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Evaluation of Non-Invasive Measurement of Haemoglobin using PPG in Clinically Ill Pediatric Patients

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Abstract*: Non-invasive haemoglobin (SpHb) estimation using Photoplethysmograph signal has gained enormous attention among researches in order to provide an earlydiagnosis to polycythemia, anaemia, various cardiovascular diseases, etc. The primary objective of this work is to evaluate the performance efficiency of SpHb monitoring using PPG in clinically ill pediatric population. PPG signal was obtained from the pediatric patients, and SpHb was calculated from the characteristic features of PPG. Haemoglobin value obtained through venous blood sample was compared with SpHb. Theabsolute mean difference between the SpHb and Hb_{ref} was 0.78g/dL (SD 0.99; 0.1 to 4.1).For a statistical analysis of the correlation between SpHb and Hb_{lab}, IBM SPSS statistics software was used. Bland-Altman analysis, T-test and Linear regression analysis were further used for finding the agreeability limits. Overestimation of SpHb value was observed for lower Hb_{lab} values, and SpHb failed to detect anaemic subjects.

Keywords: Haemoglobin, Neural Networks, Non-invasive, PPG, Regression

I. INTRODUCTION

Haemoglobin (Hb) is a complex protein molecule in red blood cells. Its main responsibility is to transport oxygen to the body's tissues. Hbmeasurement is a part of routine blood test and is one of the most widely/commonly performed laboratory tests. A routine blood test is generally advised during a general health assessment or when an individual shows indications and signs of anaemia (a very low Hb level) or polycythemia (condition with elevated Hb level) [1-3]. Haemoglobin test is one of the mandatory steps to make decisions during blood transfusions. Haemoglobin measurement is generally performed by the traditional "fingerstick method" i.e., by invasively drawing blood from the body. Although the conventional laboratory measurement is accurate, it has its own limitations such as time delay, inconvenience of the patient, exposure to biohazards and lack of real-time monitoring in critical situations.

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The above said limitations can be overcome by Non-invasive haemoglobin (SpHb) monitoring. SpHb monitoring has gained enormous attention as a point of care testing that facilitates to monitor haemoglobin concentration in a continuous, accurate, and non-invasive fashion. Various technologies and methods are employed by researches all over the globe to develop a system/device for SpHb monitoring [5-13]. Among the various methods, research on SpHb monitoring using Photoplethysmograph (PPG) is huge [14-18]. PPG signal is generally used for measuring oxygen saturation, to monitor the depth of anesthesia, heart rate, respiration monitoring and blood pressure [19-23]. Currently, SpHb, using the characteristic features of PPG signal, has shown an excellent correlation with the Haemoglobin (Hb) measured using an invasive method [4]. However, the procedure was conducted over a sample of 33 subjects and it did not include any pediatric subjects. So, the study was conducted to evaluate the performance efficiency of calculating SpHb among clinically ill pediatric population using the characteristic features of PPG and machine learning, and the results are discussed in the following sections.

II. MATERIALS AND METHODS

A. PPG Signal Acquisition

The subject database acquisition was done in Sri Ramakrishna Hospitals, Coimbatore after obtaining permission for collecting the PPG signals of pediatric patients. A formal consent was obtained from the parents or the representative of the pediatric patients before enrolment. Subjects aged between 3 and 13 years were enrolled. The subjects' data were stored in a spreadsheet of Microsoft Excel. The IR Plethysmograph transducer and Labchart software (version 7) of ADInstruments was used for signal acquisition. The sensor was placed in the forefinger of the left arm of the subjects. While the venous blood sample was collected by the trained professionals for calculating Hb_{lab}, corresponding PPG signal was acquired for a 15-period sample. The study flow of the work is presented in Fig 1. In total 132 pediatric subjects were approached, out of whom 83, aged between 3 and 13 were enrolled for the study after receiving consent. Subjects with a mean age of 8 were chosen for the study with a standard deviation (SD) of 3.3.

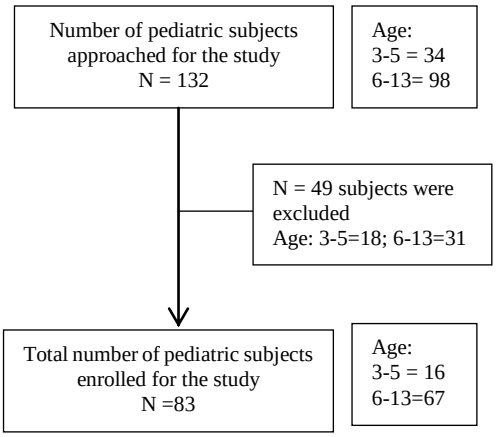

Fig. 1. Study flow

B. SpHb calculation

The original PPG signal acquired using Labchart was saved along with a spreadsheet of subject details. Along with the original PPG signal, the first and second derivative of the PPG signal was also calculated and exported to MATLAB for subsequent signal processing. Seven time-domain features as described in [3] were extractedfrom the PPG signal and its derivatives. These features along with Hb_{lab} were trained using generalized linear regression machine learning technique with linear model type [3]. The SpHb values were predicted and the Hb_{lab} stored for further analysis. For statistical analysis, Bland-Altman plot, Regression analysis, t-test, dispersion plots, Pearson product moment correlation coefficient were done on IBM SPSS statistics package.

III. RESULTS AND DISCUSSION

A total of 80 pediatric subjects were enrolled with a mean age of 8 ranging from 3 to 13 with standard deviation (SD) of 3.3. The mean Hb_{lab} recorded was 11.09 g/dL ranging from 7.1 to 13.9g/dL with SD of 1.27.The mean SpHb recorded was and 11.11 g/dL ranging from 10.2 to 13.9g/dL with SD of 0.71. For evaluating the performance, Mean Absolute Error between Hb_{lab} and SpHb (MAE), Mean Squared Error (MSE) between Hb_{lab} and SpHb, Root Mean Squared Error between Hb_{lab} and SpHb (RMSE) were used as formulated below.In the following equations, B_j denotes the Hb_{lab} value and B'_j the predicted SpHb value.

$$MAE = \frac{1}{n}\sum_{j=1}^{n} | B_j - B'_j |$$

$$MSE = \frac{1}{n}\sum_{j=1}^{n} (B_j - B'_j)^2$$

$$RMSE = \sqrt{MSE}$$

MAE, MSE and RMSE value of 0.784 g/dL with SD of 0.99, 1.6 g/dL with SD of 1.6 and 1.26 g/dL were obtained between Hb_{lab} and SpHb. Coefficient of determination-R^2 value of 0.147 was obtained along with a Pearson coefficient of 0.384 in SPSS. Dispersion diagram with R^2 is plotted in Fig 2. The high values of MAE, MSE and a low R^2, Pearson coefficient shows a poor correlation between SpHb and Hb_{lab}. But it is also observed that the estimation of SpHb was good for Hb values greater than 10 and unsatisfactory for Hb values less than 10, which is shown in Table I.

Table- I: Performance Evaluation

	Hb<10 g/dL (n=11)	Hb>10 g/dL (n=72)	Hb (n=83)
MAE	3.04 (SD 0.74)	0.45 (SD 0.39)	0.78 (SD 0.99)
MSE	9.71 (SD 4.2)	0.35 (SD 0.6)	1.6 (SD 1.6)
RMSE	3.12	0.59	1.26
R^2	0.2	0.55	0.147
Pearson coefficient	0.45	0.74	0.384

To determine if there is a significant difference between the two measurements, one sample t-test is performed considering null hypothesis which shows the confidence interval is tabulated in Table II.

Table- II: One sample t-test

Test Value = 0 (null hypothesis) on Hb_{bias}					
t-static	df	p-value	Difference (Mean)	95% Confidence Interval	
				Lower	Upper
-3.1	82	0.003	-0.40843	-0.6705	-0.1463

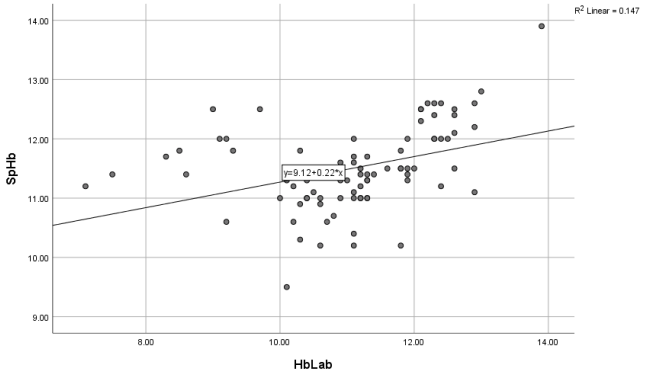

Fig. 2. Dispersion diagram

To compare the correlation and agreeability between two Hb_{ref} and SpHb, Bland Altman analysis was performed with mean on the x-axis and Hb_{bias} on y-axis.

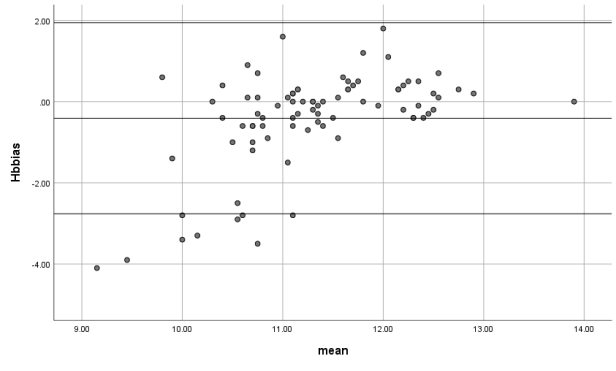

Fig. 3. Bland-Altman Plot

To analyze whether the data fit within the expectation of agreement, the upper and lower limits of agreement are plotted. The upper and lower limits of agreement are plotted as per the following formula.Upper limit of agreement = Mean Hb_{bias} + (1.96*SD of Hb_{bias})
Lower limit of agreement = Mean Hb_{bias} - (1.96*SD of Hb_{bias})

The Bland Altman plot is shown in the Fig 3 for which the upper and lower limit of 95% confidence interval agreement is 1.944 and -2.76 respectively. It can be seen that most of the data points are clustered around the mean difference line of -0.4084.It is important to look for trend among the points which are above vs below the mean difference line, since it can indicate a proportional bias. To find the trend between these two methods, linear regression is opted. The results of linear regression analysis, ANOVA (Analysis of variance) and coefficient table are shown in table III and table IV.

Table- III: Trend Analysis

Model	Sum Sq.	Deg. of freedom	Mean Square	F ratio
Regression factor	35.9	1	35.9	35.33
Residual	82.261	81	1.016	
Total	118.144	82		

Table- IV: Coefficient table

	Unstandardized Coefficients		Standardized Coefficients	
Model	B	Std. Error	Beta	t
Constant	-9.276	1.496		-6.201
mean	0.132	0.132	0.551	5.944

In the coefficient table, T value doesn't have a statistically significant t score. Hence, there is no proportional bias which indicates the absence of a trend.

IV. CONCLUSION AND FUTURE SCOPE

Coefficient of Determination R^2 value of 0.147 shows unsatisfactory results with a mean difference of 0.78 g/dL. But the R^2 value increases to 0.6 when Hb value less than 10 g/dL is excluded. SpHb measurement using PPG and generalized regression shows a better correlation for Hb values greater than 10 g/dL. Overestimation of SpHb value was observed for lower Hb_{lab} values. SpHb failed to detect the anaemic subjects. This shows that SpHb prediction using the characteristic features of PPG cannot be relied upon for detecting anaemic patients. The lowest recorded Hb value in the study is 7.1 g/dL, which is a limitation of the study. Larger prospective study over anaemic pediatric subjects is needed to confirm the results. Although the method has many positive attributes, it has to be validated in a varied population set-up with a larger sample size. A future work of evaluation of SpHb monitoring over anaemic population along with the evaluation of the work among varied population is needed. Further, better feature optimization for efficient SpHb monitoring of pediatric patients has to be developed and validated.

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