

# Do pregnant women with anemia need iron supplementation?

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As shown in the January issue of the *Journal of the Chinese Medical Association (J Chin Med Assoc—JCMA)*, we have indicated that any recommendation for supplementation of any one of trace elements, heavy metals and micronutrients, should be based on the evidence,<sup>1</sup> even though these micronutrients, for example, iron, iodine, etc., are really essentially and significantly increasing demanded in pregnant women and their deficiency might be strongly correlated with worse pregnancy outcome.<sup>2–6</sup> Among these, iron may be one of the most recommended micronutrients for pregnant women by many obstetricians, although Asadi et al<sup>7</sup> suggested no need of iron supplementation in normally healthy women, based on absence of any additional benefits, but an increased risk in the development of gestational diabetes mellitus (GDM). Since iron deficiency anemia (IDA) is very common in pregnant women with an incidence of up to 50%,<sup>1</sup> it is interesting to know the outcome of these anemic pregnant women.

In the current issue of the *JCMA*, one domestic data addressing this topic has been published.<sup>8</sup> The authors used two thresholds (10.8 g/dL and 9.9 g/dL, respectively) to evaluate the pregnancy outcome.<sup>8</sup> The results showed that pregnant women with hemoglobin <10.8 g/dL had a higher risk of primary cesarean section (odds ratio [OR] 1.12, 95% confidence interval [CI] 1.01–1.26), polyhydramnios (OR 2.53, 95% CI 1.23–5.17), and preterm premature rupture of membranes (PPROM) (OR 1.66, 95% CI 1.19–2.33), contributing to associated worse neonatal outcomes, such as early preterm birth (<34 gestational weeks) with OR of 2.16 (95% CI 1.54–3.03), very low birth weight (<1500 g) with OR of 2.08 (95% CI 1.22–3.52), and neonatal intensive care unit (NICU) transfer with OR of 1.72 (95% CI 1.31–2.26).<sup>8</sup> The worse pregnant and neonatal outcomes seemed to be more apparent in those pregnant women with severe anemia status (hemoglobin <9.9 g/dL), because the following risks were statistically increased, including primary cesarean section (OR 1.32, 95% CI 1.10–1.58), PPRM (OR 1.83, 95% CI 1.10–3.02), early preterm birth (OR 3.01, 95% CI 1.94–4.69), very low birth weight (OR 2.54, 95% CI 1.16–5.15), and NICU

transfer (OR 2.15, 95% CI 1.47–3.15).<sup>8</sup> All showed the strong correlation between anemic pregnant women and worse pregnant and neonatal outcomes. Since anemia is very common in pregnant women, the anemia-related adverse events in pregnancy should be emphasized.

It is sometimes difficult to define the anemia.<sup>1</sup> The use of the fifth percentile and 10th percentile as thresholds to study the outcome of anemic pregnant women by authors is their strength in the current study.<sup>8</sup> However, the timing to define anemia may be critical, since it is possible that anemia may be a result but not a causal factor. In fact, the authors have shown it as their limitations and the authors also agree with these potential biases, such as absence of the fixed time to obtain the hemoglobin level and no data for iron supplementation in these pregnant women.<sup>8</sup> It is well-known that hemoglobin level varies greatly in the different trimester, which is higher in the first trimester physiologically. Without the use of hemoglobin data at the same gestational weeks (e.g., initial laboratory data at the first visit to obstetricians, which are often performed in the first trimester), it is hard to claim the correlation between anemia and outcome. For example, bleeding is common in preterm labor and PPRM.<sup>9</sup> Hosny et al<sup>9</sup> found heavy vaginal bleeding was a risk factor for PPRM and preterm birth, suggesting that anemia may be a result secondary to heavy vaginal bleeding but not a cause to result in preterm labor or PPRM. Therefore, if the data containing serum ferritin, transferrin levels or others for defining anemia, of which might be reflective of chronic anemia status,<sup>10</sup> could be available in the current study, the correlation between anemia and preterm labor, PPRM or others might be more convinced.

In addition, the prevalence rate of thalassemia is restively high in Taiwan.<sup>11,12</sup> Thalassemia-carrier mothers might have a high risk of worse pregnancy and/or neonatal outcome compared to those mothers without thalassemia. If the anemia pregnant women secondary to thalassemia are not excluded, objective errors in the methods, applications, or interpretation might impede the value of the current stud. To overcome this limitation, the measurement of the aforementioned anemia markers, such as serum ferritin or transferrin levels, can easily identify concomitant iron deficiency and exclude iron loading states in women with a known hemoglobinopathy. High iron states may mediate the adverse events, including oxidative stress, increased blood viscosity, and sub-optimally effective systemic response to inflammation and infection,<sup>13–15</sup> associated with worse pregnant and neonatal outcome, such as GDM, preterm labor, PPRM, and NICU transfer.

Since pregnant women with anemia are commonly found in the clinical practice, suggesting that topic addressing the aforementioned clinical condition is worthy of our attention. After reading Dr. Chu's article, the iron supplementation in pregnant women, specifically for those with IDA can be encouraged, although much evidence is needed.

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