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The Relation Between Diabetes Type II and Anemia

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ABSTRACT

Background: Anemia is defined as a decrease in the hemoglobin concentration of blood, which accordingly decreases the oxygen-carrying capacity of red blood cells such that they are unable to meet the body's physiological requirements. Numerous reports have specified that anemia customarily occurs in patients with diabetes with renal insufficiency whereas limited studies have described the occurrence of anemia in people with diabetes prior to indication of renal impairment. Other studies have similarly recognized anemia as a risk factor for the need for renal replacement treatment in diabetes. Understanding the pathogenesis of anemia allied with diabetes can lead to the development of interventions to optimize results in these patients.

Purpose: The purpose of this study was consequently to determine the pervasiveness of anemia among patients with type 2 diabetes.

Materials and Methods: A total of 50 (25 with type 2 diabetes and 25 controls) participants were enlisted for the current study. Participants' blood samples were analyzed for fasting blood glucose, full blood count and renal function tests among others. The pervasiveness of anemia was then determined statistically.

Results: A high incidence of anemia was perceived in the cases. Of the patients with diabetes, 85 % had a hemoglobin concentration that was significantly less (males 10.88±1.78 and females 10.32±1.52) compared to that of controls (males 14.16±1.82 and females 12.49±1.11). A significantly increased fasting blood glucose, urea, sodium, potassium, and calcium ions were observed in the cases (8.02±1.28, 5.21±2.01, 141.08±7.01, 4.84±0.49 and 1.51±0.28 respectively) as compared to the controls (4.57±0.52, 3.61±2.09, 134.86±6.75, 4.38±0.61 and 1.31±0.31 respectively). Finally, a significant association between hemoglobin concentration and fasting blood glucose was also observed in the cases.

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.

Keywords: Anemia, Hemoglobin concentration, Diabetes, Renal insufficiency.

INTRODUCTION

Deficiency in the oxygen-carrying capacity of blood as a result of a reduced erythrocyte mass or reduction in the hemoglobin (Hb) concentration of the blood might specify anemia [1].

This insufficient blood supply to meet the body's physiological requirements. It is caused by either an excessive destruction or reduced production of red blood cells. Anemia is allied with increased perinatal mortality, child morbidity and mortality, increased susceptibility to lead to poisoning, immune incompetence, impaired mental development, and decreased performance at work. Anemia has a high pervasiveness and is considered a public health problem affecting developing and developed countries. It occurs at all stages of life, particularly in pregnant women and children. Globally, 1.62 billion people are anemic, consistent to 24.8 % of the global population. The highest prevalence of 47.4 % is in preschool-age children while the lowest prevalence of 12.7 % is in men [2].

Diabetes mellitus (DM) is a non-infectious sickness that correspondingly has a high occurrence worldwide [3]. It is a carbohydrate metabolism disorder which results in hyperglycemia due to either absolute insulin deficiency or reduced tissue response to insulin or both. Diabetes, particularly when poorly controlled, leads to complications such as retinopathy, nephropathy, and neuropathy in addition to numerous disordered metabolic processes including oxidative stress which causes oxidative damage to tissues and cells [4]. Anemia is one of the commonest blood

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disorders seen in patients with diabetes. Several research studies have reported that anemia frequently occurs in patients with diabetes who similarly have renal insufficiency [5]. A few other studies have also reported an incidence of anemia in diabetics prior to evidence of renal impairment [6]. Anemia occurs earlier and at a greater degree in patients presenting with diabetic nephropathy than those presenting with other causes of renal failure. The main causes of anemia can include: dietary iron deficiency; infectious diseases such as malaria, hookworm, and schistosomiasis; micronutrient deficiencies including folate, vitamin B12 and vitamin A; or inherited conditions that affect red blood cells such as thalassemia and sickle cell disease. Again, people with chronic illnesses such as kidney problems, cancer, diabetes, and related conditions are at a higher risk for developing anemia. Nevertheless, the most significant contributor to the onset of anemia is iron deficiency which has regularly been used as synonymous to anemia, and the pervasiveness of anemia used as a proxy for it [7].

Malignancy can affect bone marrow as well (bone marrow fibrosis) and this can also result in anemia. Bone marrow has a rich blood supply and is therefore a common site for a metastasis to develop [8]. Cancers of the breast, prostate, and lung are the commonest type to do this although almost all cancers have this capability. Once in the marrow the cancer cells can multiply easily and the tumor deposit enlarges, occupying more and more of the marrow space, so reducing the amount of blood-producing marrow and the subsequent anemia [9].

There are some tumors that arise from the bone marrow tissue itself, such as some types of leukemia and multiple myeloma. As these are more directly involved with the bone marrow's function they are more commonly associated with anemia.

Moreover, several diseases, conditions, and factors can cause our body to destroy its red blood cells leading to hemolytic anemia. These causes can be inherited or acquired but sometimes the cause is not known. Hemolytic anemia can lead to many health problems, such as fatigue, pain, arrhythmias, and heart failure [10]. There are many types of hemolytic anemias and treatment and outlook depend on what type and how severe it is. The condition can develop suddenly or slowly and symptoms can range from mild to severe. Hemolytic anemia often can be successfully treated or controlled. Mild hemolytic anemia may need no treatment whereas severe hemolytic anemia will require prompt and proper treatment, or it may be fatal. Inherited forms of hemolytic anemia are lifelong conditions that may require ongoing treatment but acquired forms may go away if the cause of the condition is found and corrected [11]. The following are some examples of diseases that lead to hemolytic anemia: sickle cell disease, thalassemias, hereditary spherocytosis, glucose-6-phosphate dehydrogenase (G6PD) deficiency, pyruvate kinase deficiency, acquired hemolytic anemias, immune hemolytic anemia, and mechanical hemolytic anemias [12, 13].

Results from a study by Rossing et al. showed a significant association between a lower Hb concentration and a decline in glomerular filtration rate (GFR) [14]. Other recent studies have also identified anemia as a risk factor for the need for renal replacement therapy in diabetes . Furthermore, anemia has a negative impact on the survival of patients with diabetes and is considered to be an important cardiovascular risk factor associated with diabetes and renal disease [14, 15].

There is consequently a need for more studies on the incidence and prevalence of anemia among patients with diabetes mainly those with renal malfunction. This study consequently purposed to determine the pervasiveness of anemia due to renal insufficiency among patients with type 2 diabetes and the outcome showed a high incidence of anemia among them. The findings suggest that anemia is probable to occur in patients with diabetes with renal insufficiency, mainly when it is poorly controlled. It is thus believed that presentation of the outcome will help increase the level of awareness and understanding of anemia among patients with diabetes, which will ultimately lead to the development of interventions to optimize treatment outcomes in them.

MATERIALS AND METHODS

The study was a case–control study conducted between July 2016 and January 2017. From each participant, 6 ml of an overnight fasting venous blood was collected as follows: 2 ml into an ethylenediaminetetraacetate (EDTA) tube for hematological profile, 2 ml into a plain tube for renal function tests (RFTs), and 2 ml into a fluoride tube for FBG and HbA1c analysis. Full blood count comprising red cell count, Hb, white cell count and

differentials, platelets as well as Hb indices were determined from the whole blood in the EDTA test tubes using ABX Micros 60 Haematology Analyzer (Horiba-ABX, Montpellier, France). Ferritin and TIBC were also done. Glucose is oxidized in the presence of glucose oxidase to form glucuronic acid and hydrogen peroxide. Hydrogen peroxide in the presence of peroxidase reacts with 4-aminophenazone and phenol to produce a colored quinone imine complex which is measured against a reagent blank at an absorbance of 550 nm. The FBG for each participant was estimated from the fluoride tube.

The data obtained were cleaned and entered into Statistical Package for Social Scientists (SPSS) version 20.0. Descriptive statistics such as frequencies and percentages were used to summarize categorical variables such as gender. Continuous variables such as Hb concentration, ferritin concentration, and TIBC were summarized using mean and standard deviation. An independent t-test was used to determine mean differences between means of categorical variables with two categories while an ANOVA was used for those with three categories. P- value of 0.05 was interpreted as significant.

RESULTS

The study included 50 participants, consisting of 25 participants with diabetes (8 males/17 females) and 25 participants without diabetes (7 males/18 females) who consented to participate in the study. Mean ages recorded for cases and controls were 54.89±9.98years and 45.10±14.77 years respectively (Table 1). The medical records of the participants were examined and they were taken through a physical examination for signs and symptoms of anemia. Nevertheless, 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 1: Summary of demographic characteristics of participants with diabetes

Parameters	Cases	Controls
n	25	25
Male	8	7
Female	17	18
Age (years)	54.89±9.98	45.10±14.77

Table 2 shows the hematological parameters analysis of the blood samples received from the study participants.

Hb concentration was observed to be significantly decreased in the cases as compared to the controls.

Ferritin and total iron-binding capacity (TIBC) levels were found to be within normal levels in most of the cases and lower within the control participants who were diagnosed to be anemic. The mean cell volumes (MCVs) were higher in the cases than the controls.

Table 2: Hematological parameters values of participants suffer from diabetes.

	Parameters	Cases	Controls	p value
Hb	Male (13.5–17.5 g/dL)	10.88±1.78	14.16±1.82	0.000
	Female (12.0–16.0 g/dL)	10.32±1.52	12.49±1.11	0.000
Ferritin	Male (20–200 µg/L)	83.58±1.17	92.01±1.13	0.000
	Female (20–120 µg/L)	50.36±1.09	55.35±1.33	0.000
MCV (80–95 fL)		86.19±1.09	83.87±1.08	0.000
TIBC (255–450 µg/dl)		314.80±2.74	359.80±2.78	0.001

Table 3 shows the biochemical parameters values of the blood samples that were obtained from the study participants. A significant increase in fasting blood glucose (FBG) concentration was observed in the cases compared to that of controls (p=0.000). Significant increases in urea, sodium (Na), potassium (K), and calcium (Ca) concentrations were also occurred in the cases compared to those of controls. Creatinine concentrations were almost similar in both cases and controls although they were on the high side. EPO and estimated glomerular filtration rate (eGFR) levels were lower in cases compared to controls. Glycated Hb (HbA1c) levels were also found to be higher in cases (particularly those with anemia) in comparison with controls.

Table 3: Biochemical parameters values of participants suffer from diabetes

Parameters	Cases	Controls	p value
FBG (3.8–6.1 mmol/L)	8.02± 1.28	4.57± 0.52	0.000*
Erythropoietin (4.1–19.5 mIU/mL)	6.29± 1.27	11.97± 1.87	0.000*
eGFR			
Female (80–110 ml/minute/ 1.73 m2)	84.72± 1.52	87.53± 1.14	0.000*
Male (90–120 ml/minute/ 1.73 m2)	90.16± 1.83	94.50± 1.69	0.000*
Urea (7–18 mg/dL)	5.21± 2.01	3.61± 2.09	0.000*
Na (135–145 mmol/L)	141.08 ± 7.01	134.86± 6.75	0.000*
K (3.5–5.0 mmol/L)	4.84± 0.49	4.38± 0.61	0.000*
Cl (95–105 mmol/L)	104.29 ± 4.05	104.11 ±3.71	0.000*
Ca (2.1–2.8 mmol/L)	1.51± 0.28	1.31± 0.31	0.001*
Creatinine (0.6–1.5 mg/dL)	2.41± 1.81	2.41± 1.29	0.887
HbA1c (4–7 %, 7–8 %, ≥8.5 %)	7.75± 0.98	4.45± 1.85	0.001

It was observed that participants with diabetes had a high incidence of anemia in both males and females (87.5% and 82.3% respectively) and 16.7 % of the females in the control group were also anemic. Anemia was defined by an Hb <13.0 g/dL in men and Hb <12.0 g/dL in women [16].

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).A positive correlation was found between the degree of anemia and HbA1c in patients with diabetes, supporting the hypothesis that there is a higher incidence of anemia among poorly controlled diabetics. Also a negative correlation was noted between Hb and hyperglycemia (FBG) in the diabetic population according to gender. Though, only the female population's correlation was significant (Table 4).

Table 4: Correlation between hemoglobin and hyperglycemia.

Pearson's correlations	R	p value
Hb and HG (female)	–0.455	0.005*
Hb and HG (male)	–0.411	0.163

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 men with a Hb concentration <13.0 g/dL or packed cell volume (PCV) <39 % anemic and women with Hb <12.0 g/dL or PCV <36 % to be anemic [17]. Data of the present study displayed a high occurrence of anemia (87.5% in males; 82.3% in females) in participants with diabetes, predicting the requirement to evaluate patients with diabetes for anemia during diagnosis and management. HbA1c was found to be positively correlated whereas FBG 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.

Out of the 21 studied cases who were anemic, 15 showed low eGFR, which is considered an indication that the cause of anemia may be due to renal dysfunction . They subsequently presented with normochromic normocytic anemia. The remaining 6 had higher eGFRs and possibly normal renal function; they

presented with both hypochromic microcytic 4 and normochromic macrocytic 2 anemia. These were suspected to be due to iron and B12/folate deficiency respectively. Among the controls, 5 were found to be anemic and here the majority 3 had high eGFRs and presumably normal functioning kidneys; they presented with hypochromic microcytic 3 and normochromic macrocytic 1 anemia. The remaining one had low eGFRs and were deemed to have renal insufficiency-related anemia. An earlier study reported a 15.3% occurrence of anemia in participants with diabetes without renal insufficiency [18]. 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 [19]. Again, other studies have reported that 20 % [20] and 19.6 % [19] of participants with diabetes with renal insufficiency had anemia.

The assessed pervasiveness of anemia in people with diabetes depends on essentially arbitrary criteria used to define the presence or absence of anemia. However, 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 [21]. Using this definition, almost one in four patients with diabetes (23 %) may have anemia warranting assessment. While other few studies have recommended that the pervasiveness of anemia is increased in diabetes, their surveys have generally selected patients with overt nephropathy [22].

In contrast, the Predialysis Survey on Anemia Management (PRESAM) failed to show a difference between patients with and without diabetes [23].The high frequency of anemia perceived in the current study could be as a result of the relatively small number of study participants ,about half of them presented with renal insufficiency. Anemia by reason of renal insufficiency is primarily as a result of decreased secretion of EPO by the failing kidneys, and anemia consequently arises when creatinine clearance is less than 50 mL/minute. This was perceived previously in patients with diabetes with renal insufficiency disease [6]. The high frequency of anemia can similarly be a reason of other risk factors associated to DM. Numerous studies have described factors that increase the risk of anemia, which comprise; damage to renal interstitium because of chronic hyperglycemia and consequent formation of advanced glycation end products by increased reactive oxygen species, and systemic inflammation along with decreased androgen levels induced by diabetes [6, 20]. A limiting factor worthy to mention is the sample size; a larger sample volume would have increased the significance of the conclusions of the present study . We correspondingly did not determine the HIV status of the current study participants and cannot justify the role of HIV on the pervasiveness of anemia in this specific study population, while infection with HIV has emerged as a further risk factor for the induction of anemia [24].

CONCLUSION

The results of the current study recommend that the high frequency of renal insufficiency perceived in the participants with diabetes, amid other factors, might have influenced the high frequency of anemic conditions perceived. Anemia is consequently probable to occur in poorly controlled diabetes and in patients with diabetes with renal insufficiency. Comprising routine hematological (Hb) tests in the management of diabetes and bearing in mind factors such as glycemic control and renal sufficiency among others could help in reducing anemia status in diabetes and the possible complications that could be arised consequently.

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