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ORIGINAL RESEARCH

Prevalence And Typing of Anemia in Diabetes Mellitus Type 2 Patients attending R.D.Gardi Medical College & Associated Hospitals - A cross sectional study

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Introduction

Lifestyle related diseases are increasing in 21st century with the higher pace of urbanization and industrialization. Type 2 Diabetes Mellitus is one of the most common life style related disease. Type 2 diabetes mellitus is a non-autoimmune, heterogeneous and polygenic metabolic disease in which body fails to produce enough insulin or the insulin doesn't act well on its receptors or both, also characterized by abnormal glucose homeostasis, producing state of chronic hyperglycemia. The pathogenesis of T2DM appears to involve complex interactions between genetic and environmental factors[1].

Prevalence of diabetes mellitus (T2DM) is increasing globally and has reached epidemic proportions in many countries. The recent estimate by IDF (International Diabetes Federation) there are 366 million diabetic patients worldwide which is expected to rise to 552 million by year 2030.The total predicted increase in number from 2011 to 2030 is 50.7% with an annual growth of 2.7% which is 1.7 times the annual growth of worldwide adult population. 48% of anticipated absolute global increase of 186 million people with diabetes is attributed in India and china alone. According to Wild et al, the prevalence of diabetes is predicted to double globally from 171 million in year 2000 to 366 million in 2030 with maximum rise in India.There are currently 61.3 million diabetes patients in India and this number is expected to rise to 101.2 million by year 2030. In year 2000, India topped the world in highest number of diabetic patients (India 31.7 million) in the world followed by (china 20.8 million). This higher burden of diabetes is likely to be associated with increased complications[2].

The level of morbidity and mortality due to diabetes mellitus and its complications are enormous, and pose significant burden on healthcare as well as on family and society. Worryingly, diabetes is now being shown to be associated with spectrum of complications and that too be occurring at a relatively younger age, it is one of the major cause of premature

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death, increased risk for developing cardiovascular diseases, infact T2DM is considered as CHD equivalent by different researchers in literature, incidence of cardiovascular diseases reaches 20% after a period of 7 years of diagnosis as diabetes, T2DM with duration of 10 years or more is considered a CHD equivalent for future major coronary event having risk equivalent to previous CHD .Type 2 DM occur with impaired insulin effectiveness (insulin resistance) is accompanied by the failure to produce sufficient amount of insulin. Glycosylated hemoglobin (HbA1C)is an effective tool in monitoring blood glucose control it provide an accurate estimate of average plasma glucose levels of past 8 to 12 weeks and hence it become a important marker of glycemic control in diabetes mellitus patients.

Anemia is a global public health problem affecting all age and gender in both developing and developed countries .Currently around 1.62 billion people are affected with anemia worldwide which account for approx 24% of worldwide population, anemia is more prevalent in developing countries ,maximum affecting preschool children and least affecting adult male.Anemia is one of the common preventable conditions yet overlooked especially in patients of diabetes mellitus, it is a common finding in patients with diabetic nephropathy, diabetes related chronic hyperglycemia can lead to hypoxic environment at renal interstitium which results in impaired production of erythropoietin from peritubular fibroblast cells and subsequently lead to anemia. There can be other mechanism causing anemia prior to the involvement of kidneys in patients with diabetes mellitus and might contribute to pathogenesis and progression of cardiovascular disease in diabetes mellitus patients ,anemia in diabetes patients may also aggravate and worsen the complications of T2DM like neuropathy and nephropathy, also anemia is a independent risk factor for complications like diabetic retinopathy. An emphasis on screening for anemia along with other complications of diabetes mellitus and correction of hemoglobin levels might help to delay the progression of vascular complications in these patients[3].

From previous studies anemia is a known complication of chronic kidney disease and diabetes mellitus is most common cause of chronic kidney disease but little work has done on anemia in Type 2 diabetes mellitus patients with normal renal function i.e, prior to the occurrence of advanced renal failure. This study aims at finding the prevalence of anemia in type 2 diabetes mellitus patients with normal serum creatinine values and also to study the typing of anemia occurring in patients with Type 2 diabetes mellitus patients without CRF[4].

Aims and objectives

1. To study the prevalence and typing of anemia in T2DM patients with HBA1c >6.5 % without Chronic Renal Failure.
2. To find correlation if any, between anemia and glycated hemoglobin (HBA1c), duration of T2DM, age and gender.

Materials and methods

It is a cross sectional study, constituted of 154 study cases presented with diabetes mellitus type 2 to the Deptt. of Medicine at R.D.Gardi Medical College and C.R.Gardi Hospital, Ujjain from 1st January 2018 to 31st may 2019.

A. Inclusion criteria

Patient with

- Age: Male and female aged between 18 to 65 years. And
- Recently diagnosed or Previously diagnosed cases of diabetes mellitus type 2 attending the department of medicine in O.P.D./I.P.D
- Patients given written informed consent.

B. Exclusion criteria

Patients with

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- Cases of proven GI bleed (esophagistis, gastric/peptic ulcers, varices, angiodysplasias, any GIT malignancy etc).
- Renal insufficiency (ARF and CRF) serum creatinine above 1.2mg/dl
- Associated co- morbid conditions like, Chronic Renal Failure, Congestive Cardiac Failure.
- Hematological Disorders and malignancy(Thalassemia and sickle cell anemia and any other type of hematological malignancy)
- Obstetric and Gynecological Disorders.
- Patients on Hormone Replacement Therapy.
- Pregnancy.
- Patients not given written informed consent.

Statistical analysis

Data were entered and analyzed in SPSS data sheet version 23. Frequency tables and measures of central tendency (mean) and measures of dispersion (Standard Deviation) were calculated. Correlation was assessed using the chi-square test for comparing mean of different group independent sample t-test and ANOVA were applied. Karl Pearson correlation coefficient was calculated for measuring linear relationship between GGT level and other study variable.

Observation and result

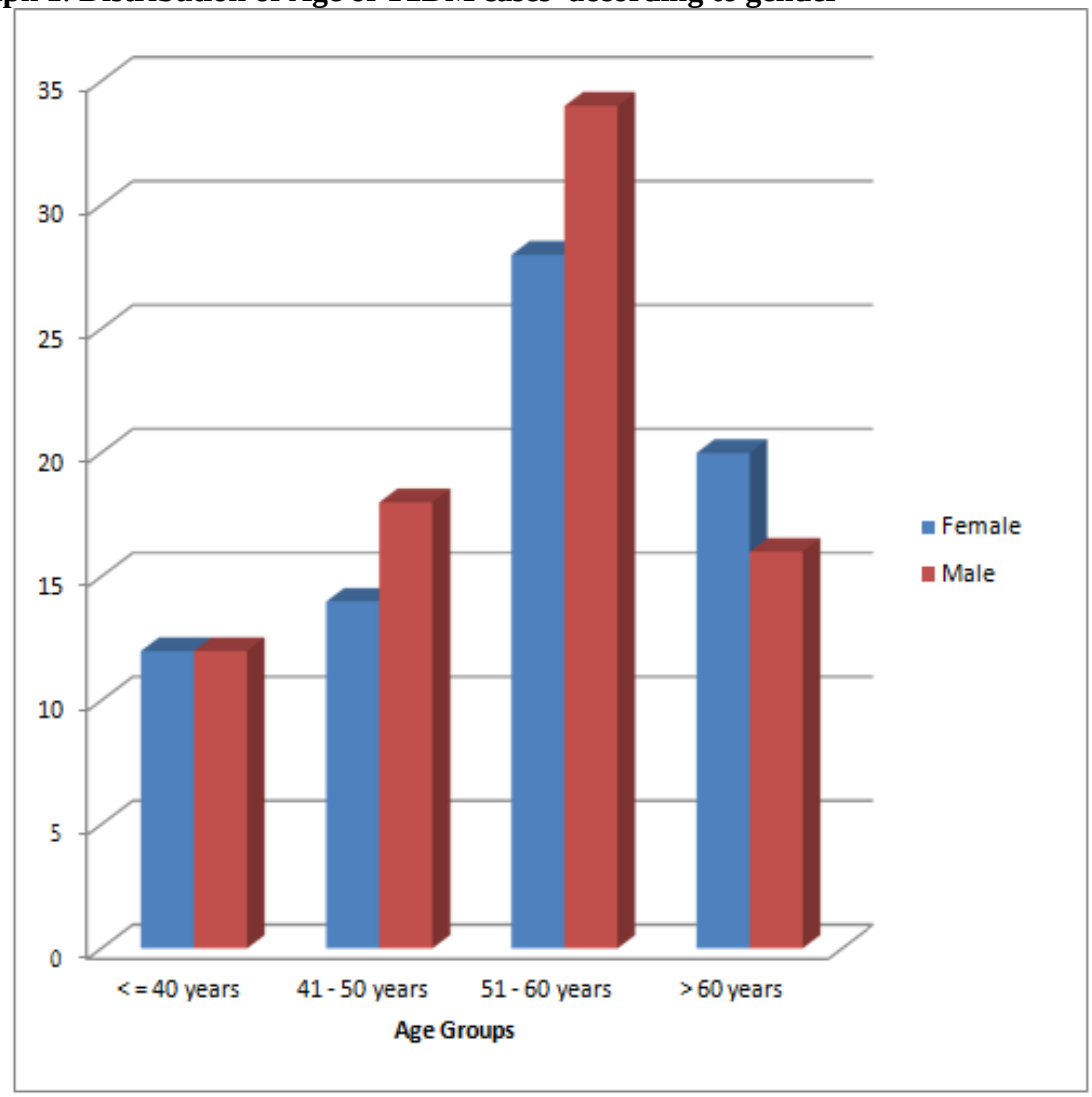
154 T2DM patients chosen by random convenient sampling are analyzed on basis of simple demographic entities like gender, age distribution divided in four groups ,age <40 years: 24 cases ,12 male and 12 female, age 41-50 years: 32 cases, 18 male and 14 female, age 51- 60 years:62 cases ,34 male and 28 female. Maximum T2DM cases fall in this age group.4.age >60 years: 36 cases, 16 male and 20 female **(Table 1) (Graph 1).**

Table 1: Distribution of Age of T2DM cases according to gender

Age groups	Sex		Total
	Female	**Male**	
< = 40 years	12	12	24
	50.0%	50.0%	100.0%
41 - 50 years	14	18	32
	43.8%	56.3%	100.0%
51 - 60 years	28	34	62
	45.2%	54.8%	100.0%
> 60 years	20	16	36
	55.6%	44.4%	100.0%
Total	**74**	**80**	**154**
	48.1%	**51.9%**	**100.0%**

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 08, 2022

Graph 1: **Distribution of Age of T2DM cases according to gender**



64/154 anemic cases are classified according to RBC morphology based on MCV in to microcytic,macrocytic and normochromic groups. Out of 64 anemic cases maximum anemic patients are found to fall in microcytic group with 43/64 cases (67.18%) followed by normocytic 16/64 cases (25%) followed by macrocytic anemia in 5 cases (7.8%)**(Table 2)**.

Table 2: Distribution of anemia according to MCV in T2DM.

MCV			**Total**
	Anemia	**Non Anemic**	
NORMOCYTIC	16	90	106
	15.1%	84.9%	100.0%
MICROCYTIC	43	0	43
	100.0%	0.0%	100.0%
MACROCYTIC	5	0	5
	100.0%	0.0%	100.0%
Total	**64**	**90**	**154**
	41.6%	**58.4%**	**100.0%**
Chi-Square = 98.06			

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 08, 2022

Table 3: Distribution of anemia according to MCV in T2DM.

HBA1C	Anemia		Total
	Anemic	Non Anemic	
Good control	5	17	22
	22.7%	77.3%	100.0%
Moderate control	9	19	28
	32.1%	67.9%	100.0%
Poor control	50	54	104
	48.1%	51.9%	100.0%
Total	**64**	**90**	**154**
	41.6%	**58.4%**	**100.0%**
Chi-Square = 6.053, p = 0.048			

64 anemic cases among T2DM group was observed for association with HBA1c signifying the glycemic control. In the good control group having HBA1c<7% carry 5/22 cases accounting for 22.7% followed by moderate glycemic control group having HBA1c between 7-8% carry 9/28 cases accounting for 32.1% and 50/104 cases accounting for 48.1% in poor glycemic control group having HBA1c above 8%. This concludes that the percentage prevalence of anemia increases with higher HBA1c that is anemia prevalence increases with poor glycemic control (table 3).

Table 4: Distribution of diabetic cases and non diabetic control according to age, gender and anemia

Age groups	Gender	Case				Control			
		Anemic		Non Anemic		Anemic		Non Anemic	
< = 40 years	Female	2	16.7%	10	83.3%	5	29.4%	12	70.6%
	Male	4	33.3%	8	66.7%	4	22.2%	14	77.8%
41 - 50 years	Female	7	50.0%	7	50.0%	7	43.8%	9	56.3%
	Male	4	22.2%	14	77.8%	4	28.6%	10	71.4%
51 - 60 years	Female	14	50.0%	14	50.0%	9	31.0%	20	69.0%
	Male	10	29.4%	24	70.6%	9	29.0%	22	71.0%
> 60 years	Female	15	75.0%	5	25.0%	4	44.4%	5	55.6%
	Male	8	50.0%	8	50.0%	5	25.0%	15	75.0%
Total	**M+F**	**64**	**41.5%**	**90**	**58.4%**	**47**	**30.5%**	**107**	**69.4%**

64 anemic cases identified out of studied 154 T2DM cases are further classified according to gender and age wise distribution. We also wanted to compare the prevalence of anemia of T2DM group to the other non diabetic patients from similar geographical area so we have taken control group of non diabetic patients admitting in same institution. There are 64/154 i.e, 41.6% anemia prevalence is observed in T2DM group as compared to 47/154 controls i.e, 30.5% in non diabetic control group, so the prevalence of anemia is higher in diabetic group as compared to non diabetic group. Age wise distribution observe maximum percentage prevalence of anemic patients falling in age group of >60 years with 15 female and 8 male standing for 75% and 50% respectively. To conclude, the percentage prevalence of anemia among T2DM is increasing with advancing age.

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 08, 2022

Discussion

The present study consisted of 154 cases of T2DM fulfilling the inclusion and exclusion criteria. Here we observed that out of 154 cases 80 are male and 74 are female counting for 51.9 % and 48.1 % respectively with male: female ratio of 1:1.08.Age of the patients studied according to our criteria was 18-65 years, the mean age of cases is found to be 36.46 years in <40 year group,45.97 years in 41-50 year group,56.63 in 51-60 year group and 64.04 year in >60 year group. Overall mean age in T2DM group was found to be 53.0065 years with SD of 9.74 years. The maximum number of patients 62(40.2%) belong to age group of 51 to 60 years. The prevalence of anemia in patients with T2DM is significantly higher (41.6%) as compared to non-diabetic population attending the same hospital (30.5%). The mean hemoglobin is also found lower in T2DM group (12.22g/dl) this result of higher prevalence of anemia in T2DM is also found consistent with many previous studies. Anemia is more common in diabetic group including both men and women; the percentage of anemia in women with T2DM is more than men. There are (38/64) female found anemic out of 64 overall anemic patients with T2DM hence female constitute 59% of anemic cases as compared to (26/64) male anemic patients out of 64 overall anemic patients with T2DM constituting 41.6%, many previous studies also found the similar result. In another study on anemia in same geographical area but on adolescent girls of different economical sections, it was found that the prevalence of anemia increases after the age of 14 years specially the severe anemia rises from 0.7% in <14 years to above 5.2% in >14 years and moderate anemia increases from 9.2% in below 14 years to 21% in above 14 years in middle income group. This study also tells us that the higher prevalence of anemia in above 14 years of female can be due to the menstruating effect with low dietary intake of iron and vitamin C with high fiber diet which limits the bioavailability of iron. Hence this results supports that female gender of child bearing age is can have higher percentage of anemia[5].

We also categorized diabetic patients according to their HBA1c in to good ,moderate and poor control groups based on HBA1c values of <7%,7-8% and >8% respectively and further studied the prevalence and type of anemia in these groups. Out of 154 T2DM cases when categorized based on their HBA1C levels in to good, moderate and poor controls,(22/154) found with good control, (28/154)are found with moderate control group and (104/154) found to have poor glycemic control. When anemia is studies further in these individual groups the result shows (5/22) 22.7% are anemic in good glycemic control group,(9/28) 32.1% are found anemic in moderate control group and (50/104) 48.1% are found anemic in poor control group. We found the percentage prevalence of anemia increases from good control to poor control group, as the HBA1c rises the percentage prevalence of anemia rises and mean hemoglobin falls.

Other observation is those with poor glycemic control has higher percentage of severe anemic patients, thus severity and prevalence both increases with poor glycemic control. This is found consistent with previous studies. According to the Nigerian study, patients who have poorly controlled diabetes were at greater risk of anemia than those with controlled diabetes and diabetic autonomic neuropathy occur early in poorly controlled diabetes mellitus which partly control the erythropoietin production and hence erythropoietin production could be prematurely impaired in patients with poor glycemic control. Out of the 154 cases if T2DM on basis of MCV, 106 are normocytic, 43 are microcytic and 5 are macrocytic. When anemia is studied among these groups based on MCV it is found that 16/106 of normocytic group are anemic, similarly 43/43 of microcytic group are anemic and 5/5 of macrocytic group are anemic. We understand from the above values that most non anemic patients of T2DM have normocytic RBC size however all those with abnormally smaller or larger sized RBC are anemic[6-8].

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 08, 2022

In our study we also found the most common type of anemia in diabetic group is microcytic anemia (43/ 64) are microcytic. This higher prevalence of microcytic anemia could be due the fact that the prevalence of anemia in the studied population without diabetes is also 30.5% as found in our control group and the predominant type of anemia in the population is found as microcytic. The prevalence of anemic in T2DM group is 41.6% which is approximately 11% higher to the anemia found in general population inhabiting same geographical area. There is increase of normocytic anemic cases in T2DM as compared to population without T2DM. However, microcytic anemia remains the most prevalent anemia in diabetic group as well. Recent analyses of the National Health and Nutrition Examination Survey IV suggest that up to 50% of patients with CKD stages 2–5 have absolute or relative (functional) iron deficiency[9-11].

Similar to the correlation established between age and anemia in T2DM in our study, the duration of illness with T2DM also correlates significantly with prevalence of anemia. It is observed in our study that anemia is more prevalent in T2DM patients with longer duration of illness, we classified all patients on the basis of duration of illness in to three groups <5 years, 5-10 years and more than 10 years. There are 18/60 cases in <5 years of duration of T2DM having group specific anemia prevalence of 18 %, the other group for 5-10 year duration contains 34/74 cases with anemia prevalence of 45.9% and the last group of more than 10 year duration of illness contains 12/19 cases having group specific anemia prevalence of 63.2%.from the above result it is clear that as the duration of illness increases the prevalence of anemia also increases. However no conclusion can be drawn on severity of anemia with the duration of illness. According to a study the proposed cause of anemia in elderly diabetics could be decreased responsiveness of the erythroid precursors. The same study also conclude that anemia prevalence increases with age which is consistent with our study and point out that this higher prevalence of anemia in elderly should not be taken as a inevitable property of age because 80% cases in anemia with elderly population can find a cause and if treated can improve the quality of life and probably decrease the mortality among elderly diabetic anemics. Mounika et al and Choi et al also conclude that anemia in T2DM increases with age and severity[12-14].

Conclusion

The prevalence of anemia is more in T2DM patients as compared to non diabetic patients, even higher among female of child bearing age. Prevalence of anemia is found to be rising with increasing age. Prevalence of anemia is found to be more with poor glycemic control (i.e. higher the HBA1C more the number of anemic cases), also the severity of anemia follows similar pattern. The prevalence of anemia is also found to be related to duration of diabetes mellitus type 2. The most common type of anemia associated with T2DM as microcytic followed by normocytic least common is macrocytic. Screening of anemia and its typing in T2DM with supplementation and correction of hemoglobin according to the type of anemia in T2DM is recommended in order to decrease and delay of complications and to improve the quality of life.

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ISSN: 0975-3583,0976-2833 VOL13, ISSUE 08, 2022

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