear to have influenced the submitted work.

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The first author affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.
Acknowledgement: BL Scholten, MD for contributing to the data

Contributorship Statement: L van Eerden, G Zeeman and A Bolte designed the study and wrote the research protocol. All authors contributed to the acquisition of data and interpretation of data.

L van Eerden, G Zeeman, G Christiaens, A Bolte and C de Groot contributed to drafting the article. All authors revised the article critically for important intellectual content.

All authors approved the final version of the article

Competing Interests: The VUmc university medical center Amsterdam has received a research grant from the Dutch Society of Obstetrics and Gynecology for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; H Scheepers reports receiving a research grant from CSE Behring for a study on clotting factors during the previous 36 months; no other relationships or activities that could appear to have influenced the submitted work.

Data Sharing Statement: No additional data
Literature:

1. www.wetboek-online.nl/wet/Sr/82a.html
4. www.perinatreg.nl/home_english
5. LVR. Landelijke Verloskundige Registratie (Dutch Perinatal Database): The Netherlands Perinatal Registry, Prismant. Prismant
7. NVOG nota verwijzing naar een perinatologische centrum. Available at www.nvog-documenten.nl/index.php
9. de Kluiver E, Offringa M, Walther FJ, Duvekot JJ, de Laat MW. [Perinatal policy in cases of extreme prematurity; an investigation into the implementation of the guidelines] [article in Dutch]. Ned Tijdsch Geneeskd. 2013;157(38):A6362


Inclusion criteria

- Gestational age 22\(^{0/7}\) – 28\(^{0/7}\)
- Severe maternal condition reason for termination
- Live fetus at onset of termination
- No fetal monitoring
- No interventions aimed at fetus

Exclusion criteria

- Gestational age \(\leq 21^{6/7}\) or \(\geq 28^{1/7}\)
- Fetal indication for termination
- Psychosocial reason for termination
- Fetal demise at onset of termination

Table 1: inclusion and exclusion criteria for this study

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<th>Indication</th>
<th>GA &lt; 24 weeks (%)</th>
<th>GA &gt; 24 weeks (%)</th>
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<tr>
<td>Overall</td>
<td>64</td>
<td>113</td>
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<td>Hypertensive disorders</td>
<td>37 (58%)</td>
<td>94 (83%)</td>
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<tr>
<td>Intra-uterine infection</td>
<td>14 (22%)</td>
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Other

- Uterine rupture
- Obstetric bleeding
- Heart failure
- Psychiatric disorders
- Malignancy

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<th>Centre</th>
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<td>19082</td>
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<td>2</td>
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<td>163052</td>
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<td>177</td>
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Table 2: Cases beyond the Dutch legal limit of 24 weeks’ gestation

Table 3: overview of terminations per center and policy of active fetal management in the period 2000-2009. GA = gestational age
Figure 1 Description of patient cohorts

Number of births from 2000 until 2009
N = 1,929,470

Non tertiary centers
N = 1,766,418

Tertiary centers
N = 163,052

TOP for maternal indications
N = 177

GA 22\frac{0}{7} – 23\frac{7}{7}
N = 64

GA 24\frac{0}{7} – 27\frac{6}{7}
N = 113

Hypertensive disorder
N = 37

PROM and infection
N = 14

Other
N = 13

Hypertensive disorder
N = 94

PROM and infection
N = 15

Other
N = 4

Figure 2: number of cases of TOP per year

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Abstract

Objective: Maternal morbidity, either pregnancy-related or pre-existent can become life-threatening and of such severity to warrant termination of pregnancy (TOP). In this situation chances of fetal survival are usually poor, either because of low gestational age, and/or because of the fetal effects of the maternal condition. Examples include severe growth restriction in pre-eclampsia and intra-uterine infection due to very early preterm prelabour rupture of membranes. There are very few reports on the prevalence of termination of pregnancy for maternal indication at the limits of fetal viability. We investigated the prevalence and indications for TOP on maternal indication in the ten tertiary care centres in the Netherlands during the past decade.

Study design: we conducted a retrospective review of the medical records of all women who underwent TOP for maternal indications between 22 to 27 completed weeks of gestation in all 10 tertiary care centres from 2000 to 2009.

Results: During the study period there were 1,929,470 deliveries. 163,052 (8.4%) of these took place in one of the ten tertiary care centres and 177 pregnancies were terminated for severe maternal disease, 131 for hypertensive disorders, 29 for intra-uterine infection and 17 for other reasons. The mean gestational age at TOP was 171 days (24\(\frac{3}{7}\) weeks) ± 10 days. No maternal deaths were recorded. The overall perinatal mortality was 99,4%.

Conclusion: Over a ten year period TOP for maternal indications was performed in 1 in 1000 deliveries in the 10 Dutch tertiary care centres. Hypertensive disorders comprised three quarters of cases.
Article summary

Strengths and limitations of the study:

- This study is one of the first to estimate the incidence of termination of pregnancy for maternal indications at the limits of fetal viability. Only two more articles on this subject have been identified.
- The results of this study raise several questions concerning policy and approach of severely sick mothers at the limits of fetal viability. The results should stimulate multidisciplinary discussion and facilitate decision making in the future.
- This study is a retrospective study and could suffer from underreporting.
- During the study period a protocol concerning active perinatal management after spontaneous preterm birth at the limits of fetal viability in The Netherlands was introduced. This might have had an impact on the approach of severely sick mothers.
Introduction

Indications for termination of pregnancy in the Netherlands can be divided in:
psychosocial reasons (unwanted pregnancies), genetic reasons (fetus with
congenital abnormalities) and maternal medical disorders including psychiatric
disorders. Under Dutch legislation, in place and unchanged since 1981, termination
of pregnancy (TOP) is possible up to the gestational age where a newborn can
survive outside the womb. This is currently considered 24\textsuperscript{0/7} weeks for adequately
grown fetuses without lethal disorders and a sufficient amount of amniotic fluid for
lung development\textsuperscript{1}. Annually there are approximately 28000 terminations of
pregnancy between 5 and 24 weeks in the Netherlands. Termination for social
indications up to 22 weeks is performed in clinics with a special license. Terminations
for genetic reasons and for medical maternal reasons are performed in obstetric units
of secondary or tertiary care centres.

In case of lethal fetal disorders such as trisomy 18, 13 or triploidy termination is also
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Termination of pregnancy beyond 24 weeks’ gestation for life-threatening maternal
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The literature lacks reports on the prevalence of termination of pregnancy for maternal indication at the limits of fetal viability. The gestational age and estimated fetal weight to consider “active perinatal management” directed towards survival has recently been lowered to 24 weeks and 500 grams in many countries, including the Netherlands. We aimed to investigate the prevalence of and indications for TOP in severely sick mothers, at the limits of fetal viability in the Netherlands between 2000 and 2009.

Methods
We conducted a retrospective review of the medical records of all women who had TOP for maternal indications between 22 and 27 completed weeks of gestation in the 10 Dutch tertiary care centres from 2000 to 2009. Cases were identified using local delivery databases. In all cases the fetus was judged to be non-viable, either because of the gestational age or because of the impact of maternal disease on the prospects for the fetus, e.g. severe growth restriction. The inclusion and exclusion criteria are listed in table 1. Data extraction from the original medical files was performed by the first or the last author (LvE and ACB) in all cases. Data on the total number of deliveries in the 10-year period were extracted from The Netherlands Perinatal Registry (PRN foundation). The indication TOP for maternal indication is not registered in this registry.

The study design was reviewed and approved by the medical ethics committee of the VU Medical Center in Amsterdam.

Results

In the ten year study period there were 1,929,470 deliveries in the Netherlands of which 163,052 (8.4%) took place in the 10 tertiary care centres. Of those 11474 deliveries occurred between 22\(^{0/7}\) and 27\(^{6/7}\) weeks of gestation. A total of 177 (1.5%) fulfilled the inclusion criteria, 172 singleton and 5 twin pregnancies. TOP was performed for hypertensive disorders and preterm prelabour rupture of membranes (PPROM) with intra-uterine infection in 131 (74%) and 29 (16%) cases, respectively. In 17 cases (9%) there was another motive to terminate the pregnancy (figure 1). The mean gestational age at TOP was 171 days (24\(^{3/7}\)) weeks ± 10 days. In the hypertension group the mean gestational age was 173 days (24\(^{5/7}\)) ± 9.7 days as compared to 167 days (23\(^{6/7}\)) ± 10.1 days in the infection group and 162 days (23\(^{1/7}\))
± 7.0 days for the other indications. The gestational age at termination was significantly higher in the hypertension group (173 days ± 9.7 days) compared to the infection group (167 days ± 10.1 days) (p= 0.006). This also applied to the hypertension group (173 days ± 9.7 days) compared to the other indications (162 days ± 7.0 days) (p<0.001).

There were no cases of maternal mortality. A total of 182 neonates were born. There was one unexpected survivor born at GA 25\textsuperscript{5/7} weeks’ gestation with a birth weight of 600 grams. This pregnancy was terminated without fetal heart rate monitoring for severe HELLP syndrome using intravenous sulprostone. The child is now four years old and has a normal development so far.

The number of pregnancies terminated beyond the limit of 24\textsuperscript{0/7} weeks’ gestation was 113 (64%). In 94 of these cases (83%) pregnancy was terminated for a severe hypertensive disorder. Fifteen pregnancies (13%) were terminated for overt intra-uterine infection in the setting of PPROM and four pregnancies (3.5%) for other indications (table 2). In cases of termination beyond 24 weeks a multidisciplinary team, consisting of at least obstetricians, neonatologists and other specialists, when indicated, discussed the intended advise for termination of pregnancy and examined alternative options before coming to a final advise to the parents.

Labour was induced with prostaglandins in 176 (99.4%) of the cases. In one case dilatation and evacuation was performed after feticide with potassium chloride. After induction two pregnancies were terminated by caesarean section. In one case a caesarean section was performed to expedite delivery because of recurrent eclamptic fits with neurological impairment. In the other case a caesarean section was performed because of an uterine rupture accompanied by a hypovolemic shock.
In 2006 a national guideline on active perinatal and neonatal management after spontaneous preterm birth at the limits of fetal viability was introduced. Before 2006, active management was generally started at 26 weeks’ gestation, whereas this was lowered to 25 weeks’ gestation in the guideline. The introduction of this guideline has had no major effect on the number of TOP for maternal indications. Figure 2 shows the number of TOP per year.

The incidence of TOP varied substantially between different centres (table 3).

Two exemplary cases:

Case 1: a nulliparous woman, with an unremarkable history, developed severe pre-eclampsia with progressive HELLP syndrome at a gestational age of 23 weeks and 2 days. She was admitted and was treated with multiple intravenous antihypertensive drugs and magnesium sulphate. Ultrasound showed an estimated fetal weight of 480 grams. She was counselled for termination of pregnancy due to the early gestational age and the progressive course of the disease and delivered a stillborn girl of 470 grams (<p10) at 24 weeks’ gestation. The delivery took place on the intensive care unit due to refractory hypertension and pulmonary oedema in the mother.

Case 2: a woman in her fourth pregnancy was admitted at a gestational age of 22 weeks. Her obstetric history revealed dilated peripartum cardiomyopathy. Pre-conceptionally, she had been strongly advised against pregnancy. She was admitted to the ICU because of severely deteriorating cardiac function. After extensive counselling by a multidisciplinary team consisting of obstetricians, cardiologists and neonatologists the pregnancy was terminated at 22 weeks and 4 days’ gestation. She delivered a stillborn son.

Comment
In the period 2000-2009 we identified 177 cases of TOP for life-threatening maternal morbidity in the ten tertiary care centres in the Netherlands. We found that there was a difference in incidence of TOP between the tertiary care centres. This may, amongst others, be due to different local interpretation on active neonatal management at the limits of viability in a period where thresholds for active management were subject to gradual change (see table 3). It is possible that some centres advised to continue the pregnancy anticipating an intra-uterine fetal demise within days.

Dutch guidelines are in place to recommend whether or not to start active neonatal management by a neonatologist in cases with spontaneous preterm labour and an expected weight appropriate for gestational age. These guidelines are periodically revised based on current (inter)national practice standards. Prior to 2006 the overall limit for active obstetric and neonatal management was 26 weeks’ of gestation. After 2006 the recommended limit was 25 weeks’ gestation, with an estimated fetal weight of at least 500 grams⁷ (figure 2). In the latest guideline dating September 2010, which was introduced after the inclusion period of this study, the recommended limit is 24 weeks’ gestation for intubation and ventilation and 25 weeks for cardiac resuscitation. Estimated fetal weight limits are no longer included⁸.

The prospects of children born at 24-25 weeks are nevertheless poor, even with active management. A recent report showed that infants who received active perinatal and neonatal management survived in 43% of cases at 24 weeks’ and in 61% of cases at 25 weeks’. Severe short term neonatal morbidity was registered in 70-80% of surviving children⁹. In case of severe maternal morbidity in pregnancy, the prospects for an intact survival for the fetus are considered to be even worse due to the combination of a low gestational age and, in most cases, severe growth
restriction or fetal inflammatory response syndrome, as well as the deleterious effects of the underlying maternal condition, such as chronic fetal hypoxia. In case it becomes inevitable for the mother’s sake to terminate the pregnancy at the limits of fetal viability, this expected extremely poor outcome of the child does not support an active fetal/neonatal management. A caesarean section puts the mother at even higher short term and long term risks. Therefore, termination via induction of vaginal delivery with prostaglandins and without fetal monitoring will often be the safest policy.

Hypertensive disease comprised three quarters of the cases and was the indication for termination in 83 % of the terminations beyond 24 weeks. Experts in the field as well as the WHO and NICE guidelines on hypertensive disorders in pregnancy, recommend that women who develop severe pre-eclampsia at less than 23 weeks should be counselled towards termination of pregnancy. Gaugler et al describe 26 pregnancies, complicated by pre-eclampsia with an onset before 24 weeks’ gestation and managed expectantly. The overall perinatal mortality was 82%, with major maternal morbidity in 65% of the women.

In 16% of overall cases and 13% of cases beyond 24 weeks, the indication for terminating pregnancy was intra-uterine infection with overt or threatening maternal sepsis. Septic shock and maternal death have been reported in pregnancies managed conservatively. Therefore, termination of pregnancy is recommended in case of serious clinical infection.

In 9% of overall cases and 3,5% of cases beyond 24 weeks pregnancy was terminated for other reasons. In the international literature papers on other reasons for pregnancy termination for maternal indications are scarce. One study from New Zealand mentions psychiatric disorders, malignancies and cardiac disorders as the
most common maternal indications for termination between 5 – 23 weeks’ gestation\(^\text{17}\). In a recent paper by Piel et al from 4 hospitals in the Parisian area covering 95000 deliveries between 2001 and 2010 the main reasons for terminating pregnancy for maternal reasons between 5 and 23 weeks of gestation were (in decreasing order of frequency): pre-eclampsia, malignancies, drug addiction, AIDS, risk of suicide, psychosis, rape, pre-existing maternal somatic or psychiatric diseases, uterine bleeding or risk of uterine rupture\(^\text{18}\). Termination for social reasons is not allowed in the Netherlands after 24\(^{0/7}\) weeks gestation.

What can we learn from our observations? There are conditions where maternal health and life are compromised to such a degree, whilst chances for healthy fetal survival so dismal, that termination of pregnancy is inevitable. This entails pregnancy-induced conditions such as pre-eclampsia and HELLP syndrome, intra-uterine infection and obstetric haemorrhage, but also pre-existing or coincidental maternal conditions such as cardiac failure or malignancies. Counselling towards termination of pregnancy in these situations is the result of a multidisciplinary perinatal team discussion involving neonatologists, and a shared decision with the mother and her partner.

We suggest that the indication for termination of pregnancy becomes a mandatory item in the Netherlands Perinatal Registry. This will gain insight in the prevalence of TOP for maternal indications. Furthermore this registration will enable audits of these cases by a medical peer-group.

Conclusion

(Inter)national literature on termination of pregnancy for maternal indication at the limits of fetal viability is scarce. In this retrospective cohort we found a prevalence of
0.1% of termination of pregnancy for maternal reasons in the ten tertiary care centres in The Netherlands between 2000-2009.

Acknowledgement:
BL Scholten, MD for contributing to the data

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Contributorship Statement
L van Eerden, G Zeeman and A Bolte designed the study and wrote the research protocol. All authors contributed to the acquisition of data and interpretation of data. L van Eerden, G Zeeman, G Christiaens, A Bolte and C de Groot contributed to drafting the article. All authors revised the article critically for important intellectual content.

All authors approved the final version of the article.

Competing Interests
All authors have completed the ICMJE uniform disclosure form at www.icmje.org/doi_disclosure.pdf and declare: The VUmc university medical center Amsterdam has received a research grant from the Dutch Society of Obstetrics and Gynecology for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; H Scheepers reports receiving a research grant from CSE Behring for a study on clotting factors during the previous 36 months; no other relationships or activities that could appear to have influenced the submitted work.
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The first author affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Data Sharing Statement

No additional data available
Literature:

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5. LVR. Landelijke Verloskundige Registratie (Dutch Perinatal Database): The Netherlands Perinatal Registry, Prismant. Prismant
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Figure Legends

Figure 1 Description of patient cohorts

Figure 2: number of cases of TOP per year
Inclusion criteria
- Gestational age 22\(\frac{0}{7}\) – 28\(\frac{0}{7}\)
- Severe maternal condition reason for termination
- Live fetus at onset of termination
- No fetal monitoring
- No interventions aimed at fetus

Exclusion criteria
- Gestational age ≤ 21\(\frac{0}{7}\) or ≥ 28\(\frac{0}{7}\)
- Fetal indication for termination
- Fetal demise at onset of termination

Table 1: Inclusion and exclusion criteria for this study

<table>
<thead>
<tr>
<th>Indication</th>
<th>GA &lt; 24 weeks (%)</th>
<th>GA &gt; 24 weeks (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>64</td>
<td>113</td>
</tr>
<tr>
<td>Hypertensive disorders</td>
<td>37 (58%)</td>
<td>94 (83%)</td>
</tr>
<tr>
<td>Intra-uterine infection</td>
<td>14 (22%)</td>
<td>15 (13%)</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Uterine rupture</td>
<td>1 (1.6%)</td>
<td>1 (0.8%)</td>
</tr>
<tr>
<td>• Obstetric bleeding</td>
<td>3 (4.7%)</td>
<td>2 (1.7%)</td>
</tr>
<tr>
<td>• Heart failure</td>
<td>3 (4.7%)</td>
<td>1 (0.8%)</td>
</tr>
<tr>
<td>• Psychiatric disorders</td>
<td>3 (4.7%)</td>
<td></td>
</tr>
<tr>
<td>• Malignancy</td>
<td>3 (4.7%)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Cases beyond the Dutch legal limit of 24 weeks’ gestation

<table>
<thead>
<tr>
<th>Centre</th>
<th>Deliveries</th>
<th>Terminations</th>
<th>Incidence (%)</th>
<th>GA at start active fetal management</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>19082</td>
<td>47</td>
<td>2.46</td>
<td>26(\frac{0}{7})</td>
</tr>
<tr>
<td>2</td>
<td>15861</td>
<td>33</td>
<td>2.08</td>
<td>26(\frac{0}{7})</td>
</tr>
<tr>
<td>3</td>
<td>18468</td>
<td>27</td>
<td>1.46</td>
<td>25(\frac{0}{7})</td>
</tr>
<tr>
<td>4</td>
<td>13391</td>
<td>19</td>
<td>1.41</td>
<td>25(\frac{0}{7})</td>
</tr>
<tr>
<td>5</td>
<td>14551</td>
<td>18</td>
<td>1.23</td>
<td>26(\frac{0}{7})</td>
</tr>
<tr>
<td>6</td>
<td>11830</td>
<td>9</td>
<td>0.76</td>
<td>24(\frac{0}{7})</td>
</tr>
<tr>
<td>No.</td>
<td>Terminations</td>
<td>GA</td>
<td>Policy of Active Fetal Management</td>
<td></td>
</tr>
<tr>
<td>-----</td>
<td>--------------</td>
<td>----</td>
<td>----------------------------------</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>16387</td>
<td>9</td>
<td>0.54</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>19523</td>
<td>6</td>
<td>0.30</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>19748</td>
<td>5</td>
<td>0.25</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>14211</td>
<td>4</td>
<td>0.28</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>163052</strong></td>
<td><strong>177</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3: overview of terminations per center and policy of active fetal management in the period 2000-2009. GA = gestational age.
Termination of pregnancy for maternal indications at the limits of fetal viability, 
in the Dutch tertiary care centres

Eerden L van\textsuperscript{a}, Zeeman GG\textsuperscript{j}, Page-Christiaens GCM\textsuperscript{c}, Vandenbussche F\textsuperscript{d}, Oei SG\textsuperscript{e}, Scheepers HCJ\textsuperscript{j}, Eyck J van\textsuperscript{a}, Middeldorp JM\textsuperscript{h}, Pajkrt E\textsuperscript{i}, Duvekot JJ\textsuperscript{b}, Groot CJM\textsuperscript{a} de and Bolte AC\textsuperscript{a}

\textsuperscript{a} = VU Medical Center Amsterdam, The Netherlands  
\textsuperscript{b} = Erasmus MC, University Medical Center Rotterdam, The Netherlands  
\textsuperscript{c} = University Medical Center Utrecht, The Netherlands  
\textsuperscript{d} = Radboud university Medical Center Nijmegen, The Netherlands  
\textsuperscript{e} = Maxima Medical Center Veldhoven, The Netherlands  
\textsuperscript{f} = Maastricht University Medical Center, The Netherlands  
\textsuperscript{g} = Isala Clinics Zwolle, The Netherlands  
\textsuperscript{h} = Leiden University Medical Center, The Netherlands  
\textsuperscript{i} = Academic Medical Center Amsterdam, The Netherlands  
\textsuperscript{j} = University Medical Center Groningen, The Netherlands

Abstract

Objective: Maternal morbidity, either pregnancy-related or pre-existent can become life-threatening and of such severity to warrant termination of pregnancy (TOP). In this situation chances of fetal survival are usually poor, either because of low gestational age, and/or because of the fetal effects of the maternal condition. Examples include severe growth restriction in pre-eclampsia and intra-uterine infection due to very early preterm prelabour rupture of membranes. There are very few reports on the prevalence of termination of pregnancy for maternal indication at the limits of fetal viability. We investigated the prevalence and indications for TOP on
maternal indication in the ten tertiary care centres in the Netherlands during the past decade.

Study design: we conducted a retrospective review of the medical records of all women who underwent TOP for maternal indications between 22 to 27 completed weeks of gestation in all 10 tertiary care centres from 2000 to 2009.

Results: During the study period there were 1,929,470 deliveries. 163,052 (8.4%) of these took place in one of the ten tertiary care centres and 177 pregnancies were terminated for severe maternal disease, 131 for hypertensive disorders, 29 for intrauterine infection and 17 for other reasons. The mean gestational age at TOP was 171 days (24\(\frac{3}{7}\) weeks) ± 10 days. No maternal deaths were recorded. The overall perinatal mortality was 99.4%.

Conclusion: Over a ten year period TOP for maternal indications was performed in 1 in 1000 deliveries in the 10 Dutch tertiary care centres. Hypertensive disorders comprised three quarters of cases.

Article summary

Strengths and limitations of the study:

- This study is one of the first to estimate the incidence of termination of pregnancy for maternal indications at the limits of fetal viability. Only two more articles on this subject have been identified.
- The results of this study raise several questions concerning policy and approach of severely sick mothers at the limits of fetal viability. The results should stimulate multidisciplinary discussion and facilitate decision making in the future.
- This study is a retrospective study and could suffer from underreporting.
During the study period a protocol concerning active perinatal management after spontaneous preterm birth at the limits of fetal viability in The Netherlands was introduced. This might have had an impact on the approach of severely sick mothers.

Introduction

Indications for termination of pregnancy in the Netherlands can be divided in:
psychosocial reasons (unwanted pregnancies), genetic reasons (fetus with congenital abnormalities) and maternal medical disorders including psychiatric disorders. Under Dutch legislation, in place and unchanged since 1981, termination of pregnancy (TOP) is possible up to the gestational age where a newborn can survive outside the womb. This is currently considered $24^{0/7}$ weeks for adequately grown fetuses without lethal disorders and a sufficient amount of amniotic fluid for lung development.\textsuperscript{1} Annually there are approximately 28000 terminations of pregnancy between 5 and 24 weeks in the Netherlands. Termination for social indications up to 22 weeks is performed in clinics with a special license. Terminations for genetic reasons and for medical maternal reasons are performed in obstetric units of secondary or tertiary care centres.

In case of lethal fetal disorders such as trisomy 18, 13 or triploidy termination is also allowed beyond 24 weeks, provided a number of criteria are fulfilled.\textsuperscript{2} These cases are audited by a committee of the Dutch Society of Obstetrics and Gynecology. Termination for severe fetal disorders in case of dismal, but not necessarily lethal, prognosis for the fetus may be excepted from legal prosecution provided adherence to stringent criteria and after assessment by an expert committee appointed by the ministries of Health and Justice. This committee consists of an obstetrician, a
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The literature lacks reports on the prevalence of termination of pregnancy for maternal indication at the limits of fetal viability. The gestational age and estimated fetal weight to consider “active perinatal management” directed towards survival has recently been lowered to 24 weeks and 500 grams in many countries, including the Netherlands. We aimed to investigate the prevalence of and indications for TOP in
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to the ICU because of severely deteriorating cardiac function. After extensive
counselling by a multidisciplinary team consisting of obstetricians, cardiologists and
neonatologists the pregnancy was terminated at 22 weeks and 4 days’ gestation. She delivered a stillborn son.

Comment

In the period 2000-2009 we identified 177 cases of TOP for life-threatening maternal morbidity in the ten tertiary care centres in the Netherlands. We found that there was a difference in incidence of TOP between the tertiary care centres. This may, amongst others, be due to different local interpretation on active neonatal management at the limits of viability in a period where thresholds for active management were subject to gradual change (see table 3). It is possible that some centres advised to continue the pregnancy anticipating an intra-uterine fetal demise within days.

Dutch guidelines are in place to recommend whether or not to start active neonatal management by a neonatologist in cases with spontaneous preterm labour and an expected weight appropriate for gestational age. These guidelines are periodically revised based on current (inter)national practice standards. Prior to 2006 the overall limit for active obstetric and neonatal management was 26 weeks’ of gestation. After 2006 the recommended limit was 25 weeks’ gestation, with an estimated fetal weight of at least 500 grams (figure 2). In the latest guideline dating September 2010, which was introduced after the inclusion period of this study, the recommended limit is 24 weeks’ gestation for intubation and ventilation and 25 weeks for cardiac resuscitation. Estimated fetal weight limits are no longer included.

The prospects of children born at 24-25 weeks are nevertheless poor, even with active management. A recent report showed that infants who received active perinatal and neonatal management survived in 43% of cases at 24 weeks’ and in
61% of cases at 25 weeks’. Severe short term neonatal morbidity was registered in
70-80% of surviving children. In case of severe maternal morbidity in pregnancy, the
prospects for an intact survival for the fetus are considered to be even worse due to
the combination of a low gestational age and, in most cases, severe growth
restriction or fetal inflammatory response syndrome, as well as the deleterious effects
of the underlying maternal condition, such as chronic fetal hypoxia. In case it
becomes inevitable for the mother’s sake to terminate the pregnancy at the limits of
fetal viability, this expected extremely poor outcome of the child does not support an
active fetal/neonatal management. A caesarean section puts the mother at even
higher short term and long term risks. Therefore, termination via induction of vaginal
delivery with prostaglandins and without fetal monitoring will often be the safest
policy.

Hypertensive disease comprised three quarters of the cases and was the indication
for termination in 83 % of the terminations beyond 24 weeks. Experts in the field as
well as the WHO and NICE guidelines on hypertensive disorders in pregnancy,
recommend that women who develop severe pre-eclampsia at less than 23 weeks
should be counselled towards termination of pregnancy. Gaugler et al describe
26 pregnancies, complicated by pre-eclampsia with an onset before 24 weeks’
gestation and managed expectantly. The overall perinatal mortality was 82%, with
major maternal morbidity in 65% of the women.

In 16% of overall cases and 13% of cases beyond 24 weeks, the indication for
terminating pregnancy was intra-uterine infection with overt or threatening maternal
sepsis. Septic shock and maternal death have been reported in pregnancies
managed conservatively. Therefore, termination of pregnancy is recommended
in case of serious clinical infection.
In 9% of overall cases and 3.5% of cases beyond 24 weeks pregnancy was terminated for other reasons. In the international literature papers on other reasons for pregnancy termination for maternal indications are scarce. One study from New Zealand mentions psychiatric disorders, malignancies and cardiac disorders as the most common maternal indications for termination between 5 – 23 weeks' gestation. In a recent paper by Piel et al from 4 hospitals in the Parisian area covering 95000 deliveries between 2001 and 2010 the main reasons for terminating pregnancy for maternal reasons between 5 and 23 weeks of gestation were (in decreasing order of frequency): pre-eclampsia, malignancies, drug addiction, AIDS, risk of suicide, psychosis, rape, pre-existing maternal somatic or psychiatric diseases, uterine bleeding or risk of uterine rupture. Termination for social reasons is not allowed in the Netherlands after 24 0/7 weeks gestation.

What can we learn from our observations? There are conditions where maternal health and life are compromised to such a degree, whilst chances for healthy fetal survival so dismal, that termination of pregnancy is inevitable. This entails pregnancy-induced conditions such as pre-eclampsia and HELLP syndrome, intra-uterine infection and obstetric haemorrhage, but also pre-existing or coincidental maternal conditions such as cardiac failure or malignancies. Counselling towards termination of pregnancy in these situations is the result of a multidisciplinary perinatal team discussion involving neonatologists, and a shared decision with the mother and her partner.

We suggest that the indication for termination of pregnancy becomes a mandatory item in the Netherlands Perinatal Registry. This will gain insight in the prevalence of TOP for maternal indications. Furthermore this registration will enable audits of these cases by a medical peer-group.
Conclusion

(Inter)national literature on termination of pregnancy for maternal indication at the limits of fetal viability is scarce. In this retrospective cohort we found a prevalence of 0.1% of termination of pregnancy for maternal reasons in the ten tertiary care centres in The Netherlands between 2000-2009.

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: The VUmc university medical center Amsterdam has received a research grant from the Dutch Society of Obstetrics and Gynecology for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; H Scheepers reports receiving a research grant from CSE Behring for a study on clotting factors during the previous 36 months; no other relationships or activities that could appear to have influenced the submitted work.

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The first author affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Acknowledgement: BL Scholten, MD for contributing to the data

Literature:

1. [www.wetboek-online.nl/wet/Sr/82a.html](http://www.wetboek-online.nl/wet/Sr/82a.html)
4. [www.perinatreg.nl/home_english](http://www.perinatreg.nl/home_english)
5. LVR. Landelijke Verloskundige Registratie (Dutch Perinatal Database): The Netherlands Perinatal Registry, Prismant. Prismant
9. de Kluiver E, Offringa M, Walther FJ, Duvekot JJ, de Laat MW. [Perinatal policy in cases of extreme prematurity; an investigation into the implementation of the guidelines] [article in Dutch]. Ned Tijdsch Geneeskd. 2013;157(38):A6362


Termination of pregnancy for maternal indications at the limits of fetal viability; a retrospective cohort study in the Dutch tertiary care centres

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**Primary Subject Heading**:
Obstetrics and gynaecology

**Secondary Subject Heading**:
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**Keywords**:
Maternal medicine < OBSTETRICS, Ultrasonography < OBSTETRICS, PERINATOLOGY
Termination of pregnancy for maternal indications at the limits of fetal viability; a retrospective cohort study in the Dutch tertiary care centres

Eerden L van\textsuperscript{a}, Zeeman GG\textsuperscript{j}, Page-Christiaens GCM\textsuperscript{c}, Vandenbussche F\textsuperscript{d}, Oei SG\textsuperscript{e}, Scheepers HCJ\textsuperscript{f}, Eyck J van\textsuperscript{a}, Middeldorp JM\textsuperscript{h}, Pajkrt E\textsuperscript{i}, Duvekot JJ\textsuperscript{b}, Groot CJM\textsuperscript{a} de and Bolte AC\textsuperscript{a}

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Abstract

Objective: Maternal morbidity, either pregnancy-related or pre-existent can become life-threatening and of such severity to warrant termination of pregnancy (TOP). In this situation chances of fetal survival are usually poor, either because of low gestational age, and/or because of the fetal effects of the maternal condition.

Examples include severe growth restriction in pre-eclampsia and intra-uterine infection due to very early preterm prelabour rupture of membranes. There are very few reports on the prevalence of termination of pregnancy for maternal indication at the limits of fetal viability. We investigated the prevalence and indications for TOP on maternal indication in the ten tertiary care centres in the Netherlands during the past decade.

Study design: we conducted a retrospective review of the medical records of all women who underwent TOP for maternal indications between 22 to 27 completed weeks of gestation in all 10 tertiary care centres from 2000 to 2009.

Results: During the study period there were 1,929,470 deliveries. 163,052 (8.4%) of these took place in one of the ten tertiary care centres and 177 pregnancies were terminated for severe maternal disease, 131 for hypertensive disorders, 29 for intra-uterine infection and 17 for other reasons. The mean gestational age at TOP was 171 days (24\textsuperscript{3/7} weeks) ± 10 days. No maternal deaths were recorded. The overall perinatal mortality was 99.4%.

Conclusion: Over a ten year period TOP for maternal indications was performed in 1 in 1000 deliveries in the 10 Dutch tertiary care centres. Hypertensive disorders comprised three quarters of cases.

Article summary
Strengths and limitations of the study:

- This study is one of the first to estimate the incidence of termination of pregnancy for maternal indications at the limits of fetal viability. Only two more articles on this subject have been identified.

- The results of this study raise several questions concerning policy and approach of severely sick mothers at the limits of fetal viability. The results should stimulate multidisciplinary discussion and facilitate decision making in the future.

- This study is a retrospective study and could suffer from underreporting.

- During the study period a protocol concerning active perinatal management after spontaneous preterm birth at the limits of fetal viability in The Netherlands was introduced. This might have had an impact on the approach of severely sick mothers.
Introduction

Indications for termination of pregnancy in the Netherlands can be divided in: psychosocial reasons (unwanted pregnancies), genetic reasons (fetus with congenital abnormalities) and maternal medical disorders including psychiatric disorders. Under Dutch legislation, in place and unchanged since 1981, termination of pregnancy (TOP) is possible up to the gestational age where a newborn can survive outside the womb. This is currently considered 24\(\frac{9}{7}\) weeks for adequately grown fetuses without lethal disorders and a sufficient amount of amniotic fluid for lung development\(^1\). Annually there are approximately 28000 terminations of pregnancy between 5 and 24 weeks in the Netherlands. Termination for social indications up to 22 weeks is performed in clinics with a special license. Terminations for genetic reasons and for medical maternal reasons are performed in obstetric units of secondary or tertiary care centres.

In case of lethal fetal disorders such as trisomy 18, 13 or triploidy termination is also allowed beyond 24 weeks, provided a number of criteria are fulfilled\(^2\). These cases are audited by a committee of the Dutch Society of Obstetrics and Gynecology.

Termination for severe fetal disorders in case of dismal, but not necessarily lethal, prognosis for the fetus may be excepted from legal prosecution provided adherence to stringent criteria and after assessment by an expert committee appointed by the ministries of Health and Justice. This committee consists of an obstetrician, a paediatrician and an ethicist, and is chaired by a lawyer\(^2\). This committee reports directly to the Attorney General, the highest legal authority in The Netherlands.

Termination of pregnancy beyond 24 weeks’ gestation for life-threatening maternal conditions in combination with dismal fetal prospects (e.g. due to severe growth restriction or anhydramnios) are generally not reported, since termination of
pregnancy in such cases is considered inevitable and the only justifiable
management option to prevent deteriorating maternal morbidity or even mortality.
According to the Guideline on Late Termination of Pregnancy of the Dutch Society of
Obstetrics and Gynecology maternal indications that warrant TOP include, but are
not limited to: hypertensive disorders with organ dysfunction, sepsis, severe
exacerbation of auto-immune disorder, severely deteriorating cardiac function,
transplant rejection, rapidly progressing malignancies as well as life-threatening
major obstetric haemorrhage. In these situations the fetus is also compromised,
either because of the gestational age, and/or because of the low estimated fetal
weight. Termination of pregnancy beyond 24 weeks' gestation for these indications
is considered to be extremely rare. The guideline on termination of pregnancy from
the Dutch Society of Gynaecology and Obstetrics states that these patients should be
referred to and treated in a tertiary care centre. Termination of pregnancy on
maternal indication is only performed after extensive multidisciplinary consultation.
The literature lacks reports on the prevalence of termination of pregnancy for
maternal indication at the limits of fetal viability. The gestational age and estimated
fetal weight to consider "active perinatal management" directed towards survival has
recently been lowered to 24 weeks and 500 grams in many countries, including the
Netherlands. We aimed to investigate the prevalence of and indications for TOP in
severely sick mothers, at the limits of fetal viability in the Netherlands between 2000
and 2009.

Methods

We conducted a retrospective review of the medical records of all women who had
TOP for maternal indications between 22 and 27 completed weeks of gestation in the

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml
10 Dutch tertiary care centres from 2000 to 2009. Cases were identified using local
delivery databases. In all cases the fetus was judged to be non-viable, either
because of the gestational age or because of the impact of maternal disease on the
prospects for the fetus, e.g. severe growth restriction. The inclusion and exclusion
criteria are listed in table 1. Data extraction from the original medical files was
performed by the first or the last author (LvE and ACB) in all cases. Data on the total
number of deliveries in the 10-year period were extracted from The Netherlands
Perinatal Registry (PRN foundation). The indication TOP for maternal indication is not
registered in this registry4.

The study design was reviewed and approved by the medical ethics committee of the
VU Medical Center in Amsterdam.

Results
In the ten year study period there were 1,929,470 deliveries in the Netherlands of
which 163,052 (8.4%) took place in the 10 tertiary care centres5-6. Of those 11474
deliveries occurred between 220/7 and 276/7 weeks of gestation. A total of 177 (1,5%)
fulfilled the inclusion criteria, 172 singleton and 5 twin pregnancies. TOP was
performed for hypertensive disorders and preterm prelabour rupture of membranes
(PPROM) with intra-uterine infection in 131 (74%) and 29 (16%) cases, respectively.
In 17 cases (9%) there was another motive to terminate the pregnancy (figure 1).
The mean gestational age at TOP was 171 days (243/7) weeks ± 10 days. In the
hypertension group the mean gestational age was 173 days (245/7) ± 9.7 days as
compared to 167 days (236/7) ± 10.1 days in the infection group and 162 days (231/7)
± 7.0 days for the other indications. The gestational age at termination was
significantly higher in the hypertension group (173 days ± 9.7 days) compared to the
infection group (167 days ± 10.1 days) (p= 0.006). This also applied to the hypertension group (173 days ± 9.7 days) compared to the other indications (162 days ± 7.0 days) (p<0.001).

There were no cases of maternal mortality. A total of 182 neonates were born. There was one unexpected survivor born at GA 25\(\frac{5}{7}\) weeks’ gestation with a birth weight of 600 grams. This pregnancy was terminated without fetal heart rate monitoring for severe HELLP syndrome using intravenous sulprostone. The child is now four years old and has a normal development so far.

The number of pregnancies terminated beyond the limit of 24\(\frac{0}{7}\) weeks’ gestation was 113 (64%). In 94 of these cases (83%) pregnancy was terminated for a severe hypertensive disorder. Fifteen pregnancies (13%) were terminated for overt intra-uterine infection in the setting of PPROM and four pregnancies (3.5%) for other indications (table 2). In cases of termination beyond 24 weeks a multidisciplinary team, consisting of at least obstetricians, neonatologists and other specialists, when indicated, discussed the intended advise for termination of pregnancy and examined alternative options before coming to a final advise to the parents.

Labour was induced with prostaglandins in 176 (99.4%) of the cases. In one case dilatation and evacuation was performed after feticide with potassium chloride. After induction two pregnancies were terminated by caesarean section. In one case a caesarean section was performed to expedite delivery because of recurrent eclamptic fits with neurological impairment. In the other case a caesarean section was performed because of an uterine rupture accompanied by a hypovolemic shock.

In 2006 a national guideline on active perinatal and neonatal management after spontaneous preterm birth at the limits of fetal viability was introduced. Before 2006, active management was generally started at 26 weeks’ gestation, whereas this was
lowered to 25 weeks’ gestation in the guideline. The introduction of this guideline has
had no major effect on the number of TOP for maternal indications. Figure 2 shows
the number of TOP per year.

The incidence of TOP varied substantially between different centres (table 3).

Two exemplary cases:

Case 1: a nulliparous woman, with an unremarkable history, developed severe pre-
eclampsia with progressive HELLP syndrome at a gestational age of 23 weeks and 2
days. She was admitted and was treated with multiple intravenous antihypertensive
drugs and magnesium sulphate. Ultrasound showed an estimated fetal weight of 480
grams. She was counselled for termination of pregnancy due to the early gestational
age and the progressive course of the disease and delivered a stillborn girl of 470
grams (<p10) at 24 weeks’ gestation. The delivery took place on the intensive care
unit due to refractory hypertension and pulmonary oedema in the mother.

Case 2: a woman in her fourth pregnancy was admitted at a gestational age of 22
weeks. Her obstetric history revealed dilated peripartum cardiomyopathy. Pre-
conceptionally, she had been strongly advised against pregnancy. She was admitted
to the ICU because of severely deteriorating cardiac function. After extensive
counselling by a multidisciplinary team consisting of obstetricians, cardiologists and
neonatologists the pregnancy was terminated at 22 weeks and 4 days’ gestation.
She delivered a stillborn son.

Comment

In the period 2000-2009 we identified 177 cases of TOP for life-threatening maternal
morbidity in the ten tertiary care centres in the Netherlands. “Since the indication for
termination of pregnancy is not specified in the Netherlands Perinatal Registry nor in
the legally required national report on termination of pregnancy, it is not possible to check our data for underreporting. However, because the guideline on late termination of pregnancy from the Dutch Society of Gynecology and Obstetrics states that women should be referred to and treated in a tertiary care centre in case of severe maternal morbidity, we assume that we found most cases of TOP for maternal indications.”

We found that there was a difference in incidence of TOP between the tertiary care centres. This may, amongst others, be due to different local interpretation on active neonatal management at the limits of viability in a period where thresholds for active management were subject to gradual change (see table 3). It is possible that some centres advised to continue the pregnancy anticipating an intra-uterine fetal demise within days.

Dutch guidelines are in place to recommend whether or not to start active neonatal management by a neonatologist in cases with spontaneous preterm labour and an expected weight appropriate for gestational age. These guidelines are periodically revised based on current (inter)national practice standards. Prior to 2006 the overall limit for active obstetric and neonatal management was 26 weeks’ of gestation. After 2006 the recommended limit was 25 weeks’ gestation, with an estimated fetal weight of at least 500 grams\(^7\) (figure 2). In the latest guideline dating September 2010, which was introduced after the inclusion period of this study, the recommended limit is 24 weeks’ gestation for intubation and ventilation and 25 weeks for cardiac resuscitation. Estimated fetal weight limits are no longer included\(^6\).

The prospects of children born at 24-25 weeks are nevertheless poor, even with active management. A recent report showed that infants who received active perinatal and neonatal management survived in 43% of cases at 24 weeks’ and in
61% of cases at 25 weeks’. Severe short term neonatal morbidity was registered in 70-80% of surviving children. In case of severe maternal morbidity in pregnancy, the prospects for an intact survival for the fetus are considered to be even worse due to the combination of a low gestational age and, in most cases, severe growth restriction or fetal inflammatory response syndrome, as well as the deleterious effects of the underlying maternal condition, such as chronic fetal hypoxia. In case it becomes inevitable for the mother’s sake to terminate the pregnancy at the limits of fetal viability, this expected extremely poor outcome of the child does not support an active fetal/neonatal management. A caesarean section puts the mother at even higher short term and long term risks. Therefore, termination via induction of vaginal delivery with prostaglandins and without fetal monitoring will often be the safest policy.

Hypertensive disease comprised three quarters of the cases and was the indication for termination in 83% of the terminations beyond 24 weeks. Experts in the field as well as the WHO and NICE guidelines on hypertensive disorders in pregnancy, recommend that women who develop severe pre-eclampsia at less than 23 weeks should be counselled towards termination of pregnancy. Gaugler et al describe 26 pregnancies, complicated by pre-eclampsia with an onset before 24 weeks’ gestation and managed expectantly. The overall perinatal mortality was 82%, with major maternal morbidity in 65% of the women.

In 16% of overall cases and 13% of cases beyond 24 weeks, the indication for terminating pregnancy was intra-uterine infection with overt or threatening maternal sepsis. Septic shock and maternal death have been reported in pregnancies managed conservatively. Therefore, termination of pregnancy is recommended in case of serious clinical infection.
In 9% of overall cases and 3.5% of cases beyond 24 weeks pregnancy was terminated for other reasons. In the international literature papers on other reasons for pregnancy termination for maternal indications are scarce. One study from Australia mentions psychiatric disorders, malignancies and cardiac disorders as the most common maternal indications for termination between 5 – 23 weeks' gestation. In a recent paper by Piel et al from 4 hospitals in the Parisian area covering 95000 deliveries between 2001 and 2010 the main reasons for terminating pregnancy for maternal reasons between 5 and 23 weeks of gestation were (in decreasing order of frequency): pre-eclampsia, malignancies, drug addiction, AIDS, risk of suicide, psychosis, rape, pre-existing maternal somatic or psychiatric diseases, uterine bleeding or risk of uterine rupture. Termination for social reasons is not allowed in the Netherlands after 240/7 weeks gestation.

What can we learn from our observations? There are conditions where maternal health and life are compromised to such a degree, whilst chances for healthy fetal survival so dismal, that termination of pregnancy is inevitable. This entails pregnancy-induced conditions such as pre-eclampsia and HELLP syndrome, intra-uterine infection and obstetric haemorrhage, but also pre-existing or coincidental maternal conditions such as cardiac failure or malignancies. Counselling towards termination of pregnancy in these situations is the result of a multidisciplinary perinatal team discussion involving neonatologists, and a shared decision with the mother and her partner.

We suggest that the indication for termination of pregnancy becomes a mandatory item in the Netherlands Perinatal Registry. This will gain insight in the prevalence of TOP for maternal indications. Furthermore this registration will enable audits of these cases by a medical peer-group.
Conclusion

(International) literature on termination of pregnancy for maternal indication at the limits of fetal viability is scarce. In this retrospective cohort we found a prevalence of 0.1% of termination of pregnancy for maternal reasons in the ten tertiary care centres in The Netherlands between 2000-2009.
Acknowledgement: BL Scholten, MD for contributing to the data

Funding: This work was funded by the Dutch Society of Obstetrics and Gynecology.

Contributor statement: L van Eerden, G Zeeman and A Bolte designed the study and wrote the research protocol. All authors contributed to the acquisition of data and interpretation of data.

L van Eerden, G Zeeman, G Christiaens, A Bolte and C de Groot contributed to drafting the article. All authors revised the article critically for important intellectual content.

All authors approved the final version of the article.

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been omitted; and that any discrepancies from the study as planned (and, if relevant,
registered) have been explained.

Data sharing statement: No additional data available

Figure legends:

Figure 1: Flowchart Patient selection. TOP = termination of pregnancy, GA =
gestational age, PROM = prelabour rupture of membranes

Figure 2: Number of TOP per year. TOP = termination of pregnancy
Literature:

1. [www.wetboek-online.nl/wet/Sr/82a.html](http://www.wetboek-online.nl/wet/Sr/82a.html)
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Inclusion criteria

Gestational age 22⁰⁷ – 28⁰⁷
Severe maternal condition reason for termination
Live fetus at onset of termination
No fetal monitoring
No interventions aimed at fetus

Exclusion criteria

Gestational age ≤ 21⁰⁷ or ≥ 28⁰⁷
Fetal indication for termination
Fetal demise at onset of termination

Table 1: inclusion and exclusion criteria for this study

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<th>Indication</th>
<th>GA &lt; 24 weeks (%)</th>
<th>GA &gt; 24 weeks (%)</th>
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<tr>
<td>Overall</td>
<td>64 (64%)</td>
<td>113 (113%)</td>
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<td>Hypertensive disorders</td>
<td>37 (58%)</td>
<td>94 (83%)</td>
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<tr>
<td>Intra-uterine infection</td>
<td>14 (22%)</td>
<td>15 (13%)</td>
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<tr>
<td>Other</td>
<td></td>
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<tr>
<td>• Uterine rupture</td>
<td>1 (1.6%)</td>
<td>1 (0.8%)</td>
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<td>• Obstetric bleeding</td>
<td>3 (4.7%)</td>
<td>2 (1.7%)</td>
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<tr>
<td>• Heart failure</td>
<td>3 (4.7%)</td>
<td>1 (0.8%)</td>
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<tr>
<td>• Psychiatric disorders</td>
<td>3 (4.7%)</td>
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<tr>
<td>• Malignancy</td>
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Table 2: Indications for termination of pregnancy. GA = gestational age

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Table 3: overview of terminations per center and policy of active fetal management in the period 2000-2009. GA = gestational age
Termination of pregnancy for maternal indications at the limits of fetal viability: a retrospective cohort study in the Dutch tertiary care centres

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\textsuperscript{d} = Radboud university Medical Center Nijmegen, The Netherlands
\textsuperscript{e} = Maxima Medical Center Veldhoven, The Netherlands
\textsuperscript{f} = Maastricht University Medical Center, The Netherlands
\textsuperscript{g} = Isala Clinics Zwolle, The Netherlands
\textsuperscript{h} = Leiden University Medical Center, The Netherlands
\textsuperscript{i} = Academic Medical Center Amsterdam, The Netherlands
\textsuperscript{j} = University Medical Center Groningen, The Netherlands

Abstract

Objective: Maternal morbidity, either pregnancy-related or pre-existent can become life-threatening and of such severity to warrant termination of pregnancy (TOP). In this situation chances of fetal survival are usually poor, either because of low gestational age, and/or because of the fetal effects of the maternal condition.

Examples include severe growth restriction in pre-eclampsia and intra-uterine infection due to very early preterm prelabour rupture of membranes. There are very few reports on the prevalence of termination of pregnancy for maternal indication at the limits of fetal viability. We investigated the prevalence and indications for TOP on
maternal indication in the ten tertiary care centres in the Netherlands during the past decade.

Study design: we conducted a retrospective review of the medical records of all women who underwent TOP for maternal indications between 22 to 27 completed weeks of gestation in all 10 tertiary care centres from 2000 to 2009.

Results: During the study period there were 1,929,470 deliveries. 163,052 (8.4%) of these took place in one of the ten tertiary care centres and 177 pregnancies were terminated for severe maternal disease, 131 for hypertensive disorders, 29 for intrauterine infection and 17 for other reasons. The mean gestational age at TOP was 171 days (24\(\frac{3}{7}\) weeks) ± 10 days. No maternal deaths were recorded. The overall perinatal mortality was 99.4%.

Conclusion: Over a ten year period TOP for maternal indications was performed in 1 in 1000 deliveries in the 10 Dutch tertiary care centres. Hypertensive disorders comprised three quarters of cases.

Article summary

Strengths and limitations of the study:

- This study is one of the first to estimate the incidence of termination of pregnancy for maternal indications at the limits of fetal viability. Only two more articles on this subject have been identified.
- The results of this study raise several questions concerning policy and approach of severely sick mothers at the limits of fetal viability. The results should stimulate multidisciplinary discussion and facilitate decision making in the future.
- This study is a retrospective study and could suffer from underreporting.
During the study period a protocol concerning active perinatal management after spontaneous preterm birth at the limits of fetal viability in The Netherlands was introduced. This might have had an impact on the approach of severely sick mothers.

Introduction

Indications for termination of pregnancy in the Netherlands can be divided in: psychosocial reasons (unwanted pregnancies), genetic reasons (fetus with congenital abnormalities) and maternal medical disorders including psychiatric disorders. Under Dutch legislation, in place and unchanged since 1981, termination of pregnancy (TOP) is possible up to the gestational age where a newborn can survive outside the womb. This is currently considered 24\textsuperscript{0/7} weeks for adequately grown fetuses without lethal disorders and a sufficient amount of amniotic fluid for lung development\textsuperscript{1}. Annually there are approximately 28000 terminations of pregnancy between 5 and 24 weeks in the Netherlands. Termination for social indications up to 22 weeks is performed in clinics with a special license. Terminations for genetic reasons and for medical maternal reasons are performed in obstetric units of secondary or tertiary care centres.

In case of lethal fetal disorders such as trisomy 18, 13 or triploidy termination is also allowed beyond 24 weeks, provided a number of criteria are fulfilled\textsuperscript{2}. These cases are audited by a committee of the Dutch Society of Obstetrics and Gynecology. Termination for severe fetal disorders in case of dismal, but not necessarily lethal, prognosis for the fetus may be excepted from legal prosecution provided adherence to stringent criteria and after assessment by an expert committee appointed by the ministries of Health and Justice. This committee consists of an obstetrician, a
paediatrician and an ethicist, and is chaired by a lawyer. This committee reports
directly to the Attorney General, the highest legal authority in The Netherlands.
Termination of pregnancy beyond 24 weeks’ gestation for life-threatening maternal
conditions in combination with dismal fetal prospects (e.g. due to severe growth
restriction or anhydramnios) are generally not reported, since termination of
pregnancy in such cases is considered inevitable and the only justifiable
management option to prevent deteriorating maternal morbidity or even mortality.
According to the Guideline on Late Termination of Pregnancy of the Dutch Society of
Obstetrics and Gynecology maternal indications that warrant TOP include, but are
not limited to: hypertensive disorders with organ dysfunction, sepsis, severe
exacerbation of auto-immune disorder, severely deteriorating cardiac function,
transplant rejection, rapidly progressing malignancies as well as life-threatening
major obstetric haemorrhage. In these situations the fetus is also compromised,
either because of the gestational age, and/or because of the low estimated fetal
weight. Termination of pregnancy beyond 24 weeks’ gestation for these indications
is considered to be extremely rare. The guideline on termination of pregnancy from
the Dutch Society of Gynaecology and Obstetrics states that these patients should be
referred to and treated in a tertiary care centre. Termination of pregnancy on
maternal indication is only performed after extensive multidisciplinary consultation.

The literature lacks reports on the prevalence of termination of pregnancy for
maternal indication at the limits of fetal viability. The gestational age and estimated
fetal weight to consider “active perinatal management” directed towards survival has
recently been lowered to 24 weeks and 500 grams in many countries, including the
Netherlands. We aimed to investigate the prevalence of and indications for TOP in
severely sick mothers, at the limits of fetal viability in the Netherlands between 2000 and 2009.

Methods

We conducted a retrospective review of the medical records of all women who had TOP for maternal indications between 22 and 27 completed weeks of gestation in the 10 Dutch tertiary care centres from 2000 to 2009. Cases were identified using local delivery databases. In all cases the fetus was judged to be non-viable, either because of the gestational age or because of the impact of maternal disease on the prospects for the fetus, e.g. severe growth restriction. The inclusion and exclusion criteria are listed in table 1. Data extraction from the original medical files was performed by the first or the last author (LvE and ACB) in all cases. Data on the total number of deliveries in the 10-year period were extracted from The Netherlands Perinatal Registry (PRN foundation). The indication TOP for maternal indication is not registered in this registry4.

The study design was reviewed and approved by the medical ethics committee of the VU Medical Center in Amsterdam.

Results

In the ten year study period there were 1,929,470 deliveries in the Netherlands of which 163,052 (8.4%) took place in the 10 tertiary care centres5-6. Of those 11474 deliveries occurred between 22^{0/7} and 27^{6/7} weeks of gestation. A total of 177 (1.5%) fulfilled the inclusion criteria, 172 singleton and 5 twin pregnancies. TOP was performed for hypertensive disorders and preterm prelabour rupture of membranes
(PPROM) with intra-uterine infection in 131 (74%) and 29 (16%) cases, respectively. In 17 cases (9%) there was another motive to terminate the pregnancy (figure 1).

The mean gestational age at TOP was 171 days ($24^{37}$) weeks ± 10 days. In the hypertension group the mean gestational age was 173 days ($24^{57}$) ± 9.7 days as compared to 167 days ($23^{67}$) ± 10.1 days in the infection group and 162 days ($23^{17}$) ± 7.0 days for the other indications. The gestational age at termination was significantly higher in the hypertension group (173 days ± 9.7 days) compared to the infection group (167 days ± 10.1 days) (p= 0.006). This also applied to the hypertension group (173 days ± 9.7 days) compared to the other indications (162 days ± 7.0 days) (p<0.001).

There were no cases of maternal mortality. A total of 182 neonates were born. There was one unexpected survivor born at GA $25^{57}$ weeks' gestation with a birth weight of 600 grams. This pregnancy was terminated without fetal heart rate monitoring for severe HELLP syndrome using intravenous sulprostone. The child is now four years old and has a normal development so far.

The number of pregnancies terminated beyond the limit of $24^{07}$ weeks' gestation was 113 (64%). In 94 of these cases (83%) pregnancy was terminated for a severe hypertensive disorder. Fifteen pregnancies (13%) were terminated for overt intra-uterine infection in the setting of PPROM and four pregnancies (3.5%) for other indications (table 2). In cases of termination beyond 24 weeks a multidisciplinary team, consisting of at least obstetricians, neonatologists and other specialists, when indicated, discussed the intended advise for termination of pregnancy and examined alternative options before coming to a final advise to the parents.

Labour was induced with prostaglandins in 176 (99.4%) of the cases. In one case dilatation and evacuation was performed after feticide with potassium chloride. After
induction two pregnancies were terminated by caesarean section. In one case a caesarean section was performed to expedite delivery because of recurrent eclamptic fits with neurological impairment. In the other case a caesarean section was performed because of an uterine rupture accompanied by a hypovolemic shock. In 2006 a national guideline on active perinatal and neonatal management after spontaneous preterm birth at the limits of fetal viability was introduced. Before 2006, active management was generally started at 26 weeks’ gestation, whereas this was lowered to 25 weeks’ gestation in the guideline. The introduction of this guideline has had no major effect on the number of TOP for maternal indications. Figure 2 shows the number of TOP per year.

The incidence of TOP varied substantially between different centres (table 3). Two exemplary cases:

Case 1: a nulliparous woman, with an unremarkable history, developed severe pre-eclampsia with progressive HELLP syndrome at a gestational age of 23 weeks and 2 days. She was admitted and was treated with multiple intravenous antihypertensive drugs and magnesium sulphate. Ultrasound showed an estimated fetal weight of 480 grams. She was counselled for termination of pregnancy due to the early gestational age and the progressive course of the disease and delivered a stillborn girl of 470 grams (<p10) at 24 weeks’ gestation. The delivery took place on the intensive care unit due to refractory hypertension and pulmonary oedema in the mother.

Case 2: a woman in her fourth pregnancy was admitted at a gestational age of 22 weeks. Her obstetric history revealed dilated peripartum cardiomyopathy. Pre-conceptionally, she had been strongly advised against pregnancy. She was admitted to the ICU because of severely deteriorating cardiac function. After extensive counselling by a multidisciplinary team consisting of obstetricians, cardiologists and...
neonatologists the pregnancy was terminated at 22 weeks and 4 days’ gestation.
She delivered a stillborn son.

Comment
In the period 2000-2009 we identified 177 cases of TOP for life-threatening maternal morbidity in the ten tertiary care centres in the Netherlands. “Since the indication for termination of pregnancy is not specified in the Netherlands Perinatal Registry nor in the legally required national report on termination of pregnancy, it is not possible to check our data for underreporting. However, because the guideline on late termination of pregnancy from the Dutch Society of Gynecology and Obstetrics states that women should be referred to and treated in a tertiary care centre in case of severe maternal morbidity, we assume that we found most cases of TOP for maternal indications.”

We found that there was a difference in incidence of TOP between the tertiary care centres. This may, amongst others, be due to different local interpretation on active neonatal management at the limits of viability in a period where thresholds for active management were subject to gradual change (see table 3). It is possible that some centres advised to continue the pregnancy anticipating an intra-uterine fetal demise within days.

Dutch guidelines are in place to recommend whether or not to start active neonatal management by a neonatologist in cases with spontaneous preterm labour and an expected weight appropriate for gestational age. These guidelines are periodically revised based on current (inter)national practice standards. Prior to 2006 the overall limit for active obstetric and neonatal management was 26 weeks’ of gestation. After 2006 the recommended limit was 25 weeks’ gestation, with an estimated fetal weight
of at least 500 grams\textsuperscript{7} (figure 2). In the latest guideline dating September 2010, which was introduced after the inclusion period of this study, the recommended limit is 24 weeks’ gestation for intubation and ventilation and 25 weeks for cardiac resuscitation. Estimated fetal weight limits are no longer included\textsuperscript{8}.

The prospects of children born at 24-25 weeks are nevertheless poor, even with active management. A recent report showed that infants who received active perinatal and neonatal management survived in 43\% of cases at 24 weeks’ and in 61\% of cases at 25 weeks’. Severe short term neonatal morbidity was registered in 70-80\% of surviving children\textsuperscript{9}. In case of severe maternal morbidity in pregnancy, the prospects for an intact survival for the fetus are considered to be even worse due to the combination of a low gestational age and, in most cases, severe growth restriction or fetal inflammatory response syndrome, as well as the deleterious effects of the underlying maternal condition, such as chronic fetal hypoxia. In case it becomes inevitable for the mother’s sake to terminate the pregnancy at the limits of fetal viability, this expected extremely poor outcome of the child does not support an active fetal/neonatal management. A caesarean section puts the mother at even higher short term and long term risks. Therefore, termination via induction of vaginal delivery with prostaglandins and without fetal monitoring will often be the safest policy.

Hypertensive disease comprised three quarters of the cases and was the indication for termination in 83 \% of the terminations beyond 24 weeks. Experts in the field as well as the WHO and NICE guidelines on hypertensive disorders in pregnancy, recommend that women who develop severe pre-eclampsia at less than 23 weeks should be counselled towards termination of pregnancy\textsuperscript{10,11,12}. Gaugler et al describe 26 pregnancies, complicated by pre-eclampsia with an onset before 24 weeks’
gestation and managed expectantly. The overall perinatal mortality was 82%, with major maternal morbidity in 65% of the women\textsuperscript{13}.

In 16% of overall cases and 13% of cases beyond 24 weeks, the indication for terminating pregnancy was intra-uterine infection with overt or threatening maternal sepsis. Septic shock and maternal death have been reported in pregnancies managed conservatively\textsuperscript{14,15,16}. Therefore, termination of pregnancy is recommended in case of serious clinical infection\textsuperscript{15}.

In 9% of overall cases and 3.5% of cases beyond 24 weeks pregnancy was terminated for other reasons. In the international literature papers on other reasons for pregnancy termination for maternal indications are scarce. One study from Australia mentions psychiatric disorders, malignancies and cardiac disorders as the most common maternal indications for termination between 5 – 23 weeks’ gestation\textsuperscript{17}. In a recent paper by Piel et al from 4 hospitals in the Parisian area covering 95000 deliveries between 2001 and 2010 the main reasons for terminating pregnancy for maternal reasons between 5 and 23 weeks of gestation were (in decreasing order of frequency) : pre-eclampsia, malignancies, drug addiction, AIDS, risk of suicide, psychosis, rape, pre-existing maternal somatic or psychiatric diseases, uterine bleeding or risk of uterine rupture\textsuperscript{18}. Termination for social reasons is not allowed in the Netherlands after 24\textsuperscript{0/7} weeks gestation.

What can we learn from our observations? There are conditions where maternal health and life are compromised to such a degree, whilst chances for healthy fetal survival so dismal, that termination of pregnancy is inevitable. This entails pregnancy-induced conditions such as pre-eclampsia and HELLP syndrome, intra-uterine infection and obstetric haemorrhage, but also pre-existing or coincidental maternal conditions such as cardiac failure or malignancies. Counselling towards termination
of pregnancy in these situations is the result of a multidisciplinary perinatal team
discussion involving neonatologists, and a shared decision with the mother and her
partner.

We suggest that the indication for termination of pregnancy becomes a mandatory
item in the Netherlands Perinatal Registry. This will gain insight in the prevalence of
TOP for maternal indications. Furthermore this registration will enable audits of these
cases by a medical peer-group.

Conclusion

(Inte)national literature on termination of pregnancy for maternal indication at the
limits of fetal viability is scarce. In this retrospective cohort we found a prevalence of
0.1% of termination of pregnancy for maternal reasons in the ten tertiary care

Competing interests:

All authors have completed the ICMJE uniform disclosure form at
www.icmje.org/coi_disclosure.pdf and declare: The VUmc university medical center
Amsterdam has received a research grant from the Dutch Society of Obstetrics and
Gynecology for the submitted work; no financial relationships with any organisations
that might have an interest in the submitted work in the previous three years; H
Scheepers reports receiving a research grant from CSE Behring for a study on
clotting factors during the previous 36 months; no other relationships or activities that
could appear to have influenced the submitted work.

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The first author affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Acknowledgement: BL Scholten, MD for contributing to the data

Contributor statement: L van Eerden, G Zeeman and A Bolte designed the study and wrote the research protocol. All authors contributed to the acquisition of data and interpretation of data. L van Eerden, G Zeeman, G Christiaens, A Bolte and C de Groot contributed to drafting the article. All authors revised the article critically for important intellectual content. All authors approved the final version of the article.
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Data sharing statement:
No additional data available

Figure legends:
Figure 1: Flowchart Patient selection. TOP = termination of pregnancy, GA = gestational age, PROM = prelabour rupture of membranes
Figure 2: Number of TOP per year. TOP = termination of pregnancy

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Number of births from 2000 until 2009
N = 1,929,470

Non tertiary centers
N = 1,766,418

Tertiary centers
N = 163,052

TOP for maternal indications
N = 177

GA 22⁴/₉⁻ 23⁷/₁₀
N = 64

Hypertensive disorder
N = 37

PROM and infection
N = 14

Other
N = 13

GA 24⁴/₉⁻ 27⁵/₁₀
N = 113

Hypertensive disorder
N = 94

PROM and infection
N = 15

Other
N = 4

155x142mm (300 x 300 DPI)