Comparison of the NBM 200 non-invasive haemoglobin sensor with Sahli's hemometer among adolescent girls in rural India

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Abbreviations: IDA- Iron deficiency anaemia, Hb- Haemoglobin, SD- Standard deviation

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Abstract

Objective: The study objective was to compare haemoglobin measurements between the NBM 200 (non-invasive haemoglobin sensor) and Sahli's hemometer in adolescent girls in a rural Indian setting.

Methods: Participants included girls aged between 13 to 17 years from 34 villages in Tuljapur and Lohara blocks of Osmanabad district, Maharashtra, India. Haemoglobin (Hb) measurements from the non-invasive sensor (NBM 200) were compared with measurements obtained from Sahli's hemometer using Bland-Altman plot, Spearman correlation coefficient, sensitivity, specificity, and area under the receiver operating characteristic curve analysis (AUROC).

Results: Paired measurements from both methods were obtained from 766 adolescent girls (N=766). Haemoglobin levels estimated by Sahli's hemometer ranged from 5.0 g/dL to 14.0 g/dL (mean: 10.1 g/dL, standard deviation (SD): 1.41), whereas measurements obtained from the NBM 200 ranged from 9.5 g/dL to 15.2 g/dL (mean: 12.8 g/dL, SD: 1.42). The Bland-Altman analysis indicated a mean difference of -2.70 g/dL (95% Confidence Intervals: -2.84 to -2.55) demonstrating an overestimation of Hb measurement by the NBM 200 compared to the Sahli's hemometer measurements. The NBM 200 showed low sensitivity (23.6%) and moderate specificity (61.8%) for the diagnosis of anaemia. The AUROC score was 0.43 indicating an underestimation of anaemia in our study population by the NBM 200.

Conclusion: Haemoglobin measurements obtained from the NBM 200 were consistently higher leading to an underestimation of anaemia prevalence compared with Sahli's hemometer estimates among adolescent girls in India.

Introduction

Iron deficiency anaemia (IDA) is a common nutritional disorder observed in Indian adolescent girls [1]. The preliminary diagnosis of anaemia is based on haemoglobin (Hb) levels [2]. In India, IDA prevalence among adolescent girls is about 56% [2], which is likely to affect physical growth, psychological development, school performance, and later reproductive health outcomes, particularly during pregnancy [3]. Thus early diagnosis of IDA and appropriate interventions are important in adolescent girls, especially in a country like India where marriage at a young age is followed by early pregnancies (18.2% girls get married by the age of 15 years, and 47.4% get married by the age of 18) [4]. Sahli's hemometer is a widely used method for haemoglobin estimation and anaemia diagnosis in rural areas of the country [5]. This is an inexpensive estimation method that requires a skilled technician. However availability of such diagnostic service is limited, particularly in geographically remote areas, where interruptions in diagnostic supplies can delay anaemia diagnosis and management [5,6].

The NBM 200 (Orsense Ltd, Nes-Ziona, Israel) is a portable non-invasive device (operating on electricity or batteries) that provides Hb measurements in 60 to 100 seconds [7]. Moreover, it has the advantage of not requiring material supplies (such as chemicals or needles) or post-testing bio-waste management services. The device provides the benefit of non-invasive testing that is not reliant on a skilled technician in areas where diagnostic facilities are limited [8]. The existing evidence-base involves comparisons of the non-invasive technology with haematology analysers or automated finger prick devices such as HemoCue (ANGELHOLM, Sweden); however, these methods are not commonly used in rural areas in India mainly because of high operational costs and limited healthcare infrastructure [4,9]. HemoCue requires a finger prick sample and is costly compared to Sahli's method due to the initial investment for the device (which ranges between 300 to 600 GBP) with higher recurring costs for testing materials compared to Sahli's approach [10,11]. Operational costs for each HemoCue test is about 35 to 40 Indian Rupees (0.35 GBP), which is twice the cost of the Sahli's method [10,11]. Similarly, automated haematology analyser machines are expensive (generally 4000 GBP onwards), and require venous blood withdrawal as well as advanced laboratory infrastructure and trained personnel. A single automated analyser test costs between 100 to 350 Indian Rupees (1.0 to 3.5 GBP) [10,11]. While the initial cost of a non-invasive device such as NBM 200 is also high (about 1100 GBP), when used on a larger scale (5000 tests and above), each test costs about 15 to 20 Indian rupees, which is similar with the cost of Sahli's hemometer. Moreover, the NBM 200 could be used in the community setting for mass screening by a healthcare auxiliary [7],[11]. Therefore, we conducted a study to compare Hb measurements generated by the NBM 200 with Sahli's hemometer to investigate the application of the non-invasive technique in an adolescent girl population from rural areas of Maharashtra state of India.

Methods

A cross-sectional survey was conducted in 34 villages of Osmanabad district of Maharashtra (~60,000 population) to investigate the prevalence and risk factors of anaemia in adolescent girls (Maharashtra Anaemia Study, Duration- 24 April 2014 to 30 June 2015). This manuscript reports on the secondary objective, which was to compare Hb measurements obtained from the non-invasive haemoglobin sensor NBM 200 and Sahli's hemometer (the reference method in our study). The study participants comprised of adolescent girls between 13 to 17 years of age who were residents of two blocks (Tuljapur and Lohara) of Osmanabad district, and were involved in the data collection in two phases. In both phases the study area had dry season with minimal temperature fluctuations. During the phase one, data were collected from April to May 2014 (2 months), and in the phase two data were collected between January and April 2015 (4 months). Participants were recruited after obtaining written consent from both individual and their local guardian in the presence of the primary investigator (AA). Data collection was performed at the participant's house or at the village health centre. Trained staff members collected information and performed haemoglobin tests by the two methods independently under AA's oversight. The NBM 200 was used according to the manufacturer's guidelines, using the thumb of the non-dominant hand [7]. Sahli's hemometer was used to conduct the invasive haemoglobin estimation under an aseptic protocol using the ring finger of the non-dominant hand [12]. Both tests were performed in a sitting position and participants were provided with written reports followed by necessary referrals to the nearest healthcare facility wherever required (based on Sahli's estimates). Anaemia was defined as a haemoglobin level of less than 12.0 g/dL (11.9 g/dL and below), and severe anaemia was defined as a haemoglobin of 7.9 g/dL and below [13].

Haemoglobin measurements obtained by both methods were compared using Bland-Altman analysis [14]. A further comparison was performed using Spearman correlation coefficient, sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV) and area under receiver operating characteristic curve (AUROC). To allow for possible confounding by environmental temperature, a sensitivity analysis of two consecutive months was analysed using the Bland-Altman analysis. All data analyses were performed using Stata Statistical Software (v13.1, Texas, USA). The study was approved by the Institutional Ethics Committee of Government Medical College Aurangabad, Maharashtra, India (reference number: Pharma/IEC/GMA/196/2014), and was also sanctioned by the Nottingham University Medical School Ethics Committee, UK (reference number: E10102013).

Results

In total, 791 eligible adolescent girls from 34 villages were contacted, and we obtained paired haemoglobin measurements using both methods from 766 adolescent girls in total (response rate 95.8%). During the phase one data were collected from 203 participants and the rest were collected in the second phase (N=563). Haemoglobin estimated by Sahli's hemometer ranged from 5.0 g/dL to 14.0 g/dL with a mean of 10.1 g/dL (standard deviation (SD): 1.41). The non-invasive sensor yielded Hb estimates in the range of 9.5 g/dL to 15.2 g/dL (SD 1.42) with a mean Hb of 12.8 g/dL. The reference method (Sahli's hemometer) showed a high prevalence of anaemia (84%) while, the NBM 200 diagnosed only 26% of participants (out of 766) as anaemic. The hemometer identified 41 participants (5%) with severe anaemia (Hb 7.9 g/dL and below), and the NBM 200 sensor did not identify any severe anaemic participants.

The Bland-Altman analysis showed a mean difference of -2.70 g/dL (95% confidence Intervals (CI): -2.84 to -2.55) in Hb estimates suggesting a systematic overestimation of haemoglobin using the non-invasive technique (Figure 1). The Bland-Altman plot showed a diamond shaped pattern suggesting that there are approximately 15 subgroups with a linear association, between Sahli's hemometer haemoglobin measurements and the difference between the two devices. Examination of this in more detail showed that this is a consequence of the difference between the two measurement techniques being similar for number of readings. A histogram plotting Hb estimates obtained using Sahli's method (reference method) showed a normal distribution, while the histogram of Hb estimates obtained using the NBM 200 was not normally distributed, and showed plateau like presentation (Figure 2). A statistically significant weak negative correlation was found between the two methods (Spearman's test rs = -0.07, p= 0.03). The NBM 200 had low sensitivity (23.6%, 95% CI: 20.4 to 27.1), moderate specificity (61.8%, 95% CI: 52.6 to 70.4), low negative predictive value (13.4%, 95% CI: 10.7 to 16.5) and moderate positive predictive value (76.4%, 95% CI: 69.9 to 82.1). The AUROC score was 0.43 suggesting poor anaemia diagnostic performance of the non-invasive sensor in our study population. Sensitivity analysis of a subgroup of data collection over two moths (April to May) resulted in a mean difference of -0.51 g/dL with wide limits of agreement (-3.46 g/dL to 2.43 g/dL), demonstrating a consistent overestimation of Hb measurement by NBM 200 compared to the hemometer.

Discussion

This study consisting of adolescent girls aged 13 to 17 years from rural India found that the non-invasive sensor NBM 200 overestimated haemoglobin when compared with Sahli's hemometer. The sensor underestimated anaemia prevalence (sensitivity 23.6%), and failed to detect severe anaemia cases in our study population.

Strengths and limitations

To our knowledge this is the first study, comparing the non-invasive technology with Sahli's hemometer [9,15] and also provided an opportunity to compare the technique in remote locations, where the Sahli's hemometer is currently used. The study had a good response rate (95.8%), and none of the study participants had thumb injury, ulceration or any skin colourants (such as Henna) thus allowing for the non-invasive measurements to be obtained in accordance with the guidelines [16].

Nevertheless, our study had certain limitations. Sahli's hemometer is not a gold standard method for measuring haemoglobin and may be susceptible to human error, but we were unable to perform additional measurements using cyanmethemoglobin technique or automated haematology analyser (gold standard method) due to logistical challenges involving transportation and hence integrity of samples collected in a hot remote rural setting [10 15]. However, we optimised the quality of the hemometer measurements to provide the best data available in this environment. Firstly, the technician involved in the MAS study had four years of laboratory experience, and received training provided the primary investigator and HMF hospital consultant. Additionally, during data collection, two study members (technician and the primary investigator) agreed on the Sahli's estimation for each participant to minimise ascertainment bias. We did not find any major differences between the two members (<0.2 g/dL). It is important to note that venous blood withdrawal is not routinely used for anaemia screening in the adolescent population in our study setting, and insisting on this for blood investigation using an automated analyser, may have adversely affected our response rate. Future studies in this area should consider using a gold standard reference measurement for haemoglobin if possible. Secondly, the Bland-Altman plot formed a diamond shaped pattern suggesting that the difference between two Hb measurement techniques was highly variable. The pattern is likely to be due to technique variability (which could affect measurements obtained from either the NBM 200 or Sahli's hemometer). The variability was more apparent for more frequently occurring Hb values (for e.g. 94 participants had an Hb value of 9.5 g/dL) and less apparent for rarer Hb values, resulting in the diamond shaped plot.

Synthesis

While we have used Sahli' hemometer as the reference method, the results are in agreement with our another study comparing the NBM 200 with the automated haematology analyser (Sysmex XP-100, Japan) in pregnant women in the same setting (N=269) [15]. Results from the pregnant women study showed that the NBM 200 overestimated haemoglobin levels with subsequent underestimation of anaemia status (sensitivity of 33.7%) [15]. Findings from the pregnant women study showed a mean difference of -1.8 g/dL (95% CI: -2.06 to -1.71) when assessed using Bland-Altman method, indicating an overestimation of Hb by the NBM 200, which is in agreement with our current adolescent girl analysis. To our knowledge, there is no published evidence comparing the NBM 200 and Sahli's hemometer. A study evaluated the finger prick technique using HemoCue (ANGELHOLM, Sweden) with NBM 200 in blood donation centres/hospitals [17]. The HemoCue uses peripheral capillary blood similar to the Sahli's hemometer, but is considered to have better precision because of reduced human error [18]. However, Kim et al. showed that compared to an automated haematology analyser (LH500, Beckman Coulter Inc., Brea, USA), both the NBM 200 and HemoCue showed low sensitivity (38% and 47% respectively)[17]. We acknowledge that Sahli's hemometer estimates are susceptible to interpretation, however, given that this is a commonly used technique in the country, it was important to compare the NBM 200 to Sahli's hemometer. The NBM 200 failed to detect severe anaemia in our study population similar to our findings from pregnant women participants [15], and thus cannot be used as an alternative to the current diagnostic technique. However, if improved substantially or re-calibrated by the manufacturer in near future to provide precise measurements in an Indian setting, non-invasive technology may be useful for anaemia screening in both remote and also in urban areas to facilitate early diagnosis and management.

Conclusion

This research is the first to provide a comparison between Sahli’s hemometer and the NBM 200 in developing country settings. The ability to obtain haemoglobin measurements involving a large representative adolescent girl population from difficult to reach communities is a major strength of the study. We report a systematic overestimation of haemoglobin using the NBM 200, which is consistent with our study involving pregnant women in the same geographical location in India. There is an urgent need to improve the non-invasive technology, as it will provide opportunities for mass screening in a country having a high prevalence of anaemia. Future studies of improved non-invasive Hb devices will be required in developing countries to validate this technology before it is used independently for anaemia diagnosis and treatment.

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Footnote for Figure 1

- Limits of agreement: -6.78 to 1.37, Mean difference: - 2.70 (95% CI: - 2.84 to -2.55), Range: 7.25 to 14.30

Conflicts of interest: Authors have no conflicts of interest to disclose that are relevant to this study.

Author contributions: The study was designed by AF, PM, LT and AA. AA obtained the data and AA, AF and PM conducted the analysis. All authors (AA, PM, AF, JD and LT) participated in manuscript preparation and approved the final manuscript for submission.

Ethical considerations and responsibilities: The study was approved by the Institutional Ethics Committee of the Government Medical College Aurangabad, Maharashtra, India (Reference number: Pharma/IEC/GMA/196/2014), and the Medical School Ethics Committee of the University of Nottingham, UK (Reference number: E10102013). All participants and their guardians provided signed informed consent for the survey and blood withdrawal separately. Other than those who declined to participate, all adolescent girls received a standardised health report including information on their haemoglobin level and anaemia status along with facilitated access to educational materials on anaemia through the health NGO, Halo Medical Foundation's (HMF) village based services. Participant health reports were also provided to the village health worker/government nurse with arrangements for free consultation and assistance if any significant health problems requiring further assessment or treatment were identified during the study. HMF's hospital was also made available for free consultation as a primary referral centre if more specialist assessment or treatment was needed. On completion of data collection, an additional reminder letter was issued to village health workers indicating details of each severe anaemic case in their village to ensure that necessary medical advice and treatment was available.

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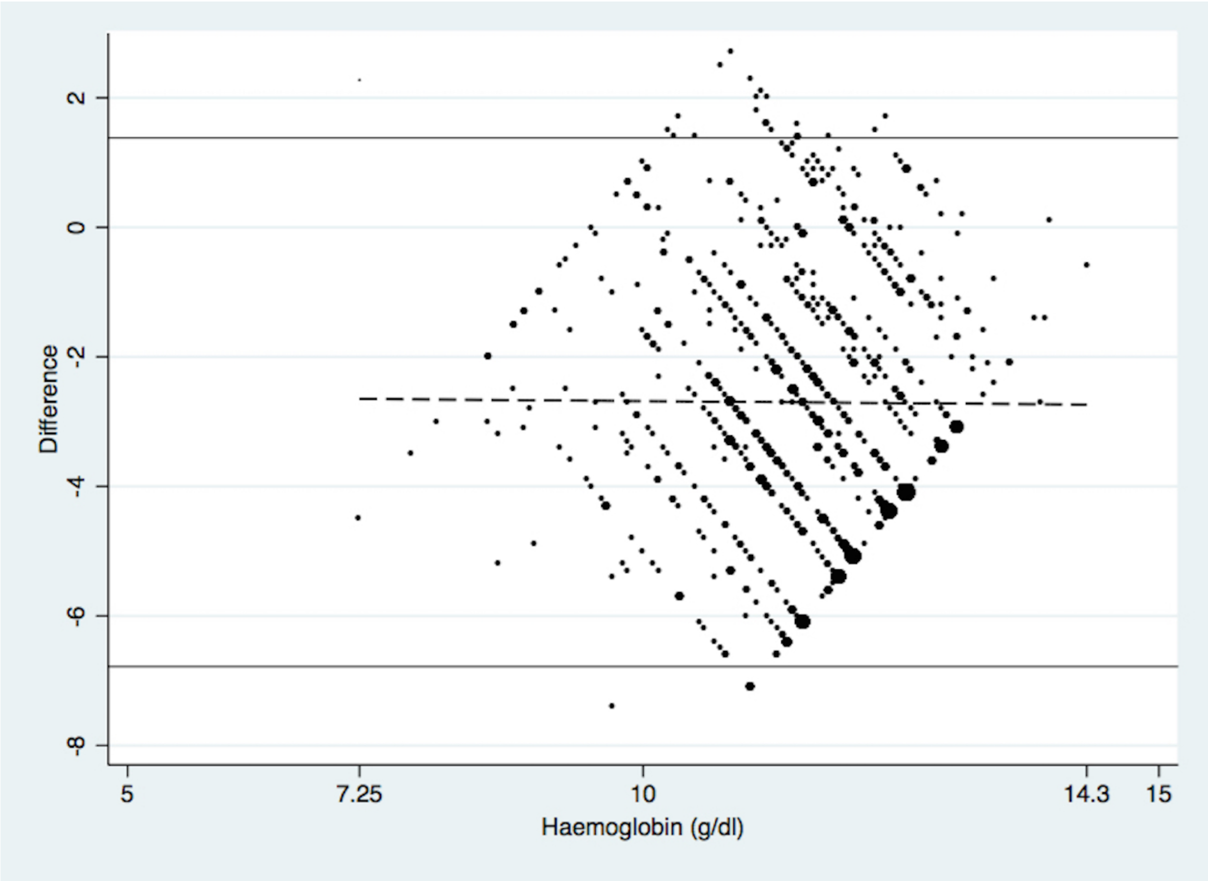
Figure 1: Bland Altman plot of NBM 200



Footnote

Limits of agreement: -6.78 to 1.37, Mean difference: - 2.70 (95% CI: - 2.84 to -2.55), Range: 7.25 to 14.30

Figure 2: Histogram of NBM 200 haemoglobin distribution