

# Prevalence of Anaemia in Individuals with Type 2 Diabetes: A Cross-sectional Study from a Tertiary Care Centre, Chennai, India

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## ABSTRACT

**Introduction:** Anaemia is frequently observed in diabetes, affecting the quality of life and also contributing to the pathogenesis of microvascular complications. However, according to the literature, there have been no previous studies on the prevalence of Anaemia in Type 2 Diabetes (T2D) without Diabetic Kidney Disease (DKD) in the south Indian population.

**Aim:** To estimate the prevalence of anaemia in T2D and study its association with glycaemic control and diabetes-related microvascular complications.

**Materials and Methods:** The present study was a cross-sectional study that included 100 patients with T2D visiting the Department of Endocrinology at Sri Ramachandra Hospital, Chennai between June and September 2019. After obtaining informed consent, samples for complete blood count, Fasting Plasma Glucose (FPG), glycosylated haemoglobin (HbA1c),

renal function tests, lipid profile, and urine microalbumin were collected from participants. Gestational diabetes, Type 1 Diabetes (T1D), and DKD on erythropoietin were excluded from this study. The test of Proportions was performed using the Chi-square test.

**Results:** The mean age of the study population was 57.91±9.50 years. The overall prevalence of anaemia in the present study was 60%, and it was higher among women (p=0.023). Anaemia was also observed to be more common in those with poor glycaemic control (p=0.340) and in cases where at least one microvascular complication had occurred (p=0.796).

**Conclusion:** Anaemia was observed in almost two-thirds of patients with T2D in this study. The prevalence of anaemia was higher in individuals with poor glycaemic control and diabetes-related microvascular complications.

**Keywords:** Glycaemic control, Diabetics, Microvascular complications

## INTRODUCTION

As the 'Diabetes capital of the world,' India has witnessed an alarming rise in the prevalence of diabetes. Alongside the impact of nutrition, lifestyle factors, increasing population, urbanisation, higher obesity rates, and longer life expectancy, there has also been a rise in the prevalence of anaemia among individuals with or without diabetes. Numerous mechanisms have shown the interlink between diabetes and anaemia. Diabetes creates a pro-inflammatory state characterised by an exaggerated expression of pro-inflammatory cytokines such as IL-6, TNF $\alpha$ , and NF $\kappa$ B. Elevated IL-6 levels exhibit an anti-erythropoietic effect by altering the sensitivity of progenitors to erythropoietin, the erythroid growth factor. Moreover, elevated IL-6 promotes apoptosis of immature erythrocytes, further reducing the number of circulating erythrocytes and leading to anaemia [1,2]. Hypoxia resulting from anaemia is also theorised to contribute to microvascular complications of diabetes, including Diabetic Nephropathy (DN), neuropathy, and retinopathy [1]. Additionally, the use of metformin has been associated with Vitamin B12 deficiency anaemia [3]. The presence of anaemia in diabetes not only negatively impacts quality of life but also contributes to disease progression, increased incidence of comorbidities, and an elevated risk of cardiovascular disease [4]. Early identification and correction of anaemia have been shown to reduce progression and delay the onset of microvascular complications [5] while improving quality of life [6]. Previous studies have investigated the prevalence of anaemia in diabetes with kidney disease [7], but data is limited for individuals with normal renal function [8]. Therefore, this study aimed to determine the prevalence of anaemia in individuals with T2D and

explore its association with glycaemic control and microvascular complications.

## MATERIALS AND METHODS

This cross-sectional study was conducted among individuals with T2D who visited the outpatient clinic of the Department of Endocrinology at Sri Ramachandra Medical College Hospital in Chennai between June and September 2019. Institutional Ethics Committee approval was obtained before commencing the study (IEC No. CSP/19/JUN/78/235).

The study included only patients with T2D who were previously diagnosed after the age of 35, based on the diagnostic criteria of the American Diabetes Association [9]. Exclusion criteria consisted of gestational diabetes, T1D, DKD beyond stage 2, and those already taking iron supplements.

The sample size was calculated using the formula  $n=3.84 \times p \times q / l^2$ , where p represents the previous prevalence, q equals 1-p, and l denotes the relative precision (20% of p). The sample size was calculated based on a previous prevalence of anaemia among T2D individuals, which was found to be 57.14% [10]. Initially, the sample size was determined as 72, but it was adjusted to 100 to account for potential non-response.

After obtaining informed consent from the participants, clinical information was collected, and a brief clinical examination was conducted. Fasting blood and urine samples were collected for complete blood count, Fasting Plasma Glucose (FPG), glycosylated haemoglobin (HbA1c), renal function tests, lipid profile, and urine microalbumin estimation.

Anaemia was defined according to WHO criteria as a Haemoglobin (Hb) level less than 13.0 g/L for men and less than 12.0 g/L for women [11]. Microcytic anaemia was defined as Mean Corpuscular Volume (MCV) <80 fL, normocytic anaemia as MCV 80-96 fL, and macrocytic anaemia as MCV >96 fL [12].

Diabetic Peripheral Neuropathy (DPN) was assessed by testing pinprick and vibration sensations on specific points on the sole of each foot. Lack of sensation in at least four out of ten points for pinprick sensation and at least three out of four points for vibration sensation, along with the absence of knee or ankle jerk in either foot, indicated the presence of DPN [13].

Diabetic Retinopathy (DR) was classified into mild Non-Proliferative Diabetic Retinopathy (NPDR), moderate NPDR, severe NPDR, and Proliferative Diabetic Retinopathy (PDR) based on fundus examination by an experienced Ophthalmologist, following the International classification of DR [14].

DN was assessed by calculating the Glomerular Filtration Rate (eGFR) using the Cockcroft-Gault formula. Based on eGFR, subjects were classified into five stages: Stage-1: eGFR  $\geq$ 90, Stage-2: eGFR 60-89, Stage-3: eGFR 30-59, Stage-4: eGFR 15-29, and Stage-5: eGFR <15 [15].

## STATISTICAL ANALYSIS

The statistical analysis was performed using the Statistical Package for Social Science (SPSS) software, version 16. Descriptive statistics were used to calculate the prevalence or proportion of variables. The Chi-square ( $\chi^2$ ) test was employed to test the statistical significance of proportions. Mean (Standard Deviation) was calculated for quantitative variables, and the t-test was conducted for significance testing. A p-value of less than 0.05 was considered statistically significant.

## RESULTS

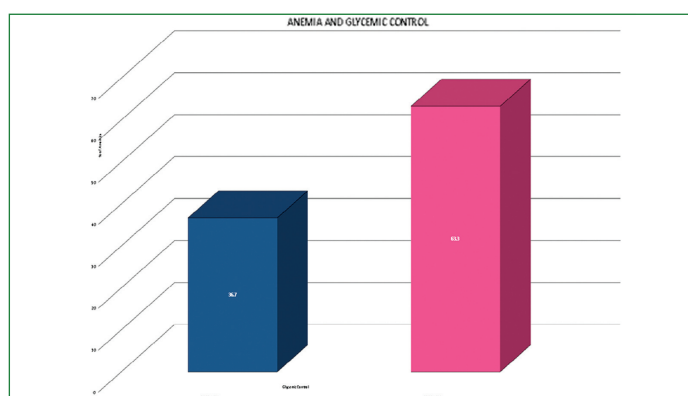
A total of 100 patients with T2D participated in this study, consisting of 68 women and 32 men. The mean age of the study population was 57.91 $\pm$ 9.50 years (range, 35-80 years), and the mean duration of T2D was 6.69 $\pm$ 4.19 years (range, 3 months to 20 years). The mean Fasting Plasma Glucose (FPG), glycosylated haemoglobin (HbA1c), serum creatinine, and urinary microalbumin levels in this cohort were 138.5 $\pm$ 54.6 mg/dL, 7.94 $\pm$ 1.68%, 0.78 $\pm$ 0.38 mg/dL, and 58.6 $\pm$ 12 mg/g, respectively.

Among the study population, 60 patients with T2D had unrecognised anaemia, including 46 women (67.6%) and 14 men (43.8%) (p=0.023). Anaemia was more prevalent in individuals above 60 years of age (p=0.03) and those who were not currently employed (p<0.001). The social, clinical, and biochemical characteristics of study participants with and without anaemia are presented in [Table/Fig-1]. The mean haemoglobin (Hb) level in this cohort was 11.74 $\pm$ 1.77 g/dL (range, 6.6 to 16.9 g/dL), with men having a mean Hb level of 12.9 g/dL and women having a mean Hb level of 11.2 g/dL. The mean Mean Corpuscular Volume (MCV) was 88.61 $\pm$ 82.56 fL. Among those with anaemia, 25 individuals (41.7%) had microcytic anaemia, while 35 individuals (58.3%) had normocytic anaemia based on MCV. Anaemia was more commonly observed in patients with poor glycaemic control, with 63.3% having HbA1c >7% and 36.7% having HbA1c  $\leq$ 7% (n=38 and n=22, respectively) [Table/Fig-2] (p=0.340). The prevalence of DN (Stage 1 and 2), DPN, and DR in this study were 46%, 33%, and 5%, respectively (n=46, n=33, and n=5, respectively). At least one microvascular complication was observed in 65% of patients, while more than one microvascular complication was present in 20% of patients, and the remaining patients did not have any microvascular complications at the time of the study. Anaemia was detected in 21 (35%) patients with DPN and 39 (65%) patients without DPN (p=0.602) [Table/Fig-3]. Only 4 (6.7%) patients with DR had anaemia (p=0.349). Of the patients, 46 had Stage 1 DKD and 34 had Stage 2 DKD based on estimated

Characteristics/Parameters		Prevalence of anaemia		p-value
		Yes (n=60)	No (n=40)	
Age	<60 years (n=52)	26 (50%)	26 (50%)	0.034
	$\geq$ 60 years (n=48)	34 (70.8%)	14 (29.2%)	
Gender	Men (n=32)	14 (43.8%)	18 (56.2%)	0.023
	Women (n=68)	46 (67.6%)	22 (32.4%)	
Family history of diabetes	Present (n=21)	14 (66.7%)	7 (33.3%)	0.483
	Absent (n=79)	46 (58.2%)	33 (41.8%)	
Employment status	Not working (Unemployed/Housewife/Retired) (n=80)	56 (70%)	24 (30%)	<0.001
	Working (n=20)	4 (20%)	16 (80%)	
Diet	Vegetarian (n=14)	8 (57.1%)	6 (42.9%)	0.814
	Non-vegetarian (n=86)	52 (60.5%)	34 (39.5%)	
Duration of diabetes	<5 years (n=31)	19 (61.3%)	12 (38.7%)	0.547
	5-10 years (n=56)	35 (62.5%)	21 (37.5%)	
	>10 years (n=13)	6 (46.2%)	7 (53.8%)	
BMI (kg/m <sup>2</sup> )	<18.5 (n=3)	3 (100%)	Nil	0.702
	18.5-22.9 (n=37)	23 (62.2%)	14 (37.8%)	
	23.0-27.5 (n=44)	24 (54.5%)	20 (45.5%)	
	>27.5 (n=16)	10 (62.5%)	6 (37.5%)	
Serum creatinine	<1.2 (n=92)	55 (59.8%)	37 (40.2%)	0.880
	$\geq$ 1.2 (n=8)	5 (62.5%)	3 (37.5%)	
Glomerular Filtration Rate (eGFR)	<60 (n=20)	17 (85%)	3 (15%)	0.038
	60-89.9 (n=34)	18 (52.9%)	16 (47.1%)	
	$\geq$ 90 (n=46)	25 (54.3%)	21 (45.7%)	
Glycaemic control (HbA1c)	Good ( $\leq$ 7) (n=33)	22 (66.7%)	11 (33.3%)	0.340
	Poor (>7) (n=67)	38 (56.7%)	29 (43.3%)	
Metformin	Yes (n=92)	53 (57.6%)	39 (42.4%)	0.098
	No (n=8)	7 (87.5%)	1 (12.5%)	
Hypertension	Yes (n=50)	32 (64%)	18 (36%)	0.414
	No (n=50)	28 (56%)	22 (44%)	
Dyslipidaemia	Yes (n=30)	20 (66.7%)	10 (33.3%)	0.373
	No (n=70)	40 (57.1%)	30 (42.9%)	
Thyroid dysfunction	Yes (n=6)	6 (100%)	Nil	0.039
	No (n=94)	54 (57.4%)	40 (42.6%)	
History of coronary artery disease	Yes (n=15)	10 (66.7%)	5 (33.3%)	0.568
	No (n=85)	50 (58.8%)	35 (41.2%)	
Complications of diabetes	Yes	39 (59%)	27 (41%)	0.796
	No	21 (61.8%)	13 (38.2%)	

**[Table/Fig-1]:** Social, clinical, and biochemical characteristics of study participants with and without anaemia (n=100).

For descriptive statistics, prevalence or proportion was calculated and for testing statistical significance of proportions,  $\chi^2$  test (Chi-square test) was used. For quantitative variables, Mean (Standard Deviation) was calculated and t-test was done for test of significance. p<0.05 was taken as statistically significant



**[Table/Fig-2]:** Prevalence of anaemia in patients with good (HbA1c  $\leq$ 7%) and poor glycaemic control (HbA1c >7%).

Microvascular complications	Anaemia	No anaemia n (%)	p-value
Retinopathy	4 (6.7)	1 (93.3)	0.35
Neuropathy	21 (35)	12 (65)	0.6
Nephropathy	25 (41.7)	21 (58.3)	0.29
Any 1 microvascular complication	39 (65)	27 (35)	0.8

**[Table/Fig-3]:** Prevalence of anaemia in patients with microvascular complications of diabetes.

Glomerular Filtration Rate (eGFR). Anaemia was found in 25 patients (41.7%) with DN and 35 (58.3%) patients without DN ( $p=0.287$ ). Anaemia was documented in 39 (65%) patients with at least one microvascular complication, while only 27 (35%) patients without any microvascular complication had anaemia, but this difference was statistically insignificant ( $p=0.796$ ). Among the patients, 53.3% with systemic hypertension and 33.3% with dyslipidaemia also had anaemia.

Primary hypothyroidism ( $n=6$ , 6%) was almost always associated with anaemia, predominantly normocytic anaemia ( $p=0.039$ ).

## DISCUSSION

In the study, the prevalence of anaemia was found to be 60%, with normocytic anaemia being the most commonly observed type. This is consistent with previous studies conducted in India, which reported prevalence rates ranging from 38-67% [16,17]. However, the findings were slightly higher than the global prevalence rate of 34-55% [17-20]. This suggested that individuals with T2D are more likely to develop anaemia compared to those without T2D, possibly due to the inflammatory nature and anti-erythropoietic effects of diabetes.

Similar to previous studies, we found that anaemia was more prevalent among women (67.6%) compared to men (43.8%) [21]. This could be attributed to factors such as poor nutrition, menstrual loss, and lack of self-care among Indian women. In addition, the study population had a higher proportion of women, which could contribute to the higher prevalence of anaemia among women.

It was also observed that anaemia was more prevalent in individuals with poor glycaemic control, with 63.3% of those with anaemia having HbA1c levels  $>7\%$ . It is hypothesised that in uncontrolled diabetes, the bone marrow's erythrocyte precursors are exposed to prolonged glucose toxicity, leading to erythrocyte dysfunction [22]. This may contribute to the development of anaemia [23].

Regarding microvascular complications [24], the authors found that 35% of individuals with anaemia had diabetic peripheral neuropathy (DPN). This is slightly higher than previous studies, suggesting that anaemia may be a risk factor for DPN in T2D. Anaemia can contribute to DPN through various mechanisms, including iron and vitamin B12 deficiencies, which are known to affect nerve function [25-28].

Retinopathy was present in 6.7% of individuals with anaemia, which was lower than previous observations [29]. However, all cases of retinopathy in the study were mild NPDR. Studies have shown that detection and treatment of anaemia can be beneficial in the management of diabetic retinopathy, as improved haemoglobin levels enhance tissue oxygenation and may reduce Vascular Endothelial Growth Factor (VEGF) production [30,31].

A high prevalence of anaemia was seen among individuals with DN, with 41.7% having anaemia [31,32]. This is consistent with previous studies linking anaemia to the progression of renal failure in diabetes [33,34]. Anaemia has been shown to increase renal sympathetic nerve activity, leading to increased glomerular pressure and proteinuria, which can accelerate the progression of DN [35].

Overall, 65% of individuals with anaemia had at least one microvascular complication, highlighting the association between anaemia and

diabetes-related complications [36]. Several mechanisms have been proposed to explain this association, including autonomic neuropathy, decreased erythropoietin production, and reduced response to hypoxia [37-39].

An association between anaemia and thyroid dysfunction, systemic hypertension, and dyslipidaemia was observed. These associations have been established in previous studies and underscore the importance of screening for anaemia in individuals with these comorbidities.

One limitation of the study is that it was conducted in a specific geographic area and may not be representative of the entire population. Additionally, the cross-sectional design of the study limits our ability to establish causality.

In conclusion, the study highlights the high prevalence of unrecognised anaemia among individuals with T2D, particularly among women and the elderly [40-42]. Appropriate screening and treatment of anaemia in this population are warranted. The associations between anaemia and microvascular complications, thyroid dysfunction, hypertension, and dyslipidaemia further emphasise the importance of addressing anaemia in the management of T2D.

## Limitation(s)

One limitation of the study is the lack of assessment of ferritin values and iron indices. This information could have provided further insights into the underlying causes of anaemia in our study population.

## CONCLUSION(S)

In our study population, the authors found that 60% of patients with T2D had unrecognised anaemia. However, a significant association between the prevalence of anaemia and glycaemic control was not found. Anaemia was documented in 65% of patients with any one microvascular complication, but only in 35% of patients without any microvascular complication. However, this difference was not statistically significant. Larger prospective studies are needed to determine the causal relationship between anaemia and diabetes-related complications.

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**PLAGIARISM CHECKING METHODS:** [Jan H et al.]

- Plagiarism X-checker: Feb 21, 2023
- Manual Googling: Jun 15, 2023
- iThenticate Software: Jul 03, 2023 (15%)

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