Title | COMPARING METHODS AND HEMOCUE DEVICES TO DETERMINE HEMOGLOBIN IN POPULATION SURVEYS

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PROBLEM STATEMENT

Hemoglobin (Hb) measurements vary when obtained using different blood sample types (venous vs. capillary pool or drop) and different analytical devices (HemoCue vs. automated analyzers), among other factors.

The use of different Hb assessment methods in population-based surveys has resulted in varying anemia prevalence estimates, causing challenges in identifying suitable interventions for reducing anemia and tracking progress in anemia reduction. This laboratory-based, multi-site comparative study aimed to identify optimal procedures and methods for Hb assessment in population surveys.

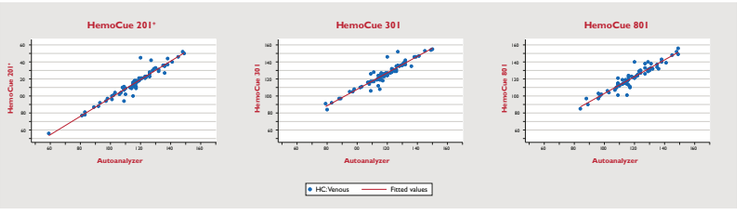
Our study included women of reproductive age (WRA) and young children (YC) 12–59-months-old and compared Hb results from venous (HC:Venous), pooled capillary (HC:Pooled), and single-drop capillary (HC:Drop) samples on different HemoCue models (201^{+}, 301, 801) against the gold standard: venous blood measured via a certified autoanalyzer (AA:Venous).

RESEARCH METHODS

The study was implemented in five sites: Cambodia, Guatemala, Lebanon, Nigeria, and Tanzania. Each site recruited up to four cohorts (one for HC:Pooled and three—one per HemoCue model—for HC:Drop comparisons) of 36 apparently healthy participants (18 WRA and 18 YC). Each participant provided paired blood samples: one venous and one capillary (HC:Pooled or HC:Drop) to allow for the following comparisons of HemoCue (201^{+}, 301, and 801) Hb measurements—HemoCue validation (AA:Venous versus HC:Venous) and sample comparison (AA:Venous versus HC:Pooled or HC:Drop).

We performed linear regression calibration (HC:Venous against AA:Venous) to account for method systematic bias (**figure 1**) per HemoCue model and we adjusted values per blood sample type. We calculated concordance correlation coefficients (CCC, adjusted and unadjusted), and average Bland-Altman (B-A) distance with 95 percent confidence intervals ([CI] or limits of agreement [LOA]).

Figure 1. Linear Correlation of Hb Concentration (in g/L) with HC:Venous (y-axis) versus AA:Venous (x-axis) in HemoCue models; example from Cambodia



FINDINGS

Across all five sites, HC:Venous versus AA:Venous showed good agreement (CCC range unadjusted: 0.75–0.97, adjusted: 0.86–0.98). Average B-A distance in HC:Venous versus AA:Venous varied from -1.7–7.3 g/L (unadjusted) to -0.9–0.2 g/L (adjusted), demonstrating improved accuracy upon adjustment. Other blood sample types resulted in improvements, albeit to a lesser degree (**table 1**). HemoCue 301 consistently overestimated Hb concentration in all countries, while the other models' performances varied by country, suggesting the need for adjustment by individual device per model.

- LOA vary by country; the difference between Hb in AA:Venous versus HC:Drop could be as high as ±25 g/L and ±28 g/L for HC:Pooled, reflecting random error possibly attributable to uncontrolled variation of Hb concentration among drops of capillary blood and/or the handling of blood samples by technicians.
- Technicians in this study were trained professionals; variation may increase with less experienced personnel, emphasizing the need for adequate training.
- In Guatemala and Cambodia HC:Pooled Hb was similar in precision to AA:Venous. However, in Tanzania and Lebanon HC:Pooled was not more precise than HC:Drop, suggesting the need for improving methodology, training, and supervision for HC:Pooled collection (**figure 2**).

Table 1: Pattern of Device Systematic Error (left side of the table) and random error or LOA (right side of the table) between the HemoCue Values with Each Blood Sample Type vs. AA: Venous

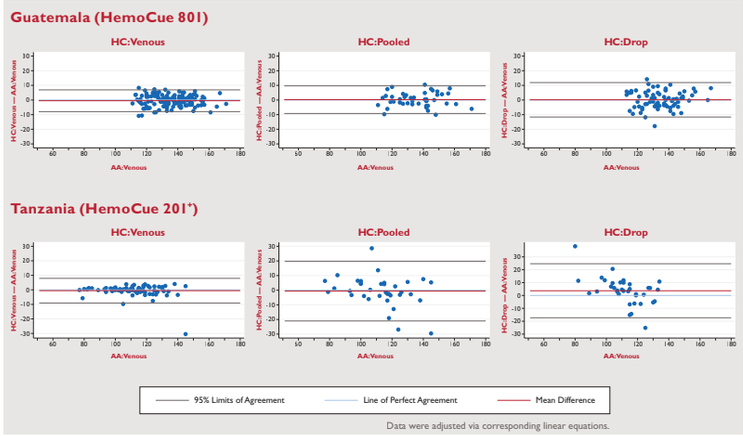
		Device Systematic Error (Hb g/L)						LOA (Hb g/L)		
		HC:Venous		HC:Pooled		HC:Drop		HC:Venous	HC:Pooled	HC:Drop
Country	HemoCue Model	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted	Adjusted	Adjusted	Adjusted
Guatemala	201^{+}									
	301									
	801									
Cambodia	201^{+}									
	301									
	801									
Tanzania	201^{+}									
	301									
Lebanon	201^{+}									
	301									
	801									
Nigeria	201^{+}									
	301									

Difference in g/L	±1	1.1–2	2.1–3.9	>4	≤10	10.1–15	15.1–20	>20

KEY TAKE-AWAY

- **HemoCue Hb measurements from capillary blood, particularly single-drop, result in unacceptably large variation; venous blood generates precise measurements.**
- **We identified model and device biases; regression calibration adjustment can address systematic bias in HemoCue devices.**

Figure 2. Examples of Difference Plots using Adjusted Hemoglobin Values from Guatemala and Tanzania



CONCLUSION

- Method performance adjustment via regression calibration increases the accuracy of Hb estimates from HemoCue devices.
- With regression adjustment, the accuracy among the three HemoCue devices was satisfactory and they can be used interchangeably.
- Venous was the most reliable for Hb blood sample type determination and should be the sample of choice.
- HC:Drop resulted in large variation in all, HC:Pooled only in some countries, emphasizing the need to avoid using HC:Drop and improving HC:Pooled before considering their use in HemoCue.

The authors declare no conflict of interest.

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