Dear Editor,

Currently, iron-deficiency anaemia (IDA) is considered one of the main public health problems affecting populations worldwide. The impact of intervention with iron supplementation or food fortification is modest, and still 802 million of preschool children and women in reproductive age are diagnosed as anemic, and it is suggested that 50% is due to iron deficiency [1]. The highest prevalence in each country is observed in populations residing at high altitudes (HA). Recent evidence suggests that this is due to the correction of threshold of haemoglobin to define anaemia at HA rather than a true condition of anaemia [2]. The rationale behind this correction is that as altitude increases, the haemoglobin levels increase and different equations to correct haemoglobin by altitude have been suggested [3]. However, an elevation of haemoglobin concentration as altitude increases is not a universal feature of all HA populations [4].

However, none of the studies suggesting correction of haemoglobin by altitude have used a gold standard to demonstrate that haemoglobin correction is correctly diagnosing iron-deficiency anaemia. This is possible by comparing area under the receiver-operating characteristic (ROC) curves using uncorrected (Fig. 1a) or corrected haemoglobin by altitude as the WHO recommends (Fig. 1b) to define anaemia and compare results with serum ferritin levels as marker of iron status. For this, we have constructed ROC curves to characterize the sensitivity and specificity based on a previously described sample of 133 healthy children from Puno (3,800 m), Peru, without inflammatory disease and aged between 6 and 24 months [5]. Haemoglobin correction by altitude reduces by 60% the prevalence of IDA but increases by three times the prevalence of anaemia. ROC curves analysis showed the highest AUC with anaemia defined with uncorrected haemoglobin values (AUC 0.87) compared to that using the haemoglobin correction by altitude (AUC 0.68). Differences between both ROC curves were significant at $p = 0.002223$. Sensitivity (true anaemics correctly identified) was 100% using uncorrected haemoglobin to define anaemia and 54.17% using corrected haemoglobin to define anaemia. Specificity (true non-anaemics correctly identified) was 74.6% with uncorrected haemoglobin and 100% with corrected haemoglobin.

Suitability of haemoglobin correction should allow demonstrating that the prevalence of anaemia after correction was closely related to iron deficiency compared to uncorrected haemoglobin. This was not observed in our results. Evidence in children residents of the highlands demonstrates that the application of the current WHO age-sex-altitude adjusted haemoglobin concentration threshold overestimates the prevalence of anaemia. The diagnosis of anaemics includes children with normal iron content, and in these cases intervention with iron will be unsuccessful.

Our results suggest that the altitude adjustment criteria to diagnose anaemia might not be appropriate to use in Andean children and support a similar proposal in Ethiopian highlanders [2]. This also may apply to populations living in other highland regions.

Since the body of evidence continues to grow, we urge for a revision of the current criteria to diagnose anaemia at HA due to the profound effects that misdiagnosis and overdiagnosis might have on public health. This is important, since 356 million inhabitants live over 1,000 m worldwide.
Fig. 1. ROC curves for anaemia defined with uncorrected haemoglobin (Hb), AUC 0.8661 (95% CI 0.799–0.932) (a). Anaemia defined with corrected Hb by the current cut-off points based on the equation: Hb correction = −0.032 (altitude × 0.0032808) + 0.022 (altitude × 0.0032808)^2, AUC 0.6833 (95% CI 0.584–0.782). ROC plot A is statistically different compared to ROC plot B (p = 0.002223). Ferritin (ng/mL) was used as an iron status marker and was measured with a commercial ELISA kit (DRG International, INC, USA). Sensitivity is the proportion of true anaemics that are correctly identified by the test. Specificity is the proportion of true non-anaemics that are correctly identified by the test. Accuracy is the proportion of correct decisions: true anaemics + true non-anaemics/number of total tested. Sensitivity: 100% (95% CI 93.3–100) (a) versus 54.17% (95% CI 40.8–68.3) (b). Specificity: 74.58% (95% CI 64.4–85.59) (a) versus specificity: 100% (95% CI 84.6–100) (b). Accuracy: 77.44% (95% CI 68.42–86.47). Sensitivity: accuracy: 57.89% (95% CI 45.9–70.6) (b).

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Author Contributions

The authors’ contributions were as follows: G.F.G., J.B., and D.E.A.-Y. conceived the article; G.F.G. and D.E.A.-Y. performed the analysis; D.E.A.-Y. and G.F.G. drafted the manuscript; and D.E.A.-Y., J.B. and G.F.G. critically reviewed and contributed to the final version.

References


