



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم



MONA MAGHRABY



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شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلم



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شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم

جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
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تحفظ هذه الأقراص المدمجة بعيدا عن الغبار



MONA MAGHRABY



Iron Deficiency Anemia in Children and Adolescents with Type 1 diabetes, is it a Real Problem?

Thesis

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in Pediatrics*

By

Asmaa Abdelnaby Mohammed Soliman

M.B., B.Ch; Ain Shams University; (2015)

Under supervision

Prof. Safinaz Adel Elhabashy

Professor of Pediatrics

Faculty of Medicine - Ain Shams University

Dr. Rasha Adel Thabet

Lecturer of Pediatrics

Faculty of Medicine - Ain Shams University

Dr. Nouran Yousef Salah El Din

Lecturer of Pediatrics

Faculty of Medicine - Ain Shams University

*Faculty of Medicine
Ain Shams University*

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قَالَ

سَبَّحَانَكَ لَا إِلَهَ إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْعَظِيمُ

صدق الله العظيم

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Asmaa Abdelnaby Mohammed Soliman

رسالة الكلية

تقوم كلية طب جامعة عين شمس بإعداد طبيب مدرب ذو مهارة تنافسية على المستوى المحلي والإقليمي، وقادر على التعليم والتعلم والتدريب مدى الحياة وملتزم بمعايير الخدمة الطبية والأخلاق المهنية، وتدعم الكلية التطوير المستمر للبرامج والمقررات والبحث العلم مع الحرص على التوسع في الأبحاث العلمية التطبيقية وبرامج الرعاية الصحية لخدمة احتياجات المجتمع وتنمية البيئة.

Faculty Mission

The Faculty of Medicine of Ain Shams University prepares a trained doctor with competitive skill at the local and regional level, capable of teaching, learning and training for life and is committed to standards of medical service and professional ethics, and the college supports the continuous development of programs, courses and scientific research while keen to expand applied scientific research and health care programs To serve the needs of society and develop the environment.

Study Protocol

What is already known on this subject? AND

What does this study add?

A higher risk for iron deficiency anemia has been noticed in children with early stages of type 1 diabetes (T1D). Anemia in diabetes is not uncommon and thus may contribute to disease complications. Hence this study is being conducted to determine the frequency of iron deficiency anemia in T1D.

1.INTRODUCTION/ REVIEW

Anemia in T1D may have a complex, multifactorial background (*Angelousi A and Larger E, 2015*). Among the most common causes of anemia in the course of T1D in children is iron deficiency, which will present as anemia with microcytosis in the blood count. Its prevalence is higher among T1D patients in comparison to people without diabetes (*Soliman et al., 2017*).

A higher risk for iron deficiency, which can lead to anemia, has been noticed in children with early stages of T1D. Anemia in diabetes is not uncommon and thus may contribute to disease complications (*Wójciak et al., 2014*).

If diagnostic procedures rule out the most common causes, co-occurrence of other autoimmune diseases (thyroiditis, celiac disease, Addison's disease, and autoimmune atrophic gastritis) that may be accompanied by anemia of various morphologies should be taken into account (*Angelousi A and Larger E, 2015*).

Adequate interpretation of the HbA1c measurement,

which is routinely performed during diabetes control visits, requires also knowing the patients' serum iron concentration, because the presence of iron deficiency anemia correlates with higher HbA1c values (*Christy et al., 2014*).

It is interesting that even though the value of a performed blood count is well known as well as the multiplicity of information it gives, there are no recommendations whether and when it should be carried out in T1D patients—neither in the guidelines published by Diabetes Poland (2018) nor those of the International Society for Pediatric and Adolescent Diabetes (*Elizabeth et al., 2018*), (*Gumprecht et al., 2018*).

2.AIM/ OBJECTIVES

Primary aim: To determine the frequency of iron deficiency anemia among T1D, Secondary aim: to identify possible etiologies of IDA and to correlate parameters to glycemic control.

3.METHODOLOGY: Patients and Methods

- **Type of Study:** A cross sectional study.
- **Study Setting:** Ain Shams University.
- **Study Period:** December 2019- July 2020
- **Study Population;**

Inclusion Criteria:

Two hundred patients with T1D aged from 2 to 18 years will be recruited from Pediatric and Adolescent Diabetes Unit (PADU), Ain shams university. Diagnosis of T1D is based upon criteria of ISPAD 2018 (*Mayer-Davis et*

al., 2018).

Exclusion Criteria:

Patients with other types of diabetes e.g. Type 2 diabetes, Maturity onset diabetes of youth (MODY).

- **Sampling Method:** Random sample of 200 patients.
- **Sample Size:** sample size was calculated using pass program. Setting the type 1 error (α) at 0.05 of the confidence interval width at 0.2 (margin of error 10%). Results from pervious study (*Thomas et al., 2004*) showed that 14% of DM cases had anemia. Calculation accordingly results in a minimal sample size of 47 approximated to 50.
- **Ethical Considerations:** Patients and accompanying parent will be informed about the study orally or will sign a written consent, and also approval of Local Ethical Committee will be obtained before patients' allocation.

- **Study Procedures**

All patients will be subjected to:

1- Detailed history including diabetic history in terms of duration, and control over last year prior study determined by frequency of hypoglycemia and or diabetic ketoacidosis, dietetic history, history of fatigue using the Fatigue Severity Scale (*Krupp et al., 1989*), history of parasitic infestations and history of menorrhagia in pubertal females.

2- Clinical examination: Full examination will be done laying stress on pallor, tachycardia according to age and gender, anthropometric measurements including weight

(kg) and height (cm). Using these values, the body mass index (BMI) will be calculated using the standard equation (the body mass in kilograms divided by the square of the body height in meters) to be plotted against centiles for age and gender (*Kuczmarski et al., 2002*).

3-Laboratory investigations:

- 1. Glycosylated hemoglobin (HbA1c) for all patients will be assessed:** through fluorescent immune-chromatography analyzing system with fine care TM FIA meter plus device.
- 2. Complete blood count for all patients:** A trained nurse will collect the sample through venipuncture, drawing the blood into a test tube containing an anticoagulant (EDTA, sometimes citrate) to stop it from clotting. Analysis begins when a well-mixed whole blood sample is placed on a rack in the analyzer. (*Buttarelli and Plebani , 2008*) Results will be interpreted according to special age and sex (*Nah et al., 2018*).
- 3. Patients with microcytic hypochromic anemia will undergo assessment of:**
 - **Serum iron, total iron-binding capacity (TIBC) and serum ferritin:** (*Gomella and Haist, 2007*) Serum iron and TIBC will be measured using Beckman Coulter method Au480, Transferrin saturation (percent of iron to total iron binding capacity) will be calculated (*Fauci et al., 2018*).
 - **Hepcidin:** Serum hepcidin concentration will be measured with a competitive enzyme-linked

immunosorbent assay (DRG Hepcidin-25 ELISA Kit (*Chernecky et al., 2013*).

- **Anti-tissue transglutaminase (IgA):** Serum anti-tissue transglutaminase IgA will be used to exclude celiac disease (*Dieterich et al., 1997*). It will be measured with enzyme linked immunosorbent assay (ELISA) technique.
- **Occult blood in stool:** It can also be used to look for active occult blood loss in anemia (*Harewood and Ahlquist , 2000*).
- **H-pylori antigen in stool**
- **Statistical analysis:**

Data will be collected and entered into the software and edited for errors. Quantitative data will be presented as mean and standard deviation or median and interquartile range. Comparison between groups will be done using paired t-test. Qualitative data will be presented as count and proportion and comparison between the groups will be evaluated using chi-square test. A p-value of 0.05 or less will be considered as the statistical significance level.

ABSTRACT

Background: Iron deficiency anemia (IDA) in children with type 1 diabetes (T1D) represents a significant burden. **Aim of the Work:** to assess iron status in children and adolescents with T1D and to correlate it with glycemic control and diabetic vascular complications. **Patients and Methods:** two hundred children and adolescents with T1D (123 male (61.5%) and 77 female (38.5%) aged 10.97 ± 3.93 years) recruited from Pediatric and Adolescent Diabetes Unit (PADU), Ain Shams University in the period from December 2019 to July 2020. History taking and examination were done stressing on anthropometric measurements. Laboratory evaluation including complete blood count, glycosylated hemoglobin (HbA1c), urinary albumin/creatinine ratio (ACR), lipid profile, serum iron, total iron-binding capacity (TIBC), serum ferritin, transferrin saturation, and patients with microcytic hypochromic anemia underwent hepcidin, quantitative anti-tissue transglutaminase (IgA), Occult blood in stool and H-pylori antigen in stool. **Results:** Seventy two of diabetic children were anemic (36%), fifty one had IDA (25.5%) and 10% has iron deficiency (ID). IDA was more prevalent in males with longer duration of diabetes. Children and adolescent with T1D and IDA experienced more clinically significant hypoglycemic episodes, more DKA attacks; high fatigue severity scale and low BMI. They also experience more micro vascular complications than those without anemia **Conclusions:** IDA occurred frequently in T1D children and adolescents. It is associated with poor glycemic control and frequent acute and chronic diabetes complications.

Key words: Iron Deficiency Anemia, Children, Adolescents, Type I diabetes, is it a Real Problem?

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List of Abbreviations

Abb.	Full term
ADHD	Attention deficit hyperactivity disorder
AMC.....	Austin Medical Centre
CCr	Creatinine clearance
FMASU REC:.....	Research Ethics Committee of Faculty of Medicine, Ain Shams University
FS	Febrile seizures
HbA1C	Hemoglobin A1C
ICH	International Council on Harmonization
ID.....	Iron deficiency
IDA	Iron deficiency anemia
IL-6	Interlukin-6
IOMS	Islamic Organization for Medical Sciences
ISPAD.....	International Society for Pediatric and Adolescent Diabetes
MCHC	Mean corpuscular hemoglobin concentration
MCV	Mean corpuscular volume
PADU	Pediatrics and Adolescent Diabetes Unit
RBC	Red blood cell
RDW	Red cell distribution width
T1D	Type 1 diabetes
TIBC	Total iron-binding capacity
WHO.....	World Health Organization