The Association between Hba1c-Derived Estimated Average Glucose (Eag) with Fasting Blood Sugar (FBS) and Post Prandial Blood Sugar (PPBS) in Patients with Type 2 Diabetes in A Cohort of Patients in a Tertiary Care Hospital in Sri Lanka

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ABSTRACT

Introduction: Type 2 Diabetes mellitus (T2DM) is a chronic illness, caused due to resistance to insulin or poor production. FBS, PPBS and Glycated Haemoglobin (HbA1c) are the major tests that are used to monitor chronic glycaemia worldwide. HbA1c level remains the gold standard test for assessment of glycanemic control at follow up and it reflects the mean glucose values in the previous three - month period. HbA1c is expressed as a percentage, whereas the day-to-day monitoring and treatment of diabetes are based on blood glucose levels expressed as milligrams per deciliter (mg/dl) or millimoles per liter (mmol/L). Due to the difference in the denominators of FBS/PPBS with HbA1c, it causes confusion to the patients regards their glycaemic control. “Estimated average glucose” or eAG derived from HbA1c has been promoted by the American Diabetes Association (ADA). American Association of Clinical Chemists concludes that the correlation (r =0.92) is strong enough to justify reporting both HbA1c and eAG which indicate the 3-month control of the average sugar of the patient. This is easy for the patient as both FBS/PPBS and eAG are expressed with the same denominator for daily glucose checks and long-term control respectively, enhancing the glycaemic control.

Objectives: To determine the statistical correlation between eAG derived from HBA1C using the Nathan’s regression equation with FBS and PPBS in patients with T2DM. To analyze the significance of eAG as opposed to HbA1C as a marker of long-term glycomic control in T2DM.

Methodology: A retrospective analytical study done at the Department of Haematology of the Sri Jayewardenepura General Hospital, Sri Lanka. A simple random sampling technique was used, over a period of one year commencing June 2019 to June 2020, to obtain the laboratory records through laboratory information system of 201 adult patients both males and females who were diagnosed with T2DM. HbA1c, FBS, PPBS done on the same day were recorded. The eAG(mg/dl) was calculated using the Nathan’s regression equation (eAG = 28.7 x HbA1c – 46.7). Three groups were generated according to the patients’ levels of FBS and PPBS.

Statistical Analysis: Data were double entered and analyzed using (SPSS) version 20. Descriptive statistical methods were used to calculate the median, mean standard deviation of age, HBA1c, FBS, and PPBS. Correlations between study variables were done with Pearson’s correlation method. The p value, lower than 0.05 was considered as statistically significant. Coefficient of determination (R Sq) was used to a statistical measure of how close the data are to the fitted regression line.

Results: The total population of patients in both the FBS and PPBS groups showed a significant statistical correlation with eAG. The individual subgroups did not conform to this correlation. The results reveal no statistical correlation in both FBS and PPBS with eAG in patients with good glycaemic control. There was a significant statistical correlation in both FBS and PPBS with eAG in the groups of patients with moderately poor control. In those with markedly poor control the FBS did not show a statistical correlation with eAG, as opposed to the PPBS.

Conclusion: The clinical importance of HbA1C/eAG in diagnosis and management of T2DM can be re-emphasized by this study. HbA1C along with eAG may be added as a test in the management of T2DM, for the better
understanding and maintenance of good glycemic control. As eAG values, derived by the Nathan’s regression equation in our study scattered very close to the regression line, it provided a more complete and representative measure of average glucose in past 3 months. We conclude that HbA1c values were reliably translated into eAG measurements which would be easily understood by the patients being of the same denominator as the FBS/PPBS.

Keywords: estimated average glucose (eAG), Type 2 Diabetes Mellitus (T2DM), Glycated Haemoglobin (HbA1c).

I. INTRODUCTION

Type 2 Diabetes mellitus (T2DM) is a chronic illness, that is caused due to resistance to insulin or when there is decrease production of Insulin by the pancreas. Self-management, education, support to prevent acute complications and reduce the risk of long-term complications are important in T2DM management [1].

(FBS), (PPBS) and Glycated Haemoglobin (HbA1c) are the major tests that are used to monitor chronic glycemia worldwide. Still estimation of HbA1c level remains the gold standard for assessment of glycemic control at follow up and it reflects the mean glucose values in the previous three-month period [2].

HbA1c is usually expressed as a percentage of hemoglobin that is glycated, whereas the day-to-day monitoring and treatment management of diabetes are based on blood glucose levels expressed as milligrams per deciliter (mg/dl) or millimoles per liter (mmol/L). As there is a discrepancy of these values regards to the patients’ glycemic control with the HbA1c value, this has known to cause confusion to the patients.

The results of the HbA1c- derived estimated Average Glucose study, published in Diabetes Care in 2008, have shown a linear relationship between HbA1c and average blood glucose levels [3]. According to this study, a new term in diabetes management, estimated average glucose or eAG has been promoted by the American Diabetes Association (ADA), joining with the European Association for the Study of Diabetes (EASD) and International Diabetes Federation (IDF). American Association of Clinical Chemists has suggested that the correlation (r = 0.92) is strong enough to justify reporting both the HbA1c result and an estimated average glucose as eAG is expressed in mg/dl and indicates the three - months control of the average sugar of the patient. This makes it very simple understanding for the patient as both the FBS/PPBS and the eAG are expressed with the same denominator result when a clinician orders the HbA1c test [4].

Use of eAG in diabetes can help to simplify the discussion between the patient and the clinician, as this value enhances the diabetes education process by focusing on a set of values with same units for both daily glucose checks and long-term control.

II. OBJECTIVES

1. To determine the statistical correlation between eAG derived from HBA1C using the Nathan’s regression equation with FBS and PPBS in patients with T2DM.

2. To analyze the significance of eAG as opposed to HbA1c as a marker of long-term glycemic control in T2DM.

III. METHODOLOGY

A. Study Design

A retrospective analytical study.

B. Center of the study

Department of Haematology of Sri Jayewardenepura General Hospital, Sri Lanka.

C. Sample selection and sample size

A simple random sampling technique was used, over a period of one year commencing June 2019 to June 2020, to obtain the laboratory records through laboratory information system of 201 adult patients both males and females who were diagnosed with T2DM.

Same day investigations of HbA1c, FBS, PPBS were recorded. The patients who diagnosed with the Type 1 Diabetes Mellitus, hypothyroidism, Cushing’s syndrome, chronic systemic illness, hepatic impairment, renal disorders, heart failure, pregnancy and cancer were excluded from the study.

D. Data Collection

Automated chemistry analyzer Mindray BS-480 and Abbott Architect plus analyzer were used for the estimation of FBS and PPBS. HbA1c was estimated by High-Performance Liquid Chromatography (HPLC) method on BIO RAD D10 analyzer.

The estimated glucose levels (mg/dl) were calculated using the Nathan’s regression equation3: (eAG = 28.7 x HbA1c – 46.7).

According to the patients’ levels of FBS, three groups were generated: group A: FBS less than 126 mg/dl; group B: FBS = (126–200) mg/ dl; and group C: FBS more than 200 mg/dl.5 According to the patients’ levels of PPBS, three groups were generated: group D: PPBS less than 140 mg/dl; group E: PPBS = (140-200) mg/ dl; and group F: PPBS more than 200 mg/dl [5].
E. Statistical Analysis

Data were double entered and were analyzed using Statistical Package for Social Sciences (SPSS) version 20. Descriptive statistical methods were used to calculate the median, mean and the ± standard deviation of age, HBA1c, FBS, and PPBS. Correlations between study variables were done with Pearson’s Correlation method. The p value, lower than 0.05 was considered as statistically significant. Coefficient of determination (R sq) was used to a statistical measure of how close the data are to the fitted regression line.

IV. Results

A total of 201 diabetic patients’ data (male=65, female=136) were recorded for the study. Age range was between 31 to 83 years and mean age ± Standard Deviation (SD) was 59.3 ± 10.56 years. The mean ± SD values of HbA1c, eAG, FBS and PPBS of total population were 7.8±1.8 %, 173.1±51.6 mg/dl, 134.0±54.6 mg/dl and 182.7±83.4 mg/dl respectively.

There was a statistically significant relationship between mean values of FBS and eAG/HbA1c in the total population (r = 0.369, p < 0.001) with the R sq of 0.136 and showing a moderate linear relationship. (Fig. 1)

The mean ± SD values of HbA1c, eAG and FBS of Group A ((FBS <126 mg/dl)) were 7.4±1.6%, 161.6±46.5 mg/dl and 102.4±14.5 mg/dl. Pearson’s correlation was done to evaluate the significance of FBS with eAG/HbA1c in this group and revealed a positive correlation (r = 0.029) which had no statistically significant relationship (p value = 0.756).

Table I and Table III revealed the descriptive data of Group B (FBS = 126 - 200 mg/dl) and Group C (FBS >200 mg/dl). There was a statistically significant positive correlation (r = 0.287, p < 0.05, R sq = 0.083) between the values of FBS and eAG/HbA1c in Group B. And no statistically significant relationship was observed between FBS and eAG/HbA1c in Group A. The eAG levels were higher in groups A and B than in group C compared to FBS levels.

TABLE I: DESCRIPTIVE DATA OF FBS GROUPS

| Variable | Total population | FBS Groups |
|----------|-----------------|------------|
|          | 201             | 116 (57.7%) | 66 (32.8%) | 19 (9.5%) |
| Frequency |                 | Group A (<126 mg/dl) | Group B (126 - 200 mg/dl) | Group C (>200 mg/dl) |
|          | Min | Max | Mean | SD | Min | Max | Mean | SD | Min | Max | Mean | SD |
| Age (Years) | 30  | 83  | 59.3 | 10.5 | 30  | 83  | 59.3 | 11.1 | 32.0 | 77.0 | 59.1 | 9.9 |
| FBS (mg/dl) | 55.7 | 425.7 | 134.0 | 54.6 | 55.7 | 125.9 | 102.4 | 14.5 | 126 | 198.8 | 150.6 | 17.9 |
| eAG (mg/dl) | 84.9 | 359.3 | 173.1 | 51.6 | 93.3 | 320.1 | 161.6 | 46.5 | 84.9 | 359.3 | 177.3 | 49.6 |
| HbA1c (%) | 4.7 | 14.5 | 7.8 | 1.8 | 5.0 | 13.1 | 7.4 | 1.6 | 4.7 | 14.5 | 8.0 | 1.7 |

TABLE II: DESCRIPTIVE DATA OF PPBS GROUPS

| Variable | Total population | PPBS Groups |
|----------|-----------------|-------------|
|          | 201             | 72 (35.8%) | 67 (33.3%) | 62 (30.8%) |
| Frequency |                 | Group D (<140mg/dl) | Group E (140-200 mg/dl) | Group F (>200 mg/dl) |
|          | Min | Max | Mean | SD | Min | Max | Mean | SD | Min | Max | Mean | SD |
| Age (Years) | 30.0 | 83.0 | 59.3 | 10.5 | 30.0 | 81.0 | 57.5 | 11.5 | 34.0 | 80.0 | 58.3 | 10.3 |
| PPBS (mg/dl) | 59.0 | 486.0 | 182.7 | 83.4 | 59.0 | 139.5 | 113.3 | 16.9 | 140.5 | 199.0 | 165.6 | 15.4 |
| eAG (mg/dl) | 84.9 | 359.3 | 173.1 | 51.6 | 84.9 | 334.1 | 153.6 | 47.3 | 107.3 | 320.1 | 169.8 | 42.9 |
| HbA1c (%) | 4.7 | 14.5 | 7.8 | 1.8 | 4.7 | 13.6 | 7.1 | 1.69 | 5.5 | 13.1 | 7.7 | 1.5 |

TABLE III: PEARSON’S CORRELATION BETWEEN PPBS AND EAG/HBA1C

| FBS Group | Total population | Group A | Group B | Group C |
|-----------|-----------------|---------|---------|---------|
| R value   | 0.369 | 0.029 | 0.287 | 0.042 |
| p value   | 0.000 | 0.756 | 0.019 | 0.865 |
| R Sq value| 0.136 | 0.015 | 0.083 | 0.002 |

TABLE IV: PEARSON’S CORRELATION BETWEEN FBS AND EAG/HBA1C

| PPBS Group | Total population | Group D | Group E | Group F |
|------------|-----------------|---------|---------|---------|
| R value    | 0.436 | 0.074 | 0.241 | 0.453 |
| p value    | 0.000 | 0.538 | 0.050 | 0.000 |
| R Sq value | 0.19  | 0.005 | 0.058 | 0.205 |

Fig. 1. FBS Vs eAG for total population.
Comparison According to the patients’ levels of PPBS, three groups were generated. Table II and Table IV revealed the descriptive data of Groups D, E and F.

Total population showed a positive correlation between the mean values of PPBS and eAG/HbA1c which had statistically significant relationship \( (r = 0.436, p<0.001) \) with the R Sq of 0.19 with moderate linear relationship. (Fig. 2).

Group E and F revealed a statistically significant positive correlation between the mean values of PPBS and eAG/HbA1c \( (r = 0.241, p < 0.05, R\ sq = 0.058) \) and \( (r = 0.453, p < 0.001) \) respectively. Group D showed no statistically significant relationship \( (r = 0.074, p= 0.538) \) between the variables.

Even though the total population of patients in both the FBS and PPBS groups showed a significant statistical correlation with eAG, the individual sub-groups of the two major groups (FBS, PPBS) did not conform to this correlation. The results reveal no statistical correlation in both FBS and PPBS (Groups A and D respectively) with eAG in the patients with well controlled glycaemic state. There was a significant statistical correlation in both FBS and PPBS with eAG in the groups of patients with moderately poor control (Groups B and E respectively). In those with markedly poor control the FBS (Group C) did not show a statistical correlation with eAG, as opposed to the PPBS (Group F) which showed a statistical correlation.

V. DISCUSSION

The relationship between the eAG and the level of HbA1c has been investigated in different studies, and various equations have been obtained [3], [6], [7] The Nathan’s regression equation, which has been recommended by the ADA to derive eAG levels and its relationship to the FBS and PPBS levels were investigated in our study.

A study done by Nathan DM et al revealed that the HbA1c-derived Average Glucose recommended translating HbA1c into eAG equivalents for monitoring glycemic control. The eAG was calculated by inserting observed HbA1c into the Nathan’s regression equation in the eAG/A1C conversion calculator of the ADA website.

A study by Bozkaya et al, has found that a strong positive correlation between fasting plasma glucose levels and estimated average blood glucose levels \( (r=0.757, p=0.05) \) [8]. Rosediani et al revealed that both PPBS and FBS correlated significantly with HbA1c but PPBS showed better correlation with HbA1c than FBS \( (r=0.604 \ vs. \ 0.575) \) [9]. Our study too revealed a similar relationship \( (r = 0.436 \ vs \ 0.369) \).

The American Diabetic Association (ADA) and American Association of Clinical Chemistry (AACC) recommend that clinical laboratories to report the eAG with HbA1C together as this has definite advantage of monitoring diabetes control [10], But this has not been implemented in Sri Lanka yet.

In 2005, a study done in Sri Lankan adults between 35 and 65 years of age in four provinces (Western, North Central, Southern and Uva) reported prevalence of diabetes of 14.2% in men and 13.5% in women [11]. The awareness of diabetes remains poor. Therefore, improving strategies for self-management of diabetes is required for the prevention of the disease.

One of these strategies is the use of eAG levels together with HbA1c values. We believe that every patient’s eAG level should be calculated and reported along with his or her HbA1c report. This strategy will help patients’ better understanding for keeping their blood glucose levels within controlled levels and this will save them from adverse complications of diabetes [12].

VI. CONCLUSION

The clinical importance of HbA1C/eAG in diagnosis and management of T2DM can be re-emphasized by this study because it showed a statistically positive correlation with FBS, PPBS and HbA1C/eAG values for the total population. HbA1C along with eAG may be added as a test in the management of T2DM, for the better understanding and maintenance of good glycemic control.

As eAG values, derived by the Nathan’s regression equation in our study, scattered very close to the regression line and it provided a more complete and representative measure of average glucose in past 3 months, we can conclude that HbA1c values were reliably translated into estimated average glucose measurements which would be
easily understood by the patients being of the same denominator as the FBS/PPBS.

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