The Journal of the International Federation of Clinical Chemistry and Laboratory Medicine

eJIFCC

Monitoring of diabetic patients with poor glycemic control. Are international recommendations met?

José Antonio Delgado[1], Josep Miquel Bauça[1,2]

[1] *Department of Laboratory Medicine, Hospital Universitari Son Espases, Palma, Spain*

[2] *Institut d'Investigació Sanitària de les Illes Balears, Spain*

ARTICLE INFO

Corresponding author:
Jose Antonio Delgado
Department of Laboratory Medicine
Hospital Universitari Son Espases
Ctra. de Valldemossa, 79, J+1
07010 Palma
Balearic Islands
Spain
Phone: +34 871205876
E-mail: jose.delgado@ssib.es

Key words:
hyperglycemia, follow-up, diabetes mellitus, biomarker, HbA1c, glycated hemoglobin

ABSTRACT

Background-aim

Diabetes mellitus is one of the most prevalent diseases worldwide. According to the ADA 2020 guidelines, individuals with unstable glycemic control should be monitored every three months by measuring glycated hemoglobin (HbA1c). The aim of this study was to evaluate the demand adequacy for HbA1c in the monitoring of patients with diabetes mellitus with a highly unstable glycemic control.

Methods

Retrospective observational study (2016-2019). All HbA1c tests from individuals ≥18 years requested by hospital physicians were considered.

Highly unstable glycemic control was defined as HbA1c≥10.0%, and their monitoring was classified as: *optimal, out of recommendations* (if>3months) and *lack of monitoring* if no further HbA1c measurement was performed by the laboratory.

For individuals classified as *lack of monitoring*, medical records were reviewed and further reclassified as: [1] due to patient's responsibility, [2] attributable to the requesting physician, [3] monitored by POCT, [4] unfeasibility of monitoring or [5] referral outside our area for follow-up.

Results

During the assessed period, 1,156 patients had an HbA1c value≥10.0%. 67.5% of them were monitored either in the clinical laboratory or as POCT (33.7% optimal monitoring), whereas 21.0% patients were not monitored due to preventable situations.

Conclusion

Lack of monitoring due to physician's reasons or patient's responsibility highlights the urgent need for an improvement.

❖❖❖❖❖

INTRODUCTION

Diabetes mellitus is a chronic and progressive disease which affects about 422 million people worldwide and may lead to serious damage to cardiovascular, nervous and renal systems, among others.[1] The measurement of glycated hemoglobin (HbA1c), in combination with fasting glucose, is the recommended strategy for the monitoring of diabetic individuals.[2] A value of HbA1c<6.5% is related with a good glycemic control, while less strict objectives (HbA1c<7.0% or HbA1c<8.0%) may be acceptable for patients with a history of severe hypoglycemia, limited life expectancy, advanced microvascular or macrovascular complications or long-standing diabetes. In such individuals, the glycemic goal might be difficult to achieve despite diabetes self-management education, and effective doses of multiple glucose-lowering agents. Hence, goals are not designed to be applied rigidly but to be used as a broad construct to guide clinical decision-making.

According to the American Diabetes Association guidelines (ADA) in 2020, individuals with a diagnosis of diabetes mellitus and unstable glycemic control (HbA1c>7.0%) or with a change in their treatments, should get tested every three months either in clinical laboratories or by means of point-of-care testing devices (POCT).[3] Other biomarkers have also recently been included in some protocols for specific cases,[4] especially where HbA1c is not suitable or interferences are present, such as in individuals with anemia, altered erythrocyte indices or certain hemoglobin variants.[5]

These recommendations are of special relevance for patients with an even higher concentration of HbA1c, such as those above 10.0%. The aim of this study was to evaluate the demand adequacy for HbA1c in the monitoring of patients with diabetes mellitus with a highly unstable glycemic control in a hospital setting.

METHODS

This is a retrospective observational study performed in the Hospital Universitari Son Espases (Mallorca, Spain), a tertiary hospital, between 2016–2019. We considered all HbA1c tests from individuals aged ≥ 18 years requested by hospital physicians (general practitioners from primary healthcare offices were excluded). Data were obtained from the laboratory information system (LIS) GestLab (Indra, Spain). HbA1c was measured on the HPLC HA-8180V platform (Menarini, ArkrayAdams, USA) using a reversed-phase cation exchange chromatographic method. Results were presented according to the Diabetes Control and Complications Trial (NGSP/DCCT).[6] Individuals with a diagnosis of hemoglobinopathy or the detection of a peak of hemoglobin variants in the chromatogram were also excluded.

Highly unstable glycemic control was defined as HbA1c≥10.0%. According to the ADA 2020 guideline, the monitoring of individuals with a HbA1c≥10.0% result was classified as: optimal

monitoring if HbA1c was retested ≤3months, out-of-recommendations monitoring if retested >3months and lack of monitoring if no further HbA1c measurement was performed by the laboratory in the assessed period.

For the individuals classified as lack of monitoring, after obtaining the approval by the Ethics Board of our institution [Research Ethics Committee of the Balearic Islands (CEI-IB)], medical records were reviewed and further reclassified as [1] no monitoring due to patient's responsibility (they do not attend the next medical appointment for follow-up), [2] no monitoring attributable to the requesting physician (no referral to specialist or general practitioner for follow-up and no retest requested), [3] POCT (HbA1c monitoring was performed, for instance at the doctor's office, but not in the clinical laboratory), [4] unfeasibility of monitoring (exitus, no medical record in the hospital information system (HIS) or patient has moved to another region/country) or [5] referral to specialist at another hospital or general practitioner for follow-up. The clinical information was obtained from the HIS Millennium (Cerner, USA).

All methods were carried out in accordance with relevant guidelines and regulations.

Means and standard deviations were calculated for each group. The Student's t-test was used for statistical analyses and significance was set at 0.05. The Excel 2010 (Microsoft Inc., USA) software was used for all calculations.

RESULTS

During the assessed period, a total of 101,145 HbA1c results were considered (98,868 patients), of which, 1,703 (1,156 patients) had a value ≥10.0%. Values above 12% represented 31% of the total number of individuals with HbA1c ≥10.0%, indicating an extremely poor glycemic control.

Among them, 249 individuals presented an optimal monitoring, 494 individuals had a monitoring out of the ADA 2020 recommendations, and 413 individuals were not monitored at all, according to the records in the LIS (Figure 1).

Nevertheless, LIS data, together with medical record review, showed that the number of monitored individuals either in the clinical laboratory or as POCT was 780 (67.5% of individuals with HbA1c ≥10.0%), whereas 243 (21.0%) patients were not monitored due to preventable situations (Table 1). All individuals with HbA1c ≥10.0% had a previous diagnosis of diabetes mellitus and were under treatment, so the finding of high values was not unexpected.

When considering the three categories of follow-up (optimal monitoring, lack of monitoring and out-of-recommendations monitoring), no statistical differences were seen in HbA1c concentrations, nor in the age or sex of individuals.

DISCUSSION

In this study, the monitoring of individuals with a poor glycemic control (HbA1c≥10.0%) was evaluated, and the causes for the lack of a proper monitoring were registered.

During the four years assessed, laboratory requests (by hospital physicians) with a high HbA1c≥10.0% represent about 1.7% of HbA1c requests. International guidelines on diabetes care,[7] recommend a close follow-up for individuals with poor glycemic control in order to consider possible changes in the therapeutic strategies and tackle comorbidities. Even though a high percentage of such individuals were monitored in our area, 32.5% of them did not show any retest of HbA1c, either in the LIS or as POCT.

Despite POCT instruments are usually not connected to the LIS, proper quality assurance programs warrant the transferability of the results obtained thereof. Some general practitioners

Figure 1 Flow diagram for the inclusion/exclusion of individuals in the study

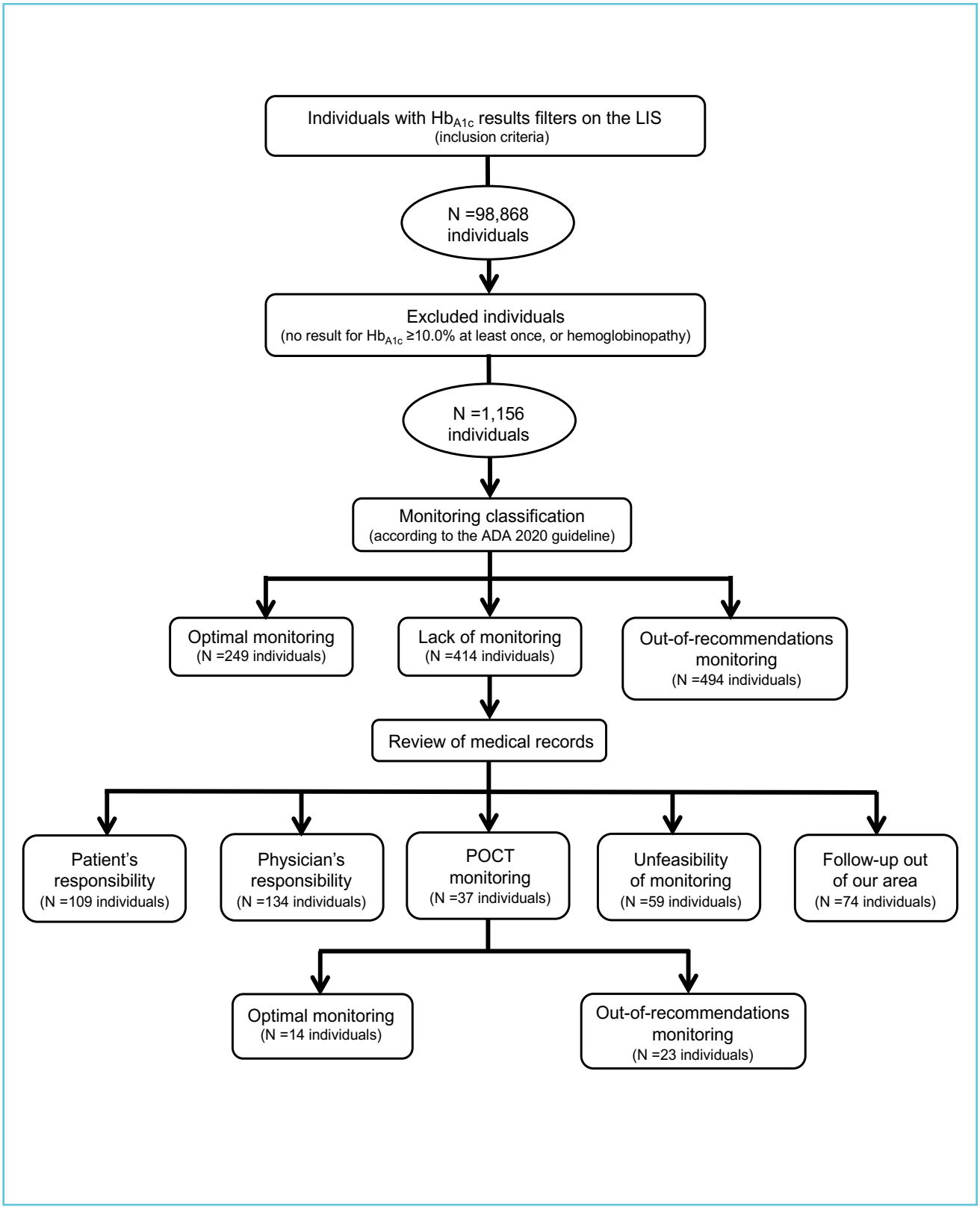

Table 1 Type of monitoring for individuals with HbA1c ≥10.0%. Results are presented as mean (standard deviation)

HbA1c ≥10.0% n =1,156	Monitoring classification					
	Optimal	Out-of-recommendations	Lack of monitoring			
			Patient's responsibility	Physician's responsibility	Unfeasibility of follow-up*	Follow-up out of our area
HbA1c, %	11.5 (1.4)	11.2 (1.2)	11.5 (1.4)	11.3 (1.2)	11.4 (1.2)	11.7 (1.3)
Retesting interval, days	48 (26)	281 (205)	-	-	-	-
Age, years	59 (19)	60 (19)	55 (17)	63 (17)	67 (25)	58 (20)
n, %	263, 22.8%	517, 44.7%	109, 9.4%	134, 11.6%	59, 5.1%	74, 6.4%

** Due to: exitus, no medical record in the hospital information system or patient has moved to another region/country.*

and endocrinologists have portable devices at their offices for a quick HbA1c test, which is used in selected patients. Therefore, in our study, individuals with a retest performed on POCT systems were considered as monitored.

A lack of monitoring due to physician's reasons or due to patient's responsibility has been reported in 21.0% of cases, which highlights the need for an improvement; as such individuals may develop serious micro and macroangiopathic comorbid situations.

To the best of our knowledge, this is one of the few studies assessing the monitoring of individuals with a poor glycemic control. Most reports on HbA1c uses for monitoring focus on the preanalytical issues related with an improper retesting interval, thus recommending a minimum of 2–3 months for a retest.[8] Automatic rules in LIS prevent the need of performing excessive retests for the same individual. Even though no study was found on whether international recommendations are followed in terms of maximum retesting intervals, nevertheless, Salinas and colleagues[9] have recently described a deficient number of HbA1c measurements in Spanish laboratories in comparison with the incidence of diabetes in the country. Their finding is emphasized with our observations.

In our study, we found a non-negligible percentage of individuals with very poor glycemic control had not been properly monitored. In this sense, clinical laboratory professionals should take a proactive attitude by alerting endocrinologists and other medical specialists to monitor them, for example by including flags in their LIS if a retest is not performed within a certain period of time. In addition, the inclusion of POCT systems has shown to improve the monitoring of these individuals.[10]

This study has some limitations, mainly related to its retrospective nature and the trust in the records from the laboratory and hospital

information systems. Besides, a lack of follow-up for an individual during the assessed period does not imply that they were not extensively studied before or after the described dates. Likewise, no information is available on the adequacy of monitoring after referral to other hospitals or primary care. Pregnancy was not considered as a variable in our study, although the success of follow-up for gestational diabetes mellitus might be different from the general population. In addition, given no differences in age, sex or HbA1c values which could explain the variability in the monitoring, there might be uncontrolled variables in this study which should have been considered, thus representing potential improvements for future projects.

Further studies on the long-term clinical impact of a lack of monitoring will enable to assess possible hyperglycemia-related micro and macroangiopathic diseases, as well as comorbid situations and mortality.

In summary, the monitoring of diabetic individuals by means of HbA1c measurement is pivotal, in order to optimize their treatment and prevent complications and is crucial especially for those with a poor glycemic control. The lack of a proper monitoring for these patients might lead to damage both for the patient's safety and for the healthcare system.

❖❖❖❖❖

ADDITIONAL INFORMATION

Ethics approval and consent to participate

The study was approved by the Ethics Board of our institution.

Consent for publication

Consent to submit has been received explicitly from all co-authors, as well as from the responsible authorities. Authors whose names appear on the submission have contributed sufficiently to the scientific work and therefore share collective responsibility and accountability for the results.

Data availability

This is a retrospective observational study performed at Hospital Universitari Son Espases (Palma de Mallorca, Spain). Analytical data were obtained from the laboratory information system GestLab (Indra, Spain), and the clinical information was extracted from the hospital information system Millennium (Cerner Corporation, USA).

Conflicts of interest

All authors declare no conflicts of interest.

Funding

This study has not received any type of public or private funding.

Authors' contributions

All authors contributed to the experimental design and approved the final version of the manuscript.

Study conception and design

JAD, JMB; acquisition of data: JAD; analysis and interpretation of data: JAD; drafting of manuscript: JAD, JMB; critical revision: JAD, JMB.

❖❖❖❖❖

REFERENCES

1. Diabetes – World Health Organization (WHO). Available at: https://www.who.int/news-room/fact-sheets/detail/diabetes. Published June 8th, 2020. Accessed November 29th, 2020.

2. Kovatchev BP. Metrics for glycaemic control – from HbA1c to continuous glucose monitoring. Nat Rev Endocrinol. 2017;13(7):425–36.

3. American Diabetes Association. 6. Glycemic targets: Standards of Medical Care in Diabetes. Diabetes Care 2020; 43(Suppl. 1):S66–S76.

4. Lees T, Nassif N, Simpson A, Shad-Kaneez F, Martiniello-Wilks R, Lin Y, et al. Recent advances in molecular biomarkers for diabetes mellitus: a systematic review. Biomarkers. 2017;22(7):604–13.

5. English E, Idris I, Smith G, Dhatariya K, Kilpatrick ES, John WG. The effect of anaemia and abnormalities of erythrocyte indices on HbA1c analysis: a systematic review. Diabetologia 2015;58:1409–21.

6. Hoelzel W, Weykamp C, Jeppsson JO, Miedema K, Barr JR, Goodall I, et al. IFCC Reference System for Measurement of Hemoglobin HbA1c in human blood and the national standardization schemes in the United States, Japan and Sweden: a method comparison study. Clin Chem. 2004;50:166–74.

7. Buse JB, Wexler DJ, Tsapas A, Rossing P, Mingrone G, Mathieu C, et al. 2019 update to: Management of hyperglycaemia in type 2 diabetes, 2018. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetologia. 2020;63:221–8.

8. Ma I, Guo M, Viczko J, Naugler C. Evaluation of a provincial intervention to reduce redundant hemoglobin HbA1c testing. Clin Biochem. 2017;50(18):1253–5.

9. Salinas M, López-Garrigós M, Flores E, Leiva-Salinas C. Glycated hemoglobin: A powerful tool not used enough in primary care. J Clin Lab Anal. 2018;32(3): e22310.

10. Tollånes MC, Jenum AK, Berg TJ, Løvaas KF, Cooper JG, Sandberg S. Availability and analytical quality of hemoglobin HbA1c point-of-care testing in general practitioners' offices are associated with better glycemic control in type 2 diabetes. Clin Chem Lab Med. 2020;58(8):1349–56.