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RESEARCH ARTICLE

COMPARATIVE STUDY OF ANAEMIA WITH THE DEGREE OF GLYCAEMIC CONTROL IN TYPE 2 DIABETES MELLITUS IN BANGLADESHI POPULATION

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ABSTRACT

Introduction: Anemia is defined as a reduction in the hemoglobin concentration of blood, which consequently reduces the oxygen-carrying capacity of red blood cells such that they are unable to meet the body's physiological needs. Several reports have indicated that anemia mostly occurs in diabetic patients with renal insufficiency while limited studies have reported the incidence of anemia in people with diabetes prior to evidence of renal impairment. Other studies have also identified anemia as a risk factor for the need for renal replacement therapy in diabetes. Understanding the pathogenesis of anemia associated with diabetes may lead to the development of interventions to optimize outcomes in these patients. The aim of this study was therefore to determine the prevalence of anemia among patients with type 2 diabetes mellitus (T2DM).

Methods: A total of 400 (250 with type 2 diabetes and 150 non diabetic subjects) participants were recruited for our study. Participants' blood samples were analyzed for fasting blood sugar, complete blood count (CBC) and renal function tests among others. The prevalence of anemia was then determined statistically.

Results: A high incidence of anemia was observed in the cases. Of the patients with diabetes, 84.8 % had a hemoglobin concentration that was significantly less (males 12.3±1.71 and females 11.38±1.64) than the non diabetic subjects (males 13.8±1.40 and females 12.0 ±1.41). Renal insufficiency determined by serum creatinine level of >1.50 mg/dL, estimated glomerular filtration rate (eGFR) <60 ml/minute/1.73m^2. A significantly increased fasting blood sugar, glycated hemoglobin (HbA1c), urea, creatinine were observed in the cases (9.44±3.57, 8.29±1.61, 36.6±29.6, 1.67±1.30 respectively) as compared to the Non diabetic subjects (4.77±0.56, 5.2±0.48, 23.3±17.7, 1.18±0.44 respectively). Finally, a significant association between hemoglobin concentration and fasting blood sugar was also observed in the T2DM.

Conclusions: The findings suggest that a high incidence of anemia is likely to occur in patients with poorly controlled diabetes and in patients with diabetes and renal insufficiency.

INTRODUCTION

Diabetes mellitus (DM) is a non-infectious disease that also has a high prevalence worldwide. It is a carbohydrate metabolism disorder which results in hyperglycemia due to either absolute insulin deficiency or reduced tissue response to insulin or both (Whiting, 2011). Diabetes, especially when poorly controlled, leads to complications such as nephropathy, retinopathy, and neuropathy as well as several disordered metabolic processes including oxidative stress which causes oxidative damage to tissues and cells (Comazzi, 2004). Anemia is the most common blood disorder and a common finding in patients with diabetes. It is also considered as a key indicator of chronic kidney disease and an important cardiovascular risk factor (Thomas, 2004). Anemia is more frequent and more severe at any level of glomerular filtration rate (GFR) in diabetics compared to nondiabetic patients (Astor, 2002 and Dikow, 2001).

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The pathogenesis of anemia in diabetes includes deficiency in erythropoietin synthesis and release, systemic inflammation, iron deficiency and chronic anemia results in tissue hypoxia, which is known to play a key role in diabetes-associated organ damage. Recent reports have suggested that anemia is an important risk factor for progression to end- stage renal disease (ESRD) in patients with chronic kidney disease, with or without diabetes (Thomas, 2004; Griac, 2007). It is therefore important to diagnose and correct anemia. The aim of this study was to determine the prevalence of anemia in type 2 diabetics and to assess its association with other variables.

MATERIALS AND METHODS

This case control study was carried out in the department of laboratory, US- Bangla Medical College Hospital from May 2016 - July 2016. A total 400 subjects of aged 30-60 years were selected purposively from the outpatient department of hospital. Patients suffering from hemoglobinopathies, iron deficiency anemia, hemolytic anemia and pregnancy were excluded from the study. Data were collected including

demographic characteristics and clinical history by utilizing a pre-designed questionnaire and were collected by direct interview from participants. Relevant physical examinations were performed on all participants. With all aseptic precaution about 5 ml blood and spot urine was collected from all of the subjects. Serum was separated after centrifuging at 3000 rpm for 10 minutes. The serum obtained and were separated. Blood glucose-both fasting and ABF, HbA1C, creatinine, eGFR, urea, CBC, iron profile level were obtained in all participants. HbA1C was estimated in whole blood by a BIO-RAD variant which was modified HPLC method.

Hemoglobin was estimated by cell counter SYSMEX XS-800i through cyanmethemoglobin method. Diabetes was diagnosed by HbA1C >6.5%. Serum creatinine values were considered abnormal if values were >1.50 mg/dL and considered as chronic kidney disease.

Definition for anemia is hemoglobin values <13.0 g/dl for male and <12.0 g/dl for female (Yun, 1999). Statistical analyses were performed with the SPSS version 21.0. Data expressed as mean (±SD) or median (range) if the variables were continuous and as percentage, if categorical.

RESULTS

Participants' demographics

The study included 400 participants, consisting of 250 participants with T2DM (115 males/135 females) and 150 participants are non diabetic subjects (68 males/82 females) who consented to participate in the study (Table 1). Mean ages recorded for cases and non diabetic subjects were 51.5±14.3 years and 43.1±10.1 years respectively. The medical records of the participants were examined and they were taken through a physical examination for signs and symptoms of anemia. However, none of them showed any signs of anemia, possibly due to the fact that there may be no symptoms in some people who have anemia. Other diseases such as cancer and myelodysplasia as well as other causes of anemia as discussed in the introduction were ruled out among the study group. Table 2 shows the hematological parameters of the blood samples we analyzed that were obtained from the study participants. Hemoglobin concentration was observed to be significantly decreased in the cases as compared to the non diabetic subjects. Ferritin and total iron-binding capacity (TIBC) levels were found to be normal in most of the cases and

Table 1. Summary of demographic characteristics of participants with diabetes (cases) and Non diabetic Subjects as Non diabetic subjects

Parameters	Type 2 Diabetes Mellitus (T2DM)	Non Diabetic Subjects
n	250	150
Male/Female	115/135	68/82

Table 2. Hematological parameters in participants with diabetes (cases) and Non diabetic subjects

Parameters	Type 2 Diabetes Mellitus (T2DM)	Non Diabetic Subjects	p value
Hb			0.000*
Male (13.5-17.5 g/dl)	12.3±1.71 (m)	13.8±1.40 (m)	
Female (12.0-16.0 g/dl)	11.38±1.64 (f)	12.0 ±1.41 (f)	
MCV (80–95 fL)	83.81±8.84	83.0±5.87	0.000*
Ferritin			0.000*
Male (20–200 µg/L)	78.53±37.63 (m)	104.90 ±27.44 (m)	
Female (20–120 µg/L)	70.90±34.00 (f)	72.82±33.38 (f)	
Iron (8.0-27.0 µmol/L)	6.9±5.8	19.9±4.5	0.0003
TIBC (255–450 µg/dl)	320.27±65.4	288.01±91.93	0.000*

Hb hemoglobin, MCV mean cell volume, TIBC total iron-binding capacity (*p value <0.05 was considered significant)

Table 3. Biochemical parameters in participants with T2DM and non diabetic subjects

Parameters	Type 2 Diabetes Mellitus (T2DM)	Non Diabetic Subjects	p value
FBS (3.8–6.1 mmol/L)	9.44±3.57	4.77±0.56	0.000*
HbA1c (4–7 %, 7–8 %, ≥8.5 %)	8.29±1.61	5.2±0.48	0.000*
Creatinine (0.6–1.5 mg/dL)	1.67±1.30	1.18±0.44	0.000*
Urea (7–18 mg/dL)	36.6±29.6	23.3±17.7	0.001*
eGFR			0.000*
Female	56.7±23.9	64.2±15.2	0.000*
(80–110 ml/minute/1.73 m^2)	42.9±16.2	79.69±32.5	
Male			
(90–120 ml/minute/1.73 m^2)			

eGFR estimated glomerular filtration rate, FBG fasting blood glucose, HbA1C glycated hemoglobin (*p value <0.05 was considered significant)

Table 4. Incidence of renal insufficiency in T2DM and non diabetic subjects

Present (%)		Absent (%)
Participants with diabetes	95 (38.0%)	155 (62.0%)
Mean	2.40±1.45	1.10±0.18
Non Diabetic Subjects	29 (19.3%)	121 (80.7%)
Mean	1.97±0.55	1.02±0.16

lower in the control participants who were found to be anemic. The mean cell volumes (MCVs) were higher in the T2DM than the non diabetic subjects. Table 3 shows the biochemical parameters of the blood samples analyzed that were obtained from the study participants. A significant increase in fasting blood sugar (FBS) concentration was observed in the T2DM compared to non diabetic subjects (p=0.000*). Significant increases in urea, creatinine, eGFR, concentrations were also observed in the T2DM as compared to non diabetic subjects. Glycated hemoglobin (HbA1c) levels were also found to be higher in T2DM (particularly those with anemia) than in non diabetic subjects. It was seen that participants with diabetes had a high incidence of anemia in both males and females (53.9 % and 68.1 % respectively) and 54.8 % of the females in the non diabetic group were also anemic. Anemia was defined by Hb <13.0 g/dL in male and Hb <12.0 g/dL in female [20]. Three types of anemia were seen morphologically and by the MCVs obtained: hypochromic microcytic (MCV<80 fL), normochromic normocytic (MCV 80–95 fL) and normochromic macrocytic (MCV>95 fL). Renal insufficiency was determined by serum creatinine level >1.50 mg/dL and eGFR <60 ml/minute/1.73 m^2. A high incidence of renal insufficiency (38.0%) was observed in the participants with diabetes compared to non diabetic subjects (Table 4). Out of the 37 (62%) cases who were anemic, 38 (62.0%) showed low eGFR, which is an indication of renal insufficiency, with the remaining 95 (38%) having higher eGFR and therefore normal renal function.

Table 5. Correlation between hemoglobin and hyperglycemia

Pearson's correlations	R	P value
Hb and FBS (female)	-0.514**	0.002
Hb and FBS (male)	0.941	0.016

Hb hemoglobin, HG hyperglycemia, *correlation is significant at p value <0.05 (two-tailed)

DISCUSSION

Anemia is defined as a low level of Hb in the blood and evidenced by fewer numbers of functioning red blood cells. The WHO considers male with a Hb concentration <13.0 g/dL or packed cell volume (PCV) <39 % anemic and female with Hb <12.0 g/dL or PCV <36 % to be anemic (Hahn, 2007). Data from our study show a high incidence of anemia (73.9 % in males 23; 62.1 % in females 37) in participants with diabetes, predicting the necessity to assess patients with diabetes for anemia during diagnosis and management. HbA1c was found to be positively correlated whereas FBS was found to be negatively correlated with anemia in the participants with diabetes. This suggests that the incidence of anemia is likely to increase in poorly controlled diabetes, and therefore reducing blood glucose levels could help reduce the risk of anemia in diabetic populations. A previous study reported a 15.3 % incidence of anemia in participants with diabetes without renal insufficiency (Adejumo, 2012). The study added that patients who have poorly controlled diabetes were at greater risk of anemia than those with controlled diabetes. Another study reported that 7.2 % of diabetics with normal renal function had anemia. Again, other studies have reported that 20 % (Adejumo, 2012) and 19.6 % (Griac, 2007), of participants with diabetes with renal insufficiency had anemia. Anemia is a key indicator of chronic kidney disease (CKD) but occurs earlier in the course of diabetic kidney disease and may be more severe than previously realized (Feteh, 2016 and Ishimura, 1998). In patients with diabetes, anemia may be the result of diminished EPO production by the failing kidney. It has been suggested in other studies that this may be due to a reduction in the number of specific EPO synthesizing interstitial cells and disruption of the interstitial anatomy or vascular architecture (Dikow, 2002 and Yun, 1999). Most patients with diabetes are rarely tested for anemia and are unaware of the link between anemia and kidney disease. A pan-European study was therefore undertaken by Stevens et al. (2003) to investigate the level of awareness and understanding of anemia among patients with diabetes (Stevens, 2003). They concluded that anemia has a significant impact on the quality of life of patients with diabetes and although patients are aware of anemia, their awareness of being tested for anemia is low (Stevens, 2003).

The estimated prevalence of anemia in people with diabetes depends on essentially arbitrary criteria used to define the presence or absence of anemia. Nonetheless, studies in patients with renal impairment suggest that deleterious effects begin with Hb <11 g/dl, meaning that 7 % of patients with diabetes may benefit from intervention according to current guidelines (National Kidney Foundation, 2001). Again a study by Thomas et al. (2003) demonstrated that anemia is an early and common complication of diabetes and patients at greatest risk of anemia can be readily identified (Thomas, 2003). In the study, 60% of patients with anemia warranting investigation had eGFR <60 ml/minute 1/1.73 m^2 and nearly half (46%) of the patients with macroalbuminuria had anemia (Levin, 2002 and Tudor-Locke, 2000). As the risk of anemia is strongly associated with eGFR in the study by Thomas et al., it seems likely that supplementation with EPO could correct anemia, particularly in the patients with anemia and adequate iron stores (Thomas, 2003). The high incidence of anemia observed in our study may be due to the relatively small number of study participants about half of whom presented with renal insufficiency (Table 5). Anemia due to renal insufficiency is primarily as a result of observed earlier in patients with diabetes with renal insufficiency or disease (Feteh, 2016). The high incidence of anemia may also be due to other risk factors related to DM. Several studies have reported factors that increase the risk of anemia, which include; damage to renal interstitium due to chronic hyperglycemia and consequent formation of advanced glycation end products by increased reactive oxygen species, and systemic inflammation as well as reduced androgen levels induced by diabetes (Adejumo, 2012 and Feteh, 2016). A limiting factor worthy of mention is our sample size; a larger sample would have increased the power of the study outcome.

Conclusion

The findings of our study suggest that the high incidence of renal insufficiency observed in the participants with diabetes, among other factors, could have influenced the high incidence of anemic conditions seen. Anemia is therefore likely to occur in poorly controlled diabetes and in patients with diabetes with renal insufficiency. Including routine hematological (Hb) tests in the treatment of diabetes and considering factors such as glycemic control and renal sufficiency among others could help reduce anemia in diabetes and the possible complications that may come with it.

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