

## Original Research Article

# Study of effect of glycemic control on haemoglobin levels in patients with type 2 diabetes mellitus

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### ABSTRACT

**Background:** Anemia is more frequent and severe in diabetics compared to non-diabetic patients. Chronic anemia results in tissue hypoxia, which is known to play a key role in diabetes-associated organ damage. Hence it is important to diagnose and correct anemia in diabetic patients. This study was done to elucidate the effect of glycemic control on haemoglobin levels in patients with type 2 Diabetes mellitus.

**Methods:** The present study is an observational, cross sectional study conducted between November 2017 to May 2019 carried out in hospitals attached to Bangalore Medical college and Research Institute. A sample of 60 patients with Diabetes mellitus were included, out of which 28 were female and 32 were male patients.

**Results:** Study was conducted on 60 patients, the age distribution was between 29yrs to 88yrs with mean age was  $56 \pm 11$  yrs. Out of 60 patients 23 patients had anemia. There was slight positive correlation between haemoglobin percentage and HbA1c. But this was not statistically significant.

**Conclusions:** The study concludes that Glycemic control was not found to influence the Haemoglobin levels in patients with Type 2 diabetes mellitus in a significant manner. In subjects with anemia, multiple other issues need to be addressed for improvement in haematocrit value and prevention of complications of diabetes apart from glycemic control.

**Keywords:** Anemia, Glycemic control, Type 2 diabetes mellitus

### INTRODUCTION

The prevalence of Type II Diabetes Mellitus worldwide is on a rise and has reached epidemic proportions in many countries. The total number of adult patients suffering from Type II Diabetes Mellitus were 366 million in 2011.<sup>1</sup>

Globally an estimated 415 million adults were living with diabetes in 2015, and it is on surge to reach to 552 million by 2030.<sup>2,3</sup> Anemia is a condition in which the number of red blood cells or their oxygen-carrying capacity is insufficient to meet physiologic needs, which vary by age, sex, altitude, smoking, and pregnancy

status.<sup>4</sup> Anemia is more frequent and severe in diabetics compared to non-diabetic patients.<sup>5</sup> The prevalence of anemia ranges from 13% to 45% in patients with diabetes mellitus, depending upon the ethnicity and diagnostic criteria used and it is especially high when associated with renal impairment.<sup>6,7</sup>

There are number of possible mechanisms for the development of anemia in diabetes patients. Failure of the kidney to increase erythropoietin (Epo) release in response to a decreasing hemoglobin (Hb) level appears to be the key contributor to the development of anemia.<sup>7</sup> However, numerous hypotheses have been proposed including efferent denervation of the kidney due to

autonomic neuropathy leading to reduced erythropoietin production, chronic renal hypoxia, tubulointerstitial disease, altered iron metabolism, drugs, hyperglycaemia and systemic inflammation.<sup>8</sup>

Chronic anemia results in tissue hypoxia, which is known to play a key role in diabetes-associated organ damage and it contributes to the progression of both microvascular and macrovascular complications in patients with diabetes mellitus.<sup>6</sup>

Hence it is important to diagnose and correct anemia in diabetic patients. Glycemic control is considered as the main therapeutic goal for prevention of organ damage and other complications of diabetes.

This study was done to elucidate the effect of glycemic control on haemoglobin levels in patients with type 2 Diabetes mellitus.

Aim of the study was to elucidate the effect of glycemic control on haemoglobin levels in patients with type 2 Diabetes mellitus

## METHODS

It's a Cross-sectional study conducted in the Department of Internal Medicine, Bangalore Medical college and Research Institute.

The cross sectional study included 60 patients diagnosed to have Type 2 diabetes mellitus as per ADA criteria. Study was conducted between November 2017 to May 2019. Patients with type 2 diabetes mellitus were screened for the presence of anemia by clinical means and use of basic laboratory tests like Complete blood counts. Those with anemia were worked up further with laboratory tests as required to know the type of anemia and cause.

For the purpose of the study the following operational standard criteria/definitions were used:

- Anemia defined as hemoglobin values <13.0 g/dl for men and <12.0 g/dl for women.<sup>5</sup>
- Type 2 Diabetes mellitus as defined by ADA<sup>9</sup>
- Normal renal function<sup>10</sup>
- Serum creatinine in female 0.5-0.9mg/dl and in males 0.6-1.2 mg/dl.
- CKD as per formula (Cockcroft-Gault equation)<sup>11</sup>
- CrCl (ml/min) = (140-age(years)x weight(kg)x [0.85 if female])/72x plasma creatinine(mg/dl).
- Previously worked up or proven cases of CKD.

## Inclusion criteria

- Patients aged ≥18 yrs.
- Patients willing to give informed written consent.
- Patients with Type 2 diabetes mellitus as per ADA criteria<sup>9</sup>

## Exclusion criteria

- Patients on any prolonged therapy with drugs known to cause bone marrow suppression.
- Patients with ongoing or with previous history of GI blood loss.
- Patients with known bleeding disorder.
- Patients with known Haemolytic disorder.
- Patients with history of blood transfusion in the past 3 months.
- Patients with history of fever and any documented intercurrent infections in the past 3 months.
- Pregnant females
- Patients on EPO or any Iron or Vitamin B supplements.

## Statistical analysis

Data was entered in Microsoft excel and was exported into SPSS version 21.0. Pearson co-relation coefficient was used to assess the relationship between HbA1C levels and Haemoglobin percentage. Also, Student 't' test was used to assess the same in 2 groups one with Chronic kidney disease and other without.

## RESULTS

Total number of study subjects were 60. Mean age of the study population was 56 years with 28 females and 32 males. Out of these, 23 subjects had chronic kidney disease and 37 had normal renal function.

A total of 23(38.3%) subjects had anemia. Out of whom 12 had Iron deficiency anemia and 11 had anemia of chronic disease. The mean HbA1c in subjects with anemia was 8.5±2.8 while it was 9.6±2.6 in those without anemia. Out of the 23 subjects with anemia 16 belonged to the CKD group.

Overall there was found to be a slight positive co-relation between Haemoglobin percentage and HbA1C levels (r=+0.177). But this was not statistically significant (p>0.05) (Figure 1).

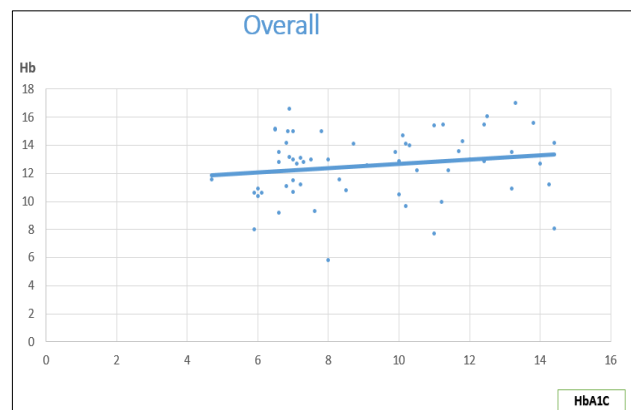
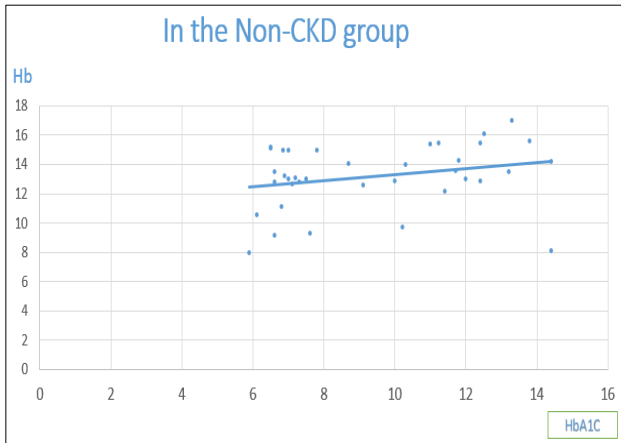


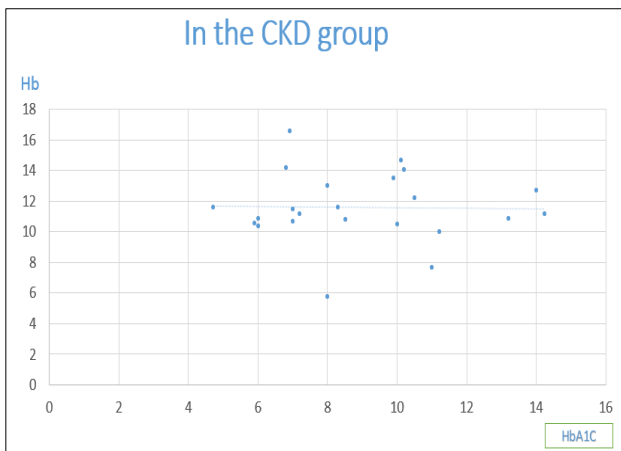
Figure 1: Scatter plot of HbA1C and Hb of all subjects.

In the non CKD group, there was slight positive correlation between the parameters( $r=+0.263$ ). However, it was statistically insignificant( $p>0.05$ ) (Figure 2).

In the group with CKD there was no co-relation between the parameters (Figure 3). The below figures show the scatter plot with haemoglobin of the population in Y axis as continuous variable and HbA1c of the population in X axis as continuous variable.



**Figure 2: Scatter plot of HbA1C and Hb of subjects with normal renal function.**



**Figure 3: Scatter plot of HbA1C and Hb of subjects with abnormal renal function.**

## DISCUSSION

Anemia in patients with diabetes mellitus might contribute to pathogenesis and progression of morbid conditions related to cardiovascular disease and aggravate diabetic nephropathy and retinopathy

It was found that Anemia occurred in 23 (38.3%) of the 60 diabetic subjects. In the non CKD group 7 (18.91%) of study subjects had anemia. In comparison to the study by KJ Craig et al, 16.12% of the study subjects with normal renal function had anemia.<sup>8</sup>

Anemia was found to occur at an increasing percentage in subjects with CKD than those without as per study by Loutradis C et al.<sup>12</sup>

Diabetic patients with anemia exhibit increased expression of pro-inflammatory cytokines as compared to diabetic patients only. In an anemic patient increase in IL-6 production, as well as B cell activity, was confirmed which affirms the association between IL-6 and antierythropoietic action.<sup>13</sup> Moreover, the diabetic and anemic patients had high levels of C-reactive protein and ferritin; however, these diabetic and anemic patients had low iron contents, showing that ferritin increases were associated with chronic inflammatory process present in diabetes.<sup>14</sup>

Inadequate bone marrow response is due 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.

Advanced glycation end products are a diverse group of end-product molecules that are formed as a result of non-enzymatic, covalent binding of glucose residues to the free amino groups of proteins, lipids, and nucleic acids. Increased production of advanced glycation end products has been implicated in the development of microangiopathy in diabetes mellitus. Increased accumulation of these products can promote non-enzymatic glycation of red-blood-cell-membrane glycoproteins and haemoglobin, which leads to impaired deformability of red blood cells in diabetes mellitus. These molecules might also increase the level of oxidative stress in diabetes mellitus by stimulating increased production of free oxygen radicals.<sup>15</sup>

Reactive oxygen species combine with nitric oxide in the endothelium to form reactive oxygen intermediates, such as peroxynitrite, which reduce the total bioavailability of nitric oxide. This change might lead to an increase in vascular tone and increased oxygen expenditure. A reduction in the renal oxygen concentration, along with impaired bioavailability of nitric oxide, might increase damage caused by free radicals in the tubular interstitium. These alterations generate a hypoxic milieu in the tubular interstitium, which inhibits the production of erythropoietin and hence may contribute to lower haematocrit in diabetic subjects.<sup>16</sup>

This study was conducted to look for any correlation between glycemic control and haemoglobin levels but, in our study, there was no statistically significant correlation between glycemic control as measured by HbA1c levels and hemoglobin levels. This was Similar to the study by Rathod GB et al, which concluded that Hb levels. The study conducted by Kojima K also showed that long standing poorly controlled diabetes was associated with anemia.<sup>17,18</sup> In contrast a study by Ji Cheol Bae in Korea revealed that Participants with lower hemoglobin had

significantly higher HbA1c at a given fasting glucose level in both men and women.<sup>19</sup>

An emphasis on regular screening for anemia in diabetics along with that of other diabetes-related complications, might help to delay the progression of micro and macrovascular complication in these patients.

But in the diabetic subjects it was found that control of blood sugars did not influence the haemoglobin levels or Haematocrit in both groups; one with normal renal function and the other with chronic kidney disease.

Small sample size was the only limitation of this study.

## CONCLUSION

Glycemic control was not found to influence the Haemoglobin levels in patients with Type 2 diabetes mellitus in a significant manner. The same was true in both groups; one with normal renal function and the other with chronic kidney disease.

In subjects with anemia, multiple other issues need to be addressed for improvement in haematocrit value and prevention of complications of diabetes apart from glycemic control.

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