

## ANAEMIA AS A RISK FACTOR FOR MICROVASCULAR COMPLICATIONS IN TYPE 2 DM- A CROSS-SECTIONAL STUDY

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### ABSTRACT

#### BACKGROUND

It is well known that diabetes adversely affects the kidneys finally leading to anaemia by various mechanisms. Several studies had postulated that anaemia developing before renal complications has an independent association with microvascular complication in type 2 diabetic patients. The aim of the study is to estimate the prevalence of anaemia in persons with type 2 diabetes mellitus and its role as a risk factor for the presence and the severity of microvascular complication in a population-based study.

#### MATERIALS AND METHODS

This is a cross-sectional study conducted in patients coming to OPD of the Department of General Medicine in Government Vellore Medical College for a duration of 3 months from June 01, 2016, to August 31, 2016. Type 2 DM patients between the age group 20-60 years attending our diabetic clinic of both sex were included in our study.

#### RESULTS

From a total of 100 patients, 41% had anaemia including 34% with normochromic normocytic, 65.85% with hyperchromic microcytic anaemia and none of the patient had macrocytic anaemia. Patients who are anaemic had more frequent microvascular complications. There was no significant difference between males and females. The average duration of diabetes has a positive correlation with anaemia. All the microvascular complications like neuropathy, nephropathy and retinopathy had significant association with the presence of anaemia in type 2 patients. Nephropathy had a significant higher frequency compared to others as a complication in type 2 DM.

#### CONCLUSION

Our study shows that there is increased prevalence of anaemia in type 2 DM patients and the prevalence of microvascular complications is significantly higher among the diabetic patients with anaemia.

#### KEYWORDS

Anaemia, T2DM, Diabetes, Microvascular Complications, Nephropathy, Neuropathy and Retinopathy.

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#### BACKGROUND

The ever increasing prevalence of diabetes is due to improved life expectancy.<sup>(1)</sup> The diabetes mellitus being a group of metabolic diseases has a significant microvascular complications leading to morbidities before it is diagnosed. In numerous studies, it is estimated that the prevalence of microvascular complications in diabetes ranges from 5%-35%.<sup>(2-5)</sup>

The most important risk factors for microvascular complications are serum albumin, albuminuria, serum

creatinine and anaemia.<sup>(6)</sup> Anaemia, a common complication, is more prevalent in persons with diabetes than in persons without diabetes.<sup>(7)</sup> DM patients tend to develop anaemia at earlier ages and with greater severity than the general population.<sup>(8)</sup> Chronic anaemia results in tissue hypoxia, which is known to play a key role in diabetes-associated organ damage. Although, anaemia due to chronic kidney disease is present in these group of patients. Anaemia is present even before the development of chronic kidney disease.<sup>(9,10)</sup> A study in Iran had shown that the prevalence of anaemia was estimated at 10% in patients with type 2 DM.<sup>(11)</sup> Even if anaemia indicates diabetic nephropathy, the presence of it before renal failure should prompt for a more robust investigation and management so as to reduce morbidity and mortality from the microvascular complications.

The outcome of heart failure and hypoxia-induced organ damage in patients with DM can also be affected by severe anaemia.<sup>(12)</sup> Presence of anaemia itself carries its own complications like exercise intolerance, poor growth,

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poor cognition and poor appetite. Since, anaemia can lead to artificially low level of glycosylated haemoglobin.

(HbA1c), it may result in missed diagnosis of hyperglycaemia as well as uninterrupted progression of diabetes-related micro- and macrovascular complications. So, it is imperative to conduct further clinical trials to study the treatment of anaemia in diabetic patients.<sup>(13)</sup>

### AIMS AND OBJECTIVES

- To estimate the prevalence of anaemia in persons with type 2 diabetes mellitus, and
- Its role as a risk factor for the presence of microvascular complications and the severity of diabetic retinopathy in a population-based study.

### MATERIALS AND METHODS

#### Materials

This study was done in patients attending our diabetic clinic as OPD. Information was collected through a preformed and pre-tested proforma from each patient. Qualified patients went for detailed history, clinical examination, biochemical examinations and detailed ophthalmic evaluation.

#### Inclusion Criteria

- Patients with type 2 DM between age group 20-70 years attending the diabetic clinic of GVMCH were all included for this study.
- Patients who are newly diagnosed with T2DM were also included for this study.

#### Exclusion Criteria

- Subjects who were suffering from type 1 diabetes mellitus.
- Gestational diabetes.
- CKD stage 3-5.
- CCF.
- Causes of anaemia like aplastic anaemia, haemolytic anaemia; thalassaemia.
- Severe infection.
- Acute cerebrovascular disease.
- Severely impaired hepatic function (AST or ALT > 2× upper limit of normal).
- Recent surgery.
- Patients with any malignancy or suffering from HIV-AIDS.

#### Examination and Laboratory Studies

For each patient, height in cms, weight (minimally dressed without shoes, using digital scales was recorded) and Body Mass Index (BMI) were calculated. Neurologic examinations were done by Michigan Neuropathy Screening Instrument. Score greater than two was taken as Diabetic Neuropathy.<sup>(10)</sup> For assessing retinopathy, all patients were referred to an ophthalmologist and the degree of eye involvement including proliferative and nonproliferative diabetic retinopathies was determined. Ophthalmologic examination was done using indirect ophthalmoscopy with dilated pupils non-sight threatening diabetic retinopathy

included cases of mild or moderate nonproliferative diabetic retinopathy. Sight-threatening diabetic retinopathy was defined as severe nonproliferative diabetic retinopathy, proliferative diabetic retinopathy and clinically significant macular oedema. The prevalence of true albuminuria was determined and other factors inducing transient albuminuria such as urinary tract infection, severe hypertension, severe hyperglycaemia, exercise and acute fever were excluded and in case of difficulty in exclusion of these factors, the patient was excluded from the study. Other studies done included 24-hour urine volume, creatinine (Cr), albumin, Fasting Blood Sugar (FBS), glycosylated Hb HbA1c, Complete Blood Count (CBC), Cr and C-Reactive Protein (CRP) were measured. Albumin levels more than 30 mg in 24 hours was defined as albuminuria (10). Creatinine clearance (ClCr) in men was calculated using MDRD formula  $186 \times (\text{Creat}/88.4) - 1.154 \times (\text{Age}) - 0.203 \times (0.742, \text{ if female}) \times (1.210, \text{ if black})$ . Anaemia was considered as Hb <13 g/dL in men and <12 g/dL in women. Mean Corpuscular Volume (MCV) of more than 100 fL and less than 80 fL were considered as macrocytic and microcytic anaemia. Normocytic anaemia was defined as MCV value between 80 and 100 fL. CBC differential normal values, Cr, FBS and albuminuria were measured by using cell counter device (BioSystem Company Kits), glucose oxidase, Jaffe and photometer methods, respectively.

#### Ethical Consideration

The study was approved by the Government Vellore Medical College. The purpose of the study was explained to all participants. Patients were informed that they were free to withdraw from the study at any time.

#### Statistical Analyses

Data analysis was done using SPSS 16 software and was compared for statistical significance by determining the 'p' value.

#### RESULTS

Total of hundred patients who fulfilled the inclusion criteria and does not have any of the exclusion criteria were included in the study.

#### Age Distribution among Diabetes

Among them 32 patients were less than 50 years of age and 68 patients were greater than 50 years of age.

#### Prevalence of Anaemia

Among the 100 type 2 diabetic patients, 41% had anaemia (15 males and 26 females) including 34% with normochromic normocytic, 65.85% with hypochromic microcytic anaemia and none of the patient had macrocytic anaemia in our study and 59 patients had no anaemia (M:30; F:29).

#### Duration of Diabetes

The average duration of diabetes in patients with anaemia was 10.4 years. and in non-anaemic was 7.2 years.

**PREVALENCE OF COMPLICATIONS**

On evaluating the complications, there was a total of 18 patients suffering from retinopathies (18%), 59 patients with nephropathies (59%) and 27 patients with neuropathies (27%) with frequent overlaps within the complications. Nephropathy was the most common complication. Patients who are anaemic had more frequent microvascular complications. The incidence of anaemia

among patients with complications were 72.2%, 62.71% and 62.96% in patients with retinopathy, nephropathy and neuropathy, respectively.

**Sex**

There was no significant difference between males and females (P value - 0.158).

**SEX DISTRIBUTION AND ANAEMIA**

	Anaemia+	Anaemia-	Marginal Row Totals
Male	15 (18.45) [0.65]	30 (26.55) [0.45]	45
Female	26 (22.55) [0.53]	29 (32.45) [0.37]	55
<b>Marginal Column Totals</b>	<b>41</b>	<b>59</b>	<b>100 (Grand Total)</b>

The average duration of diabetes in patients with anaemia was 10.4 yrs. and in non-anaemic was 7.2 years.

**RETINOPATHY AND ANAEMIA**

	Anaemia+	Anaemia-	Marginal Row Totals
Retinopathy+	13 (7.38) [4.28]	5 (10.62) [2.97]	18
Retinopathy-	28 (33.62) [0.94]	54 (48.38) [0.65]	82
<b>Marginal Column Totals</b>	<b>41</b>	<b>59</b>	<b>100 (Grand Total)</b>

There was significant correlation between Anaemia and Retinopathy (P value-0.0029).

**NEPHROPATHY AND ANAEMIA**

	Anaemia+	Anaemia-	Marginal Row Totals
Nephropathy+	37 (24.19) [6.78]	22 (34.81) [4.71]	59
Nephropathy-	4 (16.81) [9.76]	37 (24.19) [6.78]	41
<b>Marginal Column Totals</b>	<b>41</b>	<b>59</b>	<b>100 (Grand Total)</b>

There was significant correlation between nephropathy and anaemia (P Value-0.0000).

**NEUROPATHY AND ANAEMIA**

	Anaemia+	Anaemia-	Marginal Row Totals
Neuropathy+	17 (11.07) [3.18]	10 (15.93) [2.21]	27
Neuropathy-	24 (29.93) [1.17]	49 (43.07) [0.82]	73
<b>Marginal Column Totals</b>	<b>41</b>	<b>59</b>	<b>100 (Grand Total)</b>

There was significant correlation between neuropathy and anaemia with P value-0.006.

**DISCUSSION**

In our study, 32% of patients belonged to age group <50 years, which is similar to the study conducted by Padmaja Kumari et al,<sup>(14)</sup> which showed 29% of diabetic patients belonged to age group <50 years and the rest were greater than 50 yrs.

The prevalence of anaemia among diabetic population was 41% in our study, which was high when compared to 12.3% in study by Padmaja Kumari et al<sup>(14)</sup> and 30% in a study conducted by Hosseini MS et al.<sup>(15)</sup> The distribution of anaemia according to peripheral smear study and haematological indices were 34% with normocytic normochromic anaemia and 66% were microcytic hypochromic anaemia and none with macrocytic anaemia when compared to Hosseini MS et al study, which showed a distribution of normochromic normocytic in 15.1%,

hypochromic microcytic in 14.4% and 1% hyperchromic macrocytic anaemia.<sup>(15)</sup>

In our study, there was nearly equal distribution of anaemia among diabetic men (n=30) and women (n=29). But, in study conducted by David et al,<sup>(16)</sup> there was slight difference in the prevalence of anaemia among diabetic population with respect to gender difference with males 40% and females 34%. The average duration of diabetes in patients with anaemia was 10.4 yrs. in our study when compared to study of Hosseini MS et al, which showed duration of 11.4 yrs.

The prevalence of microvascular complications like retinopathy, nephropathy and neuropathy were 18%, 59% and 27% whereas in study by Hosseini MS et al, it is 35%, 77% and 44%, respectively. Also, in our study, the incidence of anaemia among patients with complications were 72.2%, 62.71% and 62.96% when compared to 51%, 80% and 61% of patients suffering from diabetic retinopathy, nephropathy and neuropathy in the study of Hosseini MS et al.

Normocytic anaemia was the most prevalent type of anaemia in patients with nephropathy. Previous studies showed anaemia as a common morbidity in diabetic kidney disease and introduced anaemia as an independent predictor of progression to end-stage renal disease.<sup>(17,18)</sup> Our study showed statistical correlation between prevalence of anaemia in patients with type 2 DM and development of diabetic retinopathy with p value of 0.0029. A study conducted by Raman et al<sup>(19)</sup> suggests that individuals with anaemia were 1.80 times more likely to develop DR than those with no anaemia. Also, in a study conducted by B.B. He, M. Xu, L. Wei et al,<sup>(20)</sup> the relationship between anaemia and subtype of microvascular complication was examined. The prevalence of anaemia was much higher in patients with DR (27.3% vs. non-DR: 19.7%,  $P < 0.001$ ), DN (35% vs. non-DN: 17%,  $P < 0.001$ ) and DPN (28.1% vs. non-DPN: 17.4%,  $P < 0.001$ ) when compared to our study with DN (63% vs. non-DN: 37%,  $P < 0.000$ ) and DPN (63% vs. non-DPN: 37%,  $P < 0.000$ ).

### CONCLUSION

Our study shows that there is increased prevalence of anaemia in type 2 DM patients and the prevalence of microvascular complications is significantly higher among the diabetic patients with anaemia. Findings from our study suggest that anaemia evaluation should be considered for inclusion in the routine management of T2DM patients and anaemia should be treated to minimise the risk of microvascular complications.

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