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EFFECT OF MICROCYTIC ANEMIA ON HbA1C VALUES IN NON-DIABETIC INDIVIDUALS

Diabetology

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ABSTRACT

(i) Objective: To determine the effect of microcytic anemia on HbA1C values in individuals without diabetes.
(ii) Methods: The study was conducted as a clinical non-interventional observation study. A sample of 200 patients with MCV less than 80 fL, FPG less than 100mg/dL was selected and in them HbA1C test was carried out using HPLC method. A control population of 40 patients with normal MCV and FPG less than 100 mg/dL was also taken and in them also HbA1C was studied.
(iii) Result: Out of the 200 cases studied 98 were males and 102 were females. The mean age for cases was 51.87 years. 28% patients had severe anemia, 64.5% patients had moderate anemia and 7.5% patients had mild anaemia. Mean MCV for cases were 71.86fL. A significant negative correlation has been found out between HbA1C and haemoglobin levels and between HbA1C and MCV.
(iv) Conclusion: There is a definite negative correlation between MCV and HbA1C in the study population. A significant correlation was also found between haemoglobin and HbA1C value.

KEYWORDS

Introduction

Glycated haemoglobin has been used in the management of diabetes as a marker of long term glycemic control. Levels of glycated haemoglobin correlate well with average blood glucose levels during the previous 2 to 3 months. The International Expert Committee recommended the use of this test for the diagnosis of diabetes, with a threshold level of 6.5% in 2009. The measurements of glycated haemoglobin for diagnosing diabetes was subsequently adopted as an optional test by the ADA in 2010 and the WHO in 2011.

In spite of some advantages, the glycated haemoglobin testing has its limitations. Depending on the assays spuriously low values may occur in patients with certain haemoglobinopathies (eg- sickle cell disease and thalassemia) or who have increased red-cell turnover (eg. Haemolytic anemia and spherocytosis) or stage 4 or 5 chronic kidney disease, especially if the patient is on erythropoetin treatment. On the other hand, falsely high glycated haemoglobin levels have been reported in association with iron deficiency and other states of decreased red-cell turnover. These potential pitfalls must be kept in mind when glycated haemoglobin testing is used for diagnosis, especially in the diagnosis of pre-diabetics, since the cut off points for this state are already somewhat arbitrary. This study is intended to determine the effect of microcytosis on HbA1C values, which could guide the diagnosis and follow up of diabetes.

Materials and Methods:

The study was conducted at Department of Internal Medicine, Govt. Medical College, Kottayam. It was a clinical non-interventional observation study. The study duration was one year from September 2011 to August 2012. The sample studied was the first consecutive 200 patients.

Inclusion criteria:

1. Patients with microcytic anemia (Microcytosis defined as MCV less than 80fL and anemia defined as Hb less than 13g/dL in men and less than 12g/dL in women)

2. Patients with fasting plasma glucose below 100mg/dL

Exclusion criteria:
1. Patients of hypochromic microcytic anemia on treatment with supplemented iron
2. Patients taking salicylates
3. Patients with chronic kidney disease

Patients with MCV less than 80fL and FPG less than 100mg/dL underwent HbA1C test (HPLC). At the same time a control group consisting of 40 patients with normal MCV (90+/- 8fL) and FPG less than 100 mg/dL were selected. HbA1C test was carried out in this group also.

Statistical Analysis

Continuous variables were expressed as mean $\pm$ sd. Pearson's correlation coefficient was used to investigate the correlation between the two variables. Microsoft Excel and SPSS 21.0 for Windows were used for data storage and analysis.

RESULT (OBSERVATIONS)

1. Distribution of sample by level of Hb and MCV

Out of 200 cases, 56 patients (28%) had severe anemia (Hb <8g/dL) , 129 patients (64.5%) had moderate anemia (HB 8-10.9g/dL) and 15 patients (7.5%) had mild anemia (Hb 11-12.9 g/dL). 7 cases (3.5%) had MCV between 50 & 60 fL and 63 cases (31.5%) had MCV between 60 & 70 fL and 130 cases (65%) had MCV between 70 &80 fL.

2. Average HbA1C by level of MCV

7 cases with MCV between 50 & 60 fL had mean HbA1C value of 6.5% $\pm$ 0.94. 63 cases with MCV between 60 and 70 fL had mean HbA1C value of 6.26% + 0.79. 130 cases with MCV between 70 & 80 fL had mean HbA1C value of 6.12 + 0.79.

3. Correlation between Hb and HbA1C

Correlation between Hb and HbA1C was calculated using Pearson Correlation Coefficient. There is significant negative correlation between HbA1C and Hb for total sample (p=0.035) and for males (p=0.002)

Table 1

	Correlation between HbA1C and Hb			
Total	Pearson Correlation	-0.149	0.035	Significant negative correlation
Males		-0.305	0.002	Significant negative correlation
Females		-0.054	0.588	No Significant correlation

4. Correlation between HbA1C and MCV

Without controlling any factors, a negative correlation was found between MCV and HbA1C and the correlation was statistically significant (p=0.048). On controlling age a statistically significant (p=0.034) more negative correlation was found. On controlling both age and FBS a statistically significant (p=0.043) negative correlation was found.

Table 2

Correlation Coefficient	P	Controlling	
Bivariate	-0.140	0.048	Nil
Partial	-0.151	0.034	Age
	-0.073	0.307	Hb
	-0.135	0.058	FBS
	-0.144	0.043	FBS, Age
	-0.074	0.304	FBS, Hb
	-0.079	0.267	Hb, Age
	-0.791	0.269	Hb, Age, FBS

5. Mean MCV and mean HbA1C in Control Population

The mean MCV for control population was 89.08 fL + 3.85 and for experimental population was 71.86fL + 5.40. This difference in MCV is statically significant (p=0.000)

The mean HbA1C for control population was 5.27% + 0.27 and for experimental population was 6.18% + 0.80. This difference in HbA1C is statically significant (p=0.000)

6. Correlation between HbA1C and MCV for control population

There is no significant correlation between HbA1C and MCV in control population

Table 3

Correlation Coefficient	P	Controlling	
Bivariate	0.084	0.606	Nil
Partial	0.093	0.575	Age

DISCUSSION

In our study a significant negative correlation has been found out between HbA1C and haemoglobin levels. Similarly a negative correlation was obtained between HbA1C and MCV. After adjusting for age the negative correlation was found to increase. Coban E et al.[1] in their study Effect of iron deficiency anemia on the level of HbA1C in non-diabetic patients reported that the mean HbA1C of 7.4 $\pm$ 0.8% in iron deficiency patients reduced to 6.2 $\pm$ 0.6% after iron therapy. Ford et al.[2] in their study Iron deficiency anemia, non –iron deficiency anemia and HbA1C among adults in the US stated that the adjusted mean concentration of HbA1C were 5.5% and 5.46% among participants with and without iron deficiency, respectively. Tarim O et al.3 in their study of Effects of iron deficiency anemia on HbA1C in Type 1 Diabetes Mellitus found that HbA1C in iron-deficient non-diabetic patients decreased from a mean of 7.6 $\pm$ 2.67 to 6.2 $\pm$ 1.4% after iron therapy. This effect of MCV on HbA1C may be due to an increase in the average life span of microcytes and also variation in the glycation rate of red blood cells in a state of iron deficiency (a common cause for microcytosis) because of the alternation in the quarternary structure of haemoglobin.[4]

CONCLUSION

Iron deficiency anemia is very much prevalent in our part of world and it is a common cause for microcytic hypochromic anemia. As has been demonstrated in this study, patients with microcytic anemia have falsely elevated HbA1C levels, it is prudent to keep in mind the potential effects of microcytosis on HbA1C before diagnosing a patient as having diabetes solely based on HbA1C test result, as well as in the assessment of glycemic control of patients with diabetes.

Limitations

Iron studies of both cases and controls could not be done because of resource constraints

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