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Original Article

Investigation of the Relationship Between Hemoglobin and Hemoglobin A1c Levels in Diabetes Mellitus Patients with and Without Anemia

Pınar Zehra Davarcı[1], Emin Murat Akbaş[2], Yusuf Kemal Aslan[3], Özlem Admış[4], İsmail Davarcı[5]

[1]Department of Public Health, Trakya University, Faculty of Medicine, Edirne, Türkiye
[2]Department of Endocrinology and Metabolic Diseases, Yalova University, Faculty of Medicine, Yalova, Türkiye
[3]Department of Biostatistics and Medical Informatics, Çukurova University, Faculty of Medicine, Adana, Türkiye
[4]Medical Biochemistry Laboratory, Mengücek Gazi Training and Research Hospital, Erzincan Binali Yıldırım University, Erzincan, Türkiye
[5]Department of Medical Microbiology, Trakya University, Faculty of Medicine, Edirne, Türkiye

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ORCID iDs of the authors: P.Z.D. 0000-0002-7709-8240, E.M A. 0000-0002-3033-0073, Y.K.A. 0000-0003-1308-8569, Ö.A. 0000-0001-5794-940X, İ.D. 0000-0002-5835-4237.

ABSTRACT

Objective: Hemoglobin A1c (HbA1c) is a glycosylated protein and shows the glycemic status for the last 2-3 months, and it is the most commonly used marker in routine practice. In this study we aimed to investigate the relationship between hemoglobin and HbA1c levels.

Methods: In total, 4278 patients with type 2 diabetes mellitus included in this study. The study was cross-sectional, and the data of the patients were recorded by scanning the hospital automation system. Hemoglobin A1c levels of patients with and without anemia who had the same fasting blood glucose levels were compared.

Results: At similar fasting blood glucose levels, HbA1c levels were found to be lower in patients with anemia than those without anemia

Conclusion: Anemia status of the patients should be considered when evaluating HbA1c.

Keywords: Anemia, diabetes mellitus, HbA1c

INTRODUCTION

Diabetes mellitus (DM) is a chronic, broad-spectrum metabolism disorder in which the organism cannot benefit sufficiently from carbohydrates, fats, and proteins due to insulin deficiency or insulin-effect defects and it requires continuous medical care.[1]

Blood glucose and non-enzymatic glycosylated proteins in blood are used as indicators of glycemic control in diabetic patients. Hemoglobin A1c (HbA1c) is a glycosylated protein and shows the glycemic status for the last 2-3 months due to the average erythrocyte life span of 120 days, and it is the most commonly used marker in routine practice and is known to be associated with chronic complications.[2,3] Hemoglobin A1c is calculated as the ratio of glycosylated hemoglobin to total hemoglobin as percentage.[3]

The American Diabetes Association has established diagnostic criteria for DM (Table 1).[4] The diagnosis of DM can be made by any of 4 methods. The diagnosis should be confirmed on the following days, preferably by the same (or different) method, except in cases where there are no severe symptoms of diabetes.[1]

Hemoglobin A1c is affected by age, race, genetic factors, hematological diseases, and many other conditions.[5] Previous studies have reported that hemolytic anemia, hemoglobinopathy, chronic liver, and chronic kidney

Corresponding Author: Pınar Zehra Davarcı, **E-mail:** zehrabuyukyazici@hotmail.com

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Table 1. Diagnostic Criteria for Diabetes Mellitus

Fasting plasma glucose	≥126 mg/dL
2-hour plasma glucose during an OGTT*	≥200 mg/dL
Random blood glucose + symptoms of diabetes	≥200 mg/dL
HbA1c	≥6.5%

OGTT, oral glucose tolerance test.
*After a glucose load of 75 g anhydrous glucose dissolved in water.

diseases affect HbA1c level.[6] When considering that 30% of the world's population has anemia, the relationship between hemoglobin and HbA1c levels arouses curiosity.[7]

The aim of this study is to investigate whether there is a difference between HbA1c levels of diabetic patients with and without anemia.

METHODS

Ethics committee approval of this study was obtained from Erzincan University (Date: May 30, 2019, Number 06/08). The study is a cross-sectional study. The population of the study consisted of patients 18 years old and above with type 2 diabetes mellitus. Patients with a history of hemolytic anemia, acute hemorrhage in the last 3 months, hemoglobinopathy, and chronic liver or kidney disease and those who were pregnant were excluded from the study. Patients were selected among the patients whose HbA1c was measured in Erzincan Binali Yıldırım University, Mengücek Gazi Training and Research Hospital Biochemistry Laboratory between January 2016 and January 2019 and whose results were recorded in the Laboratory Information System. Included patients were classified as follows according to fasting blood glucose levels: 100-134 mg/dL in group 1, 135-169 mg/dL in group 2, 170-204 mg/dL in group 3, 205-239 mg/dL in group 4, 240- 274 mg/dL in group 5, 275-309 mg/dL in group 6, and 310 mg/dL and above in group 7. Within each subgroup, the number of females and males, and the anemic and non-anemic ones were equalized randomly. This study included a total of 4278 patients with non-insulin-dependent diabetes mellitus; 2139 of them were anemic and 2139 were non-anemic.

Based on the criteria of the World Health Organization, hemoglobin level at <13 mg/dL was accepted as anemic in male patients and 12 mg/dL in female patients.[8]

MAIN POINTS

- Anemia and diabetes mellitus are common health problems.
- When evaluating HbA1c, patients' anemia conditions must be considered.

Fasting blood sugar was analyzed by enzymatic hexokinase method via Beckman Coulter AU 2700 (Beckman Coulter Inc., Fullerton, Calif, USA). Hemogram tests were taken into the laboratories in EDTA-containing tubes and performed by fluorescent flow cytometry via XN 2000 (Sysmex, Kobe, Japan) model automatic blood counting device. Hemoglobin A1c test was performed by Tosoh G8 (Tosoh Corporation, Japan) using the HPLC (high-performance liquid chromatography) method.

Statistical Analysis

Categorical variables were summarized as n (%) and continuous variables were summarized as mean ± SD value. Two-way analysis of variance was used to examine the effect of anemia and group variables on HbA1c, and both the main effects and the interaction effects were statistically tested in the model. When examining the relationship between HbA1c and continuous variables, Pearson or Spearman correlation analysis was performed according to distribution. When determining the parameters affecting HbA1c, the variables that were found to be significant as a result of univariate analyses were included in the regression model. Only one of the variables that were found as significant in the univariate analysis but were related to each other was kept in the model. *P*-value at <.05 was accepted as statistically significant. IBM Statistical Package for the Social Sciences Statistics software (SPSS), version 19.0. software (IBM Corp.; Armonk, NY, USA) was used for data analysis.

RESULTS

In the study, 50% of the included patients were female and 50% were male. The mean age of females was 63.2 ± 12.9 years, and the mean age of men was 64.7 ± 12.8 years.

Hemoglobin, white blood cells, red blood cells, neutrophil, lymphocyte, monocyte, basophil, eosinophil, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, mean platelet volume, platelet, platelet/lymphocyte, neutrophil/lymphocyte, and lymphocyte/monocyte values were examined in terms of differences between the groups. A significant difference was found between hemoglobin and mean corpuscular hemoglobin (MCH) levels.

While there was no significant difference between hemoglobin values in groups 1 and 2, significant differences were found in groups 3, 4, 5, 6, and 7. In patients with fasting blood glucose levels ranging from 100 to 170 mg/dL, similar HbA1c results were observed regardless of the presence of anemia. However, in anemic patients, lower HbA1c levels were found when fasting blood glucose levels exceeded 170 mg/dL (Figure 1, Table 2).

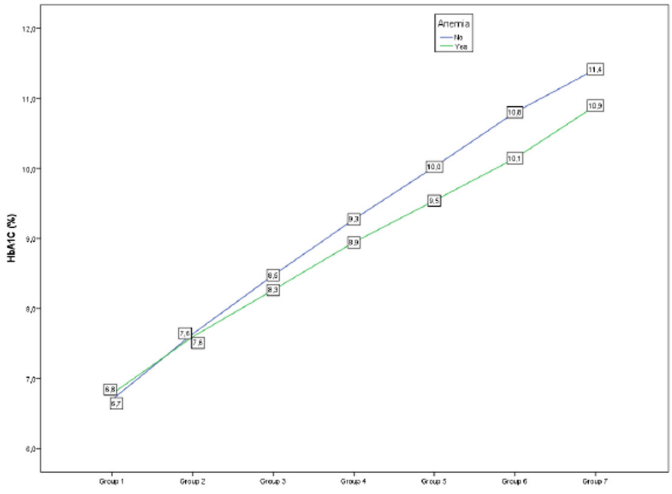


Figure 1. Variation of hemoglobin A1c according to the groups in patients with and without anemia.

As a result of regression analysis, significant correlations were found between HbA1c and variables such as anemia, group, and MCH. The mean HbA1c was found to be 0.368 units lower (beta = −0.368, $P = .036$) in anemic patients than in non-anemic patients. As the number of groups increased, the mean HbA1c increased by 0.676 units (beta = 0.676, $P < .001$). One-unit increase in MCH decreases HbA1c by 0.094 units (beta = −0.094, $P = .003$).

DISCUSSION

Anemia is defined as the inability of erythrocytes to supply the needed oxygen to the human body.[8] This need may vary according to factors such as age, gender, altitude, and smoking.[8] Although the most common cause of anemia is iron deficiency, nutritional disorders, infections, and hemoglobin synthesis defects play roles in its etiology.[8]

Diabetes mellitus is a complex metabolic disease characterized with chronic hyperglycemia.[9] Hemoglobin A1c, which is used in the diagnosis and follow-up of this disease, is affected not only by blood glucose value but also by the presence of variant hemoglobin, uremia, acute blood loss, and pregnancy.[2] Danescu et al.[10] reported that the HbA1c level of a thalassemia patient with a high blood glucose level was 1.6%. They attributed this situation to the short life span of erythrocytes.

In one of the first studies examining the relationship between anemia and HbA1c in people without diabetes, and in Coşkun et al.'s[11] study they both reported that HbA1c levels were higher in patients with anemia.[12] However, Hansen et al.[13] found no relationship between anemia and HbA1c. In a study by Kim et al.,[14] they could not establish a relationship between anemia and HbA1c in patients with HbA1c levels between 5.5% and 6.5%.

Table 2. Hemoglobin A1c Values of Patients With and Without Anemia (%)

Group	Anemia	n	Mean ± SD*	*P*
Group 1	No	545	6.7 ± 0.7	.215
	Yes	545	6.8 ± 0.8	
Group 2	No	681	7.6 ± 0.9	.493
	Yes	681	7.6 ± 1.0	
Group 3	No	389	8.5 ± 1.2	**.008****
	Yes	389	8.3 ± 1.2	
Group 4	No	230	9.3 ± 1.3	**.001****
	Yes	230	8.9 ± 1.4	
Group 5	No	146	10.0 ± 1.5	**<.001****
	Yes	146	9.5 ± 1.5	
Group 6	No	101	10.8 ± 1.6	**<.001****
	Yes	101	10.1 ± 1.7	
Group 7	No	47	11.4 ± 1.2	**.023****
	Yes	47	10.9 ± 1.3	

*Results were presented as mean and SD.

**p<0.005.

In the literature, the relationship between Hb and HbA1c has been investigated usually in people without DM. By this way, it was aimed to prevent misinterpretation of HbA1c, which is one of the diagnostic criteria of DM. However, HbA1c is an important parameter and used in the treatment follow-up of patients with DM as well. In the literature, there are very few articles investigating the relationship between Hb and HbA1c in DM patients. One of these studies is the study of Solomon et al.[15] conducted with 174 diabetic patients. In that study, HbA1c levels were found to be significantly lower in anemic patients, as in our study.

All patients included in our study were previously diagnosed with DM, and in our study there was no significant difference between anemia and HbA1c in patients with low HbA1c average (6.7% in group 1, 7.6% in group 2) similarly to studies of Hansen et al.[13] and Kim et al.[14] However, with the increase in HbA1c averages, significant differences were found between anemia and HbA1c in groups 3, 4, 5, 6, and 7. At similar fasting blood glucose levels, HbA1c levels were found to be lower in patients with anemia than in those without anemia.

Rodriguez-Segade et al.[16] reported that MCH, which is an indicator of erythrocyte life expectancy, is inversely correlated to HbA1c.

The limiting steps of our study were the lack of postprandial blood sugar levels of the patients, the lack of determination of hemolytic anemia by reticulocyte count for

each patient, and lack of hemoglobin electrophoresis for each patient. Wider and multicenter studies are needed on this subject.

Study Limitations

The main limitation of the study is that subjects were from one public hospital and the sample size was not large enough, which may cause some bias. In the future, large studies are still needed.

CONCLUSION

Diabetes mellitus type 2 and anemia are common health problems. When interpreting HbA1c, a frequently used marker in diabetes management, the anemia status of the patients must be evaluated.

Ethics Committee Approval: Ethics committee approval of this study was obtained from Erzincan University (Date: May 30, 2019, Number 06/08).

Informed Consent: Informed consent was waived due to retrospective design of the study. Approval was obtained from the hospital management where patient data was collected.

Peer-review: Externally peer-reviewed.

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REFERENCES

1. Türk Endokrinoloji ve Metabolizma Derneği (TEMD). Diabetes Mellitus Tanı, Tedavi ve İzlem Kılavuzu 2022. Available at: https://temd.org.tr/yayinlar/kilavuzlar.
2. Oğuz E, Ercan M, Yılmaz FM. Effect of iron deficiency anemia on hemoglobin A1c levels in Normoglisemic individuals. *Ank Med J*. 2014;14(1):15-18.
3. Karatoprak K, Uysal S, Akkilik ZS, Ercan M, Yılmaz FM. The relationship between serum biochemical parameters and glycaemic control in diabetes. *Turk J Bioch*. 2012;1(2):51-54. [CrossRef]
4. American Diabetes Association. Standards of medical care in diabetes-2019. 2019;42:13-28.
5. Son JI, Rhee SY, Woo JT, et al. Hemoglobin A1c may be an inadequate diagnostic tool for diabetes mellitus in anemic subjects. *Diabetes Metab J*. 2013;37(5):343-348. [CrossRef]
6. Gallagher EJ, Le Roith D, Bloomgarden Z. Review of hemoglobin A(1c) in the management of diabetes. *J Diabetes*. 2009;1(1):9-17. [CrossRef]
7. Çipil H, Demircioğlu S. Iron deficiency anemia. *Turk Klin J Fam Spec Top*. 2016;7(3):34-37.
8. World Health Organization (WHO). Anemia. (Last access date: 20.03.2022). https://www.who.int/news-room/fact-sheets/detail/anaemia.
9. Karakükçü Ç, Mert M, Karaman A. Association of labile hemoglobin A1c with blood glucose levels and MPV. *Türk Klin Biyokim Derg*. 2011;9(3):77-82.
10. Danescu LG, Levy S, Levy J. Markedly low hemoglobin A1c in a patient with an unusual presentation of beta-thalassemia minor. *Endocr Pract*. 2010;16(1):89-92. [CrossRef]
11. Coban E, Ozdogan M, Timuragaoglu A. Effect of iron deficiency anemia on the levels of hemoglobin A1c in nondiabetic patients. *Acta Haematol*. 2004;112(3):126-128. [CrossRef]
12. Brooks AP, Metcalfe J, Day JL, Edwards MS. Iron deficiency and glycosylated haemoglobin A. *Lancet*. 1980;2(8186):141. [CrossRef]
13. Gram-Hansen P, Eriksen J, Mourits-Andersen T, Olesen L. Glycosylated haemoglobin (HbA1c) in iron- and vitamin B12 deficiency. *J Intern Med*. 1990;227(2):133-136. [CrossRef]
14. Kim C, Bullard KM, Herman WH, Beckles GL. Association between iron deficiency and A1C Levels among adults without diabetes in the National Health and Nutrition Examination Survey, 1999-2006. *Diabetes Care*. 2010;33(4):780-785. [CrossRef]
15. Solomon A, Hussein M, Negash M, Ahmed A, Bekele F, Kahase D. Effect of iron deficiency anemia on HbA1c in diabetic patients at Tikur Anbessa specialized teaching hospital, Addis Ababa Ethiopia. *BMC Hematol*. 2019;19(1):2. [CrossRef]
16. Rodriguez-Segade S, Garcia JR, García-López JM, et al. Impact of mean cell hemoglobin on Hb A1c-defined glycemia status. *Clin Chem*. 2016;62(12):1570-1578. [CrossRef]