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ORIGINAL ARTICLE

Frequency of Anemia and its Types in Type II Diabetes Mellitus Patients without Renal Insufficiency

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ABSTRACT

Background: Diabetes mellitus is one of the most common diseases of twenty-first century. Anemia is 2 to 3 times more common in Diabetic Mellitus patients as compared to normal individuals.

Aims and Objective: We aimed to determine the frequency of anemia and its types in patients with type II diabetes mellitus without renal insufficiency**.**

Methodology: It was an observational study done at the Medicine department of Nishtar Medical University and Hospital Multan for six months from December 2021 to May 2022. We included 200 diabetic patients aged between 18 to 80 years. All the patients had normal renal function test with the duration of diabetes being more than one year. Men with HB level < 13.0g/dL and women with a HB level < 12.0g/dL were considered to have anemia. Data was collected through a structured proforma. SPSS version 20.0 was used for data analysis.

Results: Out of 200 patients, there were 118 (59%) females and 82 (41%) males. The mean age of patients was 49.64±13 yrs (25-79 yrs.), the mean duration of diabetes was 5.98±4.65 (1-25 years), mean hemoglobin level was 11.97±2.3 mg/dl (7-16mg/dl) and mean MCV was 86.7±9.5 (64-110). Seventy-eight (39%) had anemia, and the remaining 122 (61%) patients were non-anemic. Out of 78 anemic patients, 33 (42.3%) had microcytic anemia, 33 (42.3%) had normocytic anemia and 13 (16.6%) had macrocytic anemia. 108 (54%) had controlled diabetes mellitus and 92 (46%) had uncontrolled diabetes mellitus. There were 52 (66.7%) anemic patients with uncontrolled diabetes and 26 (33.3%) with controlled diabetes (P-value= 0.000).

Conclusion: We concluded that diabetics patients without renal insufficiency have a significant risk of anemia. Our findings also revealed that in diabetic patients without renal insufficiency, poor glycemic management, longer disease duration, and old age significantly increase the risk of anemia.

Key words: Anemia, Type 2 Diabetes mellitus, Glycosylated Hemoglobin, Renal insufficiency

INTRODUCTION

Diabetes mellitus is a collection of metabolic abnormalities defined by hyperglycemia and defect in carbohydrate, lipid, and protein metabolism as a result of decreased insulin secretion, action, or both.(1) The global epidemiological data states that the prevalence of diabetes has risen substantially from 108 million in 1980 to 463 million cases in 2019 and is anticipated to rise to 592 million by 2035. Diabetes and its complications claimed the lives of 4.2 million people in 2019. Diabetes mellitus type 2 accounts for 90–95 % of all DM and affects around 7% of the population. It is more common in third world countries. (2,3)

Anemia is common in people with diabetes, especially those with diabetic nephropathy. Diabetes significantly increased the frequency of anaemia, even in patients with maintained renal function. (4) Multiple factors contribute to the aetiology and pathophysiology of anaemia in diabetes. These factors consist of diabetic nephropathy, high levels of advanced glycation end products, iron deficiency, anti-diabetic drugs, diabetic neuropathy, chronic inflammation and decreased testosterone. (6)

Patients with diabetes are deficient in cyanocobalamin, folate, and iron, which can lead to various forms of anaemia. It indicates inadequate nutrition and declining health. (2,7) Anemia in type 2 diabetes is frequently misdiagnosed due to symptoms such as tiredness, pale complexion, chest pain, restlessness, numbness/coldness in extremities, tachycardia, SOB, and headache. Even mild anaemia can have a negative impact on one's quality of life, and untreated anaemia can have substantial poor health consequences. As a result, detecting anaemia in diabetes individuals is important. There is substantial evidence that anaemia increases the risk of diabetes-related macro- and micro-vascular problems. It can aggravate kidney, heart, and artery problems, all of which are more common in diabetic patients than in non-diabetic individuals. (8,9)

Several studies on the occurrence of anaemia in type 2 diabetic patients have been conducted in various regions, but results show that it can range from as high as 63% in Pakistan (10), India 18%. Ethiopia 34%, Malaysia 39%, Cameroon 41.4% and Saudi Arabia 55.5%. (11)

Anemia in diabetic patients with kidney failure is well-documented. The occurrence of anaemia in patients with diabetes prior to renal insufficiency has been studied very little. According to the current recommendations, Type 2 diabetics patients with maintained renal function does not need routine anaemia screening. As a result, anaemia is rarely checked in diabetics with normal renal function. Because of this, studies on the prevalence of anaemia in diabetic patients prior to renal impairment are now essential in raising diabetic patients' awareness and understanding of anaemia and in determining whether screening and treatment policies should be adjusted so that their quality of life and results might be improved.

MATERIALS AND METHODS

It was a cross-sectional observational study done at the Medicine department of Nishtar hospital Multan for six months from December 2021 to May 2022, after taking ethical approval from the IRB committee. A sample size of 200 patients was calculated using the WHO sample size calculator by considering the following parameters: absolute precision as 0.05, power as 80%, and anemia prevalence as 15.3% in diabetic patients with normal RFTs. (12) We included 200 diabetic patients aged between 18 to 80 years. All the patients had normal renal function test with the duration of diabetes being more than one year. We excluded the patients with abnormal kidney functions (s. creatinine ≥ 1.5 mg/dL). Patients with unstable cardiac, neurological, chronic liver disease, or cancers were excluded based on their medical history and records. Patients with a history of peripheral vascular disease, recent blood loss or blood donation, and hemolytic anaemia or hemoglobinopathies were all excluded.

Detailed history regarding the clinical profile including duration of disease, presence of diabetes complication was taken and associated co-morbidities and past medication history of patients was collected from patient's medical records. Blood

samples were collected from the patients under aseptic measures. SST and EDTA bottles were used to collect urea, creatinine and, complete blood analysis, glycated hemoglobin, respectively. The ion-exchange chromatography method was used to check for glycated haemoglobin. Anemia was labelled if male having HB < 13 mg/dl and female having HB < 12 mg/dl as per operational definition [13] The controlled diabetic group comprised of patients having HbA1c <7.5% and patients with HbA1c level >7.5% were labelled as poorly controlled diabetic. [12]

Data was collected through a structured proforma. SPSS version 20.0 was used for data analysis. Mean values were used to represent quantitative data e.g., age and duration of diabetes. Qualitative variables such as sex, anemia, and type were measured as frequency and percentages. The student's -test was used to compare mean values with categorical variables, and the Chi-square test was used to compare categorical variables. A p-value of more than 0.05 was not significant.

RESULTS

Out of 200 patients, there were 118 (59%) females and 82 (41%) males with a ratio of 1.4:1. The mean age of participents was 49.64±13 years (25-79 years), the mean duration of diabetes was 5.98±4.65 (1-25 yrs), mean hemoglobin level was 11.97±2.3 mg/dl (7-16mg/dl) and mean MCV was 86.7±9.5 (64-110). Seventy-eight (39%) had anemia, and the remaining 122 (61%) patients were non-anemic. Among 78 patients, there were 24 (30.7%) male and 54 (69.3%) female (P- value= 0.283). This difference was statistically not significant. Out of 78 anemic patients, 33 (42.3%) had microcytic anemia, 33 (42.3%) had normocytic anemia and 13 (16.6%) had macrocytic anemia. A total of 108 (54%) had controlled diabetes mellitus and 92 (46%) had uncontrolled diabetes mellitus as per operational definition. Among 92 patients with uncontrolled diabetes, 34 (37%) were males and 58 (63%) females. The difference between the two groups was not statistically significant (P > 0.05). There were 52 (66.7%) anemic patients with uncontrolled diabetes and 26 (33.3%) with controlled diabetes. Anemia was more common in patients with glycosylated hemoglobin level > 7.5 (P-value= 0.000).

The mean duration of diabetes among anemic and non-anemic patients was 9.05±4.9 and 4.02±3.15, respectively, indicating that the risk of anemia increases with the increasing the duration of disease (P < 0.05).

Patients with anaemia had a mean age of 58.67±10.67 years, while those without anaemia had a mean age of 43.86±10.92 years. The difference in mean age between patients with and without anaemia was statistically significant (P 0.05). This suggests that anaemia risk increases with age.

Table 1: Gender. distribution… n=200

Gender	Frequency	Percentage
Females	118.	59%
Males	82.	41%
Total	200.	100%

Table 2: Frequency of anemia among diabetic patients. n=200

Anemia	Frequency	Percentages
YES	78	39%
NO	122	61%

Table 3: Frequency of different types of anemia. n=78

Type of anemia	Frequency	Percentage
Microcytic anaemia (MCV < 80 fl)	33	42.3%
Normocytic anaemia (MCV > 80 and < 100 fl)	33	42.3%
Macrocytic anaemia (MCV > 100 fl)	13	16.6%
Total	78	100%

Table 4: Distribution of controlled and uncontrolled diabetes among anemic patients. n=78

Diabetes control	Frequency	Percentage
Controlled	26	33.3%
Uncontrolled	52	66.7%
Total	78	100%

DISCUSSION

Anemia is more prevalent in diabetes patients than in the normal individuals. This study aimed to look at the anemia profile in type 2 diabetes individuals who did not have diabetic nephropathy. Early screening could help us in detecting and treating anemia, which is known as an isolated risk factor for diabetes complication; retinopathy, neuropathy, stroke, and cardiac.

In our study, 39% of patients were found to be anemic. Barbiere et al. reported an incidence of 34.2%. anemia among type 2 diabetic patients, although he also included patients with impaired renal function. [14]. Mahjoub et al. retrospectively analyzed diabetic patients with normal renal profiles and found 41 % of patients with anemia. [15] Both studies reported a similar prevalence of anemia compared to our research. Contrarily, Another study resulted that 7.21% of people with diabetes without diabetic nephropathy were having anemia. [16] Similarly, another study that included a diabetic patient with a normal renal profile reported a very less incidence of anemia, i.e., 15.3%. [12] The higher occurrence of anemia in our study could be attributed to many patients with poorly controlled diabetes. Contrary to our study, some studies stated a very high prevalence of anemia. A study performed in Pakistan reported that 63% of anemic patients with type II diabetes mellitus. [10] In another research, out of 100 patients, 65 patients were anemic. [17] This high prevalence may be attributed to anemia being more evident in patients with decreased renal functions, as both of these studies included CKD patients.

Overall mean age of participants was 49.64±13 yrs. (25-79 years). Krishnamurthy et al. the mean age 53.4±13.6 years in their study. [4] Another study reported an almost similar mean age of 55.5 years ± 13.87. [18] We reported that the mean age of participant with anemia was 58.67± 10.67 years and without anemia was 43.86±10.92 yrs (P < 0.05). The difference in mean age indicates that the incidence of anaemia increases with age.

Out of 78 anemic patients in our study, we found 30.7% male and 69.3% female—the female to male ratio of 2.3:1. Similarly, Mahjoub et al. reported that out of 18 patients with anemia, there were more females (77.8%) than males (22.2%). [15] Solomon et al. reported that the frequency of anemia in both genders was almost the same, i.e., 19.01% and 21.1% in males and females, respectively. [19] Past studies reported occurrence of anemia in males upto 17%- 69% and in diabetic females, 11-30%. [20,21] Females, on the other hand, were more likely to suffer from anaemia than males, according to our findings. Because this study was carried out in Pakistan, where gender inequality, illiteracy, a lack of permission to make health decisions, poor diet, and a preference for men over women's health may be to blame for the higher incidence of anaemia in females.

Joshi et al. reported that microcytic anemia was most common 55.5% followed by normocytic anemia 28% and macrocytic anemia 16.8%. [22] Malnutrition, iron insufficiency, and poverty were likely factors in the greater prevalence of microcytic hypochromic anemia in diabetes mellitus. Similarly, we found that 42.3% each had microcytic and normocytic anemia, and 16.6% had macrocytic anemia. Another study testified that normocytic anemia was the most common anemia among diabetic patients 64.4%, followed by microcytic anemia 31.2%. [18] Solomon et al. resulted that among anemic patients, 81.4% had the normocytic hypochromic type of anemia. [19] According to prior research, long-term poorly controlled diabetes in patients without abnormal RFTs was linked to normocytic normochromic anemia. [23] The differences in the above results may be attributed to different populations included in the studies.

We reported that the mean duration of diabetes among anemic and non-anemic patients was 9.05±4.9 and 4.02±3.15, respectively. This indicates that the risk of anemia rises as the disease progresses (P < 0.05). According to another study, 25 % of patients with diabetes for one year had anemia, 51.6 % of diabetics for one to five years had anemia, and 64 % of diabetics for six to ten years had anemia. [18] One hypothesis proposed that persistent hyperglycemia enhances glycation-mediated regulation

of transferrin receptors, limiting receptors' ability to bind iron and diminish iron availability. [4] Rathod et al. found that people with diabetes for > five years were twice as likely to develop anaemia as those with diabetes for < 5 years. [24]

In our study, there were 52 (66.7%) anemic patients with uncontrolled diabetes and 26 (33.3%) with controlled diabetes (P-value= 0.000). In a study, out of 11 diabetic patients with anemia, 10 patients had poorly controlled diabetes [12] Similarly, Sharif et al. concluded that there were 49.5% anemic patients had HbA1C >7.5% and 13.5% had HbA1C < 7.5%. [10] It was more common in patients with glycosylated hemoglobin level > 7.5 and this difference was statistically significant. Mechanisms behind anemia risk in poorly controlled diabetes are unclear. Patients having chronic diabetes, obesity, dyslipidemias, patients on a combination of oral hyperglycemic drugs and insulin, sedentary lifestyle, poor compliance to medications, patients who do not follow proper diet chart and perform regular monitoring of glucose are more liable to poor diabetes control. Poor management of diabetes causes diabetic autonomic neuropathy. Since the autonomic nervous system partly regulates erythropoietin production, the results suggest that patients with poor glycemic control may have prematurely impaired production. Systemic inflammation, persistent hyperglycemia and diabetes-induced low testosterone levels also enhance the risk of anaemia. [25,26]

CONCLUSION

In conclusion, patients with type 2 diabetes mellitus having normal renal function tests renal have a substantial risk of developing anemia. Our findings also revealed that in diabetic patients with poor glycemic management, longer disease duration, and old age significantly increase the risk of anemia. If we timely address the anemia among diabetic patients, it may prevent diabetic complications. We believe that routine anaemia screening should be a part of the treatment criteria for diabetes.

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