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RESEARCH ARTICLE

Comparative Assessment of Serum Zinc and Iron Deficiency in Cuban Women of Reproductive Age

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Abstract:

***Background*:** Iron (Fe) deficiency anemia is the primary nutritional deficiency in Cuba, with limited documentation on serum zinc (Zn) and copper (Cu) deficiencies. This study aimed to compare the magnitude of Fe, serum Zn and Cu deficiency and its relationship with anemia and inflammation in women of reproductive age from different provinces in Cuba.

***Materials and Methods*:** A cross-sectional study conducted between 2016-2018 included a non-probabilistic sample of 654 apparently healthy women aged 18 to 40 years from Havana, the eastern region (Santiago de Cuba and Holguin), and the central region (Sancti Spiritus and Cienfuegos), who were mothers of young children. Hemoglobin, ferritin, serum Zn and Cu, high-sensitivity C-reactive protein (CRP-hs), alpha-1 glycoprotein (AGP), and ceruloplasmin (Cp) were measured. Data were analyzed to estimate quartiles, frequencies, and associations among variables, with ferritin adjusted for inflammation using SPSS 20.0 statistical package.

***Results*:** Anemia was identified in 18.1% of participants, Fe storage deficiency was 7.5% (unadjusted for inflammation) and 10.0% (adjusted); serum Zn deficiency in 36%, and serum Cu deficiency in 14.3%. Low Cp levels were found in 13.3%, and inflammation was present in 43%. Anemia showed a positive association with Fe storage deficits (OR=3.90;95%CI: 2.23-6.71) and serum Zn deficiency (OR=1.94;95%CI: 1.30-2.91), and a negative association with serum Cu deficiency (OR=0.53;95%CI: 0.30-1.10). Inflammation modified the relationship between anemia and Fe storage and serum Cu deficiencies but not the relationship with serum Zn.

***Conclusion*:** Findings reveal high rates of anemia and micronutrient deficiencies, particularly Zn, in Cuban women. These results underscore the need for interventions to improve nutritional health and address potential risks related to anemia and inflammation.

Keywords: Serum zinc, copper, inflammation, ceruloplasmin, anemia, cuba.

1. INTRODUCTION

Anemia is a global health problem commonly caused by nutrition deficiencies, in particular iron deficiency anemia [1,2,3,4,5,6,7]. Iron (Fe) and zinc (Zn) are among the micronutrients with the highest

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prevalence of deficit worldwide [7,8,9,10,11,12]. An association between Zn deficiency and Fe deficiency anemia has been identified in women of reproductive age (15-49 years) [3], particularly in low- and middle-income countries [1,8,9]. Various mechanisms have been proposed to explain the link between Zn and Hb metabolism, but to date there, there is insufficient data to demonstrate the role of Zn in the etiology of anemia [9]. Copper (Cu) deficiency also causes anemia, although the extent of Cu deficit is not well established [13-15].

All three micronutrients have structural roles in proteins, participate in redox reactions, and regulate metabolic processes [1,9,13,14,16,17,18]. The main biomarkers for assessing the nutritional status of Fe, Zn, and Cu are serum ferritin, serum Zn, serum Cu and ceruloplasmin (Cp) enzyme (EC 1.16.3.1) [7]. The concentrations of these biomarkers can vary during inflammation; therefore, it is recommended to measure them alongside inflammatory biomarkers such as the highly sensitive C-reactive protein (CRP-hs) and alpha-1 acid glycoprotein (AGP) [7,11,12,14,15,19,20].

Fe deficiency anemia is considered to be the main nutritional deficiency problem in Cuba [21]. However, there is limited information on the prevalence of Zn and Cu deficiencies and their association with anemia in Cuban women of reproductive age. Cu are essential for immune function, growth, and reproduction [13,14]. Women of reproductive age are particularly vulnerable due to their increased nutritional demands, making targeted interventions essential to break cycles of poor health and malnutrition. Thus, the objective of the study is to compare the magnitude of Fe, serum Zn and Cu deficiency and its relationship with anemia and inflammation in women of reproductive age from different provinces in Cuba.

2. METHODS

2.1. Study Design

We conducted a an analytic, cross-sectional study with a clinical and community-based approach from 2016 to 2018. The study population was comprised of mothers of children aged 6 to 59 months of age, who were included in the National Survey of Anemia and Iron Deficiency of Cuban preschool children, directed by the National Institute of Hygiene, Epidemiology and Microbiology (INHEM in Spanish) of the Ministry of Health.

2.2. Participants

The study included healthy-appearing women of reproductive age (18-40 years old) who were mothers of children from the eastern region (Santiago de Cuba and Holguin), the Central Region (Sancti Spiritus and Cienfuegos), and Havana. Pregnant and lactating women, women in the postpartum period (up to 6 months), women with sickle cell disease, or those attending medical consultation for hematological disorders were excluded. Women with conditions typically associated with an inflammatory response, such as cancer, diabetes mellitus, high blood pressure, severe asthma, chronic obstructive pulmonary disease, kidney failure, Cu metabolism disorders, physical deformities, and clinical conditions linked to Zn deficiency, such as hypothyroidism, were excluded from the study. Additionally, participants consuming mineral supplements and/or medications that interfere with the metabolism of Zn or Cu were also excluded. These conditions were identified either through self-reporting by the participants during the initial screening process or by physicians at the primary health care level. Additionally, non-fasting women were excluded. We excluded 23 hemolyzed sera and 3 with Zn values above 160.9 µg/dL, a limit considered indicative of probable contamination [22].

2.3. Procedures

2.3.1. Biochemical Measurements

Blood samples were collected after an overnight fast via antecubital vein puncture, following area disinfection. A total of 6 ml of blood was collected, with 1 ml used for hemoglobin measurement and 5 ml for serum analysis. The extraction was performed by authorized and trained personnel, adhering to recommendations for processing minerals in biological materials to avoid contamination. Hemoglobin (Hb), ferritin, serum Zn, serum Cu, Cp, CRP-hs and AGP were measured after an overnight fasting [11]. For Hb

measurement, 1 ml of blood was taken and added in a tube with 10% EDTA anticoagulant. The remaining 5 ml was used to obtain serum by centrifugation at 14,000 rpm for 5 minutes, which was then stored at -40ºC for further analysis.

Hb was measured using an ABX Micros 60 hematological analyzer (Horiba, France). Ferritin, CRP-hs, AGP, and Cp were measured using the INLAB 240 using immunoturbidimetric method (CPM Scientifica Tecnologie Biomediche, Italy). These determinations were performed by trained personnel at the INHEM Nutritional Anemia Laboratory in Havana, Cuba, using reference materials for quality control. The equipment was calibrated and certified.

Zn and Cu were measured in the INHEM Environmental Pollutant Laboratory using a Shimadzu AA-6800 atomic absorption spectrophotometer (Japan). The method followed Smith et al. [23]. Standard working solutions for calibration (0.05, 0.1, 0.2, 0.4, 0.8 µg/mL for Zn, and 0.05, 0.1, 0.2, 0.4, 0.8, 1.6 µg/mL for Cu) were prepared from appropriate dilutions of primary standard solutions of Zn and Cu (Merck, Germany) dissolved in 0.5mol/L nitric acid at a concentration of 1 mg/mL. For dilution of the standard working solutions and blank solution we used 5% distilled glycerin (99.5%) from a commercially available product (Titolchimica, Italy), and deionized water.

Before measuring Zn and Cu, a serum pool was prepared from blood samples of eligible women. The standard addition method was used for the serum pool, and recovery study showed average recovery percentages of 95.66% and 94.63% for Zn and Cu, respectively. Serum samples were diluted to 1:6 with deionized water (500 µl serum/2 mL water). For each series of determinations, curves were prepared with standard working solutions, serum pool, and fresh blank solutions. Instrumental parameters were adjusted for the determination of both Zn and Cu.

Instrumental parameters for Zn and Cu determination included hollow cathode lamps with wavelengths of 213.9 nm and 324.8 nm, acetylene air flow 2.0 L/min and 1.8 L/min, band width 0.5 nm for both minerals, lamp currents of 8 mA and 6 mA, and background correction with a deuterium lamp. All materials used in minerals analysis were treated to prevent contamination. The cut-off points used to assess serum Zn and Cu deficiencies, as well as ferritin levels, were based on expert recommendations and are appropriately referenced in Table 1.

2.3.2. Statistical Analysis

Data analysis was performed using SPSS 20.0 statistical package. Continuous variables were described by median and interquartile range due to positive skewness. Ferritin values were adjusted for inflammation using correction factors from Thurnham et al. [24]. The kappa concordance index was used to evaluate the degree of agreement between adjusted and unadjusted serum ferritin values for inflammation. Categorical variables were summarized using absolute numbers and percentages. The relationship between anemia and ferritin, serum Zn, serum Cu, Cp, and inflammation was assessed by calculating the Odds ratio (OR) and 95% confidence interval (95% CI). Serum Zn and Cu intercorrelation was evaluated using the Pearson correlation coefficient (r). The diagnostic capability of Cp as an inflammatory biomarker was assessed using a ROC curve.

2.3.3. Ethical Considerations

The study adhered to the principles of the Declaration of Helsinki [25] and was approved by the INHEM Scientific Council's Guide to Procedures for Human Research on March 21,2014. All participants signed the informed consent form and data on participants diagnosed with anemia were reported for treatment to the primary health care level corresponding to their place of residence.

Table **1** presents the study variables and their cut-off points.

3. RESULTS

A total of 654 women were evaluated. The median age of women was 28 years with a minimum age of 18 and a maximum age of 40. Table **2** presents descriptive statistics of the biochemical variables of wom-

en. Missing data in some variables was due to blood clotting or insufficient amount of serum and therefore did not represent a risk of bias for the calculation of descriptive statistics or association measures.

Table 1. Cut-off points for normality in variables used for the evaluation of women of reproductive age. Cuba, 2016-2018

Variable	Indicator	Cut-off points
Zinc	Serum Zn concentration (µg/dL)	< 70 [11]
Copper	Serum Cu concentration (µg/dL)	< 80 [26]
Ceruloplasmin (Cp)	Ceruloplasmin concentration (g/L)	0.22-0.61 [26]
Anemia	Hemoglobin (g/L)	< 120 [6]
Severity of anemia [6]	Hemoglobin (g/L)	Severe: <80
		Moderate: 80–109
		Mild: 110-119
Iron deposit deficit	Serum ferritin (µg/L)	< 15 [27]
Inflammation	C-reactive protein-hs (mg/L)	> 5 [27]
	Alpha-1 glycoprotein (g/L)	> 1 [27]

Abbreviations: Zn: zinc, Cu: copper, Hb: hemoglobin, Cp: ceruloplasmin, CRP-hs: High sensitivity C-reactive protein, AGP: alpha-1 glycoprotein acid, µg/dL: micrograms/deciliters, g/L: grams/liters, mg/L: milligrams/liters.

Table 2. Descriptive statistics as quartiles of biochemical variables in women of reproductive age.

Variable	p25	p50	p75
Hb g/L (n=639)	123.0	130.0	136.0
Serum Ferritin no adjusted (µg/L) (n=641)	29.6	54.2	84.7
Serum Ferritin adjusted (µg/L) (n=641)	26.2	44.4	70.4
Serum Zn (µg/dL) (n=654)	10.0 (65.3)	11.5 (75.1)	13.3(87.1)
Serum Cu (µg/dL) (n=645)	14.1 (89.4)	16.7 (106.0)	20.0(125.9)
Cp (g/L) (n=639)	0.27	0.34	0.42
CRP-hs (mg/L) (n=641)	1.1	2.3	6.4
AGP (g/L) (n=641)	0.6	0.8	1.0

Abbreviations: P25: 25th percentile, p50: 50th percentile, p75: 75th percentile, Hb: hemoglobin, Serum ferritin adjusted: serum ferritin adjusted for inflammation, Serum Ferritin no adjusted: serum ferritin not adjusted for inflammation, Serum zinc, Serum copper, Cp: ceruloplasmin, CRP-hs: high sensitivity C-reactive protein, AGP: alpha-1 acid glycoprotein.

Absolute and relative frequencies were as follows:

Anemia: 18.1% (116/639)

Deficit in Fe deposits: 7.5% (48/641) measured by serum ferritin not adjusted by inflammation, and 10% (63/641), serum ferritin adjusted by inflammation.

Zn deficit: 36% (233/654)

Cu deficit: 14.3% (92/645)

Decreased Cp: 13.3% (85/639)

As for biomarkers of inflammation, increased CRP-hs was detected in 31.7% (203/641) and increased AGP, in 25.1% (161/641).

In women with anemia, the deficit was mild in 81.9% (95/116), moderate in 17.2% (20/116), and severe in 0.9% of the cases (1/116). Anemia with deficit in Fe deposits was present in 18.2% (21/115) of women. After adjusting serum ferritin by inflammation, the proportion of anemic women with Fe deficiency increased to 21.7% (25/115). High concordance (kappa = 0.85) was found between deficit in Fe deposits with serum ferritin adjusted and unadjusted for inflammation. In women with anemia serum Zn deficit was present in 49.1% (57/116) and serum Cu deficit in 8.8% (10/114) of the cases.

Table **3** shows the proportion of women without deficit, or with deficiency of one or more of the three micronutrients evaluated. Multiple micronutrient deficiencies were observed in women with and without anemia, although this condition was more frequent in the anemic group. Anemia was associated with deficiency in Fe deposits (OR=3.90;95%CI: 2.23-6.71), serum Zn deficiency (OR=1.94;95%CI: 1.30-2.91) and serum Cu deficiency (OR=0.53;95%CI: 0.30-1.10).

Table 3. Proportion of women with one, two or more deficiencies in Fe, Zn and Cu, Cuba

NUM. of micronutrients in deficit	% Women with anemia (n=113)	% Women without anemia (n=507)
No micronutrient deficiency	41.2	54.2
One micronutrient deficient	42.5	36.1
Two micronutrients deficient	13.3	9.5
Three micronutrients deficient	3.0	0.2

Note: Data presented as percentage.

Of the total number of women, 43.0% (273/641) had inflammation when considering both biomarkers CRP-hs and AGP. After stratifying the sample by inflammation, a positive association was found between anemia and Fe deposits deficiency, OR=4.37 (95% CI: 2.30-8.01) and serum Zn deficiency, OR=1.90 (95% CI: 1.30-2.91). The association was negative between anemia and serum Cu deficiency OR=0.59 (95%CI: 0.30-1.10). Inflammation modifies the influence of Fe deficiency on anemia: deficiency occurs with 24.1% of anemia when there is inflammation, but with 56.2% when there is none (Table **4**).

Table 4. Anemia and deficits iron deposits, serum zinc and copper by presence or absence of inflammation, Cuba.

-		Inflammation			Non-inflammation		
		Anemia	No Anemia	Total (n)	Anemia	No Anemia	Total (n)
Fe	Deficit	7 (24.1)	22 (75.9)	29	18 (56.2)	14 (43.8)	32
	No deficit	40 (16.5)	203 (83.5)	243	50 (15.4)	275 (84.6)	325
Cu	Deficit	1 (5.3)	18 (94.7)	19	9 (13.0)	60 (87.0)	69
	No deficit	45 (18.4)	200 (81.6)	245	58 (20.2)	229 (79.8)	287
Zn	Deficit	25 (25.3)	74 (74.7)	99	32 (24.8)	97 (75.2)	129
	No deficit	22 (12.7)	151 (87.3)	173	36 (15.8)	192 (84.2)	228

Note: Data presented as n (%). Fe: iron, Cu: copper, Zn: zinc.

Figure **1** depicts the proportions of women with deficits in serum Zn and Cu and in Fe deposits in the presence and absence of inflammation. The results suggest that inflammation modified the association be-

tween anemia and deficits in serum Cu and Fe deposits, but not the association between anemia and serum Zn deficits.

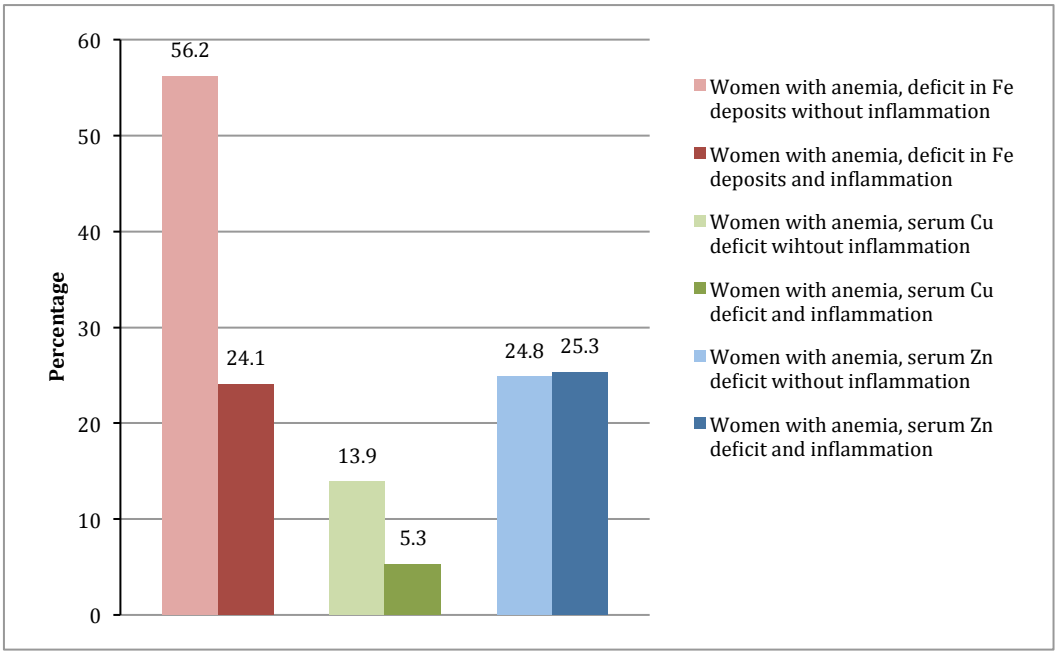

Figure 1. Effect of inflammation on Fe deposits, serum Zn and Cu deficits in anemic women.

Figure **2** illustrates the ROC curve for CP, CRP and AGP, with inflammation as the state or dependent variable. The biomarker with the highest explanatory power, as indicated by the AUC was CRP-hs, followed by AGP and Cp, with AUC and 95% CI values of 0.92 (0.90-0.94), 0.87 (0.84-0.90) and 0.72 (0.68-0.76), respectively.

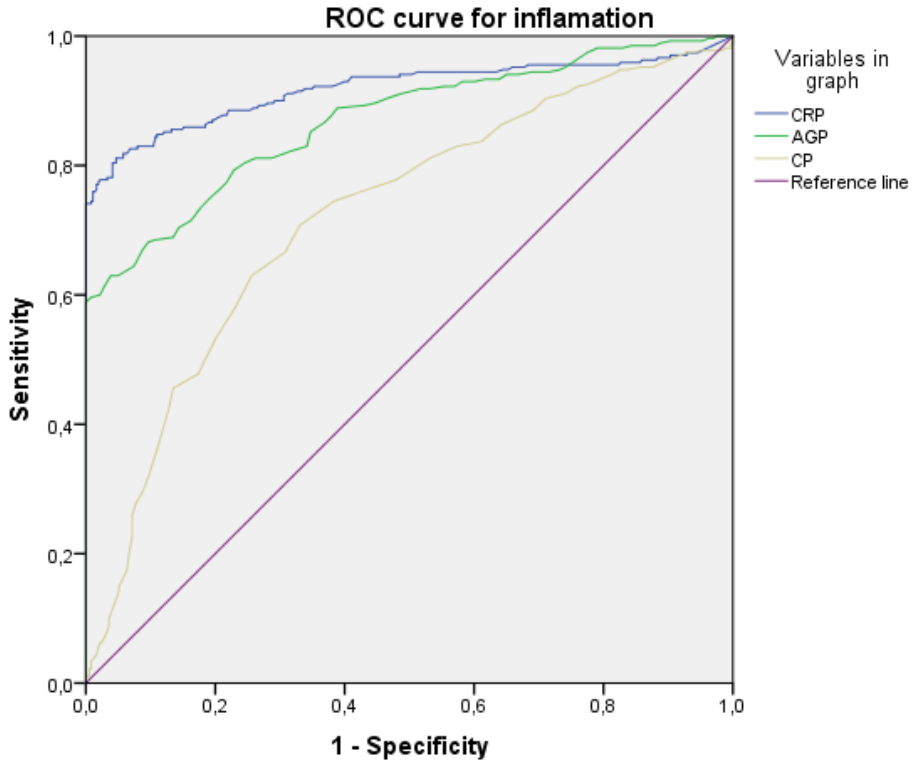

Figure 2. ROC curve analysis for Cp as a biomarker of inflammation showed an AUC of 0.72 as compared to CRP and AGP, with AUC´s of 0.92 and 0.87, respectively.

The Cp cut-off suggested by some to diagnose inflammation is close to 0.5 g/L [28,29]. However, this value showed low sensitivity (17.4%) and high specificity (93%) in the sample studied. Cut-off values in the range of 0.34 to 0.35 g/L increase sensitivity while maintaining specificity above 65%. A value of 0.35 g/L was chosen as a useful cut-off point, with a sensitivity of 71% and specificity of 67%. This cut-off value differs by 0.26 units from the upper limit of the reference range of the method used to determine Cp in the present study (Table **1**).

4. DISCUSSION

The study findings corroborated initial assumptions that more than one mineral deficiency is associated with anemia. Analysis of studies conducted from 2003 to 2019 in different countries and regions confirmed the high prevalence of Fe and Zn deficiency [8,9,10,12].

According to Stevens et al. [10], 20% or more of the women in the samples evaluated in 13 of 15 countries had serum Zn deficiency, reaching proportions higher than 50% in Cambodia, Malawi, Cameroon and Vietnam. The Fe deficit was 20% or greater in samples from 10 countries, including the United States and the United Kingdom, and reached figures greater than 40% in Azerbaijan, Mexico and Pakistan. Simultaneous deficiencies of Fe and Zn among other micronutrients were reported in Guatemala, Ecuador, United Kingdom, Vietnam, Ethiopia, Malawi, Cameroon, India, Bangladesh and Pakistan [10].

Few studies have included the evaluation of serum Cu. In a sample of Chilean women, only 2.3% had a mineral deficiency [30], while in a sample of Ghanaian women this figure was 12% [31]. In Cuba, there are few reports of evaluation of serum Zn and Cu in women of reproductive age. Taboada et al. [32] reported in 2019, in apparently healthy women, 79.4 ± 7.1 μg/dL of serum Zn and 106.8 ± 30.6 μg/dL of serum Cu, which were within the normal reference range [13,16].

The proportion of women with anemia in the present study was similar to the prevalence previously reported by Pita-Rodríguez et al. in a sample from the City of Havana (24.6%). However, the proportion of women with anemia associated with Fe deficiency in our study was markedly lower than that reported by Pita-Rodríguez et al. (82.3%). This difference could be attributed to the higher frequency of inflammation in the current study, in contrast to the results of Pita-Rodríguez et al., who reported a prevalence of 8.4% of acute inflammation and 19.9% of chronic inflammation [21]. The method of adjusting serum ferritin for inflammation used in this study may still be underestimating the Fe deficiency in our sample. Other authors have used different methodologies to perform this adjustment in women of reproductive age.

The BRINDA project used a decile linear regression model to adjust serum ferritin concentration by CRP and AGP concentrations for biomarkers reflecting inflammation and nutritional determinants of anemia [33], while Rodríguez et al. employed a quantile regression model [34]. The proportions of women with serum Zn deficiency (36.2%) and with serum Cu deficiency (19.1%) were similar and lower, respectively than those previously reported in women from Havana [21]. Cuba developed a National Plan for the prevention and control of anemia, focusing on two main strategies: Fe supplementation and food fortification [36]. However, no documentation was found regarding a similar intervention for Zn.

Implementing interventions to improve Zn nutritional status in vulnerable Cuban groups would require demonstrating that its deficiency constitutes a public health problem, defined as20% or more of the population having serum Zn values below 70 μg/dL [11]. Meats are common food sources rich in Fe, Zn and Cu. [13,16,17]. According to Jiménez et al., the Cuban diet primarily consist of rice, beans, vegetables (mainly potatoes, sweet potatoes, cassava, malanga, banana and pumpkin), eggs, and to a lesser extent, meat products. A study of children aged 6 to 23 months in Havana reported deficient Zn consumption [37]. However, data on Zn intake adequacy in women of reproductive age was not available.

The findings of this research, in which Cu deficiency is the least prevalent among the three micronutrients considered in women with anemia, both in the presence or absence of inflammation, is in line with the fact that though it is widely recognized that Cu deficiency may cause anemia, it is not mentioned among its main nutritional causes [13].

The mechanisms that regulate Cu metabolism are not fully understood, although it is known that the decrease in Cu alters Fe metabolism and erythropoiesis leading to anemia [14, 38]. However, in the curly-hair Menkes syndrome, which includes alteration of Cu metabolism and intracellular utilization, children do not have anemia [13].

Dugger et al. [38], contends that Cu deficiency anemia is almost indistinguishable from Fe deficiency anemia, but unlike the latter, it is very rare [13,38]. McArdle [13] argues that neither serum Cu nor Cp are good biomarkers to evaluate Cu nutritional status. One reason supporting this observation is that Cp, being an acute phase protein, increases during inflammation, and is the main protein that transports Cu in blood [13, 38]. However, serum Cu and Cp remain the most frequently used biomarkers to evaluate Cu nutritional status [39, 40]. Cp transports approximately 90% to 95% of blood Cu. Some causes of decrease circulating Cp include Wilson's disease, Menkes' disease, aceruloplasminemia and Cu deficiency due to nutritional causes or conditions linked to low protein intake [41]. When ruling out these diseases due to study exclusion criteria, some nutritional factors could influence the results of serum Cu deficiency.

Intestinal absorption of Fe, Zn and Cu is inhibited by phytates, and other chemical compounds present in foods such as cereals, which are consumed more rates in low- and middle-income countries [1, 16, 17, 18, 39, 42]. Inflammation is a factor that could bias the measurement of Fe, Zn and Cu. Although Cuba is considered a country with a low burden of infections [43], current results point to the presence of acute and chronic inflammation. The BRINDA study demonstrated the usefulness of controlling for inflammation when evaluating Fe nutritional status, as even in countries with low inflammation prevalence, micronutrient status biomarkers were affected [44].

Hepcidins a hormone secreted by the liver which stimulates intestinal cells and the macrophage system, with two respective effects, reduction in Fe absorption and sequestration of circulating Fe. During the inflammatory process, interleukins stimulate the secretion of Hepcidin by the liver [7].

According to Raiten et al [7], during inflammation, serum Zn enters the liver, and its blond concentration tends to decrease [7]. However, this was not demonstrated for women of reproductive age in the BRINDA project study [22]. The present study's findings are similar to those reported by BRINDA, although it remains unclear how inflammation modifies Zn metabolism in women of reproductive age, who may be influenced by hormonal factors.

Cp is one of the last proteins to rise after the inflammatory stimulus, reaching its maximum concentration within 2 to 5 days [7]. During inflammation, serum Cu leaves the liver bound to Cp, and its concentration tends to increase [30], potentially explaining the lower proportion of women with serum Cu deficiency in the group with inflammation.

The ROC curve is commonly used to estimate the diagnostic capacity of variables related to specific events [45]. The AUC> 0.7 [45,46,47], associated with the Cp ROC curve suggests that it could be used to identify individuals with inflammation. Other authors have used Cp as an inflammation biomarker in nutritional evaluation studies [29, 30]. Like AGP, Cp only increases 30 to 60% above its basal value in response to inflammation, with its maximum response occurring between the 4th and 5th day after the inflammatory stimulus. However, AGP 2 to 5 times its basal value during inflammation. CRP value in the presence of inflammation tends to be 20 to 1000 times higher than its baseline value in the first 24 to 48 h of the inflammatory stimulus [7].

Although CRP and AGP are the two most recommended frequently used biomarkers in clinical and population studies, they are not always available, especially in low-resource countries. Therefore, it is desirable to use other biomarkers, even those with lower explanatory power, such as Cp and CRP, which increase at different times after the inflammatory stimulus. The subjective choice of 0.35 g/L as the cut-off point in the present study was based on a reasonable balance between sensitivity and specificity.

The findings of this study serve as a potential alert for Cuban public health, particularly given the current context. The prevalence of low serum Zn levels exceeds 20%, the threshold established by experts to identify populations at risk of this micronutrient deficiency. These results highlight the critical importance of incorporating the assessment of inflammation into clinical protocols for investigating anemia of proba-

ble nutritional origin. Further research is strongly recommended to deepen the understanding of the relationship between anemia, serum Zn and Cu deficiencies, and the impact of inflammation, as well as to identify the underlying factors contributing to micronutrient deficiencies in women of reproductive age.

Among the limitations of this study is the lack of measurement of food intake. The absence of information on dietary intake data limits the possibility to fully interpret the relationship between micronutrient deficiencies and anemia, as well as to identify potential dietary contributors to these deficiencies. The age range used may also be considered a limitation, as women of reproductive age include adolescents from 15 years old to adults over 40 years old. The decision to focus on women aged 18 to 40 was based on the low parity of Cuban women after 40 years and the need to optimize the limited resources available. Despite these limitations, the strengths of the study include the sample size, the biochemical analyses conducted, and the robust statistical analysis employed. Another strength is that this study presents findings using the first micronutrient data from Cuban women.

CONCLUSIONS

In conclusion, the present study highlights the urgent need to address malnutrition problems, particularly micronutrient deficiencies such as Zn and Fe, and their association with anemia. These deficiencies, exacerbated by anemia and inflammation, pose a critical public health concern in Cuba and other developing countries. It also underscores the importance of considering the effect of inflammation on nutritional anemias in clinical practice. Some recommendations include the implementation of targeted interventions such as dietary diversification, nutritional education, and fortification programs, complementing existing strategies for anemia prevention. Further research is essential to explore the interplay between inflammation and micronutrient metabolism, as well as the effectiveness of tailored public policies in reducing these deficiencies. Strengthening surveillance systems to monitor nutritional biomarkers is crucial to inform and evaluate public health initiatives.

AUTHORS' CONTRIBUTIONS

The author confirms sole responsibility for the following: study conception and design, data collection, analysis and interpretation of results, and manuscript preparation.

LIST OF ABBREVIATIONS

INHEM = National Institute of Hygiene, Epidemiology, and Microbiology

FAO = Food and Agricultural Organization

CRP-hs = High Sensitivity C Reactive Protein

AGP = Alpha-1 Glycoprotein

Cp = Ceruloplasmin

Fe = Iron

Zn = Zinc

Cu = Copper

BRINDA = Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia

OR = Odds Ratio

AUC = Area Under the Curve

CONSENT FOR PUBLICATION

Not applicable.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest related to the content of this study.

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