Factors associated with the difference in HbA1c and FreeStyle Libre Glucose management indicator (GMI) in patients with type 1 diabetes

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Background

- Abbott FreeStyle Libre® flash glucose monitoring system measures interstitial fluid glucose levels.
- Increasingly used in patients with type 1 diabetes mellitus (T1DM) and selected patients with other types of diabetes.
- Large number of T1DM patients on Libre in our centre.
- Routine clinical observation is that FreeStyle Libre glucose management indicator (GMI) is similar to laboratory-measured HbA1c in most but not in all patients.
- We, therefore, set out to assess if any particular characteristic is associated with differences in HbA1c and GMI.

Patients

Persons with T1DM on FreeStyle Libre from a single diabetes centre whose sensor was active >70% of the time were included.

Methods

- Baseline characteristics, latest HbA1c, eGFR and full blood count were collected from medical records.
- HbA1c, biochemistry tests and blood count were measured respectively by Sebia Capillarys 3 Tera, Abbott Architect and Sysmex XN-9000.
- Ambulatory glucose profile data for 28-, 60- and 90-day periods ending at the date of last available HbA1c were collected from LibreView.
- An arbitrary difference in HbA1c and GMI within ±5% was considered non-significant. Characteristics of patients with HbA1c higher or lower than GMI by ≥5% were compared.
- Data were tabulated in Excel (Microsoft Corp.) and statistical analyses were performed using SPSS Statistics for Windows, version 26 (IBM Corp.).
- The GMI data were non-parametric (Shapiro-Wilk test) and therefore data were expressed as median and interquartile range (IQR).
- Spearman correlation was used to measure the degree of association and the Mann-Whitney U test was used to assess the significance of the difference.

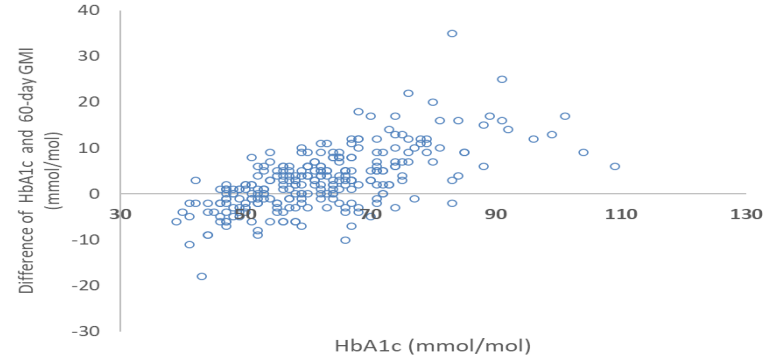

Figure 1: Difference of HbA1c and 60-day GMI plotted against HbA1c result

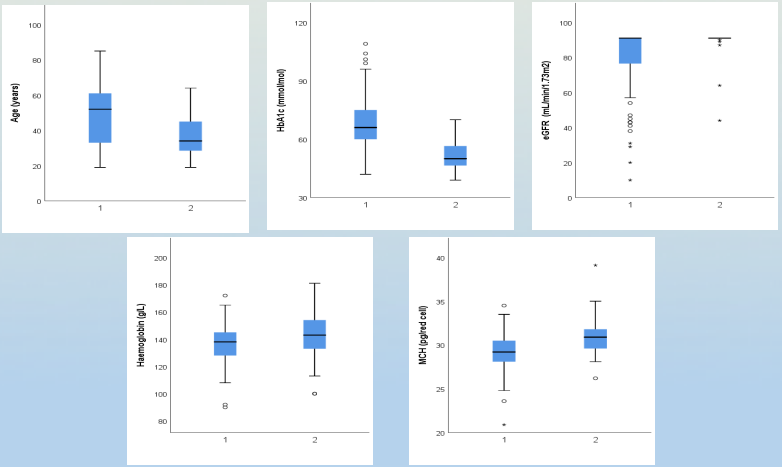

Figure 2: Age, HbA1c, eGFR, haemoglobin and MCV in patients with HbA1c higher than 60-day GMI by ≥5% (marked as group 1) and HbA1c less than 60-day GMI by ≥5% (marked as group 2)

References

[1] Nayak AU, Nevill AM, Bassett P, Singh BM. Association of glycation gap with mortality and vascular complications in diabetes. Diabetes Care. 2013;36(10):3247-3253.

[2] Jung M, Warren B, Grams M, Kwong YD, Shafi T, Coresh J, Rebholz CM, Selvin E. Performance of non-traditional hyperglycemia biomarkers by chronic kidney disease status in older adults with diabetes: Results from the Atherosclerosis Risk in Communities Study. J Diabetes. 2018 Apr;10(4):276-285.

[3] Katwal PC, Jirjees S, Htun ZM, Aldawudi I, Khan S. The Effect of Anemia and the Goal of Optimal HbA1c Control in Diabetes and Non-Diabetes. Cureus. 2020;12(6):e8431. Published 2020 Jun 3.

Results

- A total of 267 T1DM patients (53.6% females, age 45±15 years) with complete data were included in the analysis.
- Median (IQR) HbA1c, body-mass index (BMI) and haemoglobin (Hb) were 61 (53-70) mmol/mol, 26.7 (23.7-29.6) kg/m2 and 140 (130-148) g/L.
- HbA1c correlated (p<0.001) with 28-day (ρ=0.822), 60-day (ρ =0.835) and 90-day (ρ =0.817) GMI. The 60-day GMI correlated the best with HbA1c (figure 1) and, therefore, was used in subsequent data analysis in preference to the other two. HbA1c was ≥5%, within ±5% and ≤-5% of 60-day GMI in 45.3%, 38.6% and 16.1% of patients.
- When compared with patients whose HbA1c was lower than GMI by ≥5%, patients whose HbA1c was higher than GMI by ≥5% had higher age (p <0.001), higher HbA1c (p <0.001), lower eGFR (p <0.001), lower haemoglobin (p= 0.008) and lower mean corpuscular haemoglobin (MCH) (p <0.001) (figure 2).
- The difference in gender, ethnicity, BMI, red blood cell count, mean red cell volume, % time sensor is active, 60-day GMI, glucose variability or time above, below or within target was insignificant (p >0.01 for each).

Conclusions and discussion

- **Relatively advanced age, poor diabetes control and low MCH are associated with an HbA1c higher than GMI, whereas reduced renal function, relatively low haemoglobin and high MCH are associated with an HbA1c lower than GMI.**
- An HbA1c higher than fructosamine-derived standardized predicted HbA1c has previously been noted in patients with higher HbA1c [1].
- Anaemia and CKD are well known to affect HbA1c [2][3]. The effect of anaemia on HbA1c is varied and depends on the aetiology of the anaemia [3]. That information, however, was not available for our cohort.
- The difference of HbA1c and GMI could also be due to calibration bias of either the HbA1c measured in the laboratory or average glucose measured by Libre which is then used to derive GMI, based on a set linear regression equation. This, however, may also indicate a potential for further optimisation of the regression equation.