



## Letter to the Editor

# Response to the assessment of the Matos & Carvalho index by Hoffmann and Urrechaga



Dear Editor,

Hoffmann and Urrechaga evaluated the Matos & Carvalho Index (MCI),<sup>1</sup> however they performed their analyses characterizing the population differently from that used by us. In Matos et al.,<sup>2</sup> anemia was characterized as hemoglobin (Hb) <12 g/dL for women and <13 g/dL for men.<sup>3</sup> Conversely, Hoffmann and Urrechaga characterized anemia using the value of Hb <13 g/dL, independent of the sex of the patients, which is not recommended by the World Health Organization.<sup>3</sup> In addition, the characterization of iron deficiency anemia (IDA) performed in our study was based on the ferritin level according to the gender, that is, <6 ng/mL for women and <28 ng/mL for men. Hoffmann and Urrechaga characterized IDA using ferritin <15 µg/L regardless of gender. This variation in the definition of cases of anemia, particularly IDA, may affect the results, since in the study conducted by Hoffmann and Urrechaga, false positive women with Hb values greater than 12 g/dL and less than 13 g/dL were included in the study. Moreover, women with IDA and ferritin levels >6 and <15 ng/mL (false positive) and true positive men with ferritin levels >15 and <28 ng/mL were excluded. It is important to highlight that different criteria in the sample selection may interfere with the results of sensitivity, specificity and area under the curve.

Following the above, some other aspects deserve clarification:

Firstly, in Brazil, some studies have already been carried out to determine the frequency of the 3.7 kb deletion, the main mutation causing  $\alpha$ -thalassemia, with frequencies between 20% and 25% being found in the population studied.<sup>4,5</sup> Despite this high frequency, the correct diagnosis of this disorder depends on molecular tests that are not accessible to a large proportion of the Brazilian population. Although used in many clinical laboratories, the hemoglobin (Hb) H test shows low sensitivity. The prevalence of the  $\beta$ -thalassemia trait in Brazil is certainly lower than that observed in Mediterranean countries.

Secondly, with regard to the prevalence of IDA, it is possible to observe that this disorder is more prevalent in all groups and age ranges when comparing non-industrialized to industrialized countries.<sup>6</sup> Thus, considering the reality of the Brazilian population, an index that shows good sensitivity for the diagnosis of IDA, a common condition that causes microcytosis in Brazil, would be important.

It should be noted that the objective of Matos et al. was to develop a screening tool that could guide the physician as to which clinical conduct should be adopted as mentioned in the discussion of the article.<sup>2</sup> The inability of the MCI to discriminate between IDA and the thalassemia trait (TT) is a limitation of this formula clearly described in the discussion of the article.<sup>2</sup> However, we consider that this index may be useful as a screening tool in a population with similar epidemiological characteristics as the same laboratory diagnostic criteria were adopted for IDA and the TT.

In order to further clarify the usefulness of the MCI, we highlight part of the discussion by Matos et al.<sup>2</sup>: "Despite the advantages and simplicity of the implementation of the MCI in the laboratory practice, there is a limitation of MCI and other discriminating formulas since they are not able to differentiate all cases of IDA from TT. In light of this, two situations can occur that deserve special attention: (i) the index indicated TT, but the patient had IDA and (ii) the application of the index indicated IDA, but the patient was a TT carrier. In the first case, patient follow-up is necessary and will indicate, over time, a significant reduction in circulating hemoglobin levels, prompting the physician to request investigative tests of iron metabolism. In the latter situation, patient follow-up is also needed which will show the need for medical procedures. In this case, the prescription of iron would not increase the hemoglobin level due to the genetic disorder. In cases of concomitant diseases, monitoring can also clarify the best medical approach. Therefore, MCI is a useful tool in guiding the physician regarding the initial conduct to be adopted; however, it does not eliminate the need of a follow-up that eventually may require confirmatory tests".

With regard to the MCI using the mean corpuscular hemoglobin concentration (MCHC), this parameter is calculated by hematology analyzers and is not obtained directly similar to the other parameters and this may weaken its discriminative value. However, all the parameters obtained directly from hematology analyzers were tested by a professional with recognized competence in the area of statistics at the time of index development and MCHC combined with the red blood cell count, provided the best discriminant power.

Finally, we agree with the comment of Hoffmann and Urrechaga regarding the recommendation to laboratories that any newly published index should be used only after additional validation in their own patient population.

### Conflict of interest

The authors declare no conflicts of interest.

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