Poor Validity of Noninvasive Hemoglobin Measurements by Pulse Oximetry Compared with Conventional Absorptiometry in Children in Côte d'Ivoire

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Abstract. Anemia remains a major public health issue in many African communities. We compared a novel, commercially available noninvasive hemoglobin (Hb)–measuring device to direct Hb measurements by finger-prick samples in a pediatric cohort in rural Côte d'Ivoire. Noninvasive Hb measurements were attempted in 191 children 2–15 years of age and obtained in 102 (53.5%) children. The median Hb for the 102 children was 12.0 g/dL (interquartile range [IQR] = 11.3–12.7 g/dL) for conventional absorptiometry and 13.3 g/dL (IQR = 12.1–14.2 g/dL) for noninvasive measurements. A Bland–Altman analysis demonstrated a median bias of +1.1 g/dL (IQR = 0.4–2.0 g/dL), with greater overestimation of Hb by noninvasive testing occurring at low Hb values. This overestimation of the noninvasive Hb–measuring device to direct Hb measurements persisted across preschool- and school-aged children, and both sexes. The Pearson correlation coefficient was 0.50 for children 4–9 years of age, and 0.33 for children 10–15 years of age. Further study and development of noninvasive Hb devices is necessary prior to implementation in African pediatric populations.

INTRODUCTION

Approximately 60% of African children are affected by anemia with signs of a potentially worsening problem.¹ Anemia contributes to ill-health and debilitation, diminished work capacity, reduced ability to execute activities of daily living, increased maternal mortality risks, and reduced cognitive function, whereas chronic anemia that develops in infancy and childhood may have additional long-lasting effects on well-being and function.^{1–4} Assessing the causes of anemia is challenging. In low- and middle-income countries, the key factors are dietary insufficiencies (e.g., folic acid or vitamin A deficiencies), chronic diseases and inflammation (e.g., human immunodeficiency virus and tuberculosis), malaria (resulting in hemolysis), malabsorption, and iron loss due to gastrointestinal infections (e.g., hookworm, *Schistosoma* spp., and *Helicobacter pylori*).^{4,5} It is likely that multiple mechanisms mediate anemia in the context of schistosomiasis.⁶ More than 750 million people are at risk of schistosomiasis and at least 250 million individuals are infected, mainly with *Schistosoma haematobium*, *Schistosoma mansoni*, and *Schistosoma japonicum*.⁷ Between 1990 and 2010, schistosomiasis-related anemia was one of the few anemic conditions to increase in prevalence.⁸ Schistosomiasis is highly prevalent in the area where this project was conducted and is a significant contributor to anemia of chronic diseases in this region.

Anemia is most reliably assessed by measuring hemoglobin (Hb) levels, rather than by clinical signs. Because assessment requires phlebotomy, the extent of illustrative surveys on the etiology of anemia is sparse.¹ Measurement of blood Hb is therefore crucial to clinical care and research throughout the world; however, obtaining blood via phlebotomy presents several unique challenges in certain resource-constrained

settings. These include limited infrastructure to draw and process blood⁹ and, occasionally, cultural beliefs and rumors such as sorcery and blood selling.¹⁰ Noninvasive Hb testing may provide a solution to some of these problems. Several devices are now commercially available and have been studied in a variety of settings with somewhat mixed results when compared with both invasive point-of-care devices and venous blood samples processed on a laboratory analyzer.^{11–15} A recent meta-analysis identified 39 relevant studies and concluded that noninvasive Masimo Pronto-7[®] devices provide an unbiased, pooled estimate of laboratory Hb, yet have lower precision and wider 95% limits of agreement than invasive HemoCue devices.¹⁶

Representative data on anemia are sparse in settings where anemia is most prevalent and particularly in settings without clinical facilities, where noninvasive methods are welcomed by both patients and medical personnel. However, some data have suggested that there is low accuracy of noninvasive Hb devices in patients with dark skin pigmentation.¹² To our knowledge, noninvasive Hb devices have not yet been tested in an African setting. Hence, the aim of our study was to compare a novel, noninvasive device to measure Hb values with a calibrated finger-prick blood sample in an African pediatric population.

METHODS

The current investigation was integrated into a larger study pertaining to efficacy, safety, and pharmacodynamics of praziquantel in preschool-aged (2–5 years) and school-aged (6–15 years) children infected with *S. mansoni* (results to be presented elsewhere). Ethical approval was obtained from the Ethics Committee of Northwestern and Central Switzerland (EKNZ; reference no. 162/2014) and the Comité National d'Ethique et de la Recherche du Ministère de la Santé et de l'Hygiène Publique in Côte d'Ivoire (no. 50/2014). The study is registered on the ISRCTN registry (unique identifier: 15280205).

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FIGURE 1. Study flow.

In December 2014, a total of 302 children (179 school-aged children 6–15 years of age and 124 preschool-aged children 2–5 years of age) were examined in the villages of Allain, Elevi, Makouguié, M'Bromé, and Odoguie in the district of Agboville, south Côte d'Ivoire. Baseline Hb values were obtained from all children via finger prick, using a calibrated HemoCue device (HemoCue 301 system; Ångelholm, Sweden). On the same day, during clinical examination, Hb levels were measured with a Masimo Pronto-7® non-

invasive Hb measuring device (Masimo; Irvine, CA). This device uses pulse oximetry to predict Hb levels in individuals. The study staff was skilled at both Hb measuring systems. The same study staff used the Hb-measuring devices throughout the study. We followed operational instructions and used specific pediatric finger gloves (for children weighing 10–50 kg). Results from each device were entered into a spreadsheet (Microsoft Excel 2010; Microsoft, Redmond, WA) and data were analyzed with R (R Foundation for

FIGURE 2. Bland–Altman plot of difference in hemoglobin measurement between noninvasive pulse oximetry device (Masimo Pronto-7®) and conventional absorptiometry (HemoCue), as a function of measurement by the conventional test. The solid line indicates the median difference, dashed lines indicated 25th and 75th percentiles, and the dotted line indicates a null difference.

TABLE 1

Diagnostic operating parameters of conventional absorptiometry vs. noninvasive pulse oximetry hemoglobin measurements in children in Côte d'Ivoire

Children	Conventional absorptiometry hemoglobin measurement, HemoCue, g/dL, (IQR) N = 102	Noninvasive pulse oximetry hemoglobin measurement, [Masimo Pronto-7 [®]], g/dL, (IQR) N = 102	Pearson product correlation between both devices
All	12.0 (11.3–12.7)	13.3 (12.1–14.2)	
Age 4–9 years	11.7 (11.2–12.3)	12.9 (12.0–14.2)	0.50
Age 10–15 years	12.3 (11.5–13.1)	13.4 (12.7–14.2)	0.33
Male	12.1 (11.4–12.8)	13.5 (12.9–14.4)	0.25
Female	12.0 (11.2–12.6)	12.8 (12.0–13.7)	0.53

IQR = interquartile range.

Statistical Computing; Vienna, Austria). The staff was blinded to any prior Hb values during the course of this study.

RESULTS AND DISCUSSION

The study flow is presented in Figure 1. Noninvasive Hb measurement using the portable pulse oximetry device was attempted on 191 school-aged and preschool-aged children, for which Hb values with the HemoCue system were obtained. Noninvasive Hb values were obtained for 102 individuals (53.4%); the device was unable to provide a reading on the remaining 89 (46.6%) children. Of note, as it was time consuming and cumbersome to keep retrying the measurements, the use of the device was abandoned after the 12th preschool-aged child.

Of the 102 children for whom an Hb measurement with both devices was obtained, the median age was 10 years (interquartile range [IQR] = 8–11 years). The median Hb by conventional absorptiometry for the 102 children was 12.0 g/dL (IQR = 11.3–12.7 g/dL). Median Hb by the noninvasive pulse oximetry device was 13.3 g/dL (IQR = 12.1–14.2 g/dL). No results were obtained by the noninvasive pulse oximetry device from children aged 2 to 3 years. Our results demonstrate a poor correlation between noninvasive Hb measurements from the noninvasive pulse oximetry device and values from a calibrated HemoCue device. This persisted across multiple age groups and both sexes, with a pattern of significant overestimation of Hb, particularly at lower values. A Bland–Altman nonparametric analysis demonstrated a median bias of +1.1 g/dL and IQR of 0.4–2.0 g/dL, with greater overestimation of Hb by noninvasive testing occurring at low Hb values ($\beta = -0.35$, $P < 0.001$; Figure 2). Pearson product moment correlation coefficient was 0.50 for children 4–9 years of age, and 0.33 for children 10–15 years of age. Pearson coefficient was 0.25 for males and 0.53 for females. Summary statistics are given in Table 1.

The reasons for the poor correlation between the two devices are not entirely clear, in particular since they were compared in the same setting, at the same time, and in children with the same medical condition. Earlier attempts showing discrepancies among Hb devices were not compared in a single study,¹² hence differences in the outcome might be somewhat expected. One possibility is the limitation previously described for patients with darker skin pigmentation, which is plausible since measurements are based on light passing through skin and soft tissue to a photodetector. Moreover, the overestimation was higher in patients with lower Hb levels, which are rather typical for children in malaria-endemic resource-constrained regions of west Africa.¹⁷ As a related note, one limitation of our

study is the use of a finger-prick device as a comparison, since this is not the gold standard method for measuring Hb. Indeed, the finger prick itself can overestimate Hb in certain patient populations, for example, those with absent iron stores.¹⁸ Regardless, the finger-prick technique is an extremely common and well-validated mode of Hb measurement in clinical, public health, and research settings in low- and middle-income countries, often used as a diagnostic 'gold' standard in these settings.¹⁹ Another limitation is our use of only a single noninvasive pulse oximetry device for measurement for all comparisons.

In conclusion, our data demonstrate the need for further study of noninvasive Hb devices prior to implementation in African pediatric populations. Optimally, such studies would not only provide evidence, but could inform better design and/or manufacturing for tropical resource-constrained rural settings, where they are most needed. Although these devices have many positive attributes, they must be validated in different populations prior to scale-up.

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