SHORT ARTICLE

Validity of point-of-care device for diagnosing anemia in workers exposed to lead

Ankit Viramgami[1], Soundarya Soundarajan[2], Ankit Sheth[3], Kuldip Upadhyay[4]

[1]Scientist-C (Medical), Health Science Division, Indian Council of Medical Research - National Institute of Occupational Health, Ahmedabad, Gujarat; [2]Scientist-B (Medical), Health Science Division, Indian Council of Medical Research - National Institute of Occupational Health, Ahmedabad, Gujarat; [3]Scientist-E (Medical), Health Science Division, Indian Council of Medical Research - National Institute of Occupational Health, Ahmedabad, Gujarat; [4]Scientist-C, Chemical Science Division, Indian Council of Medical Research - National Institute of Occupational Health, Ahmedabad, Gujarat

Corresponding Author

Dr Kuldeep Upadhyay, Chemical Science Division, Indian Council of Medical Research - National Institute of Occupational Health, Meghaninagar, Ahmedabad, Gujarat, India - 380016
E Mail ID: drkuldip_upadhyay@rediffmail.com

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Abstract

Detecting anemia in occupational health settings is critical in a high-risk population for anemia like the lead-exposed. Whether the point-of-care devices are sensitive to detect anemia in individuals with high levels of lead exposure is unknown. We compared hemoglobin (Hb) levels from HemoCue® Hb 301 System and standard analyzer, Mindrey-BC 5300, in individuals (n=58) exposed to lead (mean levels = 44.9 µg/dL) for a chronic period (mean duration of exposure = 105 months). We observed high sensitivity (0.95), specificity(0.95) in detecting anemia by hemocue, and high agreement between the methods. The significant difference in Hb values between the methods (0.171g/dL, p=0.018) was clinically minimal. We conclude that hemocue is a good method for rapidly detecting anemia and estimating Hb levels among the lead-exposed in resource-limited settings.

Keywords

Lead; Point-of-Care Systems; Occupational Health; Hemoglobin; Anemia

Introduction

Anemia is a known risk factor for recurrent infections, reduced cognitive performance, and reduced workplace productivity (1-3). About 25% of Indian men suffer from anemia (4). And, occupational risk like lead exposure further adds to the burden.

Lead prevents the heme synthesis by inhibiting the enzymatic activity of ***δ***-Amino levulinic acid dehydratase and ferrochelatase, and subsequent decreases in blood hemoglobin (Hb). This results in the development of microcytic, hypochromic anemia.

Accurate screening of anemia at the individual level in occupational health setting is important to identify those who require treatment. Thus, methods for Hb measurement must be sensitive, specific, accurate, reproducible, and cost-effective. Portable point-of-care Hb devices like Hemocue have picked up pace recently as screening procedures as they offer rapid testing. Also, this can be a preferred method in low-resource settings like India. However, point-of-care results must be accurate to avoid false exclusion, inclusion, and clinical misdiagnosis.

In this view, few studies have reported testing Hemocue as a point-of-care device to detect anemia, in community settings and studies focusing on children and women (5, 6). However, whether hemocue results would be influenced by lead levels in the blood is unknown. Thus, screening for anemia in occupational health settings is of primary importance.

Aims & Objectives

To investigate whether the estimation of Hb levels in blood samples of occupationally lead-exposed individuals with high blood-lead concentrations by a portable point of care device (HemoCue 301) is sensitive and in addition to

validate the precision of Hb estimation in comparison with automated hematology analyzer (Mindray-BC 5300).

Material & Methods

Validation of Measurement: Present validation work for point-of-care portable hemoglobin (Hb) estimation device (HemoCue® Hb 301 System) was performed from Oct'19 - Nov'19 as a part of a large cross-sectional study aimed to determine the health effects of lead among the workers of a lead smelting plant (situated in the western part of India). During the first phase of the project, nearly one-third of study subjects (58 out of 201 participants) were randomly selected for estimation of Hb with an automated blood cell counter (Mindrey-BC 5300, as a standard laboratory test) and portable point-of-care device (HemoCue® Hb 301 System). Institutional ethical committee approval was received before the initiation of participant recruitment. On receipt of written informed consent from each study participant, relevant socio-demographic and occupational details were collected using a pre-validated structured questionnaire. After completion of the clinical evaluation of each subject, 5 ml of venous blood was collected using an aseptic technique for laboratory investigations. From the collected sample, about 1-2 ml of blood was stored in EDTA vacutainer at 2-8 °C until laboratory evaluation. Within 48 hours of sample collection, Hb estimation was performed with Mindrey-BC 5300 and HemoCue® Hb 301 System as recommended by the manufacturers. To ensure the quality of the report, for HemoCue® Hb 301 control cuvette (Eurotrol Sr. No. 93350, 93351 & 93352) for known concentration standards (low, normal & high; respectively) were used. Similarly, in the case of Mindrey-BC 5300 internal quality assurance tri-level controls (high, normal & low; BC-5D Mindray Hematology Control Sr. NO. BC2001B) were run before Hb estimation of study samples. Guidelines of WHO were followed to classify study subjects with Hb <13.0 g/Dl as anemic (7).

Statistical Analysis: Interrelations among the variables were tested by the bivariate Spearman test. The difference in Hb values between the methods was tested by paired-t-tests. All correlations were spearman and covariates were controlled in partial correlations. To understand the diagnostic accuracy of Hemocue methods, we calculated sensitivity and specificity in detecting anemia. To assess the agreement between the methods for Hb estimation, we used a Bland-Altman plot, after calculating the mean differences (mean bias) between the estimated methods. All analyses were run in R studio (8).

Results

In total, 58 participants (Mean age = 35.9, SD = 6.9, range: [23, 53]) were included in the study. All participants were males with average lead levels (M = 44.49, SD = 10.7) µg/dL, with a mean lead exposure duration of (M = 105.6, SD = 25.9) months. There were significant correlations between the studied variables: age, Hb levels by hemocue and standard, lead levels, and duration of lead exposure (Table1).

Hb levels from both methods were significantly negatively correlated with age as well as blood lead levels. The higher the age, the lesser the Hb values. To understand whether this relationship is due to lead levels and their exposure, we controlled for them in partial correlations. Even when controlling for lead levels and duration of lead exposure the correlation between age and Hb levels by both the methods was negative and significant: standard (r=-0.382,p=0.003) and hemocue (r=-0.405,p=0.002).

Lead levels were significantly negatively correlated with Hb levels from both methods. This suggests higher lead levels are associated with lower Hb values detected by both methods. However, on controlling for age and duration of lead exposure, the correlations between lead and Hb levels were no longer significant (Standard: r=-0.195, p=0.148 and Hemocue: r=-0.204, p=0.132).

On comparing the mean Hb scores between both methods, we observed Hb values from the hemocue (M = 13.61, SD = 1.9) were significantly higher than the standard (M = 13.44, SD = 1.8) test values. This difference (0.171, 95% CI[0.030,0.311]) was statistically significant, t(57)=2.43, p=0.018.

High diagnostic accuracy and precision between hemocue and standard method

19 subjects had anemia based on the standard test assessing hemoglobin; sensitivity and specificity of hemocue in identifying anemia were 0.95 (0.74,1.00) and 0.95 (0.83.0.99) respectively, with positive and negative predictive values 0.90 (0.68,0.99) and 0.97 (0.86, 1.00) respectively. ROC curve for detecting anemia using hemocue compared with standard autoanalyzer among lead-exposed individuals is depicted in Figure-1. The Area under the curve (AUC) for hemocue was 97%, for anemia detection.

High agreement between h

emocue and standard method

From the Bland-Altman plot (Figure 2), The mean difference was 0.176 with an SD of 0.5. The mean differences were normally distributed per the Shapiro-Wilk test (W = 0.98, p-value = 0.579). The Bland-Altman plot indicates good agreement between the methods and differences lie close to the mean bias of 0.176. Clinically this difference in hemoglobin is not significant. The limits of the agreement were -0.898 and 1.239

Kappa values were noted to be 0.884 (p<0.001) and Lin's concordance between the estimated methods was statistically significant, ρc = 0.96 with 95% CI[0.93,0.97] (Figure 3) and this is substantial according to McBride G et al [9).

Discussion

A rapid, valid and accurate screening for anemia in occupational health settings is critical, especially in

populations at-risk for anemia like the lead-exposed. This study aimed to validate hemocue, a point of care device to detect anemia in occupational health settings. Especially the precision of Hb estimation in lead-exposed individuals without any interference of lead levels in the blood was explored. We observed excellent sensitivity and specificity of Hemocue in detecting anemia in the lead-exposed and significant and high agreement between hemocue and standard autoanalyzer-based estimates of Hb. Both methods showed a significant negative correlation between lead and Hb levels. Our study demonstrates that Hemocue is a rapid point-of-care device in occupational screening for anemia among the lead exposed.

Our study indicated high sensitivity and specificity for hemocue to detect anemia in lead-exposed individuals. For a diagnostic test to be useful, the sum of sensitivity and specificity should be greater than 1.5 [10). In our study, this sum was 1.9, which is high. We observed high agreement between the methods, as indicated by substantial correlation in Lin's concordance and Bland-Altman methods. Thus, as a rapid testing method, hemocue can be a better alternative than time-consuming standard methods in occupational screening settings.

Even though we had a statistically significant difference among the methods, the difference in the Hb level was only 0.17g/dl, which is clinically a very small value. Also, compared to many other studies in hemocue reporting ranges of differences from 0.2- 0.35 g/dl even among the paired samples [11), the difference between the methods in our study (0.17g/dl) is quite low. We also observed a significant correlation between the lead levels and Hb values in both methods. However, this did not withstand correction for age. Hence, we hypothesize that lead levels do not affect hemocue readings, and thus it is a viable alternative to detect anemia rapidly, even among lead-exposed.

Conclusion

In conclusion, our study suggests hemocue method has good accuracy and is in good agreement with the standard estimations of Hb values.

Recommendation

Hemocue, a point-of-care device has good accuracy and offers a viable, economical and a rapid method for screening anemia in occupational setting in resource limited country like India.

Limitation of the study

Our study has a limited sample size for comparing methods of anemia detection. However, to the best of our knowledge, this is the first study to test the precision of hemocue in the lead-exposed workplace. Also, we could not test for inter-rater reliability in this sample, future studies should compare and contrast results among different testers of this method.

Relevance of the study

Whether accuracy of point-of-care device like hemocue results would be influenced by lead levels in the blood is unknown. However, the current study provides statistical evidence that Hemocue has good accuracy as well as good agreement with standard estimations of Hb even in lead exposed individuals.

Authors Contribution

AV and KU conceptualized and designed the study and collected the data. AV, SS and AS did the data and statistical analysis. AV and AS did the literature search. AV, SS, AS and KU prepared the manuscript. AS edited and reviewed the manuscript.

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Tables

TABLE 1 MEANS, STANDARD DEVIATIONS, AND CORRELATIONS AMONG STUDIED VARIABLES

Variable	M	SD	1	2	3	4
1. Age	35.90	6.94				
2. Hemocue	13.61	1.94	-.45***			
3. Standard	13.44	1.84	-.42***	.95****		
4. Lead level	44.49	10.74	.23	-.28*	-.27*	
5. Duration	105.55	25.89	.024	-.034	-.0006	-.047

*Note: M and SD are used to represent mean and standard deviation, respectively. * indicates p < .05. ** indicates p < .01.*

Figures

FIGURE-1. ROC CURVE

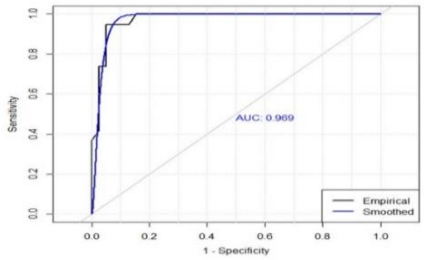

Figure legends: Receiver-operating characteristic (ROC) curve for anemia prediction based on Hb levels measured by hemocue and the standard methods. Hb: hemoglobin; AUC: Area under the curve

FIGURE-2: BLAND-ALTMAN PLOT FOR THE RELATION BETWEEN THE TWO METHODS EMPLOYED FOR HB ESTIMATION

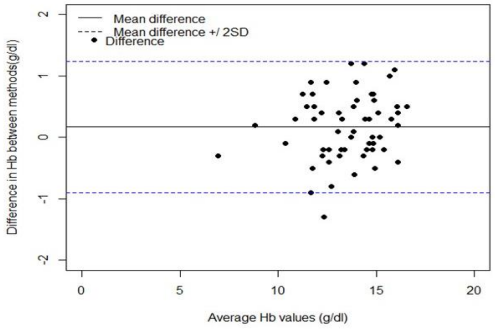

Figure legends: This is a scatterplot depicting the relationship between the average value and the differences in values between the measures. The black line indicates the mean of the differences between hemocue and the standard method of Hb estimation. The Upper and lower limits of the interval of the agreement are indicated in blue. They are +2SD and -2SD, respectively. The black line corresponds to -0.170, and the upper and lower limits are 0.876 and -1.218, respectively. 95% of the differences between the estimated methods lie within this range.

FIGURE-3: LIN'S CONCORDANCE SCATTERPLOT

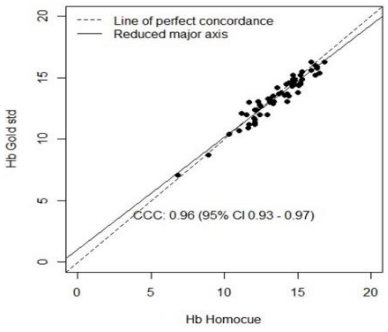

Figure legends: This scatterplot depicts Lin's concordance with 95% CI. The x-axis represents the Hb values from the Hemocue and the Y-axis represents the Gold standard values.