Prevalence Of Anemia In Different Degrees Of Glycemic Control In Type Ii Diabetes Mellitus And Its Association With Crp

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ABSTRACT
Aims and objectives: The present study was conducted to study the prevalence of anemia in mild, moderate and severe degrees of hyperglycemia in type II Diabetes Mellitus, to study the Association of CRP with levels of HbA1c in type II Diabetes Mellitus, to study the Association of CRP with degree of Anemia and to compare the hematological parameters (Hb%, MCV, CRP) among the patients of type 2 diabetes mellitus with HbA1c levels below 6.5% and above 6.5%.
Results: Mild anemia was 57%, moderate anemia was 31% and severe anemia was 12%. Higher infection (>6) CRP has higher HbA1c (15) level and was statistically significant. Comparison of anemia with CRP and HBA1C were showed statistically significant results. Hematological parameters (Hb%, MCV, CRP) were statistically significant among the patients of type 2 diabetes mellitus with HbA1c levels. Lower HbA1c level (<6.5) was showed higher Hematological levels. (Hb%, MCV, CRP)
Conclusion: Prevalence of anemia was found significant with increasing severity of hyperglycemia and higher incidence of anemia is likely to occur in patients with poorly controlled diabetes. Our study indicates lower levels of CRP can be achieved with better glycemic control. Further good glycemic control in diabetes mellitus is associated with better hemoglobin levels and a lesser incidence of anemia
Keywords: HbA1c, anemai, diabetes mellitus

Introduction
Anaemia can be defined as a condition in which the number of red blood cells has decreased leading to reduced oxygen carrying capacity which is insufficient to meet the body's physiological needs.The World Health Organization (WHO) guidelines recommend investigation of anaemia when the Hb is less than 12g/dl in women and less than 13g/dl in men.[1]

Diabetes mellitus is a group of metabolic diseases characterized by elevated blood glucose levels (hyperglycemia) resulting from defects in insulin secretion, insulin action or both. Chronic hyperglycemia is associated with micro vascular and macro vascular complications that include neuropathy, retinopathy, coronary artery disease and stroke. Diabetes mellitus can be put into two groups:

8.3% of people around the world have diabetes mellitus, which affects about 382 million people.In Kuwait, 2.8% of expatriates and 2.3% of natives between the ages of 0 and 20 have type 1 diabetes. 25.4% of Asian expats between the ages of 30 and 60 have type 2 diabetes, which is higher than the rate among natives.[2]

Glycosylated Haemoglobin (HbA1c) is an effective tool to know the glycemic control in T2DM. HbA1c values gives an accurate estimate of average plasma glucose level from past 8 to 12 weeks. Now instead of glycemic control, HbA1c is used to detect diabetes and ADA has set guidelines to diagnose diabetes based on glycosylated haemoglobin values. Desirable value of HbA1c to be maintained suggesting a good glycemic control is 6.5%. Values of HbA1c of more than 6.5% is considered as poor glycemic control in T2DM.

Anemia is twice as likely to happen to people with type 2 diabetes as it is to people without diabetes. Presence of anaemia in diabetes, leads to progression of micro and macro vascular complications of diabetes mellitus. Anaemia can lead to falsely low HbA1c values which may result in under treatment of hyperglycemia, which in turn will further lead to the progression of micro and macro vascular complications of diabetes mellitus.

Systemic inflammation, blocking the release of erythropoietin, damage to the renal interstitium, severe symptomatic autonomic neuropathy causing efferent sympathetic denervation of the kidney and loss of appropriate erythropoietin, drugs, changes in iron metabolism, and high blood sugar are all thought to be reasons why diabetics get anaemia more quickly.[3]

Some studies have shown that diabetic patients with renal insufficiency are more likely to get anaemia than diabetics without renal insufficiency because their kidneys are less able to make erythropoietin. Also, diabetic neuropathy affects the hormone that makes red blood cells (RBCs), which leads to anaemia.[4] People with diabetes also have low levels of cyanocobalamin, folate, and iron in their bodies, which can lead to different types of anaemia. Metformin may make it harder to absorb cyanocobalamin, which can lead to anaemia from not getting enough vitamin B12. Anemia and type 2 diabetes have many of the same symptoms, like pale skin, chest pain, numbness or coldness in the extremities, shortness of breath, and headaches. Because of this, most people with type 2 diabetes don't know they have anaemia. So, it's important for diabetics to know if they have anaemia.

The liver is the organ responsible for producing C-reactive protein. As an acute phase reactant, C-reactive protein (CRP) will activate the complement classical route after tissue injury or inflammation has taken place. The level of circulating C-reactive protein, which is mostly controlled by the amount of interleukin-6 in the blood, is a predictor of coronary heart disease in healthy persons. A CRP test with high sensitivity may detect a lower concentration of the protein. It is a quantitative test of CRP in plasma, and it provides a novel way for identifying persons at high risk who have ruptured plaque.[5]

In diabetic patients, there will be development of macrovascular changes, when there is a poor control of glycemic level. CRP is a significant risk factor for the development of cardiovascular diasease. Increase levels of c-reactive protein ia also linked in increase risk for development of diabetes in later stages. Hence the study has been taken up to know the relation between the Hba1c and CRP in type 2 diabetes mellitus.

Material and methods

It was a cross- sectional study and was include all patients consulting Mahatma Gandhi Hospital - both OPD and IPD.

This study was conducted from March 2021 to September 2022 in Mahatma Gandhi Medical College and Hospital, Jaipur.

The inclusion criteria comprised of all patients consulting MGMCH with type II Diabetes Mellitus. (HbA1c > 6.5%).

Methodology:

- Present study was Hospital based Cross-sectional study.
- Data was collected using a pretested proforma meeting the objectives of the study.
- Detailed history and necessary investigations were undertaken. The purpose of the study was explained to the patient and informed consent obtained.
- Patients were selected for study who satisfied all inclusion and exclusion criteria. Relevant history including symptoms and signs at presentation, past medical history, drug history and examination findings are to be noted.
- Anemia, diabetes mellitus type II, degree of glycemic control, CRP, Hb, MCV, PBF, HbA1c, RBS was noted from the investigations.

Type: Hospital based Cross-sectional study.

Study population:

All patients diagnosed with diabetes mellitus type II (HbA1c > 6.5%) presenting to Department of Medicine, Mahatma Gandhi Hospital, Jaipur, from March 2021 to September 2022, was included in the study, patients of both genders were studied.

Place of Study: Mahatma Gandhi Medical College and Hospital, Jaipur.

Duration of Study: March 2021 to September 2022.

Inclusion Criteria:

- All patients giving informed and written consent.
- All patients diagnosed with diabetes mellitus type II (HbA1c > 6.5%) presenting to Department of Medicine, Mahatma Gandhi Hospital, Jaipur, from March 2021 to September 2022, will be included in the study.
- Patients of both genders were studied.

Exclusion Criteria:

- Patients age <18 years / Patients with type 1 diabetes mellitus.
- Patients not willing to give consent or not willing to participate.
- Patients with history of alcohol consumption for any duration of time was excluded.
- Steroid induced Diabetes, was excluded from the study
- Patients who are on drugs for AnemiaOr drugs causing anemia.
- Pregnancy
- Association with malignancy.

The approval from the Institutional and ethical committee was taken before undertaking the study.

Written and inform consent was taken from all participants before enrolment into the study.

SAMPLE SIZE:

·   All patients diagnosed with diabetes mellitus type II (HbA1c > 6.5%) presenting to Department of Medicine, Mahatma Gandhi Hospital, Jaipur , from March 2021 to September 2022, was included in the study.

IV. TYPE OF PATIENTS:

1.   All patients diagnosed with diabetes mellitus type II (HbA1c > 6.5%) presenting to Department of Medicine, Mahatma Gandhi Hospital, Jaipur, from March 2021 to September 2022, was included in the study.

2.   Vulnerable / special group subjects which include:
- elderly
- illiterate
- handicapped
- seriously ill
- economically & socially backward

Statistical analysis

The data was coded and entered into Microsoft Excel spreadsheet. Analysis was done using SPSS version 20 (IBM SPSS Statistics Inc., Chicago, Illinois, USA) Windows software program. Descriptive statistics included computation of percentages, means and standard deviations. The data were checked for normality before statistical analysis using Kolmogorov Simonov test. The unpaired t test (for quantitative data to compare two independent observations) and ANOVA test (for quantitative data to compare two and more than two observations) were applied. Level of significance was set at P≤0.05. **OBSERVATION AND RESULTS:**

The frequency of diabetes was highest among patients belonging to more than > 70 years (29%) The majority of patients were male (71%). The majority of patients were having the condition since 1-5 years (56%) followed by 5-10 (37%) and 10-15 (7%) duration of DM

The majority of patients had RBS in 120-200 (57%) followed by 200-250 (31%) and 250-300 (12%).

Mild anemia was 57%, moderate anemia was 31% and severe anemia was 12%

Table 1: Association of CRP with levels of HbA1c

	N	Mean	Std. Deviation	P value
<6 CRP	5	8.12	2.21	0.001 (S)
>6 CRP	95	15.00	.00	

Higher infection (>6) CRP has higher HbA1c (15) level and was statistically significant.

Table 2: Comparison of anemia and HbA1C:

	N	Mean	Std. Deviation	P value
Mild	57	8.43	2.46	0.01 (S)
Moderate	31	8.04	2.506	
Severe	12	7.41	1.81	

Mild anemia had higher HBA1C (8.43), moderate and severe anemia have low HBA1C i.e. 8.04 and 7.41. Comparison of anemia and HBA1C was showed statistically significant results.

Table 3: Comparison of anemia and CRP

	N	Mean	Std. Deviation	P value
Mild	57	78.53	107.43	0.001 (S)
Moderate	31	52.05	72.79	
Severe	12	38.98	74.89	

Mild anemia had higher CRP (78.53), moderate and severe anemia have low CRP i.e. 52.05 and 38.98. comparison of anemia and CRP was showed statistically significant results.

Table 4: Hematological parameters (Hb%, MCV, CRP) among the patients of type 2 diabetes mellitus with HbA1c levels

		N	Mean	Std. Deviation	P value
HB	<6.5 HbA1c	13	8.66	0.19	0.01 (S)
	>6.5 HbA1c	87	8.07	0.58	
MCV	<6.5 HbA1c	13	96.24	4.16	0.001 (S)
	>6.5 HbA1c	87	88.98	5.05	
CRP	<6.5 HbA1c	13	321.53	91.802	0.001 (S)
	>6.5 HbA1c	87	46.91	70.26	

Hematological parameters (Hb% , MCV, CRP) were statistically significant among the patients of type 2 diabetes mellitus with HbA1c levels
Lower HbA1c level (<6.5) was showed higher Hematological levels. (Hb%, MCV, CRP)

Discussion
The frequency of diabetes was highest among patients belonging to more than > 70 years (29%) In a study by Aldallal, S et al, the average age of patients with anemia was found to be 60.69 ± 0.198 years.[6] In a study by Barbieri J et al, the study population had an average age of 60,9 ± 8,9 years.[7] Choi et al (2004) have also shown that the prevalence of anemia increases with the increasing age. The possible reasons for this increased prevalence with age might be due to deficiencies of vitamins such as folate, cyanocobalamin or bone marrow disorders and higher number of comorbidities.[8]
The majority of patients were male (71%). However, in study by Aldallal, S et al, There is a statistically significant relation between prevalence of anemia and gender, i.e. the prevalence of anemia is significantly greater in diabetic females than diabetic males (P < 0.05). This finding is consistent with the findings of Alsayegh et al (2017) which reported prevalence as 35.8% vs. 21.3% in diabetic females versus diabetic males.[9] The possible reason for higher prevalence of anemia in females might be due to poor nutrition, less importance given to their own health due to lack of empowerment. This can be improved by educational interventions such as health awareness programs in the rural areas, provision of iron rich food, prescription of vitamin and iron supplements and knowledge of the diabetic complications[10]
The majority of patients were having the condition since 1-5 years (56%). In a study by Barbieri J etal,[4] median of disease diagnosis time of 5,0 years (0,5–40,0 years). The prevalence of anemia (hb) in mild, moderate and severe degrees of hyperglycemia was statistically significant. Similarly in a study by Aldallal S et al.[3] The prevalence of anemia is significantly greater in poorly controlled diabetics than those with glycemic status under control (P < 0.05). In patients with poorly controlled diabetes, the erythrocyte precursors of the bone marrow might be prone to prolonged direct toxicity to glucose toxicity or the mature erythrocytes can be affected by oxidative stress leading to disturbances in the erythrocyte function.
In the present study it was noted that the majority of patients were CRP > 6 (95%). Association of CRP with levels of HbA1c was >6 . It is observed that the diabetic and anemic patients had high levels of C-reactive protein and ferritin ultra-sensible; however, these diabetic and anemic patients had low iron contents, showing that ferritin increases were associated with chronic inflammatory process present in diabetes. It was observed if there is decreased values of hemoglobin, hematocrit, and red blood cells in anemic patients, it can be associated with a normocytic normochromic anemia, characteristic of an anemia of chronic disease (ACD). ACD is a light-to-moderate anemia shortening the survival of red blood cells (about 80 days instead of 120 days normal). This phenomenon is attributed to hyperactivity

state mononuclear phagocyte system, triggered by the infectious, inflammatory, or neoplastic process, leading to the early removal of circulating red blood cells. Inadequate bone marrow response observed is due basically to inappropriately low Secretion of Erythropoietin (EPO), decreased bone marrow response to EPO, and decreased erythropoiesis consequent to lower supply of iron to the bone marrow. [11, 12]

In the present study it was seen that the hematological parameters (Hb%, MCV, CRP) were statistically significant among the patients of type 2 diabetes mellitus with HbA1c levels. In a study by Prabhu S et al Anaemia was seen in 71% of patients with poor glycaemic control as compared to ones with good glycaemic control, in which only 39% of patients had anaemia. Mean haemoglobin was significantly lower in group with poor glycaemic control as compared to group with good glycaemic control. It was noted that There was a statistically significant negative correlation between Haemoglobin percentage and HbA1c.[13]

Several studies have reported factors that increase the risk of anaemia, which include damage to renal interstitium due to chronic hyperglycaemia and consequent formation of advanced glycation end products by increased reactive oxygen species, and systemic inflammation as well as reduced androgen levels induced by diabetes as shown by Adejumo et al,[35] and Fetch et al.[14]

Conclusion

Anemia is a common finding in Type 2 Diabetes Mellitus patients when compared with the general population. Prevalence of anemia was found significant with increasing severity of hyperglycemia and higher incidence of anemia is likely to occur in patients with poorly controlled diabetes. Higher degrees of CRP levels in diabetics indicates risk of development of macro and microvascular complications of diabetes especially increases cardiovascular disease burden. Our study indicates lower levels of CRP can be achieved with better glycemic control. Further good glycemic control in diabetes mellitus is associated with better hemoglobin levels and a lesser incidence of anemia.

Hence in diabetic patients, it would be desirable to evaluate the hemoglobin levels often, even when the renal parameters are within the normal limits for a better quality of life.

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