Evaluation of serum ferritin and thyroid function in the second trimester of pregnancy

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Abstract. Ferritin is a universal intracellular protein that acts as an iron carrier. Several studies have indicated that iron deficiency affects thyroid function in non-pregnant women. Our objective was to assess the relationship between serum ferritin levels and thyroid function in pregnant women during the second trimester. Pregnant women with sufficient iodine intake and normal antithyroid antibodies during the second trimester were recruited from the obstetric outpatient department of the Fifth People’s Hospital of Fudan University. Serum ferritin (SF) levels, thyroid function, anti-thyroid antibodies and vitamin B12 were determined by electrochemiluminescence immunoassay kit. Maternal serum iron (Fe), unsaturated iron binding capacity (UIBC), hemoglobin (Hb), creatinine (Cr), fasting blood glucose (FBG), and alanine aminotransferase (ALT) were also evaluated. Stepwise regressions performed to evaluate the associations between SF and other maternal parameters. In the second trimester, 11.4% pregnant women had a SF concentration less than 12 μg/L, and 7.6% pregnant women were anemic. SF levels were negatively correlated with serum TSH levels ($r = –0.219, p < 0.05$), and positively correlated with FT4 levels ($r = 0.203, p < 0.05$). Linear regression analysis showed only SF, age, week of gestation were significant predictors of regression with TSH as the dependent variable ($β$: –0.007, –0.059, and 0.118 respectively; all $p < 0.05$). However consistent relation between the SF levels and FT4 was not observed in stepwise linear regression. Maternal iron status is a determinant of TSH concentrations during pregnancy in pregnant women during the second trimester.

Key words: Serum ferritin, Thyroid function, Thyroid stimulating hormone, Pregnancy, The second trimester

THYROID DISEASE is a common endocrine disorder prevalent in pregnant women. The prevalence of subclinical hypothyroidism and hypothyroxinemia during the second trimester of pregnancy is 5.96% and 2.29%, respectively in China [1]. Maternal thyroid dysfunction has been reportedly associated with gestational hypertension, gestational diabetes, spontaneous abortion, fetal loss, dysplasia, and inadequate neuropsychological development in children [2-5]. Chronic autoimmune thyroiditis is the main cause of hypothyroidism during pregnancy [6, 7]. Iodine deficiency during pregnancy is also an important cause of maternal thyroid dysfunction [8]. Additional variables include obesity and surgical history. Maternal high-fat diet induces obesity and thyroid dysfunction [9] resulting in higher weight in pregnant women with lower FT4 [10-12], isolated hypothyroxinemia with decreasing maternal FT4 and increasing FT3:FT4 ratio [13]. However, other factors affect maternal thyroid function. Several studies are investigating the complex etiology of thyroid dysfunction during pregnancy.

Iron deficiency is the most common nutritional deficiency in the world. There were more than 0.8 billion people suffer from anemia or iron deficiency, and pregnant women are the most vulnerable [14, 15]. Ferritin is a universal intracellular protein that stores iron in most tissues. However, small amounts are secreted into the serum where it functions as an iron carrier. In humans, it acts as a buffer against iron deficiency and iron overload. Hence, serum ferritin has been used for the diagnosis and treatment of iron deficiency anemia (IDA) [16, 17]. In our clinical practice we have noticed TSH elevated rap-
Idly along with the decrease of Hb and SF levels in pregnant women. A few clinical studies have indicated that iron deficiency affects thyroid function during pregnancy. Yu X et al. found that iron deficiency (ID) is an independent risk factor for isolated hypothyroxinemia during the first trimester of pregnancy with appropriate iodine intake in China [18]. Zimmermann MB provided data suggesting that poor maternal iron status predicts higher TSH and lower TT4 during pregnancy in areas of borderline iodine deficiency [19]. However, few studies focused on the role of ferritin in thyroid status of pregnant women during the second trimester excluding the effects of iodine and thyroid autoimmunity. Our objective was to investigate whether maternal serum ferritin is a determinant of TSH and/or free T4 concentrations during pregnancy in an iodine-sufficient area of China.

Materials and Methods

Study Population

This study was carried out in Minhang District, Shanghai, which is an iodine-sufficient area in China. We extracted data from pregnant women screened for thyroid disease as part of their first routine evaluation in obstetric outpatient department of the Fifth People’s Hospital of Fudan University from September 2014 to April 2015. Only pregnant women screened in the second trimester (gestational age ranging between 13 and 24 weeks, calculated on the basis of the last menstrual period) were consecutively enrolled in the study. Recruitment criteria included urban residence; age between 18 and 40 years; and a singleton pregnancy at 13 to 24 weeks of gestation; sufficient iodine intake according to the WHO Technical Consultation recommendation for pregnant women: urinary iodine concentration (UIC) ranging between 150 μg/L and 499 μg/L [20]; a normal titer of thyroid peroxidase antibody (TpoAb) (<34 IU/mL) and anti-Tg antibodies (TgAb) (<115 IU/mL). Exclusion criteria were: multiple pregnancies; patients with history of thyroid disease or other chronic conditions (diabetes, cancer, hypertension, and tuberculosis); anemia before pregnancy and during the first trimester; patients on oral contraceptive (OC) regimens before pregnancy or any medical regimen that may affect thyroid function, such as glucocorticoids, dopamine, or antiepileptic drugs, treatment for infertility, a positive test for HIV and HBsAg. All the participants were asked to complete the questionnaires pertaining to demographic data, parity, education level, history of thyroid diseases and other chronic diseases, and medication usage.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the Helsinki declaration. The study protocols were approved by the Medical Ethics Committee of the Fifth People’s Hospital of Shanghai Fudan University (NO. 002). Informed consent was obtained from all individual participants included in the study.

Sample collection

Totally 209 pregnant women were recruited between September 2014 and April 2015. All the venous blood samples and spot urine samples were collected in the morning (07:00–09:00 h) after an overnight fast of more than 8 h. Blood samples were centrifuged to obtain serum, which was sent to the clinical laboratory for testing or storage in a serum bank at –80°C until further analysis.

Thyroid function test and antithyroid antibodies

The levels of free thyroxine (FT4) (reference range, 12–22 pmol/L), TSH (reference range, 0.27–4.2 mIU/L), TpoAb (cut-off level, 34 IU/mL), and TgAb (cut-off level, 115 IU/mL) were determined in all the subjects on the same day of sampling, utilizing a commercial electrochemiluminescence immunoassay kit (Roche Diagnostics, Cobas 8000 analyzer e602 module, Germany). The intra-assay CVs of TSH, FT4, TpoAb, and TgAb were 1.73% to 2.44%, 1.73% to 2.51%, 4.07% to 7.13%, and 4.20% to 6.60%, respectively. The inter-assay CVs of TSH, FT4, TpoAb, and TgAb were 2.05% to 4.12%, 2.11% to 2.57%, 5.04% to 8.49%, and 5.33% to 7.22%, respectively.

Iron nutrition: indices and biochemical criteria

Maternal serum ferritin (SF) and vitamin B12 were measured using the electrochemiluminescence immunoassay (Roche Diagnostics, Cobas 6000 analyzer e601 module, Germany). An abnormal value of SF was defined as less than 12 μg/L. The intra-assay CV of ferritin and vitamin B12 were 1.38% to 4.3%, 2.90% to 4.92%, respectively. The interassay CV of ferritin and vitamin B12 were 5.11% to 7.52%, 3.14% to 5.37%, respectively. Maternal serum iron (Fe), unsaturated iron binding capacity (UIBC), creatinine (Cr), alanine aminotransferase (ALT), and fasting blood glucose (FBG) were measured using automated chemical analyzer MODULAR P 800 (Roche Diagnostics, Germany). The
intra-assay CVs of Fe, UIBC, Cr, ALT, and FBG were 1.31% to 3.04%, 2.24% to 6.40%, 3.11% to 4.07%, 3.31% to 4.95%, and 2.11% to 3.25%, respectively. The inter-assay CVs were 0.90% to 1.50%, 1.03% to 6.10%, 3.07% to 3.49%, 3.16% to 4.74%, and 2.04% to 2.39%, respectively. Total iron binding capacity (TIBC) was calculated as Fe plus UIBC, and the transferrin saturation (TS) was determined as the ratio of Fe to TIBC. Maternal UIC was measured using the ammonium persulfate method based on Sandell-Kolthoff reaction. The intra-assay and inter-assay CVs of UIC were 2.15% to 4.82%, and 3.06% to 5.66%, respectively. Hemoglobin (Hb) was measured using an automated hematology analyzer XE 2100 D (Sysmex Diagnostics, Japan). Women were classified as anemic if Hb was less than 105 g/L in the second trimester.

**Statistical analysis**

Statistical analysis was performed using the SPSS software (version 17.0; Chicago, IL). Pregnant women were divided into three groups by tri-sectional quantiles method according to maternal SF levels as follows: Group A, ferritin level less than 31.71 μg/L; Group B, ferritin level between 31.71 μg/L and 58.08 μg/L; and Group C, ferritin value more than 58.08 μg/L. Data are presented as mean ± standard deviation or median with 25th and 75th percentiles. Student’s t-test and ANOVA were used for continuous variables. Non-Gaussian parameters were directly compared with Kruskal-Wallis H test. Pearson or Spearman correlation and stepwise linear regression analysis were used to establish the relationship between ferritin and other maternal parameters. p < 0.05 was considered to be statistically significant.

**Results**

**Clinical characteristics of pregnant women with different serum ferritin levels**

On the base of serum ferritin (SF) concentration, we assigned pregnant women into groups A (SF < 31.71 μg/L), B (31.71 ≤ SF ≤ 58.08 μg/L) and C (SF > 58.08 μg/L). The sample characteristics and laboratory data of 209 pregnant women in the second trimester are listed in Table 1. 11.4% (24/209) pregnant women were observed SF concentration less than 12 μg/L, and 7.6% (16/209) pregnant women were anemic. No significant differences in age, BMI and systolic blood pressure (SBP) were found among the different SF concentration groups. On the other hand, the week of gestation decreased progressively with increased SF concentration (p < 0.05).

Interestingly, the TSH level exhibited a significantly decreased trend with increased SF concentration (p < 0.05). Compared with Group A, Group B and Group C pregnant women exhibited significantly lower TSH levels: (2.55 ± 1.64 vs. 3.25 ± 1.72 mIU/L, p < 0.05) and (2.18 ± 1.33 vs. 3.25 ± 1.72 mIU/L, p < 0.05), respectively. The TSH levels were similar in Groups B and C pregnant women (2.55 ± 1.64 vs. 2.18 ± 1.33 mIU/L). 24.8% (52/209) of pregnant women exhibited TSH greater than 4.0 mIU/L. The SF level showed no significant difference in pregnant-week matching women with TSH ≥ 4.0 mIU/L and those with TSH < 4.0 mIU/L (45.11 ± 6.53 vs. 52.96 ± 3.50 μg/L, p > 0.05). Significant differences were also observed in FT4 levels among different SF concentration groups (p < 0.05). Compared with Group C, FT4 levels were substantially different in Group A (14.26 ± 1.45 vs. 14.81 ± 1.65 pmol/L, p < 0.05) and Group B (14.09 ± 1.43 vs. 14.81 ± 1.65 pmol/L, p < 0.05), respectively. FT4 levels in Groups A and B did not show remarkable alteration (14.26 ± 1.45 vs. 14.09 ± 1.43 pmol/L). On the contrary, no significant differences were found in TpoAb and TgAb levels among different SF groups.

Significant differences in Hb, Fe, TIBC, UIBC, TS, vitamin B12 and ALT existed among the three SF groups. Compared with Group A, pregnant women in Groups B and C showed remarkably higher Hb, Fe and TS levels, but significantly lower TIBC, and UIBC levels. However, the levels of Hb, Fe, TIBC, UIBC and TS were similar in Groups B and C. Compared with Group A, only Group C displayed higher ALT and vitamin B12 levels, and the ALT and vitamin B12 levels between Groups A and B along with Groups B and C did not vary significantly. Furthermore, no significant differences in Cr and FBG were observed among the three groups.

There was little impact of low SF level on the obstetrical outcome due to quick medicine prevention. None of 24 pregnant women with SF < 12 μg/L was observed miscarriage and premature delivery because the pregnant women were informed to immediately supplement 100–200 mg iron element per day when SF concentration was less than 12 μg/L, while miscarriage and premature delivery rate in SF ≥ 12 μg/L pregnant women were 1.1% (2/185) and 2.1% (4/185) respectively. No significant differences were found in birth weight among different groups A, B and C (3.342.12 ± 57.06 g, 3.321.12 ± 50.56 g, 3.399.02 ± 64.86 g, respectively, p > 0.05).
Correlation analysis of SF and FT4 or TSH levels revealed that SF levels were positively correlated with FT4 levels ($r = 0.203, p < 0.05$) (Fig. 1), and negatively correlated with serum TSH levels ($r = -0.219, p < 0.05$) (Fig. 2), but were not correlated with TpoAb ($r = -0.022, p = 0.758$) nor TgAb ($r = 0.017, p = 0.813$) in pregnant women during the second trimester.

**Table 1** Clinical characteristics of pregnant women with different serum ferritin levels during the second trimester

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group A (SF &lt; 31.71 μg/L)</th>
<th>Group B (31.71 ≤ SF ≤ 58.08 μg/L)</th>
<th>Group C (SF &gt; 58.08 μg/L)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>69</td>
<td>70</td>
<td>70</td>
<td>—</td>
</tr>
<tr>
<td>Age (years)*</td>
<td>26.85 ± 4.90</td>
<td>27.54 ± 4.60</td>
<td>27.20 ± 3.88</td>
<td>0.66</td>
</tr>
<tr>
<td>BMI (kg/m²)*</td>
<td>21.08 ± 3.25</td>
<td>21.07 ± 2.55</td>
<td>21.28 ± 3.59</td>
<td>0.87</td>
</tr>
<tr>
<td>Gestational age (weeks)*</td>
<td>19.33 ± 2.99</td>
<td>16.88 ± 2.69</td>
<td>15.76 ± 2.17</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>FT4 (pmol/L)*</td>
<td>14.26 ± 1.45</td>
<td>14.09 ± 1.43</td>
<td>14.81 ± 1.65</td>
<td>0.01</td>
</tr>
<tr>
<td>TSH (mIU/L)*</td>
<td>3.25 ± 1.72</td>
<td>2.55 ± 1.64</td>
<td>2.18 ± 1.33</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>TpoAb (IU/mL)+</td>
<td>9.70 (9.30–14.30)</td>
<td>10.90 (9.60–13.40)</td>
<td>9.85 (9.78–14.48)</td>
<td>0.47</td>
</tr>
<tr>
<td>TgAb (IU/mL)+</td>
<td>10.00 (10.00–15.95)</td>
<td>10.00 (9.20–13.30)</td>
<td>10.05 (10.00–15.09)</td>
<td>0.45</td>
</tr>
<tr>
<td>Hb (g/L)*</td>
<td>114.01 ± 10.92</td>
<td>119.59 ± 9.44</td>
<td>120.90 ± 8.30</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Fe (μmol/L)*</td>
<td>17.78 ± 5.31</td>
<td>23.17 ± 6.68</td>
<td>25.32 ± 6.28</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>UIBC (μmol/L)*</td>
<td>54.36 ± 10.73</td>
<td>37.99 ± 8.99</td>
<td>32.33 ± 11.70</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>TIBC (μmol/L)*</td>
<td>72.34 ± 7.69</td>
<td>60.94 ± 6.54</td>
<td>57.65 ± 10.44</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>TS (%)*</td>
<td>25.41 ± 8.63</td>
<td>37.66 ± 11.66</td>
<td>44.82 ± 12.07</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>ALT (U/L)*</td>
<td>14.80 ± 3.15</td>
<td>20.40 ± 4.38</td>
<td>22.26 ± 4.29</td>
<td>0.01</td>
</tr>
<tr>
<td>Cr (μmol/L)*</td>
<td>40.77 ± 5.17</td>
<td>41.14 ± 4.90</td>
<td>42.64 ± 5.90</td>
<td>0.09</td>
</tr>
<tr>
<td>FBG (mmol/L)*</td>
<td>4.32 ± 0.43</td>
<td>4.36 ± 0.44</td>
<td>4.38 ± 0.39</td>
<td>0.68</td>
</tr>
<tr>
<td>VitB12 (pg/mL)</td>
<td>291.01 ± 15.04</td>
<td>326.93 ± 14.46</td>
<td>364.79 ± 16.11</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

* Mean ± standard deviation.
+ Median with interquartile range.
▲ TS : transferrin saturation

![Fig. 1](image1.png)  ![Fig. 2](image2.png)

**Correlation between serum ferritin and other maternal parameters**

Correlation analysis of SF and FT4 or TSH levels revealed that SF levels were positively correlated with FT4 levels ($r = 0.203, p < 0.05$) (Fig. 1), and negatively correlated with serum TSH levels ($r = -0.219, p < 0.05$) (Fig. 2), but were not correlated with TpoAb ($r = -0.022, p = 0.758$) nor TgAb ($r = 0.017, p = 0.813$) in pregnant women during the second trimester.
women during the second trimester. Linear regression analysis showed that SF levels were correlated with TSH and FT4 when TSH and FT4 acted as dependent variables and the covariate only included SF (Table 2). Similar results were also obtained after stepwise addition of further potential risk factors such as age, BMI, Hb and ALT into the model. It’s worth noting that after week of gestation adding into the model the association could be obtained between the TSH and SF. However, no but any consistent relation between the FT4 and SF levels was not observed ($\beta = 0.004$, $p = 0.216$). In brief, only SF ($\beta = -0.007$, $p = 0.020$), age ($\beta = -0.059$, $p = 0.024$), week of gestation ($\beta = 0.118$, $p = 0.007$) were significant predictors of regression with TSH as the dependent variable.

### Discussion

During the second trimester, pregnant women are high vulnerable to iron deficiency (ID) anemia [21]. Serum ferritin reflects body’s iron reserves, which are the most important clinical indicators of ID anemia. Low SF was mainly due to iron requirements along with expansion of blood volume are greater than at other times to maintain maternal tissues, placenta and fetal need, especially in the second and the third trimesters [22]. Diet was another cause of low SF during pregnancy. Golub MS et al. disclosed inadequate intake of diet can induce iron deficiency anemia during pregnancy in rhesus monkeys [23]. However in our experiment, we have not recorded the everyday intake calorie and type of food, so we can’t conclude whether diet is the cause of low SF for pregnancy in our study. Intriguingly, vitamin B12 level exhibited a significantly decrease trend with the decline of SF concentration. Because SF and Vitamin B12 all absorbed in small intestine, we speculated the different absorption capacity of small intestine in pregnancy perhaps affected the SF level. But further research should be carried out to verify this hypothesis and detailed mechanism.

During pregnancy, maternal thyroid functionally adapts to meet the increased maternal and fetal needs. Inadequate synthesis of maternal thyroid hormone is associated with multiple obstetric and neonatal adverse outcomes [24]. Our results suggest that maternal TSH was correlated with serum ferritin levels during the second trimester in pregnant women with adequate iodine levels in China. To our knowledge, this is the first study to explore such a relationship. In our study we predicted SF along with age and week of gestation as risk factors contributing to TSH variation. SF levels were positively correlated with FT4 levels using Pearson correlation method. However consistent relation between the SF levels and FT4 was not observed in superior stepwise linear regression. Yu X et al. found that serum TSH levels were negatively correlated with total body iron (TBI) levels at 4 to 12 weeks of gestation [18]. Flora Veltri et al. found iron deficiency was frequent during the first trimester of pregnancy and was associated with a higher prevalence of thyroid autoimmunity, higher serum TSH and lower FT4 levels [25]. Because the prevalence of low body iron was substantially increased in pregnant women in the second trimesters than in the first trimesters (14.3 ± 2.1% vs. 6.9 ± 2.2%) [21], we investigated pregnant women from 13 to 24 weeks of gestation in the second trimester. Zimmermann MB et al. also indicated that SF was a significant predictor of TSH levels during the second and third trimesters of pregnancy in an area of borderline iodine deficiency [19]. Our study excluded the effects of iodine and thyroid autoimmunity by recruiting pregnant women with normal urinary iodine levels and thyroid autoimmune antibodies. In addition, we enrolled 24.8% pregnant women with TSH greater than 4.0 mIU/L while Zimmermann MB et al. included 6% pregnant women with TSH exceeding 4.0 mIU/L [19]. However, SF is not

### Table 2 Correlation between TSH or FT4 with SF level in adjusted linear regression models

<table>
<thead>
<tr>
<th></th>
<th>TSH</th>
<th>FT4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\beta$</td>
<td>$SE$</td>
</tr>
<tr>
<td>Model 1 (SF)</td>
<td>-0.008</td>
<td>0.002</td>
</tr>
<tr>
<td>Model 2 (SF, age, BMI)</td>
<td>-0.008</td>
<td>0.002</td>
</tr>
<tr>
<td>Model 3 (SF, age, BMI, Hb)</td>
<td>-0.010</td>
<td>0.003</td>
</tr>
<tr>
<td>Model 4 (SF, age, BMI, Hb, ALT)</td>
<td>-0.011</td>
<td>0.003</td>
</tr>
<tr>
<td>Model 5 (SF, age, BMI, Hb, ALT, Gestational week)</td>
<td>-0.007</td>
<td>0.003</td>
</tr>
</tbody>
</table>

SF: serum ferritin
the only determining factor that affects thyroid function. Ravanbod M et al. provided the absence of significant differences in Hb and TSH before and after 90 days of iron treatment in non-pregnant patients with ID anemia and subclinical hypothyroidism (SCH), which hinted that iron factor alone does not change the TSH level in non-pregnant patients with ID anemia and SCH [26]. No significant differences were found in Hb and SF before and after levothyroxine treatment, which suggested that thyroid hormone alone does not influence SF level. However, there were significant increases in Hb and SF and significant decreases in TSH in the group treated with iron plus levothyroxine. Hence, the combination of levothyroxine and iron salt is effective for patients with ID anemia and SCH. Although this study suggested that iron is not the only factor that affects thyroid function in non-pregnant patients with anemia, iron has a significant auxiliary effect on thyroid function. We suggest that when TSH levels elevated above pregnancy-specific TSH reference ranges with short-term, we should provide patients with immediate oral administration of levothyroxine according to 2017 American Thyroid Association guidelines for thyroid disease during pregnancy (strong recommendation for TPO antibody negative women with TSH \( \geq 10.0 \) mU/L, weak recommendation for those with 4.0 mIU/L \( \leq \) TSH < 10.0 mU/L) [27]. What’s more, clinicians need to evaluate the alteration of the Hb and SF levels in recent periods. Early treatment with iron combined with levothyroxine is essential for rapid correction of thyroid function in pregnant women.

Several studies showed that iron deficiency anemia affects thyroid function via several mechanisms. Iron deficiency decreases serum total and free T3, T4 concentrations and TPO activity [28, 29]. Iron deficiency decreases pituitary TSH response to TRH [30, 31]. Iron deficiency decreases the activity of hepatic T4 de-iodination and T3 turnover rates [31, 32], increases peripheral type III de-iodinase activity resulting in high T4 and T3 clearance rate [29]. The most striking effect of imbalance in Fe relates to compromised intellectual function. Fe deficiencies disrupt brain development via reduction in circulating and brain thyroid hormone levels resulting in aberrant hippocampal structure and function, hypomyelination of axons, altered brain energy metabolism, and altered neuronal signaling [29, 33, 34]. Actually there was little impact of low SF level on obstetrical outcomes including miscarriage, birth weight and premature delivery due to quick supplement 100–200 mg iron element per day when SF concentration was less than 12 μg/L. But we have not evaluated the cognition function of women during pregnancy or after delivery. Furthermore, Terefe B et al. found that SF concentrations are significantly lower in newborns delivered by IDA mothers than in normal mothers [35]. Neurochemical and behavioral abnormalities associated with Fe deficiencies are irreversible and persist into adulthood [36]. Prenatal iron supplementation is critical to improve maternal Hb and iron status and reduce intellectual damage of offspring.

We speculate SF may be a risk factor for thyroid dysfunction during pregnancy although the occurrence of thyroid dysfunction in pregnant women is influenced by a lot of factors with complicated interaction. Thyroid function and SF status should be normalized rapidly in gestational women. However, our study has a few limitations. First, we should investigate thyroid function and SF in different trimesters, especially during the first and the third trimesters of pregnancy. Second, the study should be extended to the population in iodine deficient or excessive area. Further research is needed to determine the role of maternal thyroid dysfunction with iron deficiency in fetal development.

Acknowledgement

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Disclosure

None of the authors have any potential conflicts of interest associated with this research.

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