Adjusting Iron Biomarkers for Inflammation in Pregnant Women: Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia (BRINDA) Project

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Objectives: Accurate assessment of iron deficiency during pregnancy is essential for program planning and interventions. We aimed to examine the relationship between serum ferritin (SF) and soluble transferrin receptor (sTfR) and inflammation and examine the impact of inflammation on the prevalence of iron deficiency in a large multi-country analysis.

Methods: Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia (BRINDA) project provided 17 pregnancy datasets (n = 14,077) from 15 countries including at least one iron (serum ferritin, SF; soluble transferrin receptor, sTfR) and inflammation biomarker (C-reactive protein, CRP or α-1-acid glycoprotein, AGP). Spearman rank correlations between CRP or AGP and iron biomarkers (SF, sTfR) were examined. We report unadjusted and adjusted prevalence of iron deficiency, using the BRINDA regression correction approach to adjust for inflammation on behalf of the BRINDA Pregnancy Workgroup.

Results: Ferritin concentrations were positively correlated with CRP in 6 out of 14 surveys (ρ from 0.65 in Mexico, $P < 0.0001$ to 0.06 in Vietnam, $P < 0.05$) and AGP in 8 out of 9 surveys (correlation coefficients (ρ) ranging from 0.41, in Guatemala to 0.19 in Pakistan, $P < 0.0001$). Among the 8 datasets with both CRP and AGP, adjustment for both AGP and CRP increased the estimated prevalence of iron deficiency (ferritin < 15 μg/L) by a median of 18.8 percentage points (pp) compared to 15.6 pp for AGP alone and 10.5 pp for CRP alone. sTfR concentrations were positively correlated with AGP in 4 out of 12 surveys (ρ ranging from 0.36 in Vietnam to 0.09 in Pakistan, $P < 0.01$) and positively associated with CRP in 4 out of 10 surveys (ρ ranging from 0.20 in Vietnam to 0.07 in US and Ghana, $P < 0.05$).

Conclusions: Failing to adjust for inflammation during pregnancy appears to underestimate iron deficiency using serum ferritin during pregnancy. Given the weak and inconsistent association between sTfR and inflammation, adjustment of sTfR biomarkers during pregnancy does not appear warranted at this time.

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