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Iron Deficiency Anemia in Children and Adolescents with Type I Diabetes, Is it a Real Problem?

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Abstract

Background: Iron deficiency anemia (IDA) in children with type I diabetes (T1D) represents a significant burden.

Aim of Study: To asses iron status in children and adolescent with T1D of and to correlate it with glycemic control and diabetic vascular complications.

Patients and Methods: Two hundred children with T1D recruited from Pediatrics and Adolescent Diabetes Unit (PADU), Ain Shams University in the period from December 2019 to July 2020. They were 123 males (61.5%) and 77 females (38.5%) aged 10.97±3.93 years (Range: 2-18 years). History taking, fundus examination and general examination were done stressing on anthropometric measurements. Laboratory evaluation including complete blood count, glycosylated haemoglobin (HbA1c), urinary albumin/creatinine ratio (ACR), lipid profile and patients with microcytic hypochromic anaemia underwent Serum iron, total iron-binding capacity (TIBC), serum ferritin, Hepcidin, Anti-tissue transglutaminase (IgA), Occult blood in stool and H-pylori antigen in stool.

Results: Seventy two of diabetic children were anemic (36%) and fifty one had IDA (25.5). IDA was more prevalent in males. Children with T1D and IDA experienced more clinically significant hypoglycemic attacks, more DKA attacks, high fatigue severity scale and history of menorrhagia. Low body weight, low BMI, low mean corpuscular volume (MCV), high TIBC and low hepcidin level were present in diabetic children with IDA. They also had high HbA1c, neuropathy, high triglycerides and high level of low density lipoprotein (LDL cholesterol).

Conclusions: IDA is a significant morbidity among children with T1D and it should be screened. Serum hepcidin levels are significantly associated with iron status in children, and could be useful indicators of ID.

Key Words: *Iron deficiency anemia – Children – Adolescents – Type I diabetes – Is it a Real Problem?.*

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Introduction

ANEMIA in type 1 diabetes (T 1 D) may have a complex, multifactorial background. Among the most common causes of anemia in the course of T1D in children is iron deficiency. Its prevalence is higher among T1D patients in comparison to people without diabetes **[1]**.

Iron deficiency (ID) and iron deficiency anemia (IDA) can impair glucose homeostasis and may negatively affect glycemic control and predispose to more complications in diabetic patients **[2]**.

Anemia is associated with an increased risk of diabetic complications including nephropathy, retinopathy and macro vascular disease. Anemia may also be significant in determining the outcome of heart failure and hypoxia-induced organ damage in diabetes. While several factors contribute to the increased prevalence of anemia in diabetes, the failure of the kidney to increase erythropoietin in response to falling hemoglobin appears to be the dominant factor **[3]**.

On the other hand diabetes and its complications are associated with anemia and its correction improves diabetes control and may prevent or delay the occurrence of complications **[2]**.

Iron replacement therapy decreases HbA1c in both diabetic and non-diabetic individuals. This implies that the iron states must be considered during the interpretation of HbA1c concentrations in diabetic or non-diabetic patients. Early diagnosis and treatment of ID in diabetic patients can improve their glycemic control and may prevent or delay complications **[2]**.

Aim of the study:

To determine the frequency of iron deficiency anemia among type I diabetic children and to

identify possible etiologies of iron deficiency anemia and to correlate different hematological parameters to glycemic control and diabetic vascular complications.

Patients and Methods

Study design and sampling:

A cross-sectional study was conducted on 200 children with T 1 D aged from 2 to 18 years over 6 months from December 2019 to July 2020 at Pediatrics and Adolescent Diabetes Unit (PADU), Ain Shams University.

Sample size was calculated using pass program. Setting the type I error (a) at 0.05 of the confidence interval width at 0.2 (margin of error 10%). Results from pervious study Thomas et al. [3] showed that 14% of DM cases had anemia. Calculation accordingly results in a minimal sample size of 47 approximated to 50.

Ethical considerations:

Ethical approval and advice for study design and sample size was obtained from the Research Ethics Committee of Faculty of Medicine, Ain Shams University (FMASU REC). The FMASU REC is organized and operated according to guidelines of the International Council on Harmonization (ICH) Anesthesiology and the Islamic Organization for Medical Sciences (IOMS), the United States Office for Human Research Protection and the United States Code of Federal Regulations and operates under Federal wide (Assurance no. MS234/2020).

Parents or legal guardians were informed about the purpose and the anticipated benefits of the research and confidentiality of data was ensured. An informed consent in simple Arabic language was obtained from the legal guardians prior to enrollment in the study.

Study population:

Two hundred patients with T1D were recruited from Ain Shams University Pediatrics and Adolescent Diabetes Unit. Diagnosis of type I diabetes is based upon criteria of ISPAD 2018 [4].

Children with other types of diabetes e.g. Type 2 diabetes, Maturity onset diabetes of youth (MODY) and patients with any chronic disease affecting iron status such as autoimmune diseases, neoplasia, chronic kidney disease, and chronic liver disease were excluded from the study.

Study procedure:

All enrolled children were subjected to the following:

1- Interview-based questionnaire:

The main researcher interviewed the guardians to collect the following data:

Personal data:

Data on child's age, gender, order of birth, number of siblings, area of residence, father's and mother's educational level and occupation was collected to determine the socioeconomic status of study participants.

Socioeconomic status (SES) was assessed using the Modified scale for social level of families for usage in health research which was modified after the original scale of Fahmy and El-Sherbini where subjects were given a score from 54 and were further classified into 3 social classes; low, medium, or high, according to their score [5].

Diabetes history:

In terms of duration, and control over last two year prior study determined by frequency of hypoglycaemia and or diabetic ketoacidosis, history of fatigue using the Fatigue Severity Scale [6], history of parasitic infestations and history of menorrhagia in pubertal females.

Dietetic history:

Included type of feeding in early infancy; either exclusive breastfeeding, non-exclusive breast feeding (mixed feeding) or formula feeding, as well as a review of foods introduced during weaning, and a 24-hour recall of diet aimed at assessing the intake of required macro- and micro-nutrients to determine quality of diet.

Weaning was judged either to be faulty or correct depending on timing of its initiation and types of foods introduced, and according to WHO recommendations for infant feeding.

Medical history:

Parents were also asked if they noticed that their child experienced any symptoms of anemia such as development of pallor, easy fatigue, and lack of concentration, pica or palpitations and fatigue severity scale questionnaire was obtained from them [6].

2- Examination:

Anthropometric evaluation including weight in kilograms (Kg), height in centimeters (cm) and

Body mass index (BMI) was calculated as follows weight (kg)/height (m)^2.

Weight, height and BMI Z scores was measured using z score reference for Egyptian children and adolescent [7].

Examination for tachycardia, radial pulse rate was performed a. Inspection for pallor at palms, nail beds, conjunctiva, oral mucosa and tongue was also done. Cardiac examination for hemic murmur and to exclude any underlying illness. Chest examination for dyspnea. Abdominal examination for hepato-splenomegaly. Slit-lamp biomicroscopy was done to evaluate retinopathy.

3- *Laboratory investigations:*

Complete Blood Count (CBC) was done for all subjects; Samples were collected by a trained nurse under complete aseptic condition. 2ml of blood were withdrawn into EDTA containing (purple top) tubes. CBC was performed using the Sysmex XT-1800i (Sysmex, Kobe, Japan) results will be interpreted according to special age and sex [8].

Glycated haemoglobin (HbA1c): A well-trained nurse had withdrawn the samples by pricking a finger and collecting finger capillary blood sample then the blood sample was added to the buffer and was shacked well to mix the blood with the buffer and through fluorescent immunochromotography analyzing system with fine care TM FIA meter plus device the result were collected.

Fasting lipid profile (triglycerides, total cholesterol, high density lipoproteins and low density lipoproteins which are done on Cobas c 111 (Roche Diagnostics, Mannheim, Germany) to detect dyslipidemia.

Patients with microcytic hypochromic anaemia underwent assessment of:

Serum iron and serum ferritin: 2ml of blood were with drawn into Gold-top serum separator tube (SST) and analysis was done using a 5010 spectrophotometer supplied by Roche diagnostics (GmbH, SandhoferStrasse 116, D-68305 Mannheim) [9].

Total iron-binding capacity (TIBC) measurement consists of three steps: The first step involves addition of supra physiological amounts of FeCl3 to saturate the free binding sites on transferrin; the second is the removal of unbound excess iron by adsorption onto solid magnesium carbonate, charcoal or an ion exchange resin; the third is the determination of iron that dissociated from transferrin at acidic pH (done on Cobas c 111) (Roche Diagnostics, Mannheim, Germany).

Hepcidin: Venous blood samples of 2ml were collected. Separated serum was frozen to 70 ° Celsius for storage and transport, and later thawed and analyzed in a single batch. Serum hepcidin was measured by a competitive enzyme-linked immunoassay (C-ELISA). Results from the C-ELISA were determined from standard curves developed from calibrators run simultaneously with study samples.

Anti-tissue transglutaminase (IgA): 1ml serum sample were collected in a red topped tube or gel barrier tube Serum anti-tissue transglutaminase IgA will be used to exclude celiac disease [10]. It will be measured with enzyme linked immunosorbent assay (ELISA) technique.

Occult blood in stool: It is used to look for active occult blood loss in anemia [11]. The stool samples were collected in a clean container and evaluated by detecting color changes on a test cardusing a microscope by immunochromatography technique.

H -pylori antigen in stool: Fresh fecal samples were collected in 60ml clean clearly labeled containers with wide mouths and screw-caps. Helicobacter Pylori Ag was measured by immunochromatography technique.

Assessment of diabetic chronic complication:

Diabetic neuropathy:

Diabetic neuropathy by performing simple rabid neuropathy test [12].

Diabetic nephropathy:

Albumin/creatinine ratio (ACR) in urine was examined to assess degree of diabetic nephropathy.

Statistical analysis:

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative data were presented as mean, standard deviations and ranges when their distribution found parametric and median with inter-quartile range (IQR) when their distribution found non parametric. Also qualitative variables were presented as number and percentages.

The comparison between two groups regarding qualitative data were done by using Chi-square test and Fisher exact test instead of Chi-square test when the expected count in any cell found less than 5.

The comparison between two independent groups with quantitative data and non-parametric distribution were done by using Mann-Whitney test while the comparison between more than two groups was done by using Kruskall-Wallis test.

Spearman correlation coefficients were used to assess the correlation between two quantitative parameters in the same group.

Receiver operating characteristic curve (ROC) was used to assess the best cut off point with its sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and area under curve (AUC).

Logistic regression analysis was used to assess the relations with outcome with odds ratio and 95% confidence interval (95% CI).

Kaplan Mayer analysis was used to assess the relations with overall survival using Log Rank test.

The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following:

- *p*-value >0.05: Non significant (NS).
- *p*-value <0.05: Significant (S).
- *p*-value <0.01: Highly significant (HS).

Results

The study was carried on 200 children with type 1 diabetes.

Demographic data:

The study included 200 children with T1D, IDA collectively was found in 51 children with percentage positivity (25.5%).

Young male, clinically significant hypoglycemia, DKA and menorrhagia were found significantly higher in diabetic children with IDA than those without IDA.

Children with T1D and IDA had Low socioeconomic status, were formula fed, faulty and early weaned, less protein intake in a week, tachycardic and pale and had neuropathy.

Microcytosis, high HbA1c, Low serum iron, high TIBC, low hepcidin, high triglycerdies, high LDL cholesterol and presence of occult blood in stool were significantly present in diabetic children with IDA compared to those without IDA.

Positive correlation was found between IDA and male sex, lower age, hypoglycemic attacks, DKA attacks, positive menorrhagia history, fatigue severity scale, neuropathy, tachycardia, presence of pallor, low MCV, lower body weight, BMI lower than 19.93, TIBC more than 315, high HbA1c, low hepcidin, early faulty weaning, formula feeding, less times of protein intake, high level of LDL cholesterol and high triglycerides.

Table (1): Demographic and clinical characteristics of children with T1D (n=200).

	Total No.=200
Gender:	
Females	77 (38.5%)
Males	123 (61.5%)
Age (years):	
Mean ± SD	10.97±3.93
Range	2-18
Diabetes duration (years):	
Median (IQR)	2 (1 5)
Range	1-15
Insulin dose (IU/kg/day):	
Mean ± SD	1.06±0.28
Range	0.5-2.2
Clinically significant hypoglycemia/year:	
Median (IQR)	0 (0-1)
Range	0-4
Diabetic ketoacidosis/year:	
Median (IQR)	1 (0-2)
Range	0-5
Socioeconomic class:	
Low	77 (38.5%)
Medium	100 (50.0%)
High	23 (11.5%)
Early life feeding:	
Breast fed.	106 (53.0%)
Formula fed.	43 (21.5%)
Mixed feeding	51 (25.5%)
Weaning:	
Correct	136 (68.0%)
Faulty	64 (32.0%)
Time of weaning:	
Correct	139 (69.5%)
Early	43 (21.5%)
Late	18 (9.0%)
Protein intake/week:	
Median (IQR)	3 (2-3)
	1-7
Multi-vitamins or fortified food intake:	
No	192 (96.0%)
Yes	8 (4.0%)
Fatigue severity scale:	
Median (IQR)	2.2 (1.8-3)
Range	1-6
Neuropathy:	
Negative	179 (89.5%)
Positive	21 (10.5%)

Table (1): Cont.

	Total No.=200
Nephropathy:	
Negative	169 (84.5%)
Positive	31 (15.5%)
Retinopathy:	
Negative	187 (93.5%)
Positive	13 (6.5%)
Parasitic infestation history:	
Negative	152 (76.0%)
Positive	48 (24.0%)
Menorrhagia history:	
No menstruation	31 (15.5%)
No menorrhagia	33 (16.5%)
Menorrhagia	13 (6.5%)
Males	123 (61.5%)
Heart rate (beat/minute):	
Mean ± SD	89.35±8.29
Range	70-112
Pallor:	
Negative	131 (65.5%)
Positive	69 (34.5%)
Weight (kg):	
Mean ± SD	36.88± 15.47
Range	11-85
Weight z-score:	
Median (IQR)	0 (-1-1)
Range	-3-3
Height (cm):	
Mean ± SD	133.37± 19.08
Range	84-175
Height z-score:	
Median (IQR)	-1 (-2-0)
Range	-3-3
Body mass index (BMI):	
Mean ± SD	19.94±5.00
Range	11.89-40.4
BMI z-score:	
Median (IQR)	1 (0-1)
Range	-3-3
BMI:	
Underweight	86 (43.0%)
Normal	88 (44.0%)
Overweight	18 (9.0%)
Obese	8 (4.0%)

Table (2): Laboratory data of the studied children with T1D (n=200).

	Total No.=200
Hemoglobin gm/dl:	
Mean ± SD	12.10± 1.77
Range	8-16.2
Anemia:	
No	128 (64.0%)
Yes	72 (36.0%)
Types of anemia:	
No anemia and no microcytosis	108 (54.0%)
Non microcytic anemia	21 (10.5%)
Microcytosis without anemia	20 (10.0%)
Iron deficiency anemia	51 (25.5%)
Mean corpuscular volume fl:	
Mean ± SD	75.96±8.33
Range	50-99.8
Red cell distribution width %:	
Mean ± SD	14.14± 1.78
Range	11-21
Glycated hemoglobin (Hba1c) %:	
Mean ± SD	9.18± 1.17
Range	7.4-13
Serum ferritin ng/dl:	
Median (IQR)	45 (25-78)
Range	10-350
Serum ferritin level:	
Low normal <60	47 (66.2%)
Normal	24 (33.8%)
Serum iron mg/dl:	
Mean ± SD	79.00±24.36
Range	30-120
Total iron binding capacity (TIBC) mg/dl:	
Mean ± SD	316.18±66.16
Range	165-455
Hepcidin pg/dl:	
Median (IQR)	1300 (850-2900)
Range	550-4800
Anti-tissue transglutaminase IgA eu/ml:	
Median (IQR)	7 (5-9)
Range	1-14
Occult blood:	
Negative	68 (97.1 %)
Weak positive	2 (2.9%)
Positive	0 (0.0%)
H -pylori antigen in stool:	
Negative	56 (80.0%)
Weak positive	10 (14.3%)
Positive	4 (5.7%)
Cholesterol:	
Mean ± SD	163.41±28.84
Range	93-238
HDL cholesterol:	
Mean ± SD	65.00± 18.81
Range	25-141
LDL cholesterol:	
Mean ± SD	92.80±23.52
Range	45-164
Triglyceride:	
Mean ± SD	74.50±27.94
Range	34-213

Table (3): Comparison between diabetic children with IDA and without IDA in clinical and demographic data.

	No iron deficiency anemia (IDA) No.=149	Iron deficiency anemia No.=51	Test value	*p*-value
Gender:				
Females	69 (46.3%)	8 (15.7%)	15.048*	<0.001
Males	80 (53.7%)	43 (84.3%)		
Age (years):				
Mean ± SD	11.33±3.91	9.91±3.84	2.246•	0.026
Range	2-18	4-18		
Diabetes duration (years):				
Median (IQR)	2 (1-4)	3 (1.5-5)	–1.571≠	0.116
Range	1-15	1-11		
Insulin dose (unit/kg/day):				
Mean ± SD	1.05±0.30	1.06±0.21	–0.108•	0.914
Range	0.5-2.2	0.5-1.4		
Clinically significant hypoglycemia/year:				
Median (IQR)	0 (0-0)	2 (0-2)	–6.883≠	<0.001
Range	0-3	0-4		
Diabetic ketoacidosis/year:				
Median (IQR)	1 (0-1)	2 (1-3)	–5.883≠	<0.001
Range	0-4	0-5		
Parasitic infestation history:				
Negative	110 (73.8%)	42 (82.4%)	1.515*	0.218
Positive	39 (26.2%)	9 (17.6%)		
Menorrhagia history:				
No menstruation	29 (19.5%)	2 (3.9%)	21.634	<0.001
No menorrhagia	32 (21.5%)	1 (2.0%)		
Menorrhagia	8 (5.4%)	5 (9.8%)		
Males	80 (53.7%)	43 (84.3%)		
Socioeconomic class:				
Low	31 (20.8%)	46 (90.2%)	77.513*	<0.001
Medium	95 (63.8%)	5 (9.8%)		
High	23 (15.4%)	0 (0.0%)		
Early life feeding:				
Breast fed.	100 (67.1%)	6 (11.8%)	71.202*	<0.001
Formula fed.	12 (8.1%)	31 (60.8%)		
Mixed feeding	37 (24.8%)	14 (27.5%)		
Weaning:				
Correct	126 (84.6%)	10 (19.6%)	73.672*	<0.001
Faulty	23 (15.4%)	41 (80.4%)		
Time of weaning:				
Correct	126 (84.6%)	13 (25.5%)	62.569*	<0.001
Early	16 (10.7%)	27 (52.9%)		
Late	7 (4.7%)	11 (21.6%)		
Protein intake in a week:				
Median (IQR)	3 (3-4)	2 (1-2)	–8.396≠	<0.001
	1-7	1-3		
Multi-vitamins or fortified food intake:				
No	141 (94.6%)	51 (100.0%)	2.852*	0.091
Yes	8 (5.4%)	0 (0.0%)		
Fatigue severity scale:				
Median (IQR)	2 (1.8-2.5)	3 (2-4.5)	–4.635≠	<0.001
Range	1-5	1-6		

Table (3): Cont.

	No iron deficiency anemia (IDA) No.=149	Iron deficiency anemia No.=51	Test value	*p*-value
Neuropathy:				
Negative	142 (95.3%)	37 (72.5%)	20.931 *	<0.001
Positive	7 (4.7%)	14 (27.5%)		
Nephropathy:				
Negative	126 (84.6%)	43 (84.3%)	0.002*	0.966
Positive	23 (15.4%)	8 (15.7%)		
Retinopathy:				
Negative	139 (93.3%)	48 (94.1%)	0.043*	0.836
Positive	10 (6.7%)	3 (5.9%)		
HR:				
Mean ± SD	88.50±8.47	91.82±7.26	–2.501•	0.013
Range	70-112	80-110		
Pallor:				
Negative	123 (82.6%)	8 (15.7%)	75.171 *	<0.001
Weight (kg):				
Mean ± SD	38.66±15.81	31.68±13.25	2.831•	0.005
Range	11-85	13-66		
Weight z-score:				
Median (IQR)	0 (-1-1)	0 (-1-1)	–0.722≠	0.471
Range	-3-3	-2-2		
Height (cm):				
Mean ± SD	134.58±19.49	129.80±17.52	1.55•	0.123
Range	84-170	99-175		
Height z-score:				
Median (IQR)	-1 (-2-0)	-1 (-1-0)	–1.082≠	0.279
Range	-3-3	-3-2		
BMI:				
Mean ± SD	20.60±5.20	17.99±3.77	3.302•	0.001
Range	11.89-40.4	12.16-31.8		
BMI z-score:				
Median (IQR)	1 (0-1)	0 (0-1)	–1.380≠	0.168
Range	-2-3	-3-3		
BMI:				
Underweight	56 (37.6%)	30 (58.8%)	9.175*	0.027
Normal	69 (46.3%)	19 (37.3%)		
Overweight	17 (11.4%)	1 (2.0%)		
Obese	7 (4.7%)	1 (2.0%)		

BMI: Body mass index.
p-value >0.05: Non significant.
p-value <0.05: Significant.
p-value <0.01: Highly significant.
*: Chi-square test.
•: Independent *t*-test.
≠: Mann-Whitney test.

Table (4): Laboratory difference among diabetic children with and without IDA.

	No iron deficiency anemia (IDA) No.=20	Iron deficiency anemia No.=51	Test value	*p*-value
Serum ferritin ng/ml:				
Median (IQR)	50 (32.5-60)	45 (20-80)	–0.935≠	0.350
Range	10-250	10-350		
Serum Iron ug/ml:				
Mean ± SD	96.95±17.86	71.96±23.02	4.360•	<0.001
Range	55-120	30-115		
TIBC ug/ml:				
Mean ± SD	280.90±35.15	330.02±70.47	–2.967•	0.004
Range	165-341	213-455		
Hepcidin pg/ml:				
Median (IQR)	2900 (2450-3180)	1000 (750-2100)	–4.234≠	<0.001
Range	750-4800	550-4200		
Anti-tissue transglutaminase eu/ml:				
Median (IQR)	8 (5-9)	7 (5-9)	–0.597≠	0.550
Range	3-10	1-14		
Occult blood:				
Negative	18 (90.0%)	51 (100.0%)	5.248 *	0.022
Weak positive	2 (10.0%)	0 (0.0%)		
Positive	0 (0.0%)	0 (0.0%)		
H-pylori antigen in stool:				
Negative	15 (75.0%)	42 (82.4%)	0.808*	0.668
Weak positive	4 (20.0%)	6 (11.8%)		
Positive	1 (5.0%)	3 (5.9%)		
MCV fl:				
Mean ± SD	79.38±5.74	65.96±6.44	13.950•	<0.001
Range	58.3-99.8	50-80		
RDW%:				
Mean ± SD	14.01±1.74	14.52±1.85	–1.763•	0.079
Range	11-21	12-20.7		
HbA1c %:				
Mean ± SD	8.84±0.94	10.16±1.23	–7.965•	<0.001
Range	7.4-12	8-13		
Cholesterol:				
Mean ± SD	163.36±28.99	163.55±28.68	–0.041•	0.967
Range	96-23 8	93-225		
HDL cholesterol:				
Mean ± SD	65.60±18.96	63.25±18.46	0.767•	0.444
Range	25-137	37-141		
LDL cholesterol:				
Mean ± SD	90.62±24.08	99.18±20.75	–2.266•	0.025
Range	45-164	60-155		
Triglyceride:				
Mean ± SD	72.12±26.47	81.43±31.12	–2.071•	0.040
Range	34-196	35-213		

TIBC: Total iron binding capacity.
MCV: Mean corpuscular volume.
RDW: Red cell distribution width.
HbA1c: Glycated hemoglobin.
HDL: High density lipoprotein.
LDL: Low density lipoprotein.

p-value >0.05: Non significant.
p-value <0.05: Significant.
p-value <0.01: Highly significant.
*: Chi-square test.
•: Independent *t*-test.
≠: Mann-Whitney test.

Table (5): Univar ate logistic regression analysis for factors associated with IDA.

	B	S.E.	Wald	*p*-value	Odds ratio (OR)	95% C.I. for (OR)	
						Lower	Upper
Sex (males)	1.534	0.419	13.425	<0.001	4.636	2.041	10.531
Age (years) < 10	1.085	0.338	10.300	0.001	2.959	1.526	5.740
LDL cholesterol >80	1.231	0.420	8.591	0.003	3.426	1.504	7.805
Triglyceride >82	1.033	0.337	9.373	0.002	2.809	1.450	5.440
Hypoglycemic coma >1	2.623	0.400	43.054	0.000	13.776	6.293	30.155
Diabetic ketoacidosis times >1	2.164	0.369	34.342	0.000	8.707	4.222	17.957
Neuropathy	0.697	0.349	3.986	0.046	2.008	1.013	3.982
HR >84	1.421	0.467	9.253	0.002	4.141	1.658	10.343
Pallor	3.236	0.441	53.738	<0.001	25.428	10.705	60.401
MCV <75.4	5.562	1.034	28.924	<0.001	260.417	34.302	1977.065
Weight (kg) <30	1.171	0.339	11.934	0.001	3.225	1.660	6.268
HbA 1 c >9.4	2.251	0.380	35.102	<0.001	9.493	4.509	19.988
BMI < 19.39	1.050	0.349	9.081	0.003	2.859	1.444	5.661
S Iron <75	-0.414	0.641	0.418	0.518	0.661	0.188	2.321
TIBC >315	2.473	0.797	9.627	0.002	11.864	2.487	56.595
Hepcidin < 1900	2.807	0.704	15.908	<0.001	16.564	4.169	65.808
Formula feeding	0.804	0.196	16.747	<0.001	2.234	1.520	3.283
Faulty weaning	3.112	0.419	55.079	<0.001	22.461	9.875	51.089
Early time of weaning	1.770	0.288	37.775	<0.001	5.868	3.337	10.317
Protein intake in a week <2	3.060	0.436	49.274	<0.001	21.321	9.074	50.099

CI: Confidence interval.

Table (6): Multivariate logistic regression analysis for factors associated with IDA.

	B	S.E.	Wald	*p*-value	Odds ratio (OR)	95% C.I. for (OR)	
						Lower	Upper
Hepcidin < 1900	2.950	0.901	10.725	0.001	19.104	3.269	111.652
Neuropathy	–0.632	1.119	0.320	0.572	0.531	0.059	4.761
HbA 1 c >9.4	1.510	0.784	3.711	0.054	4.525	0.974	21.023
Diabetic ketoacidosis times >1	1.661	1.013	2.692	0.101	5.267	0.724	38.326
LDL cholesterol >80	2.050	1.110	3.410	0.065	7.764	0.882	68.373
Triglyceride >82	0.571	0.837	0.466	0.495	1.771	0.343	9.131

Table (7): Correlation between factors related to IDA and TID.

	S F		S Iron		TIBC		Hepcidin	
	r	*p*-value	*r*	*p*-value	*r*	*p*-value	*r*	*p*-value
S F			0.029	0.812	-.014-	0.907	0.053	0.662
S Iron	0.029	0.812			–0.797**	0.000	.904**	0.000
TIBC	–0.014	0.907	–0.797**	0.000			–0.709**	0.000
Hepcidin	0.053	0.662	0.904**	0.000	–0.709**	0.000		
Age (years)	–0.103	0.392	0.022	0.854	–0.053	0.660	0.020	0.867
Cholesterol	0.122	0.309	0.114	0.343	–0.041	0.736	0.131	0.277
HDL cholesterol	–0.07	0.561	–0.001	0.996	0.022	0.854	–0.051	0.671
LDL cholesterol	–0.031	0.801	0.082	0.495	0.003	0.98	0.098	0.414
Triglyceride	0.062	0.61	0.117	0.331	–0.044	0.718	0.116	0.334
Diabetes duration (years)	0.046	0.705	–0.307**	0.009	0.235*	0.049	–0.223	0.062
Insulin dose (KG/day)	0.201	0.096	–0.124	0.305	0.053	0.665	–0.047	0.699
Hypoglycemic coma	0.251*	0.035	–0.292*	0.014	0.246*	0.039	–0.285*	0.016
Diabetic ketoacidosis times	0.152	0.205	–0.240*	0.044	0.183	0.126	–0.211	0.077
Fatigue severity scale	–0.072	0.550	–0.417**	0.000	0.299*	0.011	–0.430**	0.000
HR	–0.020	0.867	–0.091	0.450	0.063	0.600	–0.066	0.583
Weight (kg)	–0.134	0.265	–0.010	0.935	–0.040	0.741	–0.020	0.866
Weight z-score	–0.400**	0.001	–0.170	0.158	0.135	0.261	–0.158	0.188
Height (cm)	–0.035	0.771	0.066	0.582	–0.118	0.326	0.071	0.557
Height z-score	0.048	0.691	0.042	0.729	–0.065	0.588	0.015	0.903
BMI	–0.178	0.137	–0.078	0.517	0.071	0.558	–0.103	0.394
BMI z-score	–0.021	0.860	–0.196	0.102	0.217	0.069	–0.193	0.107
HGB	–0.107	0.377	0.599**	0.000	–0.437**	0.000	0.546**	0.000
MCV	–0.231	0.053	0.473**	0.000	–0.517**	0.000	0.431**	0.000
RDW	–0.096	0.427	–0.329**	0.005	0.358**	0.002	–0.237*	0.046
HbA1c	0.183	0.126	–0.540**	0.000	0.397**	0.001	–0.481**	0.000
Protein intake in aweek	–0.127	0.290	0.556**	0.000	–0.413**	0.000	0.514**	0.000
Anti-tissue transglutaminase	0.032	0.795	0.132	0.275	–0.021	0.861	0.066	0.588

Discussion

Type I diabetes (T1D) is one of the most common chronic diseases of childhood and is caused by immune-associated destruction of insulin-producing pancreatic beta-cells. Iron deficiency (ID) is common in children with T1D. Since ID in children is associated with adverse effects, such as cognitive and behavioral impairment, it is important to assess their iron status **[13]**.

Until present, there have not been many studies assessing the prevalence of anemia among children with T1D. There is a range of publications regarding patients with type 2 diabetes and anemia, usually accompanying renal complications.

Analysis of the collected data in this study revealed that, the overall prevalence rate of anemia among 200 children with type I diabetes is 36% while Prevalence rate of iron deficiency anemia among 200 children with type I diabetes is 25.5% this result is similar to that of Wójciak et al. **[14]** who studied 100 children with type I diabetes, aged 6 to 17 years and found that the incidence of iron deficiency anemia is 26% in newly diagnosed children with type I diabetes.

While in an analysis of 200 children with T1D conducted in Egypt, anemia was diagnosed in 37% of cases. Among patients with anemia 54.7% had iron deficiency **[15]**.

Also in a cross sectional study including 109 people with type I diabetes (54.1% male, mean age 56.2 years) at the diabetes clinic of the Goethe University Hospital. Decreased serum iron and ferritin levels were observed in 18 (16.8%) and 28 (26.7%) patients, respectively. Anemia was present in 20 patients 18.34% **[16]**.

While a two-center prospective observational study in which the iron status of Dutch children with DM type I was determined during a regular check-up. Absolute iron deficiency and functional iron deficiency were found in 13/227 (5.7%) and 100/214 (47%) patients, respectively, while only 15/113 (13%) patients also had anemia **[17]**.

Demographic data:

In our study low socioeconomic class was highly significantly present in diabetic children with IDA than those without IDA this is similar to Abdel-Rasoul et al. **[18]**, who find that children from low and middle socioeconomic standard had a two-fold increased risk of developing IDA [OR 1.59, 95% confidence interval (CI) 1.1-2.4]. This is in agreement with the study carried out by Neuman et al. **[19]** in Brazil, in which IDA was more prevalent in children from low socioeconomic backgrounds. This can be as attributed to the fact that poverty is a contributing factor to IDA because families living at or below the poverty line may not be consuming enough iron-rich foods.

In our study from 200 patient there were 123 male (61.5%) and 77 patients (38.5%) were females. Their ages ranged from 2 years to 18 years with mean age 10.9±3.93 years (SD). Median duration of T 1 D was 2 (1-5) years IQR.

On the other side, a study was done by Wójciak et al. **[14]** on 94 children with T1D (55 females) 58.5% and 39 males 41.4% at Diabetic Outpatient Clinic, Upper Silesian Centre for Child's Health in Katowice, Poland. Their mean age at study time was 12.5±4.1 years (SD) (ranging from 3 to 19 years). Mean duration of T1D was 4.2 ±3.6 years (SD).

In our study IDA was more common in males than in female this was statistically highly significant (*p*-value 0.000).

This is consistent with the results of Solomon et al. **[20]** who studied 87 patients diagnosed with IDA, where 53 (60.9%) were male and 34 (39.1%) were female. Of the 87 non-IDA diabetic patients, 51 (58.6%) were female and 36 (41.4%) were male.

While according to Andriastuti et al. **[21]** who studied two groups children age group and the adolescent and found that there were a total of 45 subjects in the children age group, which included 21 females (46.7%) and 24 males (53.3%). Twenty percent (nine subjects) had anemia. The overall prevalence of IDA, ID, and iron depletion was 11.1%, 15.6%, and 4%, respectively. The prevalence of anemia and iron deficiency was higher in the male population.

The adolescent group consisted of 162 subjects, and 51.2% were females and 48.8% were males. The prevalence of anemia, IDA, ID, and iron depletion was higher in the female group.

He defines school-aged children as children aged 6-9 years old; we describe adolescents as young people between the age of 10 and 18 years old **[21]**.

On the other hand Abdel-Rasoul et al. **[18]** found that IDA occurred in both sexes, but more among females (57.5%), although no significant difference found; this in agreement with Mohamed et al. **[22]** No sex differences were found in the prevalence of anemia, although a slight difference was noted (12.8%) for girls and for boys (11.4%). This may be due to unhealthy food consumption and blood loss during menstruation in older girls.

Dietetic history:

In this study we find that formula feeding, faulty and early weaning were found significantly higher in diabetics with iron deficiency anemia than in diabetics without IDA.

This is This is consistent with the results of Kim et al. **[23]** who observed IDA more frequently in infants whose nutrition was supplied only by breastfeeding for more than 6 months, in those who were fed weaning food with low iron content and in those who took a long time to adapt to the weaning food **[23]**.

This is similar to Al Ghwass et al. **[24]** who studied 345 children aged 6 months to 12 years and found that the frequency of IDA was 64% among them. This high prevalence of iron deficiency among study population explained by the consumption of unfortified cow's milk feeding during the 1st year of life, low intake of iron-rich foods, unmet increased needs for iron due to rapid growth.

While the prevalence of IDA was higher in infants fed with the formula without iron (20%), much lower in those fed with iron-fortified formula (0.6%), and medium in infants fed with human milk (15%). In another study, an increased prevalence of IDA in infancy was observed in infants fed with nonformula cow's milk >600ml or more daily or >6 breast feeds per day **[25]**.

There was a significant positive correlation between increased number of meals containing animal meat, chicken meat, liver, and IDA. This is in agreement with Mamdooh; there was a significant association between the consumption of food rich in iron and IDA. This can be as attributed to the fact that liver and meat are very rich in heme iron **[18]**.

Diabetes complications:

Acute complication:

The current study found that the presence of hypoglycemic coma, DKA were significantly higher

in diabetics with iron deficiency anemia than in diabetics without IDA this is consistent with Soliman et al. [2] who found that Iron deficiency (ID) and IDA can impair glucose homeostasis in human and negatively affect glycemic control and predispose to more complications like hypoglycemia and diabetic ketoacidosis in diabetic patients.

Chronic complication:

The present study revealed that the frequency of neuropathy in children with T1DM was 26.5% (53/200).

Similarly the European Diabetes Prospective Complications Study reported that the neuropathy prevalence was 28% at baseline [26].

On the other hand a study at Zagazig University Hospitals revealed that the frequency of neuropathy in children with T1DM was 42.5% (17/40) [27]. In addition, a study conducted by Moser and coworkers reported that of 151 youth with type I diabetes 11% were diagnosed with diabetic peripheral neuropathy (DPN).

This difference in frequency of neuropathy in diabetic patient may be due to difference in duration of diabetes among study populations.

In our study we found that the frequency of diabetic nephropathy in children with T1DM was 15.5% (31/200).

While 25% to 40% of patients with T1D develop diabetic kidney disease approximately 20% to 30% of T1D have microalbumiuria after mean diabetes duration of 15 years and the overall incidence of end stage renal disease is reported to be 4% to 17% at 20 to 30 years from T1D diagnosis [28].

While on the other hand in 86 patients, prevalence of micro albuminuria was 6% [29].

While Diabetic nephropathy was diagnosed in 10 patients (31%), 2 with microalbuminuria and 8 with proteinuria [30].

This variation in prevalence rates for micro albuminuria might be explained by differences in study populations, such as age range, diabetes duration, glycemic control, and length of follow-up ranging.

In our study, we have demonstrated the prevalence of retinopathy to be 6.5% (13/200) for any retinopathy in children and adolescents while Klein et al. [31] demonstrated that the prevalence of retinopathy was less than 10% during the first 5 years after onset of type I diabetes, in children younger than 13 years. While Kernell et al. [32] a have demonstrated the prevalence of retinopathy to be 14.5% for any retinopathy and 2.3% for proliferative and preproliferative retinopathy in children and adolescents.

Parasitic infection:

The prevalence of parasitic infestation among our 200 patient was 24% (48/200) while the prevalence of intestinal parasites in 1920 school-age children from eight schools located in Thailand was presented in Table (1). The overall prevalence of intestinal parasites was 12.6% (242/1920) [33].

A previous study conducted in Jeddah, KSA reported that the overall prevalence of the parasitic infection was 48%, A study conducted in Morocco showed that the mono- or polyparasitism was detected in 34.5% of the children [34].

The high prevalence of intestinal parasites recorded in the study could be attributed to exposure of the children to predisposing factors to intestinal parasitic infections; such as (poor sewage disposal system, unsafe sources of water, poor sanitary conditions, poor housing and lack of awareness on the part of the parents and children).

The prevalence of IDA among children with a positive medical history for diarrhea and parasitic infestation was higher than that among children with a negative medical history for diarrhea and parasitic infestation. This result is in agreement with Abdel-Rasoul et al., diarrheal and parasitic infestations were reported in different studies in the Gaza Strip and have been shown to be associated with anemia among school-age children in Gaza. Also Abdel-Rasoul et al. [18] who found that of IDA among children with a positive medical history for diarrhea and parasitic infestation was higher than that among children with a negative medical history for diarrhea and parasitic infestation (59.9 and 80.3%, respectively). This may be because diarrhea and parasitic infestation affect absorption and may lead to loss of blood from gastro intestinal tract (GIT).

Anthropometric measures:

In this study, mean BMI in IDA diabetic group was low compared to non-IDA diabetic group 17.99 ±3.77, 20.60±5.20kg/m^2 patients with highly significant statistical difference (p-value=0.001). Also patients with IDA were shorter and lighter than non-anemic patient but this didn't reach statistical significance.

Similarly Al Ghwass et al. [24] showed that stunting, wasting and underweight were associated among iron deficient anemic children, but underweight only was statistically significant.

This agrees with Luo et al., who reported that IDA during the first 2 years of life significantly impairs growth, and there is a significantly correlation between growth velocity and SF concentration. Also Luo et al. [35] mentioned that children with anemia were shorter for their age, and a higher percentage of them of them had stunted growth.

Clinical data:

In our study the mean heart rate was significantly higher among cases with IDA than those without IDA (91.82±7.26 bpm vs. / 88.50±8.47 bpm). Similarly Mustafa et al. [36] found the same results the mean heart rate was significantly higher among anemic patients compared to the control group (84.4±22.4 bpm vs. 72.6± 13.2 bpm; p=0.005.

In this study presence of pallor was highly significantly higher in diabetic children with iron deficiency than those without iron deficiency anemia.

This is consistent with the results of Stoltzfus et al. [37] that studied five different study samples and provide information on the performance of clinical pallor to detect low hemoglobin based on observations of 5,760 individuals, 3,072 of whom were anemic, and 192 of whom had hemoglobin concentrations <70g/Land found that Hemoglobin concentration significantly lower in group with pallor compared to without pallor for all sites, p<0.001.

Similarly, This has been a consistent finding in all of the published studies of the clinical assessment of anemia that we were able to identify [38,39].

Laboratory result:

The present study revealed that mean HbA1c is higher in IDA group (10.16± 1.23) compared to the group without IDA (8.84±0.94) (p<0.000).

Similarly a prospective study including 37 patients with type I diabetes (1 1 patients were ID and the remaining 26 were iron sufficient). Patients with ID had higher levels of HbA1c than patients without iron deficiency [2].

Also in 200 type I diabetic patients attending a pediatric diabetic clinic in Cairo, HbA1c levels were statistically significantly higher in iron-deficient than in non-iron-deficient patients (p<0.01) [15].

This is supported by studies done by, Ford et al., in [11], Silva et al., in [41], have obtained higher HbA1c level in IDA patients.

In contrary Solomon et al. [20] revealed that HbA1c (%) is significantly lower in IDA group (6.18± 1.57) compared to the control group (7.74 ±1.81) (p<0.05). This is supported by studies done by Sinha et al., in [42], Cavagnolli et al., in [43].

They all stated that HbA1c concentration tends to be lower in the presence of iron deficiency anemia. According to Sinha et al. [42] suggestion, the reason for lower HbA1c is due to the severity of anemia in the study participants.

Christy et al., in [44] found a positive correlation between IDA and increased A1C levels.

The present study revealed that mean cell volume is lower in IDA group (65.96±6.44) compared to non-IDA group (79.38 ±5.74) this result was highly significant (p-value 0.000).

Similarly Solomon et al. [20] mean hemoglobin, mean cell volume (MCV), was lower in IDA group compared to non-IDA diabetic patients.

In this study, median hepcidin was lower in IDA group compared to non-IDA diabetic children 1000 (750-2100), 2900 (2450-3180) ug/ml with highly significant statistical difference.

Similarly a study evaluated serum hepcidin concentrations in relation to iron status in 215 children with T1D found that: In patients with absolute iron deficiency there is lower hepcidin concentrations compared to patients with normal iron status. (p-value=0.000) [13].

This is consistent with the results of Choi et al. [45] who studied 59 children (23 males and 36 females) and found that mean serum hepcidin levels were significantly lower in the ID (7.72 ±8.03 ng/mL) and IDA groups (2.01 ±2.30ng/mL). Low serum hepcidin in ID and IDA can be attributed to the lower total iron stores in these groups than that in the normal controls.

Similarly Girelli et al. [46] found the same results In IDA, hepcidin levels are generally suppressed.

In addition D'Angelo [47] found the same results In pure iron deficiency anemia (IDA), serum and urinary hepcidin concentrations are significantly

decreased and even in the absence of anemia, hepcidin appears to be a sensitive indicator of iron deficiency. Moreover, compared to hematocrit or hemoglobin, a decrease in hepcidin is an early marker of iron deficiency together with transferrin saturation and decreased ferritin.

In our study, mean serum ferritin was lower in IDA group compared to non-IDA diabetic 45 (20-80), 50 (32.5-60) ng/ml patients but with no significant statistical difference (p-value=0.350).

This is consistent with the results of Madanat **[48]** mean serum ferritin for the iron deficiency anemia group was 39.1ng/mg as compared to 84.7ng/ml for the normal group. Even though the serum ferritin level was lower in the iron deficiency group, the difference in the means did not reach statistical significance.

Similarly Bouri and Martin **[49]** found the same results In IDA the ferritin, serum iron and transferrin saturations are low, but the TIBC increases.

Summary:

Iron deficiency anemia a prevalent finding in patients with type I diabetes and represents a significant unrecognized burden.

In this study, we aim to study prevalence of iron deficiency anemia among type I diabetic children and to identify possible etiologies of iron deficiency anemia and to correlate parameters to glycemic control.

This is particularly important as iron deficiency anemia is associated with impaired psychomotor and mental development in infants, and neurocognitive impairment in adolescents.

This case-control study included two hundred children with type I diabetes recruited from Pediatrics and Adolescent Diabetes Unit (PADU), Ain shams university in the period from December 2019 to July 2020.

Cases (123 males and 77 females) are children with type I diabetes. Diagnosis of type I diabetes are based upon criteria of ISPAD 2018. Their mean age was 10.97±3.93 years (Range: 2-18 years).

Cases were subjected to full history taking; general examination with laying stress on heart rate, pallor and anthropometric measurements and laboratory evaluation including complete blood count, glycated haemoglobin (HbA1c) and Patients with microcytic hypochromic anaemia underwent assessment of:

Serum iron, total iron-binding capacity (TIBC) and serum ferritin, Hepcidin, Anti-tissue transglutaminase (IgA), Occult blood in stool and H-pylori antigen in stool.

Our results showed upon comparison of cases with IDA to those without IDA: Cases with IDA had significantly higher values as regards male sex, lower age, hypoglycemic attacks, DKA attacks, menorrhagia history, higher fatigue severity scale, neuropathy, tachycardia, pallor, lower MCV, lower body weight, lower BMI, higher TIBC and lower hepcidin level.

Also longer diabetes duration, higher insulin dosage retinopathy, higher RDW, lower Hba1c, lower height and h-pylori antigen in stool are higher in cases with IDA than in cases without IDA with no statistical difference.

36% of diabetic patient were anemic and 25.5% had iron deficiency anemia.

Our study has several limitations. The study sample was small and based solely on diabetic children who were recruited from our clinic. This study used a case control study design so that the causality between iron deficiency anemia and type I diabetes could not be established, just the association between them that could be suggested.

Conclusions:

The incidence of anemia in the early stages of the disease justifies conducting the screening in all children with type I diabetes and taking appropriate preventive measures toward the patients at risk for iron-deficiency anemia.

Serum hepcidin levels are significantly associated with iron status in children, and could be useful indicators of ID. Further studies are necessary to confirm the value of serum hepcidin measurement in the diagnosis of ID and to determine the reliable reference range and cutoff values in children.

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أنيميا نقص الحديد فى الأطفال والمراهقين المصابين بمرض السكر من النوع الأول

يعد فقر الدم الناجم عن نقص الحديد السبب الرئيسى لفقر الدم فى الأطفال كما يعتبر تحدياً عالمياً. فما يقرب من ٤٠٪ من الأطفال مصابون بفقر الدم فى مختلف الأوساط الأفريقية والآسيوية.

فى هذه الدراسة، نهدف إلى دراسة معدل انتشار فقر الدم الناجم عن نقص الحديد بين الأطفال المصابين بالسكرى من النوع الأول وتحديد المسببات المحتملة له وربط ذلك بضبط نسبة السكر فى الدم.

وهذا فى غاية الأهمية حيث أن فقر الدم الناجم عن نقص الحديد يرتبط بخلل فى النمو الحركى والعقلى عند الرضع، وضعف الإدراك العصبى لدى المراهقين.

ولقد تضمنت هذه الدراسة مائتى طفل يعانون من مرض السكرى من النوع الأول تم تجميعهم من وحدة طب الأطفال ومرض السكرى لدى المراهقين، جامعة عين شمس فى الفترة من ديسمبر ٢٠١٩ إلى يو ليو ٢٠٢٠.

هذه الدراسة تشمل مائتى طفل (١٢٣ من الذكور و ٧٧ من الإناث) هم أطفال يعانون من داء السكرى من النوع الأول، ويستند تشخيص مرض السكرى من النوع الأول إلى معايير.

وكان متوسط أعمارهم ١٠.٩٧±٣.٩٣ سنة (النطاق : ٢–١٨ سنة).

وقد خضعت الحالات لأخذ تاريخ مرضى كامل، وفحص عام للجسم مع التركيز على معدل ضربات القلب، والشحوب والقياسات البشرية وتم اجراء التقييمات المخبرية التى تشمل تعداد الدم الكامل، والهيموغلوبين السكرى أما المرضى الذين يعانون من فقر الدم النا قص الصغر خضعوا لتقييمات اضافية وتشمل :

نسبة الحديد بالدم، القدرة الكلية على الارتباط بالحديد ونسبة الفيريتين بالدم، فحص حساسية الجلوتين، الهبسيدين، الدم الخفى فى البراز ومستضد جرثومه المعدة فى البراز.

وبالمقارنة بين الأطفال الذين يعانون من أنيميا نقص الحديد بأولئك الذين لا يعانون منها أظهرت نتائجنا أن الحالات المصابة أكثر فى الذكور ذو الأعمار الأقل من ١٠ سنوات ويعانون من نوبات نقص السكر بالدم ونوبات ارتفاع السكر بالدم و لهم تاريخ من غزارة الطمث ولهم قيم أعلى فى مقياس شدة التعب ويعانون من إلتهاب الأعصاب والشحوب وارتفاع فى ضربات القلب وانخفاض فى الوزن وانخفاض مؤشر كتلة الجسم بشكل أكثر من الذين لا يعانون من أنيميا نقص الحديد.

كما وجد أن مستوى الهبسيدين فى الدم أقل ومتوسط حجم كريات الدم الحمراء أقل والقدرة الكلية على الارتباط بالحديد أعلى فى أولئك الذين يعانون من أنيميا نقص الحديد.

من خلال هذه الدراسة وجد أن ٣٦٪ من مرضى السكرى النوع الأول يعانون من فقر الدم و ٢٥.٥٪ يعانون من فقر الدم الناجم عن نقص الحديد.