

Dedication

To source of my life...

To the spirit of my father...

And my mother...

**To source of my interesting in
life...**

My husband...

To source of my happiness..

**My daughter Dania...and her
sisters and brother**

To my sisters and my brother..

I dedicate this works ...

Amani

Acknowledgement

First grateful thanks to Allah..

Then to my supervisor Dr. Mohi Eldin Abass Abdall for his guidance and constant supervision as well as for providing necessary information regarding the project and also for his support in completing the project .My thanks also extended to my co supervisor Dr. fatehelrahman Mahdi I am deeply indebted to Dr.Mahmoud Elgari & Dr. Hassan Elsiddig for their help and advice, staff of medical laboratory of Atbra Teaching Hospital, Ministry of Health in River Nile State. My gratitude extends to Mrs. samah Hassan,and staff ofAli Hajj

Hammed Medical Laboratory and to all those who encouraged and supported me to finish this research. I am deeply indebted to the women who participate on this project.

Finally, lot of thanks to the members of my family and all my friends...

Amani

Abstract

This is cross sectional descriptive analytical study, conducted at River Nile state. During the period from November 2011 - June 2013 to determine the frequency of iron deficiency anemia among Sudanese pregnant women in River Nile state.

Three hundred (300) pregnant women were informed about the study and agreed for participation, a questionnaire was designed to collect information about the study group such as age, number of pregnancies, state of trimesters, miscarried, iron treatment, pathological blood loss and nutritional, economic state, 2.5 ml of venous blood was collected in EDTA anticoagulant container, thin blood film and reticulocyte count were done, screening was done by measurement of HbF and HbA2 levels HbS using capillary Hemoglobin Electrophoresis; CBC was done using a Sysmex™ Kx21n, serum iron, ferritin and TIBC were done using Biosystems A25. The results were analyzed by statistical package for social science (SPSS version 11.5)

The study showed that the frequency of the anemic group was (42.3%) related to all study groups. The study shows that the incidence of the iron deficiency anemia was (46.5%) thalassia anemia (3.9%) sickle cell anemia was (2.4) and other anemia (46.2%) in anemic group.

The means of Hb level, RBCs count, HCT% Red Cell indices (MCV, MCH, MCHC) were 7.6g/dl \pm 1.2, $3.6 \times 10^{12}/\pm 1.8$, 25.3% \pm 2.6, 78.2fl \pm 9.2, 24.5pg \pm 4.1 28.4g/dl \pm 3.8 respectively, and there was

statistical significant difference in the means of those values among anemic study group when compared with control group ($P < 0.05$).

The means of serum iron and serum ferritin among women of iron deficiency anemia group were $23.2\text{mg/dl} \pm 2.9$, $10.9\text{mg/dl} \pm 1.2$ respectively, were significantly lower than control group ,and total iron binding capacity was $481.4\text{mg/dl} \pm 9.4$, it was significant higher in comparison with means obtained in control group (p value < 0.05),

Iron deficiency anemia is the most common occurring among multiparous pregnant women (29.1%), than in normal child spacing pregnant women (16.5%) and prolonged child spacing pregnant women (0.8%).

In thalassemia carrier group the hemoglobin electrophoresis showed significant increase mean levels of HbA₂, and HbF were $5.8\% \pm 0.8$, $3.6\% \pm 0.5$, and lower level of HbA $90.6\% \pm 0.5$ in comparison with hemoglobin electrophoresis in control group (P value < 0.04). In homozygous sicklers HbA₂ was $2.2\% \pm 0.5$, and there was no significant differences in comparison with control group (p . value > 0.05), while HbF 26.8 ± 0.3 and HbS 70.3 ± 0.6 , were showed significant elevation respectively in comparison with control group (p . value < 0.05).

ملخص الدراسة

هذه الدراسة وصفية تحليلية أجريت في ولاية نهر النيل في الفترة ما بين نوفمبر 2011 - يونيو 2013م. وقد هدفت الدراسة إلى تحديد تكرار الإصابة بفقر الدم الناتج عن نقص الحديد والثلاسيميا والانييميا المنجلية عند السودانيات الحوامل في ولاية نهر النيل. أخذت (300) عينة من نساء حوامل بعد أخطارهن بهذه الدراسة وأهميتها وأخذت موافقتهن علي المشاركة . صمم أستبيان لجمع معلومات عن المشاركات في الدراسة بالنسبة للعمر وتاريخ العائلة في الإصابة بالانييميا عدد مرات الحمل ، فترة الحمل ، تاريخ وجود إجهاض ، علاج الحديد ، تاريخ وجود نزيف والحالة الاقتصادية وحالة التغذية . تم جمع عينة دم 3 مل في حاوية تحتوي على مانع تجلط (ثنائي أمين الإيثيلين رباعي حمض الخليك) تم عمل مسحه رقيقه للدم Hb F Hb A2 وحساب تعداد كريات الدم الحمراء الشعبية ثم قياس خضاب الدم بواسطة الرحلان الكهربى لجهاز (الهيموجلوبين إلكترولفوريسس) كما تم Hb S استخدام جهاز (سيسمكس) لتحليل تعداد الدم الكامل والذي يعمل اوتوماتيكيا، أيضا تم حساب تركيز الحديد في مصل الدم وتركيز فرتين مصل الدم وسعة ارتباط والذي يعمل اوتوماتيكيا وتم تحليل A25الحديد الكلى باستخدام جهاز (بايوسيسستم SPSS). النتائج إحصائيا باستخدام برنامج الحزم الإحصائية (الإصدار 11.5

أوضحت الدراسة أن تكرار المجموعة المصابة بفقر الدم (43.3%) بالنسبة لكل المجموعة تحت الدراسة . كذلك أوضحت الدراسة أن تكرار فقر الدم الناتج عن نقص الحديد (45.5%) وفقر الدم نوع الثلاسيميا (3.9%) وفقر الدم المنجلي المتجانس (2.4%) وفقر الدم نسبة لأنواع أخرى (46.2%) في المجموعة المصابة بفقر الدم . وتم حساب المتوسط مستوى خضاب الدم (الهيموغلوبين) ومتوسط عدد كريات الدم الحمراء ومكداس الدم الأحمر ومؤشرات الخلية الحمراء (متوسط حجم الخلية ، متوسط خضاب الخلية الدموي ، متوسط تركيز خضاب $3.6 \times 10^{12} / \text{ml} \pm 1.8$ ، $7.6 \pm 1.2 \text{ g/dl}$ الخلية الدموي) وكانت النتائج كالآتي: $25.3\% \pm 2.6$, $78.2 \text{ fl} \pm 9.2$, $24.5 \text{ pg} \pm 4.1$, $28.4 \text{ g/dl} \pm 3.8$ بالترتيب، كما أن هناك اختلاف ذو دلالة إحصائية واحتمالية أقل من (0.05%) في هذه القيم لدى النساء الحوامل بالمقارنة مع المجموعة الضابطة .

وفي مجموعة النساء المصابات بفقر الدم الناتج عن نقص الحديد وجد أن متوسط تركيز الحديد في مصل الدم ، ومتوسط تركيز فرتين مصل الدم كالآتي: بالترتيب، و كانت هذه القيم منخفضه $23.2 \text{ mg/dl} \pm 2.9$, $10.9 \text{ mg/dl} \pm 1.2$. بفرق إحصائي معنوي بالمقارنة مع المجموعة الضابطة .

وهي أعلى ، $9.4 \pm \text{mg/dl}$ وكانت قيمة متوسط سعة ارتباط الحديد الكلي 481.4 من متوسط المجموعة الضابطة والفرق ذو قيمة إحصائية معنوية . كما أوضحت نتائج الدراسة أيضاً أن فقر الدم الناتج عن نقص الحديد أكثر شيوعاً بين السيدات ذوات الحمل المتعدد (29.1%) مقارنة بذوات الحمل طبيعى الفترات ()

16.5%) والحمل طويل الفترات (0.8%). في المجموعة المصابة بفقر الدم
الثلاسيما وجد أن الرحلان الكهربائي لخضاب الدم كالتالي : ارتفاع خضاب الدم من
بالترتيب, كما $3.6\% \pm 0.5$, $0.8\% \pm 0.8$ للذان كانت قيمتهما $HbF 5.8$ HbA_2 النوع
بالمقارنة مع قيم الرحلات الكهربائي عند $HbA 0.5\% \pm 0.5$ وجد أيضا "إنخفاض 90.6
المجموعة الضابطة والفرق له دلالة إحصائية, وفي النساء المصابات بمرض فقر
الدم المنجلي المتجانس وجد أنه لا اختلاف في متوسط الرحلات الكهربائي لخضاب
ومتوسطه في المجموعة الضابطة , كما وجد فرق $2.2\% \pm 0.5$ HbA_2 الدم النوع
والنوع $Hb F 70.3 \pm 0.6$ إحصائي بين متوسط الرحلان الكهربائي لخضاب الدم نوع
. حيث كانا مرتفعان في مرض فقر الدم المنجلي $HbS 26.8 \pm 0.3$

Contents

NO	SUBJECT	PAGE
1	Dedication	I
2	Acknowledgement	II
3	Abstract(English)	III
4	Abstract(Arabic)	IV
5	Contents	V
6	Tables	XI
7	Figures	XIII
8	Abbreviations	XIV
Chapter one: introduction and literature review		
1.1	General Introduction	1
1.2	Literature Review	3
1.2.1	Blood	3
1.2.1.1	Blood Function	3
1.2.1.2	Blood composition	3
1.2.1.2.1	Plasma	4
1.2.1.2.2	Blood Cells	4
1.2.2	Anemia	9
1.2.2.1	Classification of Anemia	10
1.2.2.1.1	Morphological classifications of Anemia	10
1.2.2.1.2	Etiological classifications of Anemia	10
1.2.2.1.3	Physiological classifications of anemia	11
1.2.2.1.4	Kinetic Classification	11
1.2.2.2	Pathophysiology of Anemia	12
1.2.2.3	Frequency of anemia	12

1.2.2.4	Mortality and Morbidity by Anemia	13
1.2.2.5	Race and Anemia	13
1.2.2.6	Gender and Anemia	13
1.2.2.7	Age and Anemia	14
1.2.2.8	Causes of anemia	14
1.2.2.9	Signs and symptoms of anemia	15
1.2.3	Iron in the Human Body	15
1.2.3.1	Iron Distribution (Iron Compartment)	16
1.2.3.2	Function of iron	17
1.2.3.3	Transport of iron	17
1.2.3. 4	Iron Metabolism	19
1.2.3.5	Iron Absorption	19
1.2.3.6	Iron Deficiency Anemia	20
1.2.3.6.1	Etiology of iron deficiency anemia	21
1.2.3.6.2	Causes of Iron Deficiency anemia	21
1.2.3.6.3	Laboratory Diagnosis for Iron Deficiency Anemia	22
1.2.3.6.4	Iron deficiency specific tests	22
1.2.4	Pregnancy	24
1.2.4.1	Physiological change during pregnancy	26
1.2.4.2	Normal Hematological Changes during Pregnancy	26
1.2.4.3	Iron metabolism during pregnancy	28
1.2.4.4	Anemia in Pregnancy	29
1.2.4.4 .1	The physiologic anemia of pregnancy	29
1.2.4.4.2	Iron deficiency anemia and pregnancy	30
1.2.4.4.3	Etiology of Iron Deficiency in Pregnant Women	31
1.2.4.4.4	Causes of anemia during g Pregnancy	33
1.2.4.4.5	Nutritional Anemia of Pregnancy	33
1.2.4.4.6	Megaloblastic anemia and pregnancy	34
1.2.4.4.7	Clinical Features of Megaloblastic Anemia	35

1.2.5	Incidence of IDA in pregnancy in Sudan and worldwide	35
1.2.5.1	Incidence of IDA in pregnancy in the world wide	35
1.2.5.2	Incidence of IDA among pregnancy in Sudan	37
1.2.6	Rationale	39
1.2.7	Objectives:	40
1.2.7.1	General objective:	40
1.2.7.2	Specific objectives	40
Chapter two: Materials and Methods		
2.1	Study design	41
2.2	Ethical consideration	41
2.3	Study area	41
2.4	Sample size	41
2.5	Sample collection	41
2.6	Thin blood films spreading & staining Technique	43
2.7	Complete blood count	43
2.7.1	Principle of sysmex KX 21hematological analyzer	44
2.8	Reticulocyte count	45
2.8.1	Absolute Reticulocyte counts (ARC)	45
2.8.2	Corrected reticulocyte count (CRC)	46
2.8.3	Reticulocyte production index (RPI)	46
2.9	Principle and Procedure of Serum iron determination	47
2.10	Serum ferritin Principle and procedure	48
2.11	Total Iron Binding Capacity (TIBC) & Transferrin Saturation	49
2.12	Transferrin Saturation	50
2.13	Biosystems A25 instrument back ground and principle	50

1.14	Preparation of Red Cell hemolysate	51
2.15	Alkaline Hemoglobin Electrophoresis Principle	51
2.16	Statistical analysis	Freq uenc y of Red Cell Disor ders amon g Suda nese Preg nant Wom en in River Nile State 53
Chapter three: Results		
3-1	Clinical History of Study group	54
3-2	Frequency of anemic pregnant women among study group	56
3-3	Mean of Hb, hematocrit, RBCs count, RBCs indices and reticulocyte count in study group compared with control group	57
3-4	Iron profile status in study group compared to normal control	58
3-5	Frequency of anemia's among study group	59

3-6	Patterns of peripheral blood picture among study group	59
3-7	Frequency of anemias among multiparous women related to gap of pregnancy	60
3-8	Mean of HB-electrophoresis in normal healthy women of reproductive age	61
3-9	Hemoglobin A, Hb A ₂ and Hb F levels of Thalassemic group compared to control group	62
3-10	Hemoglobin A, Hb A ₂ and Hb F levels of sickle cell anemic group compared to normal control	63
Chapter four: Discussion, conclusion, Recommendation and References		
Discussion		64
Conclusion		68
Recommendation		69
References		70
Appendices		78

Tables

No	T itle	Page
1-1	Reference value of red cell indices in non pregnant women	8
1-2	Factors affect in iron absorption	20
1-3	Iron requirements in pregnancy	29
3-1	Clinical History of Study group	54
3-2	Frequency of anemic pregnant women among study group	56
3-3	Mean of Hb, hematocrit, RBCs count, RBCs indices and reticulocyte count in study group compared with control group	57
3-4	Iron profile status in study group compared to normal control	58
3-5	Frequency of anemia's among study group	59
3-6	Patterns of peripheral blood picture among study group	59
3-7	Frequency of anemias among multiparous women	60

	related to gap of pregnancy	
3-8	Mean of HB-electrophoresis in normal healthy women of reproductive age	61
3-9	Hemoglobin A, Hb A ₂ and Hb F levels of Thalassemic group compared to control group	62
3-10	Hemoglobin A, Hb A ₂ and Hb F levels of sickle cell anemic group compared to normal control	63

Figures

NO	Title	PAGE
1-1	Iron cycle in the Body	16
1-2	Microcytic hypochromic RBCs	21

List of abbreviations

ACD	Anemia of chronic disease
ARC	Absolute reticulocyte count
CBC	Complete blood count
CO₂	Carbon dioxide
CRC	Corrected reticulocyte count
ELISA	Enzyme linked immunosorbent assay
Fe⁺³	Ferric ions
Fe+2	ferrous ions
FeOOH	Ferric oxyhydroxide
FI	Femtoliters
HB	Hemoglobin
HB F	Fetal Hemoglobin
HCT	Hematocrit
IDA	Iron deficiency anemia
K2EDTA	Potassium Ethylene Diamine Tri acetic Acid
L/L	Liter per liter
LCD	Lucid Crystal Displyer
MCH	Mean Cell Hemoglobin
MCHC	Mean Cell Hemoglobin Concentration
MCV	Mean cell volume
MPV	Mean Platelet Volume
NRBCs	Nucleated red blood cells

PBP	Peripheral blood Picture
PC	Program computer
PCV	Packed cell volume
Pg	Picogram
RBCs	Red blood corpuscular cell
RC	Reticulocyte count
RE	Reticuloendothelia
RPI	Reticulocyte Production index
SCD	Sickle cell disease
SI	Serum Iron
STFR	Serum Trans Ferrin receptor
TEB	Tris/ EDTA/ Borate
TIBC	Total iron binding capacity
TRF	Transferrin
TWBCs	Total white blood cells