

# BMJ Open Elective caesarean: does delay in cord clamping for 30 s ensure sufficient iron stores at 4 months of age? A historical cohort control study

Ola Andersson,<sup>1,2</sup> Lena Hellström-Westas,<sup>1</sup> Magnus Domellöf<sup>3</sup>

**To cite:** Andersson O, Hellström-Westas L, Domellöf M. Elective caesarean: does delay in cord clamping for 30 s ensure sufficient iron stores at 4 months of age? A historical cohort control study. *BMJ Open* 2016;**6**:e012995. doi:10.1136/bmjopen-2016-012995

► Prepublication history for this paper is available online. To view these files please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2016-012995>).

Received 20 June 2016  
Revised 24 September 2016  
Accepted 27 September 2016



CrossMark

<sup>1</sup>Department of Women's and Children's Health, Uppsala University, Uppsala, Sweden

<sup>2</sup>Department of Research and Development, Region Halland, Sweden

<sup>3</sup>Department of Clinical Sciences, Pediatrics, Umeå University, Umeå, Sweden

## Correspondence to

Dr Ola Andersson;  
olamedmac@gmail.com

## ABSTRACT

**Objective:** To compare iron stores in infants born after elective caesarean section (CS) and a 30 s delay of umbilical cord clamping with those born vaginally after early ( $\leq 10$  s) or delayed ( $\geq 180$  s) cord clamping.

**Design:** Prospective observational study with historical control.

**Setting:** Swedish county hospital.

**Population:** 64 infants born after elective CS were compared with a historical control of 166 early clamped and 168 delayed clamped after vaginal birth.

**Methods:** Blood and iron status were measured in blood samples collected at birth, 48–96 hours after birth, 4 and 12 months of age.

### Primary and secondary outcome measures:

Ferritin at 4 months of age was the primary outcome, second outcome measures were other indicators of iron status, and haemoglobin, at 4 and 12 months of age, as well as respiratory distress at 1 and 6 hours after birth.

**Results:** At 4 months infants born by elective CS had better iron status than those born vaginally subjected to early cord clamping, shown by higher adjusted mean difference of ferritin concentration (39  $\mu\text{g/L}$  (95% CI 10 to 60)) and mean cell volume (1.8 fL (95% CI 0.6 to 3.0)); and lower levels of transferrin receptors ( $-0.39$  mg/L (95% CI  $-0.69$  to  $-0.08$ )). No differences were seen between infants born after elective CS and delayed clamped vaginally born infants at 4 months. No differences were found between groups at 12 months of age.

**Conclusions:** Waiting to clamp the umbilical cord for 30 s after elective CS results in higher iron stores at 4 months of age compared with early cord clamping after vaginal birth, and seems to ensure iron status comparable with those achieved after 180 s delayed cord clamping after vaginal birth.

## INTRODUCTION

During the two last decades, evidence has accumulated regarding the benefits of waiting to clamp the umbilical cord for 2–3 min in term births.<sup>1–3</sup> Research has

## Strengths and limitations of this study

- This study compares iron status and haematological parameters up to 12 months in term infants after caesarean section (CS) with those born vaginally in relation to time to umbilical cord clamping.
- As an observational study with historical controls, results must be interpreted with caution because of potential bias from confounding.
- Nutrition and growth rate is expected to influence iron status at a later age, and we could control for these data.
- Only 35–40% of eligible pregnancies were included, why readiness to participate may be a confounding factor.
- A limitation for the conclusion is that cord clamping at 30 s at elective CS has not been compared with the usual practice of immediate cord clamping at elective CS.

mainly included vaginal births, omitting the global increase in elective caesarean section (CS) births.

Newborns subjected to delayed cord clamping (DCC) have higher haemoglobin (Hb) concentrations at 24–48 hours of life, and improved iron stores at 4–6 months.<sup>4</sup> After delivery, the newborn may receive up to 30 mL/kg blood from its placental circulation within 3–5 min,<sup>5 6</sup> contributing 75 mg iron which is equivalent to the infant's requirements for 3–4 months.

Iron deficiency is associated with impaired development,<sup>7</sup> and a main reason for adopting DCC has been to reduce iron deficiency. Recently, we have shown that DCC is associated with improved fine motor skills at 4 years of age.<sup>8</sup>

Less is known about the placental transfusion after prelabour elective CS. Elective CS can be performed for several reasons, including maternal, fetal and preferential factors.<sup>9</sup> The obstetrician has to weigh possible

benefits against possible disadvantages for the mother and child. To ensure that this decision is evidence based, research must contribute to a wider understanding of long-term consequences of these actions.

Pioneering physiological studies in the 1960s by Lind and colleagues showed that there was less placental transfusion after CS than after early cord clamping (ECC) following vaginal delivery.<sup>10</sup> More recently it was demonstrated that it is possible to harvest a higher volume of blood to stem cell banks after CS, also pointing to a reduced placenta to child transfusion after CS.<sup>11</sup>

CS was associated with anaemia at 12 and 58 months in two large longitudinal Chinese birth cohorts,<sup>12</sup> and a systematic review and meta-analysis found that CS compared with vaginal delivery was associated with a reduced placental transfusion and poor iron-related haematological indices in both cord and peripheral blood.<sup>13</sup>

We set out to prospectively study infants after elective CS, and follow them with the same protocol used for our cord clamping trial, using the vaginally born children as a historic control group. After delayed umbilical cord clamping at 180 s after vaginal births was introduced at the hospital, the board of obstetricians chose to perform cord clamping at 30 s after the delivery of the child in elective CS as a pragmatic attempt to allow for at least some placental blood transfusion.

Our hypothesis was that iron stores measured by ferritin at 4 months in children delivered by CS with cord clamping after 30 s would be lower than children born vaginally after DCC and thus similar to those born vaginally after ECC.

## METHOD

### Study design

This is a prospective observational study of children delivered by CS, using reference data from a study<sup>3</sup> of children randomised to DCC versus ECC after vaginal delivery.

### Setting

During the period of 6 June 2010 and 29 February 2012, women planned for elective CS were approached by the midwife, informed of the study and asked for consent, which was then signed by both parents. The historical control group consisted of 382 term newborns included in a randomised controlled trial between 16 April 2008 and 22 May 2009. The results from this trial have been reported in several papers.<sup>3 8 14</sup> The study was performed at the Hospital of Halland, Halmstad, Sweden.

### Participants

Pregnant women were eligible if they met the following criteria: non-smoking; normal pregnancy (no pre-eclampsia, no diabetes, no prolonged rupture of membranes or signs of infection) and term pregnancy (gestational age 37+0 to 41+6 weeks). The mother also

had to understand Swedish well enough to participate in the study. Exclusion criteria were serious congenital malformations, syndromes or other congenital diseases that could affect the outcome measures. For the elective CS group, an additional eligibility criterion was admission for a scheduled CS.

For the reference groups, eligibility also included being randomised to ECC or DCC in the performed randomised trial, having the intervention as allocated (per protocol), and being born vaginally.

After delivering the infant, the obstetrician placed the baby on the mother's thighs or beside her on the operation table and waited 30 s to clamp the umbilical cord, as advised by the present routine at the hospital. The timing at 30 s had been chosen by the board of obstetricians at the hospital before initiation of the current study. The timing of the clamping was noted. After clamping, blood samples for blood gas evaluation was taken routinely from the placental side of the umbilical vessels, and for the research project samples were taken for analysis of blood status; Hb and mean cell volume (MCV), and iron status; transferrin saturation (TS), soluble transferrin receptor (sTfR) and ferritin. Although ferritin is considered the most useful iron status marker, it is not sufficiently validated in children.<sup>15</sup> We chose to also include TS (lower in iron deficiency) and sTfR (higher in iron deficiency) as they, as well as Hb and MCV, provided additional information on the iron status of the infant.

As inflammation is known to influence iron status markers,<sup>16</sup> blood samples with C reactive protein (CRP)  $\geq 10$  mg/L were excluded from analysis.

Apgar scores, birth weight, length and head circumference were recorded according to routine. At 1 and 6 hours after birth, the midwife assessed the infant's well-being, and prospectively noted in the protocol whether there were any respiratory difficulties (grunting, presence of nostril flaring, respiratory frequency above 60 breaths/min and intercostal retractions) as well as if the baby had been breast fed.

At the time for routine venous blood sampling for metabolic screening at 2 days postpartum, additional blood samples were collected, that is, blood and iron status, and CRP.

At 3 months of age, a letter was sent to ask the parents to return with their child at 4 months for sampling of blood status, iron status and CRP. Again, at 11 months of age, an invitation to return at 12 months was sent. Venous blood samples for blood status, iron status and CRP were obtained.

Blood was collected in EDTA tubes (BD Vacutainer, Plymouth, UK) for blood status, and in serum separator tubes (BD Vacutainer) for iron status, and CRP.

Complete blood counts were analysed with an automated haematology analyser (Sysmex XE 2100, Sysmex, Kobe, Japan). Iron status indicators, and CRP were analysed with Cobas 6000 (Roche Diagnostics, Basel, Switzerland).

At 4 months, mothers reported their infant's feeding habits in a three-day diary and infant's length and weight was measured.

### Definitions

#### At 2 days

Anaemia: Hb<145 g/L,<sup>17</sup> polycythaemia: haematocrit >0.65.<sup>18</sup>

#### At 4 months

Anaemia: Hb<105 g/L,<sup>15</sup> iron deficiency: two indicators of iron status outside reference range (ferritin <20 µg/L,<sup>15</sup> MCV<73 fL,<sup>19</sup> TS<10%,<sup>20</sup> sTfR>7 mg/L<sup>3</sup>).

#### At 12 months

Anaemia: Hb<110 g/L, iron deficiency: two indicators of iron status outside reference range (ferritin <12 µg/L, MCV<70 fL, and TS<10%, sTfR>5.6 mg).<sup>21</sup>

### Outcomes

The primary outcome was infant serum ferritin at 4 months of age. Secondary outcomes included infant Hb and iron status (measured as serum ferritin, TS, sTfR, MCV) at 4 and 12 months of age, Apgar score at birth, and observations on breast feeding and respiratory symptoms at 1 and 6 hours after birth.

### Confounders

To be able to compare the included children with the historical reference group and to ensure that inclusion criteria were met, data on the mother (reported illness, medication, parity, weight, height, smoking habits, blood group Rhesus factor status and Hb concentration at the time of admission to antenatal care) were obtained from medical records. Nutrition and growth may affect iron status at 4 months; to adjust for this we controlled feeding habits at 4 months of age. As birth weight can be affected by the size of placental transfusion, we decided to only use length as a proxy for growth from birth to 4 and 12 months.

### Sample size

Our hypothesis was that the difference in ferritin at 4 months in children born by elective CS and DCC would be the same as that shown between DCC and ECC in a previous study,<sup>3</sup> that is a difference in log<sub>10</sub> ferritin between 2.07 and 1.90 with a SD of 0.34. To show this difference, a sample size of 63 was needed.

### Statistical analysis

For the group comparison of continuous variables, we used one-way analysis of variance (ANOVA) for variables with normal distribution and Bonferroni as post hoc test for pairwise comparisons. Categorical variables were compared between pairwise groups by using Fisher's exact test and across all three groups with Pearson  $\chi^2$  test. Ferritin concentration was log<sub>10</sub> transformed for

analysis. A  $p<0.05$  was considered significant. We used SPSS, V.22.0 (IBM, Armonk, New York, USA).

For adjusted analyses, analysis of covariance (ANCOVA) was used for test scores with Bonferroni post hoc test for pairwise comparisons. For adjustment variables, background variables (table 1) with a difference between groups with a  $p<0.1$  were chosen, resulting in mothers' age and gestational age.

### RESULTS

During the inclusion period, 505 infants were born after CS, 98 (19%) preterm and 34 (7%) post-term, figure 1. Among the term newborns (n=373), CS were classified as acute (174, 47%), elective with a medical reason (145, 39%), and elective with no medical reason (54, 14%). From the 199 elective term CS, 26 could not be included due to maternal disease (diabetes, n=12), pre-eclampsia, n=6, intrauterine growth restriction (IUGR), n=6 and combination of pre-eclampsia and IUGR, n=2. Additionally, five women smoked at admission to antenatal care, leaving 168 possible for inclusion. One hundred and four declined participation, resulting in the inclusion of 64 deliveries with elective CS. We did not record the reason to decline out of respect for parents' privacy, but reluctance to return for repeated blood sampling was the most common objection. Furthermore, 166 ECC and 168 DCC controls were available for analysis, figure 1. We did compare data between the 64 included elective CS with the available data from the 104 who declined inclusion and no significant differences in maternal age, gestational age, infants' birth weight, length or head circumference was found, nor any differences in Apgar score or umbilical blood gases, pointing to our sample being representative for the whole cohort (results not shown).

At 4 months 59 (92.2%) infants in the elective CS group returned for blood sampling between 6 October 2010 and 28 June 2012. Corresponding blood samples had been obtained from 153 (92.2%) in the ECC group and from 156 (92.9%) in the DCC group between 8 August 2008 and 1 October 2009. At 12 months, 56 (87.5%) infants returned in the elective CS group between 31 May 2011 and 20 February 2013, while in the control group, 144 (86.7%) samples were available from the ECC and 149 (88.7%) from the DCC group (collected between 8 April 2009 and 21 May 2010; see figure 1).

For baseline characteristics, see table 1. The sex distribution was comparable between groups; 28 (44%) were males in the CS group, 83 (50%) in the ECC group and 73 (44%) in the DCC group,  $p=0.44$ . As expected, the gestational age was lower in the elective CS group than in the ECC group,  $-1.2$  weeks (95% CI  $-1.5$  to  $-0.8$ ,  $p<0.001$ ), and DCC group,  $-1.1$  weeks (95% CI  $-1.5$  to  $-0.8$ ,  $p<0.001$ ). The maternal age was also higher in the elective CS group than the in DCC group, 2.2 years (95% CI 0.5 to 3.9,  $p=0.005$ ).

**Table 1** Maternal and birth characteristics and early outcomes after elective CS or vaginal birth after early ( $\leq 10$  s) or delayed ( $\geq 180$  s) umbilical cord clamping\*

Maternal characteristics	CS	n	ECC	n	DCC	n	p Value‡	Mean difference (95% CI)†			
								CS vs ECC	p Value§	CS vs DCC	p Value§
At admission to antenatal care											
Weight, kg	69.3 (14.8)	56	66.4 (12.0)	164	67.3 (12.2)	168	0.32				
Length, cm	166.8 (6.6)	56	167.9 (6.4)	147	167.5 (5.1)	141	0.44				
Body mass index, kg/m <sup>2</sup>	24.8 (4.3)	56	23.6 (3.8)	146	23.9 (3.6)	141	0.16				
Haemoglobin, g/L	126.4 (10.1)	57	128.0 (8.8)	161	128.0 (10.8)	168	0.55				
At day of giving birth											
Age, years	33.0 (5.6)	64	31.7 (4.2)	166	30.8 (4.9)	168	0.006	1.4 (−0.3 to 3.0)	0.15	2.2 (0.5 to 3.9)	0.005
Parity (including study child)	1.9 (1.0)	64	1.8 (0.9)	166	1.8 (0.7)	168	0.88				
Early infant characteristics	CS	n	ECC	n	DCC	n	p Value‡	Adjusted† mean difference (95% CI)			
								CS vs ECC	p Value¶	CS vs DCC	p Value¶
Gestational age, weeks	38.9 (0.6)	64	40.0 (1.1)	166	40.0 (1.1)	168	<0.001	−1.2 (−1.5 to −0.8)	<0.001	−1.1 (−1.5 to −0.8)	<0.001
Apgar score at 1-min	9.0 (1.0)	64	8.8 (0.8)	166	9.0 (0.4)	168	0.008	0.2 (−0.1 to 0.4)	0.42	−0.1 (−0.3 to 0.2)	>0.99
Length, cm	50.4 (82.0)	64	50.7 (1.9)	165	50.9 (1.9)	168	0.23	0.7 (0.0 to 1.3)	0.046	0.4 (−0.2 to 1.1)	0.31
Birth weight, gram	3537 (567)	64	3523 (483)	166	3632 (464)	168	0.10	224 (51 to 398)	0.006	104 (−70 to 277)	0.45
Head circumference, cm	35.8 (1.5)	64	34.7 (1.3)	166	35.0 (1.37)	168	<0.001	1.7 (1.2 to 2.1)	<0.001	1.4 (0.9 to 1.9)	<0.001
pH in umbilical cord artery	7.29 (0.05)	57	7.27 (0.08)	159	7.26 (0.08)	144	0.04	0.02 (−0.01 to 0.05)	0.33	0.025 (−0.01 to 0.06)	0.16
Base deficit	2.0 (2.5)	56	4.4 (3.4)	158	4.8 (3.7)	143	<0.001	−2.0 (−3.4 to −0.6)	0.002	−2.4 (−3.8 to −1.0)	<0.001

\*Data are mean (SD) or mean difference (95% CI).

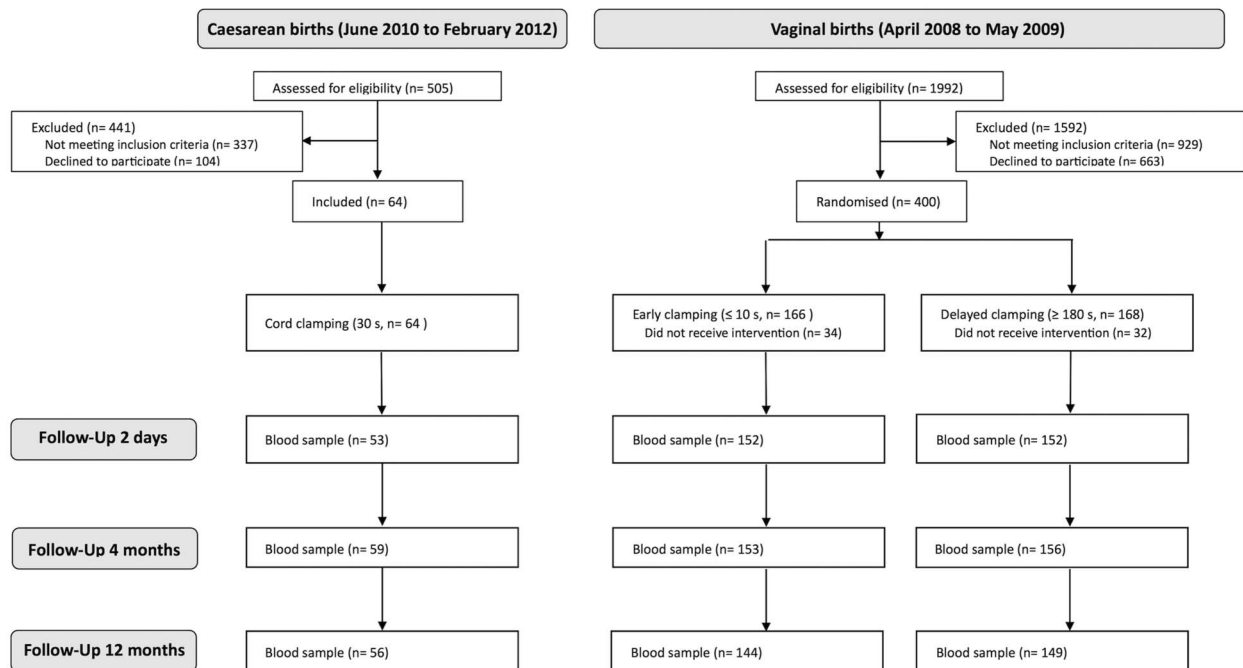
†Adjusted for maternal age and gestational age.

‡The p values were calculated using one-way ANOVA.

§The p values were calculated using one-way ANOVA with Bonferroni post hoc comparison.

¶The p values were calculated using analysis of covariance with Bonferroni post hoc comparison.

ANOVA, analysis of variance; CS, caesarean section; DCC, delayed cord clamping; ECC, early cord clamping.



**Figure 1** Trial profile. Flow diagram.

Apgar scores at 1 and 5 min were comparable between groups.

Hb was lower in umbilical cord blood in the elective CS group, when compared with the ECC group, adjusted mean difference (AMD)  $-13.5$  (95% CI  $-20.3$  to  $-6.6$ ,  $p < 0.001$ ) g/L and the DCC group, AMD  $-8.5$  g/L (95% CI  $-15.4$  to  $-1.5$ ,  $p = 0.01$ ). However, at 48–72 hours of age, the Hb level did not differ between groups. The Hb level after delivery increased more in the DCC (31.3 g/L [7.8],  $n = 121$ ) and CS (35.6 g/L [16.8],  $n = 38$ ) groups as compared with the ECC group (11.5 g/L [16.8],  $n = 121$ ),  $p < 0.001$ , indicating a larger placental transfusion.

At 4 months, differences in ferritin, MCV, and transferrin receptors (but not in TS) indicated better iron status in the CS group compared with the ECC group (table 2). The proportions of infants having abnormal values for iron status parameters did not differ between the CS group, and the ECC and DCC groups, respectively (table 3).

At 12 months, no differences between groups in iron status or blood status could be shown (tables 2 and 3).

### Auxiliary analysis

Postnatally, children born after CS were more likely to not having been breast fed 1 hour after delivery as compared with the ECC, relative risk (RR) 2.1 (95% CI 1.5 to 2.9) and DCC groups, RR 2.5 (95% CI 1.7 to 3.5). The CS group had a higher risk of respiratory distress at 6 hours after birth compared with ECC, RR 3.4 (95% CI 1.1 to 10.5) and DCC, RR 4.4 (95% CI 1.4 to 14.9). Respiratory distress at 1-hour of age and breast feeding frequency at 6 hours did not differ between groups.

At 4 months, exclusive breast feeding was equally prevalent among the groups, CS 27 (47%), ECC 78

(52%) and DCC 84 (56%),  $p = 0.45$ . Exclusive breast feeding correlated positively to the infants' serum ferritin level ( $r = 0.144$ ,  $p = 0.007$ ), but not to any other blood sample analysed at 4 months. If 'exclusive breast feeding' was included in the ANCOVA, results were not different for any variable in any significant way, except for TS, where the elective CS group attained a significantly higher value than ECC: AMD 2.0% (95% CI 0.0 to 4.0),  $p = 0.049$ .

The length and weight at 4 and 12 months of age were comparable across groups, also when adjusted for gestational age. Also weight and length gain from birth was comparable between groups at 4 and 12 months of age (data not shown). Adding 'length gain' into the adjusted model did not alter differences in any significant way.

## DISCUSSION

### Main findings

The findings in this prospective observational study indicate that in infants born after elective CS with umbilical cord clamping after 30 s, iron stores at 4 months are comparable to iron stores in vaginally born infants subjected to DCC ( $\geq 180$  s), and improved compared with vaginally born infants subjected to ECC ( $\leq 10$  s).

### Strengths and limitations

The main strength of the present study is to report data on iron status and haematological parameters in term infants after CS, as compared with vaginal deliveries and in relation to time to umbilical cord clamping. Haematological and iron status after different timings of umbilical cord clamping have previously been reported

**Table 2** Laboratory status at different time points after elective CS or vaginal birth after early ( $\leq 10$  s) or delayed ( $\geq 180$  s) umbilical cord clamping\*

	CS	n	ECC	n	DCC	n	p Value§	Adjusted† mean difference (95% CI)			
								CS vs ECC	p Value¶	CS vs DCC	p Value†
<b>Umbilical cord</b>											
Haemoglobin, g/L	147.9 (19.0)	52	163.3 (14.9)	144	158.0 (17.6)	144	<0.001	-13.5 (-20.3 to -6.6)	<0.001	-8.4 (-15.4 to -1.5)	0.01
Ferritin, µg/L‡	160 (8 to 853)	61	181 (12 to 1112)	163	183 (25 to 735)	164	0.38				
<b>48–72 hours after birth</b>											
Haemoglobin, g/L	179.9 (20.5)	40	174.9 (18.6)	104	188.5 (16.4)	107	<0.001	7.5 (-0.7 to 15.8)	0.09	-6.6 (-14.9 to 1.7)	0.17
<b>4 months</b>											
Haemoglobin, g/L	113.4 (7.5)	57	113.0 (7.1)	153	112.8 (7.5)	147	0.88				
MCV, fL	79.3 (2.6)	57	77.9 (3.1)	153	79.1 (3.1)	147	<0.001	1.8 (0.6 to 3.0)	0.001	0.5 (-0.7 to 1.7)	0.96
Ferritin, µg/L‡	103 (14 to 401)	55	80 (6 to 760)	153	117 (20 to 880)	149	<0.001	39 (10 to 60)	0.007	2 (-41 to 33)	>0.99
Transferrin saturation, %	17.1 (6.5)	56	15.8 (5.6)	153	18.2 (6.1)	148	0.002	2.1 (-0.3 to 4.5)	0.11	-0.3 (-2.7 to 2.1)	>0.99
Transferrin receptors, mg/L	3.70 (0.75)	55	4.00 (0.80)	153	3.72 (0.69)	149	0.002	-0.39 (-0.69 to -0.08)	0.007	-0.10 (-0.40 to 0.21)	>0.99
<b>12 months</b>											
Haemoglobin (g/L)	117.5 (8.0)	52	119.4 (8.2)	131	117.6 (7.8)	129	0.14				
MCV, fL	76.8 (3.6)	52	76.9 (3.3)	131	76.6 (3.3)	129	0.77				
Ferritin, µg/L‡	35 (8 to 107)	48	34 (8 to 135)	136	35 (10 to 281)	129	0.84				
Transferrin saturation, %	16.2 (7.1)	49	15.4 (7.3)	135	15.3 (6.0)	130	0.72				
Transferrin receptors, mg/L	4.40 (0.82)	49	4.48 (0.99)	136	4.37 (0.87)	130	0.61				

\*Data are mean (SD) or mean difference (95% CI).

‡Ferritin is presented as geometric mean (geometric SD).

†Adjusted for maternal age and gestational age.

§The p values were calculated using one-way ANOVA.

¶The p values were calculated using analysis of covariance with Bonferroni post hoc comparison.

ANOVA, analysis of variance; CS, caesarean section; DCC, delayed cord clamping; ECC, early cord clamping; MCV, mean cell volume.

**Table 3** Infants with anaemia or abnormal iron indices outside reference ranges at 4 and 12 months after elective CS or vaginal birth after early ( $\leq 10$  s) or delayed ( $\geq 180$  s) umbilical cord clamping\*

	CS	n	ECC	n	DCC	n	p Value	Absolute risk reduction (95% CI), %	
								CS vs ECC	CS vs DCC
<b>4 months</b>									
Anaemia (Hb<105 g/L)	6 (10.5%)	57	20 (13.1%)	153	20 (13.6%)	147	0.84		
Anaemia and iron deficiency	0 (0%)	52	2 (1.3%)	153	0 (0%)	148	0.27		
Iron deficiency (2 of the 4)†	0 (0%)	52	8 (5.2%)	153	1 (0.7%)	144	0.02	5.2 (-2.9 to 5.2)	0.7 (-1.8 to 0.7)
MCV<73 nm	0 (0%)	57	8 (5.2%)	153	3 (2.0%)	147	0.09	5.2 (-2.3 to 5.2)	2.0 (-3.0 to 2.0)
Ferritin <20 umol/L	1 (1.8%)	55	11 (7.2%)	153	0 (0%)	149	0.002	5.4 (-3.8 to 7.7)	-1.8 (-1.8 to 0.5)
Transferrin saturation <10%	6 (10.7%)	56	22 (14.4%)	153	8 (5.4%)	148	0.03	3.7 (-8.9 to 12.0)	-5.3 (-14.5 to 2.8)
Transferrin receptors <7 mg/L	0 (0%)	55	0 (0%)	153	0 (0%)	149	NA		
<b>12 months</b>									
Anaemia (Hb<110 g/L)	9 (17.3%)	52	16 (12.2%)	131	22 (17.1%)	129	0.49		
Anaemia and iron deficiency	1 (2.1%)	46	1 (0.8%)	130	0 (0%)	128	0.30		
Iron deficiency (2 of the 4)†	2 (4.3%)	47	7 (5.3%)	132	3 (2.3%)	128	0.464		
MCV<73 nm	0 (0%)	52	3 (2.3%)	131	3 (2.3%)	129	0.54		
Ferritin <20 umol/L	2 (4.2%)	46	3 (2.2%)	136	2 (1.6%)	129	0.58		
Transferrin saturation <10%	6 (12.2%)	49	25 (18.5%)	135	22 (16.9%)	130	0.60		
Transferrin receptors <5.92 mg/L	4 (8.2%)	45	10 (7.4%)	136	9 (6.9%)	130	0.96		

\*Data are numbers (%).

†Defined as having two or more of iron status indicators (low ferritin, low MCV, low transferrin saturation and/or high transferrin receptors) out of reference range.

CS, caesarean section; DCC, delayed cord clamping; ECC, early cord clamping; Hb, haemoglobin; MCV, mean cell volume; NA, not applicable.

in several studies.<sup>4</sup> Among available studies with 4 months or longer follow-up on iron stores, three excluded infants born after CS<sup>2 3 22</sup> while one included CS but did not separate results from vaginal birth.<sup>23</sup> From an ethical, and in many cases also medical point of view, it is impossible to randomise women to either elective CS or vaginal birth. As the trial is observational, and not randomised, the interpretation of the study's results is limited by the possibility of bias and confounding factors. These include in particular unidentified differences in baseline characteristics between groups, including prenatal maternal as well as perinatal and postnatal infant influences. Except for iron stores at birth, nutrition and growth rate is expected to influence iron status at a later age, and we could control for these data that did not alter the main outcomes. In all three groups, only 35–40% of eligible pregnancies were included. Data from the included EC cohort were not significantly different from those who declined consent, indicating similarity between included and 'declined inclusion' pregnancies. A limitation for the conclusion is that cord clamping at 30 s at elective CS has not been compared with the usual practice; immediate clamping at elective CS.

### Interpretation

Previous studies have implied less placental transfusion after CS. Consequently our findings are not in line with the relatively scarce literature on this subject. One explanation of our finding that CS rather improves iron stores compared with ECC at 4 months of age could be that the obstetrician actually waited 30 s to clamp the cord. The timing to umbilical cord clamping after CS has usually not been reported in other studies, but we presume it to have been performed immediately after delivery. Another potentially contributing factor to the improved iron stores is that infants born after elective CS have a lower blood pressure due to less circulating adenosine and catecholamines,<sup>24 25</sup> facilitating a faster blood transfusion from the placenta. Unfortunately, we did not record the time for the first breath/cry, but earlier reports indicate that most newborns had started breathing before the cord was clamped in the CS group.<sup>26</sup>

Hb in the umbilical cord blood sample was significantly lower after elective CS compared with ECC and DCC, a finding in coherence with a recent systematic review and meta-analysis.<sup>13</sup> This finding suggests that umbilical cord Hb may not be a reliable marker of iron status in newborns, as the result may reflect both iron status and mode of delivery.

Our study supports the pragmatic approach to wait for 30 s before clamping after CS, as we could not demonstrate any negative effect on iron homeostasis compared with the vaginally born groups. Our findings might imply that whatever negative consequences on the child's health CS is associated with, waiting for 30 s to clamp the cord reduces those that could possibly be explained by a diminished placental blood transfusion.

### CONCLUSION

Erickson-Owens *et al*<sup>27</sup> have suggested umbilical cord milking as a possible procedure to facilitate the placental transfusion after CS in term infants. Our results suggest that the less invasive method of a 30 s DCC might be sufficient to ensure the placental transfusion after elective CS. Large observational studies, most preferably prospective with vaginally born matched controls, are indicated and warranted.

In summary, our study demonstrated that infants born after elective CS with cord clamping at 30 s had iron stores similar to those born vaginally with DCC and better than those born vaginally with ECC at 4 months of age.

**Twitter** Follow Ola Andersson at @olamedmac

**Acknowledgements** The authors thank RN Eivor Kjellberg and RN Monika Nygren for assistance in collecting the data, the staff at the Department of Obstetrics and Gynaecology at Hospital of Halland, Halmstad, and all mothers and infants who participated in the study.

**Contributors** OA, LH-W and MD planned the study. OA was responsible for staff training, study management and data collection with support from LH-W and MD. OA, LH-W and MD analysed the data. OA drafted the manuscript. All authors revised the manuscript and accepted the final version. OA is the guarantor.

**Funding** The study was supported by grants from the Regional Scientific Council of Halland; the Southern Healthcare Region's common funds for development and research; and H.R.H. Crown Princess Lovisa's Society for Childcare.

**Disclaimer** The funders had no involvement in study design; the collection, analysis and interpretation of data; neither in the writing of the report or in the decision to submit the manuscript for publication.

**Competing interests** None declared.

**Ethics approval** The original study was approved by the Regional Ethical Review Board at Lund University (2008/41), and the new cohort including elective CS was approved by an amendment (2009/344).

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data sharing statement** No additional data are available.

**Open Access** This is an Open Access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

### REFERENCES

1. Grajeda R, Pérez-Escamilla R, Dewey KG. Delayed clamping of the umbilical cord improves hematologic status of Guatemalan infants at 2 mo of age. *Am J Clin Nutr* 1997;65:425–31.
2. Chaparro CM, Neufeld LM, Tena Alavez G, *et al*. Effect of timing of umbilical cord clamping on iron status in Mexican infants: a randomised controlled trial. *Lancet* 2006;367:1997–2004.
3. Andersson O, Hellström-Westas L, Andersson D, *et al*. Effect of delayed versus early umbilical cord clamping on neonatal outcomes and iron status at 4 months: a randomised controlled trial. *BMJ* 2011;343:d7157.
4. McDonald SJ, Middleton P, Dowswell T, *et al*. Effect of timing of umbilical cord clamping of term infants on maternal and neonatal outcomes. *Cochrane Database Syst Rev* 2013;(7):CD004074.
5. Yao AC, Moinian M, Lind J. Distribution of blood between infant and placenta after birth. *Lancet* 1969;2:871–3.
6. Farrar D, Airey R, Law GR, *et al*. Measuring placental transfusion for term births: weighing babies with cord intact. *BJOG* 2011;118: 70–5.



7. Doom JR, Georgieff MK. Striking while the iron is hot: understanding the biological and neurodevelopmental effects of iron deficiency to optimize intervention in early childhood. *Curr Pediatr Rep* 2014;2:291–8.
8. Andersson O, Lindquist B, Lindgren M, *et al.* Effect of delayed cord clamping on neurodevelopment at 4 years of age: a randomized clinical trial. *JAMA Pediatr* 2015;169:631–8.
9. Branch DW, Silver RM. Managing the primary cesarean delivery rate. *Clin Obstet Gynecol* 2012;55:946–60.
10. Yao AC, Wist A, Lind J. The blood volume of the newborn infant delivered by caesarean section. *Acta Paediatr Scand* 1967;56:585–92.
11. Yamada T, Okamoto Y, Kasamatsu H, *et al.* Factors affecting the volume of umbilical cord blood collections. *Acta Obstet Gynecol Scand* 2000;79:830–3.
12. Li HT, Trasande L, Zhu LP, *et al.* Association of cesarean delivery with anemia in infants and children in 2 large longitudinal Chinese birth cohorts. *Am J Clin Nutr* 2015;101:523–9.
13. Zhou YB, Li HT, Zhu LP, *et al.* Impact of cesarean section on placental transfusion and iron-related hematological indices in term neonates: a systematic review and meta-analysis. *Placenta* 2014;35:1–8.
14. Andersson O, Hellström-Westas L, Andersson D, *et al.* Effects of delayed compared with early umbilical cord clamping on maternal postpartum hemorrhage and cord blood gas sampling: a randomized trial. *Acta Obstet Gynecol Scand* 2013;92:567–74.
15. Domellöf M, Braegger C, Campoy C, *et al.* Iron requirements of infants and toddlers. *J Pediatr Gastroenterol Nutr* 2014;58:119–29.
16. Baker RD, Greer FR. Diagnosis and prevention of iron deficiency and iron-deficiency anemia in infants and young children (0-3 years of age). *Pediatrics* 2010;126:1040–50.
17. Dallman PR. Red blood cell values at various ages. In: Rudolph A. ed. *Pediatrics*. 16th edn. New York: Appleton-Century-Crofts, 1977:1111.
18. Pappas A, Delaney-Black V. Differential diagnosis and management of polycythemia. *Pediatr Clin North Am* 2004;51:1063–86.
19. Domellöf M, Dewey KG, Lönnerdal B, *et al.* The diagnostic criteria for iron deficiency in infants should be re-evaluated. *J Nutr* 2002;132:3680–6.
20. Saarinen UM, Siimes MA. Developmental changes in red blood cell counts and indices of infants after exclusion of iron deficiency by laboratory criteria and continuous iron supplementation. *J Pediatr* 1978;92:412–16.
21. Dallman PR, Siimes MA, Stekel A. Iron deficiency in infancy and childhood. *Am J Clin Nutr* 1980;33:86–118.
22. van Rheeën P, de Moor L, Eschbach S, *et al.* Delayed cord clamping and haemoglobin levels in infancy: a randomised controlled trial in term babies. *Trop Med Int Health* 2007;12:603–16.
23. Ceriani Cernadas JM, Carroli G, Pellegrini L, *et al.* [The effect of early and delayed umbilical cord clamping on ferritin levels in term infants at six months of life: a randomized, controlled trial]. *Arch Argent Pediatr* 2010;108:201–8.
24. Irestedt L, Dahlin I, Hertzberg T, *et al.* Adenosine concentration in umbilical cord blood of newborn infants after vaginal delivery and cesarean section. *Pediatr Res* 1989;26:106–8.
25. Hagnevik K, Faxelius G, Irestedt L, *et al.* Catecholamine surge and metabolic adaptation in the newborn after vaginal delivery and cesarean section. *Acta Paediatr Scand* 1984;73:602–9.
26. te Pas AB, Davis PG, Hooper SB, *et al.* From liquid to air: breathing after birth. *J Pediatr* 2008;152:607–11.
27. Erickson-Owens DA, Mercer JS, Oh W. Umbilical cord milking in term infants delivered by cesarean section: a randomized controlled trial. *J Perinatol* 2012;32:580–4.