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Frequency of Anemia in Type 1 Diabetic Adolescent Patients in Tertiary Care Hospital of Karachi, Pakistan

Sagheer Uddin[1*], Taif Hameed[1], Sana Barkat Ali[2], Muhammad Saeed[3], Aroosa Anjum[4] and Mir Mubarak[5]

[1]Department of Biochemistry, Mekran Medical College, Turbat, Pakistan
[2]Department of Physiology, Bahria University Health Science, Karachi, Pakistan
[3]Department of Physiology, Mekran Medical College, Turbat, Pakistan
[4]Department of Physiology, Baqai Medical University, Karachi, Pakistan
[5]Department of Community Medicine, Mekran Medical College, Turbat, Pakistan

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***Corresponding Author:**
Sagheer Uddin
Department of Biochemistry, Mekran Medical College, Turbat, Pakistan
shahbaloch96@hotmail.com

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ABSTRACT

Anemia in type 1 diabetes (T1D) can impair glucose management by reducing red blood cells, reducing oxygen delivery and affecting insulin sensitivity. Low hemoglobin levels may cause falsely higher HbA1c readings, misleading healthcare providers about glycemic control. **Objective:** To determine the frequency of anemia in type 1 diabetic adolescent patients. **Methods:** A cross-section study was conducted at Baqai Medical University, Karachi, from April 2023 to November 2023. The sample size was 169 diagnosed type 1 diabetes patients. After getting informed consent, HbA1c and Complete Blood Count (CBC) were measured. In the CBC of individuals with hypochromic microcytic anemia, the particular subjects underwent further investigation of serum iron, ferritin and total iron binding capacity (TIBC) levels. All data analyses were performed on SPSS version 23.0. **Results:** The study analyzed adolescent T1Dpatients, focusing on their age and anthropometric parameters. Out of 169 type 1 diabetes patients, 81 were diagnosed with anemia while 88 weren't. There is a statistically significant difference in anthropometric parameters among anemic and non-anemic type T1D patients. The hematological parameters between T1Dsubjects with anemic and non-anemic were significantly lower in those with anemia, with p-values of 0.000**. Out of 81 anemic patients, 47 had iron deficiency anemia with lower levels of iron and ferritin and higher levels of TIBC. **Conclusions:** It was concluded that the study highlights a substantial prevalence of anemia among adolescents with T1D. Hematological analysis showed lower blood parameters and higher TIBC in anemic patients. HbA1c is higher in anemic T1D patients than in non-anemic ones.

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by insufficient insulin synthesis or an inadequate response to the insulin receptor. Hyperglycemia is a serious adverse effect of uncontrolled diabetes that damages numerous systems, including blood vessels, retina and neurons [1]. According to International Diabetes Federation (IDF) in 2021, it was estimated that 537 million people living with diabetes, globally make up 10.5% of the world population. The number is predicted to increase to 643 million by 2030 and 783.2 million by 2045 [2]. The prevalence of diabetes was common in both sex man and women. According to the World Health Organization (WHO), DM is the sixth leading cause of death. IDF reported that 26.7% of people in Pakistan were diagnosed with diabetes mellitus in 2022, for almost 33.3 million people living with DM [3]. Diabetes is classified into many classes such as type 1 diabetes (T1D), type 2 diabetes (T2D), gestational diabetes mellitus (GDM) and neonatal diabetes. T2D is a major class of diabetes. It is estimated about 80 to 90 % diabetic population have T2D. GDM is a kind of diabetes that is not pre-existing and diagnosed during 2nd and 3rd trimester of pregnancy [4]. Neonatal

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diabetes starts before six months. A primary monogenic etiology can be found in about 80% to 85% of cases [5]. Maturity onset of Diabetes in Young commonly exhibits early progress of hyperglycemia typically earlier than 25 years; however, diagnosis can occur at older ages [6]. T1D was previously known as "insulin-dependent diabetes" or "juvenile-onset diabetes". The immune system damages pancreatic beta cells that produce insulin. 5% to 10% of people with diabetes have T1D, worldwide [7]. Death of T-mediated cells contributes significantly to the pathophysiology of T1D, even though the exact cause of the disease is unknown. Anemia is defined Hemoglobin (Hb) less than 12 g/dL in females and below 13 g/dL in males. Normal ranges of Hb are 12-16 g/dL (local cut-offs) [8]. Compared to the healthy population, subjects with T1D had a higher prevalence of anemia [9]. Anemia in T1D adolescent patients can result in numerous challenges, due to the interaction between these two conditions. The β-cell of the pancreas produces insulin that requires iron to function properly. It can weaken insulin secretion and sensitivity, making it stiff to regulate plasma sugar. This may lead to more episodes of hyperglycemia and hypoglycemia, decreasing the efficiency of T1D management [10]. Anemia can reduce physical growth and development in adolescents. Iron intake is vital for puberty-related growth secretions and achieving health, especially in adolescent girls. Insufficient iron levels in a body can cause growth delays and decrease cognitive function. Iron deficiency Anemia (IDA) can absorb other essential macro and micronutrients, including vitamins and minerals, vital for maintaining overall health and controlling T1D. The health of adolescents with T1D patients may worsen due to a disturbance in the dietary cycle. IDA class of anemia is more common in Pakistan particularly in adolescent subjects with T1D across various ethnic groups. Anemia occurs due to fewer intakes of iron-rich foods including meat, leafy green vegetables and fortified cereals [11]. The amount of these meals has a higher concentration of particular nutrition which may prevent anemia due to socioeconomic circumstances may be restricted by some ethnic groups. Limited access to healthcare can result in undiagnosed or untreated anemia, particularly in rural or remote areas, due to limited awareness about the importance of iron-rich diets, iron supplementation and the consequences of anemia can contribute to its prevalence among the majority of the population in Pakistan particularly in adolescents T1D patients [12]. Therefore, the present study was conducted to anticipate the frequency of anemia in T1D patients visiting Outpatient Departments at the Tertiary care hospital in Karachi, Pakistan. This will help in the identification of anemia in individuals with T1D and subsequently assist diabetologists in managing glycemic control. Anemia can falsely elevate HbA1c levels which may mislead the proper treatment of T1D and its complications. Anemia is a global health concern, particularly in developing countries like Pakistan. T1D is prevalent in children and young adults. This research aims to examine anemia frequency in Pakistani type 1 diabetic patient; inaccurately elevated HbA1c measurements due to low hemoglobin levels might potentially deceive medical professionals on glycemic management. Early identification of anemia in Type 1 diabetic patients is crucial for effective management and improved patient outcomes. Addressing this issue is essential due to the growing prevalence of Type 1 diabetes and anemia worldwide.

Anemia, particularly iron deficiency anemia, poses a significant yet underrecognized complication in adolescents with Type 1 Diabetes (T1D), as it not only impairs glycemic regulation and insulin sensitivity but also falsely elevates HbA1c levels, potentially misleading clinicians in their management decisions. Despite the growing global burden of both T1D and anemia, particularly in developing nations like Pakistan where iron deficiency is highly prevalent, there remains a critical lack of locally focused studies examining the frequency and characteristics of anemia specifically within T1D adolescent populations. The inconsistency in existing literature — compounded by limited data from Pakistani tertiary care settings creates a significant research gap regarding how anemia interacts with glycemic markers and anthropometric parameters in this vulnerable age group. This study aims to determine the prevalence of anemia, particularly iron deficiency anemia, in adolescents with Type 1 Diabetes patients and to investigate the association between anemia and HbA1c levels in type 1 diabetic patients.

METHODS

This cross-sectional study was conducted at the Department of Biochemistry, Baqai Medical University. The diagnosed T1D patients were recruited from Baqai Institute of Diabetology and Endocrinology, Karachi, from April 2023 to November 2023 after approval from the Institutional Review and Ethics Board and Advance Research Study Board with reference (BMU-EC/05-22). The sample size was 169 diagnosed type 1 diabetic adolescent patients, calculated through open Epi with a 95% confidence interval and a 5% margin of error. The power of the study was used at 80%. Blood sample collection was done by trained phlebotomist. The data were collected by using convenience nonprobability sampling. The inclusion criteria were adolescents (both male and female) diagnosed with T1D with the age range of 10 to 19 years [13]. The exclusion criteria were subjects with type 2 diabetes; T1D patients with thalassemia, sickle cell anemia, and end-

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stage renal and liver disorders were excluded from the study. After getting informed consent from the patients, parents, or guardians, age and anthropometric measurements, including weight, height, body mass index, and waist and hip circumference, were measured via standard protocols [14]. The ethnicity and socio-economic class of every participant were asked by pre-papered questionnaires designed. Initially, the Complete Blood Count (CBC) and HbA1c were done for every subject included in the study who visited the OPD. The CBC was performed using the Sysmex XT-1800i (Sysmex, Kobe, Japan) [15]. HbA1c was measured by the high-performance liquid chromatography method. Approved by standardized Diabetes Control and Complication assay [16]. Anemia was categorized by Hb levels less than 13 g/dL in men and 12 g/dL in women. The mean corpuscular volume (MCV) below 76 fL or above 96 fL and mean corpuscular hemoglobin (MCH) below 26 pg. was considered microcytic hypochromic anemia. T1D patients diagnosed with hypochromic microcytic anemia underwent further investigation of serum iron, ferritin, and TIBC levels. Serum iron level was performed through a spectrophotometer. Serum ferritin level is done by an enzyme-linked immunosorbent assay (ELISA) laboratory method, and the total iron-binding capacity (TIBC) test was performed by a calculation method. All data analyses were performed on SPSS version 23.0. Appropriate statistical tests such as chi-square and Fisher exact test were applied for data analysis. The result was analyzed and a conclusion was drawn.

RESULTS

Results show the basic anthropometric and hematological characteristics of T1D adolescent patients included in the study and it is seen that the mean age of the participants was 15.34 ± 2.69 years. The gender distribution in the study was 93, (55.0) male and 76, (45.0) female included. The mean weight, height, BMI, waist and hip circumference, HbA1c, Hb, MCV and MCH were 45.54 ± 13.49 Kg, 98 ± 14.60 cm, 19.74 ± 8.1, 74.94 ± 10.78 cm, 79.8 ± 13.13 cm, 9.65 ± 2.40%, 12.33 ± 2.56 g/dL, 79.7 ± 10.21 fL and 29.85 ± 5.69 pg respectively, (Table 1).

Table 1: Anthropometric and Hematological Characteristics of the Adolescent T1D Patients

Variables (n=169)	Mean ± SD
Age (Years)	15.34 ± 2.69
Male	93 (55.0%)
Female	76 (45.0%)
Weight (kg)	45.54 ± 13.49 kg
Height (cm)	152.98 ± 14.60 cm
BMI	19.74 ± 8.1
HbA1c (%)	9.65 ± 2.40%
Waist Circumference (cm)	74.94 ± 10.78 cm
Hip Circumference (cm)	79.8 ± 13.13 cm
Hb (g/dL)	12.33 ± 2.56 g/Dl
MCV (fL)	79.7 ± 10.21 fL
MCH (pg)	29.85 ± 5.69 pg.

A Study was shown among 169 adolescents subject to T1D, 81, (47.7%) individuals were diagnosed with anemia and 88, (52.4) were non-anemic (Figure 1).

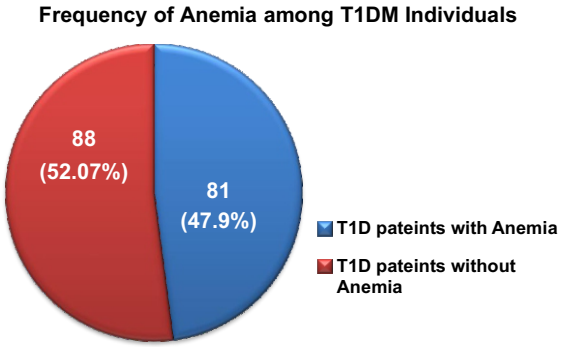


Figure 1: Frequency of Anemia among T1D Patients

Table shows the comparison of anthropometric and hematological characteristics of adolescent subject with T1D with Anemia and without Anemia and it is seen that the mean age of individuals with anemia is significantly lower than without anemic counterparts (p=0.026). Gender distribution shows no significant difference between the two groups. However, several anthropometric measurements exhibit significant variations with anemic presenting significantly lower mean weight, height, hip circumference, and waist circumference (p=0.031*), (p=0.040*), (p=0.030*) (p=0.001**) respectively compared to non-anemic T1D subjects. The mean Hb level was significantly lower in individuals with T1D with anemia (11.03 ± 1.5 g/dL) compared to them without anemia counterparts (13.64 ± 1.06 g/dL) p=0.000**, the MCV values in anemic T1D subjects (75.19 ± 11.83 fL) are significantly reduced compared to non-anemic (84.21 ± 8.6 fL), suggesting a microcytic nature of anemia. MCH is significantly lower in anemic (27.72 ± 4.96 pg.) compared to non-anemic (31.98 ± 6.43 pg.) p=0.000**. HbA1c levels are significantly lower in anemic (9.1 ± 2.11%) compared to without anemic (10.2 ± 2.7%) (Table 2).

Table 2: Comparison of Anthropometric and Hematological Characteristics of Adolescents Individuals with T1D with Anemia and without Anemia

Variables (n=169)	Anemic T1D subjects (n=81)	Without anemia (88)	p-Value
Age (Years)	14.88 ± 2.8	15.81 ± 2.59	0.026*
Male	46 (56.8%)	47 (53.4%)	0.659
Female	35 (43.2%)	41 (46.6%)	
Weight (Kg)	43.29 ± 13.95kg	47.8 ± 13.03kg	0.031*
Height (cm)	150.65 ± 13.83cm	155.32 ± 15.38cm	0.040*
BMI	18.59 ± 4.22	20.9 ± 11.98	0.090

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Hip Circumference (cm)	77.65 ± 13.93cm	81.95 ± 12.33cm	0.030*
Waist Circumference (cm)	72.17 ± 11.55cm	77.72 ± 10.02cm	0.001**
Hb (g/dL)	10.89 ± 1.51g/dL	10.86 ± 1.94g/dL	0.953
MCV (fL)	68.73 ± 9.49fL	84.12 ± 8.5fL	<0.001**
MCH (pg)	24.81 ± 3.22pg.	31.75 ± 4.03pg.	<0.001**
HbA1c (%)	9.18 ± 2.39	8.94 ± 1.67	0.612

An Independent t-test was applied. p-value<0.05 was considered significant

Analysis shows the comparison of biochemical parameters between adolescents with T1D with IDA and other anemia yielded significant variations. T1D subjects with IDA exhibited a markedly lower mean serum Iron level of 48.87 ± 22.86 µg/dL compared to those diagnosed with other anemias have a substantially higher mean of 96.51 ± 13.69 µg/dL, this difference was statistically significant (p=<0.001**). The TIBC was significantly higher in the IDA group (583.34 ± 140.51 µg/dL) compared to the other anemia (466.59 ± 132.32 µg/dL) with a p-value of <0.001** (Table 3).

Table 3: Comparison of Iron Profile between Adolescents Individuals with T1D with IDA and without IDA

Variables	T1D Patients with Other Anemia (N=34)	T1D Patients with Iron Deficiency Anemic Subject (n=47)	p-Value
Mean ±SD			
Serum Iron	96.51±13.69	48.87±22.86	<0.001**
Serum Ferritin	50.03±29.19	54.54±131.92	0.845
Serum TIBC	466.59±132.32	583.34±140.51	<0.001**

An Independent t-test was applied for comparison. p-value<0.05 was considered significant

DISCUSSION

Anemia is a widespread issue in public health. Although it affects people of all ages, pregnant women and children of school age are the most affected subjects [8]. An iron deficiency is known to be the most frequent cause of anemia, accounting for around 30% to 50% of cases of anemia globally. The IDA is also the most common cause of anemia in Pakistan. Low hemoglobin levels may cause falsely higher HbA1c readings, misleading healthcare providers about glycemic control. The present study investigated the prevalence of anemia with T1D patients, among, 169 patients, 81 were diagnosed with anemia. In contrast, 88 patients, did not exhibit signs of anemia. These results underline the relatively common co-occurrence of anemia in adolescents with T1D patients. The prevalence of anemia in over half of the study population with T1D suggests potential implications for healthcare professionals, urging a closer examination of the relationship between T1D and anemia. One of the previous research showed similar result trends by Safinaz *et al.*, [17]. The prevalence of anemia was 14% in T1D children diagnosed with anemia. These studies supported the findings and reported a higher prevalence of anemia in T1D subjects. According to the present study the mean age of subjects with anemia was found to be lower than (14.88 ± 2.8), (15.81 ± 2.59) non-anemic subjects, which was shown in another study by. Nosheen *et al.*, [18]. Out of 90 children with T1D, 60 had anemia and their mean age was less than non amenic subjects. According to present study in gender distribution, no significant difference was observed b/w anemic & non-anemic, suggests that anemia prevalence does not exhibit a gender bias within the studied population. Another study was conducted by *H. Kırmzbekmez et al.*, [19], in which the gender of the subjects with T1D did not matter in the comorbidity of anemia. According to present the anthropometric and hematological measurements in anemic subjects had lower mean values in weight, height, BMI, hip, waist circumference, Hb, MCV, MCH and HbA1c respectively compared to their non-anemic subjects, which also showed in another study Safinaz *et al.*, [17], in which anthropometric & hematological parameters were lower in anemic individuals with T1D as compared to a non-anemic population. Furthermore, the study explores glycemic control through HbA1c levels, revealing a significant difference between anemic and non-anemic adolescents with T1D. Anemic subjects with T1D have higher HbA1c levels (9.1±2.11%) compared to non-anemic (8.94±1.67). Previous studies Akkermans *et al.*, have found similar findings and stated that anemic subjects have higher HbA1c levels as compared to non-anemic. The study concluded that among T1D patients, anemia is associated with higher concentrations of HbA1c [20]. Researchers looked at the iron levels of T1D patients and IDA. They found that T1D patients with IDA had significantly lower iron levels (48.87 ± 22.86 µg/dL) than other anemia subjects (96.51 ± 13.69 µg/dL) (p=<0.001**). The comparison of serum total iron-binding capacity (TIBC) further supports the distinction between the IDA and non-IDA groups. Subjects with T1D and IDA demonstrate a significantly higher mean TIBC of 583.34 ± 140.51 µg/dL, in contrast to the other anemic group with a mean of 466.59 ± 132.32 µg/dL (p-value=<0.001**). A high TIBC level means that the body is trying to take in more iron, which means that iron transport proteins can bind more iron because there is less iron in the blood.

This study was limited by its cross-sectional design, single-center recruitment from one tertiary hospital in Karachi, convenience sampling methodology, and a relatively modest sample size of 169 patients, all of which restrict the generalizability of findings to the broader Pakistani adolescent T1D population. Additionally, dietary assessment and socioeconomic data, though referenced

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as contributing factors, were not systematically analyzed as independent variables influencing anemia prevalence. Future research should employ multicenter, longitudinal study designs with larger and more geographically diverse samples to better establish causality between T1D and anemia, while also evaluating the impact of iron supplementation on both HbA1c levels and overall glycemic control outcomes in this population.

CONCLUSIONS

It was concluded that the study highlights the higher prevalence of anemia in type 1 diabetes patients. This study shows that iron deficiency anemia is the most common cause of anemia among type 1 diabetic patients. There was variation in age, anthropometric, and hematological parameters in anemic and non-anemic type 1 diabetic patients. There were seen low iron and ferritin levels and higher TIBC levels in iron deficiency anemia than in other anemic patients. There is also a higher level of HbA1c seen among anemia and non-anemic patients with type 1 diabetes.

Authors' Contribution

Conceptualization: SU
Methodology: SU, TH, SBA, MS, AA, MM
Formal analysis: SU, TH, SBA, AA, MM
Writing and Drafting: SU, TH, MM
Review and Editing: SU, TH, MM

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

The authors declare no conflict of interest.

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