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The risk of intrapartum/neonatal mortality and morbidity following birth at 37 weeks of gestation: a nationwide cohort study

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Objective To assess intrapartum/neonatal mortality and morbidity risk in infants born at 37 weeks of gestation compared with infants born at 39–41 weeks of gestation.

Design Nationwide cohort study.

Setting The Netherlands.

Population A total of 755 198 women delivering at term of a singleton without congenital malformations during 2010–14.

Methods We used data from the national perinatal registry (PERINED). Analysis was performed with logistic regression and stratification for the way labour started and type of care.

Main outcome measures Intrapartum or neonatal mortality up to 28 days and adverse neonatal outcome (neonatal mortality, 5-minute Apgar <7, and/or neonatal intensive care unit admission).

Results At 37 weeks of gestation intrapartum/neonatal mortality was 1.10‰ compared with 0.59‰ at 39–41 weeks ($P < 0.0001$). Adjusted odds ratio (aOR) for 37 weeks compared with 39–41 weeks was 1.84 (95% CI) 1.39–2.44). Adverse neonatal outcome at 37 weeks was 21.4‰ compared with 12.04‰ at 39–41 weeks ($P < 0.0001$) with an aOR 1.63 (95% CI 1.53–1.74). Spontaneous start of labour at 37 weeks of gestation was significantly associated with increased intrapartum/neonatal mortality with an aOR of 2.20 (95% CI 1.56–3.10), in both primary (midwifery-led) care and specialist care. Neither induction of labour nor planned caesarean section showed increased intrapartum/neonatal mortality risk.

Conclusions Birth at 37 weeks of gestation is independently associated with a higher frequency of clinically relevant adverse perinatal outcomes than birth at 39–41 weeks. In particular, spontaneous start of labour at 37 weeks of gestation doubles the risk for intrapartum/neonatal mortality. Extra fetal monitoring is warranted.

Keywords 37 weeks of gestation, level of care, start of labour, term adverse neonatal outcome, term intrapartum mortality, term neonatal mortality.

Tweetable abstract Birth at 37 weeks of gestation gives markedly higher intrapartum/neonatal mortality risk than at 39–41 weeks, especially with spontaneous start of labour.

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Introduction

Birth at term is defined as a pregnancy that has reached 37 weeks + 0 days of gestation up to and including 41 weeks + 6 days of gestation (37–41 weeks). Term birth is considered low risk when risk factors such as multiple pregnancy, fetal growth restriction, congenital malformations, hypertensive disorders, diabetes and/or complicated obstetric history are absent.[1] However, term births are not a homogeneous group, and those born in the early-term period, 37–38 weeks, are known to have a higher risk of mortality and morbidity than infants born at 39–41 weeks of gestation.[2–11]

Most studies on early-term births considered the combined group of births at 37 and 38 weeks of gestation.[3,7,12,13] The main outcome measures in many studies of early-term births are neonatal mortality and morbidity (low Apgar score, meconium aspiration syndrome or other respiratory morbidity requiring neonatal intensive care unit [NICU] admission).[6,9,11,14] Some studies are performed only in tertiary maternity hospital settings,[5–7] or for term

infants admitted to NICUs[6] or in low-risk settings.[5,8,15–17] We found no studies on both mortality and morbidity for birth at 37 weeks as a separate gestational age group.

In the Netherlands women with uncomplicated term pregnancies (37–41 weeks of gestation) are considered low risk and are under the care of independent midwives – or sometimes general practitioners (primary care, midwifery-led care, level 1 care) – during pregnancy, labour and delivery. When complications (threaten to) occur women are transferred to the obstetrician (specialist care, level 2 care).

Fleischman et al. made an appeal to epidemiologists and clinicians to collect data specific to the varying intervals of term births to provide new insights and strategies for improving birth outcomes.[4]

The aim of this study is to assess intrapartum/neonatal mortality and adverse neonatal outcome of pregnancies ending at 37 weeks of gestation compared with pregnancy outcomes ending at 39–41 weeks in a recent 5-year national cohort of term singleton pregnancies without congenital malformations.

Methods

Data sources

The study used data from the national perinatal database containing information on pregnancies, deliveries and neonatal (re)admissions until 28 days after birth (Perined, www.perined.nl).[18,19] The registry covers approximately 99% of all births in the Netherlands. The committee for research and ethics of Perined approved the study protocol (Perined approval 16.40). Patients were not involved in the development of the research.

We selected all term singleton infants born at 37–41 weeks of gestation (from 37 weeks + 0 days up to and including 41 weeks + 6 days) without congenital malformations born between 1 January 2010 and 1 January 2015, and registered in the Perined database. Mortality is defined as intrapartum or neonatal mortality during the first 4 weeks of life. Adverse neonatal outcome is defined as neonatal mortality and/or low 5-minute Apgar score (<7) and/or admission to one of the ten NICUs in the Netherlands with a stay of at least 24 hours.

There are no missing values for the main outcome measurements and no loss to follow up. Missing values for the main characteristics were low (<0.02%) and as we wanted to include all women in the analysis the missing values were assigned as follows:

Missing maternal age (n = 19) was imputed with the mean age of 30 years (reference group).

The 11 585 records (1.5%) with missing zip code were assigned to the mid socio-economic status (SES) (reference group), (data on SES were obtained from The Netherlands Institute for Social Research/SCP).

Missing parity (n = 36) was assigned to nulliparity (high-risk group and most likely category when missing).

The 6511 records (0.9%) with unknown ethnicity were coded as non-western (high-risk group and most likely category when missing).

Missing birthweight (n = 224, 0.35%) was assigned to the non-SGAp10 group (small-for-gestational-age, <10th birthweight centile; low-risk group).

Statistical analysis

The prevalence of intrapartum/neonatal mortality and adverse neonatal outcome is calculated for singleton infants born at 37 weeks of gestation and compared with infants born at 39–41 weeks. The chi-square test was used to test for differences. Both crude and adjusted odds ratios (aOR) with 95% CI were calculated with logistic regression. The odds ratios for all outcome measures were at first adjusted for parity (nulliparity/primi- and multiparity), age (<25, 25–34, ≥35 years), ethnicity (Caucasian ethnicity/non-Caucasian ethnicity (South Asian, African, Mediterranean or other non-Caucasian ethnicity), socio-economic status (SES: low <25th centile/mid 25th to 75th centile/high >75th centile). Subsequently, we also adjusted for hypertensive disorder (essential hypertension, pregnancy-induced hypertension, [pre]eclampsia) and small-for-gestational-age <10th birthweight centile according to parity, sex and ethnicity (SGA<p10).[20]

Sensitivity analysis was conducted by excluding breech presentation for the main outcome measure.

Stratified analyses were performed for intrapartum/neonatal mortality and the way labour started (spontaneous, induction of labour or planned caesarean section) and level of care (primary care-level 1 or specialist care-level 2) at spontaneous start of labour.

All statistical analyses were performed using SAS (version 9.3, SAS Institute Inc., Cary, NC, USA).

Results

Characteristics of the mothers and infants born at 37, 38 and 39–41 weeks of gestation show differences (Table 1). At birth, at 37 weeks mothers were more likely to be nulliparous, with maternal age <25 years, non-Caucasian ethnicity and low SES compared with birth at 39–41 weeks of gestation. Hypertensive disorders were four times more common in birth at 37 weeks of gestation compared with birth at 39–41 weeks, and more male infants and SGA<p10 infants were born at 37 weeks. Induction of labour was doubled at 37 weeks compared with birth at 39–41 weeks. At 37 weeks of gestation, labour started half as often (30%) with primary care (independent midwife or general practitioner) than at 39–41 weeks (60%).

Differences in intrapartum/neonatal mortality and adverse neonatal outcome were higher for birth at 37 weeks than at

Table 1. Outcome and characteristics of 755 198 mothers and children in different term groups

	37 weeks		38 weeks		39–41 weeks		P-value	
All births	*n* = 55 629		*n* = 124 788		*n* = 574 781		overall	37 vs 39–41 weeks
Outcome								
	n		*n*		*n*			
Intrapartum/neonatal mortality	61	1.10‰	81	0.65‰	336	0.59‰	*	*
Adverse neonatal outcome	1189	21.4‰	161	12.9‰	6912	12.0‰	*	*
Characteristics	*n*	%	*n*	%	*n*	%		
Maternal								
Nulliparity	26 787	48.2%	52 659	42.2%	257 109	44.7%	*	*
Maternal age								
<25 years	7247	13.0%	14 510	11.6%	63 954	11.1%	*	*
25–34 years	36 697	66.0%	82 820	66.4%	394 510	68.6%	*	*
≥35 years	11 685	21.0%	27 458	22.0%	116 317	20.2%	*	*
Non-Caucasian ethnicity	11 005	19.8%	26 383	21.1%	108 668	18.9%	*	*
Socio-economic status								
Low	14 467	26.0%	32 229	24.0%	137 948	24.0%	*	*
Mid	28 619	51.4%	63 221	50.6%	291 033	50.6%	*	*
High	12 543	22.5%	29 338	25.4%	145 800	25.4%	*	*
Hypertensive disorders	13 080	23.5%	15 657	12.6%	32 924	5.7%	*	*
Child								
Male gender	29 493	53.0%	65 018	52.1%	288 546	50.2%	*	*
SGA<p10[$]	5233	9.4%	10 706	8.4%	48 103	8.4%	*	*
Delivery								
Spontaneous start of labour	29 470	53.0%	69 266	55.5%	450 439	78.4%	*	*
Planned caesarean section	5209	9.4%	17 872	14.3%	26 423	4.6%	*	*
Induction of labour	20 950	37.7%	37 650	30.2%	97 919	17.0%	*	*
Start labour with primary care	16 791	30.2%	45 861	36.8%	345 958	60.2%	*	*
Delivery with primary care	10 239	18.4%	28 747	23.0%	196 706	34.2%	*	*

*$P < 0.0001$; [$]SGA < p10 = small for gestational age < 10th percentile.

38 weeks compared with birth at 39–41 weeks (Table 1, and see Supplementary material, Figure S1). For infants born at 37 weeks of gestation, intrapartum/neonatal mortality was higher, 1.10‰ compared with 0.59‰ for infants born at 39–41 weeks ($P < 0.0001$). Adverse neonatal outcome at 37 weeks of gestation was increased, 21.4‰ compared with 12.0‰ for infants born at 39–41 weeks ($P < 0.0001$) (Table 2).

Adjustment for parity, age, ethnicity and SES gives an odds ratio for 37 weeks of gestation compared with 39–41 weeks for intrapartum/neonatal mortality of 1.86 (95% CI 1.41–2.44) and additional adjustment for hypertensive disorders and SGA gave a similar odds ratio (Table 3). For adverse perinatal outcomes, full adjustment showed significant increased risk with an odds ratio of 1.63 (95% CI 1.53–1.74).

Exclusion of births with breech presentation at 37 weeks gave the same significant results for intrapartum/neonatal mortality and adverse neonatal outcome (see Supplementary material, Table S1).

For infants born at 38 weeks of gestation, there was a higher risk for adverse neonatal outcome than for infants born at 39–41 weeks, but this was not the case for intrapartum/neonatal mortality risk (see Supplementary material, Table S2 and Figure S1). After full adjustment no differences were seen (see Supplementary material, Table S3).

Table 4 shows the effect of the way of start of labour and level of care at 37 weeks of gestation compared with 39–41 weeks. Spontaneous start of labour showed the highest risk for intrapartum/neonatal mortality with aOR 2.20 (95% CI 1.56–3.10). Induction of labour and planned caesarean section showed no increased intrapartum/neonatal mortality risk.

When labour started spontaneously under primary care, intrapartum/neonatal mortality risk was elevated with an aOR of 1.95 (95% CI 1.19–3.21); it was also elevated with start of labour under specialist care (aOR 2.15; 95% CI 1.31–3.52).

Discussion

Main findings

Gestational age of 37 weeks has an overall odds ratio of 1.8 for intrapartum/neonatal mortality and 1.6 for adverse

Table 2. Intrapartum/neonatal mortality and adverse neonatal outcome in infants born at 37 weeks of gestation compared with infants born at 39–41 weeks

	37 weeks		39–41 weeks		*P*-value
All births	55 629		574 781		
	n	‰	*n*	‰	
Antepartum deaths	128		432		
Alive at start of labour	55 501		574 349		
Intrapartum deaths	20	0.36	110	0.19	0.008
Live births	55.481		574.239		
Neonatal mortality	41	0.74	226	0.39	0.0002
Intrapartum/neonatal mortality	61	1.10	336	0.59	<0.0001
5-minute Apgar <7	787	14.2	5763	10.0	<0.0001
NICU admission*	475	8.6	1791	3.1	<0.0001
Adverse neonatal outcome**	1189	21.4	6912	12.04	<0.0001

*Admission to third level NICU with ≥24 hours stay.
**Neonatal mortality, and/or 5-minute Apgar <7, and/or NICU admission (therefore the figure does not add up).

Table 3. Odds ratios for intrapartum/neonatal mortality and adverse neonatal outcome in infants born at 37 weeks of gestation compared with infants born at 39–41 weeks

37 weeks		Odds ratio	95% CI	
Intrapartum/neonatal mortality	Crude	1.88	1.43	2.47
	Adjusted*	1.86	1.41	2.44
	Adjusted**	1.84	1.39	2.44
Adverse neonatal outcome	Crude	1.79	1.69	1.91
	Adjusted*	1.73	1.63	1.84
	Adjusted**	1.63	1.53	1.74

*Adjusted for parity, maternal age, ethnicity, socio-economic status, gender.
**Adjusted for parity, maternal age, ethnicity, socio-economic status, gender, SGA, hypertensive disorder.

Table 4. Intrapartum/neonatal mortality at 37 completed weeks of gestation compared with 39–41 completed weeks, start of labour and care at spontaneous start of labour

	Total birth *n*	Intrapartum/ neonatal mortality *n*	aOR*	95% CI	
Start of labour					
Spontaneous	29 426	37	2.20	1.56	3.10
Induction	20 870	18	1.62	0.95	2.77
Planned caesarean section	5205	6	1.17	0.48	2.85
Total	55 501	61			
Care at spontaneous start of labour					
Primary (midwifery-led) care	16 473	17	1.95	1.19	3.21
Specialist care	12 814	20	2.15	1.31	3.52
Unknown care	139	0	n.a.		
Total	29 426	37			

n.a., not applicable.
*Adjusted for parity, maternal age, ethnicity, socio-economic status, gender, SGA<p10, hypertensive disorder.

neonatal outcome compared with 39–41 weeks. These differences are not explained by differences in parity, age, ethnicity, SES, hypertensive disorder or SGA<p10.

Spontaneous start of labour at 37 weeks gave a significantly increased risk for intrapartum/neonatal mortality with an odds ratio of 2.2, whereas induction of labour and planned caesarean section gave no increased risk. Whether labour started spontaneously under primary (midwifery-led) care or specialist care, the elevated intrapartum/neonatal mortality risk was the same.

Strengths and limitations

Our study is one of the few studies exploring 37 weeks of gestation separately as an independent determinant in a large and recent nationwide population-based cohort of births for both intrapartum/neonatal mortality and adverse neonatal outcome.

As body mass index and smoking are not yet registered items in the Perined database, we could not adjust for these risk factors in the logistic regression models. These factors are important for perinatal intrapartum/neonatal mortality and morbidity. However, we showed that the adjustment for hypertensive disorder or SGA, often considered intermediate risk factors for body mass index and smoking, did not cause much change in the effect of 37 weeks of gestation, and therefore, we believe that adjustment for body

mass index and smoking will also have low impact on the odds ratios.

Interpretation

It is difficult to compare our results with earlier studies on this subject. Many studies take 37 and 38 weeks of gestation as a combined group, apparently due to lack of power for using only data on 37 weeks separately.[3,7,13] There are a few regional or hospital studies on perinatal mortality but as they include multiple births and congenital malformations they are not comparable with our study.[21,22]

Neonatal mortality of 0.7 per 1000 live-born infants at 37 weeks of gestation, found in our study, is in agreement with studies in the USA.[11,23] Higher rates were found in the study of Reddy et al. with 1.6 per 1000 births for singletons born at 37 weeks. In that study, birth defects were included so it is not quite comparable with our study.[13]

We found 8.6 per 1000 births admission to NICU for at least 24 hours. This is much lower than the 55 per 1000 births in the study of Linder et al. in a low-risk population of infants born at 37–38 weeks of gestation in a third-level hospital.[5] Caughey and Musci[22] found for 37 weeks of gestation 74 NICU admissions per 1000 live births, Parikh et al.[9] found for the combined group of 37 and 38 weeks of gestation 81 NICU admissions per 1000 live births. All of these figures are much higher compared with our findings. In our country, only admission to a level III NICU department for at least 24 hours are counted as such, which might explain the differences.

Low Apgar score is an important component of adverse neonatal outcome in our study. A low 5-minute Agar score (<7) is sometimes questioned as a valid measure of birth asphyxia because of subjective elements.[23] In term-born infants without congenital malformations a 5-minute Apgar score <7 may be caused by intrauterine asphyxia and is an essential part of the Adverse Outcome Index.[24–26] An Apgar score <7 at 5 minutes was found in our study for 14.2 per 1000 live births at 37 weeks of gestation. Other studies were not comparable because of a low-risk setting or because the study pertains to a regional cohort.[5,15,17,27]

A remarkable finding in our study is the different risk at 37 weeks of gestation when we regard the way labour started. When labour started spontaneously, intrapartum/neonatal mortality risk was clearly higher when compared with when labour started with induction of labour or a planned caesarean section. When induction of labour or planned caesarean section takes place at 37 weeks of gestation higher risk is present or suspected, and continuous fetal monitoring is applied. When labour starts spontaneously at 37 weeks this is in general regarded as normal and expectant policy is usual. Intrapartum/neonatal mortality risk at spontaneous start of labour was nearly equal under primary (midwifery-led) care and specialist care. Start of labour under primary care means, in principle, that pregnancy was uncomplicated. Apparently, spontaneous start of labour at 37 weeks of gestation carries more risk in itself, which needs more intensive monitoring during labour, delivery and in the first days/weeks of life.

Our findings provide a reason to regard the start of labour at 37 weeks of gestation not as low risk but as an intermediate group between preterm and term birth with clearly elevated perinatal risk.

Conclusion

In conclusion, birth at 37 weeks of gestation is independently associated with a higher frequency of clinically relevant perinatal outcomes than birth at 39–41 weeks.

Spontaneous start of labour at 37 weeks is associated with a doubling of the risk for intrapartum/neonatal mortality. More intensive monitoring during labour, delivery and the neonatal period seems warranted.

Disclosure of interests

FG reports personal fees from the Dutch government, outside the submitted work; FG has a patent 2-iminobiotin for neuroprotection issued. None of the other authors have a conflict of interest to report. Completed disclosure of interest forms are available to view online as supporting information.

Contribution to authorship

ME and AR conceived the study question, collected the data and performed the statistical analyses. ME and AR drafted the first version of the manuscript and it was revised and approved by SE, FG, AA, AR and ME.

Details of ethics approval

The committee for research and ethics of Perined approved the study protocol (Perined approval 16.40 d.d. 12-7-2016).

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1. Intrapartum/neonatal mortality and adverse neonatal outcome by gestational age.

Table S1. Odds ratios for intrapartum/neonatal mortality and adverse neonatal outcome in infants born at 37 weeks of gestation compared with infants born at 39–41 weeks (infants born with breech position excluded).

Table S2. Intrapartum/neonatal mortality and adverse neonatal outcome in infants born at 38 weeks of gestation compared with infants born at 39^0–41^6 weeks.

Table S3. Odds ratios for intrapartum/neonatal mortality and adverse neonatal outcome in infants born at 38 weeks of gestation compared with infants born at 39–41 weeks. ■

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