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Ability of serum ferritin to diagnose iron deficiency anemia in an elderly cohort

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ABSTRACT

Background: Diagnosis and treatment of iron deficiency anemia in older subjects improves their quality of life. Serum ferritin as a marker of iron stores is an acute phase protein. In older subjects who usually have many concomitant chronic medical conditions, serum ferritin may increase in response to inflammatory processes irrespective of iron stores. This study was performed to determine the diagnostic properties of serum ferritin in the diagnosis of iron deficiency anemia in older subjects.

Methods: This case–control study included all the inhabitants of Amirkola town who participated in the Amirkola Health and Aging Project. Diagnosis of anemia was confirmed based on a hemoglobin level <13 g/dL in men and <12 g/dL in women and iron deficiency anemia by percent transferrin saturation <15%. A receiver operating characteristic curve was constructed to determine an optimal serum ferritin cutoff value to differentiate patients with and without iron deficiency anemia at the highest sensitivity and specificity.

Results: Eighty patients with iron deficiency anemia and 160 cases of anemia without iron deficiency (mean age: 72.9 ± 8 and 71.6 ± 7.6 years, respectively; *p*-value = 0.37) were analyzed. In iron deficiency anemia, the mean serum ferritin was significantly lower (*p*-value = 0.036) compared to patients without iron deficiency anemia. Serum ferritin with a cutoff level of 100 ng/mL differentiated patients with and without iron deficiency anemia with a sensitivity of 60% and specificity of 59% and area under the receiver operating characteristic curve of 0.615 ± 0.040 (95% confidence interval: 0.536–0.694; *p*-value = 0.004).

Conclusion: These findings indicate that in elderly subjects, iron deficiency anemia may develop with higher levels of serum ferritin. Hence, the conventional cutoff of serum ferritin for the diagnosis of iron deficiency anemia in young adults is not appropriate for the elderly population.

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Introduction

Anemia affects one third of the world population with nearly half of the patients with anemia suffering from iron deficiency.[1]

In elderly people, even low levels of anemia affect the quality of life and increase the risk of mortality resulting in many medical conditions such as cardiovascular and cognitive disorders, osteopenia, muscle weakness, falls and fractures, and depression.[2] Several factors such as inflammatory processes, chronic renal failure, and gastrointestinal and nutritional disorders are associated with anemia, in particular iron deficiency anemia (IDA). In the aged, the prevalence of anemia increases with age and ranges from 8% to 25%, nonetheless the causes of anemia, including the diagnosis of the iron deficiency state, remain undetermined in many patients.[3–6] Currently, serum ferritin (SF) (ranging from 40 to 200 ng/mL) is a measure of iron stores in healthy adults. However, its diagnostic capability varies across different studies with regard to cutoff points.[7–9]

In elderly populations, changes in SF concentrations do not always correlate with variations in iron stores because ferritin is an acute phase protein and is affected by inflammatory processes irrespective of the iron store status.

Many chronic medical conditions in the general population such as obesity, metabolic syndrome, chronic obstructive pulmonary disease and diabetes are also prevalent in the elderly.[10–19] These conditions are usually associated with inflammation.[10,11,20,21] Coexistence of these comorbidities in aged people may be associated with elevated levels of acute phase proteins including SF. This situation results in the development of functional IDA (anemia of inflammation) which is associated with disproportionate release of iron from iron stores to compensate body demands with subsequent IDA. In these cases, in contrast to absolute IDA, SF does not reduce concomitantly with iron stores.

This issue creates difficulties in the diagnostic capability of the ferritin test to diagnose IDA. Thus, the classic cutoff value of SF as applied to young adults may be inappropriate for the diagnosis of IDA in the elderly. These observations warrant further investigations to determine a SF level with more reliable diagnostic properties. A systematic review of 55 studies found variations in SF test results across populations with and without inflammatory processes, liver disease or neoplastic diseases. Although ferritin is not an excellent measure of iron stores, it is a practical and widely used method to assess iron stores.[22]

For these reasons, the present study was designed to determine an optimal SF level to differentiate elderly patients with and without IDA with greater sensitivity and specificity. The secondary purpose of this study was to determine the diagnostic properties of different levels of SF in the diagnosis of IDA in a cohort of the elderly subjects aged 60 years and older.

Methods

The patients of this case–control study were recruited among the participants of the Amirkola Health and Aging Project (AHAP). This project was carried out in Amirkola, Babol, a town located near the Caspian Sea, northern Iran. The project was funded by the Vice-Chancellery of Research and Technology, Babol University of Medical Sciences for the investigation of geriatric medical problems such as falling, bone fragility and fractures, cognitive impairment and dementia, poor mobility and functional dependence. The baseline stage of this project was carried out in 2011 and 2012. All inhabitants aged 60 years and over were invited to participate in this study with 72.3% of the invited subjects participating.[12] All patients with anemia, defined as a hemoglobin level lower than 13 g/dL in men and 12 g/dL in women, were included in the study. Participants with a history of transfusion within six months prior to the start of this study, those taking iron supplements, and patients with chronic renal failure and on maintenance hemodialysis were excluded.

All patients gave informed consent and the proposal of this study was approved by the Ethics Committee of the Babol University of Medical Sciences, Babol, Iran.

Data were collected regarding serum iron, percent of transferrin saturation and SF and the prevalence of coexistent chronic medical conditions was recorded.

Data regarding chronic diseases were provided by clinical examination, interviews and review of medical records. The diagnosis of IDA was confirmed based on transferrin saturation levels of less than 15%. Details of patient selection, data collection and laboratory test results have been described elsewhere.[12]

In the statistical analysis, the participants of this study were classified as patients with and without IDA. Eighty patients with IDA were compared with 160 patients with anemia without iron deficiency. The two groups were compared regarding SF and percent of transferrin saturation.

The diagnostic ability of SF was determined by receiver operating characteristic (ROC) curve analysis. The optimal cutoff levels that differentiated patients with and without IDA at the highest sensitivity and specificity rates were determined using Youden's index calculated by sensitivity + specificity − 1. The accuracy of test was assessed based on area under the ROC curve (AUC). The distribution of all variables was tested for normality using the Kolmogorov–Smirnov test. Parametric and non-parametric tests were used for analyses of variables with and without normal distribution, respectively. Statistical Package for the Social Sciences (SPSS) software version 18 was employed for analysis.

Results

The Amirkola Cohort Profile included all inhabitants living in the 34 districts of Amirkola town, 2234 of whom were aged 60 years or older when this study began (1158 men and 1076 women). Thirty-five out of 2234 participants were excluded and 114 women and 126 men out of 1994 participants (12.03%) who had anemia were studied. Eighty patients with IDA, with a mean age of 72.9 ± 8 and 160 patients without IDA with a mean age of 71.6 ± 7.6 years old (p-value = 0.37) were analyzed (Table 1).

Coexistent common chronic medical diseases such as, hypertension, urinary incompetence, diabetes, chronic lung