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Evaluation of Calculated HbA1c as a Low-Cost Alternative for management of Diabetes Mellitus for possible use in Low-resource settings.

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KEYWORDS

Glycated Hemoglobin; Hemoglobin A1c protein; Glycemic control; Blood glucose

ABSTRACT:

Background: Diabetes Mellitus is a significant burden in low-middle income countries (LMICs), with 80% of the global diabetic population residing in these regions. The management of diabetes is often hindered by limited resources, particularly in rural areas. HbA1c is a crucial diagnostic marker for monitoring glucose control, but its high cost limits its accessibility in LMICs. This study aimed to implement to calculate HbA1c from fasting blood glucose levels as a possible replacement for estimated HbA1c in low resource settings.

Methods: The calculated HbA1c (cHbA1c) was compared with estimated HbA1c (eHbA1c) in 203 study subjects from a tertiary care center in South India.

Results: The results showed a significant positive correlation between eHbA1c and cHbA1c, with a mean difference of 0.82 ± 1.00 and limits of agreement (-1.13, 2.78).

Conclusion: The study suggests that cHbA1c can be a reliable and cost-effective alternative for diabetes management in low-resource settings, particularly in rural areas of LMICs. However, larger multicentric studies are needed to confirm these findings. The use of cHbA1c can help bridge the gap in diabetes care in resource-constrained settings, enabling early detection and prevention of complications like chronic kidney disease and cardiovascular disease.

1. Introduction

Of the world diabetic population, 80% were reported to be prevalent in low middle income countries (LMICs) as the prevalence increases rapidly (1). With rapid transition and urbanisation globally, the burden of the Diabetes Mellitus has become a nuisance for the low and low-middle income countries, especially in managing the rural population (1,2). India faces challenges in managing diabetes mellitus due to fact that it deals with a population for diverse socioeconomic status (3). Although some parts of the urban population has high resource availability than the rural, the economic burden of the accessible population plays key role in utilizing the facility which might post delay in treatment leading to long term metabolic complications such as chronic kidney disease and cardiovascular disease(4). HbA1c is one of the promising diagnostic marker for the monitoring long term glucose control for the management of diabetes Mellitus(5). As the cost of this test is relatively high for the accessibility of common man, the need for an alternative but effective diagnostic test is essential for the management of diabetes mellitus. A mathematical model was developed with the fasting glucose level using Truncated Fourier series along with standard Structured Query Language (SQL) Database

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implementation to use the calculated HbA1c in place of analysed HbA1c values(6).

2. Objectives

In order to assess the feasibility and reliability of these calculated inlow middle income countries, we have made an attempt to associate the measured HbA1c values, with the calculated HbA1c for its possible effective use in low resource settings such as rural India. The objective of the study were 1. To calculate Glycosylated Hemoglobin (HbA1c) using plasma fasting glucose in diabetic patients. 2. To compare calculated HbA1c and estimated HbA1c levels for use in low resource settings.

3. Methods

This study was a cross-sectional study conducted in a tertiary care center of South India and the study was approved by the Institute's human ethical clearance. The biochemical data such as fasting blood glucose and glycated Hemoglobin levels were collected from the study subjects with normal and diabetes mellitus were recruited for the study. In order to analyse the variation among the control and diabetes groups, the data of the study subjects were categorised into three groups based on their HbA1c values such as Group I: Healthy control range (<5.7%), Group II: Prediabetic range (5.7 – 6.4%) and Group III: Diabetes Mellitus range (>6.5) as per the guidelines of the Americal Diabetes Association (ADA). Patients with hemoglobinopathies, thyroid disorder, severe anemia, hypertension, renal disorder, pregnancy women, cardiovascular disease, liver and muscle disease were excluded from this data analysis. 2ml blood samples were collected in both serum separator tube and EDTA vacutainer for analysis of fasting blood glucose and glycated haemoglobin analysis respectively. The Biochemical analysis carried out on the same day was included for the analysis. The fasting blood glucose (FBG) was estimated by glucose oxidase and peroxidase method analysed using fully automated clinical chemistry analyser (M/s Roche Cobas c311, Germany) and the glycated Hemoglobin levels were estimated using D10 Hemoglobin testing system (M/s Bio rad Inc., USA) as per the manufacturer's instruction. The calculated HbA1c was calculated based on the formula "Calculated HbA1c = 2.6 + 0.03 × FBG (mg/dl)" (7). In this study, the HbA1c data of 203 study subjects were calculated for calculated HbA1c using the above formula and values were evaluated check for the agreement between the values with 80% power and 95% confidence interval. The data are represented as mean and standard deviation and limits of agreement were calculated as per the Bland Altman plot analysis (8). The comparison between the estimated and calculated HbA1c was carried out by independent t test and the limits of agreement with in ±1% were considered acceptable clinically. The statistical analysis were carried out using Statistical Package for the Social Sciences, version 19.0

Results

In this study, the Fasting blood glucose and the estimated HbA1c of 203 subjects were enrolled for the analysis which includes 56 in Group I, 65 in Group II and 82 in Group III. It is found that the cHbA1c were significantly decreased (5.93 ± 1.41) compared to eHbA1c (6.85 ± 1.82) with p value <0.001. It is observed that a significant correlation between the eHbA1c and the cHbA1c (r= 0.841, P value <0.01) as shown in the graph (figure 1). The study groups were further divided into three groups as mentioned above and the mean value shows a significant difference among the groups (figure 2).

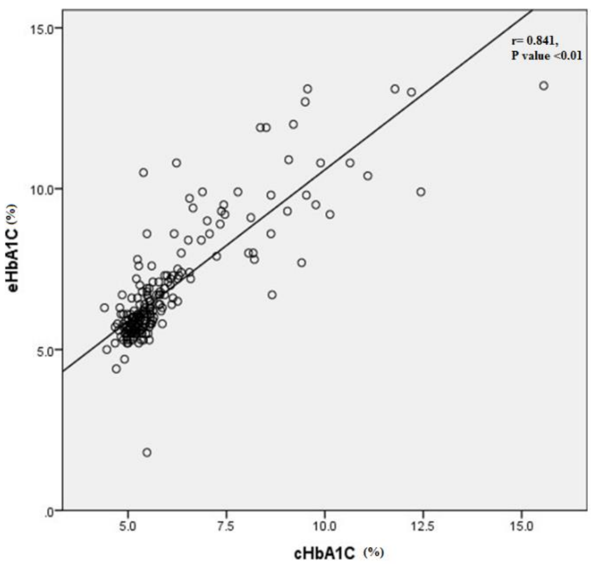

Figure. 1: Correlation between Estimated HbA1c and calculated HbA1c scores

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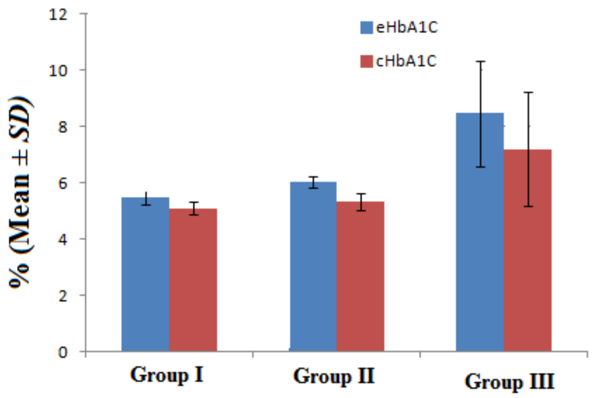

Figure 2: Comparison of Estimated HbA1c and calculated HbA1c scores among group 1 (eHbA1c<5.7%), Group 2 (eHbA1c 5.8 -6.4%) and Group 3 (eHbA1c >6.4%)

Estimated average plasma glucose is 170.67 ±43.63 mg/dL in diabetic cases and 104.5 ± 4.59 mg/dL in controls. However when analyzed for the agreement between the estimated and calculated HbA1c parameters using Bland Altman plot which is plotted with mean difference of two measurement against the mean of two measurements ie., eHbA1c and cHbA1c using the bias ±SD, 0.82±1.00 and limits of agreement (-1.13, 2.78) with 95% CI as in Figure 3A. The values are plotted for the three different ranges individually for group I to III and the Bland Altman plot was plotted as shown in figure 3 B,C,D.

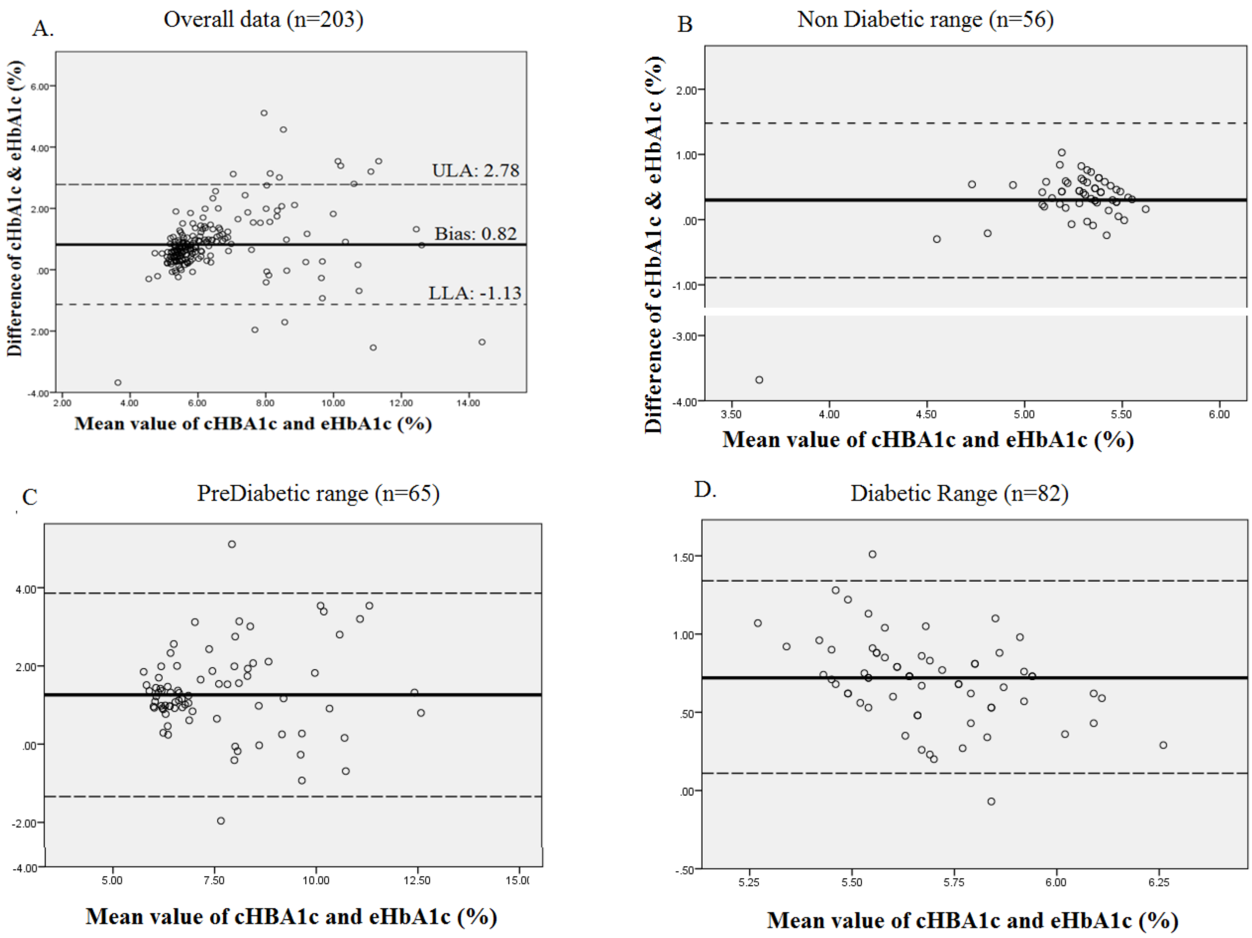

Figure 3: The Bland-Altman plot for the cHbA1c with respect to the eHBA1c levels in A. All the study subjects data (n=208), B. Group I, Non diabetic (n=56), C. Group II. PreDiabetic (n=65) and Diabetic range (n=82) respectively.

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4. Discussion

HbA1c (glycated hemoglobin) is a critical marker for monitoring long-term glucose control in diabetes management and it is more reliable as it shows strong correlation with continuous glucose monitoring (CGM) (5). Its importance in low-resource settings is underscored by its ability to provide a reliable measure of average blood glucose levels over several months without the need for fasting, making it a practical tool in these environments. However the testing for HbA1c is expensive in low resource settings and rural part of the low- and middle-income countries face difficulty in monitoring the diabetic patients from getting severe complications of diabetes mellitus (9).

A study conducted in a Northern part of India (A low middle income country) among the rural and urban population on the prevalence shows that the proportion of diabetes were more among urban than the rural (10). However, it is observed that the estimated low prevalence report in low and low middle income countries such as India and other countries could be due to low availability of resource for diagnosis and management of diseases (11,12). Although, the facilities are available in some low middle income countries and in the urban part, the economic burden for the diagnosis and management of the disease more among the common man to utilize the facility (4,13,14). As the diabetes related chronic kidney disease is major burden, the need for low cost test atleast in the rural settings and in low or low middle income countries could be crucial for managing the disease burden of Diabetes mellitus (15). The comparison between estimated HbA1c (eHbA1c) is crucial for understanding their accuracy and applicability in diabetes management. Both these metrics aim to reflect laboratory-measured HbA1c, but they differ in methodology and precision. The present study shows that there is significant positive correlation between the eHbA1c and cHbA1c. However an acceptable agreement between the eHb1c and calculated HbA1c shows that the cHbA1c can be used as a replacement in low resource settings when the Resource and the cost of the measuring HbA1c is a concern. This studies have been in agreement with similar studies (16). However some studies have contradicting results showing negative bias in patients iwth DM to hyperglycemia (17) although it is recommended for use in patients with good glycemic control (18,19).

Limitation of the study:

The study data was included from a single centred tertiary care centre in South india and the sample size with larger study subjects and multicentric data may give a more promising evidence to use for the management of diabetes mellitus.

Conclusion:

Although the calculated HbA1c inferior the estimated HbA1c and it is recommended to use only case of patients with well controlled glycemic status, the calculated hbA1c can be a promising tool in low resource settings such as rural parts of low and low middle income countries to efficiently manage the diabetic complications.

Ethical statement:

The study was approved by the institute Human Ethical Clearance vide registered number, MGMCRI/IRC/61/2021/01/IHEC/76 for the conduct of the study in accordance with the guidelines by Indian Council of Medical Research 2017.

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