Original Research Article

A cross-sectional study on anemia in diabetic patients as a risk factor for development of diabetic retinopathy

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Abstract

Background: Anemia is a serious public health problem as harmful as the epidemic of infectious disease, especially in developing countries like India. With both the problems occurring together in an individual, the development of complications due to diabetes is severe and much earlier.
Aim of the study: To estimate the prevalence of anemia in persons with type 2 diabetes mellitus and its role as a risk factor for the presence and the severity of diabetic retinopathy, in a population-based study.
Materials and methods: This was a cross-sectional study conducted in about 200 diabetic inpatients in Government Royapettah Hospital, Chennai over a period of 6 months to study the correlation between low hemoglobin and development of diabetic retinopathy.
Results: Fundus examination in anemic group showed normal interpretation in 49 patients, NPDR in 40 patients and 11 had PDR. In the non-anemic group, 68 patients had normal fundus examination, 26 had NPDR and 6 had PDR. The number of patients having diabetic retinopathy was greater in the anemic group than in the non-anemic group.
Conclusion: Thus this study showed a positive correlation between anemia and earlier development of diabetic retinopathy. Hence, treatment of anemia must also be considered as a routine entity at the time of diagnosis of diabetes mellitus.

Key words

Anemia, Diabetes Mellitus, Diabetic Retinopathy, Vascular Complications.

Introduction

Anemia is considered as a public health problem because it affects the majority of its population, especially in the economically productive age group [1]. The sedentary lifestyle along with genetic factors and other determinants has made diabetes mellitus as one of the common problems in India. When anemia is accompanied by diabetes mellitus, the development of complications is accelerated and more severe [2]. Anemia decreases the amount of oxygen delivery to tissues and creates some amount of background damage to the organs. With the diabetes mellitus and with its increasing duration, the already damaged retinal tissue with the effect of anemia is prone to excessive damage as a result of vascular changes in diabetes mellitus [3]. Various factors are associated with the development and severity of DR including high blood pressure, proteinuria, duration of DM, administration of insulin and renal disease. Anemia is suggested as another long term complication of DM and defined as hemoglobin level less than 13g/dl in men and 12g/dl in women. The prevalence of anemia in DM patients is reported as 14-48% [4]. Anemia is supposed to be an independent risk factor for the development and progression of cardiovascular complications and heart failure chronic renal disease and DR in DM patients. In DM patients, with any amount of glomerular filtration compared to non-DM patients with the same renal function, anemia is more prevalent and more severe [5]. High glycosylated hemoglobin, diabetic neuropathy, low serum albumin, younger age and also low hematocrit were reported as risk factors for the development of a more severe form of DR (high-risk proliferative DR) and visual loss [6]. Macular edema (ME) may appear at any stage of DR and is the main cause of central visual loss in diabetic patients. It is defined as an increase in tissue fluid, which causes a thickening of the retina and secondarily causes structural and functional alterations with important clinical consequences [7].

Materials and methods

This cross-sectional study was conducted in Government Royapettah hospital, Chennai for duration of 6 months from April 2018 to September 2018. A proper ethical approval was obtained from the Institutional Ethical Committee. The study was conducted after getting written informed consent from all the subjects involved in this study.

Inclusion criteria

Diabetics in this study were defined by the American Diabetes Association as either

- Diagnosis by a physician before the survey, or
- Fasting plasma glucose (FBS) of >126 mg/dL or
- Postprandial blood sugars(2Hr)> 200 mg/dL

Anemia was defined by hemoglobin concentration

- In males <13g/dL
- In females <12g/dL

Exclusion criteria

- Normocytic Normochromic anemia
- Chronic Kidney Disease Stage 3-5
- Uncontrolled Hypertension
- Type 1 Diabetes mellitus
- Gestational Diabetes mellitus
- Glaucoma or family history of Glaucoma

Methodology

Hemoglobin concentration for each patient was obtained using an automated analyzer. Peripheral smear study was made for all patients who were anemic and those with normocytic normochromic picture were eliminated from the study. Fundus examination was made all the patients using Welch Allyn direct ophthalmoscope. Fundus findings were recorded and the retinopathy changes were classified according to ETDRS classification. The collected data were analyzed with IBM.SPSS statistics software 23.0 Version. To describe about the data descriptive statistics frequency analysis, percentage analysis was used for categorical variables and the mean and S.D were used for continuous variables. To find the significant

difference between the bivariate samples in Independent groups the Unpaired sample t-test was used. To find the significance in categorical data Chi-Square test was used. In both the above statistical tools the probability value 0.05 is considered as significant level.

Statistical analyses: Data analysis was done using SPPS 16 software and was compared for statistical significance by determining the 'p' value.

Results

In this study, the study population in 2 groups – anemic and non-anemic was categorized according to age. In the anemic group, the population in 50-59 years was the majority contributors followed by the age group category of ≥60 years and the 30-39 years contributed the least. In the non-anemic category, the majority were from 50-59 years category followed by 30-39 years, while the least contribution was from ≥60 years category. The study population consisted of almost equal males and females, with about 101 females and 99 males. The mean hemoglobin in anemic population was 8.19g/dL. The mean hemoglobin concentration in non-hemoglobin group was 13.14 g/dl. Fundus examination in anemic group showed normal interpretation in 49 patients, NPDR in 40 patients and 11 had PDR. In the non-anemic group, 68 patients had normal fundus examination, 26 had NPDR and 6 had PDR. The number of patients having diabetic retinopathy was greater in the anemic group (50) than in the non-anemic group (31). There was a significant statistical association between patients with anemia and diabetic retinopathy (**Table – 1**).

Table – 1: Total individuals in the study with and without diabetic retinopathy.

Diabetic retinopathy	Groups		Total
	Anemia	Non-Anemia	
No	50	69	119
Yes	50	31	81
Total	100	100	200

Discussion

One of the microvascular complications due to diabetes mellitus causing blindness is diabetic retinopathy. It is more common in type 2 than in type 1 diabetes mellitus [9]. The hallmark of diabetic retinopathy is microvascular occlusion and microvascular leakage. Microvascular occlusion leads to hypoxia and causes release of growth factors, which leads to neovascularization [10]. According to a recent study, 86% of diabetic patients with nephropathy had retinopathy, whereas 24% of patients with retinopathy had nephropathy. Excess glucose causes increased sorbitol production, which increases the activity of protein kinase, leading to pericyte loss and capillary leakage. Excess glucose also caused auto-oxidation and free radical production, leading to endothelial damage and capillary leakage [11]. Hypoxia due to decreased perfusion causes release of vascular endothelial growth factor causing angiogenesis. Microvascular leakage leads to formation of hard exudates, hemorrhage, and macular edema [12]. Thomas MC, et al. in Finland in 1691 DM patients found that the DM patients with hemoglobin level lower than 12 mg/dl were two times more likely to develop DR. Consistently, we found that anemic DM patients were 2.4 times more likely to develop DR [13]. Yang W, et al. reported that low hematocrit is a risk factor of development and advanced DR. The etiology and pathogenesis of anemia in DM patients are multifactorial. Decreased erythropoietin production is an important cause of development of anemia in DM patients. Chronic hyperglycemia is involved in the pathogenesis of anemia by means of creating abnormalities in RBCs, oxidative stress, autonomic neuropathy, and renal sympathetic denervation. These conditions put the renal interstitium in a hypoxic state and consequently, the production of erythropoietin by peritubular fibroblasts is impaired. The other possible causes of anemia include functional erythropoietin deficiency, diabetic nephropathy, chronic inflammation, high levels of ultimate glycosylated products, iron deficiency, anti- DM drugs and low testosterone

levels suggested by others. Regarding the effect of anemia on DR, it seems that anemia-induced hypoxia leads to the increased release of vaso-proliferative factors (X factor) and bring about the progression of DR. Preceeding studies reported that the flexibility of RBCs in DM patients is much less compared to normal individuals and this may be involved in the exacerbation of diabetic microangiopathy [14]. Mohanram, et al. studied 426 DM patients for 17 years and reported a direct relationship between hemoglobin level and the development and deterioration of proliferative DR and concluded that the level of hemoglobin was a predictive factor for the development of proliferative DR in type 1 DM patients [15].

Conclusion

There is a significant association between anemia in diabetic patients and earlier development of diabetic retinopathy. Hence, diagnosis and treatment of low hemoglobin must be made at the time of diagnosis of diabetes mellitus in order to reduce the complications of diabetes mellitus. Findings from our study suggest that anemia evaluation should be considered for inclusion in the routine management of T2DM patients and anemia should be treated to minimize the risk of microvascular complications.

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