

:Dedication

To my wife Um Ala' , for her great
, encouragement and patience

To my sons: Ala', Baha', Bara', Asma',
, and Doa' with great love

To my brothers and sisters with great
.respect

: Acknowledgment

I would like to express my special thanks to my supervisor Dr. Mohammed Siddiq Mohammed Ali for his assistance and .help

I also thank my co-supervisor Dr. Malik .Hassan Ibrahim Mustafa

I would like to express my gratitude to Razi Hospital and it's administration and the head master Mr. Fawwaz Hammad .for his encouragement and help

I would like to thank my colleagues in .Razi hospital

I would also like to express my appreciation to all those who helped me . to complete this study

List of Contents

No	Subject	Page
I	Dedication	I
II	Acknowledgment	II
III	List of contents	III
IV	List of tables	V
V	List of figures	VI
VI	List of abbreviations	VII
VII	Abstract in English	IX
VIII	Abstract in Arabic	XI
	Chapter one (Introduction and literature review)	
1.1	Introduction	1
1.2	Literature review	5
1.2.1	Haemoglobin structure	5
1.2.2	Haemolytic anaemia	10
1.2.2.1	Membrane disorders	11
1.2.2.2	Enzymatic disorders	12
1.2.2.2.1	G6PD deficiency	12
1.2.3	Haemoglobinopathies	13
1.2.3.1	Defect in haemoglobin synthesis	15
1.2.3.1.1	Sickle cell anaemia	16
1.2.3.1.2	Hb-C	19
1.2.3.1.3	Hb-D	20
1.2.3.1.4	Hb-E	20
1.2.3.1.5	Hereditary persistence of fetal haemoglobin	21
1.2.3.1.6	Thalassaemias	22
1.2.3.1.6.1	Alpha Thalassaemia	22
1.2.3.1.6.2	Beta Thalassaemia	27
1.2.3.1.6.2.1	Beta Thalassaemia major	29
1.2.3.1.6.2.2	Beta Thalassaemia trait	31
1.2.3.1.6.2.3	Treatment of beta Thalassaemia	32
1.2.4	Iron over load and chelation	32

1.2.5	Previous studies	35
1.2.6	Prognosis and progress	41
1.2.7	Promising therapy	42
1.2.8	Laboratory technology for haemoglobinopathies	42
1.2.8.1	Cell counters	42
1.2.8.2	Electrophoresis	44
1.2.8.3	Hb-A ₂ quantitation and chromatography	44
1.2.9	Ethnicity	46
	Chapter two (Objectives)	
2.1	General objectives	48
2.2	Specific objectives	48
	Chapter three (Materials and methods)	
3.1	Study design	49
3.2	Study area	49
3.3	Study duration	49
3.4	Study population	49
3.5	Sampling	49
3.6	Procedures	49
3.6.1	Complete Blood Count	50
3.6.2	Electrophoresis	50
3.6.3	Hb-A ₂ quantitation	55
	Chapter four (Results)	57
	Chapter five (Discussion and Recommendations)	70
5.1	Discussion	70
5.2	Recommendations	73
	References	74
	Appendices	85

List of Tables

No	Title	Page
4.1	Means of Hb-A, Hb-A ₂ , Hb-F and Hb-S concentrations among the major Palestinian families	58
4.2	Means of Hb-A, Hb-A ₂ , Hb-F, and Hb-S concentrations in relation to gender in the major Palestinian families	59
4.3	Means of the total haemoglobin (Hb), Packed Cell Volume (PCV), Red Blood Cells (RBC), Mean Cell Volume (MCV) and Mean Cell Haemoglobin Concentration (MCHC) among the major tribes in Palestine	60
4.4	The association between the mean concentration of Hb-A, Hb-A ₂ , Hb-F and Hb-S and the type and color of the hair of the major Palestinian families	61
4.5	Mean of the concentration of Hb-A, Hb-A ₂ , Hb-F and Hb-S in relation to color of eye in individuals belong to the major families in Palestine	62
4.6	The correlation between length of Palestinian individuals and concentration of Hb-A, Hb-A ₂ , Hb-F and Hb-S	63
4.7	Test of significance between different types of haemoglobins and some Complete Blood Count and red cell indices detected in Palestinian families	64
4.8	comparison between the two methods used to determination of Hb-A ₂ (gel electrophoresis and chromatography-ion exchange resin)	65

List of Figures

No	Title	Page
1.1	Location of the genes of globin chains on chromosomes in the embryonic stage	7
1.2	Location of genes of globin chains on chromosomes in fetal and adult life	8
1.3	Synthesis of individual globin chains in prenatal and postnatal life	9
1.4	Genes in normal red cells and different types of alpha Thalassaemia	24
1.5	Alpha genes deletion in alpha Thalassaemia	25
3.1	Example for interpretation of the migration of normal and abnormal haemoglobins	53
3.2	Examples for the interpretation of the final result of electrophoresis curve and some haemoglobins present	54
4.1	The number of individuals/family	57
4.2	Means of the concentration of elevated Hb-A ₂ (>3.7%) in the major families in Palestine	66
4.3	Percentages of elevated Hb-F concentration (>2.0%) in the major families in Palestine	67
4.4	The occurrence of Hb-S in the major families in Palestine	68
4.5	The number of cases of normal and abnormal haemoglobins in all families	69

List of abbreviations

α	Alpha
β	Beta
γ	Gamma
δ	Delta
AIDS	Acquired Immune Deficiency Syndrome
Hb	Haemoglobin
Hb-A	Adult Haemoglobin
mRNA	Messenger Ribo Nucleic Acid
Hb-F	Fetal Haemoglobin
HS	Hereditary Spherocytosis
G6PD	Glucose 6 Phosphate Dehydrogenase
ATP	Adenosine Tri Phosphates
NADPH	Phosphorylated Nicotinamide Adenine Dinucleotide
GSH	Reduced Glutathione
HPFH	Hereditary Persistence of Fetal Haemoglobin
Hb-S	Sickle Haemoglobin
Hb-E	Haemoglobin E
Hb-C	Haemoglobin C
Hb-D	Haemoglobin D
PO ₂	Oxygen tension
HbSC	Haemoglobin SC
DNA	Deoxy Ribo Nucleic Acid
Hb-H	Haemoglobin H
MCV	Mean Corpuscular Haemoglobin
MCH	Mean Corpuscular Haemoglobin
RBCs	Red Blood Corpuscles
KSA	Kingdome of Saudi Arabia
SCD	Sickle Cell disease
USA	United States of America
PCR	Polymerase Chain Reaction
HPLC	High Performance Liquid Chromatography

HbA1c	Glycosylated Haemoglobin A1c
BC	Before Christmas
Km	Kilo meter
EDTA	Ethylene Diamine Tetra Acetic Acid
ml	Millie liter
mg	Millie gram
CBC	Complete blood Count
PCV	Packed Cell Volume
WBCs	White Blood Cells
MCHC	Mean Corpuscular Haemoglobin Concentration
RDW	Red Cell Distribution Width
NaCl	Sodium Chloride
mA	Millie Ampere
nm	Nano meter
rpm	Round per minute

Abstract

Thalassaemias are group of genetic disorders of haemoglobin synthesis, resulting from reduced rate of production of one or more of globin chains. It is prevalent in many countries and about 3% of the world population carries the gene. The study was conducted on 263 individuals belong to 10 different families in Jenin area in Palestine in the period Jan.2007 to Dec.2008.

A descriptive cross-sectional study was conducted to find out the distribution of beta Thalassaemia and other Hb variants in that families. Blood samples were subjected for Complete Blood Count (CBC), gel electrophoresis and ion exchange chromatography. The results were filed and subjected to SPSS for analysis.

The study showed that beta Thalassaemia present in high percentages (elevated Hb-A₂ and Hb-F) in Torokman (25%) and Aboalrob (23%) with overall percent of (15%). The study detects sickle cell Hb (HbS) in Qalalweh(41%), Noairat(27%) and Aboalrob(14%) and does not present in Ziud, Daraghmeh, Jaradat and Torokman.

The Hb concentration and other blood indices vary significantly among families. Also shows no correlation between color of eye, color of hair, type of hair and length of individuals and the concentration of Hb variants. The study also correlate between electrophoresis and chromatography with respect to Hb-A₂ measurement.

The study recommended that individuals belong to Torokman, Aboalrob, Qalalweh and Noairat should be subjected to haematological screen and advice to avoid carrier partners. Those individuals with reduced Hb, PCV, MCV and MCHC should be subjected to electrophoresis. The study

also recommended giving the persons in the community information's about Thalassaemia and sickle cell anaemia.

Further studies are recommended in other families in the area and Palestine.

• □ □ □ □ □ □ □ □ □

تعتبر أنيميا البحر المتوسط مجموعة من الاعتلالات الوراثية للهيموجلوبين، تنشأ عن انخفاض مستوى إنتاج أحد أنواع سلاسل البروتين (غلوبين).

تنشر في العديد من الدول بنسبة عالمية تقدر بحوالي 3%.

أجريت هذه الدراسة على 263 شخصاً ينتمون إلى 10 عائلات مختلفة في محافظة جنين في فلسطين في الفترة ما بين كانون الثاني (يناير) 2007 وحتى كانون أول (ديسمبر) 2008.

دراسة وصفية تم إجراؤها للتحري عن مدى انتشار أنيميا البحر المتوسط وأنماط أخرى من اعتلالات المريء وأمن المراشة الموجهة في المنطقة

حيث تم جمع العينات من الأشخاص، وتم عمل الفحوصات التالية لكل

عنده

- ❖ فحص دم أولي (CBC).
- ❖ فصل الأنواع Hb (فصل الأنواع بواسطة التيار الكهربائي)
- ❖ Ion-exchange chromatography بواسطة Hb-A₂ quantitation

تم جمع النتائج وعرضها على برنامج التحليل الإحصائي SPSS (Statistical Package for Social Science)

أظهرت الدراسة بأن أنيميا البحر المتوسط موجودة بنسبة عالية في كل من عائلات تركمان، أبو الرب، تلها العائلات الأخرى بنسبة أقل. تبين من خلال الدراسة أن الجين المسؤول عن الأنيميا المنجلية موجود بنسبة عالية في كل من عائلات قلالوة، نعيرات، أبو الرب، موجود بنسبة قليلة في عائلات أخرى، ولا يوجد في كل من عائلات زيدود، درا غمة، حرادات وعائلة تركمان.

ذلك أظهرت الدراسة تبايناً في قيم الأهيوجلوبين وبعض معايير الدم الأخرى بين العائلات، ولم تظهر الدراسة آية علاقة ما بين كل من أنواع الأهيوجلوبين وكل من لون العيون، لون الشعر، نوع الشعر وطول القامة.

كذلك تم المقارنة بين نتائج Electrophoresis و Hb-A₂ في كل من exchange chromatography.

وخرجت الدراسة بتوصيات إلى كل الأشخاص من عائلات تركمان، أبو الرب، نعيرات، قلالوة بعمل فحوصات ما قبل الزواج بشكل كامل، كذلك كل شخص تكون عنده قيم فحوصات الدم الأولية من Hb, PCV, MCV قليلة، عليه عمل Electrophoresis مباشرة.

كذلك أوصت الدراسة بعمل نشرات تشيفيفية عن أنيميا البحر المتوسط وأنيميا المنجلية لأنباء المجتمع الفلسطيني وان يصار إلى عمل دراسات أخرى على عائلات أخرى في المنطقة وفي سائر إنجاء فلسطين.