

# Anemia in patients with type II diabetes mellitus with and without diabetic retinopathy

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## Abstract

**Background:** Anemia has been recognized as a chronic complication of diabetes mellitus. Oxidative stress created by chronic hyperglycemia leads to RBC damage and is involved in the pathogenesis of anemia. Anemia induced hypoxia leads to vaso-proliferation in the retina and in turn to development and deterioration of diabetic retinopathy.

**Objective:** The aim of the study was to find out whether anemia is prevalent in cases of type II diabetes mellitus (DM). To find out whether there exist a relationship between anemia and diabetic retinopathy.

**Materials and Methods:** The study was done on total 135 subjects. The control group (Group-A) included 45 age and sex matched healthy subjects. The case group was divided into 2 groups, 45 subjects diagnosed with type II DM without diabetic retinopathy (Group-B) and 45 subjects of type II DM with diabetic retinopathy (Group-C). The mean hemoglobin level, total red blood cell (RBC) count and packed cell volume (PCV) were compared in 2 groups.

**Result:** The mean hemoglobin level in Group-A, B, and C were 14.23±0.83 gm/dl, 12.22±0.11 gm/dl, and 10.44±0.23 gm/dl, respectively ( $p<0.001$ ). The mean PCV in Group-A, B, and C were 44.21±0.34%, 41.11±1.22%, and 37.86±1.12%, respectively ( $p<0.001$ ). The mean RBC count in Group-A was 5.9 ±0.11 million/mm<sup>3</sup>, Group-B was 5.4±0.83 million/mm<sup>3</sup>, and in the Group-C was 4.6±1.3 million/mm<sup>3</sup>. The mean hemoglobin level, RBC count, and PCV were found to be significantly lower in subjects with diabetes as compared to non-diabetic subjects. The values were further statistically significantly lower in diabetic subjects with retinopathy.

**Conclusion:** We conclude that unrecognized anemia exists in diabetic subjects. The severity of anemia is greater in subjects with retinopathy. It is suggested that the hematological parameters should be evaluated and treated periodically in diabetic patients to reduce the load, of ocular morbidity due to retinopathy.

**KEY WORDS:** Anemia, Diabetes, Diabetic retinopathy, Type II diabetes mellitus

## Introduction

The changing lifestyle and dietary habits have increased the incidence of diabetes multifold times. The increasing incidence of diabetes mellitus is a major public health concern.

Improvements in healthcare and specific treatments have increased the life expectancy and survival rate of the diabetic patients. On the other hand increased life span is associated with higher prevalence of diabetes mellitus related complications and in turn poor life quality of patients.<sup>[1]</sup> Retinopathy, nephropathy, and neuropathy are various microangiopathic complications associated with diabetes. Diabetes is a well-established cause of diminution of vision and retinopathy is the commonest etiology for it. Retinopathy is a well-known complication of diabetes mellitus.

Anemia is a long-term complication of diabetes mellitus. The prevalence of anemia in diabetic patients is reported as 14–48%.<sup>[2,3]</sup> The etiology and pathogenesis of anemia in diabetes mellitus (DM) patients are multifactorial including inflammation,

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**Table 1:** Patients characteristics of 3 groups

	Non-diabetic (Group-A)	Diabetic without retinopathy (Group-B)	Diabetic with retinopathy (Group-C)
Total subjects	45	45	45
Male subjects	22	24	20
Female subjects	23	21	25
Mean age (years)	63.1±0.12	62.3 ±0.98	65.78±0.56
Mean duration of disease (years)	NA	7.8±0.45	14.3±0.6
Mean BMI (kg/m <sup>2</sup> )	23.78±1.11	24.12±1.3	24.78±1.42
Mean body weight (kg)	63.67±1.2	65.69±1.6	67.89±1.45

nutritional deficiency, drugs, and nephropathy. Hyperglycemia in diabetes leads to increased expression of inflammatory markers like IL-6 and TNF- $\alpha$ . These cytokines have anti-erythropoietic effect leading to lowered hematocrit values. The longer the duration of the disease and poorer the glycemic control more severe is the inflammatory response.<sup>[4,5,6]</sup>

Anemia leads to development, progression, and proliferation of diabetic retinopathy and other comorbidities associated with diabetes mellitus.<sup>[7]</sup> The severity of retinopathy is inversely related to the hematocrit values.<sup>[1]</sup> Subjects with hemoglobin levels <12 gm% are having double risk of having retinopathy as compared to subjects with a normal value of hemoglobin. They are also at 5% additional increased risk of developing proliferative retinopathy.<sup>[8]</sup> Anemia usually remains unrecognized and untreated in the diabetic population. Treatment of anemia apart from improving exercise tolerance also decreases the rate of micro and macrovascular complications.<sup>[7,9,10]</sup> Early recognition and treatment of anemia in the diabetic population decreases morbidity and mortality and leads to better life quality of diabetic subjects. So, we conducted this study to find out whether anemia is prevalent in the diabetic population. Whether there exists an association between anemia and diabetic retinopathy (DR).

## Materials and Methods

The current case-control study was conducted in the Department of Physiology in collaboration with Department of Ophthalmology. Institutional Research Committee and Institutional Ethics Committee clearance was procured. Informed consent was obtained from all the participants. The study was done on total 135 subjects. The control group (Group-A) included 45 age, sex, and body built matched healthy subjects. The case group included 90 diabetic subjects. They were further subdivided into 2 groups: Group-B consisting of 45 subjects of type II DM without diabetic retinopathy and Group-C consisting of 45 subjects of type II DM with diabetic retinopathy. The patients with a history of any cause of anemia like acute or chronic blood loss, malignancy or under treatment for anemia were excluded from the study. Basic data such as age, duration of disease, history of hyperlipidemia, blood pressure were recorded in the study performed. We have used criteria according to the World Health

**Table 2:** Prevalence of anemia in 3 groups

	No. of subjects non-anemic	No. of subjects anemic	% anemia
Group-A	37	08	17.8%
Group-B	33	12	26.67%
Group-C	28	17	37.78%

Organization (WHO) definition, i.e. hemoglobin level <13 gm/dl in men and <12 gm/dl in women to define anemia.<sup>[11]</sup> All patients underwent an ophthalmologic examination of the anterior segment under slit lamp and retina examination by an indirect ophthalmoscope. The patients were investigated for hemoglobin level, total red blood cells (RBC) count and packed cell volume (PCV).

## Results

Out of total 45 subjects in the control group, there were 22 males and 23 females. Among the diabetic subjects, there were 44 males and 46 females. The mean age of the non-diabetic subjects was 63.1±0.12 years and mean age of diabetic subjects without retinopathy was 62.3±0.98 years and with retinopathy was 65.78 ± 0.56 years. The mean duration of disease of the subjects without retinopathy was 7.8±0.45 years and the mean duration of disease of subjects with retinopathy was 14.3±0.6 years. The mean anthropometric parameters were comparable in both case and control group (Table 1). The incidence of anemia was higher in Group-B and C as compared to Group-A (Table 2). The mean hemoglobin level, RBC count, and PCV of the 3 groups are described in Table 3.

## Discussion

In our study, the incidence of anemia was higher in the diabetic group (26.67%) as compared to non-diabetic group (17.8%). The incidence was further higher in diabetics with retinopathy (37.78%). Thomas *et al.* in their study on anemia in diabetic population found anemia prevalent in the diabetic population. They found 15% females and 13% males with

**Table 3:** Mean hemoglobin, RBC count, and PCV in 3 groups

	RBC count (million/mm <sup>3</sup> ) (Mean ± SD)	Hemoglobin (gm/dl) (Mean±SD)	PCV% (Mean ± SD)
Group-A	5.9 ±0.11	14.23 ±0.83	44.21±0.34
Group-B	5.4±0.83	12.22±0.11	41.11±1.22
Group-C	4.6 ±1.3	10.44±0.23	37.86±1.12
P value	<0.001*	<0.001*	<0.001*

Statistical comparison done using ANOVA test  $p < 0.05^*$  considered significant

type I diabetes to have anemia.<sup>[10]</sup> Janet B et al. in their study found that prompt treatment of anemia leads to decreased morbidity and mortality in diabetic subjects. The authors also found anemia as a cause associated with disease progression and development of comorbidities.<sup>[12]</sup> Other investigators have documented increased pro-inflammatory cytokines like C-reactive proteins in diabetic patients with anemia. Obesity is responsible for most of the cases for the acceleration of inflammation. TNF- $\alpha$  and IL-6 are the pro-inflammatory adipokines that are correlated both with increased body weight and insulin resistance.<sup>[13-15]</sup>

We found significantly lower mean hemoglobin level, RBC count, and PCV in the diabetic individuals (Group-B) as compared to non-diabetics (Group-A) ( $p < 0.001$ ). Further lower values of hematocrit, hemoglobin, and RBC count were observed in diabetic patients with retinopathy. Chronic hyperglycemia in DM is involved in the pathogenesis of anemia by means of creating abnormalities in RBCs due to oxidative stress, autonomic neuropathy, and renal sympathetic denervation. Erythropoietin deficiency, nephropathy, chronic inflammation, anti-DM drug, and low testosterone levels are other suggested causes of anemia in diabetes. Anemia induced hypoxia leads to Vasoproliferation in retina and progression of diabetic retinopathy. Qiao et al. in his study found that the DM patients with hemoglobin level lower than 12 mg/dl were 2 times more likely to develop DR.<sup>[8]</sup> Diabetes is a leading cause of chronic kidney disease and anemia is common among diabetics with kidney disease.<sup>[16]</sup> Renal disease in diabetes is progressive and anemia plays a role in the progression of kidney disease in the diabetics possibly due to renal ischemia caused by reduced oxygen delivery.<sup>[17,18]</sup> Bahar et al. found lower hemoglobin level and a higher incidence of anemia in diabetic patients with retinopathy.<sup>[1]</sup> Davis et al. and Conway et al. reported a direct relationship between hemoglobin level and the development and deterioration of proliferative diabetic retinopathy. Anemia is an important accompanist of diabetes mellitus and has been reported by multiple researchers in the past.<sup>[19-21]</sup> Ranil PK et al. in their study concluded that every 10th individual in a population of diabetes mellitus could be anemic.<sup>[22]</sup> The findings of our study were in accordance with the previous investigators.

Anemia in diabetic subjects leads to development and progression of cardiovascular disease and aggravation of other comorbidities like retinopathy and nephropathy. Regular

screening and timely intervention for anemia in diabetic individuals may be helpful in delaying the progression of vascular complications in diabetic subjects.<sup>[23]</sup> Singh et al. in their case report noted spontaneous closure of microaneurysms on the treatment of anemia in type I diabetes mellitus with background diabetic retinopathy.<sup>[24]</sup> Shorb et al. also reported a rapid progression to proliferative retinopathy in patients with iron deficiency anemia.<sup>[25]</sup> Friedman et al. reported their experience of resolution of macular hard exudates in patients treated with erythropoietin for anemia.<sup>[26]</sup> This consensus statement released after the meeting of Indian Diabetologists and Nephrologists on the treatment of anemia in patients with diabetic kidney disease recommended early identification and treatment of anemia to improve patient outcome with diabetic kidney disease. The patient usually requires treatment in form of erythropoiesis-stimulating agents (ESA) along with parenteral iron therapy.<sup>[27-29]</sup>

Similar to the previous investigators, we noted a higher incidence of anemia in the diabetic population as compared to the non-diabetics. Increased incidence and severity of anemia were noted in diabetic subjects with retinopathy. In conclusion, we would like to say that unrecognized anemia exists in diabetic subjects. The severity of anemia is increased in subjects having retinopathy. We suggest that the hematological parameters should be evaluated periodically. Identification and treatment of anemia would make a positive impact in preventing micro vascular complications such as retinopathy. Our sample size was small further mass level studies can be done on larger sample size. In our study, we have not evaluated the beneficial effect of treatment of anemia in the diabetic population. Study need to be done to elucidate the effect of treatment of anemia on the progression of diabetic comorbidities in type I as well as type II diabetes mellitus.

## Conclusion

We conclude that unrecognized anemia exists in diabetic subjects. The severity of anemia is greater in subjects with retinopathy. It is suggested that the hematological parameters should be evaluated and treated periodically in diabetic patients to reduce the load, of ocular morbidity due to retinopathy.

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- List of abbreviations:  
DM diabetes mellitus  
RBC red blood cell  
PCV packed cell volume  
Gm/dl gram /deciliter  
mm<sup>3</sup> cubic millimeter  
DR diabetic retinopathy  
WHO World Health Organization  
TNF tumor necrosis factor  
IL interleukins  
ESA erythropoiesis stimulating agent

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