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The iron status of a healthy South African adult population

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ABSTRACT

Introduction: Iron deficiency is associated with significant morbidity and mortality, can present with or without haematological changes and is a major cause of microcytic anaemia. In South Africa and Africa in general, there is a paucity of studies on the iron status of healthy adult non pregnant females and males >18 years of age. The aim of the study was to determine the prevalence of iron deficiency in a healthy South African population.
Methods: A total of 651 healthy adults >18 years were included in the study. Blood samples were taken for the determination of iron status, haematological and inflammatory parameters. A ferritin level of <30 μg/L was used to define iron deficiency and these subjects were further divided into those with and without anaemia. Diet and menstrual history in females was further investigated.
Results: Overall, the prevalence of anaemia was 12.6% and iron deficiency was found in 78% of anaemic subjects. The prevalence of iron deficiency was 39.8% in all participants and females and Black Africans had a very high prevalence of 56.6% and 50.7% respectively. Significant ($p < 0.05$) differences were found in concentrations of ferritin, haemoglobin, iron, transferrin, transferrin saturation, MCV and MCH between the groups.
Conclusion: Anaemia is a minor health problem but a large proportion of subjects with iron deficiency do not present with anaemia. The prevalence of iron deficiency was high especially in females and Black African participants.

1. Introduction

Iron is an essential trace element that plays a crucial role in various metabolic functions. It is a structural component of haem-containing proteins like haemoglobin (Hb) and myoglobin which bind oxygen for delivery to the tissues. It is also involved in energy production, redox reactions and DNA synthesis. However, free iron is toxic and therefore it is tightly regulated by its binding and incorporation into proteins [1].

A reduction in the total body iron is referred to as iron deficiency (ID) and it can occur as a result of reduced intake, decreased absorption or increased losses of iron [2,3]. ID progresses through three stages namely depleted iron stores, iron deficient erythropoiesis and finally iron deficiency anaemia (IDA) [4]. In iron depletion, the total body iron is decreased but erythropoiesis is unaffected whereas in iron deficient erythropoiesis, due to insufficient supply of iron to erythroid tissues, erythropoiesis is affected. However, the Hb is still within normal limits and thus referred to as iron deficiency without anaemia (IDWA). The last and severe stage of ID presents with anaemia [5]. ID is the most common nutritional deficiency and the top ranking cause of anaemia in the world [6]. Children, pregnant and lactating women are considered at high risk because of the increased iron requirements. Non-pregnant women of reproductive age are also at risk of ID due to the loss of blood through menstruation [3].

In adults, anaemia is defined as an Hb concentration of below 13 g/dL in males and below 12 g/dL in non-pregnant females [7]. Anaemia is easy to diagnose, however to confirm that the anaemia is a result of ID can prove to be difficult. The gold standard for the diagnosis of ID is a bone marrow aspirate (BMA) which is highly specific but invasive and expensive [8]. Serum ferritin is the most specific non-invasive biochemical test to diagnose ID, as it reflects total body iron stores. A serum ferritin level below 12 μg/L is generally accepted as consistent with depleted iron stores [9]. However, Mast et al. found that the sensitivity and specificity of ferritin below 12 μg/L compared to BMA was 25% and 98% respectively. The sensitivity increased to 92% and the specificity remained the same when a cut-off of 30 μg/L was used [10]. Importantly, this cut-off may only be used in the absence of inflammation as ferritin is an acute phase protein and levels will be higher in the presence of

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inflammation [5,8]. The WHO and Centres for Disease Control and Prevention (CDC) Joint Report recommends that ferritin, Hb, mean cell volume (MCV), soluble transferrin receptors and zinc protoporphyrin are the best indicators of iron status in all populations. The performance of other tests such as iron, transferrin and transferrin saturation are improved when used in conjunction with the above tests [8].

Importantly, IDA is associated with significant morbidity and mortality as it can affect neurocognitive development and function, work productivity and even result in death [11]. In 2000, Nojilana et al. [12] estimated that 0.4% of all deaths in South Africa were a result of IDA. Various studies examined the prevalence of IDA in the South African population; however, these studies have been conducted mostly in children, pregnant women and the elderly population [12–15]. There is a paucity of studies on the iron status of healthy adult non pregnant females and males over 18 years of age [16–18]. Thus, the aim of this study was to determine the prevalence of iron deficiency in a healthy population representative of South Africa.

2. Methods

2.1. Study population

From a database of the 'Establishing Adult Reference Intervals for Selected Analytes in South Africa' study consisting of 1433 subjects, 651 adults meeting the inclusion criteria were included in our study. The study involved the recruitment of healthy individuals aged 18 years and older from the general public as well as students, hospital and laboratory staff. The protocol and standard operating procedures used in the main study are published elsewhere [19]. All participants completed a questionnaire and written informed consent was obtained. The questionnaire included the following: (i) demographic details i.e. age, gender and ethnicity; (ii) personal habits i.e. smoking and alcohol history; (iii) physical activity and exercise; (iv) dietary information; (v) current health status i.e. recent infections, medication intake including nutritional supplements and allergies; (vi) menstrual history in females. The study was approved by the Health Research Ethics Committee of Stellenbosch University, Cape Town, South Africa (S12/05/147).

We excluded the following individuals: those not born in South Africa; with recent results pointing to a severe disease; a recent illness or hospitalisation 2 weeks prior to recruitment; who donated blood up to 3 months prior to recruitment; known carriers of Hepatitis B, Hepatitis C or Human Immunodeficiency Virus (HIV); pregnant or within one year of childbirth; and those who participated in a research study involving an investigational drug in the past 12 weeks. Additional exclusion criteria included: missing data for ferritin, iron, transferrin, transferrin saturation, highly sensitive C-reactive protein (hsCRP), Hb, MCV and mean cell haemoglobin (MCH); and participants with hsCRP concentrations ≥10 mg/L and WCC > 11 (×10^9).

2.2. Biochemical analysis

Blood samples were collected, following a 12–14 h fast, after subjects were seated for 20–30 min. Biochemical parameters were analysed at an ISO 15189 accredited Pathology practice (PathCare Reference Laboratory, Cape Town, South Africa).

The measurement of serum ferritin was performed on the Beckman Coulter Access immunoassay system (Beckman Coulter Inc. Brea, CA, USA). The assay is a paramagnetic particle, chemiluminescent immunoassay and the calibrator is traceable to the World Health Organisation (WHO) 3rd International standard for ferritin (IS 94/572). The assay has a linear range of 0.2–1500 μg/L. Transferrin, iron and hsCRP measurements were performed on the Beckman DXC automated analyser (Beckman Coulter Inc. Brea, CA, USA). Transferrin was measured in serum using an immunoturbidimetric method that utilises anti-human transferrin antibodies. The assay's linear range is 0.75–7.5 g/L. Hs-CRP was determined in serum by an immunoturbidimetric assay utilising anti-CRP antibody coated latex particles with a linear range of 0.08–80 mg/L. Serum iron was measured using a colorimetric assay that utilises 2,4,6-tripyridyl-*s*-triazine (TPTZ) as a chromogen. TPTZ reacts with ferrous iron to form a blue coloured complex that is measured photometrically. The linear range of the assay is 2–179 μmol/L. Transferrin saturation was calculated according to the formula: % saturation = [iron / (transferrin × 25.6)] × 100%.

The Beckman Coulter A^C•T diff2 haematology analyser (Beckman Coulter Inc. Brea, CA, USA) was used for the determination of Hb, MCV, MCH and WCC using EDTA whole blood. This analyser is based on the Coulter principle of sizing and counting for quantitative determination of Hb, MCV, MCH and WCC.

2.3. Definitions & statistical analysis

Serum ferritin was used to define iron deficiency. A cut-off level of 30 μg/L for serum ferritin was chosen to distinguish between participants with ID (ferritin <30 μg/L) and those who are iron replete (IR) (ferritin >30 μg/L). For the diagnosis of anaemia, an Hb of <13 g/dL in males and <12 g/dL in females was used (WHO criteria). We used the laboratory reference ranges to define microcytic hypochromic anaemia as an Hb below cut-off for gender as well as an MCV <81 fl (microcytosis) and MCH <28 pg (hypochromia). Subjects with ID (ferritin <30 μg/L) were further subdivided into two groups namely IDA (Hb below cut-off for gender) and IDWA (Hb above cut-off for gender).

Data was analysed using Microsoft Excel® (Microsoft, Redmond, WA, USA) and SPSS® v20 statistical software (SPSS, Chicago, IL, USA). The Shapiro Wilk test was performed and non-parametric tests were applied as not all the data fitted a Gaussian distribution. Descriptive data is reported as median values and interquartile ranges (IQR). The Mann Whitney *U* test was used for comparisons between the groups. Statistically significant differences were indicated by $p < 0.05$.

3. Results

3.1. Characteristics of study population

Of the 651 participants included, 410(63%) were female and 241(37%) male. The majority of participants were of Caucasian origin (55.5%) followed by Mixed ancestry (33.9%) and Black African (10.6%). The age of all participants ranged from 18 to 76 years with a median age of 30 (22–44) years.

3.2. Prevalence of anaemia

The prevalence of anaemia in all participants was 12.6%. Female participants had a much higher prevalence of anaemia (18.3%) compared to 2.9% in male participants. Anaemia was more prevalent (31.9%) in Black Africans compared to 17.2% and 6.1% in the Mixed-ancestry and Caucasians respectively. Microcytic hypochromic anaemia was present in only 22 (26.8%) participants of which 20(91%) were female. However, ID (ferritin <30 μg/L) was found in 64 (78%) of the participants with anaemia. The cause of anaemia was not determined in the 18 (22%) subjects in the IR group (Table 1).

3.3. Iron status of study participants

We found a prevalence of 39.8% for ID in this study population. Black African participants had the highest prevalence of ID (50.7%) compared to 43.4% and 35.5% in the Mixed ancestry and Caucasian participants respectively (Table 1). Table 2 shows the medians and IQRs of iron status and haematological parameters. There was a statistically significant ($p < 0.001$) difference in the concentrations of ferritin, transferrin, iron, transferrin saturation, Hb, MCV and MCH between the ID and IR groups (Table 2).