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Glycemic control in diabetes mellitus in patients assisted by a university hospital in the state of Piauí (Brazil)

Jose Arimatéa NERY-NETO[1] , Andrew Oliveira dos SANTOS[1] , Larissa Conceição da SILVA[1] ,
Elison Costa HOLANDA[1] , Maria Carolina BRITO[1] , Lorena Almeida LIMA[1] , Jonas Nascimento de SOUSA[1] ,
Carla Escórcio DOURADO[1]

[1]Universidade Federal do Piauí, Piauí, Brasil

Corresponding author: Dourado CE, csmdourado@gmail.com

Abstract

Objectives: To investigate glycemic control in outpatient clinics at a university hospital, as well as to correlate HbA1c with fasting glucose and postprandial glycaemia, in order to assess which variable best correlates with HbA1c. **Methods**: This is a descriptive and cross-sectional study, in which the data were collected from the electronic medical records of patients monitored at a university hospital located in the city of Teresina (Piauí, Brazil), from random consultation of the medical request for blood glucose dosage. To check glycemic control, the parameters defined by the Brazilian Diabetes Society (2017-2018) were used, namely: fasting glucose < 100 mg/dL, HbA1c < 7% and postprandial glycaemia < 160 mg/dL. The statistical analysis was performed with the aid of the SPSS® program (version 13.0), adopting $p<0.05$ as statistical significance level. **Results**: A total of 250 medical records were evaluated (87 men and 163 women), with a mean age of 60.1 ± 12.9 years old. Fasting glycaemia was altered beyond the recommended in 80.8% of the individuals evaluated, HbA1c in 45.2% of the cases, and 66% of the participants presented higher postprandial glycaemia values than the recommended goals. The correlations noticed between HbA1c and fasting glucose (rs=0.74) and between HbA1c and postprandial glycaemia (rs=0.60) were strong and moderate, respectively. **Conclusions**: A significant percentage of the individuals evaluated did not present good glycemic control. The correlation between fasting glucose and HbA1c confirmed that HbA1c is the best parameter for monitoring blood glucose levels in diabetes mellitus. In addition to that, the fasting glucose/HbA1c correlation showed greater strength than the postprandial glycaemia/HbA1c correlation.

Keywords: blood glucose; glycated hemoglobin; hyperglycemia; diabetes mellitus.

Controle glicêmico no diabetes mellitus em pacientes assistidos por um hospital universitário no estado do Piauí (Brasil)

Resumo

Objetivos: Investigar o controle glicêmico em indivíduos ambulatoriais de um hospital universitário, bem como correlacionar a HbA1c com a glicemia de jejum e a glicemia pós-prandial, a fim de avaliar qual variável melhor se correlaciona com a HbA1c. **Métodos:** Trata-se de um estudo descritivo transversal, no qual os dados foram coletados dos prontuários eletrônicos ambulatoriais de pacientes acompanhados em um hospital universitário localizado na cidade de Teresina (Piauí, Brasil), a partir da consulta aleatória da solicitação médica da dosagem da glicemia. Para verificação do controle glicêmico foram utilizados os parâmetros estabelecidos pela Sociedade Brasileira de Diabetes (2017-2018): glicemia de jejum < 100 mg/dL, HbA1c < 7% e glicemia pós-prandial <160 mg/dL. A análise estatística foi realizada com o auxílio do programa SPSS® (versão 13.0), adotando-se $p<0.05$ como nível de significância estatística. **Resultados:** Foram avaliados 250 paciente (87 homens e 163 mulheres) com média de idade igual a 60.1 ± 12.9 anos. A glicemia de jejum estava alterada além do recomendado em 80.8% dos indivíduos avaliados, HbA1c em 45.2 % dos casos e 66% dos participantes também apresentaram glicemia pós-prandial além das metas preconizadas. A correlação observada entre HbA1c/glicemia de jejum (rs=0.74) e HbA1c/glicemia pós-prandial (rs=0.60) foi forte e moderada, respectivamente. **Conclusões:** Uma parcela significativa dos indivíduos avaliados não possuía um bom controle glicêmico. A correlação entre a glicemia de jejum e a HbA1c confirmou que a HbA1c é o melhor parâmetro para monitoração dos níveis glicêmicos no diabetes mellitus. Além disso, a correlação da glicemia de jejum/HbA1c mostrou maior força de correlação que a glicemia pós-prandial/HbA1c.

Palavras-chave: glicemia; hemoglobina glicada; hiperglicemia; diabetes mellitus.

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Introduction

Diabetes Mellitus (DM) is a chronic metabolic disorder in which the resulting hyperglycemia generates a cascade of pathophysiological changes, such as oxidative stress, inflammation, apoptosis, necrosis and fibrosis.[1] These factors trigger macrovascular and microvascular complications, such as cardiovascular diseases, diabetic retinopathy, kidney disease and neuropathy.[2] According to the Brazilian Diabetes Society (*Sociedade Brasileira de Diabetes*, SBD) (2017),[3] DM has worldwide prevalence and is pointed out by the World Health Organization (WHO)[4] as one of the five main global risk factors for mortality, as well as hypertension, tobacco use, sedentary lifestyle and obesity.

Diagnosis occurs by detection of high blood glucose levels (hyperglycemia).[5] Early detection of diabetes/pre-diabetes through screening increases the likelihood of identifying asymptomatic individuals and can promote provision of the appropriate treatment to reduce the burden of diabetes and its complications.[6] Therefore, after identifying hyperglycemia, glycemic control is fundamental, and it can help direct the assistance provided to the individual, reducing hospitalization time, clinical complications and morbidity and mortality rates.[7]

Currently, glycated hemoglobin (HbA1c), which represents the percentage of hemoglobin that is bonded to glucose, is considered as the basic reference for glycemic control.[8] In adults, maintenance of the HbA1c level below 7% is defined as one of the main goals in DM control adopted by different scientific societies.[3] Studies conducted in Greece and Malaysia showed that 57.1% and 69% of the patients evaluated, respectively, did not present good glycemic control.[9,10] In Brazil, a study conducted in the most populous state of the country (São Paulo) showed that 60.3% of the patients did not attain the goal of HbA1c below 7%.[11] In Piauí, however, only 37% of the patients with DM1, assisted by the Pharmacy at the Specialized Component of Pharmaceutical Assistance (*Componente Especializado da Assistência Farmacêutica*, CEAF), presented satisfactory HbA1c levels.[12]

Adequate glycemic control is fundamental to prevent and delay complications in DM.[13] Therefore, to investigate glycemic control, it was proposed to correlate HbA1c with fasting and postprandial glycaemia, in order to assess which variable best correlates with HbA1c, in outpatients treated in the Clinical Analysis Laboratory of a University Hospital (UH), based on the following hypothesis: HbA1c is the best parameter to monitor glycemic levels in DM. Previous studies described by Ketema and Kibret (2015)[14] in a systematic review also correlate the aforementioned variables with HbA1c.

The relevance of knowing the glycemic control profile of the individuals treated at a UH in northeastern Brazil lies in the fact that this characterization can help us to draw a profile of these people for the development of quality of life programs, in order to reduce the number of clinical complications and risk factors related to the disease.

Methods

This is a descriptive and cross-sectional study carried out by surveying data from individuals assisted in the Clinical Analysis Laboratory of the University Hospital at the Federal University of Piauí (*Hospital Universitário da Universidade Federal do Piauí*, HU-UFPI), between October and November 2018.

The sample consisted in outpatients of both genders and over 18 years of age, selected from random consultation of the medical request for the fasting glucose dosage, HbA1c and postprandial glycaemia. For the analysis, only the samples with concomitant dosage of these three parameters were considered. Individuals with anemia, variant hemoglobins, chronic kidney disease, hypothyroidism, hyperthyroidism and liver cirrhosis were excluded, as these conditions can interfere with HbA1c dosage.[3,15]

The data were collected in medical records. To verify glycemic control, the parameters established by the Brazilian Diabetes Society (SBD 2017-2018) were used, namely: fasting glucose < 100 mg/dL, HbA1c < 7% and postprandial glycaemia < 160 mg/dL.

The statistical analysis was performed with the aid of the SPSS® program (version 13.0), adopting $p<0.05$ as the statistical significance level. The continuous variables were expressed as mean ± standard deviation and the categorical variables were presented as proportions (%). After submitting the fasting glucose, HbA1c and postprandial glycaemia values to the Kolmogorov-Smirnov test to assess data normality, it was found that the sample did not present normal distribution, requiring the performance of non-parametric statistical tests. Mann-Whitney's U test was used to verify the statistical differences between the genders. To correlate the quantitative analyses with each other, Spearman's correlation (rs) was performed using the cutoff points described by Mukaka (2012)[16] to classify the stability level of the answers: values between 0 and 0.3 are biologically negligible; those between 0.31 and 0.5 are weak positive correlations; between 0.51 and 0.7, moderate; those between 0.71 and 0.9 are strong correlations; and > 0.9 are considered as very strong.

This study was approved by the Committee of Ethics in Research with Human Beings of the University Hospital at the Federal University of Piauí (HU-UFPI) under CAAE No. 44530815.4.00005214.

Results

A total of 250 participants aged from 26 to 94 years old (mean of 60.1 ± 12.9 years old) were included in this study: 87 men and 163 women.

According to the laboratory criteria adopted by the SBD, 19.2% of the individuals were normoglycemic (< 100 mg/dL), 21.6% had DM or increased risk for the disease ($\geq$ 100 and < 126 mg/dL) and 59.2% had hyperglycemia (> 126 mg/dL), where 80.8% of them presented higher fasting glucose values than those recommended by the SBD[3] (Table 1).

Table 1. Fasting glucose according to the age group of the patients treated in the Clinical Analysis Laboratory of the University Hospital (Piauí- Brazil, 2018).

Fasting glucose (mg/dL)					
Age Group (years old)	Gender	n	<100 n (%)	≥100 and <126 n (%)	≥126 n (%)
Up to 59	M	46	6 (2.4)	11 (4.4)	29 (11.6)
	F	68	15 (6.0)	10 (4.0)	43 (17.2)
≥60	M	41	6 (2.4)	10 (4.0)	25 (10.0)
	F	95	21 (8.4)	23 (9.2)	51 (20.4)
Total	M	87	12 (4.8)	21 (8.4)	54 (21.6)
	F	163	36 (14.4)	33 (13.2)	94 (37.6)
Total		250	48 (19.2)	54 (21.6)	148 (59.2)

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Comparing the means of fasting glucose, HbA1c and postprandial glycaemia between men and women, the Mann-Whitney's U test found that gender exerted no effect on the parameters evaluated (p>0.05) (Table 2).

Regarding glycemic control assessed by HbA1c, 45.2% (n=113) of the study participants did not have satisfactory glycemic control (HbA1c < 7%), and there was no statistically significant difference between the genders (p>0.05) (Table 2).
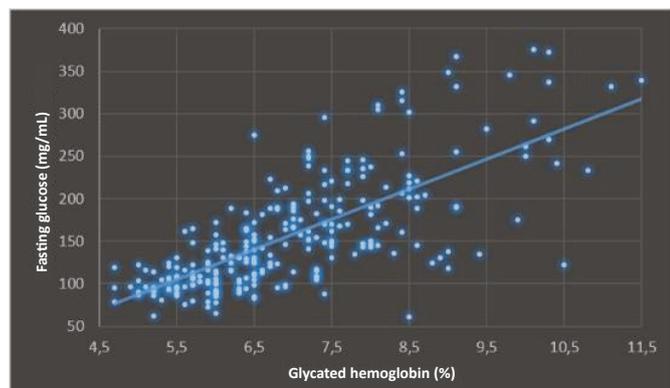
Table 2. Comparison between the means of fasting glucose, HbA1c and postprandial glycaemia in relation to the gender of the patients treated in the Clinical Analysis Laboratory of the University Hospital (n = 250, Piauí - Brazil, 2018)

Parameter	Gender	
	M	F
Fasting glucose (mg/dL)	161.62±62.42	155.66±67.2
HbA1c (%)	6.96±1.24	7±1.43
Postprandial glycaemia (mg/dL)	223.39±116.88	208.35±98.87

Key: HbA1c: Glycated hemoglobin

The Spearman's correlation test resulted in a value of 0.74 between the HbA1c and fasting glucose variables (p<0.01), indicating a strong positive correlation (Figure 1). On the other hand, for the HbA1c and postprandial glycaemia variables, the correlation reached a value of 0.60 (p<0.01), indicating a moderate positive correlation (Figure 2).

Figure 1. Correlation between fasting glucose and HbA1c of the patients treated in the Clinical Analysis Laboratory of the University Hospital (n = 250, Piauí- Brazil, 2018).

Figure 2. Correlation between postprandial glycaemia and HbA1c of the patients treated in the Clinical Analysis Laboratory of the University Hospital (n = 250, Piauí- Brazil, 2018).
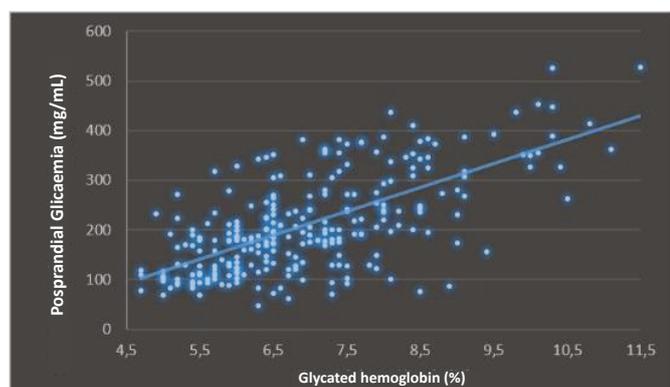
Discussion

Our findings revealed that nearly 80% of the medical records evaluated presented higher values than those recommended by the SBD, which is fasting glucose lower than 100 mg/dL, and that approximately 45% of the participants in this study had HbA1c > 7%, indicating deficient glycemic control. For glycemic monitoring, the measure of fasting plasma glucose is adopted due to its practicality. However, this diagnosis modality *per se* is not sufficient to provide a quantitative and reliable glycaemia assessment during a prolonged period of time.[17] In this sense, HbA1c dosage becomes necessary and presents greater advantages such as convenience (no fasting required), possibly greater pre-analytical stability and fewer day-to-day disturbances during stress and illness.[18] In addition, when compared to fasting glucose, baseline HbA1c is pointed out as a stronger predictor of diabetes and of underlying cardiovascular events.[19]

HbA1c is considered as the gold standard test to assess long-term glycemic control,[20] as it reflects the blood glucose levels in the last 2 or 3 months.[21] This control is defined in the HbA1c < 7% range.[20] In our sample, most of the individuals were older adults (> 60 years old), which are considered particularly more vulnerable to hypoglycemia.[18] According to Funamizu *et al.* (2020)[21], hypoglycemia is associated with an increased risk of all-cause mortality, which casts doubt about very strict glycemic control in diabetic patients.

Postprandial hyperglycemia is the result of excessive production of glucose associated with its reduced peripheral uptake, which can evolve to a chronic state, producing glycotoxicity. It is characterized by a progressive reduction in secretion by the beta cell, or by the progressive loss of the glycostatic function of the pancreas, progressively deteriorating the hyperglycemic state.[22] In our study, 66% of the individuals presented postprandial glycaemia above the goals recommended by the SBD, which is < 160 mg/dL. A similar result was described by Bonora (2002)[23] (around 70%) when checking postprandial glycaemia after two hours at breakfast and lunch in patients with Type 2 Diabetes Mellitus. Postprandial glycaemia does not play any role in DM diagnosis due to the difficulty establishing adequate reference values.[3] However, its control has proved to be an essential factor for general glucose control, with high postprandial glycaemia levels being associated with a higher risk of developing microvascular and macrovascular complications in patients with diabetes.[24]

In this study, when correlating HbA1c and fasting glucose, the result found was rs=0.74. A similar result was reported in a study carried out in the United States with 11,092 patients, in which a strong positive correlation was described between HbA1c and fasting glucose (r=0.73).[19] In addition, Christiansen *et al.* (2012),[25] when evaluating data from 10,065 Danish individuals with simultaneous dosage of HbA1c and fasting glucose, obtained a correlation of r=0.77, with no difference between the genders. The results found in this study indicated a strong and positive linear correlation between the plasma levels of fasting glucose and HbA1c, in line with previous studies, in which the higher the HbA1c value, the higher the fasting glucose level. However, some individuals presented fasting glucose in the acceptable range, whereas the HbA1c levels were high. Therefore, the need is verified to measure HbA1c concomitantly with fasting glucose during routine tests, as the relationship between fasting glucose and HbA1c may depend on the glycemic control degree, especially because some diabetics have difficulty understanding the concept

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of deficient glycemic control through the HbA1c value, when they do not present very high fasting glycaemia. Therefore, checking the discrepancies between the fasting blood glucose and HbA1c values can help to determine whether the individual is having good glycemic control or not.[26]

Ketema and Kibret (2015),[14] when carrying out a meta-analysis with evidence on the importance of fasting and postprandial plasma glucose and its correlation with HbA1c, described that 63.5% (n=7) of the articles evaluated found better or stronger correlations between postprandial glycaemia and HbA1c than between fasting blood glucose and HbA1c. However, 36.5% (n=3) of the studies reported a better correlation between fasting glucose and HbA1c. Unlike most of these studies, our findings indicated a stronger positive correlation between the fasting glucose levels and HbA1c (rs=0.74) than the correlation between postprandial glycaemia and HbA1c (rs=0.60).

The positive correlation shown between fasting glucose and HbA1c was already expected, as it is known that the HbA1C value depends on fasting glucose concentration and on erythrocyte lifetime. Thus, recent glycaemia, in the last thirty days prior to dosage, is the one that most influences HbA1C formation, contributing 50% of its value. Another 25% will formed in the second month prior to the exam; and the remaining 25%, in the third and fourth months. Thus, lack of control of the glycemic concentrations exposes the patient to the risks of chronic hyperglycemia, to microvascular complications such as nephropathy, retinopathy and neuropathy, and to macrovascular complications such as stroke and acute myocardial infarction, which are responsible for the high morbidity and mortality rates among diabetics. Our findings reinforce the need to improve patients' access and frequency regarding appointments in the Basic Health Unit (BHU) as a primary strategy for initial DM control.[10]

The brief collection period with a small sample size stands out as a limitation of this study. In addition to that, the study was conducted in a single health center, hindering externalization of the results.

As a perspective for investigating the topic, there is the need for studies with larger sample sizes and that include collection of information in interviews with the patients, in order to establish which factors could be interfering with good glycemic control.

Conclusion

The data presented indicated that a significant percentage of the individuals monitored by a university hospital located in the state of Piauí did not have adequate glycemic control, presenting higher values than those recommended by the Brazilian Diabetes Society for fasting/postprandial glycaemia and HbA1c. The correlation analysis between fasting glucose and HbA1c showed a stronger correlation than postprandial glycaemia/HbA1c. The use of data from laboratory tests, especially fasting glucose and HbA1c, allow for the monitoring of chronic diseases, especially diabetes, serving as a basis for evaluating the measures implemented. Thus, this study contributes to the knowledge about the glycemic control degree of the outpatients in the aforementioned hospital and reinforces the need for multidisciplinary interventional practices in order to avoid future chronic microvascular and/or macrovascular complications resulting from diabetes mellitus.

Conflict of interest statement

The authors declare no conflicts of interest in relation to this article.

References

1. Yaribeygi H, Maleki M, Sathyapalan T et al. Anti-inflammatory potentials of incretin-based therapies used in the management of diabetes. Life Sci. 2020; 241: 1-6.

2. Canto ED, Ceriello A, Rydén L, et al. Diabetes as a cardiovascular risk factor: An overview of global trends of macro and micro vascular complications. Eur. j. prev. cardiol. 2019; 26(25): 25-32.

3. SOCIEDADE BRASILEIRA DE DIABETES. Diretrizes da Sociedade Brasileira de diabetes. 2017-2018. Rio de Janeiro: 2017. Available: https://www.diabetes.org.br/profissionais/images/2017/diretrizes/diretrizes-sbd-2017-2018.pdf. Accessed on: March 5, 2020.

4. World Health Organization. Global health risks: mortality and burden of disease attributable to selected major risks. Geneva, Switzerland: World Health Organization. 2009. Available: https://www.who.int/healthinfo/global_burden_disease/GlobalHealthRisks_report_full.pdf. Accessed on: October 8, 2020.

5. MearnsH, Otiku PK, Shelton M, et al. Screening strategies for adults with type 2 diabetes mellitus: a systematic review protocol. Syst Rev. 2020;9(1):1-11.

6. Chawla R, Madhu SV, Makkar BM et al. RSSDI-ESI Clinical Practice Recommendations for the Management of Type 2 Diabetes Mellitus 2020. Indian J Endocrinol Metab. 2020;24(1):1-122.

7. Panarotto D, Teles AR, Schumacher MV. Fatores associados ao controle glicêmico em pacientes com diabetes tipo 2. Rev Assoc Med Bras. 2008; 54(4): 314-21.

8. Rossaneis MA, Andrade SM, Gvozd R, et al. Fatores associados ao controle glicêmico de pessoas com diabetes mellitus. Ciênc. saúde coletiva. 2019; 24(3): 997-1005.

9. Souliotis K, Koutsovasilis A, Vatheia G. Profile and factors associated with glycaemic control of patients with type 2 diabetes in Greece: results from the diabetes registry. BMC Endocr Disord. 2020;20(16): 1-10.

10. Abdullah MFILB, Sidi H, Ravindran A, et al. How Much Do We Know about the Biopsychosocial Predictors of Glycaemic Control? Age and Clinical Factors Predict Glycaemic Control, but

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Revista Brasileira de Farmácia Hospitalar e Serviços de Saúde

Psychological Factors Do Not. J Diabetes Res. 2020;2020: 1-11.

11. Harder L, Andrade TK, Serra FB *et al.* Number of type 2 diabetes patients achieving HbA1c goal and Related Factors in Brazil: A real world evidence study. Research Square. 2020: 1-16.

12. Martins JA, Santos RB, Leal BS *et al.* Perfil clínico e epidemiológico dos portadores de Diabetes Mellitus tipo I assistidos pelo componente especializado do Piauí. Revista de Casos e Consultoria. 2020;11(1):1-18.

13. Fasil A, Biadgo B, Abebe M. Glycemic control and diabetes complications among diabetes mellitus patients attending at University of Gondar Hospital, Northwest Ethiopia. Diabetes Metab Syndr Obes. 2019; 12: 75-83.

14. Ketema EB, Kibret KT. Correlation of fasting and postprandial plasma glucose with HbA1c in assessing glycemic control: systematic review and meta-analysis. Arch Public Health. 2015; 73(43): 1-9.

15. Cho JH, Kim HJ, Lee JH, *et al*. Poor glycemic control is associated with the risk of subclinical hypothyroidism in patients with type 2 diabetes mellitus. Korean J Intern Med. 2016;31(4):703-711.

16. Mukaka MM. Statistics corner: A guide to appropriate use of correlation coefficient in medical research. Malawi Med J. 2012; 24(3): 69-71.

17. Rizzardi L, Cunha TN. O diabetes mellitus e a hemoglobina glicada e sua correlação com a glicemia média estimada. Rev Saúde e Desenvol. 2013;3(2): 150-167.

18. Standards of Medical Care in Diabetes — 2014, American Diabetes Association. Diabetes Care. 2014; 37(1): S14-S80;

19. Selvin E, Steffes MW, Zhu H et al. Glycated hemoglobin, diabetes, and cardiovascular risk in nondiabetic adults. N Engl J Med. 2010;362(9):800–811.

20. Wang S, Ji X, Zhang Z *et al.* Relationship between Lipid Profiles and Glycemic Control Among Patients with Type 2 Diabetes in Qingdao, China. Int J Environ Res Public Health. 2020; 17(15): 1-10.

21. Funamizu T, Iwata H, Nishida Y *et al.* Increased risk of cardiovascular mortality by strict glycemic control (pre-procedural HbA1c<6.5%) in Japanese medically-treated diabetic patients following percutaneous coronary intervention: a 10-year follow-up study. Cardiovasc Diabetol. 2020; 19(21): 1-12.

22. Geloneze B, Lamounier RN, Coelho OR. Hiperglicemia Pós-Prandial: Tratamento do seu Potencial Aterogênico. Arq Bras Cardiol. 2006; 87(1): 660-670.

23. Bonora E. Post-prandial peaks as a risk factor for cardiovascular disease: epidemiological perspectives international. J Clin Pract Suppl. 2002; 29(1): 5-11.

24. Miura J, Imori M, Nishiyama H *et al*. Ultra-Rapid Lispro Efficacy and Safety Compared to Humalog® in Japanese Patients with Type 1 Diabetes: PRONTO-T1D Subpopulation Analysis. Diabetes Ther. 2020;11(9):2089-2104.

25. Christiansen R, Rasmussen LM, Nybo H *et al*. The relationship between HbA1c and fasting plasma glucose in patients with increased plasma liver nzyme 320 measurements. Diabetic Med. 2012; 29(6): 742-7.

26. Bettencourt-Silva R, Costa E, Teles MJ *et al.* Associação entre glicose média estimada e glicose plasmática em jejum em adultos em seguimento ambulatório. Rev Portuguesa de Diabetes. 2018;3(1): 3-13.

27. Chandalia HB, Krishnaswamy PR. Glycated Hemoglobin — Current Science. 2002; 83(12):1522-1532.