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Published in:
Acta Obstetricia et Gynecologica Scandinavica

DOI (link to publication from Publisher):
10.1111/aogs.14572

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Publication date:
2023

Document Version
Publisher's PDF, also known as Version of record

Link to publication from Aalborg University

Citation for published version (APA):
Andersson, C. B., Thellesen, L., Kesmodel, U. S., Petersen, J. P., & Johnsen, S. P. (2023). Implementation of universal umbilical cord pH analysis in Denmark. A national register-based study. *Acta Obstetricia et Gynecologica Scandinavica*, *102*(7), 854-864. https://doi.org/10.1111/aogs.14572

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Received: 27 November 2022 | Revised: 27 February 2023 | Accepted: 22 March 2023

DOI: 10.1111/aogs.14572

ORIGINAL RESEARCH ARTICLE

Implementation of universal umbilical cord pH analysis in Denmark. A national register-based study

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Abstract

Introduction: Umbilical cord blood gas analysis provides information about intrapartum hypoxia and is considered an important measure of quality in maternity care. Universal measurement of umbilical cord pH (UC-pH), as part of umbilical cord blood gas analysis, has been recommended in Denmark since 2009. The recommendation is that UC-pH is measured from the umbilical cord artery (pH_{UA}) and vein (pH_{UV}). The aim of this study was to evaluate the national implementation of universal measurement of UC-pH.

Material and methods: The study consisted of two parts. First, an evaluation of the implementation, that is, the proportion of births with measured UC-pH since the recommendation was introduced. Second, an evaluation of the cases in which UC-pH was missing. This analysis only involved births with gestational age ≥35 + 0 weeks.

Results: In the period 2009 to 2018 there were 560 889 singleton, live births with registered gestational age in Denmark. The proportion of births with measured pH_{UA} and pH_{UV} increased from 12.4% in 2009 to 82.8% in 2015 and then declined to 76.9% in 2018 ($p < 0.001$). When comparing the group with missing pH from one or both vessels to the group with both pH_{UA} and pH_{UV} we found lower occurrence of pregnancy and births complications in the first group, body mass index ≥35 (unadjusted RR: 0.89, 95% CI: 0.85–0.93), pregnancy induced medical conditions (RR: 0.86, 95% CI: 0.84–0.89), fetal distress during birth (RR: 0.77, 95% CI: 0.76–0.79), emergency cesarean section (RR: 0.80, 95% CI: 0.78–0.83) and serious births events (RR: 0.80, 95% CI: 0.74–0.86). In contrast, the occurrence of placental insufficiency (RR: 1.07, 95% CI: 1.03–1.11), small for gestational age (RR: 1.36, 95% CI: 1.30–1.43, for <2.3th percentile), hypothermia treatment (RR: 1.60, 95% CI: 1.21–2.14) and neonatal death (RR: 1.96, 95% CI: 1.40–2.74) were higher in the group without measured pH_{UA} and pH_{UV}.

Conclusions: The use of UC-pH measurement has increased markedly in Denmark since universal measurement was recommended in 2009. Missing UC-pH from one

Abbreviations: CI, confidence interval; DNPR, Danish National Patient Register; DNQDB, Danish National Quality Database for Births; pHUA, pH in umbilical cord artery; pHUV, pH in umbilical cord vein; RR, risk ratio; SGA, small for gestational age; UCBGA, umbilical cord blood gas analysis; UC-pH, umbilical cord pH.

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or both vessels was associated with less complicated pregnancies and with small for gestational age, hypothermia treatment and neonatal death.

KEYWORDS
birth, fetal monitoring, neonatology, obstetrics, umbilical cord pH

1 | INTRODUCTION

Identification of hypoxia from birth is important since hypoxia is associated with adverse outcomes immediately after birth and later in life.[1–4]

Umbilical cord blood gas analysis (UCBGA) provides crucial information that serves several purposes. Measurements performed immediately after birth reveal if acidosis is present, as a measure of fetal hypoxia, and may help the clinician decide on observation and treatment of the child. Furthermore, UCBGA adds substantial information about the pathogenesis of neurological disabilities in childhood (eg cerebral palsy) and is important for medicolegal reasons.[5–7]

UCBGA is an important measure of quality in maternity care and is valuable for educational reasons.[8] Previous studies have shown that universal UCBGA can reduce the proportion of hypoxic children over time, and a cost-effectiveness analysis showed that changing the recommendation from selective to universal UCBGA reduced costs, mainly through a reduction in admissions to special care nursery for children with birthweight >2499 g.[8,9]

In settings where universal measurement of UCBGA is recommended, mostly single hospitals or administrative regions, the proportion of births with UCBGA varies from 49% in Alabama, USA, to 81% in Victoria, Australia, with UCBGA still missing in a substantial proportion of births.[5,10,11]

Prior to 2009 policy in Danish maternity wards varied from no UCBGA to UCBGA in cases with suspicion of hypoxia. In 2009 the Danish Society of Obstetrics and Gynecology introduced a national recommendation of universal measurement of umbilical cord pH (UC-pH) as part of UCBGA. From 2012, the proportion of births with UC-pH became part of a national quality improvement initiative, and in 2014 the proportion was included as an indicator in the Danish National Quality Database for Births (DNQDB).[12,13] DNQDB results are reported monthly to the hospitals and published annually in a national, publicly accessible report.

With this study we aimed to evaluate the implementation of universal UC-pH measurement in Denmark and to examine characteristics of births, where UC-pH was not measured after the recommendation was implemented.

Key message

Experiences from implementation of universal umbilical cord pH in Denmark showed that it was possible to obtain umbilical cord pH in up to 83% of all births. Missing umbilical cord pH was associated with less complicated pregnancies and births, and with seriously ill children.

2 | MATERIAL AND METHODS

2.1 | Design

We performed a national study including all singleton hospital births in Denmark between 2009 and 2018 with a liveborn child with registered gestational age (GA).

2.2 | Setting

The birth rate in Denmark is approximately 60 000 per year, of which 97% take place in one of the 21 public hospitals or clinics, the rest being homebirths. Children born from singleton pregnancies constitute 98.5% and the proportion of stillbirths after 22 weeks of pregnancy is 0.3%.[14] In Denmark midwives are handling uncomplicated vaginal births, and obstetricians are only involved if complications arise. All pregnant women in Denmark are offered free and comprehensive antenatal and obstetric care.

2.3 | Data source

Data were retrieved from DNQDB and from the Danish National Patient Register (DNPR), which holds information on all somatic hospitalizations including births in Denmark since 1977.[15] Via a unique 10-digit civil registration number given to all residents in Denmark at birth or immigration, data were linked to The Danish Civil Registration System and The Register of Causes of Death and Statistics Denmark. This allowed linkage between mother and child and information on death, migrant status, income, and education. Reporting to the DNPR is mandatory.

In addition to information on procedures performed during birth and maternal and child outcomes (including UC-pH), DNQDB holds information on multiple obstetric background factors including maternal prepregnancy weight, height, smoking status, obstetric history, and relevant comorbidities, all registered at the beginning of pregnancy, and updated at the regular antenatal controls. GA is set by ultrasound scan in the early second trimester in 92% of cases, and for the remaining pregnancies GA is estimated by head circumference at a late second trimester scan.[16]

2.4 | UC-pH measurements

Blood samples from the umbilical cord artery and vein are collected by a midwife within the first minute after birth in case the cord is not

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clamped, and within 30 min if the cord is clamped. Blood is sampled in preheparinized syringes. It is recommended that blood gasses are analyzed within 30 min from birth.[17]

Hypoxia is defined from pH-measurement(s) from the umbilical artery (pH_{UA}). To ensure that pH-measurement is from the artery, which is difficult to measure because the vessel is thin and has muscles in the wall, pH must be measured from both the umbilical cord artery and vein (pH_{UV}). The samples are considered to be from two different vessels when the difference in pH between the two measurements is ≥0.02 units.[10]

To avoid invalid information, pH values below 6.0 and over 8.0 were considered as missing data.

In the following we operate with three groups of UC-pH measurements: (1) pH_{UA} and pH_{UV} (two samples with a difference ≥0.02 units); (2) Missing pH; (3) Only 1 pH or two measurements with a difference <0.02 units, the latter being considered from the same vessel and therefore referred to as only 1 pH.

2.5 | Covariates

Maternal body mass index was calculated from prepregnancy weight and height, and maternal age defined as maternal age at delivery. Smoking was defined as smoking at any time during pregnancy, prepregnancy medical conditions included insulin dependent diabetes mellitus, hypertension, thyroid diseases, neurological diseases, polycystic ovary syndrome, respiratory diseases, and anemia. Pregnancy induced medical conditions included gestational diabetes mellitus, pregnancy induced hypertension, pre-eclampsia/eclampsia, and intrahepatic cholestasis of pregnancy. Placental insufficiency included signs of fetal distress before birth; Pathological signs on the cardiotocograph, intrauterine weight deviation (<2 SD), oligohydramnios or abnormal flow in the umbilical artery, middle cerebri arteries, ductus venosus or uterine arteries. Induction of labor included medical induction with prostaglandins or oxytocin or mechanical induction including artificial rupture of membranes or induction with a balloon catheter. Fetal distress included pathological signs on the cardiotocograph, meconium-stained amniotic fluid, pathological result of a scalp blood sampling, pathological doppler flow on an ultrasound scan or a significant event on ST analysis (STAN). Spontaneous vaginal birth was defined as births without cesarean section or operative vaginal delivery. Serious birth events included shoulder dystocia, uterine rupture, placental abruption, cord prolapse or bleeding from vasa previa. A full list of International Statistical Classification of Diseases (ICD)10 codes is presented in Table S1.

Migrant status was categorized as immigrants and residents born in Denmark, income was defined as equivalized disposable yearly income, which is the total income of a household, after tax and other deductions, that is available for spending or saving, divided by the number of household members converted into equalized adults; household members are equalized or made equivalent by weighting each according to their age, using the modified Organization for Economic Co-operation and Development (OECD) equivalence scale.[18] Maternal education was categorized into three groups; <10, 10–12 or >12 years.

Small for gestational age (SGA) was presented as <10th percentile (1 SD), <2.3th percentile (2 SD) and <first percentile (3 SD). Apgar score was reported after one and 5 min, and neonatal outcomes comprised procedures used at the neonatal department: continuous positive airway pressure (CPAP), mechanical ventilation, treatment with inhaled nitric oxide (NO treatment) and/or hypothermia treatment. Neonatal death was defined as death within 28 days after birth.

2.6 | Statistical analyses

In the first part of the study, we evaluated the change in the proportion of births with measured pH_{UA} and pH_{UV} from 2009 to 2018. The proportion was calculated for all births as well as for selected pregnancy, birth and neonatal conditions/outcomes known to be associated with hypoxia from birth; placental insufficiency diagnosed in pregnancy, suspicion of fetal distress during birth, serious birth events, birthweight below the 2.3th percentile (2 SD), preterm birth, low Apgar score (0–3 after 1 min, 4–7 after 1 min and <7 after 5 min), hypothermia treatment and neonatal death. For the selected outcomes we compared the proportion of births with measured pH_{UA} and pH_{UV} in two periods: 2009–2010, at the time routine UC-pH was introduced in the national guideline, and 2014–2018 after the proportion of births with measured pH_{UA} and pH_{UV} had reached a plateau.

In a subanalysis we calculated the proportion of births with pH_{UA} and pH_{UV} or at least 1 pH according to GA (Figure 3).

Subsequently we analyzed the characteristics related to the woman, the birth, and the child in the group with missing or only 1 pH compared to the group with pH_{UA} and pH_{UV} to examine in which clinical situations UC-pH was measured as recommended (Table 1).

In a subanalysis we compared the group with missing UC-pH with the group with at least one UC-pH to examine in which clinical situations UC-pH measurements was performed (Table 2).

To avoid bias from low GA (in which the proportion of measured UC-pH is low) we included only births from GA ≥ 35 + 0 weeks in the second part of the study, and we included only births from 2014 to 2018 after the proportion of births with measured pH_{UA} and pH_{UV} had reached a plateau.

Binary logistic regression models were used to identify characteristics for missing/one UC-pH compared with measured pH_{UA} and pH_{UV} (reference) and for missing UC-pH compared to at least 1 pH (reference). The results were estimated as crude risks and risk ratios (RR) with 95% confidence intervals (CIs) (Table 1).

STATA release 15 was used for the statistical analyses (StataCorp. 2017. Stata Statistical Software: Release 15. StataCorp LLC).

2.7 | Ethics statement

This study was approved by the Danish Data Protection Agency (dnr number 2018-107, North Denmark Region) on June 19, 2018.

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TABLE 1 Maternal, birth and child characteristics of the group missing/one umbilical cord pH (UC-pH) and the group with pH in umbilical cord artery (pH_{UA}) and pH in umbilical cord vein (pH_{UV}).

	Missing or one UC-pH[a] *n* = 53 940 *n* (%)	PH_{UA} and PH_{UV} *n* = 217 633 *n* (%)	Missing or one UC-pH compared to pH_{UA} and pH_{UV} RR (95% CI)
Maternal characteristics			
Maternal age mean, (interquartile range)	29.8 (26–30)	29.8 (26–33)	
Maternal age ≥40 years	1577 (2.9)	6404 (2.9)	0.99 (0.94–1.05)
Maternal BMI mean, (interquartile range)	23.6 (20.6–26.3)	24.1 (20.8–26.6)	
BMI ≥ 35	2231 (4.1)	13 822 (6.4)	0.89 (0.85–0.93)
Nulliparas	23 081 (42.8)	94 960 (43.6)	0.98 (0.97–0.99)
Smoking	3710 (6.9)	14 828 (6.8)	1.01 (0.98–1.05)
Pregestational medical conditions[b]	5060 (9.4)	20 547 (9.4)	0.99 (0.96–1.02)
Pregnancy induced medical conditions[c]	4977 (9.2)	23 267 (10.7)	0.86 (0.84–0.89)
Placental insufficiency[d]	3104 (5.8)	11 745 (5.4)	1.07 (1.03–1.11)
Education			
<10 years	7286 (13.5)	28 579 (13.1)	
10–12 years	16 465 (30.5)	68 189 (31.3)	
>12 years	28 772 (53.3)	116 117 (53.4)	
Equivalized disposable income[e] (Euro)	31 310	31 166	
Mean, (interquartile range)	(21 468–37 621)	(21 786–37 494)	
Migrant status[f]			
Immigrant	9894 (18.8)	37 858 (17.5)	
Interventions in pregnancy			
Planned cesarean section	4570 (8.5)	20 712 (9.5)	0.89 (0.86–0.92)
Induction of labor	11 960 (22.2)	53 562 (24.6)	0.90 (0.89–0.92)
Birth			
Breech (vaginal delivery)	1773 (3.3)	6866 (3.2)	0.97 (0.88–1.08)
Suspected fetal distress[g]	7931 (14.7)	41 414 (19.0)	0.77 (0.76–0.79)
Spontaneous vaginal birth[h]	42 101 (78.1)	159 884 (73.5)	1.06 (1.06–1.07)
Emergency CS	4498 (8.3)	22 554 (10.4)	0.80 (0.78–0.83)
Operative vaginal delivery	3134 (5.8)	16 033 (7.4)	0.79 (0.76–0.82)
Serious births events[i]	813 (1.5)	4098 (1.9)	0.80 (0.74–0.86)
Child			
SGA < 10th percentile	7113 (13.2)	22 831 (10.5)	1.26 (1.23–1.29)
SGA < 2.3th percentile	2212 (4.1)	6561 (3.0)	1.36 (1.30–1.43)
SGA < 1st percentile	702 (1.3)	1877 (0.9)	1.51 (1.38–1.64)
Apgar 0–3/1	533 (1.0)	2203 (1.0)	0.98 (0.89–1.07)
Apgar 4–6/1	1233 (2.3)	6523 (3.0)	0.76 (0.72–0.81)
Apgar 0–6/5	378 (0.7)	1349 (0.6)	1.13 (1.00–1.27)
CPAP	2418 (4.5)	11 548 (5.3)	0.84 (0.81–0.88)
Mechanical ventilation	241 (0.5)	820 (0.4)	1.17 (1.02–1.35)
NO treatment	33 (0.1)	112 (0.1)	1.19 (0.81–1.75)

Continued

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TABLE 1 Continued

	Missing or one UC-pH[a] $n = 53\,940$ n (%)	PH_{UA} and PH_{UV} $n = 217\,633$ n (%)	Missing or one UC-pH compared to pH_{UA} and pH_{UV} RR (95% CI)
Hypothermia treatment	65 (0.1)	163 (0.1)	1.60 (1.21–2.14)
Neonatal death (<28 days)	51 (0.1)	105 (0.1)	1.96 (1.40–2.74)

Note: Included are births from gestational age 35 + 0 weeks in the period 2014–2018. Values are numbers (percentages) unless otherwise stated.

Abbreviations: CPAP, continuous positive airway pressure; NO treatment, treatment with inhaled nitric oxide.

[a]One UC-pH or two UC-pH measurements with a difference <0.02.

[b]Pregestational medical conditions: Insulin dependent diabetes mellitus, thyroid diseases, neurological diseases, respiratory diseases, anemia.

[c]Pregnancy induced medical conditions; Gestational diabetes, hypertension, preeclampsia/eclampsia, intrahepatic cholestasis of pregnancy.

[d]Placental insufficiency; Sign of fetal distress before births; Pathological signs on the cardiotocograph (CTG), intrauterine weight deviation (<−22%), oligohydramnios or abnormal flow in the umbilical artery, the middle cerebral artery, ductus venosus or uterine artery.

[e]The equivalized disposable yearly income is the total income of a household, after tax and other deductions, that is available for spending or saving, divided by the number of household members converted into equalized adults; household members are equalized or made equivalent by weighting each according to their age, using the modified OECD equivalence scale.

[f]Migrant status; Immigrants: All patients not born in Denmark. Information on migrant status was present in 267 749/271 570 cases.

[g]Suspected fetal distress: Pathological signs on the cardiotocograph (CTG), meconium-stained amnion fluid, pathological result of a scalp blood sampling, pathological doppler flow on a UL scan or a significant event on ST analysis (STAN). Registrations are used when it leads to an intervention.

[h]Spontaneous vaginal birth: No emergency CS, planned CS or operative vaginal delivery.

[i]Serious births events: Shoulder dystocia, uterine rupture, abruptio placentae, cord prolapse or vasa previa.

According to Danish law, register-based studies do not require ethical approval or patient consent.

3 | RESULTS

In the period from 2009 to 2018 there were 560 891 live singleton hospital births with registered GA in Denmark. Figure 1 presents the proportion of births with missing UC-pH, one UC-pH/two UC-pH measurements with a difference <0.02 units, pH_{UA} and pH_{UV}, and at least one UC-pH among all included births from 2009 to 2018. The proportion of births with measured pH_{UA} and pH_{UV} increased from 12.4% (95% CI: 12.2–12.7) in 2009 to 82.8% (95% CI: 82.5–83.1) in 2015 and hereafter declined to 76.9% (95% CI: 76.6–77.3) in 2018 ($p < 0.001$). The proportion of births with at least one UC-pH reached 95.9% (95% CI: 95.8–96.1) in 2015 but declined to 95% (95% CI: 94.8–95.1) in 2018 ($p < 0.001$).

The same pattern was seen for all subgroups except for extremely preterm births and in cases of neonatal death (Figure 2). In these cases, the proportion of births with measured pH_{UA} and pH_{UV} also increased but only to a level of 46.6% and 40.9% respectively.

In the subanalysis examining the proportion of births with measured pH_{UA} and pH_{UV} according to GA we found that the proportion of births with pH_{UA} and pH_{UV} increased from 41.9% (95% CI: 32.9–51.5) in GA 24 weeks to 79.4% (95% CI: 76.8–81.8) in GA 33 weeks, and after GA 33 weeks the proportion was nearly stable. The proportion of births with at least one UC-pH reached 80% already from GA 25 weeks (Figure 3).

Table 1 presents the maternal, birth and child characteristics of the group with missing or only one UC-pH and the group with pH_{UA} and pH_{UV} and a comparison with pH_{UA} and pH_{UV} as reference. In general, we found the differences between the two groups to be small.

There was no difference in the occurrence of preexisting medical conditions in the two groups (RR: 0.99, 95% CI: 0.96–1.02), but the occurrence of body mass index ≥35 was lower in the group with missing UC-pH/only one UC-pH (RR: 0.89, 95% CI: 0.85–0.93).

Compared to the group with pH_{UA} and pH_{UV} women in the group with missing UC-pH/only one UC-pH had a lower occurrence of nulliparity (RR: 0.98, 95% CI: 0.97–0.99) and pregnancy induced medical conditions (RR: 0.86, 95% CI: 0.84–0.89) but the occurrence of placental insufficiency was higher (RR: 1.07, 95% CI: 1.03–1.11). Regarding the births, there was a lower occurrence of induction of labor (RR: 0.90, 95% CI: 0.89–0.92), planned cesarean section (RR: 0.89, 95% CI: 0.86–0.92), suspicion of fetal distress (RR: 0.77, 95% CI: 0.76–0.79), vacuum or forceps delivery (RR:0.79, 95% CI: 0.76–0.82), emergency cesarean section (RR: 0.80, 95% CI: 0.78–0.83) and serious births events (RR: 0.80, 95% CI: 0.74–0.86) in the group with missing/only one UC-pH.

In the group with missing/only one UC-pH, fewer children had low Apgar after 1 min (RR: 0.76, 95% CI: 0.72–0.81 for Apgar 4-6) or/and were treated with continuous positive airway pressure (CPAP) (RR: 0.84, 95% CI: 0.81–0.88). In contrast, seriously ill children in need of hypothermia treatment and neonatal death were overrepresented in the group with missing/one UC-pH (RR: 1.60, 95% CI: 1.21–2.14 and RR: 1.96, 95% CI: 1.40–2.74), as well were children who were SGA defined as <10th percentile, (RR: 1.26, 95% CI: 1.23–1.29), <2.3th percentile (RR: 1.36, 95% CI: 1.30–1.43) and <1st percentile (RR: 1.51, 95% CI: 1.38–1.64).

There were no notable differences in socioeconomic status measured as income and education, and there was no difference between women born in Denmark or immigrants (Table 1).

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TABLE 2 Maternal, birth and child characteristics in the group with missing umbilical cord pH (UC-pH) and in the group with at least one UC-pH.

	Missing UC-pH *n* = 13 422 *n* (%)	One UC-pH[a] or pH_{UA} and pH_{UV} *n* = 258 148 *n* (%)	Missing UC-pH compared to one UC-pH[a] or pH_{UA} and pH_{UV} RR (95% CI)
Maternal characteristics			
Maternal age mean, (interquartile range)	30.0 (27–33)	29.8 (26–33)	
Maternal age ≥40 years	429 (3.2)	7552 (2.9)	1.09 (0.99–1.20)
Maternal BMI mean, (interquartile range)	23.1 (20.5–26.0)	24.0 (20.8–26.6)	
BMI ≥ 35	530 (4.0)	11 798 (4.6)	0.86 (0.79–0.94)
Nulliparas	5402 (40.3)	112 639 (43.6)	0.92 (0.90–0.94)
Smoking	864 (6.4)	17 674 (6.9)	0.94 (0.88–1.00)
Pregestational medical conditions[b]	1271 (9.5)	24 336 (9.4)	1.00 (0.95–1.06)
Pregnancy induced medical conditions[c]	1146 (8.5)	27 098 (10.5)	0.81 (0.77–0.86)
Placental insufficiency[d]	643 (4.8)	14 206 (5.5)	0.87 (0.81–0.94)
Education			
<10 years	1782 (13.3)	34 983 (13.2)	
10–12 years	3969 (29.6)	80 685 (31.3)	
>12 years	7198 (53.6)	137 641 (53.3)	
Equivalized disposable income[e] (Euro) Mean, (interquartile range)	31 286 (21 485–37 965)	31 187 (21 758–37 497)	
Migrant status[f]			
Immigrant	2319 (18.0)	45 162 (17.8)	
Interventions in pregnancy			
Planned cesarean section	1222 (9.1)	24 060 (9.3)	0.98 (0.92–1.03)
Induction of labor	2630 (19.6)	62 892 (24.4)	0.80 (0.78–0.83)
Birth			
Breech (vaginal delivery)	445 (3.3)	8194 (3.2)	0.96 (0.79–1.16)
Suspected fetal distress[g]	1650 (12.3)	47 695 (18.5)	0.67 (0.64–0.70)
Spontaneous vaginal birth[h]	10 359 (77.2)	101 626 (74.2)	1.04 (1.03–1.05)
Emergency CS	1203 (9.0)	25 849 (10.0)	0.90 (0.85–0.95)
Operative vaginal delivery	732 (5.5)	18 435 (7.1)	0.76 (0.71–0.82)
Serious births events[i]	215 (1.6)	4696 (1.8)	0.88 (0.77–1.01)
Child			
SGA < 10th percentile	1444 (10.8)	28 500 (11.0)	0.97 (0.93–1.02)
SGA < 2.3th percentile	467 (3.5)	8306 (3.2)	1.08 (0.99–1.19)
SGA < 1st percentile	154 (1.2)	2425 (0.9)	1.22 (1.04–1.44)
Apgar 0–3/1	131 (1.0)	2605 (1.1)	0.97 (0.81–1.15)
Apgar 4–6/1	254 (1.8)	7511 (2.9)	0.63 (0.55–0.71)
Apgar 0-6/5	101 (0.8)	1626 (0.6)	1.19 (0.98–1.46)
CPAP	494 (3.7)	13 472 (5.2)	0.71 (0.65–0.77)
Mechanical ventilation	59 (0.4)	1011 (0.4)	1.12 (0.86–1.46)
No treatment	9 (0.1)	136 (0.1)	1.27 (0.65–2.50)

Continued

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TABLE 2 Continued

	Missing UC-pH $n = 13\,422$ n (%)	One UC-pH[a] or pH_{UA} and pH_{UV} $n = 258\,148$ n (%)	Missing UC-pH compared to one UC-pH[a] or pH_{UA} and pH_{UV} RR (95% CI)
Hypothermia treatment	20 (0.2)	208 (0.1)	1.85 (1.17–2.93)
Neonatal death (<28 days)	29 (0.2)	127 (0.1)	4.39 (2.94–6.57)

Note: Included are births from gestational age 35 + 0 weeks in the period 2014–2018. Values are numbers (percentages) unless otherwise stated.

Abbreviations: CPAP, continuous positive airway pressure; NO treatment, treatment with inhaled nitric oxide.

[a]One UC-pH or two UC-pH measurements with a difference <0.02.

[b]Pregestational medical conditions: Insulin dependent diabetes mellitus, thyroid diseases, neurological diseases, respiratory diseases, anemia.

[c]Pregnancy induced medical conditions; Gestational diabetes, hypertension, preeclampsia/eclampsia, intrahepatic cholestasis of pregnancy.

[d]Placental insufficiency; Sign of fetal distress before births; Pathological signs on the cardiotocograph (CTG), intrauterine weight deviation (<− 22%), oligohydramnios or abnormal flow in the umbilical artery, the middle cerebral artery, ductus venosus or the uterine artery.

[e]The equivalized disposable yearly income is the total income of a household, after tax and other deductions, that is available for spending or saving, divided by the number of household members converted into equalized adults; household members are equalized or made equivalent by weighting each according to their age, using the modified OECD equivalence scale.

[f]Migrant status; Immigrants: All patients not born in Denmark. Information on migrant status was present in 267 749/277 455 cases.

[g]Suspected fetal distress: Pathological signs on the cardiotocograph (CTG), meconium-stained amnion fluid, pathological result of a scalp blood sampling, pathological doppler flow on a UL scan or a significant event on ST analysis (STAN). Registrations are used when it leads to an intervention.

[h]Spontaneous vaginal birth: No emergency CS, planned CS or operative vaginal delivery.

[i]Serious births events: Shoulder dystocia, uterine rupture, abruptio placentae, cord prolapse or vasa previa.

In the subanalysis, comparing the group with missing UC-pH with the group with at least one UC-pH (reference), we found results comparable to the above, but the occurrence of placental insufficiency was smaller in the group with missing UC-pH (RR: 0.87, 95% CI: 0.81–0.94) and there was only increased occurrence of SGA below the 1st percentile in the group with missing UC-pH.

4 | DISCUSSION

The proportion of births in Denmark with measured pH_{UA} and pH_{UV} increased markedly in the years after a national recommendation of universal UC-pH was issued in 2009. A plateau was reached at 82.8% in 2015, and subsequently the proportion decreased to 76.9%. For all the pregnancies, births, and neonatal conditions we investigated there was an increase in the proportion of births with pH_{UA} and pH_{UV}, but in extremely preterm births and in births ending in neonatal death, the proportion only reached 46.6% and 40.9%. Concerning GA, we found that the proportion of births with pH_{UA} and pH_{UV} equaled the proportion in term births if GA was above 33 weeks.

When comparing the group with missing/only one UC-pH to the group with pH_{UA} and pH_{UV}, among births from GA 35 + 0 weeks, we found that the first group consisted of women with fewer complications in pregnancy and birth, but we also found an overrepresentation of placental insufficiency, SGA < 10th percentile, hypothermia treatment and neonatal deaths. When comparing missing UC-pH with at least one UC-pH results were comparable, but the occurrence of placental insufficiency was smaller, and only SGA < 1st percentile was increased in the group with missing UC-pH.

The proportion of births with measured pH_{UA} and pH_{UV} was high in our study compared to previous studies, where reported proportions have been 50%–75%.[5,8,19] A possible explanation for this could be the central registration in Denmark, allowing monthly electronic feedback to departments and an annual publicly accessible national report. In the years 2012 to 2014 there was an increased focus on the area caused by an extensive national project aiming to reduce the proportion of births with hypoxia in Denmark.[20] In subsequent years the proportion of UC-pH from both umbilical artery and vein remained at 82% but declined to 77% in 2018 ($p < 0.001$). Several changes in the obstetric national landscape may have played a part in this. The organization in some departments has changed towards a separation into clinics handling uncomplicated births and departments handling complicated births, and some complications, such as severe post-partum hemorrhage, has increased, both changes with a plausible impact on pH-measurement. We do, however, suggest that a receding focus towards the end of the study period is the most likely cause. From Figure 1 it is seen that while the proportion of measured pH_{UA} and pH_{UV} slowly decreased after 2015, the proportion of births with only one sample or two samples from the same vessel, in the same period, increased from 13.3% to 18.5%. This indicates that the measuring UC-pH is well implemented, but either less effort is done in measuring correctly, or skills are decreasing.

There is an ongoing debate on whether UCBGA should be recommended on a selective or universal basis.[21] If the recommendation is selective UCBGA, the recommendation is often UCBGA in cases, where the child is born with low Apgar score or in births with a high risk of fetal hypoxia. Ahlberg et al. compared departments in Sweden with the two different approaches and found that the proportion of at least one UCBGA in high risk deliveries (preterm birth, breech birth, abnormal cardiotocography tracings during delivery and small- and large-for-gestational age infants) and in cases with low Apgar score was higher in settings with a universal approach.[6] This corresponds to the increase in measured UC-pH in births complicated with uterine rupture, bleeding from vasa previa,

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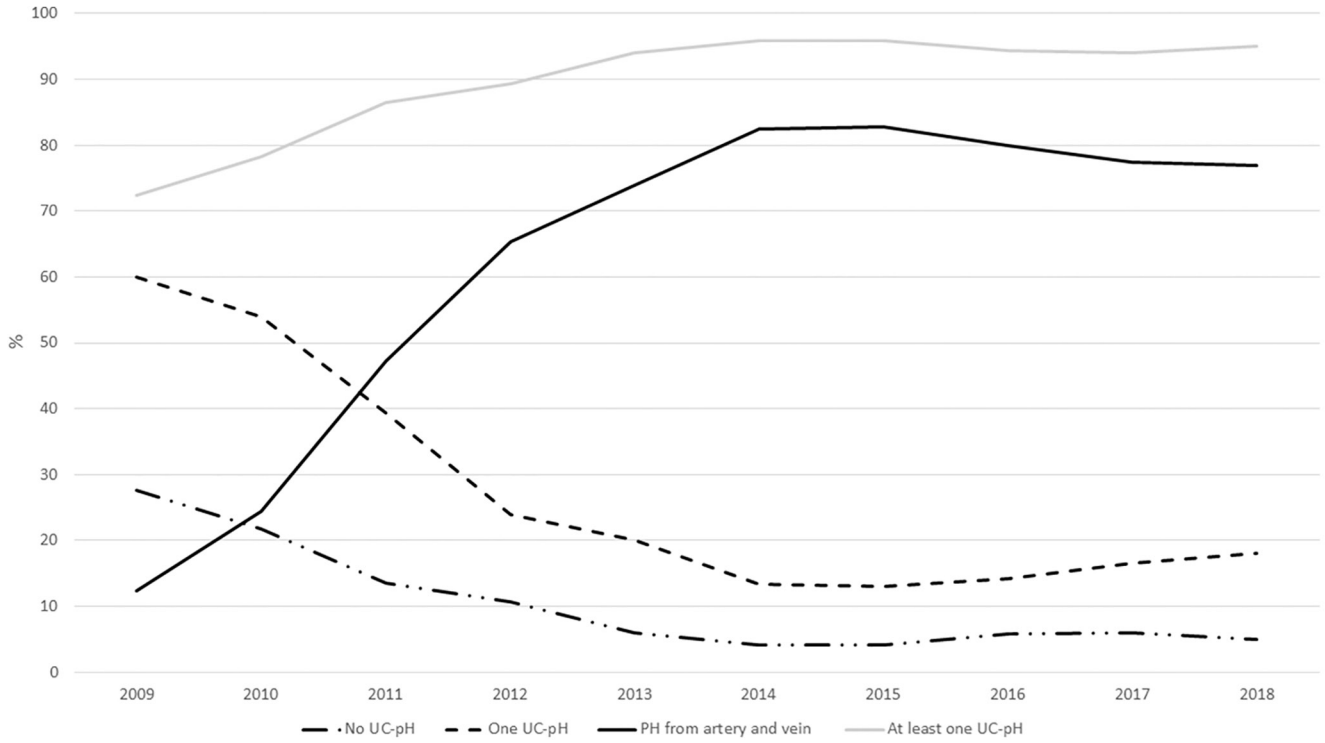

FIGURE 1 Development in the proportion of births with pH in umbilical cord artery (pH_{UA}) and pH in umbilical cord vein (pH_{UV}), one umbilical cord (UC-), at least one UC-pH and missing UC-pH in the period from 2009 to 2018 in the total study population.

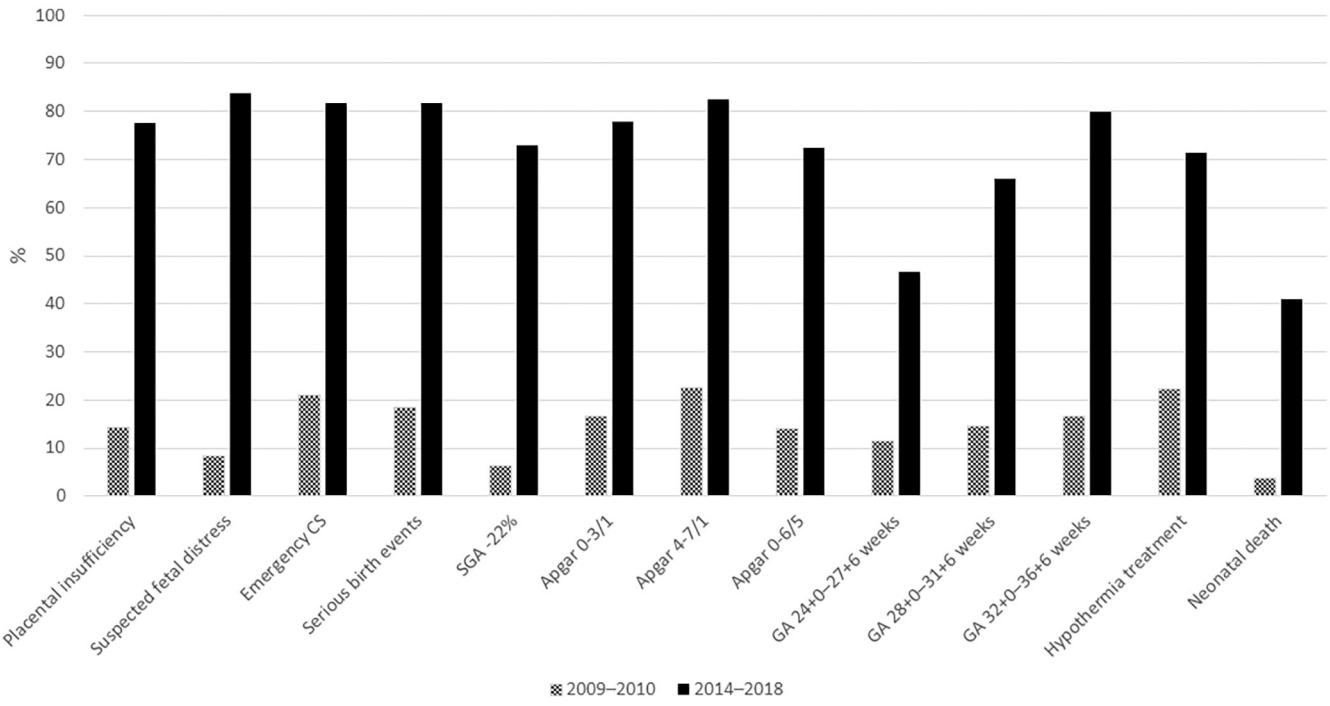

FIGURE 2 Proportion of births with pH in umbilical cord artery (pH_{UA}) and pH in umbilical cord vein (pH_{UV}) in selected maternal, pregnancy and neonatal conditions. 2009–2010 compared to 2014–2018. CS, cesarean section; GA, gestational age; SGA, small for gestational age.

cord prolapse or placental abruption, and in cases with low Apgar score seen in Denmark after the implementation of universal UC-pH measurement.

The reason that spontaneous vaginal births, without severe births complications, are overrepresented in the group with missing/one UC-pH among births after GA 35 + 0 weeks is unknown. Some

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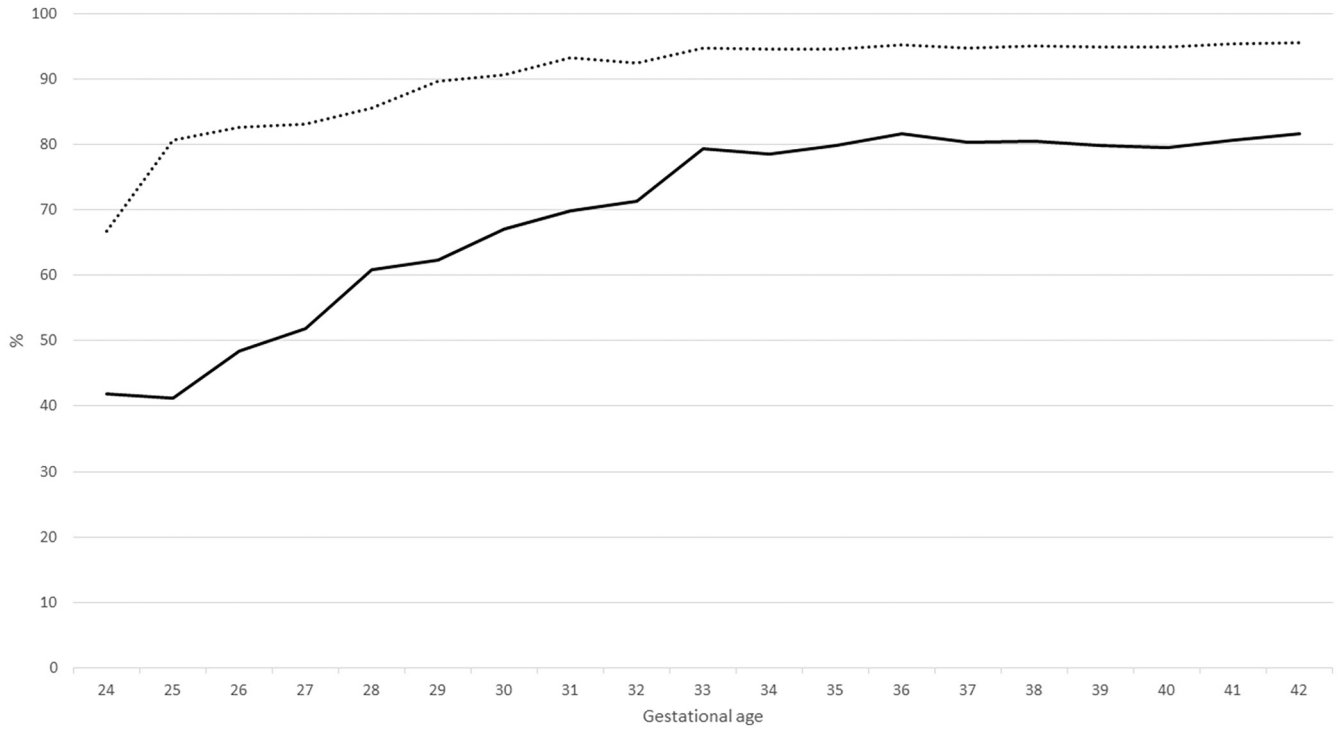

FIGURE 3 The proportion of births with at least one umbilical cord pH (UC-pH) in gestational age 24 + 0–42 + 6 weeks. Included are births from 2014 to 2018. The black line illustrates the proportion with umbilical cord artery (pHUA) and pH in umbilical cord vein (pHUV) and dotted line the proportion with at least on UC-pH.

of the births may be births in water, in which UC-pH measurements may not be performed at the same frequency. Also, midwives may have put less emphasis on collecting UC-pH, when they assumed risk of fetal hypoxia was low, however, these hypotheses cannot be assessed in the current dataset. The overrepresentation of births with severe child complications in the group with missing/one UC-pH can be caused by technical issues (eg thin umbilical cord), or emergency scenarios in which the samples were not prioritized.

Central registration of UC-pH in DNPR from all births in Denmark and the possibility to link mother and child via the national registration numbers were a prerequisite for this nationwide study. The same was the central registration of obstetric demographic factors, procedures performed during birth and maternal and neonatal outcomes. The size of the study population furthermore allowed us to include rare complications such as hypothermia treatment, neonatal death, and shoulder dystocia.

Even though the aim of this study was to evaluate the implementation of pH_{UA} and pH_{UV} in all births we also evaluated the group of births with at least one UC-pH. Since it is easier to sample the blood from the vein than from the artery, it is most likely that a single sample or two samples with a difference of <0.02 units are from the vein. In an everyday clinical setting, it is better to know one (venous) sample than no samples at all, since a high value in one vessel most probably rules out the risk of hypoxia (<1% if pH > 7.22).[19] In our study we found an overrepresentation of placental insufficiency and SGA among children with only one UC-pH. In these cases, the risk of hypoxia is increased, and it is especially important to know UC-pH, even if it is not possible to measure pH from both vessels.

In 2009, when the recommendation of universal UC-pH was introduced in a national guideline, and later when the proportion of measured pH_{UA} and pH_{UV} was introduced as a quality indicator in DNQDB, not all maternity wards had the equipment required to measure pCO_2, pO_2, lactate and base deficit. For that reason, it was decided only to register UC-pH in DNPR. Lacking registration on pCO_2 and pO_2 it was not possible to fully meet the criteria for validation of the paired UCBGA described by Westgate et al.[10] Preferably all parts of UCBGA should be registered, especially when used for scientific purposes, for example, to compare the outcome from hypoxia. However, arterial UC-pH has been shown to be the most important parameter in predicting adverse neonatal outcome, thus having an important value on its own.[5,22,23]

The validity of the study results depends on valid registration by the clinicians. The five regions in Denmark had different IT systems, and in some regions the UC-pH values were added manually in the register, and in general the UC-pH registrations have not been validated for scientific purposes. Some obstetric data from DNPR have been validated in previous studies. In general, validation studies show that registration of clinically significant conditions and interventions such as placenta previa and cesarean section are more valid than less significant events.[24,25] We do not suspect any systematic differences in registration for births with measured UC-pH and with no registered UC-pH.

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Experiences from implementation of universal UC-pH measurement in Denmark show that by introduction of a national guideline, central registration, and publication of the results from all departments as part of a national quality program it is possible to obtain pH_{UA} and pH_{UV} in up to 83% of all births. Results from this study may guide clinicians, administrations and quality organizations aiming to introduce universal UC-pH. Knowledge about timespan and in which cases it is difficult to collect umbilical blood samples is valuable in the implementation process. Further, our results may impact research on causes and consequences of intrapartum hypoxia.

5 | CONCLUSION

Implementation of a national guideline on universal UC-pH in Denmark combined with introduction of a national quality indicator measuring the proportion of births with measured UC-pH and reporting results to all Danish regions monthly, resulted in an increase in measured pH_{UA} and pH_{UV} from 12% to 77%–82% of all births in Denmark over a period of 5 years. Missing pH_{UA} and pH_{UV} was associated with less complicated pregnancies and births and with placental insufficiency, SGA, hypothermia treatment and neonatal death.

AUTHOR CONTRIBUTIONS

CBA, USK, JPP, LT and SPJ designed the study. CBA and SPJ acquired the data and CBA did the data management. CBA, USK, JPP, LT and SPJ analyzed and interpreted the data. The manuscript was drafted by CBA, with all other authors critically revising the manuscript. CBA is guarantor of the study. CBA and SPJ had full access to all the data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. CBA is responsible for the overall content as guarantor.

CONFLICT OF INTEREST STATEMENT

None.

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How to cite this article: Andersson CB, Thellesen L, Kesmodel US, Petersen JP, Johnsen SP. Implementation of universal umbilical cord pH analysis in Denmark. A national register-based study. *Acta Obstet Gynecol Scand*. 2023;102:854-864. doi:10.1111/aogs.14572

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