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Impact of maternal, antenatal and birth-associated factors on iron stores at birth: data from a prospective maternal-infant birth cohort

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Running title Factors associated with iron stores at birth

Conflict of interest No conflicts of interest to declare

Contributors EKM carried out data collection, database construction and data analysis. EKM and MK designed the study and drafted the manuscript. DMM is the overall principal investigator (PI) of the Cork BASELINE Birth Cohort Study and JOBH, LCK, ADI and MK are co-PIs and specialist leads. LCK is the PI of the SCOPE Ireland pregnancy cohort study. All authors reviewed and approved the final submission.

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ABSTRACT

Background/objectives Low serum ferritin concentrations at birth, which reflect neonatal iron stores, track through to early childhood and have been associated with poorer neurodevelopmental outcomes. We aimed to identify maternal, antenatal and birth-associated factors that are associated with iron stores at birth in a prospective maternal-infant birth cohort.

Subjects/methods In a population-based, longitudinal, prospective birth cohort in Ireland, 413 maternal-infant dyads with prospectively collected lifestyle and clinical data from 15 weeks' gestation had umbilical cord serum ferritin concentrations measured. Regression models were developed to identify independent factors associated with cord ferritin concentrations.

Results Median [IQR] cord ferritin concentrations were 185.7 [131.7, 385.5] µg/L and 8% (*n*=33) of infants had low iron stores (ferritin <76µg/L) at birth. Maternal obesity (BMI ≥30kg/m^2) at 15 weeks' gestation (adj. estimate [95% confidence interval (CI)]: -66.4 [-106.9, -25.9] µg/L, *P*<0.0001) and delivery by Caesarean section (-38.8 [-70.2, -7.4] µg/L, *P*=0.016) were inversely associated with cord ferritin concentrations. While maternal smoking at 15 weeks' gestation (adj. odds ratio [95% CI]: 2.9 [1.2, 7.0], *P*=0.020) and being born small-for-gestational age (3.4 [1.3, 8.9], *P*=0.012) were associated with an increased risk of low iron stores (ferritin <76µg/L) at birth.

Conclusions We have identified a number of potentially modifiable lifestyle factors that influence iron stores at birth, with the important role of overall maternal health and lifestyle during pregnancy highlighted. Public health policies targeting women of child-bearing age to improve nutrition and health outcomes should be prioritised for the health of the next generation.

Keywords iron stores, birth cohort, neonate, pregnancy, caesarean section, serum ferritin.

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INTRODUCTION

Adequate iron status is of particular importance during pregnancy and the first two years of a child's life to ensure healthy physical growth, immune function and development of the central nervous system.[1-3] Iron deficiency, with and without anaemia in early childhood has been consistently associated with lower cognitive, motor and behavioural outcomes, with the effects long-lasting.[4, 5] The interpretation of iron status in neonates can be difficult, due to the changes in iron metabolism that occur during the first weeks of life, as the infant goes from a relatively hypoxic intrauterine environment to an oxygen-rich atmosphere.[1] However, it is accepted that ferritin concentrations in umbilical cord blood serum reflect neonatal iron stores.[6, 7]

Iron stores in neonates have been shown to track through to early childhood; those with the lowest serum ferritin concentrations at birth continue to have significantly lower ferritin concentrations up to two years of age.[8, 9] Given the altered iron metabolism in the neonatal period, the thresholds used to define depleted iron stores and iron deficiency in young children are not applicable to neonates. However, studies have identified thresholds for use in the neonatal population, with suggested thresholds for depleted iron stores (<76 µg/L) and iron deficiency (<35 µg/L, estimated to reflect iron deficiency in the brain) associated with lower developmental test scores up to five years of age.[10, 11]

Iron stores at birth are affected by a multitude of factors associated with pregnancy and childbirth.[9, 12] However, few studies have explored multiple potential determinants in a single cohort and those that have are somewhat limited by study design and size. Therefore, the aim of the current study was to explore maternal, antenatal and birth-associated factors that influence iron stores at birth in an extensively-characterised sample of children from a prospective, longitudinal maternal-infant birth cohort in Ireland.

METHODS

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Study design and participants

Neonatal participants were recruited as part of the Cork BASELINE (Babies after SCOPE: Evaluating the Longitudinal Impact using Neurological and Nutritional Endpoints) Birth Cohort Study (www.clinicaltrials.gov NCT01498965) between March 2008 and January 2011 from women who had participated in the SCOPE (Screening for Pregnancy Endpoints) Ireland pregnancy study (http://www.anzctr.org.au ACTRN12607000551493). In SCOPE, 1 768 low risk, nulliparous women with a singleton pregnancy were recruited prior to 15 weeks' gestation from Cork University Maternity Hospital, as part of an international, multicentre study aimed at investigating early indicators of pregnancy complications. Specific exclusion criteria for the SCOPE study included women with a predetermined high risk of preeclampsia, small-for-gestational age (SGA) infants or spontaneous preterm birth because of underlying medical conditions as outlined in full previously.[13, 14]

Women in the SCOPE Ireland study provided written informed consent to the BASELINE Study for their infants (n = 1 537) at 15 weeks' gestation. The women and their infants were followed prospectively throughout pregnancy and through to five years of age, with a detailed methodology for the BASELINE Study outlined elsewhere.[15] Both the SCOPE and BASELINE studies were conducted in accordance with the Declaration of Helsinki and ethical approval was granted by the Clinical Research Ethics Committee of the Cork teaching hospitals (SCOPE: ECM5(10)05/02/2008, BASELINE: ECM 5(9) 01/07/2008).

Data collection

At 15 weeks' gestation, research midwives collected information on maternal socioeconomic status, occupation, education, relationship status and a complete medical history. Information on nutritional supplement use, recreational activity, cigarette and alcohol use were recorded for the three month period prior to conception and during the first trimester. Maternal

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anthropometric (height and weight) and clinical measurements (blood pressure, biological samples) were also collected. Prior to 20 weeks' gestation, maternal haemoglobin concentrations were measured and adjusted to account for cigarette smoking prior to/in early pregnancy in accordance with World Health Organisation (WHO) criteria.[16, 17] Information on pregnancy outcomes (including preeclampsia, gestational diabetes mellitus (GDM)) were collected prospectively throughout pregnancy and validated subsequently.

At birth, the mode of delivery was recorded and infants' birth weight, length and head circumference were measured and customised birth weight centiles for the population were developed. SGA was defined as a birth weight <10th customised centile adjusted for maternal height, booking weight, ethnicity, infant gestation and sex.[18] Data was entered at the time of appointments into an internet-based, secure, custom database developed by Medical Science Online (MedSciNet, Sweden) and monitored extensively to avoid illogical or erroneous data.

Biological samples

At birth, umbilical cord blood was collected from BASELINE Study participants, processed to serum within three hours of collection and stored at -80°C until use. Serum ferritin and high sensitivity C-reactive protein (CRP) were measured in the laboratory of the Cork Centre for Vitamin D and Nutrition Research, University College Cork, by immunoturbidimetric assay using the RX Monaco Clinical Chemistry Analyser (Randox Laboratories Ltd., Co. Antrim, UK). Participants with an elevated CRP (>5 mg/L) were excluded.[19]

Statistical analysis

Data were analysed using IBM SPSS® for Windows™ version 21 (IBM Corp., Armonk, NY, USA). Descriptive statistics were generated and normative distribution of the data was examined by skewness/kurtosis. Differences between groups were explored by Chi square (χ^2)

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tests and independent t-tests or non-parametric tests for continuous variables, depending on their distribution. Associations with cord ferritin concentrations were explored using Spearman correlations.

Multiple linear regression models were developed to explore potential factors associated with cord serum ferritin concentrations. Factors were first explored in unadjusted models and those with a P <0.1 were included in the final multivariate model (gender included as an *a priori* variable). The residuals of the final linear regression model were normally distributed and associations were expressed as adjusted mean differences and 95% confidence intervals (CI). In a secondary analysis, crude and adjusted logistic regression models were developed to explore factors associated with low iron stores at birth, indicated by cord ferritin concentrations <76 µg/L.[10] Unadjusted and final adjusted models were developed using the same protocol as for the linear regression analysis and associations were expressed as odds ratios (OR) and 95% CI. Analyses were performed on complete datasets only, without recoding or imputation of missing values.

Potential factors explored in the univariate analyses included maternal data collected at 15 weeks' gestation including education, employment, household income, relationship status, iron supplement use, haemoglobin concentrations, smoking status, alcohol consumption, physical activity levels, BMI, complications during pregnancy (preeclampsia, GDM), maternal age at delivery, mode of delivery and infant gender, gestational age, birth weight, length, head circumference and born SGA.

RESULTS

Participants

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Of the 1 537 infants initially recruited antenatally to the BASELINE Study, 1 436 participated in the first study assessment. At the time of this analysis, umbilical cord blood samples were available for 1 050 of these participants. As the measurement of ferritin concentrations in umbilical cord blood serum samples was not an *a priori* objective of the BASELINE Study and given the restrictions on the availability of samples, a subsample of the cohort (n = 413) was selected to have cord ferritin concentrations measured, if they had 1) a complete maternal-infant dataset and 2) matched blood samples collected at the 24-month study assessment (n = 706 with samples). The principal characteristics of those with cord ferritin concentrations measured and their comparison with the rest of the BASELINE cohort are presented in **Table 1**.

The distribution of cord serum ferritin concentrations in the 413 participants and in males and females separately is presented in **Table 2**. Using the previously suggested thresholds for neonatal ferritin concentrations, low iron stores (ferritin <76 µg/L[10]) were observed in 8% (n = 33) and iron deficiency (ferritin <35 µg/L[11]) was observed in 2% (n = 9) of participants.

Maternal and antenatal factors

Maternal BMI at 15 weeks' gestation was inversely associated with cord ferritin concentrations (Spearman r = -0.157, P <0.0001). Given the previously reported health consequences of maternal obesity in pregnancy,[20] we looked specifically at the association between a maternal BMI ≥30 kg/m^2 at 15 weeks' gestation and cord ferritin. Infants of obese mothers had lower median [interquartile range (IQR)] cord ferritin concentrations (137.8 [110.9, 178.3] vs. 198.3 [137.1, 390.0] µg/L, P <0.0001) and a higher proportion of them had concentrations <76 µg/L (16.0 vs. 6.9%, P = 0.05) than infants whose mothers were not obese. Infants born to mothers who were smoking at 15 weeks' gestation had lower cord ferritin than non-smokers (160.2 [115.5, 360.8] vs. 187.8 [135.3, 386.7] µg/L, P = 0.08), while a higher proportion of infants

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born to smoking mothers had concentrations <76 µg/L (17.0 vs. 6.7%, *P* = 0.022). Neither maternal alcohol consumption nor physical activity levels at 15 week's gestation were associated with cord ferritin concentrations.

Preeclampsia (systolic blood pressure ≥140 mm Hg or diastolic ≥90 mm Hg, or both, after 20 weeks' gestation, with either proteinuria or any multisystem complication) was diagnosed in 3.4% (*n* = 14) of mothers. Infants of mothers with preeclampsia had lower ferritin concentrations at birth than those without preeclampsia (141.8 [93.2, 234.2] vs. 187.5 [133.4, 386.5] µg/L, *P* = 0.052). Sixteen (3.9%) mothers were diagnosed with GDM; infants born to mothers with GDM had median [IQR] ferritin concentrations of 144.5 [92.1, 350.5] µg/L compared to 187.2 [133.3, 386.0] µg/L in the rest of the sample (*P* = 0.259).

The median [IQR] haemoglobin concentration of mothers in early pregnancy was 129.0 [124.0, 136.0] g/L and 1.7% (*n* = 7) had concentrations <110 g/L, indicative of anaemia.[19] There was no association between maternal haemoglobin and cord ferritin concentrations. Three-quarters (75.6%) of mothers took iron-containing supplements during their pregnancy, although the dose and duration of use of these supplements was not recorded. Iron supplement users had cord ferritin concentrations of 193.3 [137.7, 386.8] µg/L and non-users had concentrations of 174.8 [117.9, 397.5] µg/L (*P* = 0.146).

Birth-associated factors

Infants delivered vaginally had higher cord ferritin than those delivered by Caesarean section (193.1 [136.1, 394.8] vs. 162.6 [111.2, 334.5] µg/L, *P* = 0.005). The prevalence of concentrations <76 µg/L among infants delivered vaginally was about half that of infants delivered by Caesarean section (6.5 vs. 12.6%, *P* = 0.089). There was no difference in cord ferritin between infants delivered by elective (*n* = 28) or emergency Caesarean section.

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Ferritin concentrations were lower in preterm infants (159.7 [110.5, 237.2] µg/L) than term infants (186.5 [132.9, 385.7] µg/L, $P = 0.511$), although only 15 infants in this study were born premature. Neither weight, length or head circumference at birth was associated with cord ferritin. SGA and non-SGA infants had similar cord ferritin concentrations (166.8 [101.9, 372.9] vs. 188.5 [133.2, 386.7] µg/L, $P = 0.166$), however, more SGA infants had cord ferritin <76 µg/L (20.0 vs. 6.9%, $P = 0.016$) and <35 µg/L (14.3 vs. 1.1%, $P < 0.0001$), respectively.

Factors associated with cord serum ferritin concentrations

Factors associated with cord ferritin concentrations included in the final linear regression model, expressed as the unadjusted and adjusted mean difference in µg/L (95% CI) are presented in **Table 3**. Maternal BMI at 15 weeks' gestation (kg/m^2) was inversely associated with cord ferritin concentrations (-5.1 [-8.4, -1.7] µg/L, $P = 0.003$), with the effect of maternal obesity most notable. Delivery by Caesarean section was associated with decreased cord ferritin concentrations, while the adverse effect of maternal smoking at 15 weeks' gestation was attenuated in the final adjusted model. In a separate model, maternal obesity combined with delivery by Caesarean section ($n = 17$) had a pronounced negative influence on cord ferritin (-81.5 [-147.2, -15.8] µg/L, $P = 0.015$).

Factors associated with the risk of low iron stores at birth (ferritin <76 µg/L) included in the final logistic regression model are depicted in **Table 4**, displayed as both unadjusted and adjusted OR and 95% CI. From the final adjusted model, infants born SGA were three times more likely to have low iron stores at birth in comparison to non-SGA infants, while maternal smoking during pregnancy and delivery by Caesarean section were also associated with an increased risk of low iron stores at birth. The adverse effect of maternal obesity was attenuated in the final adjusted model.

DISCUSSION

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188 This study has explored multiple potential factors that are associated with iron stores at birth
189 in a large, prospective maternal-infant birth cohort. Delivery by Caesarean section, being born
190 SGA and an unhealthy maternal lifestyle, characterised by smoking and obesity during
191 pregnancy, were all associated with significantly lower ferritin concentrations and an increased
192 risk of low iron stores at birth in this cohort.

193 A number of studies have explored individual determinants of cord ferritin concentrations in
194 isolation.[21-23] However, few studies have explored multiple potential determinants in a single
195 cohort and those that have, have been somewhat limited by smaller sample sizes or a reliance
196 on retrospectively collected data.[9, 24, 25] Much of the focus of previous research has been on
197 the influence of maternal iron status during pregnancy on neonatal iron status. In this study,
198 we observed no association between maternal anaemia in early pregnancy and cord ferritin
199 concentrations, in contrast to findings in a number of early studies.[26-28]

200 Maternal BMI at 15 weeks' gestation and maternal obesity in particular was inversely
201 associated with cord ferritin concentrations in the current study. Obesity in pregnancy has been
202 associated with an increased risk of suboptimal pregnancy outcomes and adverse health
203 outcomes for both the mother and infant.[20] With regards its effect on neonatal iron status, only
204 four studies, all recent, have explored such associations.[29-32] The mechanism behind this
205 association remains to be fully elucidated but many suggested mechanisms involve the iron
206 transporter protein, hepcidin. The low-grade, chronic pro-inflammatory state associated with
207 obesity results in an overexpression of hepcidin, inhibiting intestinal iron absorption and the
208 release of iron from hepatic stores, thus decreasing circulating iron in the mother.[29] Hepcidin
209 may also interfere directly with placental iron transfer to the fetus, resulting in less maternal
210 iron available to the fetus.[29, 30] In addition, obesity during pregnancy is often associated with
211 the concurrent diagnosis of other conditions that impact on neonatal iron status independently,
212 including GDM, hypertension and preeclampsia.[20, 33]

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Infants born by Caesarean section had significantly lower cord ferritin concentrations and an increased risk of low iron stores at birth compared to those delivered vaginally. Delivery by Caesarean section has previously been shown to result in a decreased level of iron-related haematological indices, including haemoglobin, haematocrit and erythrocyte, in neonatal cord or peripheral blood compared to infants delivered vaginally.[34] However, our study is one of the first to demonstrate the effect of Caesarean delivery on neonatal iron stores specifically. Caesarean deliveries result in a reduced placental transfusion attributable to a weaker transfusion force, mainly due to a lack of utero squeezing and gravity, and a shorter transfusion period due to immediate umbilical cord clamping.[34, 35] The cumulative adverse effect of Caesarean delivery in obese mothers reported in the current study is also of particular importance, given the elevated rates of Caesarean deliveries observed in obese mothers.[20] Delayed clamping of the umbilical cord (≥180 seconds or after cord pulsations stop) has been shown to result in an increased transfusion of blood to the neonate, improving iron status with no associated increased risks of neonatal mortality or morbidity.[36] Despite delayed cord clamping now being recommended as standard care for full term deliveries after uncomplicated pregnancies,[37, 38] the practice is still not yet universal.

The intrauterine environment has previously been shown to influence neonatal iron status, with smoking during pregnancy associated with chronic fetal hypoxia and decreased utero-placental blood flow.[22] In this study, maternal smoking in early pregnancy was associated with an increased risk of low iron stores at birth, in agreement with previous observations.[9, 23] Additionally, we observed that infants born SGA, often due to growth restriction *in utero*, were three times more likely to have low iron stores at birth. Of the infants with cord ferritin <35 µg/L, a threshold suggested to reflect neonatal iron deficiency, over half were born SGA, further emphasising the influence of the intrauterine environment on neonatal iron stores.

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This large, prospective study has identified a number of potentially modifiable lifestyle factors that impact neonatal iron stores. The implications of such findings are important as firstly, low iron stores at birth track through to early childhood[8, 9] and secondly, low iron stores at birth have previously been associated with adverse neurodevelopmental outcomes in childhood.[10, 11] The identification of specific risk factors for low iron stores at birth may help clinicians identify the infants most at risk, thus potentially enabling earlier intervention to prevent iron deficiency and its associated consequences, especially for neurodevelopment, later in childhood.

The importance of overall maternal health and lifestyle for neonatal iron status has been highlighted. The effect of maternal obesity reported in this study is particularly important, given its possible cumulative detrimental effect and the rising prevalence of obesity in pregnant women,[39] the potential for a concomitant rise in iron deficiency rates in neonates is of concern. Public health policies and health promotion interventions for women of child-bearing age are needed with the promotion of a healthy lifestyle among young women essential to protect future generations.

The current study has several strengths. To our knowledge, this is the largest study to describe maternal, antenatal and birth-associated factors that influence serum ferritin concentrations at birth in a single prospective maternal-infant cohort. The prospective, longitudinal design of both the SCOPE study and the Cork BASELINE Birth Cohort, with the collection of a detailed dataset for participants from 15 weeks' gestation has enabled this novel exploration. The generalizability of our results may be somewhat limited, given the specific inclusion criteria of the cohort; however, they are generalizable to other healthy, low risk maternal-infant populations. The low prevalence of certain pregnancy outcomes such as GDM and preeclampsia in this healthy cohort may have limited our ability to accurately investigate their influence on neonatal iron stores, while the lack of data collected on maternal serum ferritin concentrations or other indicators of iron status and diet during pregnancy is another limitation.

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No information on the timing of umbilical cord clamping was recorded, however, delayed cord clamping was not routine in our service during the study period.

Conclusions

In this large, prospective maternal-infant cohort, we have identified a number of potentially modifiable lifestyle factors that influence iron stores at birth. In particular, the important role of overall maternal health and lifestyle as opposed to iron status has been emphasised. Given the reported consequences of low iron stores at birth for later iron status and developmental outcomes, strategies to improve neonatal iron status should be considered. Public health policies targeting young women to improve nutrition and health outcomes and the universal implementation of delayed cord clamping in the obstetric field are two potential strategies.

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Conflict of interest No conflicts of interest to declare.

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Table 1 Principal characteristics of participants with (*n* = 413) and without (*n* = 1023) cord serum ferritin concentrations measured in the Cork BASELINE Birth Cohort Study

	Cord ferritin measured (*n* = 413)	**Cord ferritin not measured (*n* = 1023)**	**p value***
Maternal characteristics			
Age (at delivery, years)	31.0 [29.0, 33.0]	31.0 [28.0, 33.0]	0.560
Caucasian	409 (99)	993 (98)	0.266
Education			0.920
≤12 years	48 (12)	114 (11)	
>12 years	365 (88)	898 (89)	
Marital status			0.264
Single	21 (5)	70 (7)	
Married/*defacto*	392 (95)	953 (93)	
Household income			0.298
<€21,000	34 (9)	68 (7)	
€21,000-€63,000	175 (44)	385 (40)	
€64,000-€105,000	144 (36)	389 (40)	
>€105,000	45 (11)	123 (13)	
Body mass index (kg/m^2)			0.124
<18.5	3 (1)	11 (1)	
≥18.5 and <25.0	227 (55)	620 (61)	
≥25.0 and <30.0	133 (32)	268 (26)	
≥30.0	50 (12)	123 (12)	
Smoking			0.640
Never in pregnancy	308 (75)	771 (75)	
Quit while pregnant	64 (15)	166 (16)	
Still smoking	41 (10)	86 (9)	
Alcohol consumption			0.655
Never in pregnancy	74 (18)	190 (19)	
Quit while pregnant	277 (67)	662 (65)	
Still drinking	62 (15)	171 (16)	
Mode of delivery			0.036
Caesarean section	95 (24)	259 (29)	
Vaginal	306 (76)	618 (71)	
Infant characteristics			
Male	221 (54)	507 (50)	0.195
Preterm birth (<37 weeks)	15 (4)	56 (6)	0.241
Small-for-gestational age	35 (9)	113 (11)	0.174
Birth weight (kg)	3.5 [3.3, 3.8]	3.4 [3.1, 3.8]	0.033
Birth length (cm)	50.5 [49.0, 51.9]	50.1 [48.9, 51.8]	0.051
Head circumference at birth (cm)	35.0 [34.0, 36.0]	35.0 [34.0, 36.0]	0.599

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Data presented as median [IQR] or numbers (%). Maternal data collected at 15 weeks' gestation unless otherwise stated.
* *P* values are comparisons between groups with χ^2 or Mann-Whitney U tests.

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Table 2 Distribution of cord serum ferritin concentrations (μg/L) in total population and in males and females separately

	All	**Males**	**Females**
	n = 413	*n* = 221	*n* = 192
Mean	236.5	227.7	246.5
SD	136.1	134.9	137.1
Median	185.7	176.5	188.5
5th centile	58.7	52.7	67.7
25th centile	131.7	124.5	137.5
75th centile	385.5	379.9	393.9
95th centile	446.8	440.6	452.2

Difference between males and females explored by Mann-Whitney U test ($P = 0.144$).

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Table 3 Factors associated with cord serum ferritin concentrations (μg/L) in infants in the Cork BASELINE Birth Cohort Study (*n* = 413)

Characteristic	Unadjusted mean difference (μg/L, 95% CI)	p value	Adjusted mean difference[1] (μg/L, 95% CI)	p value
BMI				
<30 kg/m^2	Reference		Reference	
≥30 kg/m^2	-79.3 (-118.9, -39.6)	<0.0001	-76.5 (-118.7, -34.3)	<0.0001
Smoking status				
Non-smoker	Reference		Reference	
Smoker	-39.9 (-83.9, 3.9)	0.074	-42.6 (-90.4, 5.2)	0.080
Mode of delivery				
Vaginal	Reference		Reference	
Caesarean section	-42.7 (-73.9, -11.5)	0.008	-38.8 (-70.2, -7.4)	0.016

Maternal data collected at 15 weeks' gestation unless otherwise stated.
[1] Final model included infant sex, gestational age, maternal education, income, BMI, smoking and mode of delivery.

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Table 4 Factors associated with low iron stores (ferritin <76 µg/L) at birth in infants in the Cork BASELINE Birth Cohort Study (*n* = 413)

Characteristic	Unadjusted OR (95% CI)	p value	Adjusted OR[1] (95% CI)	p value
Smoking status				
Non-smoker	Reference		Reference	
Smoker	2.8 (1.2, 6.5)	0.014	2.9 (1.2, 7.0)	0.020
BMI				
<30 kg/m^2	Reference		Reference	
≥30 kg/m^2	2.6 (1.1, 6.1)	0.031	1.8 (0.7, 4.6)	0.193
Mode of delivery				
Vaginal	Reference		Reference	
Caesarean section	2.1 (0.9, 4.4)	0.060	2.2 (1.0, 4.9)	0.046
Small-for-gestational age infant				
No	Reference		Reference	
Yes	3.4 (1.4, 8.5)	0.009	3.4 (1.3, 8.9)	0.012

Maternal data collected at 15 weeks' gestation unless otherwise stated.
[1] Final model included infant sex, small-for-gestational age, maternal education, income, BMI, smoking and mode of delivery. Reference: cord ferritin concentrations ≥76 µg/L.

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