



“A STUDY OF EFFECT OF MICROCYTIC ANEMIA ON HbA1c IN NON DIABETIC PATIENTS”

General Medicine

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ABSTRACT

Background: Diabetes mellitus is one of the most common diseases worldwide with significant morbidity and mortality. HbA1c remains one of the most important methods for diagnosis and monitoring of the disease. Since HbA1c is a reflection of the glucose attached to red blood cells, factors affecting hemoglobin and red blood cells half-life can influence HbA1c measurements. **Objective :** To study the correlation between the severity of microcytic anemia and the derangements of HbA1c levels in an adult non diabetic population. **Methods :** A cross sectional study was conducted at Mahadevappa Rampure Medical college, Kalaburgi during the period of August 2022-January 2024 on 300 patients admitted to in patient department of general medicine with anemia and evaluated for the same. **Results :** Study observed that out of 300 patients; 183(61.0%) of patients were microcytic hypochromic anemia, 25(8.3%) patients were dimorphic, 38(12.7%) were macrocytic and 54(18.0%) of patients were normocytic normochromic anemia. Comparison of severity of Microcytic hypochromic anemia with HbA1c showed significant association, as severity of anemia increased in this group HbA1c also increased (p value=0.001). When we compared other anemias like dimorphic anemia, macrocytic anemia and normocytic normochromic anemia individually with HbA1c we did not find any correlation in our present study. **Conclusion :** Microcytic hypochromic anemia is the commonest anemia in this group of patients. As severity of microcytic hypochromic anemia increased HbA1c also increased. This false increase in HbA1c level may lead to misdiagnosis of diabetes mellitus so it is worthwhile to crosscheck haemoglobin before using HbA1c for diagnosing diabetes mellitus in anemic individuals.

KEYWORDS

HbA1c – Glycosylated hemoglobin

INTRODUCTION:

Globally, anemia continues to be a crucial health issue for countries which are developed as well as those which are still developing, and affects all age groups. According to the WHO, definition of anemia is hemoglobin (Hb) levels <13.0 g/dL in males and <12.0 g/dL in females.¹

According to the World Health Organization's 2019 report, Anemia is estimated to affect half a billion women 15–49 years of age and 269 million children 6–59 months of age worldwide. In 2019, 30% (539 million) of non-pregnant women and 37% (32 million) of pregnant women aged 15–49 years were affected by anaemia.² The normal values of hemoglobin may vary with gender, ethnicity and the physiologic status of the population. Various etiological factors such as physiological and pathological mechanisms account to anemia. The classification and diagnosis of anemia is mainly based on the history of patient, hematologic parameters and thorough physical examination.³ During morphological presentation in examination of a peripheral blood smear, anemia can be macrocytic type, microcytic hypochromic type, normocytic normochromic type and dimorphic type. Varied etiologies are present with each of these morphological types.⁴

Diabetes mellitus is another condition with increased global prevalence along with anemia. The most important diagnostic values in evaluating glycemia are postprandial blood sugar, fasting blood sugar and hemoglobin A1c (HbA1c). The report of WHO in 2011 summarized the evidence on the usage of HbA1c for the diagnosis of Diabetes Mellitus and its quality with the help of GRADE methodology. The report says that for diabetes mellitus, HbA1c can be used as a diagnostic test with strict quality assurance tests in place along with assays standardized to criteria aligned to the international reference values, and there are no conditions present which preclude its accurate measurement.⁵ The measure of HbA1c is the most widely accepted diagnostic test used, especially in community-based studies, as it needs no fasting blood glucose and has lesser inter-observer variability.⁵ The World Health Organization along with the American Diabetes Association has promoted the use of HbA1c for diagnosing type 2 diabetes mellitus with 6.5% or higher considered as a cut off value.⁶

The value of HbA1c can be altered by conditions unrelated to diabetes mellitus. Factors which influence an increased HbA1c value include iron deficiency, decreased erythropoiesis and vitamin B₁₂ deficiency,

whereas low values of HbA1c could be influenced by administration of erythropoietin, vitamin B₁₂ or iron and reticulocytosis or chronic liver disease, while genetic or chemical alterations in hemoglobin such as hemoglobinopathies, fetal hemoglobin (HbF), methemoglobin can decrease or increase HbA1c.⁵ The hemolytic anemias, because of reduction in erythrocyte lifespan can cause a decrease in HbA1c value. Whereas, iron deficiency anemia results in increased HbA1c estimates, contrasting to the previous types of anemia.⁶

Deficiency of iron occurs due to decreased intake of iron, reduced absorption of iron, loss of blood, menstrual bleeding or pregnancy. Thus with several etiologies, iron deficiency anemia characterises as two separate disease processes; mainly anemia and iron deficiency. Further, the severity of iron deficiency against anemia might differ by gender due to menstrual cycles in females.

Works of literature have examined iron deficiency and anemia as two separate entities independently and studied the impact of diabetes and prediabetes prevalence using HbA1c values. An extensive longitudinal study by China Health and Nutrition Survey utilised covariate and descriptive adjusted models to evaluate the relative risk of diabetes as well as prediabetes using only Fasting Blood Glucose (FBG), only hemoglobin A1c and FBG and hemoglobin A1c, in normal, anemia exclusively, and in IDA study population. The study population was 7308 adults aged eighteen to seventy-five years. The analysis showed that the prediabetes adjusted prevalence using HbA1c alone was twenty-two per cent for male with anemia alone, but thirteen per cent for male population with iron/hemoglobin at normal levels. Oppositely, the pre-estimated prediabetes widespread presence using only hemoglobin A1c came to be eight per cent for female population having only IDA, compared with thirteen percent for females with iron/hemoglobin at normal levels. Hence, such findings recommend, the prevalence of diabetes was under diagnosed in females with deficiency of iron using HbA1c alone and over diagnosed in males with anemia. Therefore, there is an increased chance of misdiagnosing the population to be diabetic using HbA1c, especially in region of highly prevalent deficiency of iron and anemia.⁷ A systematic review results also suggest HbA1c could be affected by iron deficiency and iron deficiency anemia with a false rise in HbA1c. Whereas, subjects without iron deficiency anemia may generate a lower HbA1c value. This further leads to chaos in the diagnosis of diabetes with HbA1c.⁸

Objectives :

To study the correlation between the severity of microcytic anemia and the derangements of HbA1c levels in an adult non diabetic population..

MATERIALS AND METHODS:

A cross sectional study was conducted at Mahadevappa Rampure Medical college , Kalaburgi during the period of August 2022-January 2024 on 300 patients admitted to in patient department of general medicine with anemia and evaluated for the same. Data was analysed using appropriate inferential statistics .

Study Design : Hospital based cross sectional study
Source Of Data : The study will be conducted on out patients and inpatients admitted in Basaveshwara Teaching and General Hospital attached to Mahadevappa Rampure Medical College Kalaburagi during the time period of August 2022-January 2024 were evaluated .

- Inclusion Criteria :**
- 1) Patients above the age of 18 years.
 - 2) Patients with anemia

- Exclusion Criteria :**
- 1) Cases of diabetes
 - 2) Pregnant women
 - 3) Patient with known hemoglobinopathies
 - 4) Patient with hemolytic anemias
 - 5) Patient with chronic renal failure
 - 6) Patient with chronic liver disease

Sample Size Estimation : 300 cases based on the hospital in patient admissions and appropriate age in accordance to our hospital statistics was selected.

Statistical Analysis : Statistical data was analyzed by IBMSPSS25.0 version software. Collected data were spread on excel sheet and prepared master chart. Through the master chart tables and graphs were constructed. For quantitative data analysis mean and standard deviations were calculated, t-test was applied for statistical significant. For qualitative data analysis chi-square test and Fisher exact probability tests were applied for statistical significance. If P-value was less than 0.05 considered as significant.

RESULTS:

Table No:1. Types of Anemia table

peripheral smear	Frequency	Percent
Dimorphic	25	8.3
Macrocytic	38	12.7
Microcytic Hypochromic	183	61.0
Normocytic Normochromic	54	18.0
Table Total	300	100.0

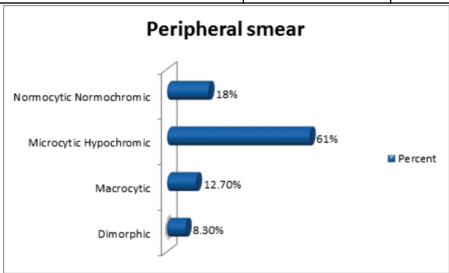


Figure 1:

Peripheral smear study revealed that 183 patients (61%) had microcytic hypochromic picture, dimorphic picture was present in 25 patients (8.3%) , 38 patients (12.7%) with macrocytic (megaloblastic) blood picture and 54 patients (18%) had Normocytic and normochromic blood picture.

Table No:2 Comparison of microcytic hypochromic Anemia with HbA1c

peripheral smear	HbA1c	SEVERITY OF ANEMIA			Total
		MILD	MODERATE	SEVERE	
Microcytic Hypochromic	<5.6	15	25	38	78
		19.2%	32.1%	48.7%	100.0%
	5.6-6.4	11	5	79	95

		11.6%	5.3%	83.2%	100.0%
	>6.4	1	3	6	10
		10.0%	30.0%	60.0%	100.0%
	Total	27	33	123	183
		14.8%	18.0%	67.2%	100.0%

*chi-square statistic = 27387, p-value = 0.001 (highly significant association)

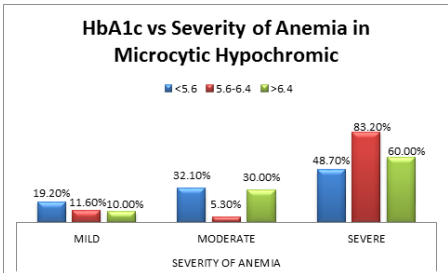


Figure 2:

The above table depicts severity of Microcytic hypochromic anemia alone with HbA1c and was found to have significant correlation (p value 0.001)

DISCUSSION

In the present study of 300 patients, the effect of severity of anemia on HbA1c was carried out. In our study, we observed patient age ranged from 18-86 years. In our study, further we attempted to categorize our 300 patients based on Peripheral smear it was found to have Microcytic hypochromic anemia in 183 patients (61%), dimorphic anemia in 25 patients (8.3%) and 38 patients (12.3%) had macrocytic anemia and 54 patients (18%) had Normocytic normochromic blood picture. We found comparison of HbA1c with severity of microcytic hypochromic anemia in our study population to be significant (p value 0.001) whereas, some authors have found a correlation of HbA1c with iron deficiency in moderate to moderately severe iron deficiency anemia. Majority of our patients were severely anemic, with most of them having microcytic hypochromic anemia. We observed in 12 patients the HbA1c $\geq 6.5\%$. Of these 12 patients 10 patients had microcytic hypochromic anemia(6 belong to severe anemia, 3 belonged to moderate anemia and 1 belonged to mild anemia group ,the observation was statistically significant).Remaining 2 one in each Dimorphic anemia and normocytic normochromic anemia.A study by Rajagopal L et al.⁹ and Basil A. Alzahrani et al.¹⁰ has found with increasing severity of iron deficiency anemia, a positive correlation with HbA1c levels (p value <0.05).They have found HbA1c levels increase as severity of anemia worsens. Comaparison of severity of Microcytic hypochromic anemia with HbA1c showed significant association, as severity of anemia increased in this group HbA1c also increased. A study by Nobuaki Sakamoto et al.¹¹ found different anemias influence HbA1c differently.When we compared other anemias like dimorphic anemia, macrocytic anemia and normocytic normochromic anemia individually with HbA1c we did not find any correlation in our present study. We feel it is worth taking different variables like age, sex, types of anemia, severity of anemia and its influence on HbA1c levels with a large sample size. This is because many times we do come across blood sugars being normal(fasting blood sugars and post prandial blood sugars), but the HbA1c is more than cut off levels. With a large sample size, it would be possible to overcome these biases as stated above.

CONCLUSION

The study was conducted to know whether or not HbA1c is influenced by various variables like age, sex, types of anemia or severity of anemia. In our study, based on HbA1c cut off values, 12 patients had an HbA1c $\geq 6.5\%$, but none had fasting or post prandial blood sugar abnormalities. We feel that it is worth while to take a large sample size and compare these confounding factors like age, sex, chronic illnesses, types of anemia and severity of anemia to see whether truly there is a relationship with these variables or not as often in clinical scenarios, we do come across situations when blood sugars are normal but HbA1c is abnormal.

So we feel, with a large sample size these issues have to be addressed, comparing HbA1c with different variables. We also feel that follow up with treatment of these anemic patients and its effect on HbA1c needs

to be studied.

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