MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.59218/makrjms.2023.10.57.61

OPEN ACCESS

Key Words
Anemia, diabetes mellitus, HbA1C haemoglobin

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Received: 20 September 2023
Accepted: 7 October 2023
Published: 8 October 2023

Citation: Sudhangshu Majumder, Hema Malathi Rath, Subhashis Chakraborty, Biva Bhakat, Prantik Bhattacharya and Debarshi Jana, 2023. Evaluation of Anemia with Age and Duration of Diabetes in Type 2 Diabetes Mellitus: A Study in a Tertiary Care Hospital of Eastern India. Res. J. Med. Sci., 17: 57-61, doi: 10.59218/makrjms.2023.10.57.61

Evaluation of Anemia with Age and Duration of Diabetes in Type 2 Diabetes Mellitus: A Study in a Tertiary Care Hospital of Eastern India

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ABSTRACT
One of the major non-communicable illnesses with significant morbidity and consequences, diabetes mellitus has emerged as a major worldwide health issue. The diverse range of environmental and genetic etiologies that cause diabetes mellitus result in a state of chronic hyperglycemia, which over time causes substantial harm to the heart, blood vessels, eyes, kidneys and nerves. People with type 2 diabetes typically have relative (as opposed to absolute) insulin insufficiency as well as insulin resistance (IR). To identify the types, prevalence and risk factors for anemia in people with type 2 diabetes mellitus, as well as the anemia among these people's risk factors. This cross-sectional analytical investigation was conducted in a hospital. The study was carried out at the N.R.S. Medical College, Kolkata over a one year period from July 2022 to June 2023. This study included 240 patients. More than two thirds (67.1%) of the subjects had an HbA1C% control status. According to the FBG and PPBG levels, control status was attained in 65.4 and 47.1% of the subjects, respectively. For the PPBG levels, it was discovered that the control status was poor. Anemia was present in one out of every five T2DM patients, even in those with acceptable eGFR values, indicating normal renal function. A minor form of anemia was present in the majority of the individuals. The normocytic normochromic anemia was the most common form morphologically.

INTRODUCTION

One of the major non-communicable illnesses with significant morbidity and consequences, diabetes mellitus has emerged as a major worldwide health issue. The diverse range of environmental and genetic etiologies that cause diabetes mellitus result in a state of chronic hyperglycemia, which over time causes substantial harm to the heart, blood vessels, eyes, kidneys and nerves. People with type 2 diabetes have both relative (as opposed to absolute) insulin insufficiency and insulin resistance (IR).

One of the greatest issues facing humanity in the 21st century is the global diabetes epidemic. Diabetes mellitus has become a significant public health issue on a global scale in recent decades[1]. The prevalence of diabetes is rising, according to studies done in various contexts[2]. The bulk of the approximately 422 million individuals with diabetes globally reside in low- and middle-income nations and diabetes is directly responsible for 1.6 million annual fatalities. By 2035, it's predicted to reach 592 million. According to statistics from the World Health Organization, diabetes was the sixth most common cause of death in 2016. Diabetes-related premature mortality increased by 5% between 2000 and 2016[3].

India has the highest percentage of diabetic patients worldwide, according to reports from the World Health Organization (WHO). Diabetes affects 88 million people in the South East Asian region and that number is expected to rise to 153 million by 2045[4]. In India, 8.9% of people aged 20-79 have diabetes mellitus, which currently affects 77 million people and is anticipated to reach 123.5 million people by 2040[5]. The rapid epidemiological change, which was followed by urbanization and socioeconomic development, is blamed for the rise.

Type 2 diabetes mellitus typically manifests at age 42.5. Every year, diabetes claims about a million lives in India. According to an analysis by the American Diabetes Association, India would experience the largest rise in the number of diabetics receiving a diagnosis by the year 2030[6].

Typical signs and symptoms of diabetes mellitus include thirst, polyuria, blurred eyesight and weight loss. Ketoacidosis or a non-ketotic hyperosmolar state may occur in its most severe stages, which may cause stupor, coma and in the absence of adequate treatment, may result in death. Because symptoms are frequently mild or nonexistent, hyperglycemia that is severe enough to induce pathological and functional abnormalities may exist for a considerable amount of time before the diagnosis is made.

MATERIALS AND METHODS

Study design: A hospital based cross sectional analytical study was conducted among the type 2 diabetic mellitus patients in the department of General Medicine and Cardiology, NRSMCH, Kolkata.

Study duration: The study was conducted for a period of one year from July 2022 to June 2023.

Study population: All consecutive patients attending at Medicine outpatient clinic, Cardiology clinic and admitted in medicine and Cardiology ward during the study period with diagnosis of type 2 diabetes mellitus.

Inclusion criteria: Patients with type 2 diabetic mellitus aged 30 years and above attending Medicine outpatient clinic, cardiology clinic and admitted in medicine and Cardiology ward will be included in the study.

Exclusion criteria

Patients (with/who):

- Type 1 diabetes
- Known hematological disorders
- Known CKD with causes other than diabetes mellitus
- Comorbidity like congestive cardiac failure and chronic liver disease
- Malignancy
- Acute illness/critically ill
- Have undergone major surgeries/blood loss and Undergone blood transfusion
- Pregnant
- Iron deficiency anemia/treatment for anaemia
- On ACE inhibitors

RESULTS

Diabetes was present for an average of 5.8 (3.0) years, ranging from 1 year to a maximum of 18 years. The average time span was 6 (3-8) years (Table 1).

More than two thirds (67.1%) of the subjects had an HbA1C% control status. According to the FBG and PPBG levels, control status was attained in 65.4 and 47.1% of the subjects, respectively. For the PPBG levels, it was discovered that the control status was poor (Table 2).

The median creatinine level was 0.9 (0.3) mg dL^{-1}, ranging from 0.4-1.9 mg dL^{-1}. Eight patients had a creatinine clearance of less than thirty. In 9 patients, proteinuria was 2 or higher (Table 3).

11.3% of type 2 diabetes mellitus patients had retinal disease. In the study's participants, non-proliferative diabetic retinopathy affected 8.0% while proliferative diabetic retinopathy affected 3.3% (Table 4).

Table 1: Clinical profile of the participants

Duration of diabetes mellitus (years)	Frequency	Percentage
Mean (SD)	5.8	2.8
Median (IQR)	6.0	3-8
Type of treatment		
Oral hypoglycaemic drugs	170	70.8
Oral hypoglycaemic drugs+insulin	61	25.4
Insulin	9	3.80

Table 2: Distribution of participants by control status

Control status	Frequency	Percentage
HbA_1C		
Under control ($HbA_1C \leq 7.0\%$)	161	67.1
Not under control ($HbA_1C > 7.0\%$)	79	32.9
Fasting blood glucose (mg dL^{-1}) n (%)		
Under control (80-130)	157	65.4
Not under control (>130)	83	34.6
Post prandial blood glucose (mg dL^{-1}) n (%)		
Under control (<180)	113	47.1
Not under control (180 and above)	127	52.9

Table 3: Distribution of participants by their renal function

Creatinine level (mg dL^{-1})	Frequency	Percentage
Mean (SD)	0.9	0.3
Creatinine clearance (Cockcroft-Gault formula)		
≤30	8	3.3
31-60	50	20.8
61-90	107	44.6
>90	75	31.3
Proteinuria		
Trace	155	64.6
1+	76	31.7
2+ or more	9	3.8

Table 4: Distribution of participants by type of anaemia

Type of anaemia	Frequency	Percentage
Microcytic hypochromic	40	56.3
Normocytic normochromic	169	43.7

Table 5: Association of type of treatment with Haemoglobin level

	Haemoglobin level (%)		
Type of treatment	Mean (g)	SD (g)	*p-value
Oral hypoglycaemic drugs	13.4	1.4	<0.001
Oral hypoglycaemic drugs+insulin	12.3	1.7	
Insulin	10.9	1.1	

Table 6: Macrovascular complications among the study participants (N = 240)

Macrovascular complication	Frequency	Percentage
Hypertension		
Yes	65	27.1
No	175	72.9
Coronary artery disease		
Yes	22	9.2
No	218	90.8
Cerebral-vascular accidents		
Yes	14	5.8
No	226	94.2
Peripheral arterial disease		
Yes	10	4.2
No	230	95.8

When compared to patients solely receiving oral hypoglycemic medications, patients receiving insulin therapy alone had lower mean hemoglobin levels than patients receiving both insulin and oral hypoglycemic medications and this difference was determined to be statistically significant. The significance was present between each category on post-hoc analysis with Bonferroni adjustment (Table 5).

Hypertension was present in 28.1% of the participants. Coronary artery disease, cerebro-vascular accidents and peripheral arterial disease was reported by 9.2, 5.8 and 4.2% of the patients with tyoe-2 diabetes mellitus, respectively (Table 6).

DISCUSSIONS

Diabetes mellitus (DM), a metabolic illness, has a significant global effect. Anemia is a prevalent occurrence among people with diabetes mellitus who also have renal insufficiency, although anaemia is inevitable in all patients. Anemia has a substantial impact on a diabetes patient's quality of life and is linked to the development of complications. However, until the issue manifests, the haemoglobin reading is often disregarded. Therefore, this study was required to examine the truth, which would aid in our better comprehension and, ultimately, better management of diabetes problems.

The patients in our research had a mean age of 57.1 (6.6) years and 2/3 of the participants were between the ages of 41 and 60. The findings of our investigation are consistent with numerous other studies carried out throughout the world[7-10]. This discovery suggests that the patients may have been afflicted much earlier in their lives or that there may have been a delay in diagnosis, both of which raise the risk of problems. It may be claimed that because of this, it was crucial that the study be carried out with the key goal of averting the difficulties at an earlier stage.

A bit in contrast to the research that is currently accessible, which mostly suggests that the condition is either equal among males and females or somewhat greater in males, almost two thirds (63.3%) of the participants were females with a M:F of 0.58:1[7,11]. It's unknown why the aforementioned observation was made.

According to our study, there were 36.3% of overweight individuals and 27.0% of obese participants. Our study discovered no correlation between anemia and BMI status, in contrast to the findings of other studies, which reported a greater incidence of anemia among people with higher BMI[12,13]. The widely held and accepted theory is that obesity, a high body mass index (BMI) and a large waist circumference are all associated with anemia in diabetes individuals. The establishment of an inflammatory state that predisposes to the development of insulin resistance is linked to obesity or the buildup of circulating fatty acids. Particularly in adipocytes and muscle cells, where glucose absorption is mediated by insulin, insulin resistance lowers glucose tolerance. As a result, there is an increase in blood glucose levels and a hyperglycemic condition. The increased inflammatory activity in obese individuals' adipose tissue encourages the creation of hepcidin, which is enhanced during infection and inflammation in chronic disease-related anemia and lowers blood iron levels through a mechanism that restricts the availability of iron. Numerous researchers have frequently proven the link between increased iron

reserves and diabetes and insulin resistance. The improved control status within our research population may be a contributing factor to the observed result in our investigation.

Anaemia was more common (and much more prevalent) among people with hypertension and coronary artery disease (p<0.001). Given that hypertension in diabetics raises the risk of cardiovascular problems such heart failure, stroke, tissue inflammation and atherosclerosis, this link is concerning[14].

With a minimum of 1 year and a maximum of 18 years, diabetes was present on average for 5.8 (3.0) years. More over two thirds (67.1%) of the subjects had a HbA1C control status. According to the FBG and PPBG levels, control status was attained in 65.4% and 47.1% of the subjects, respectively. The PPBS levels were determined to have a low control status. In comparison to our study, several other investigations found rather low control status[15]. The discovery may have been made by chance or as a result of greater drug adherence. Another explanation might be that our research population's mean duration of diabetes was 5.8 years, which is less than in previous studies.38,56,91. Since the patients in our research were chosen through purposive sampling, this may have been the result of selection bias.

11.3% of type 2 diabetes mellitus patients had retinal disease. In the study's participants, non-proliferative diabetic retinopathy affected 8.0% while proliferative diabetic retinopathy affected 3.3%. In 30.4% of the individuals with type 2 diabetes, dyslipidaemia was found.

Type-2 diabetes mellitus patients had an anaemia prevalence of 29.6% (95% CI: 23.9-35.9%). According to certain research carried out in many nations, this is the case. Nevertheless, two investigations carried done in rich nations. Thomas *et al*.[11] has found that individuals with type-2 diabetes had a lower frequency of anemia. These variations could be brought on by variations in the country's level of development, which has an impact on the quality of health care delivery, ethnicity, age of study participants, duration of DM and geographical elevation above sea level. Surprisingly, our study's findings were significantly lower than those of several other studies carried out in India, which indicated that anaemia prevalence ranged from 38.0-74.0%[9,16]. It is important to take this data seriously since it raises the potential that our population's lower prevalence was caused by a lower mean duration of diabetes mellitus, which may have happened as a result of selection bias.

Anemia of inflammation or infection, also known as mild-to-moderate anemia, is frequently present in patients with chronic diseases like diabetes. The findings of the authors of Anemia of Chronic Disease show that diabetic individuals with anemia express more proinflammatory cytokines than those with only diabetes. Increased IL-6 synthesis and B cell activity were seen in an anemic patient, supporting the link between IL-6 production and antierythropoietic activity. Additionally, the diabetic and anemic patients had high levels of C-reactive protein and ferritin ultrasensitive but these patients had low iron contents, demonstrating that ferritin elevations were linked to the chronic inflammatory process seen in diabetes.

Microcytic hypochromic anemia was observed in 56.3% of the participants among the anemic patients, whereas normocytic normochromic anemia was prevalent in 43.7% of the individuals. The term ACD is used to describe this behavior. ACD is a mild to severe anemia that reduces red blood cell survival from 120-80 days. The cause of this phenomena is thought to be the hyperactive condition mononuclear phagocyte system, which is brought on by an inflammatory, infectious, or malignant process and causes the early elimination of circulating red blood cells. The main causes of the reported inadequate bone marrow response include improperly low erythropoietin secretion, a diminished bone marrow response to erythropoietin and decreased erythropoiesis as a result of a reduced iron availability to the bone marrow. This explanation may be the cause of the phenomena that led to identical findings in other investigations[17].

Age, the length of diabetes, the kind of therapy and the hemoglobin level all had a negative link that was statistically significant (p<0.001). FBG and PPBG significantly correlated negatively with the research participants' hemoglobin levels. HbA1C did not, however, correlate with hemoglobin levels. The patients' anemic condition significantly correlated with both proteinuria and creatinine clearance. The incidence of anemia did not, however, significantly correlate with peripheral artery disease or cerebral vascular accidents (p>0.05).

The fact that the study was conducted on a randomly selected population sample allowed the results to be extrapolated to similar environments, which is one of its key strengths. One of the drawbacks of our study, as with many previous cross sectional studies, might be the inability to determine the cause-and-effect link. Additionally, there is a probability that selection bias contributed to our research population's higher control status but this is not definite because it is always possible that better compliance contributed to the better control status.

CONCLUSION

With a M:F ratio of 0.58:1, the 240 patients had a mean age of 57.1 (6.6) years and were approximately two thirds female. Diabetes was present on average

for 5.8 (3.0) years. More over two thirds (67.1%) of the subjects had a HbA1C control status. According to the FBG and PPBG levels, control status was attained in 65.4 and 47.1% of the subjects, respectively. Type-2 diabetes mellitus patients had an anaemia prevalence of 29.6% (95% CI: 23.9%-35.9%). Microcytic hypochromic anaemia was seen in 56.3% of the participants among the anemic individuals. 11.3% of people with diabetes had diabetic retinopathy, of which 8.0% had non-proliferative diabetic retinopathy. Thirty.4% of the patients had dyslipidemia and 28.1% had hypertension. 9.2, 5.8 and 4.2% of patients with type-2 diabetes reported having coronary artery disease, strokes, or peripheral arterial disease, respectively. Age, the length of diabetes, the kind of therapy and the hemoglobin level all had a negative link that was statistically significant ($p<0.001$). FBG and PPBG significantly correlated negatively with the research participants' hemoglobin levels. The patients' anemic condition significantly correlated with both proteinuria and creatinine clearance. Patients with coronary artery disease, hypertension and diabetic retinopathy had a greater frequency of anemia ($p<0.05$). Therefore, even in the absence of renal involvement, diabetics should have routine anemia screenings since anemia might raise the risk of cardiovascular disease. A large multicenter research with a longitudinal follow up is also required. The diabetic population must be made aware of the danger of anemia and other consequences of diabetes at the time of their diagnosis.

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