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Original Research Article

Prevalence of Anemia in Type 2 Diabetes Mellitus and its Association with Vitamin B12 Deficiency

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Abstract:

Background: The world's diabetes epicenter is in India nearly 21% of the total new diabetes cases every year are from India, which already has highest number of cases in any country. Since many years ago, vitamin B12 deficiency has been recognized as a significant adverse effect in diabetic patients on metformin for longer than 5 to 10 years. The purpose of this study was to identify the prevalence of anemia in people with type 2 diabetes mellitus (T2DM) and its relationship to vitamin B12 insufficiency brought on by metformin treatment.

Methods: The study comprised 100 males and females with type 2 diabetes mellitus (T2DM). All participants provided blood in tubes without anticoagulant for measurements of Hba1c and Fasting blood glucose. By using automated cell counters, hemoglobin and mean corpuscular volume (MCV) were assessed. Only individuals who presented with macrocytic anemia had their levels of vitamin B12 measured.

Results: Out of 100 patients, 57 were vegetarians. In this study's participant population, anemia was prevalent in 33 (33.0%). A diagnosis of Normocytic Normochromic Anemia was given to 6, Microcytic Hypochromic Anemia to 11, Macrocytic Anemia to 13, and Dimorphic Anemia to 3 (6.98%) individuals. Vitamin B12 levels were checked in these 16 patients who had macrocytic and dimorphic anemia at the time of testing. For 12 patients, the vitamin B12 level was less than 200 pg/ml, whereas for the remaining 4 patients, it was more than 200 pg/ml. On Metformin were 63 individuals.

Conclusion: Our findings imply that treating anemia may play a significant role in preventing other diabetic complications, and as a result, we advise that routine hematological testing and annual testing for Vitamin B12 deficiency be included in the criteria for treating T2DM.

Keywords: Macrocytic Anemia, Type-2 Diabetes Mellitus.

Introduction

Diabetes prevalence is rising alarmingly quickly around the world.1 The world's diabetes epicenter is in India. 80 to 87 million Indians will have diabetes by 2030, while 438 million adults (7.8%) worldwide are predicted to have the disease.[2] The loss of life from premature death among people with diabetes is largest in underdeveloped countries, despite the fact that it is occasionally thought of as the main worry for industrialized countries.[1] According to the Third National Health and Nutrition Examination Survey (NHANES-III), people with diabetes had a double the likelihood of anemia compared to those who had renal impairment from other causes at a similar level.[3] those with diabetes get iron deficiency anemia more frequently than those without diabetes, and the problem is exacerbated in people with impaired renal function.[4] Since many years ago, vitamin B12 deficiency has been recognized as a significant adverse effect in diabetic patients on metformin for longer than five to ten years.[5] Patients with diabetes who are vitamin B12 and/or iron deficient may be at increased risk of developing diabetic retinopathy, nephropathy, neuropathy, and cardiovascular disease. In addition to renal failure, the etiology of red blood cell fragility in diabetes patients is multifaceted and includes aggravation, various insufficiencies, associated immune system diseases, medications, and hormonal changes.[4] Cobalamin, often known as vitamin B12, is a water-soluble vitamin that is essential for neurological health, healthy hemopoiesis, and DNA synthesis.[6] It frequently causes pancytopenia and macrocytic (megaloblastic) anemia, and in severe cases, both. Paresthesia, peripheral neuropathy, and demyelination of the corticospinal tract and dorsal columns (subacute combined systems illness) are among the neurologic consequences of vitamin B12 insufficiency.[7] Neverthe-

less, the proportion of diabetic patients with anemia who do not have renal impairment is rising. There is currently a dearth of information about anemia in diabetics.8 Therefore, the purpose of this study was to identify the prevalence of anemia in people with type 2 diabetes mellitus (T2DM) and its relationship to vitamin B12 insufficiency brought on by metformin use.

Material and Methods

Males and females with type 2 diabetes who visited Sri Krishna Medical College and Hospital in Muzaffarpur, Bihar, from June 2022 to May 2023 made up the study groups.

This study excluded people with type I diabetes, hematological disorders, pregnant women, and smokers.

As a result, all eligible volunteers who met the requirements of the study protocol and gave their written consent to participate in the study. When the hemoglobin (Hb) concentration is below 12 g/dl for females and <13 g/dl for males, according to WHO criteria, anemia should be investigated. We can address the subject of macrocytic anemia if we add mean corpuscular volume (MCV) more than 100fL. On the basis of WHO recommendations, anemia was categorized as mild, moderate, and severe.[9]

Table 1: WHO criteria for diagnosing anemia and grading

Grading	HaemoglobinConcentration
Mild	11- 12.9 g/dl
Moderate	8- 10.9 g/dl
Severe	<8 g/dl

We evaluated the patients and carefully reviewed their clinical histories. EDTA-containing tubes containing 5 ml of the patient's blood were used for the automated cell counter analysis, which also performed a peripheral smear examination and measured MCV and hemoglobin. The peripheral smears were stained with Leishman's reagent.On a peripheral blood smear, which reveals oval macrocytes, hypersegmented granulocytes, and anisopoikilocytosis, these deficits are easily recognized. Red blood cell inclusions in severe anemia may contain Howell-Jolly bodies, Cabot rings, and punctate basophilia. Collection of blood for HbA1c levels and fasting blood sugar levels were assessed in each individual. Blood was drawn into tubes without any anticoagulant.Only individuals who presented with macrocytic anemia had their levels of vitamin B12 measured. Low serum vitamin B12 levels typically less than 200pg per mL (150 pmol/L) along with clinical illness evidence have historically been used to make the diagnosis of vitamin B12 insufficiency.[7]

Results

The study collected data on 100 T2DM patients in total. The distribution of the patients' demographic and clinical traits is shown in Table 1. 63 patients (about 63%) were men. 32 patients were between the ages of 50 and 60, whereas 29 patients were under 50. 39 patients fell under the category of people older than 60. The average age was 56.8. 61 (61%) patients had T2DM for less than 5 years. 13 individuals had a HbA1c of 5.7 to 6.4, whereas the remaining 4 patients had a HbA1c of >6.5. 63 of the 100 patients with diabetes who had already received a diagnosis were using metformin. There were 57 patients on a vegetarian diet.

Table 2: Demographics and clinical characteristics of study population

Variables	N (%)
Gender	M63 (63%), F 37 (37%)
Age	<50=29(29%), 51-60=32(32%), >60=39(39%)
Duration of T2DM	<5 YRS=39(39%), >5 YRS=61(61%)
HbA1c	<5.6=4(4%), 5.7-6.4=13(13%), >6.5=83(83%)
Dietary Habits	Vegetarian= 57(57%), Mixed= 43(43%)
Patients on Metformin	31
Anemia	Present=33(33%), Absent=67(67%)
Vitamin B12	<200 pg/ml=12, >200pg/ml=4

Anemia was prevalent in this study population at 33 (33%; Table 2), with 19 (58.4%) patients having hemoglobin below the recommended level of <11 g/dl, 10 (30.7%) patients having moderate anemia (8–10.9 g/dl), and 4 (12.12%) patients having severe anemia (<8 g/dl). According to WHO standards, patients were evaluated and categorized.[9] Anemia was also carefully examined, with several types identified based on the appearance of the peripheral smear.

Table 3: Classification of anemia based on clinical grading

Grading	N= 33
Mild (female: 11 – 11.9 g/dL; male: 11-12.9 g/dL)	19(58.4%)
Moderate (8-10.9 g/dL)	10(30.7%)
Severe (< 8 g/dL)	4(12.12%)

Among these 33 anaemic individuals, we discovered that 6 (13.95%) had Normocytic Normochromic Anemia, 11 (25.58%) had Microcytic Hypochromic Anemia, 13 (30.23%) had Macrocytic Anemia, and 3 (6.08%) had Dimorphic Anemia. (Table 3). Dimorphic anemia refers to anemias that exhibit both macrocytic and microcytic traits in their morphology. Vitamin B12 levels were checked in these 16 patients who had macrocytic and dimorphic anemia at the time of testing. For 12 patients, the vitamin B12 level was less than 200 pg/ml, whereas for the remaining 4 patients, it was >200 pg/ml.

Table 4: Classification of anemia based on morphology.

Features, Morphology	N=33
Normocytic Normochromic (MCV 80-95 fL, MCH ≥ 27 pg)	6(13.95%)
Microcytic Hypochromic (MCV < 80 fL, MCH < 27 pg)	11(25.58%)
Macrocytic Normochromic (MCV > 100 fL)	13(30.23%)
Dimorphic (Both Macrocytic and Microcytic)	3(6.98%)

Discussion

Our study and those conducted by Thomas MC10, Adejomo BI11, and Thambiah SC[8] are quite similar. Our study population is primarily under 60 years old, which is equivalent to the gender percentage in other studies.

Comparatively to other research, our study found a significant rate of anemia in T2DM (32.5%). The majority of these patients in our study (60.5%) had their T2DM diagnosis more than five years prior, and their glucose management was generally subpar, with a mean FBS of 7.6 mmol/L and a HbA1c of 8.05. This could be the cause. Due to diabetic autonomic neuropathy, poorly managed DM can cause decreased erythropoietin production and release. The autonomic nerve system regulates erythropoietin release and production in part, which raises the possibility that erythropoietin production may be prematurely diminished in individuals with poor glycemic control and diabetic autonomic neuropathy.[11]

Macrocytic anemia was the most common kind (30.23%), whereas microcytic anemia (25.58%), normocytic anemia (13.95%), and dimorphic anemia (6.98%) were less common.

Compared to other research, our study's prevalence of Macrocytic anemia (including dimorphic anemia) at 37.21% was high. B12 deficiency is the most typical cause of macrocytic anemia. B12 deficiency has long been known to be a serious adverse effect in diabetic patients taking metformin for longer than 5–10 years, which 31 (or 69.0%) of the participants in the study did. The absorption of vitamin B12 is hampered by metformin.12 The most used medication worldwide for treating diabetes (often type 2 diabetes) is metformin. It has a fantastic safety profile for the majority of people and an effectiveness that is on par with or greater than several other medications already on the market.4 After starting metformin therapy, vitamin B12 malabsorption and levels may begin to decline as early as the fourth month. Clinical symptoms of a vitamin B12 deficiency, however, may start to show up after 5 to 10 years due to storage in the liver.[13]

Biguanides like metformin hydrochloride reduce type 2 diabetics' fasting and post-prandial glucose levels. It primarily works by enhancing insulin sensitivity and reducing hepatic glucose synthesis.14 Although not all experts agree, using metformin appears to lower blood folate concentrations. This can depend on the population. One of the contributing factors to macrocytic anemia is low folate levels.[15]

Liver, egg yolks, pork, cheese, and other foods are the main sources of vitamin B12.[13] However, in our study, the majority (56.5%) of the participants are vegetarians, which may potentially be a contributing factor in the rise in the number of patients presenting with macrocytic anemia.

Anemia in 46.51% of the patients was Microcytic Hypochromic (including dimorphic anemia), which may have been caused by iron deficiency, which is common in DM and CKD patients. The remaining study participants were Normocytic Normochromic. Due to renal involvement, this kind of anemia can be noticed in people with poorly managed T2DM.

Similar research was conducted in Malaysia by Thambiah SC[8] on 165 T2DM patients. Due to renal dysfunction, 39.4% of patients had anemia, and 80% of these patients had normocytic normochromic anemia.

Thomas SC[10], Adejumo BI[11], and Bharathi K[2] investigated the hematological profile and its

importance in T2DM patients. As a result of renal involvement and reduced erythropoietin production and release brought on by diabetic autonomic neuropathy, the majority of the patients in these investigations had normocytic and microcytic anemia. Renal function loss is significantly associated with an increased risk of anemia. These diabetes consequences are a result of chronic DM that is not well-controlled.

Conclusion

The study helped us re-evaluate the association of Type 2 diabetes mellitus with Vitamin B12 deficiency.

Diabetes is frequently accompanied by anemia. It may be related to poorly managed diabetes that causes renal impairment or due to the use of Metformin that causes Vitamin B12 malabsorption.

The primary care setting should therefore start regular, early monitoring of the Hb level of T2DM. Therefore, supplementation and annual testing for Vitamin B12 insufficiency should be used to treat T2DM. We advise that routine hematological testing be included in the diabetes treatment criteria since treating anemia may play a key role in preventing additional diabetic complications.

References

1. Akhtar SN, Dhillon P. Prevalence of diagnosed diabetes and associated risk factors: Evidence from the large-scale surveys in India. J Soc Health Diabetes 2017; 5:28-36.
2. Bharathi K. Study of hematological profile and its significance in type 2 diabetes mellitus patients. Journal of Diagnostic Pathology and Oncology, 2016;1(1):14-7.
3. Astor BC, Muntner P, Levin A, et al. Association of kidney function with anemia – The Third National Health and Nutrition Examination Survey (1988–1994). Arch Intern Med 2002;162(12):1401–8.
4. Onel AF, Cotorâci1 CA, Răducan D, Trofenciuc NM, Onel C, Popa AR. Metformin and macrocytic anemia. Medical connections 2016;3(43):35-6.
5. Gholoobi A. A Case of Metformin-Related Megaloblastic Anemia Presenting with Palpitation. Patient SafQualImprov. 2015;3(1):234-7.
6. Kibirige D, Mwebaze R. Vitamin B12 deficiency among patients with diabetes mellitus: is routine screening and supplementation justified? Journal of Diabetes & Metabolic Disorders 2013; 12:17
7. Robert C, David L. Vitamin B12 Deficiency. American Family Physician, 2003;67(5):979-86.
8. Thambiah SC, Samsudin IN, George E, Ranjit LK, Saat NS, Hussein Z, et al. Anaemia in Type 2 Diabetes Mellitus (T2DM) Patients in Hospital Putrajaya. Malaysian Journal of Medicine and Health Sciences 2015;11(1):49-61.
9. World Health Organization: Nutritional Anemia: Report of a WHO Scientific Group. Geneva, World Health Org., 1968
10. Thomas MC, Macisaac RJ, Tsalamandris C, Power D, Jerums G. Unrecognized Anemia in Patients with Diabetes. Diabetes Care 2003; 26:1164–9.
11. Adejumo BI, Dimkpa U, Ewenighi CO, Onifade AA, Mokogwu AT, Erhabor TA, et al.Incidence and risk of anemia in type-2 diabetic patients in the absence of renal impairment. Health 2012; 4:304-8.
12. Sanket K, Swati C. A Study of the Prevalence of Serum Vitamin B12 and Folic Acid Deficiency in Western Maharashtra. J Family Med Prim Care. 2015 Jan-Mar;4(1):64–8.
13. Jeetendra S, Tushar B. Metformin Use and Vitamin B12 Deficiency in Patients with Type-2 Diabetes Mellitus. MVP Journal of Medical Sciences, 2016;3(1):67-70.
14. Cheong B. Metformin: A Differential Diagnosis for Weight Loss, Altered Bowel Habits and B12 Deficiency Anemia in an Elderly. DiabeticMed J Malaysia, 2013;68(5):441-2.
15. Hillson R.Diabetes and the blood–red cells. Practical Diabetes, 2015;32(4):1-2.