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904.OUTCOMES RESEARCH-NON-MALIGNANT CONDITIONS

Direct Effect of Iron Deficiency Independent of Anemia on Adverse Perinatal Outcomes- a Scoping Review

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Introduction
Iron is required throughout pregnancy by both the pregnant individual and the fetus. Iron stores can be depleted during pregnancy resulting in iron deficiency (ID), which is the most common cause of anemia in pregnancy. Iron deficiency anemia (IDA) is associated with an approximately two-fold increase in adverse perinatal outcomes (APO) such as low birth weight (LBW), preterm delivery, and stillbirth. It is uncertain whether depleted iron store in a non-anemic pregnant individual affects fetal growth and well-being. The effect of ID per se on these outcomes, independent of anemia, is the central focus of this scoping review.
If an independent association between iron deficiency without anemia (IDWA) and these APO is established and given the potential for non-anemic iron deficiency to progress to IDA, early screening, and intervention before the development of IDA may be important in preventing these morbidities and mortality. Our objective is to determine the current state of existing knowledge concerning IDWA and APO. The specific aims are to determine the prevalence of IDWA in pregnant individuals, assess predictors and determine types of APO associated with IDWA.
Methods
We performed a comprehensive systematic scoping review of the independent effect of IDWA on APO. The search for relevant studies involved Ovid Medline, Cochrane Database of Systematic Reviews, Cochrane Control Register of Controlled Trials, and hand search of citations of relevant articles for cohort and cross-sectional studies, randomized controlled trials, systematic reviews, and meta-analyses, scoping and narrative reviews from the inception of the databases. We used all relevant Medical Subject Headings terms and subheadings with no language restrictions.
Two reviewers independently screened titles, abstracts, and full text based on the outlined inclusion and exclusion criteria. The inclusion criteria include relevant studies reporting on IDWA in pregnancy and APO. Exclusion criteria include studies not reporting IDWA and APO, and the presence of medical conditions such as hemoglobinopathies, polycythemia, iron overload, autoimmune and inflammatory conditions. Discrepancies were resolved through discussion and consensus. Covidence ® systematic review software was used for screening, automatically eliminating duplicates and data extraction. PRISMA for Scoping Reviews reporting guidelines was used. The selection process and results of included and excluded studies were presented with a PRISMA flow chart. A narrative summary was conducted to descriptively summarize the findings.
Results
A total of 4389 articles were identified from the searched databases after all duplicates were removed. Two studies conducted between 2005-2008 and 2017-2018 respectively met the inclusion criteria and were eligible for data extraction. A total of 5684 participants made up of 5479 Danish and 205 Spanish cohorts were included. The prevalence of IDWA in Denmark was 14.2% based on serum ferritin of $<30\mu g/L$ and hemoglobin $\geq 110g/L$ and 20% in Spain using thresholds of SF $<12\mu g/L$ and Hb$\geq$110g/L. The mean (standard deviation, SD) age of participants was 31.8 ± 5.0 years in Denmark, and the mean (95% CI) was 31.0 (29.4-32.6) years in Spain. In the Danish study, the babies had a mean (SD) birth weight of 3508±523g and were on average 192g smaller (p=0.028). The mean (SD) gestational age (GA) at delivery was 39.8±1.7 weeks, adjusted odds ratio

(95%CI) of LBW was 0.6 (0.4-1.0), stillbirth 4.0(1.0-14.3) and gestational diabetes mellitus 1.1 (0.7-1.7) in the IDWA group. The Spanish study reported a mean (95% CI) infant birth weight (IBW) of 3140 (3067-3213) g, reduction in adjusted IBW of -192.4 (-363.6, -21.2)g, p=0.028, $R^2_{c.100} = 35.4$, $F_{194,11} = 9.3$, $p<0.001$ in IDWA. Both studies reported the covariates and predictors of APO including parity, race, body mass index, and socioeconomic status.

Conclusion

Overall, there is limited research on this important obstetric hematology topic. The few available studies identified higher odds of non-causal association between IDWA, stillbirth, and smaller birth weight. Similarly, there was a non-significant causal association with most predictors and maternal medical complications of pregnancy. These findings will motivate further research work by our team. The study will involve the use of large population-based data to establish a potential causal association between IDWA and APO.

Disclosures No relevant conflicts of interest to declare.

Figure 1: PRISMA flow chart

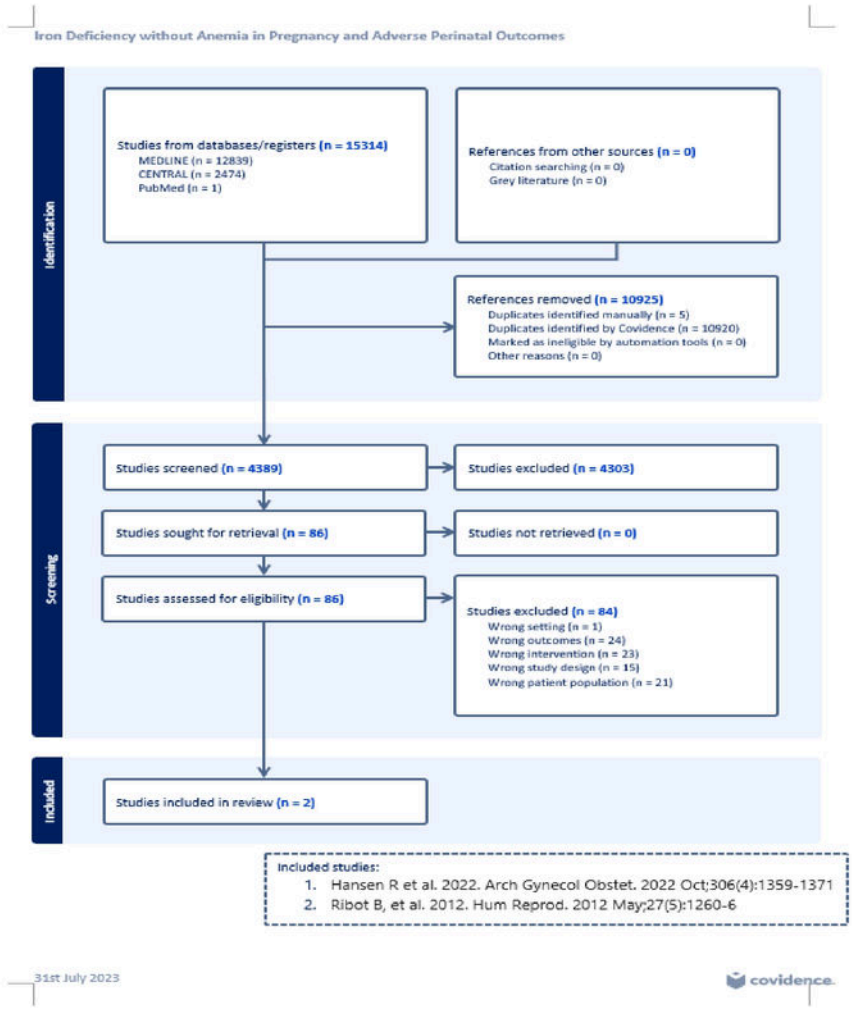

Table 1: Characteristics of participants and perinatal outcomes

Study	Age of participants (years) Mean (SD)	Age of participants (years) Mean (95% CI)	GA (weeks) Mean (SD)	Gestational length (weeks) Mean (95% CI)	BWT (grams) Mean (SD)	IBW (grams) Adjusted for gestation weeks	LBW Crude OR	LBW AOR	Preterm % (95%CI)	Stillbirth Crude OR	Stillbirth AOR
Hansen et al. 2022, Denmark (2017-2018). n=5479	31.8 ± 5.0		39.8±1.7		3508±523		0.7 (0.4–1.0)	0.6 (0.4–1.0)		3.0 (0.8–9.5)	4.0 (1.0–14.3)
Ribot et al. 2012, Spain (2005-2008). n=205		31.0 (29.4–32.6)		38.7 (38.2–39.2)		3140 (3067–3213)			5.4 (-1.5–12.3)		

BWT= Birth weight, GA= Gestational age at delivery, SD= Standard deviation, CI= Confidence interval, OR= Odds ratio, AOR= Adjusted Odds ratio, LBW= Low birth weight, IBW= Infants birth weight

Figure 1

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