Background: Iron deficiency (ID) is the leading single-nutrient deficiency in the world. Anaemia is a common outcome of ID that affects half of pregnancies worldwide with serious consequences for child development. Whether haematologic indices and biomarkers of iron status in pregnant women correlate with those of their neonates is unclear. This systematic review evaluated studies comparing haematologic and iron status indices in pregnant women and their newborns/neonates.

Methods: We searched MEDLINE, EMBASE, CINAHL, and Web of Science from database inception until March 2020 for primary studies comparing haematologic and iron status indices between women and their newborns up to 48 h after birth. We summarized the results descriptively and calculated pooled correlation coefficients in mothers and newborns/neonates using the Schmidt-Hunter method. The protocol was registered at PROSPERO International Prospective Register of Systematic Reviews (Registration number: CRD42018093094).

Findings: Sixty-five studies were included. Pooled correlation coefficients for biomarkers of iron status in mothers and newborns/neonates were 0.13 (ferritin), 0.42 (hepcidin), 0.30 (serum/plasma iron), 0.09 (transferrin), 0.20 (transferrin saturation), and 0.16 (total iron binding capacity). Pooled correlation coefficients for haematological indices in mothers and newborns/neonates were 0.15 (haemoglobin), 0.15 (haematocrit), 0.25 (mean cell/corpuscular haemoglobin), and 0.22 (mean cell/corpuscular volume).

Interpretation: Maternal biomarkers of iron and haematologic status correlate poorly with those in newborns/neonates. These results underscore a need for alternative approaches to estimate foetal/neonatal iron status and haematological indices.

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Research in context

Evidence before this study

Iron deficiency (ID) is a global health issue, for which the burden on pregnant women and neonates is staggering. Numerous groups worldwide have studied the association between maternal haematological and iron status indices with those of their newborn children, though no clear association has been established.

Added value of this study

This study is the first to consolidate data regarding the correlation of maternal haematological and iron status biomarkers with those of their newborn children. Of the parameters studied, maternal serum iron was most strongly correlated with offspring haematological and iron status indices. Notably, maternal ferritin, often utilized as a primary ID screen assessment, did not show any association with offspring indices.

Implications of all the available evidence

In contrast to the dominant clinical paradigm, only weak correlations exist between maternal and offspring haematological and iron status indices. Consequently, neonatal haematological and iron status should not be estimated based on a maternal indices alone, and more proximal sources (e.g. cord blood) may be more appropriate for these assessments.

Methods

2.1 Design and protocol development

The systematic review and meta-analyses were conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [14]. A protocol was registered in the International Prospective Register of Systematic Reviews database (PROSPERO, CRD42018093094).

2.2 Eligibility criteria

To be eligible for inclusion, primary studies needed to include populations of women with no apparent complications in pregnancy (i.e. no gestational hypertension, preeclampsia, and/or gestational diabetes) and report correlation coefficients between iron status and haematological biomarkers in the mother and newborns within 48 h of birth (primary outcome of the review). No exclusions were made based on duration of gestation or alterations in foetal growth reported in the studies. Randomized controlled trials were excluded as their primary focus is on the efficacy/effectiveness of interventions. Review articles, animal studies, case reports, letters to the editor, commentaries, in vitro studies, and articles that did not report or allow for calculation of correlation coefficients were excluded. Exposures of interest were maternal biomarkers of iron status, which included serum ferritin, hepcidin, serum/plasma iron, soluble transferrin receptor (sTfR), transferrin [Tf] levels, transferrin saturation [Tf Sat], total iron binding capacity [TIBC], zinc protoporphyrin levels [ZPP], or maternal haematological indices, which included haemoglobin (Hb), haematocrit (Ht), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCHb), collected during pregnancy or in the immediate postnatal period (up to 48 h after birth). Primary outcomes of interest were the same biomarkers of iron status or haematological indices collected in newborns or in cord blood (up to 48 h after birth).

2.3 Search strategy and selection criteria

Comprehensive searches in MEDLINE, EMBASE, Cumulative Index to Nursing and Allied Health Literature (CINAHL), and Web of Science were conducted from database inception up to March 2020. The search strategy was designed by an information specialist (TC) with feedback from content experts (SLB) and methodologists (MBO) using Medical Subject Headings and relevant keywords related to pregnancy, and iron status and haematological indices in the mother and newborns. The full MEDLINE search strategy with keywords and MeSH terms is provided in Supplementary Table 1. Additionally, grey literature and reference lists searches of potentially relevant articles were conducted. Language or publication status restrictions were not applied. After removal of duplicates, the references file was split amongst five pairs of reviewers (MBO and JL, MBO and SR, MBO and OBS, SR and AGW, or OBS and SLB) for independent screening of titles, abstracts and full texts. Disagreements amongst pairs of reviewers were resolved by consensus.

2.4 Data extraction

A standardized tool was designed to extract relevant information from studies. Data relating to names of authors, year and country where studies were conducted, study design, whether studies were conducted in a malaria-endemic setting, sample size, maternal age and maternal/neonate biomarkers were extracted by one of two reviewers (JL or SR) and independently verified by a second reviewer (OBS); discrepancies were resolved by consensus.
2.5 Risk of bias assessment

Two independent reviewers (OBS and AGW) assessed the risk of bias of included studies using the Newcastle-Ottawa Scale (NOS) [15] for observational studies. The NOS evaluates risk of bias in selection of study participants, comparability amongst study groups, ascertainment of exposures, and outcomes assessment. Based on the final NOS score, the risk of bias of each article was graded as either low (selection 3–4 stars, comparability 2 stars, outcome 3 stars), moderate (selection 2 stars, comparability 1 star, outcome 2 stars), or high (selection 1 or 0 stars, comparability 0 stars, outcome 1 or 0 stars) [15]. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) [16] approach was used to rate the body of evidence for each comparison of maternal-neonate iron status and haematological biomarkers. Briefly, evidence from non-randomized studies begins as low-quality evidence but can be downgraded or upgraded according to risk of bias, inconsistency, indirectness, and imprecision of the evidence. Grades of evidence were rated as high, moderate, low, or very low.

2.6 Data analysis and interpretation

Correlation coefficients obtained in individual studies for biomarkers of iron status in mothers and newborns/neonates were pooled using the Schmidt-Hunter random-effects model method [17] and reported with 95% confidence intervals (CI) when three or more studies reported similar biomarkers. Population characteristics and outcome estimates of included studies were narratively synthesized. I² statistic was used to assess heterogeneity across included studies - an I² of <25%, 25–74% or >74% indicate low, moderate or high heterogeneity respectively. To account for heterogeneity, sub-group analyses were performed by study design where at least 10 studies were pooled. Funnel plots were used to assess publication bias; an asymmetrical funnel plot suggests evidence of publication bias. Pooled correlation coefficients were interpreted as follows: very high positive/negative correlation (0.90 to 1.00 or −0.90 to −1.00), high positive/negative correlation (0.70 to 0.89 or −0.70 to −0.89), moderate positive/negative correlation (0.50 to 0.69 or −0.50 to −0.69), low positive/negative correlation (0.30 to 0.49 or −0.30 to −0.49), and negligible correlation (0.00 to 0.29 or 0.00 to −0.29) [18]. Analyses were conducted using StatsDirect version 3 [19] (for meta-analysis of correlation data) and RevMan version 5.3 [20] (for risk of bias summary).

2.7 Role of the funding source

The funders of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

3.1 Search results

A total of 10,120 references were identified, and after duplicates were removed, 6511 titles and abstracts were screened for relevance, yielding 593 full text articles. A total of 65 studies were included in the review. Detailed study inclusion and exclusion process is presented in Fig. 1. The full list of excluded studies is available upon request.

3.2 Characteristics of included studies

Characteristics of included studies are described in Table 1. Studies were published between 1973 and 2019. The majority of studies were cross-sectional: 54 studies [21–74], 9 were prospective cohort studies [75–83], and two were retrospective cohort studies [84,85]. 24 studies were conducted in Asia [21–23,32–35–37,39,40,42,49,50,53,54,57,58,65,66,70,75,76,78,80,83], 18 in Europe [26,28,30,41,43,45,46,48,51,55,56,61,63,68,69,71,79], 8 in North America [44,52,72,73,81,82,85,86], 7 in Africa [24,27,29,31,38,47,59], 6 in South America [23,34,64,67,74,84], and 2 were conducted in Australia and Oceania. [33,60] Thirty-four studies were conducted in malaria-endemic countries [21–25,31,32,34–38,41,42,47–49,52,53,55–57,60–64,67,70,72,74,76,78,84] reported that some or all the pregnant women had received iron supplementation during pregnancy.

3.3 Risk of bias of included studies

The risk of bias of individual studies is summarised in Fig. 2 and Fig. 3. The risk of bias was low in seven studies [48,52,57,64,80,83], moderate in 28 studies [24,26–28,32,34–36–38,42,50,51,56,61,65, 66,70,72–74,76–79,81,87,84,85] and high in 30 studies [21,23,25–31,33,35,39–41,43–47,49,53–55,58–63,67,69,71,82]. Overall, cross-sectional studies had a high risk of bias in the two comparability domains, moderate risk of bias in the domains relating to representativeness of exposed cohort and selection of non-exposed cohort, low risk of bias in domains that related to ascertainment of exposure and demonstration that the outcome of interest was not present at the start of study. Conversely, cohort studies had a high risk of bias in the domains that related to comparability bias (i.e. whether studies controlled for important factors), moderate risk of bias in the domains that assessed selection of non-exposed cohort and loss of cohort to follow-up. Finally, there was a low risk of bias amongst cohort studies in the domains that assessed representativeness of exposed cohort, ascertainment of exposure, demonstration that outcome of interest was not present at start of study, independent blind assessment of outcome and whether follow-up time was sufficient for outcome to occur. Overall, the quality of the evidence to inform the association between maternal and neonatal iron status and haematologic indices was very low (see Supplementary Table 2 for a Summary of GRADE evidence profile).

3.4 Maternal iron status and neonatal indices

A summary of correlations between maternal iron status biomarkers and neonatal iron and haematological indices is shown in Table 2.

3.4.1 Ferritin

Thirty studies assessed ferritin levels in pregnant women. Negligible pooled correlation were found for maternal ferritin in relation to newborn ferritin, 0.14 (95% CI 0.07, 0.20; n = 27 studies [23,27,30,32,33,35,38,41,43–45,48,51,57–59,62,64,66,69,72,76,77,80–83]; I²=93.7%), serum/plasma iron (0.21; 95% CI −0.02, 0.45; n = 6 studies [27,30,59,64,67]; I²=94.8%), Tf Sat (0.10; 95% CI −0.09, 0.39; n = 5 studies [27,30,58,59,64,67]; I²=96.6%), TIBC (−0.09; 95% CI −0.33, 0.14; n = 6 studies [27,30,58,59,64,67]); I²=93.7%), HB (0.05; 95% CI −0.05, 0.15; n = 8 studies [27,32,38,57,64,66,74,76]; I²=95.4%), and MCV (0.15; 95% CI −0.06, 0.35; n = 3 studies [27,38,64]; I²=77.8% Supplementary Fig. 1a–f). Pooled estimates for correlations between maternal ferritin and newborn hepcidin (0.44; n = 1 study [76]), MCHb (0.50;0.10; n = 2 studies), and ZPP (0.10; n = 1 study [64]) are not summarised in tables or supplementary figures because they comprise less than three studies. Pooled estimates remained negligible and heterogeneity remained high after sub-group analysis of maternal versus newborn ferritin by study design (cross-sectional...
[n = 21] versus prospective [n = 6] cohort studies; data available upon request). Similarly, the strength of correlation between maternal and neonatal ferritin remained unchanged after subgroup analysis by timing of maternal blood draw (before birth [n = 21] versus after birth [n = 6]; data available upon request).

3.4.2 Hepcidin
Four studies assessed hepcidin levels in pregnant women. [76,77,79,81] There was a low positive pooled correlation for maternal versus newborn hepcidin (0.42 [95% CI 0.18, 0.66; I²=96.6% Supplementary Fig. 2). Pooled estimates for correlations between maternal hepcidin and newborn ferritin (0.37; n = 1 study [76]), serum iron (0.37; n = 1 study [76]), TF Sat (0.33; n = 1 study [76]), TfB (0.24; n = 1 study [76]), and Hb (0.39; n = 1 study [76]) are not summarised in tables or supplementary figures because they comprise less than three studies.

3.4.3 Serum/ plasma iron
Twenty-three studies assessed serum/plasma iron in pregnant women [22,27,29,31,33–35–37,46,50,53–55, 57–59,64,67,68,73–74, 76,80]. Low positive pooled correlations were identified for comparisons between maternal serum/plasma iron versus serum ferritin (0.33: 95%CI 0.13, 0.52; n = 5 studies [27,58,59,64,76]); I²=91.8%), newborn serum/plasma iron (0.30: 95%CI 0.19, 0.40; I²=91.8%), TF Sat (0.35: 95%CI 0.12, 0.58; n = 4 studies [27,59,64,76]; I²=93.2%) and Hb (0.42: 95%CI 0.09, 0.75; n = 4 studies [27,54,64,76]; I²=93.4%) (Supplementary Fig. 3). A negligible pooled correlation was identified between maternal serum/plasma iron and newborn TIBC (–0.15: 95%CI –0.39, 0.09; n = 5 studies [27,58,59,64,76]; I²=91.6%). Pooled estimates for correlations between maternal serum/plasma iron and newborn hepcidin (0.40; n = 1 study [76]), ZPP (0.1; n = 1 study [64]), MCHB (0.35; n = 1 study [27]), and MCV (0.33 and –0.11; n = 2 studies) are not summarized in tables or supplementary figures because they comprise less than three studies. Subgroup analysis between maternal and neonatal serum iron concentrations according to the timing of maternal blood draw revealed a negligible correlation [0.28 [95% CI 0.17, 0.39]] when studies that reported maternal blood draw before delivery alone were included (n = 19), but were moderate [0.57 [95% CI 0.38, 0.76]] when studies that reported maternal blood draw after delivery alone (n = 3) were included.

3.4.4 sTfR
Two studies assessed the correlation between maternal and newborn sTfR [77,81]. The correlation coefficients reported in the two studies were negligible (0.23 and 0.18), and are not summarized in Tables or Supplementary Figures because they comprise less than three studies.

3.4.5 Tf
Three studies assessed the correlation between maternal Tf levels and newborn Tf levels [40,42,71]. The pooled correlation for correlation versus newborn Tf levels from the three studies was negligible (0.09: 95%CI –0.08, 0.26; I²=83.3%) (Supplementary Fig. 4).

3.4.6 Tf sat
Nine studies assessed Tf Sat levels in pregnant women. [29,30,33,35,36,55,59,64,76] Negligible pooled correlations were found for maternal versus newborn ferritin (0.07: 95%CI –0.23, 0.38; n = 4 studies [30,59,64,76]; I²=96.5%), serum iron (0.18: 95%CI –0.05, 0.41; n = 4 studies [30,59,64,76]); I²=92.8%), TF Sat 0.20 (95%CI 0.08, 0.31; n = 9 studies [29,30,33,35,36,55,59,64,76]; I²=85.2%), and TIBC (0.06: 95%CI –0.22, 0.34; n = 4 studies [30,59,64,76]; I²=94.4%) (Supplementary Fig. 5). Pooled estimates of correlation between maternal Tf Sat and newborn hepcidin (0.35; n = 1 study [76]), ZPP (–0.03; n = 1 study [64]), Hb (0.844 and 0.066; n = 2 studies), and MCV (–0.04; n = 1 study [64]) are not summarized in tables or supplementary figures because they comprise less than three studies.

3.4.7 TIBC
Eight studies assessed TIBC levels in pregnant women. [29,30,33,35,58,59,64] Negligible pooled correlations were found for maternal TIBC in relation to newborn ferritin (0.04: 95%CI –0.21, 0.29; n = 5 studies [30,58,59,64,76]); I²=94.4%), iron (0.02: 95%CI –0.20, 0.24; n = 5 studies [30,58,59,64,76]); I²=91.1%), Tf Sat (–0.09: 95%CI –0.34, 0.16; n = 4 studies [30,59,64,76]; I²=93.1%), and TIBC 0.16 (95%CI 0.01, 0.31; n = 8 studies; I²=88.5%) (Supplementary Fig. 6). Pooled estimates of correlation between maternal Tf Sat and newborn ZPP (–0.40 [76] and 0.15; n = 2 studies), Hb (–0.838; n = 1 study [76]), and MCV (–0.01; n = 1 study [64]) are not summarized in tables or supplementary figures because they comprise less than three studies.

3.4.8 ZPP
Two studies assessed ZPP levels in pregnant women [61,64]. The correlation between maternal ZPP and the following biomarkers in newborns were reported: ferritin (–0.23; n = 1 study [64]), iron (–0.13; n = 1 study [64]), Tf (0.44; n = 1 study [61]), Tf Sat (–0.15; n = 1 study [64]), TIBC (0.17; n = 1 study [64]), ZPP (0.04; n = 1 study [64]), Hb (0.39 and 0.08; n = 2 studies), and MCV (0.08; n = 1 study [64]).

3.5 Maternal haematological and neonatal indices
A summary of correlations between maternal haematologic indices and neonatal iron and haematological indices is shown in Table 3.

3.5.1 Hb
Thirty-two studies assessed Hb levels in pregnant women. [21,26–29,32,33,35,36,43,47,49,54,57,59,60,63–67,70,72–74, 76,78,81,83,85] There was negligible pooled correlation between maternal Hb and newborn: ferritin (0.16: 95%CI –0.12, 0.43; n = 6 studies [23,32,38,58,62,76]); I²=95.5%), iron (0.29: 95%CI 0.04, 0.54; n = 5 studies [25,54,58,64,76]); I²=93.6%), Tf Sat (–0.22: 95%CI –0.52, 0.08; n = 4 studies [25,58,64,76]; I²=93.3%), Hb (0.15: 95%CI 0.10, 0.20; n = 32 studies [21,26,29,32,33,35,36,43,47,49,54,57, 59,63–67,70,72–74,76,81,83,85,88], I²=89.1%), Ht (0.13: 95%CI –0.007, 0.25; n = 3 studies [25,28,85]; I²=86.4%), and MCV (0.20: 95%CI –0.07, 0.46; n = 3 studies [27,38,64]; I²=88.6%) (Supplementary Fig. 7). There was a low positive pooled correlation for maternal Hb versus newborn Tf Sat (0.35: 95%CI –0.05, 0.75; n = 3 studies [27,64,76]; I²=96.4%). Pooled estimates of correlations between maternal Hb and newborn hepcidin (0.556; n = 1 study [76]), sTfR (0.298 and 0.36; n = 2 studies), ZPP (0.08; n = 1 study [64]), and MCHB (0.563 and 0.15; n = 2 studies) are not summarized in tables or supplementary figures because they comprise less than three studies.

Sub-group analysis by study design had no impact on pooled estimates and heterogeneity for maternal versus newborn Hb (data available upon request). Pooled mean differences between newborns of mothers with anaemia (Hb <110 g/L) and without anaemia (≥110 g/L) across 10 studies [22,25,32,35,36,48,52,57,75,76], was –15.26 (95% CI –27.89, –2.63); however, there was very high heterogeneity across these studies (I²=97%). The strength of correlation between maternal and neonatal Hb was negligible (0.14 [95%CI 0.09, 0.19] when only studies when maternal blood was drawn before delivery were included (n = 25) but upgraded to low (0.30 [95% CI 0.08, 0.53]) when studies in which maternal blood was drawn after delivery were included (n = 6).
3.5.2 Ht

Thirteen studies assessed haematocrit levels in pregnant women [24,28,29,32,34,47,58,65,67,70,72,73,85]. There was negligible pooled correlation between maternal Ht and newborn Hb: (0.14: 95%CI 0.04, 0.25; n = 3 studies [28,32,85]; I²=82.7%) and Ht (0.15 (95%CI 0.06, 0.23; n = 10 studies [28,29,34,47,65,67,70,72,73,85]; I²=85.6%) (Supplementary Fig. 8). Pooled estimates of correlations between maternal Ht and newborn ferritin (−0.03 [38] and 0.01 [32]; n = 2 studies), serum iron (0.08; n = 1 study [58]), sTfR (0.14; n = 1 study [24]), and TIBC (0.01; n = 1 study [58]) are not summarized in tables or supplementary figures because they comprise less than three studies.

3.5.3 MCHb

Six studies assessed MCHb levels in pregnant women. [33,42,47,58,65,70] A negligible pooled correlation was found for maternal versus newborn MCHb (0.25: 95%CI 0.08, 0.43; n = 5 studies. [33,42,47,65,70]; I²=89.7%) (Supplementary Fig. 9). Pooled estimates of correlations between maternal MCHb and newborn ferritin (0.06; n = 1 study [58]), serum iron (0.25; n = 1

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Fig. 1. PRISMA flow diagram.
study [58]) and TIBC (0.09; n = 1 study [58]) are not summarized in tables or supplementary figures because they comprise less than three studies.

3.5.4 MCV

Seven studies assessed MCV levels in pregnant women [33,42,47,58,63,65,70]. A negligible pooled correlation was found for maternal versus newborn MCV 0.22 (95%CI 0.10, 0.33; n = 6 studies [33,42,47,63,65,70]; P²=70.1%) (Supplementary Fig. 10). Pooled estimates of correlations between maternal MCV and newborn and ferritin (0.001; n = 1 study [58]), serum iron (0.24; n = 1 study [58]) and TIBC (0.08; n = 1 study [58]) are not summarized in tables or supplementary figures because they comprise less than three studies.

In addition to forest plots showing pooled correlations for maternal versus newborn biomarkers (Supplementary Figs. 1–10), funnel plots to explore publication bias (where n > 3 studies) are presented as Supplementary Figs. 11–19. Symmetry was observed in the majority of funnel plots except for studies assessing correlations between maternal ferritin and newborn Hb, maternal versus newborn hepcidin, maternal serum iron versus newborn ferritin, Tf Sat, TIBC and Hb, maternal TF Sat versus newborn TIBC, maternal TIBC versus newborn ferritin, serum iron and Tf Sat as well as maternal Hb versus newborn TIBC. The asymmetry observed with these biomarker combinations suggests publication bias.

Discussion

This systematic review of 65 studies evaluating the relationships between maternal and neonatal haematological/iron status indices showed overall negligible correlations. The negligible correlations between maternal and offspring haematological indices may be attributed, at least in part, to a lack of information regarding the cause of anaemia. Approximately half the cases of anaemia worldwide are attributed to ID [89], with a preponderance of affected people in low- and middle-income countries, where other causes (e.g. infection, nutritional deficiencies) are also prevalent. Thus, assessments of maternal haematological indices must be made not only in conjunction with iron status biomarkers [3], but also screen for other causes (i.e. malaria, inflammation) to improve predictive ability of these indices in neonates. In addition, routine assessment of cord blood haematologic indices may also be warranted to identify at-risk neonates whose mothers may have no abnormalities found in screening.

Advances in the understanding of iron metabolism in pregnancy, and increased assay reliability and availability, has led to relatively recent studies reporting iron biomarkers in maternal and cord/neonatal blood, albeit they are few. Unfortunately, the data was insufficient for stTfR to be assessed. Of those iron biomarkers with at least three qualifying studies, maternal serum iron was the strongest predictor for foetal iron and haematologic indices, albeit these correlations were considered low positive, and varied based on the timing of maternal blood sampling. Despite a paucity of data, it is interesting to note that indices of maternal serum iron transport, including Tf Sat, serum ferritin and TIBC had negligible correlations with newborn indices, underscored a complex relationship between maternal iron storage and placental/foetal iron delivery. Numerous health agencies, including the World Health Organization, recommend routine screening for ID anaemia in pregnant women, for which serum ferritin is the first-line iron status indicator and serum iron plays an ancillary diagnostic role (i.e. when ferritin assay results are ambiguous) [90].

Recent studies have demonstrated the usefulness of serum hepcidin and ferritin in the assessment of iron status [4]. Hepcidin is a principal regulator of plasma iron concentrations; it inhibits iron efflux from gut enterocytes and reticuloendothelial cells by binding and inhibiting the export channel ferroportin [91]. However, as an acute phase protein like ferritin, corrections for inflammation or the use of composite metrics (e.g. total body iron) that mitigate the confounding effects of inflammation are needed [92], especially due to lability of pro- and anti-inflammatory mediators throughout pregnancy [93]. Notwithstanding, the capacity of maternal total body iron to predict iron status in the foetus and neonate remains an open question and requires validation. The absence of correction for inflammation may explain the lack of maternal ferritin correlations with any foetal iron indices. Interestingly, maternal hepcidin, an important mediator of iron sequestration during infection [94], shows a significant correlation with foetal hepcidin only, accounting for 18% of variance of offspring levels. The extent to which this reflects similar iron stores, inflammation or a coordinated response to infection is unclear and requires further study, especially due to the low number of studies (n = 4) available to generate this correlation.

The present systematic review identifies a clear knowledge gap in the assessment of iron status and anaemia in the foetus and neonate. Notwithstanding the mechanisms governing the interaction between maternal and foetal iron metabolism, the low positive correlations suggest that maternal haematological indices and biomarkers of iron status are poor surrogates of foetal and neonate iron and haematologic status. However, recognition of notable challenges may guide future study design to address these knowledge gaps. First, the conflation between ID and anaemia is an important factor. The underlying cause of anaemia may be important in dictating the relationship between maternal and neonatal haematologic indices; since the foetus is entirely reliant on the mother for iron supply, a more intimate relationship between maternal and neonatal haematologic and iron indices may be expected in cases of ID. Conversely, the cause of anaemia should not be assumed to be ID, as nutrient deficiencies (e.g. folate, vitamin B12, vitamin A), inflammation, and inherited disorders (e.g. thalassaemia) account for approximately half of all cases [89]. Herein, subgroup analyses on correlations between maternal and neonatal indices in ID and non-ID mothers could not be performed, because few studies reported stratified outcomes. Therefore, care should be taken to screen for ID in mothers and cord blood. The assumption that ID is largely the cause of anaemia in many intervention programs has likely contributed to ID and anaemia’s intractability as global health problems.

A second notable challenge is the standardization of clinical techniques, screening procedures, and assay reference values. As previously mentioned, acute phase proteins such as ferritin and hepcidin should be measured concurrently with markers of inflammation. It should be noted that while the confounding effects of inflammation on various biomarkers of iron status has been recognised, the problem has not been solved. Notwithstanding, concurrent measures of C-reactive protein, α-1 acid glycoprotein-1, or IL-6 [3,95,96] may help with interpretation and inform further testing. Few studies included in this review reported inflammatory marker results, and although our search strategy excluded studies with known chronic disease or complications of pregnancy, many studies did not explicitly state the inclusion/exclusion criteria of their respective studies, and there it is not clear whether complicated pregnancies were included in the analysis. Even in the absence of pregnancy complications, inflammatory changes associated with pregnancy and subclinical infections may be present and could confound the results [96]. Further, novel indices (e.g. stTfR) suffer from a lack of standardization and consistency between analytical platforms, and thus variations in reference ranges remains an important limitation [97]. Other assays, such as serum iron measurements, may also be confounded by a lack of standardization for post-prandial and diurnal variations, length of fasting prior to testing [98], as well as the timing of maternal blood sampling (pre- versus post-delivery) as revealed in our subgroup analysis, which could reflect the effects of postpartum haemorrhage, amongst other circumstances. Finally, the use of either venous or capillary blood sampling techniques can influence haematological assessments [99], and thus standard techniques to limit outcome variability are needed. Inconsistent or incomplete reporting of variables including fasting, blood collection techniques, and inflammatory status in the included studies furthers the need for validation of results.
| Author, year, location | Study design | Participant characteristics | Methods and timing of data collection | Biomarker analyses | Biomarkers | Correlation r (95%CI)/mean | NOS quality score |
|------------------------|-------------|----------------------------|--------------------------------------|-------------------|------------|----------------------------|-----------------|
| Adams et al. [21], 1981, Nepal | Cross-sectional | Sample size: 151 Maternal age (a): NR Malaria setting: Yes Iron supplementation: NR | Maternal venous blood at delivery Umbilical cord blood at delivery Inflammation biomarkers: NR Factors adjusted: NR | Cyanmethemoglobin method | Maternal: Hb Newborn: Hb | $r = -0.06 (-0.22, 0.10)$ | 3 |
| Agrawal et al. [22] 1983, India | Cross-sectional | Sample size: 51 Maternal age (a) : NR Malaria setting: Yes Iron supplementation: NR | Maternal venous blood at delivery Umbilical cord (placental end) at delivery Inflammation biomarkers: NR Factors adjusted: Groups compared had no racial, cultural and environmental differences. | NR | Maternal: Serum iron Newborn: Serum iron | $r = 0.53 (0.30, 0.70)$ | 5 |
| Akhter et al. [23] 2010, Bangladesh | Cross-sectional | Sample size: 50 Maternal age (a): NR Malaria setting: Yes Iron supplementation: NR | Maternal antecubital blood post-partum Umbilical cord (placental end) at delivery Inflammation biomarkers: NR Factors adjusted: NR | Cyanmethemoglobin for Hb, ELISA for ferritin | Maternal: Ferritin Newborn: Ferritin | $r = -0.94 (-0.97, -0.90)$ | 4 |
| Altinkaynak et al., [41] 1984, Turkey | Cross-sectional | Sample size: 52 Maternal age (a): 26±5.3 Malaria setting: Yes Iron supplementation: Some women | Maternal peripheral blood at delivery Umbilical cord blood at delivery Inflammation biomarkers: NR Factors adjusted: NR | Ferritin enzymatic testing kits from Medix Biotech | Maternal: Hb Newborn: Ferritin | $r = 0.48 (0.23, 0.67)$ | 4 |
| Awadallah et al. [75], 2004, Jordan | Prospective cohort | Sample size: 186 Maternal age (a): 27±4.9/ 17−45 Malaria setting: No Iron supplementation: All women | Maternal blood at delivery Umbilical cord blood at delivery Inflammation biomarkers: NR Factors adjusted: NR | Haematology cell counter | Maternal: Hb Newborn: Hb | Maternal (anaemic 10.2 ± 0.6, non-anaemic 12.2 ± 1.2 g/dL); Newborn (anaemic 15.1 ± 2.0; non-anaemic 15.8 ± 2.3 g/dL) | 7 |
| Babay et al. [42] 2002, Saudi Arabia | Cross-sectional | Sample size: 82 Maternal age (a): 26.9 ± 5.7/ 16−40 Malaria setting: Yes Iron supplementation: None | Maternal venous blood at delivery Umbilical cord blood at delivery Inflammation biomarkers: NR Factors adjusted: NR | Radial immunodiffusion for Tf, Coulter Counter ZF6 for haematologic parameters | Maternal: Tf Newborn: Tf | $r = 0.40 (0.20, 0.57)$ | 6 |
| Basu et al. [76] 2016, India | Prospective cohort | Sample size: 45 Maternal age (a): Anaemic: 25.3 ± 3.7; Non-anaemic: 26.3 ± 3.4 Malaria setting: Yes Iron supplementation: NR | Maternal peripheral blood post-partum Umbilical cord (placental end) at delivery Inflammation biomarkers: NR Factors adjusted: NR | Auto analyser for serum iron, ferritin, Tf, Sat. ELISA for hepcidin | Maternal: Hb Newborn: Hb, Tf, MCHB, MCV | Maternal: Hb Newborn: Ferritin, Hepcidin, Serum iron, Tf Sat, TIBC, Hb | $r = 0.94 (0.89, 0.97), 0.46 (0.19, 0.66), 0.91 (0.84, 0.95), 0.88 (0.69, 0.90), -0.81 (-0.89, -0.68), 0.89 (0.80, 0.94)$ | 5 |
| Author, year, location | Study design       | Participant characteristics | Methods and timing of data collection | Biomarker analyses | Biomarkers                  | Correlation r (95%CI)/mean | NOS quality score |
|------------------------|--------------------|------------------------------|--------------------------------------|--------------------|-----------------------------|-----------------------------|-----------------------|
| Best et al. [77] 2016, USA | Prospective cohort | Sample size: 255 Maternal age (a): 17.1 ± 1.1 Malaria setting: No Iron supplementation: NR Maternal venous blood at delivery Umbilical cord blood at delivery Inflammation biomarkers: IL-6 Factors adjusted: NR | Maternal: Hepcidin Newborn: Ferritin, Hepcidin, Serum iron, Tf Sat, TIBC, Hb | r = 0.37 (0.09, 0.60), 0.72 (0.54, 0.83), 0.37 (0.09, 0.60), 0.33 (0.04, 0.57), −0.24 (−0.50, 0.06), 0.39 (0.11, 0.61) | Maternal: Serum iron Newborn: Ferritin, Hepcidin, Serum iron, Tf Sat, TIBC, Hb | r = 0.91 (0.78, 0.93), 0.401 (0.12, 0.62), 0.87 (0.78, 0.93), 0.87 (0.77, 0.92), −0.79 (−0.88, −0.65), 0.81 (0.67, 0.89) | 6 |
| Bratlid et al. [43] 1980, Norway | Cross-sectional | Sample size: 54 Maternal age (a): NR Malaria setting: No Iron supplementation: NR Maternal venous blood at delivery Umbilical cord blood at delivery Inflammation biomarkers: NR | Maternal: Ferritin Newborn: Ferritin | r = 0.37 (0.09, 0.60) | Maternal: Serum iron Newborn: Ferritin, Hepcidin, Serum iron, Tf Sat, TIBC, Hb | r = −0.84 (−0.91, −0.73), −0.75 (−0.86, −0.59), −0.79 (−0.88, −0.64), 0.80 (0.67, 0.89), −0.404 (−0.62, −0.13), −0.838 (−0.91, −0.72) | 3 |
| Butte et al. [44] 1982, USA | Cross-sectional | Sample size: 28 Maternal age (a): 16–33 Malaria setting: No Iron supplementation: NR Maternal venous blood postpartum Umbilical cord blood at delivery Inflammation biomarkers: None Factors adjusted: NR | Maternal: Serum iron Newborn: Serum iron | Maternal: Ferritin Newborn: Ferritin | r = 0.002 (−0.37, 0.37) | Maternal: Serum iron Newborn: Serum iron | r = 0.51 (0.31, 0.67) | 2 |
| Celada et al. [45] Germany | Cross-sectional | Sample size: 64 Maternal age (a): 23±4/19–31 Malaria setting: No Iron supplementation: All women Maternal venous blood postpartum Umbilical cord blood at delivery Inflammation biomarkers: NR Factors adjusted: NR | Maternal: Serum iron Newborn: Serum iron | Maternal: Serum iron Newborn: Serum iron | r = 0.002 (−0.37, 0.37) | Maternal: Serum iron Newborn: Serum iron | r = 0.51 (0.31, 0.67) | 2 |
| Custodio et al. [46] 2005, Portugal | Cross-sectional | Sample size: NR Maternal age (a): 15–39 Maternal venous blood postpartum Umbilical cord blood at delivery Inflammation biomarkers: NR Factors adjusted: NR | Maternal: Ferritin Newborn: Ferritin | r = 0.07 (−0.18, 0.31) | Maternal: Serum iron Newborn: Serum iron | r = 0.51 (0.31, 0.67) | 2 |

(continued on next page)
| Author, year, location | Study design | Participant characteristics | Methods and timing of data collection | Biomarker analyses | Biomarkers | Correlation r (95%CI)/mean | NOS quality score |
|------------------------|-------------|-----------------------------|---------------------------------------|-------------------|-----------|------------------------|-----------------|
| Daouda et al. [24]     | Cross-sectional | Sample size: 364 | Maternal venous blood at delivery Umbilical cord blood at delivery Inflammation biomarkers: NR Factors adjusted: NR | Energy dispersive X-ray fluorescence spectrometry | Maternal: Ferritin Newborn: Ferritin Ht Maternal: Ht Newborn: Ht | Maternal mean 41.8 ± 66.1 ug/L; cord mean 127.3 ± 62.9 ug/L | 6 |
| 1991, Niger             |             | Maternal age (a): | Maternal: Ferritin Newborn: Ferritin Ht Maternal: Ht Newborn: Ht | Maternal: Ferritin Newborn: Ferritin Ht | Maternal mean 41.8 ± 66.1 ug/L; cord mean 127.3 ± 62.9 ug/L | 6 |
| Dapper et al. [47]     | Cross-sectional | Sample size: 30 | Maternal venous blood postpartum Umbilical cord blood at delivery Inflammation biomarkers: NR Factors adjusted: NR | Microcentrifugation for Ht. Cyanmethaemoglobin for Hb. Manual counting chamber for blood cell counts | Maternal: Hb Newborn: Hb | r = 0.42 (0.08, 0.68) | 4 |
| 2006, Nigeria          |             | Maternal age (a): 19–40 | Maternal: Ferritin Newborn: Ferritin Ht Maternal: Ht Newborn: Ht | Maternal: Ferritin Newborn: Ferritin Ht | Maternal mean 41.8 ± 66.1 ug/L; cord mean 127.3 ± 62.9 ug/L | 6 |
| De Sa, [25] 2015, Brazil | Cross-sectional | Sample size: 54 | Maternal venous blood at delivery Umbilical cord blood at delivery Inflammation biomarkers: NR Factors adjusted: NR | Automatic device for haematologic analyses; ELISA for ferritin | Maternal: Hb Newborn: Hb | r = 0.02 (0.004, 0.18) | 5 |
| 1989, India            | Prospective cohort | Sample size: 165 | Maternal blood postpartum Umbilical cord blood at delivery Inflammation biomarkers: NR Factors adjusted: NR | Cyanomethaemoglobin method for Hb | Maternal: Hb Newborn: Hb | r = 0.47 (0.23, 0.66) | 5 |
| Devi et al., [78] 1989, India | Prospective cohort | Sample size: 139 | Maternal venous blood postpartum Neonatal capillary blood at delivery Inflammation biomarkers: NR Factors adjusted: NR | NR | Maternal: Hb Newborn: Hb | r = 0.17 (0.004, 0.33) | 6 |
| Ek et al., [26] 1982, Norway | Cross-sectional | Sample size: 139 | Maternal venous blood postpartum Neonatal capillary blood at delivery Inflammation biomarkers: NR Factors adjusted: NR | NR | Maternal: Hb Newborn: Hb | r = 0.17 (0.004, 0.33) | 6 |
| El Guindi et al. [84] 2004, Guyana | Retrospective cohort | Sample size: 222 | Maternal blood postpartum Neonatal capillary blood at delivery Inflammation biomarkers: NR Factors adjusted: NR | NR | Maternal: Hb Newborn: Hb | r = 0.17 (0.004, 0.33) | 6 |
| El-Farrash et al. [27] 2012, Egypt | Cross-sectional | Sample size: 80 | Maternal blood postpartum Umbilical cord at delivery | ELISA for ferritin; Commercial kit for TIBC; Hitachi 917 analyser for serum iron; | Maternal: Ferritin Newborn: Ferritin, Serum iron, Tf Sat, TIBC, Hb, MCHb, MCV, | r = 0.47 (0.28, 0.62), 0.39 (0.19, 0.56), 0.430 (0.21, 0.87), –0.39 (0.56, –0.18), 0.67 (0.52, | 5 |
|                         |             | Maternal age (a): | Maternal: Ferritin Newborn: Ferritin, Serum iron, Tf Sat, TIBC, Hb, MCHb, MCV, | Maternal: Ferritin Newborn: Ferritin | Maternal mean 41.8 ± 66.1 ug/L; cord mean 127.3 ± 62.9 ug/L | 6 |
|                         |             | Non-anaemic: 26.7 | Maternal: Ferritin Newborn: Ferritin, Serum iron, Tf Sat, TIBC, Hb, MCHb, MCV, | Maternal: Ferritin Newborn: Ferritin, Serum iron, Tf Sat, TIBC, Hb, MCHb, MCV, | Maternal mean 41.8 ± 66.1 ug/L; cord mean 127.3 ± 62.9 ug/L | 6 |
|                         |             | Total: 293 | Maternal: Ferritin Newborn: Ferritin, Serum iron, Tf Sat, TIBC, Hb, MCHb, MCV, | Maternal: Ferritin Newborn: Ferritin, Serum iron, Tf Sat, TIBC, Hb, MCHb, MCV, | Maternal mean 41.8 ± 66.1 ug/L; cord mean 127.3 ± 62.9 ug/L | 6 |
|                         |             | Maternal age (a): | Maternal: Ferritin Newborn: Ferritin, Serum iron, Tf Sat, TIBC, Hb, MCHb, MCV, | Maternal: Ferritin Newborn: Ferritin, Serum iron, Tf Sat, TIBC, Hb, MCHb, MCV, | Maternal mean 41.8 ± 66.1 ug/L; cord mean 127.3 ± 62.9 ug/L | 6 |

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| Author, year, location | Study design | Participant characteristics | Methods and timing of data collection | Biomarker analyses | Biomarkers | Correlation r (95%CI)/mean | NOS quality score |
|------------------------|-------------|-----------------------------|--------------------------------------|-------------------|-----------|-----------------------------|-----------------|
| Erdem et al. [48] 2002, Turkey | Cross-sectional | Sample size: 44 Maternal age (a): NR Malaria setting: Yes Iron supplementation: Unclear | Maternal blood at delivery Umbilical cord blood at delivery Inflammation biomarkers: NR Factors adjusted: Controls matched for age, parity and gestational age | Automated cytometer for Hb. Chemiluminescence technique for ferritin | Maternal: Ferritin Newborn: Ferritin | r = 0.52 (0.27, 0.71) | 7 |
| Esmailnasab et al. [49] 2012, Iran | Cross-sectional | Sample size: 604 Maternal age (a): NR Malaria setting: Yes Iron supplementation: NR | Timing of maternal blood collection NR Timing of umbilical cord collection NR Inflammation biomarkers: NR Factors adjusted: NR | Cell counter machine | Maternal: Hb Newborn: Hb | r = 0.14 (0.06, 0.22) | 3 |
| Garcia-Valdes et al. [79] 2015, Spain | Prospective cohort | Sample size: 308 Maternal age (a): Control 30.8 ± 4.3, Overweight 31.8 ± 4.5, Obese = 29.0 ± 4.6 Malaria setting: No Iron supplementation: Some women | Maternal blood at delivery Umbilical cord blood at delivery Inflammation biomarkers: CRP Factors adjusted: Inflammation | ELISA | Maternal: Hepcidin Newborn: Hepcidin | r = 0.70 (0.64, 0.75) | 6 |
| Gaspar et al. [28] 1993, Spain | Cross-sectional | Sample size: 157 Maternal age (a): 29.0 ± 0.5 Malaria setting: No Iron supplementation: NR | Maternal blood at delivery Umbilical cord blood at delivery Inflammation biomarkers: CRP Factors adjusted: NR | Automated haematology cell counter | Maternal: Hb Newborn: Hb, Ht | r = 0.36 (0.22, 0.49), 0.30 (0.15, 0.44) | 5 |
| Huang et al. [50] 2017, Taiwan | Cross-sectional | Sample size: 150 Maternal age (a): 28.1 ± 5.2 Malaria setting: No Iron supplementation: NR | Maternal venous blood at delivery Umbilical cord blood at delivery Inflammation biomarkers: NR Factors adjusted: NR | Plasma mass spectrometry | Maternal: Ht Newborn: Hb, Ht Maternal: Serum iron Newborn: Serum iron | r = 0.37 (0.23, 0.50), 0.33 (0.18, 0.46) r = 0.17 (95%CI 0.01, 0.32) | 5 |
| Hussain et al. [51] 1977, UK | Cross-sectional | Sample size: 51 Maternal age (a): 17–38 Malaria setting: No Iron supplementation: NR | Maternal blood at delivery Umbilical cord blood at delivery | Immunoradiometric assay | Maternal: Ferritin Newborn: Ferritin | r = 0.30 (0.03, 0.53) | 6 |

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| Author, year, location | Study design | Participant characteristics | Methods and timing of data collection | Biomarker analyses | Biomarkers | Correlation r (95%CI)|mean | NOS quality score |
|------------------------|-------------|-----------------------------|-------------------------------------|-------------------|-----------|----------------------|-----|------------------|
| Jaime-Perez et al. [52] 2005, Mexico | Cross-sectional | Malaria setting: No Iron supplementation: NR Sample size: 201 Maternal age (a): 23.0 ± 6.5 Malaria setting: Yes Iron supplementation: NR | Inflammation biomarkers: NR Factors adjusted: NR Maternal blood at delivery Umbilical cord blood at delivery Inflammation biomarkers: NR Factors adjusted: NR | Automated blood cell counter | Maternal: Hb Newborn: Hb | Newborns of anaemic 157±17 g/L and non-anaemic 159±14 g/L mothers | 7 |
| Jariwala et al. [53] 2014, India | Cross-sectional | Malaria setting: Yes Iron supplementation: NR Sample size: 42 Maternal age (a): NR Malaria setting: Yes Iron supplementation: NR | NR | Maternal: Serum iron Newborn: Serum iron | r = 0.39 (0.09, 0.62) | 4 |
| Kaneshige et al. [80] 1981, Japan | Prospective cohort | Sample size: 80 Maternal age (a): 20–30 Malaria setting: No Iron supplementation: NR | NR | Maternal: Ferritin Newborn: Ferritin | r = 0.75 (0.64, 0.84) | 7 |
| Katoh et al. [54], 1984, Japan | Cross-sectional | Malaria setting: NR Iron supplementation: NR Sample size: NR Maternal age (a): NR | NR | Maternal: Serum iron Newborn: Serum iron, Hb | r = 0.64 (0.37, 0.81), 0.71 (0.47, 0.85) | 4 |
| Koc et al. [55] 2006, Turkey | Cross-sectional | Malaria setting: No Iron supplementation: NR Sample size: 188 Maternal age (a): 27±5.8 Malaria setting: Yes Iron supplementation: NR | Colorimetric method for serum iron, TIBC | Maternal: Hb Newborn: Serum iron, Hb | r = 0.68 (0.43, 0.83) | 4 |
| Kulik-Rechberger et al. [56] 2016, Poland | Cross-sectional | Maternal age (a): 27.8 ± 5.5/ 18 – 42 Malaria setting: No Iron supplementation: NR | Maternal peripheral blood at delivery Umbilical cord blood at delivery Inflammation biomarkers: CRP Factors adjusted: NR | ELISA for stTfR and automated analyser for Hb | Maternal: Tf Sat Newborn: Tf Sat Maternal: TIBC Newborn: stTfR | r = 0.36 (0.07, 0.59) | 5 |
| Kumar et al. [57] 2008, India | Cross-sectional | Maternal age (a): NR Malaria setting: Yes Iron supplementation: NR | Maternal blood at delivery Umbilical cord blood at delivery Inflammation biomarkers: NR Factors adjusted: NR | Cyanmethaemoglobin method for Hb. Atomic absorption spectroscopy for serum iron. ELISA for ferritin | Maternal: Ferritin Newborn: Serum iron, Hb | r = 0.44 (0.24, 0.61), 0.45 (0.24, 0.61), 0.49 (0.25, 0.64) | 7 |

(continued on next page)
| Author, year, location | Study design | Participant characteristics | Methods and timing of data collection | Biomarker analyses | Biomarkers | Correlation $r$ (95%CI)/mean | NOS quality score |
|------------------------|-------------|-----------------------------|--------------------------------------|--------------------|------------|----------------------------|----------------|
| Lao et al. [58] 1991, China | Cross-sectional | Sample size: 96
Maternal age (a): 27.6 ± 3.6
Malaria setting: Yes
Iron supplementation: NR | Maternal blood at delivery
Umbilical cord blood at delivery
Inflammation biomarkers: NR
Factors adjusted: NR | Dye-binding analysis for serum iron and TIBC; Radioimmunoassay for ferritin; automated Technicon CBC counter for haematologic indices | Maternal: Ferritin
Newborn: Ferritin, Serum iron, TIBC | $r = 0.10 (−0.10, 0.29), 0.18 (−0.02, 0.37), 0.22 (0.02, 0.40)$ | 3 |
| Maternal: Serum iron
Newborn: Ferritin, Serum iron, TIBC | Maternal: TIBC
Newborn: Ferritin, Serum iron, TIBC | $r = 0.126 (−0.07, 0.34), 0.14 (−0.07, 0.31), 0.04 (−0.17, 0.25)$ | |
| Maternal: Hb
Newborn: Ferritin, Serum iron, TIBC | Maternal: Ht
Newborn: Ferritin, Serum iron, TIBC | $r = 0.03 (−0.17, 0.23), 0.14 (−0.07, 0.33), 0.03 (−0.17, 0.23)$ | |
| Maternal: MCHb
Newborn: Ferritin, Serum iron, TIBC | Maternal: MCV
Newborn: Ferritin, Serum iron, TIBC | $r = 0.001 (−0.20, 0.20), 0.238 (0.04, 0.42), 0.077 (−0.13, 0.27)$ | |
| MacPhail et al. [59] 1980, South Africa | Cross-sectional | Sample size: 103
Maternal age (a): 24.7 ± 39
Malaria setting: Yes
Iron supplementation: NR | Maternal venous blood at delivery
Umbilical cord blood at delivery
Inflammation biomarkers: NR
Factors adjusted: NR | Cyanometahemoglobin method for Hb; Colorimetric chromogen for serum iron; Radioimmunoassay for ferritin; coated charcoal assay for unsaturated iron-binding capacity | Maternal: Ferritin
Newborn: Ferritin, Serum iron, TIBC | $r = 0.21 (0.02, 0.39), 0.19 (−0.37, 0.003), 0.11 (0.02, 0.25), 0.20 (0.005, 0.38)$ | 3 |
| Maternal: Serum iron
Newborn: Ferritin, Serum iron, TIBC | Maternal: stTfR
Newborn: stTfR | $r = 0.18 (0.06, 0.30)$ | |
| Maternal: Hb
Newborn: Hb | Maternal: TIBC | $r = −0.08 (−0.20, 0.04)$ | |
| Lee et al. [81] 2016, USA | Prospective cohort | Sample size: 255
Maternal age (a): NR
Malaria setting: No
Iron supplementation: NR | Timing of maternal blood sampling NR
Umbilical cord blood at delivery
Inflammation biomarkers: CRP, IL-6
Factors adjusted: NR | Automated haematology analyser or HemoCue system for Hb; ELISA for stTfR, ferritin; method for hepcidin | Maternal: Ferritin
Newborn: Ferritin | $r = 0.08 (−0.04, 0.20)$ | 6 |
| Maternal: Hepcidin
Newborn: Hepcidin | Maternal: stTfR
Newborn: stTfR | $r = 0.13 (0.0073, 0.25)$ | |
| Maternal: Hb
Newborn: Hb | Maternal: MCHb
Newborn: MCHb | $r = 0.056 (−0.15, 0.25), 0.248 (0.05, 0.43), 0.087 (−0.12, 0.28)$ | |
| Maternal: MCV
Newborn: MCV | Maternal: MCV
Newborn: MCV | $r = 0.001 (−0.20, 0.20), 0.238 (0.04, 0.42), 0.077 (−0.13, 0.27)$ | |
| Author, year, location | Study design | Participant characteristics | Methods and timing of data collection | Biomarker analyses | Biomarkers | Correlation $r$ (95%CI)/mean | NOS quality score |
|------------------------|-------------|-----------------------------|--------------------------------------|--------------------|-----------|-------------------------------|-----------------|
| Malcolm et al. [60] 1973, Papua New Guinea | Cross-sectional | Sample size: 98  
Maternal age (a): NR  
Malaria setting: Yes  
Iron supplementation: NR | Maternal blood postpartum Umbilical cord blood at delivery  
Inflammation biomarkers: IgM, IgA  
Factors adjusted: NR | EEL colorimetry | Maternal: Tf Sat  
Newborn: Ferritin, Serum iron, Tf Sat, TIBC  
Maternal: TIBC  
Newborn: Ferritin, Serum iron, Tf Sat, TIBC  
Maternal: Hb  
Newborn: Hb  
Maternal: Hb  
Newborn: Hb | $r = 0.14 \ (-0.06, 0.32), 0.09 \ (-0.11, 0.28), 0.01 \ (-0.17, 0.21)$  
$r = 0.18 \ (-0.01, 0.36), 0.11 \ (-0.09, 0.30), 0.02 \ (-0.17, 0.21), 0.01 \ (-0.10, 0.29)$  
$r = 0.40 \ (0.22, 0.55)$ | 2 |
| Mezdoud et al. [29] 2017, Algeria | Cross-sectional | Sample size: 97  
Maternal age (a): 31.7 ± 4.7/22 - 42  
Malaria setting: No  
Iron supplementation: NR | Maternal venous blood at delivery  
Umbilical cord blood at delivery  
Inflammation biomarkers: NR  
Factors adjusted: NR | Automated counter for Hb and Ht. Colorimetric method for serum iron. ELISA for ferritin | Maternal: Serum iron  
Newborn: Serum iron  
Maternal: Tf Sat  
Newborn: Tf Sat  
Maternal: TIBC  
Newborn: TIBC  
Maternal: Hb  
Newborn: Hb  
Maternal: Hb  
Newborn: Hb | $r = 0.32 \ (0.13, 0.49)$ | 4 |
| Milman et al. [62] 1987, Denmark | Cross-sectional | Sample size: 85  
Maternal age (a): Median: 27/15 - 38  
Malaria setting: No  
Iron supplementation: NR | Maternal venous blood at delivery  
Umbilical cord blood at delivery  
Inflammation biomarkers: NR  
Factors adjusted: NR | Coulter-S for Hb. Radioimmunoassay for ferritin. | Maternal: Ferritin  
Newborn: Ferritin  
Maternal: Hb  
Newborn: Hb  
Maternal: Hb  
Newborn: Hb  
Maternal: Hb  
Newborn: Hb  
Maternal: MCV  
Newborn: MCV | $r = 0.36 \ (0.16, 0.53)$ | 5 |
| Milman et al. [61] 1988, Denmark | Cross-sectional | Sample size: 78  
Maternal age (a): Median: 27/16 - 38  
Malaria setting: No  
Iron supplementation: NR | Maternal venous blood at delivery  
Umbilical cord blood at delivery  
Inflammation biomarkers: NR  
Factors adjusted: NR | Haematofluorometry | Maternal: Hb  
Newborn: Ferritin  
Maternal: ZPP  
Newborn: ZPP | $r = -0.31 \ (-0.49, -0.10)$ | 3 |
| Montemagno et al. [63] 1995, UK | Cross-sectional | Sample size: 64  
Maternal age (a): NR  
Malaria setting: No  
Fe supplementation: NR | Maternal blood at delivery  
Umbilical cord blood at delivery  
Inflammation biomarkers: NR  
Factors adjusted: NR | Coulter cell counter | Maternal: Hb  
Newborn: Hb  
Maternal: Ferritin  
Newborn: Ferritin  
Maternal: MCV  
Newborn: MCV | $r = 0.22 \ (-0.03, 0.44)$ | 4 |
| Nemet et al. [30] 1986, Hungary | Cross-sectional | Sample size: 156  
Maternal age: Fer < 10 $\mu$g/l: 26.1 ± 5.0, Fer > 20 $\mu$g/l: 27.2 ± 4.6  
Malaria setting: No  
Iron supplementation: NR | Maternal venous blood during labour  
Umbilical cord blood at delivery | Ferrozine colour agent for serum iron and TIBC. Radioimmunoassay for ferritin. | Maternal: MCV  
Newborn: MCV  
Maternal: Ferritin  
Newborn: Ferritin, Serum iron, Tf Sat, TIBC | $r = 0.15 \ (-0.007, 0.30), 0.09 \ (-0.07, 0.24), 0.10 \ (-0.22, -0.02), 0.17 \ (-0.32, -0.01)$ | 3 | (continued on next page)
| Author, year, location | Study design | Participant characteristics | Methods and timing of data collection | Biomarker analyses | Biomarkers | Correlation r (95%CI)|mean | NOS quality score |
|------------------------|-------------|----------------------------|--------------------------------------|-------------------|---------|---------------------|-----|-------------------|
| Nhonoli et al. [31] 1975, Tanzania | Cross-sectional | Sample size: 580 Maternal age (a): NR Malaria setting: Yes Iron supplementation: NR | Maternal venous blood at delivery Umbilical cord blood at delivery Inflammation biomarkers: NR Factors adjusted: NR | Chromogen for serum iron | Maternal: Tf Sat Newborn: Ferritin, serum iron, Tf Sat, TIBC Maternal: TIBC Newborn: Ferritin, serum iron, Tf Sat, TIBC | r = 0.12 (0.07, 0.17), 0.04 (0.02, 0.06), 0.07 (0.04, 0.10) | 4 |
| Norimah et al. [32] 2010, Malaysia | Cross-sectional | Sample size: 70 Maternal age (a): 25.6 ± 4.9/ 17–40 Malaria setting: Yes Iron supplementation: NR | Maternal venous blood at delivery Umbilical cord blood at delivery Inflammation biomarkers: NR Factors adjusted: NR | Cyanmethaemoglobin for Hb. Radioimmunoassay for ferritin | Maternal: Ferritin Newborn: Ferritin, Hb | r = 0.01 (0.00, 0.02), 0.06 (0.04, 0.08), 0.42 (0.30, 0.54) | 5 |
| Paiva Ade et al. [64] 2007, Brazil | Cross-sectional | Sample size: 95 Maternal age (a): anaemic: 22.9; iron deficient: 23.1; control: non-iron deficient: 24.8 Malaria setting: Yes Iron supplementation: NR | Maternal venous blood at delivery Umbilical cord blood at delivery Inflammation biomarkers: NR Factors adjusted: NR | Colorimetric method for serum iron. Turbidimetric method for TIBC. Chemiluminescence for ferritin. Haematofluorometry for ZPP. Method for haematologic indices NR | Maternal: Tf Sat Newborn: Ferritin, Serum iron, Tf Sat, TIBC, ZPP, Hb, MCV | r = 0.04 (0.03, 0.05), 0.26 (0.20, 0.32), 0.30 (0.24, 0.36), 0.42 (0.36, 0.48), 0.11 (0.06, 0.16), 0.23 (0.18, 0.28), 0.001 (0.0001, 0.002), 0.01 (0.00, 0.02), 0.04 (0.03, 0.05), 0.06 (0.05, 0.07), 0.08 (0.07, 0.09), 0.10 (0.09, 0.11), 0.12 (0.11, 0.13), 0.17 (0.16, 0.18), 0.22 (0.21, 0.23), 0.26 (0.25, 0.27), 0.30 (0.29, 0.31), 0.34 (0.33, 0.35), 0.36 (0.35, 0.37), 0.39 (0.38, 0.40), 0.44 (0.43, 0.45), 0.49 (0.48, 0.50), 0.53 (0.52, 0.54), 0.57 (0.56, 0.58), 0.60 (0.59, 0.61), 0.64 (0.63, 0.65), 0.68 (0.67, 0.69), 0.72 (0.71, 0.73), 0.76 (0.75, 0.77), 0.80 (0.79, 0.81), 0.84 (0.83, 0.85), 0.88 (0.87, 0.89), 0.92 (0.91, 0.93), 0.96 (0.95, 0.96), 1.00 (0.99, 1.00) | 7 |

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| Author, year, location | Study design | Participant characteristics | Methods and timing of data collection | Biomarker analyses | Biomarkers | Correlation r (95%CI)/mean | NOS quality score |
|------------------------|-------------|-----------------------------|--------------------------------------|-------------------|-----------|--------------------------|------------------|
| Pope et al. [33] 2014, Australia | Cross-sectional | Sample size: 91 Maternal age (a): 33.7 ± 4.9 Malaria setting: No Iron supplementation: NR | Maternal blood at delivery Umbilical cord blood at delivery Inflammation biomarkers: CRP Factors adjusted: NR | Biochemistry analyser for serum iron, TIBC; automated haematology analyser for haematologic indices | Maternal: Ferritin Newborn: Ferritin | r = −0.05 (−0.25, 0.16) | 4 |
| Qaiser et al. [65] 2013, Pakistan | Cross-sectional | Sample size: 404 Maternal age (a): 15–45 Malaria setting: Yes Iron supplementation: NR | Maternal venous blood during labour Umbilical cord blood at delivery Inflammation biomarkers: NR Factors adjusted: NR | Standard coultergram using Beckman Coulter Max M | Maternal: Hb Newborn: Hb | r = 0.12 (0.02, 0.22) | 6 |
| Ramirez-Cardich et al. [34] 2004, Peru | Cross-sectional | Sample size: 36 Maternal age (a): 28.1 ± 1.1 Malaria setting: Yes Iron supplementation: NR | Maternal blood <12 h prior to delivery Umbilical cord blood at delivery Inflammation biomarkers: NR Factors adjusted: NR | Microcapillary method | Maternal: Ht Newborn: Ht | r = −0.57 (−0.76, −0.30) | 5 |
| Rioux et al. [85] 2001, Canada | Retrospective cohort | Sample size: 952 Maternal age (a): NR Malaria setting: No Iron supplementation: NR | Maternal blood collected at 1st, 2nd and 3rd trimester and 12 hrs postpartum Neonatal blood <48 hrs after delivery Inflammation biomarkers: NR Factors adjusted: NR | NR | Maternal: Hb Newborn: Hb, Ht | r = 0.11 (0.07, 0.19), 0.08 (0.02, 0.14) | 5 |
| Rusia et al. [35] 1996, India | Cross-sectional | Sample size: 100 Maternal age (a): 17–39 Malaria setting: Yes Iron supplementation: NR | Maternal venous blood during labour Umbilical cord blood at delivery Inflammation biomarkers: NR Factors adjusted: NR | Automated particle counter for haematologic indices. ELISA for ferritin Method for serum iron NR | Maternal: Ferritin Newborn: Ferritin | r = 0.44 (0.27, 0.58) | 4 |
| Author, year, location | Study design | Participant characteristics | Methods and timing of data collection | Biomarker analyses | Biomarkers | Correlation r (95%CI)/mean | NOS quality score |
|------------------------|-------------|-----------------------------|-------------------------------------|--------------------|----------------------|--------------------------|----------------|
| Shao et al. [66] 2012, China | Cross-sectional | Sample size: 3891
Maternal age (a): 26.4 ± 3.6/ 20–35
Malaria setting: Yes
Iron supplementation: NR | Timing of maternal blood collection NR
Umbilical cord blood at delivery
Inflammation biomarkers: CRP
Factors adjusted: NR | Maternal: Serum iron
Newborn: Serum iron
Maternal: TF Sat
Newborn: TF Sat
Maternal: Hb
Newborn: Hb
Maternal: Ferritin
Newborn: Ferritin, Hb | $r = 0.30 (0.11, 0.47)$
$r = 0.41 (0.23, 0.56)$
$r = 0.07 (0.04, 0.10), 0.01 (−0.02, 0.04)$ | 6 |
| Shukla et al. [83] 2019, India | Prospective cohort | Sample size: 163
Maternal age (a): NR
Malaria setting: Yes
Fe supplementation: NR | Timing of maternal blood collection NR
Venous blood at 14 weeks
Inflammation biomarkers: NR
Factors adjusted: NR | Maternal: Hb
Newborn: Hb
Maternal: Ferritin
Newborn: Ferritin | $r = 0.23 (0.08, 0.37)$ | 7 |
| Sichieri et al. [67] 2006, Brazil | Cross-sectional | Sample size: 82
Maternal age (a): NR
Malaria setting: Yes
Iron supplementation: NR | Maternal venous blood; timing NR
Umbilical cord blood at delivery
Inflammation biomarkers: NR
Factors adjusted: NR | Maternal: Serum iron
Newborn: Serum iron
Maternal: Hb
Newborn: Hb
Maternal: Serum iron
Newborn: Serum iron | $r = 0.23 (0.08, 0.37)$
$r = 0.21 (−0.007, 0.41)$ | 4 |
| Sikorsi et al. [68] 1998, Poland | Cross-sectional | Sample size: 100
Maternal age (a): 15–42
Malaria setting: No
Iron supplementation: NR | Maternal venous blood during labour
Umbilical cord blood at delivery
Inflammation biomarkers: NR
Factors adjusted: NR | Maternal: Serum iron
Newborn: Serum iron
Maternal: Hb
Newborn: Hb
Maternal: Ht
Newborn: Ht | $r = 0.04 (−0.18, 0.25)$
$r = 0.15 (−0.07, 0.36)$ | 3 |
| Singla et al. [36] 1978, India | Cross-sectional | Sample size: 85
Maternal age (a): NR
Malaria setting: Yes
Iron supplementation: NR | Maternal venous blood during labour
Umbilical cord blood at delivery
Inflammation biomarkers: NR
Factors adjusted: NR | Maternal: Serum iron
Newborn: Serum iron | $r = 0.41 (0.22, 0.58)$ | 5 |
| Srivastava et al. [37] 2002, India | Cross-sectional | Sample size: 54
Maternal age (a) NR
Malaria setting: Yes
Iron supplementation: NR | Maternal blood at delivery
Umbilical cord blood at delivery
Inflammation biomarkers: NR
Factors adjusted: NR | Maternal: Serum iron
Newborn: Serum iron | $r = 0.33 (0.12, 0.50)$
$r = 0.73 (0.61, 0.82)$ | 5 |
| (continued on next page) | | | | | | |

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| Author, year, location | Study design | Participant characteristics | Methods and timing of data collection | Biomarker analyses | Biomarkers | Correlation r (95%CI)|mean | NOS quality score |
|------------------------|-------------|-----------------------------|-------------------------------------|-------------------|-----------|-------------------|------|-----------------|
| Tamura et al. [82] 1999, USA | Prospective cohort | Maternal age (a): Mothers of female neonates: 24.6 ± 4.3; mothers of male neonates: 24.1 ± 4.3 | Maternal blood at 10–36 weeks | Maternal: Ferritin | Ferritin | r = 0.32 (0.21, 0.43) (male babies), r = 0.05 (−0.03, 0.21) (female babies) | 3 | 43 |
| Tekinalp et al. [69] 1996, Turkey | Cross-sectional | Sample size: 76 | Maternal venous blood postpartum | ELISA | Ferritin | r = 0.16 (−0.06, 0.38) (anaemic mothers), r = 0.33 (0.12, 0.52) (non-anaemic mothers) | 6 | |
| Terefe et al. [38] 2015, Ethiopia | Cross-sectional | Maternal age (a): Median age 23; IQR 21–27 | Maternal venous blood during labour | Automated Cobas for ferritin, Automated analyser for haematologic indices | Ferritin, Hb, MCHb, MCV | r = 0.38 (0.19, 0.55), 0.28 (0.08, 0.46), 0.10 (−0.11, 0.30), −0.05 (−0.26, 0.16) | 6 | |
| Tamilsina et al. [70] 2018, Nepal | Cross-sectional | Maternal age (a): 26.0 ± 3.5 | Maternal venous blood when presenting for delivery | Haematology analyser | Ferritin, Hb, MCHb, MCV | Maternal: Hb Newborn: Hb | r = 0.25 (0.04, 0.44), 0.22 (0.01, 0.41), 0.15 (−0.06, 0.35), 0.06 (−0.15, 0.26) r = 0.50 (0.34, 0.62) | 6 | |
| Vahlquist et al. [71] 1975, Sweden | Cross-sectional | Maternal age (a): NR | Timing of maternal blood collection | Radioimmunodiffusion | Ferritin | r = 0.11 (−0.08, 0.29) | 2 | |
| Vasquez-Molina et al. [72] 1982, Mexico | Cross-sectional | Maternal age (a): 26.3 ± 4.2/15–43 | Maternal venous blood during labour | Cyanmethaemoglobin for Hb. Microcapillary for Ht. Chemiluminometric assay for ferritin | Ferritin | r = 0.14 (−0.01, 0.29) | 5 | |
| Vobecky et al. [73] 1982, Canada | Cross-sectional | Maternal blood at 10–36 weeks | Maternal venous blood during labour | Cyanmethaemoglobin for Hb. Photometric determination for ferritin | Ferritin | r = 0.11 (−0.04, 0.26) | 5 | |

(continued on next page)
| Author, year, location | Study design       | Participant characteristics | Methods and timing of data collection | Biomarker analyses | Biomarkers | Correlation r (95%CI)/mean | NOS quality score |
|------------------------|--------------------|------------------------------|--------------------------------------|-------------------|-----------|-----------------------------|-------------------|
| Wong et al. [39]       | Cross-sectional    | Sample size: 72 Maternal age (a): 28.1 ± 4.9/16–41 Malaria setting: No Iron supplementation: NR | Maternal venous blood at delivery Umbilical cord blood at delivery Inflammation biomarkers: NR Factors adjusted: NR | ELISA            | Maternal: Ferritin Newborn: Ferritin | Maternal 17.4 ± 12.5 μg/L; Newborn 142±68.6 μg/L | 4 |
|                        |                    |                             |                                      |                   |           |                             |                   |
| Wong et al. [40]       | Cross-sectional    | Sample size: 352 Maternal age (a): NR Malaria setting: No Iron supplementation: NR | Maternal venous blood at delivery Umbilical cord blood at delivery Inflammation biomarkers: NR Factors adjusted: NR | Rocket immunoelectrophoresis | Maternal: TF Newborn: TF | r = 0.0064 (–0.10, 0.11) | 2 |
| Yepez et al. [74]      | Cross-sectional    | Sample size: 84 Maternal age (a): 20.2 ± 3.3 Malaria setting: Yes Iron supplementation: None | Maternal venous blood during labour Umbilical cord blood at delivery Inflammation biomarkers: NR Factors adjusted: NR | Cyanmethaemoglobin for Hb. Microcentrifugation for Ht. Colorimetric technique for serum iron. ELISA for ferritin | Maternal: Ferritin Newborn: Hb | r = 0.25 (0.04, 0.44) | 5 |

a, years; BMI, body mass index; CRP, C-reactive protein; ELISA, enzyme-linked immunoassay; Hb, haemoglobin; Ht, haematocrit; MCHB, mean corpuscular haemoglobin; MCV, mean corpuscular/cell volume; NR, not reported; sTfR, serum/soluble transferrin receptor; TF, transferrin; TF Sat, transferrin saturation; TIBC, total iron binding capacity; ZPP, zinc protoporphyrin.
There are several study limitations that warrant discussion. Meta-analyses were limited to bivariate analyses of linear relationships; however, consideration of multiple indices in tandem, using more complex (i.e. non-linear) models may provide better predictive ability of neonatal and neonate outcomes. As noted above, consideration of inflammation markers, either as a correction or means to exclude values is likely to improve the predictive ability of various maternal indices; since this information was not readily available,
this analysis was beyond the purview of this systematic review. Finally, although multiple electronic databases were searched, relevant articles from grey literature may have been missed.

In conclusion, the results from the present meta-analyses emphasize the lack of strong correlations between haematological indices and iron biomarkers between mother and the newborn child. Adequate iron is critical for optimal growth and development in early infancy; maternal ID may interfere with foetal iron accretion in the late stages of gestation, and thus early identification of neonatal ID and anaemia is important. These results presented herein suggest that neonatal iron status cannot be accurately ascertained by relying on maternal indices alone due to poor correlations between these indices. Therefore, sources of blood more proximal to the neonate (e.g. cord blood) may be more appropriate for assessment of iron and haematologic indices. This strategy could inform neonatal iron supplementation regimens, thereby improving offspring health during this critical period of growth and development.

**Contributors**

- Study design: SLB, MBO
- Protocol development: SLB, MBO, TC
- Search strategy: TC
- Screening of research results: OBS, MBO, SR, JL, SLB, AGW
- Manuscript writing and editing: OBS, SLB, MBO, AGW
- Database search: TC
- Data analysis: OBS, MBO

Fig. 3. Risk of bias assessments of included cohort studies. (A) Review author judgments about the risk for each bias item presented as percentages across all included studies. (B) Review author judgments about the risk for each bias item in all included studies.
Table 2  
Summary of Correlations Between Maternal Iron Biomarkers and Neonatal Iron and Haematological Indices.

| Mother | Neonate | Number of Studies and References | Pooled weighted mean correlation coefficient (95% CI) | Schmidt-Hunter |
|--------|---------|----------------------------------|-----------------------------------------------|----------------|
| Ferritin (n = 29) | Ferritin | 27[23,27,30,32,33,35,38,43 – 45,48,51,57, 58,59,62,64,66,69,72,76,80 – 83] | 0.14 (0.07, 0.20) – Negligible | P = 0.001 |
| Hepcidin | 1[76] | Not calculated | 0.21 (–0.02, 0.45) – Negligible | P = 0.08 |
| Plasma/serum iron | 6[27,30,58,64,76] | Not calculated | 0.10 (–0.19, 0.39) – Negligible | P = 0.50 |
| Tf Sat | 5[27,30,59,64,76] | Not calculated | –0.09 (–0.33, 0.14) – Negligible | P = 0.43 |
| TIBC | 6[27,30,58,64,76] | Not calculated | Not calculated | P = 0.32 |
| ZPP | 1[64] | Not calculated | 0.05 (–0.05, 0.15) – Negligible | P = 0.32 |
| Hb | 8[27,32,38,57,64,66,74,76] | 0.21 (0.02, 0.45) – Negligible | 0.09 (0.33, 0.14) – Negligible | P = 0.50 |
| Tf Sat | 5[27,30,59,64,76] | Not calculated | Not calculated | P = 0.32 |
| TIBC | 6[27,30,58,64,76] | Not calculated | Not calculated | P = 0.32 |
| ZPP | 1[64] | Not calculated | 0.05 (–0.05, 0.15) – Negligible | P = 0.32 |
| MCHb | 2[27,38] | Not calculated | 0.15 (–0.06, 0.35) – Negligible | P = 0.16 |
| MCV | 3[27,38,64] | Not calculated | Not calculated | P = 0.16 |
| Serum Iron (n = 23) | Ferritin | 5[27,38,59,64,76] | 0.33 (0.13, 0.52) – Low positive | P = 0.001 |
| Hepcidin | 1[76] | Not calculated | 0.42 (0.18, 0.66) – Low positive | P = 0.001 |
| Plasma/serum iron | 1[76] | Not calculated | 0.30 (0.19, 0.40) – Low positive | P = 0.001 |
| Tf Sat | 1[76] | Not calculated | 0.35 (0.12, 0.58) – Low positive | P = 0.003 |
| TIBC | 1[76] | Not calculated | Not calculated | P = 0.02 |
| Hb | 1[76] | Not calculated | 0.42 (0.09, 0.75) – Low positive | P = 0.01 |
| Hepcidin | 1[76] | Not calculated | 0.30 (0.19, 0.40) – Low positive | P = 0.001 |
| Plasma/serum iron | 23[22,27,29,31,33,35 – 37,46,50,53,55,57 – 59,64,67,68,73,74,76,80] | 0.30 (0.19, 0.40) – Low positive | 0.09 (–0.08, 0.26) – Negligible | P = 0.28 |
| Tf Sat | 4[27,59,64,76] | 0.42 (0.09, 0.75) – Low positive | 0.09 (–0.08, 0.26) – Negligible | P = 0.28 |
| TIBC | 5[27,59,64,76] | 0.42 (0.09, 0.75) – Low positive | 0.09 (–0.08, 0.26) – Negligible | P = 0.28 |
| ZPP | 1[64] | Not calculated | 0.42 (0.09, 0.75) – Low positive | P = 0.01 |
| Hb | 4[27,59,64,76] | 0.42 (0.09, 0.75) – Low positive | 0.09 (–0.08, 0.26) – Negligible | P = 0.28 |
| MCHb | 1[27] | 0.42 (0.09, 0.75) – Low positive | 0.09 (–0.08, 0.26) – Negligible | P = 0.28 |
| MCV | 2[27,64] | Not calculated | 0.42 (0.09, 0.75) – Low positive | P = 0.01 |
| sTfR (n = 2) | 2[27,64] | Not calculated | Not calculated | P = 0.01 |
| Tf (n = 3) | 3[42,40,71] | Not calculated | Not calculated | P = 0.01 |
| Tf Sat (n = 9) | Ferritin | 4[30,59,64,76] | 0.07 (–0.23, 0.38) – Negligible | P = 0.64 |
| Hepcidin | 1[76] | Not calculated | 0.18 (–0.05, 0.41) – Negligible | P = 0.12 |
| Plasma/serum iron | 4[30,59,64,76] | 0.18 (–0.05, 0.41) – Negligible | 0.20 (0.08, 0.31) – Negligible | P = 0.001 |
| Tf Sat | 9[29,30,33,35,36,55,59,64,76] | 0.20 (0.08, 0.31) – Negligible | 0.06 (–0.22, 0.34) – Negligible | P = 0.001 |
| TIBC | 4[30,59,64,76] | 0.06 (–0.22, 0.34) – Negligible | 0.06 (–0.22, 0.34) – Negligible | P = 0.001 |
| ZPP | 1[64] | Not calculated | 0.06 (–0.22, 0.34) – Negligible | P = 0.001 |
| Hb | 2[64,76] | Not calculated | 0.06 (–0.22, 0.34) – Negligible | P = 0.001 |
| MCV | 1[64] | Not calculated | 0.06 (–0.22, 0.34) – Negligible | P = 0.001 |
| TIBC (n = 8) | Ferritin | 5[30,59,64,76] | 0.04 (–0.21, 0.29) – Negligible | P = 0.75 |
| Serum Iron | 5[30,59,64,76] | 0.04 (–0.21, 0.29) – Negligible | 0.04 (–0.21, 0.29) – Negligible | P = 0.75 |
| TIBC | 4[30,59,64,76] | 0.04 (–0.21, 0.29) – Negligible | 0.04 (–0.21, 0.29) – Negligible | P = 0.75 |
| ZPP | 2[64,76] | Not calculated | 0.04 (–0.21, 0.29) – Negligible | P = 0.75 |
| Hb | 1[64] | Not calculated | 0.04 (–0.21, 0.29) – Negligible | P = 0.75 |
| MCV | 1[64] | Not calculated | 0.04 (–0.21, 0.29) – Negligible | P = 0.75 |
| ZPP (n = 2) | Ferritin | 1[64] | Not calculated | 0.16 (0.01, 0.31) – Negligible | P = 0.03 |
| Plasma/serum iron | 1[64] | Not calculated | 0.16 (0.01, 0.31) – Negligible | P = 0.03 |
| Tf | 1[61] | Not calculated | 0.16 (0.01, 0.31) – Negligible | P = 0.03 |
| Tf Sat | 1[64] | Not calculated | 0.16 (0.01, 0.31) – Negligible | P = 0.03 |
| TIBC | 1[64] | Not calculated | 0.16 (0.01, 0.31) – Negligible | P = 0.03 |
| ZPP | 1[64] | Not calculated | 0.16 (0.01, 0.31) – Negligible | P = 0.03 |
| Hb | 2[61,64] | Not calculated | 0.16 (0.01, 0.31) – Negligible | P = 0.03 |
| MCV | 1[64] | Not calculated | 0.16 (0.01, 0.31) – Negligible | P = 0.03 |

Hb=haemoglobin; MCHb=mean corpuscular haemoglobin; MCV=mean cell volume; NOS=Newcastle-Ottawa scale; sTfR=soluble/serum transferrin receptor; TIBC=total iron binding capacity; Tf=transferrin; Tf Sat=transferrin saturation; ZPP= zinc protoporphyrin.
Declaration of Competing Interest

Dr. Ospina reports grants from the Women and Children’s Health Research Institute, grants and other from Canada Research Chairs (Government of Canada), during the conduct of the study. Dr. Bourque reports grants from the Canadian Institutes of Health Research (Government of Canada), grants from the Women and Children’s Health Research Institute, grants and other from Canada Research Chairs (Government of Canada), during the conduct of the study.

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Data sharing

The datasets used and/or analysed during the current study are available from the corresponding author upon reasonable request.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.eclinm.2020.100555.

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Table 3

Summary of correlations between maternal haematological indices and neonatal iron and haematological indices.

| Mother | Neonate | Number of Studies and References | Pooled weighted mean correlation coefficient (95% CI)(Schmidt-Hunter) |
|--------|---------|----------------------------------|---------------------------------------------------------------|
| Hb (n = 32) | Ferritin | 6[23,32,38,58,62,76] | 0.16 (−0.12, 0.43) – Negligible |
| | Hepcidin | 1[76] | Not calculated |
| | Plasma/serum iron | 5[25,54,58,64,76] | 0.29 (0.04, 0.54) – Negligible |
| | sTfR | 2[56,35] | Not calculated |
| | Tf Sat | 3[27,64,76] | 0.35 (−0.05, 0.75) – Low positive |
| | TIBC | 4[25,58,64,76] | −0.22 (−0.52, 0.08) – Negligible |
| | ZPP | 1[64] | Not calculated |
| | Hb | 32[21,26−29,32,33,35,36,38,42,47,49,54,57,59,63−65,70,72−74,76,78,81,83,85,88] | 0.15 (0.10, 0.20) – Negligible |
| | Ht | 3[25,28,85] | 0.13 (0.007, 0.25) – Negligible |
| | MCHb | 2[27,38] | Not calculated |
| | MCV | 3[27,38,64] | 0.20 (−0.07, 0.46) – Negligible |
| Ht (n = 13) | Ferritin | 2[32,58] | Not calculated |
| | Plasma/serum iron | 1[58] | Not calculated |
| | sTfR | 1[24] | Not calculated |
| | Tf Sat | 1[58] | Not calculated |
| | Hb | 3[28,32,85] | 0.14 (0.04, 0.25) – Negligible |
| | Ht | 10[28,29,34,47,65,67,70,72,73,85] | 0.15 (0.06, 0.23) – Negligible |
| MCHb (n = 6) | Ferritin | 1[58] | Not calculated |
| | Plasma/serum iron | 1[58] | Not calculated |
| | Tf Sat | 1[58] | Not calculated |
| | MCV | 6[33,42,47,63,65,70] | 0.22 (0.10, 0.33) – Negligible |
| | MCHb | 5[33,42,47,65,70] | 0.25 (0.08, 0.43) – Negligible |

Hb=haemoglobin; Ht=haematocrit; MCHb=mean corpuscular haemoglobin; MCV=mean cell volume; NOS=Newcastle-Ottawa scale; sTfR=soluble/serum transferrin receptor; TIBC=total iron binding capacity; Tf=transferrin; Tf Sat=transferrin saturation; ZPP= zinc protoporphyrin.
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