Original Article
Association between serum ferritin levels and metabolic syndrome: an updated meta-analysis

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Abstract: It is definite that the serum iron level has a positive correlation with the risk of obesity. However, the association between increased serum ferritin levels and the metabolic syndrome still remains controversial. The purpose of this meta-analysis is to confirm the association between serum ferritin levels and metabolic syndrome. We searched PubMed and the China National Knowledge Infrastructure (CNKI) for relevant articles that assessed the association between serum ferritin levels and metabolic syndrome and were published between 2006 and 2014. Review Manage 5.3 software was used to collect and analysis the data cited in the ultimately selected papers. The variance was exhibited using the forest plot and the heterogeneity among studies was examined using the I² index. We use the funnel plot to evaluate the publication bias. Cross-sectional study, case-control study and prospective cohort study met our inclusion criteria including data from a total of 4,797 participants. The pooled odds ratio (OR) for the metabolic syndrome comparing the highest and lowest category of ferritin levels was 1.20 (95% CI: 0.69, 1.71; I²=96%). The meta-analysis demonstrates that elevated ferritin levels are positive associated with metabolic syndrome.

Keywords: Ferritin, metabolic syndrome, meta-analysis

Introduction

The metabolic syndrome, a pathological status that a variety of abnormal metabolism accumulate [1], was a significant risk factor for cardiovascular disease and endocrine disease [2, 3]. Recently, some studies suggested that it was also hazardous element for cancer [4] and clustered several clinical symptoms including central obesity or overweight, hypertension, hypertriglyceridemia, insulin resistance and low high-density lipoprotein cholesterol (HDL) [5].

Ferritin was a kind of intracellular protein that increased the iron and regulated the iron homeostasis [6]. However, increasing evidence indicated that elevated serum iron levels may have an adverse impact on the body [7]. In some meta-analyses, there was a positive relationship among elevated ferritin, hypertension, type 2 diabetes, abdominal obesity and hyperlipidemia [8, 9]. However, no meta-analysis has focused on serum iron concentration in relation to the metabolic syndrome.

Thus, the purpose of this meta-analysis was to update the existing evidence, to further confirm the association between serum ferritin levels and metabolic syndrome.

Methods

Search strategy

We searched PubMed and the China National Knowledge Infrastructure (CNKI) for relevant articles that assessed the association between serum ferritin levels and metabolic syndrome and were published between 2006 and 2014. We used the following Medical Subject Heading (MeSH) terms “ferritin”, “metabolic syndrome”, “meta-analysis”. We only searched the articles written in Chinese and English. The search period was all-inclusive until April 2015. In addition,
we also reviewed the reference lists of the retrieved original articles.

**Study selection**

Included criteria of the eligible studies were the following: 1) studies in humans; 2) observational studies (case-control study, cohort study and cross-sectional study); 3) the subjects didn’t intate the drugs that affect the levels of ferritin; 4) the studies were conducted to assessed the association between serum ferritin levels and metabolic syndrome.

Exclusion criteria included: 1) studies in animals; 2) no original research (reviews, editorials); 3) case reports and case series; 4) study subjects without metabolic syndrome.

**Data extraction**

Journal title, family name of the first author, year of the publication, study design, country of origin, size of study added, serum ferritin levels and number of participants were extracted in article included. Data extraction was performed independently by reviewers (Lianping He and Yi Chen).

**Statistical analysis**

The extracted data was used to perform the meta-analysis using the standard mean difference (SMD) and 95% confidence intervals (CI). The SMD were calculated by using random-effects models. The heterogeneity among stud-
Table 1. Basic characteristic of these studies

<table>
<thead>
<tr>
<th>First author</th>
<th>Year</th>
<th>Country</th>
<th>Study design</th>
<th>Resource</th>
<th>Size of study added</th>
<th>Experiment/control</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>S.N. Rajpathak [11]</td>
<td>2009</td>
<td>USA</td>
<td>Case-control</td>
<td>Diabetes, Obesity and Metabolism</td>
<td>560</td>
<td>50.4/50.2</td>
<td>0.6/0.6</td>
</tr>
<tr>
<td>Qihai Lin [12]</td>
<td>2010</td>
<td>China</td>
<td>Cross-sectional</td>
<td>Journal of Zhejiang University of Traditional Chinese</td>
<td>1645</td>
<td>102.4/82</td>
<td>65.95/59.20</td>
</tr>
<tr>
<td>Linghua Tang [14]</td>
<td>2007</td>
<td>China</td>
<td>Case-control</td>
<td>Chin J Lab Diagn</td>
<td>123</td>
<td>199.5/112.45</td>
<td>60.23/45.89</td>
</tr>
<tr>
<td>Ying Li [15]</td>
<td>2006</td>
<td>China</td>
<td>Case-control</td>
<td>Zhejiang Medical Journal</td>
<td>120</td>
<td>196.35/110.28</td>
<td>72.15/68.32 (ug/mL)</td>
</tr>
<tr>
<td>Xincai Xiao [16]</td>
<td>2011</td>
<td>China</td>
<td>Case-control</td>
<td>Journal of Hygiene Research</td>
<td>189</td>
<td>243.4/156.5</td>
<td>65.3/47.3</td>
</tr>
<tr>
<td>S. Iwanaga [17]</td>
<td>2014</td>
<td>Japan</td>
<td>Cohort</td>
<td>Obesity Research &amp; Clinical Practice</td>
<td>785</td>
<td>204.7/96.4</td>
<td>140.9/91.9</td>
</tr>
</tbody>
</table>
crucial role in the process of the body’s metabolism, including the section of generating adenosine triphosphate (ATP) in the oxidative respiratory of the chondriosome. However, when serum iron was superfluous, it had an adverse effect on the activity of the various enzymes [18]. At the basis of pathologies like type 2 diabetes mellitus, neoplasm and degenerative brain disorders, this effect would be enhanced [19, 20]. Although the former studies had proved that the high iron levels are associated with the pathological statue, the concrete data is ambiguous for us. On account of regional difference, gender gap and the distinction between premenstrual and menstrual for the same woman, perhaps they are the real reasons why the heterogeneity of statistics analysis is so evident. Therefore, we need to have a concrete analysis for those data. In general, the serum ferritin levels is higher in men with metabolic syndrome than women with metabolic syndrome [21].

The World Health Organization (WHO) has provided the data in the aspect of storing and regulating iron (>200 ug/L for men and >150 ug/L for Women) [22]. However, the value of ferritin was lower than the given value in the WHO. In women with metabolic syndrome, the value of ferritin was also lower than the values of iron overload defined by the WHO in the postmenopausal [23]. Due to iron losses by menstrua-

**Figure 2.** Forest Plot of the meta-analysis assessed the association between serum ferritin levels and the metabolic syndrome.

**Figure 3.** Funnel Plot of the present meta-analysis.

```plaintext
<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>IV/Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hye-ja lee2014</td>
<td>41.94</td>
<td>17.82</td>
<td>51</td>
<td>36.67</td>
<td>19.58</td>
<td>1299</td>
<td>12.8%</td>
<td>0.27 [-0.01, 0.55]</td>
</tr>
<tr>
<td>Iwanaga, S.2014</td>
<td>204.7</td>
<td>109.4</td>
<td>47</td>
<td>96.4</td>
<td>91.9</td>
<td>638</td>
<td>12.7%</td>
<td>1.17 [0.86, 1.47]</td>
</tr>
<tr>
<td>J Scott Gabrielsen2012</td>
<td>260</td>
<td>23</td>
<td>38</td>
<td>185</td>
<td>21</td>
<td>87</td>
<td>11.3%</td>
<td>3.45 [2.87, 4.03]</td>
</tr>
<tr>
<td>LU Ying2006</td>
<td>196.35</td>
<td>72.15</td>
<td>60</td>
<td>110.28</td>
<td>68.32</td>
<td>60</td>
<td>12.3%</td>
<td>1.22 [0.83, 1.61]</td>
</tr>
<tr>
<td>Lin Qhai2010</td>
<td>102.4</td>
<td>65.95</td>
<td>166</td>
<td>82</td>
<td>50.2</td>
<td>1479</td>
<td>13.1%</td>
<td>0.34 [0.18, 0.50]</td>
</tr>
<tr>
<td>S.N. Raipathak2009</td>
<td>50.4</td>
<td>6.2</td>
<td>280</td>
<td>50.2</td>
<td>6.2</td>
<td>280</td>
<td>13.1%</td>
<td>0.33 [0.17, 0.50]</td>
</tr>
<tr>
<td>Tang Linghua2007</td>
<td>189.5</td>
<td>60.23</td>
<td>60</td>
<td>112.45</td>
<td>45.89</td>
<td>63</td>
<td>12.2%</td>
<td>1.62 [1.21, 2.03]</td>
</tr>
<tr>
<td>XAO Xinciai2011</td>
<td>243.4</td>
<td>65.3</td>
<td>166</td>
<td>156.5</td>
<td>47.3</td>
<td>102</td>
<td>12.6%</td>
<td>1.54 [1.21, 1.88]</td>
</tr>
</tbody>
</table>

Total (95% CI) 789 4000 100.0% 1.20 [0.68, 1.71]
Heterogeneity: Tau² = 0.50; Ch² = 194.17, df = 7 (P = 0.00001); I² = 96%
Test for overall effect: Z = 4.65 (P = 0.00001)

Favours [experimental]   Favours [control] 100
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Serum ferritin levels and metabolic syndrome

The serum ferritin levels in the menstrual were lower than in ante menstruationem. In other words, the latter has a higher probability to develop the metabolic syndrome [24]. Our meta-analysis suggests that the men or pre-menopausal women whose serum ferritin levels are lower than the WHO cut-offs for iron overload could suffer from metabolic syndrome easily. In the early stages, high serum ferritin levels could be as an indicator by health examination to detect the risk of developing the metabolic syndrome. For this purpose, data from the final selected citations will be helpful for us to explore the relationship between serum ferritin levels and metabolic syndrome whether the value was greater than the WHO or not.

Limitation

It is obvious that moderate subjects exist in our study, thus the limitation was inevitable. Because our meta-analysis has a high heterogeneity and lack of enough groups, we can’t have a subgroup analysis. Therefore, further studies need to be explored.

Conclusion

In summary, the consequence of our meta-analysis manifest that the serum ferritin levels has a distinctly positive relationship with the metabolic syndrome.

Acknowledgements

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Disclosure of conflict of interest

None.

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References

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[18] Vardanyan Z and Trchounian A. Fe(III) and Fe(II) ions different effects on Enterococcus hirae cell growth and membrane-associated ATPase activity. Biochem Biophys Res Commun 2012; 417: 541-545.


[23] Vardanyan Z and Trchounian A. Fe(III) and Fe(II) ions different effects on Enterococcus hirae cell growth and membrane-associated ATPase activity. Biochem Biophys Res Commun 2012; 417: 541-545.