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ARTICLE

Increasing trends in a low 5-min Apgar score among (near) term singletons: a Dutch nationwide cohort study

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OBJECTIVE: To investigate trends in low Apgar scores in (near) term singletons using the Dutch Perinatal Registry.
METHODS: In a cohort of 1,583,188 singletons liveborn ≥35 weeks of gestation in the period 2010–2019, we studied trends in low 5-min Apgar scores (<7 and <4) using Cochrane Armitage trend tests.
RESULTS: The proportion of infants with low Apgar scores <7 and <4 increased significantly between 2010–2019 (1.04–1.42% ($p < 0.001$), 0.17–0.19% ($p = 0.009$), respectively). Neonatal mortality remained unchanged. Induction of labour, epidural analgesia and planned caesarean section showed an increasing trend. Instrumental vaginal delivery and emergency caesarean section were performed less frequently over time, but these intervention subgroups showed the highest relative increase in infants with low Apgar scores.
CONCLUSIONS: In the Netherlands, the risk of a low 5-min Apgar score increased over the last decade. The highest relative increase was observed in subgroups of instrumental vaginal delivery and emergency caesarean section.

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INTRODUCTION

The neonatal period is the most vulnerable period for a child's survival. The child's risk of dying is the highest in the first 28 days of life. One of the leading causes of neonatal death is birth asphyxia. The World Health Organization (WHO) defines birth asphyxia as "the failure to initiate and sustain breathing at birth" [1]. In birth asphyxia, the marked impairment of blood flow or gas exchange to or from the fetus in the period before, during or directly after birth, leads to progressive hypoxemia, hypercapnia, and significant metabolic acidosis. Globally, birth asphyxia is responsible for an estimated 900,000 neonatal deaths each year, and it is the main cause of death in term infants admitted to the neonatal intensive care unit (NICU) [2, 3]. Furthermore, birth asphyxia is a major cause of morbidity with both significant short and long-term consequences [4, 5].

The Apgar score provides a rapid assessment of the infant's clinical status immediately after birth and of the response to resuscitation if needed [6, 7]. In term infants without severe congenital malformations, a low 5-min Apgar score has the best predictive value for neonatal mortality and is highly associated with subsequent neurological disability such as cerebral palsy, cognitive impairment, attention deficit/hyperactivity disorder, and epilepsy even in the era of therapeutic hypothermia [8–12].

Previous studies showed that the risk of a low 5-min Apgar score <7 among term singletons slightly decreased in the period 1999–2009 in the Netherlands, but significantly increased in the subsequent period (from 9.9/1000 in 2010 to 10.9/1000 in 2014, $p < 0.001$) [13–15]. This latter observation is worrisome. An association with epidural analgesia was suggested, because the study presenting data from 2010–2014 also showed that the strongest risk factor for an Apgar score <7 was the use of epidural analgesia [14]. To the best of our knowledge, there are no studies presenting more recent trends in the Netherlands for a low Apgar score in the Netherlands, including Apgar score <4.

The primary aim of the present study was to investigate recent trends in low 5-min Apgar score, as indicator of birth asphyxia, over the last decade (2010–2019) in the Netherlands. The secondary aim was to identify risk factors for a low 5-min Apgar score, and to describe trends over time in low Apgar scores in subgroups of infants based on obstetric interventions and level of care.

METHODS

Data sources

Data for this study were extracted from a national cohort using the Netherlands Perinatal Registry (www.Perined.nl). The Perined registration

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consists of population-based clinical and laboratory data on pregnancies, deliveries, and neonatal (re)admissions until 28 days after delivery. Data in this national registry are collected by caregivers. The database covers about 96% of all deliveries at more than 22 completed weeks of gestation in the Netherlands [16].

For this study, we selected all singletons liveborn between 35^{+0} and 42^{+6} weeks of gestation in the period between January 1st 2010 and December 31st 2019. We did not include more recent years 2020 and 2021 because of the possible influence of the COVID-19 pandemic [17]. Infants with severe congenital malformations and infants who died before or during birth (defined as fetal mortality) were excluded.

Outcome measures

The primary outcome of this study was a low 5-min Apgar score, defined as Apgar <7 and Apgar <4 among liveborn infants. The following secondary outcomes were studied as other indicators of birth asphyxia: NICU admission for 24 h or more, low umbilical artery pH (pH <7.1 and pH <7.0), and neonatal mortality (within 7 and 28 days after birth). We limited NICU admissions to admissions for at least 24 h to prevent misclassification of infants admitted for transient symptoms of fetal-to-neonatal transition.

Covariates

Several sociodemographic characteristics and factors related to pregnancy, labour and health care were collected and studied as risk factors for a low Apgar score. Sociodemographic characteristics included maternal age (<25 years, 25–34 years, and ≥35 years), ethnicity (Western vs. non-Western), urbanisation (very urban with >2500 addresses per square kilometre (km^2), intermediate with 500–2500 households/km^2 and very rural with <500 households/km2), and neighbourhood socioeconomic status (SES; in quintiles (Q1 very low/deprived to Q5 very high)) [18]. Variables related to pregnancy were: parity (nulliparous P0, multiparous P1-P2 and multiparous P3+), hypertensive disorder including pre-eclampsia, maternal diabetes including gestational diabetes, medical history with caesarean section, and severe vaginal bleeding during gestation.

Variables studied related to labour were: obstetric interventions (induction of labour, instrumental vaginal delivery, planned (primary) and emergency (secondary) caesarean section, and use of epidural analgesia), presentation at birth (cephalic vs. non-cephalic), prelabour rupture of membranes (>24 h before birth), prolonged second stage of labour (>120 min for nulliparous women and >60 min for multiparous women), and meconium-stained amniotic fluid. Characteristics at birth were: month of birth, year of birth, fetal sex, gestational age in weeks, and small (SGA) or large for gestational age (LGA). SGA was defined as <10th percentile and LGA as >90th percentile according to the Dutch reference curves [19]. As health care related factors we studied: time of birth (daytime 8–17 h, evening 18–24 h or night 24–8 h), day of birth on a week or weekend day and level of care (primary vs. secondary at onset of birth and at delivery). Level of care was studied because the Dutch maternity care model is based on risk selection. Antepartum-judged low-risk pregnancies are under surveillance of primary care, whereas high-risk pregnancies are under secondary care. Primary care is provided by midwives, and on a small scale general practitioners, and includes home births, and births in a birth centre or in a hospital under the care of a midwife. Secondary obstetric care is provided by an obstetrician in a general hospital or tertiary academic centre [20].

Statistical analysis

First, we studied trends over time in our primary and secondary outcome measures. We calculated the number and rate of births with the outcome measurements for each year of the study. To analyse possible trends over time, we performed Cochrane-Armitage trend tests. The absolute difference was the outcome in year 2019 minus 2010. The relative difference (in percentage) was the absolute difference divided by the outcome in year 2010.

Second, we investigated risk factors for a low 5-min Apgar score, both <7 and <4, by calculating risk per 100 births and performing logistic regression analysis. We assessed crude and adjusted odds ratios (ORs) with 95% confidence intervals (CI). The Population Attributable Risk (PAR), which takes the number of exposed individuals into account, was calculated for the variables with statistically significant ORs for Apgar score, both <7 and <4.

Thirdly, we studied trends in prespecified obstetric interventions (induction of labour, use of epidural analgesia, planned and emergency caesarean section, and instrumental delivery) and in level of care. In subgroups based on these obstetric interventions, we also separately assessed trends in low Apgar scores.

Finally, we performed a multivariate logistic regression analysis to adjust for the co-variates. Collinearity diagnostics was performed to find possible interaction of factors. Data of co-variates were missing in less than 0.5% of the cases. The missing data were imputed using a single imputation method. Continuous variables were imputed with the mean and dichotomous or categorical variables with the larges/main groups.

None of the outcome measurements were missing, except for arterial umbilical cord blood pH's, which are not routinely collected in clinical care. These pH measurements were only available in 9.6% of all liveborn infants ($n = 152{,}653$).

All statistical analyses were carried out with SAS software version 9.4 (SAS Institute Cary, North Carolina, USA). A p-value of less than 0.05 was considered statistically significant.

RESULTS

Study population

In the Perined registry, 1,602,867 singletons were registered with gestational age between 35^{+0} and 42^{+6} weeks in the period between January 1st 2010 and December 31st 2019 (Supplementary Fig. 1). We excluded 17,504 infants with severe congenital anomalies, and 2175 deliveries with fetal mortality, leaving 1,583,188 liveborn eligible singletons for this study. Fetal mortality after a pregnancy of ≥35 weeks decreased significantly by 23.5% over the years (from 0.17% ($n = 279$) in 2010 to 0.13% ($n = 193$) in 2019 ($p < 0.0001$)—Supplementary Table 1).

Trends in outcome measurements

Table 1 shows the trends in the primary outcomes, both 5-min Apgar score of <7 and <4. An Apgar score <7 was present in 1.20% of all liveborn singletons, and significantly increased by 36.5% over the years (from 1.04% in 2010 to 1.42% in 2019 ($p < 0.0001$)). A 5-min Apgar score <4 was recorded in 0.18% of all liveborn infants. The Apgar score <4 increased significantly by 11.8% over time (from 0.17% in 2010 to 0.19% in 2019, $p = 0.0003$).

Table 2 shows the trends in the secondary outcome measurements. Neonatal mortality within the first week of life was 0.049%, and within the first month was 0.059%. Both remained stable over the study period. The percentage of infants being admitted to the NICU for 24 h or more increased by 19.3% from 0.57% in 2010 to 0.68% in 2019 ($p < 0.0001$). Arterial umbilical cord blood pH's were available in 9.6% of all liveborn infants during the whole study period. The availability increased from 6.8% in 2010 to 10.8% in 2019 ($p < 0.001$). Over the years, we observed a significant increase in proportion of infants with an umbilical artery pH <7.1 and pH <7.0. An umbilical artery pH <7.1 was present in 9.0% of cases with available umbilical artery pH in 2010 and in 10.3% in 2019. This is a relative increase of 14.4% ($p < 0.0001$). The trend in pH <7.0 was also significant over the years ($p < 0.0001$), but less clear. An umbilical artery pH <7.0 was available in 2.2% of cases with available umbilical artery pH and varied between 1.7 and 2.5% over the years.

Risk factors for a low 5-min Apgar score

Supplementary Table 2 describes risk factors for a low 5-min Apgar score <7 and <4. Many perinatal characteristics showed a significant association with low Apgar scores. The intermediate risk factors for an Apgar score <7 with a high crude OR and PAR were: emergency caesarean section (OR 4.84, 95% CI: 4.63–5.05), delivery in secondary care (OR 4.25, 95% CI: 4.01–4.47), instrumental vaginal delivery (OR 3.49, 95% CI: 3.33–3.65). Risk factors for an Apgar score <7 with a high crude OR and PAR were: nulliparity (OR 1.99, 95% CI: 1.93–2.05, PAR = 29.0%), prolonged second stage of labour (OR 1.94, 95% CI: 1.87–2.00, PAR = 12.1%), male sex (OR 1.28, 95% CI: 1.24–1.31, PAR = 15.4%), epidural analgesia (OR 1.48, 95% CI: 1.44–1.54, PAR = 17.1%), induction of

Table 1. Trends in low 5-min Apgar score in 1,583,188 liveborn singletons ≥ 35 weeks of gestation.

	Total liveborn	Apgar score < 7		Apgar score < 4	
Year	*n*	*n*	%	*n*	%
2010	164,343	1714	1.04	284	0.17
2011	164,337	1755	1.07	270	0.16
2012	162,174	1825	1.13	235	0.14
2013	155,561	1738	1.12	273	0.18
2014	160,586	1866	1.16	276	0.17
2015	156,421	1898	1.21	280	0.18
2016	158,937	1967	1.24	288	0.18
2017	155,491	2042	1.31	326	0.21
2018	151,857	2008	1.32	283	0.19
2019	153,481	2174	1.42	298	0.19
Total	1,583,188	18,987	1.20	2813	0.18
p-value trend test			<0.0001		0.0003
Difference[a]					
Absolute			0.38		0.02
Relative (%)			36.5		11.8

[a]Difference in 2019 compared to 2010 (both absolute and relative in percentage).

labour (OR 1.42, 95% 1.38–1.47, PAR 8.2%), and meconium-stained amniotic fluid (OR 1.76, 95% CI: 1.70–1.83, PAR = 8.0%)).

For an Apgar score <4, the most notable risk factors were overall comparable to the risk factors for an Apgar <7. With a slightly stronger effect for non-western ethnicity, non-cephalic presentation, and a weaker effect for induction of labour.

Trends in obstetric interventions, level of care and low Apgar scores in subgroups

Table 3 shows trends in the five prespecified obstetric interventions and the incidences of a low Apgar score (<7 and <4) in these subgroups. The incidence of induced labour, use of epidural analgesia and planned caesarean section increased significantly between 2010 and 2019 (from 19.8 to 23.9% ($p < 0.0001$), from 15.2 to 20.5% ($p < 0.0001$), and from 6.5 to 7.2% ($p < 0.0001$), respectively). Epidural analgesia showed the strongest increase, with a significant relative increase of 34.8% between 2010 and 2019 (from 15.2% in 2010 to 20.5% in 2019). In total, 8.4% of all infants were born by instrumental vaginal delivery and 8.1% by emergency caesarean section. Incidences of both interventions showed a decreasing trend; instrumental vaginal deliveries decreased from 10.2 to 7.1% (−31.4% relative difference, $p < 0.0001$), and emergency caesarean sections from 9.0% in 2010 to 7.9% in 2019 (−10.8% relative difference, $p < 0.0001$).

Within all five obstetric intervention subgroups, a significant increase in infants with an Apgar score <7 was observed. The highest increase in low Apgar score <7 was observed in the subgroups of instrumental vaginal delivery (relative increase of 52.4%, with absolute percentages increasing from 2.1% in 2010 to 3.2% in 2019 ($p < 0.0001$)), and emergency caesarean section (relative increase of 63.3%, with absolute percentages increasing from 3.0% in 2010 to 4.9% in 2010 ($p < 0.0001$)).

For the Apgar score <4, a significant trend was only observed in the subgroups of instrumental vaginal delivery and emergency caesarean section. In the subgroup of instrumental vaginal delivery, the proportion of infants with Apgar score <4 increased with 32% (from an absolute percentage of 0.24% in 2010 to 0.32% in 2019, $p < 0.001$). For the subgroup of emergency caesarean section, the relative increase in low Apgar score <4 was 30% (from an absolute percentage of 0.63 in 2010 to 0.82 in 2019, $p < 0.0001$).

Table 4 shows the results of the analysis performed for level of care. Overall, 28.7% of infants was born in primary care and 71.3% in secondary care. As expected, the risk of a low Apgar score <7 and <4 was higher for infants born in secondary care compared to primary care. Both in primary and secondary care there was a significant increase in infants with a low Apgar score <7, but the highest increase was observed in secondary care. Over time, the Apgar score <4 remained stable in primary care. In secondary care, the proportion of infants with Apgar score <4 increased significantly (from 0.22 to 0.26%, with a relative difference of 18.2%) in subgroup with onset of birth in secondary care, and from 0.22 to 0.25% (significant relative increase of 18%) in subgroup with delivery in secondary care).

In the multivariate analysis, where we controlled for the co-factors in separate models, still the trend in the low 5-min Apgar <7 (1.04, 95% CI: 1.04 to 1.05) and Apgar <4 (1.03, 95% CI: 1.02 to 1.03) was significantly increased (Supplementary Table 3).

DISCUSSION

In this nationwide Dutch study, we found a significant increase in low 5-min Apgar scores, <7 and <4, in (near) term liveborn singletons over the period 2010–2019. Neonatal mortality remained unchanged. Risk factors for an Apgar score <7 with a high crude OR and PAR were: nulliparity, prolonged second stage of labour, male gender, epidural analgesia, induction of labour and meconium-stained amniotic fluid.

The obstetric interventions planned caesarean section, induction of labour and epidural analgesia showed a significant increase over the last ten years. Instrumental vaginal delivery and emergency caesarean section showed and opposite trend and were performed less frequently over this decade. The highest relative increase in low Apgar scores (<7 and <4) was observed in the intervention subgroups of instrumental vaginal delivery and emergency caesarean section. In primary care, we observed an overall low risk for a low Apgar score.

Ravelli et al. previously showed that the risk of a low 5-min Apgar score <7 among term singletons in the Netherlands increased in the period 2010–2014 (from 9.9/1000 in 2010 to 10.9/1000 in 2014, $p < 0.001$) [13, 14]. This observation was

Table 2. Trends in neonatal mortality, NICU admission and arterial umbilical cord blood pH in liveborn singletons ≥ 35 weeks of gestation.

	Total live born	Neonatal mortality < 7 days		Neonatal mortality <28 days		NICU admission > 24 hr		Umbilical artery pH available		Umbilical artery pH < 7.1[a]		Umbilical artery pH < 7.0[a]	
Year		*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
2010	164,343	98	0.060	122	0.074	931	0.57	11,134	6.8	1002	9.0	278	2.5
2011	164,337	87	0.053	100	0.061	929	0.57	13,683	8.3	1114	8.1	308	2.3
2012	162,174	69	0.043	79	0.048	867	0.53	16,135	9.8	1263	7.8	269	1.7
2013	155,561	52	0.033	66	0.040	823	0.53	16,191	9.9	1360	8.4	337	2.1
2014	160,586	69	0.043	90	0.055	822	0.51	15,780	9.6	1341	8.5	361	2.3
2015	156,421	72	0.046	88	0.054	882	0.56	14,850	9.1	1305	8.8	332	2.2
2016	158,937	72	0.045	90	0.055	839	0.53	18,277	11.1	1634	8.9	401	2.2
2017	155,491	91	0.059	106	0.064	1,081	0.70	17,784	10.8	1735	9.8	392	2.2
2018	151,857	79	0.052	95	0.058	919	0.61	11,146	6.8	1128	10.1	238	2.1
2019	153,481	92	0.060	102	0.062	1,048	0.68	17,673	10.8	1822	10.3	435	2.5
Total	1,583,188	781	0.049	938	0.059	9,141	0.58	152,653	9.6	13,704	9.0	3351	2.2
p-value trend test			0.29		0.51		<0.0001		<0.0001		<0.0001		<0.0001
Difference[b]													
Absolute			N.A.		N.A.		0.11		4.0		1.3		0.0
Relative (%)			N.A.	.	N.A.		19.3		58.8		14.4		0.0

[a]Percentage of infants with a low umbilical artery pH in whom an umbilical artery pH was available.
[b]Difference in 2019 compared to 2010 (both absolute and relative in percentage).
N.A. not applicable.

Table 3. Trends in obstetric interventions and the incidence of low 5-min Apgar scores in the intervention subgroups.

	Induction of labour			Epidural analgesia			Instrumental delivery			Planned caesarean section			Emergency caesarean section		
Year	Inc.[a]	AS < 7 %	AS < 4 %	Inc.[a]	AS < 7 %	AS < 4 %	Inc.[a]	AS < 7 %	AS < 4 %	Inc.[a]	AS < 7 %	AS < 4 %	Inc.[a]	AS < 7 %	AS < 4%
2010	19.8%	1.4	0.22	15.2%	1.9	0.29	10.2%	2.1	0.24	6.5%	1.3	0.20	9.0%	3.0	0.63
2011	21.0%	1.4	0.22	16.5%	1.9	0.30	9.9%	2.4	0.31	6.4%	1.4	0.28	8.9%	3.1	0.54
2012	20.7%	1.4	0.14	16.8%	2.0	0.24	9.2%	2.4	0.20	6.5%	1.4	0.18	8.6%	3.5	0.52
2013	20.7%	1.4	0.23	17.3%	2.1	0.30	8.6%	2.5	0.39	7.0%	1.4	0.18	8.4%	3.6	0.64
2014	20.7%	1.5	0.20	18.5%	2.1	0.29	8.4%	2.7	0.24	7.3%	1.5	0.25	8.2%	3.6	0.64
2015	21.2%	1.5	0.24	20.2%	2.0	0.24	8.1%	2.8	0.35	7.6%	1.6	0.23	8.3%	4.0	0.57
2016	21.6%	1.6	0.20	19.9%	2.2	0.29	7.6%	2.7	0.34	7.4%	1.5	0.29	7.7%	4.4	0.64
2017	22.1%	1.7	0.25	20.7%	2.3	0.29	7.1%	3.2	0.49	7.3%	1.5	0.26	7.1%	4.6	0.69
2018	22.1%	1.7	0.20	20.0%	2.2	0.24	7.1%	3.1	0.28	7.2%	1.6	0.13	7.2%	4.2	0.62
2019	23.9%	1.8	0.26	20.5%	2.2	0.30	7.1%	3.2	0.32	7.2%	1.6	0.13	7.9%	4.9	0.82
Total	21.4%	1.6	0.22	18.5%	2.1	0.28	8.4%	2.7	0.31	7.0%	1.5	0.21	8.1%	3.9	0.63
p-value[b]	<0.0001	<0.0001	0.17	<0.0001	<0.0001	0.90	<0.0001	<0.0001	0.026	<0.0001	0.0091	0.19	<0.0001	<0.0001	0.014
Difference[c]															
Absolute	4.1	0.4	N.A.	5.3	5.3	N.A.	−3.1	1.05	0.12	0.7	0.31	N.A.	−1.1	1.9	0.19
Relative	20.7	28.6	N.A.	34.8	15.8	N.A.	−31.4	52.4	33.3	10.8	23.1	N.A.	−12.2	63.3	30.1

AS Apgar score, *Inc.* incidence, *N.A.* not applicable.
[a]Incidence in the total cohort of 1,583,188 liveborn singletons per year; [b]*p*-value trend test; [c]Difference in 2019 compared to 2010 (both absolute and in percentage) if there was a significant trend.

Table 4. Trends in level of care at onset of birth and delivery and low 5-min Apgar score in level of care subgroups of infants.

	Onset of birth in primary care			Onset of birth in secondary care			Delivery in primary care			Delivery in secondary care		
Year	Inc.[a]	AS < 7 %	AS < 4 %	Inc.[a]	AS < 7 %	AS < 4 %	Inc.[a]	AS < 7 %	AS < 4 %	Inc.[a]	AS < 7 %	AS < 4 %
2010	53.0%	0.8	0.13	47.0%	1.3	0.22	28.7%	0.4	0.06	71.3%	1.3	0.22
2011	52.6%	0.8	0.11	47.4%	1.4	0.22	28.5%	0.4	0.05	71.5%	1.4	0.21
2012	52.8%	0.8	0.10	47.2%	1.5	0.19	28.7%	0.3	0.05	71.3%	1.4	0.18
2013	52.0%	0.8	0.13	48.0%	1.4	0.22	26.8%	0.4	0.08	73.2%	1.4	0.21
2014	52.6%	0.9	0.13	47.4%	1.5	0.22	28.3%	0.3	0.07	71.7%	1.5	0.21
2015	52.7%	0.9	0.13	47.3%	1.6	0.24	28.7%	0.3	0.08	71.3%	1.6	0.22
2016	53.5%	0.9	0.12	46.2%	1.7	0.25	29.5%	0.3	0.05	70.5%	1.6	0.24
2017	52.8%	1.0	0.15	47.2%	1.7	0.28	29.4%	0.4	0.08	70.6%	1.7	0.26
2018	51.8%	0.9	0.14	48.2%	1.7	0.24	29.7%	0.4	0.08	70.3%	1.7	0.23
2019	50.2%	1.0	0.13	49.8%	1.8	0.26	28.4%	0.5	0.06	71.6%	1.8	0.25
Total	52.4%	0.9	0.13	47.6%	1.6	0.26	28.7%	0.4	0.07	71.3%	1.5	0.22
p-value[b]	<0.0001	<0.0001	0.1075	<0.0001	<0.0001	0.0017	<0.0001	0.0127	0.1238	<0.0001	<0.0001	0.0006
Difference[c]												
Absolute	−2.8	0.2	N.A.	2.8	0.5	0.04	−0.3	0.1	N.A.	0.3	0.2	0.03
Relative	−5.3	25.0	N.A.	6.0	38.5	18.2	−1.0	25.0	N.A.	0.4	38.5	13.6

AS Apgar score, *Inc.* incidence, *N.A.* not applicable.
[a]Incidence in the total cohort of 1,583,188 liveborn singletons per year; [b]*p*-value trend test; [c]Difference in 2019 compared to 2010 (both absolute and in percentage) if there was a significant trend.

worrisome because it had been reported in numerous studies that a low Apgar score is associated with adverse neonatal outcome [8–12, 21, 22]. However, studies reporting more recent data on low Apgar scores are currently lacking for the Netherlands. Overall, the rates of low Apgar scores that we found in this Dutch study are in line with the literature. We report that 1.20% of (near) term liveborn singletons had a 5-min Apgar score <7. A study from the United Kingdom found similar results: 1.54% of all liveborn infants had an Apgar score <7 [23]. The EURO-Peristat project, covering twenty-three countries or regions in Europe, reported rates between 0.3–2.4% for Apgar scores <7 for the period 2004 to 2010 [24]. For the more recent period 2015–2019, unfortunately, data on Apgar scores were not reported by the EURO-Peristat project [25].

A low 5-min Apgar score was chosen as main outcome measure of this study. The Apgar score has been widely embedded into clinical practice as an accepted method for standardised assessment of the neonate immediately after birth on the basis of heart rate, respiration, colour, muscle tone and reflex irritability [6]. There are numerous factors, apart from birth asphyxia, that can influence Apgar scores, including maternal medication or anaesthesia, gestational age, congenital malformations, trauma, and interobserver variability of the Apgar assessment [26, 27]. A low Apgar score alone is not sufficient to diagnose birth asphyxia [7]. However, in term infants without congenital malformations a low 5-min Apgar score most likely reflects birth asphyxia [8]. In this study, including only (near) term singletons without congenital malformations, we therefore used a low 5-min Apgar score as proxy for birth asphyxia.

A major limitation of this study is the lack of information on long-term outcomes. However, it has been shown in large population-based studies that low Apgar scores are well correlated with long-term outcomes in a dose-dependent manner across the entire range of Apgar scores. Prior studies showed a strong association between 5-min Apgar scores below 7 and cerebral palsy, epilepsy, special needs and cognitive impairment [8–12, 21, 22]. Selvaratnam et al. recently showed that there is an adverse relation between the 5-min Apgar score and poor developmental and educational outcomes. The least favourable outcomes were seen for infants with an Apgar score of 0 to 3, compared to those with an Apgar score of 10. Increasingly favourable outcomes were observed for infants with Apgar closer to 10, but Apgar scores of 7, 8 and 9 were also associated with poorer educational outcomes [28]. These observations seem to suggest that the current study, showing an increasing trend in low 5-min Apgar scores, is clinically relevant and needs further attention. Although the incidence of low 5-min Apgar scores (and our secondary outcomes) is low in the whole population, the relative increases we observed were high and in absolute numbers (with on average 160,000 singletons ≥35 weeks being born each year in the Netherlands) it's an increase of hundreds of infants at risk for these long term adverse neonatal outcomes.

Our observations suggest an increase in infants with a low Apgar score. The trends observed in low Apgar scores are supported by the increasing trends in NICU admissions and low umbilical artery pHs over the past decade. Because of our observational study design, we were not able to study causality and we can therefore only speculate about the reasons for these observations. The highest PARs were found for nulliparity, epidural analgesia, emergency caesarean section, instrumental vaginal delivery, prolonged second stage of labour, male sex and delivery in secondary care. Nulliparity and male sex are risk factors that cannot be changed, but the other variables can be influenced and are, therefore, of special interest for future research. A part of the increase in low 5-min Apgar scores might be explained by the decrease in fetal mortality after a pregnancy of ≥35 weeks, assuming that the surviving foetuses (who would otherwise have died) have an increased risk of poor Apgar scores.

It is remarkable that the intervention subgroups of instrumental vaginal delivery and emergency caesarean section show the highest increase in low 5-min Apgar scores. For Apgar score <7 we observed a relative increase of 52.4 and 63.3%, respectively, compared to an increase of 36.5% in the total cohort. For Apgar score <4, this was 33.3 and 30.1%, respectively, compared to 11.8% in the total cohort. Both interventions are generally performed when fetal distress is suspected. In our study, these interventions were less frequently performed over the last decade, but these intervention subgroups showed a relatively high increase in low Apgar scores. There might be two possible explanations for these observations. The first explanation is a better selection of infants with fetal distress over time due to improved fetal monitoring, with the interventions only being performed when there is a strong medical indication. However, a second potential explanation could be a more reluctant attitude towards obstetric interventions emergency caesarean section and instrumental vaginal delivery. This reluctance might cause a delay in time to intervention, and thus have a negative impact on the outcome of pregnancies resulting in more infants with lower Apgar scores. These two explanations, or a combination of both, and residual confounding may play a role, but the current study design, being an observational study cohort, is not designed to investigate causality.

The level of care was studied because of the unique Dutch maternity care system. As expected, in primary care, with only low-risk pregnancies, the overall risk of a low Apgar score was remarkably low. The increase in low Apgar scores (<7 and <4) was relatively high in secondary care compared to primary care. This could implicate that health care factors, implemented in secondary care (such as obstetric interventions), are the most relevant.

The main strength of our study is that we studied a large cohort of more than one million infants using a national registry that covers nearly all births (98%) in the Netherlands. An important limitation, besides the lack of the long-term outcome, is that data about therapeutic hypothermia were missing. As therapeutic hypothermia was not registered yet as item in the national registry, we could not study trends in the main treatment for severe birth asphyxia. We want to collect these data for future studies.

In this study, we did not focus on higher 5-min Apgar scores of 7, 8 and 9, but there is growing evidence that children with these Apgar scores are also more likely to have developmental vulnerability at population level, compared to children with Apgar score of 10 [28]. It would be interesting to analyse trends in these higher Apgar scores in future studies.

CONCLUSIONS

In the Netherlands, the risk of a 5-min Apgar score <7 and <4 increased significantly over the last decade. Neonatal mortality remained unchanged. The incidence of secondary caesarean section and instrumental delivery decreased over time, but in these obstetric intervention subgroups the highest relative increase in infants with a low Apgar score was observed.

DATA AVAILABILITY

The data that support the findings of this study are available from Perined but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are, however, available from the authors upon reasonable request and with permission of Perined.

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AUTHOR CONTRIBUTIONS

CT contributed to the design of the study, wrote initial draft of the manuscript, reviewed and revised the manuscript and approved the final manuscript as submitted. AR contributed to the design of the study, performed the analysis, reviewed and revised the manuscript and approved the final manuscript as submitted. WO, PB, FG, AR, LB, and JB contributed to the design of the study, reviewed and revised the manuscript and approved the final manuscript as submitted. All members of the N3 benchmarking group contributed to the data collection and approved the final manuscript as submitted.

COMPETING INTERESTS

The authors declare no competing interests.

ETHICAL APPROVAL

The committee for research and ethics of Perined approved the study protocol (Perined approval 21.13). The registry contains anonymous data and takes the European privacy policy into account. Medical ethical approval and individual informed consent for participation were not necessary.

ADDITIONAL INFORMATION

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