

D

**Serum Neopterin Concentrations in Childhood
Hematological and Lymphoproliferative
Malignancies**

Thesis

**Submitted for partial fulfilment of Master Degree in
Pediatrics**

By

**Sheriene Samir Malak
(M.B.B.Ch 1991)**

Supervised by

Prof. Dr. Kotb Ahmed Tolba

**Professor of Pediatrics
Faculty of Medicine
Ain Shams University**

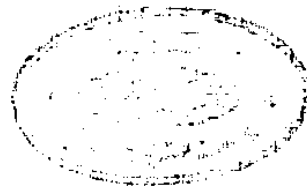
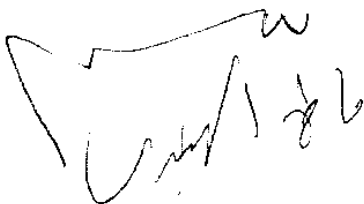
Dr. Sahar Mohamed Ahmed

**Lecturer of Pediatrics
Faculty of Medicine
Ain Shams University**

Dr. Nagy Abdalla Iskander

**Lecturer of Chemical Biochemistry
National Center for Radiation Research and Technology
Atomic Energy Authority**

618.920075
Sh.S





Acknowledgment

I wish to express my gratitude to my professor Dr. Kottb Ahmed Tolba professor of pediatrics, Faculty of Medicine Ain Shams University, for giving me the privilege to work under his supervision and for his continuous encouragement and guidance.

I also wish to thank Dr Sahar Mohammed Ahmed Lecturer of pediatrics, Faculty of Medicine, Ain Shams University for her encouragement and her patience with me in this study.

I also wish to thank Dr. Nagy Abdalla Iskander Lecturer of Chemical Biochemistry, National Center for Radiation Research and Technology, Atomic Energy Authority for his direct supervision and his guidance throughout the practical part of this work.

I also wish to thank Dr. .Azza Abdel-Gawad Tanatawi. Lecturer of pediatrics, Faculty of Medicine, Ain Shams University for her follow up of this work and her great effort with me in this study.

CONTENTS

	<u>Pages</u>
Introduction.....	1
Aim of work.....	2
Review of literature	
• Childhood acute leukemia	
Introduction.....	3
Epidemiology of AL in childhood.....	4
Etiology of AL.....	7
Classification of AL.....	10
Clinical presentation of AL.....	15
Diagnosis of AL.....	17
Prognostic factors in AL.....	19
Therapy of AL.....	22
• Childhood lymphomas	
Introduction.....	27
A - Hodgkin`s disease.....	27
Epidemiology of H.D.....	27
Aetiology of HD.....	28
Clinical presentation of HD..	29
Staging classification of HD.....	30
Diagnosis of HD.....	32
Prognosis of HD.....	34
Therapy of HD.....	35
B-Non Hodgkin`s Lymphoma.....	37
Introduction.....	37
Epidemiology of NHL.....	37
Aetiology of NHL.....	38
Classification of NHL.....	40
Clinical presentation of NHL.....	42

Diagnosis of NHL.....	43
Staging of NHL.....	44
Prognosis of NHL.....	45
Treatment of NHL.....	48
Neopterin	
Introduction.....	49
Chemistry of neopterin.....	49
Biosynthesis of neopterin.....	50
Immunology of neopterin.....	52
Physiology of neopterin.....	52
Circadian rhythm of neopterin.....	53
Measurments of neopterin.....	53
Concentrations of neopterin in healthy subjects	54
Bioppterin and neopterin in various milk and infant formulas.....	55
Conditions associated with high neopterin levels	56
Subjects and Methods	
Results.....	73
Discussion.....	98
Summary and Conclusions.....	105
Recomendations.....	107
References.....	108
Arabic summary	

List of tables

	Pages
Table (1) :	FAB classification of ALL11
Table (2) :	FAB classification of ANLL.....12
Table (3) :	Immunology markers of ALL.....13
Table (4) :	Cytochemical classification of ALL.....14
Table (5) :	The general strategy for the therapy of ALL.....22
Table (6) :	Ann Arbor staging of HD.....31
Table (7) :	Rye's classification of HD.....32
Table (8) :	Factors of high risk of different stages of HD.....34
Table (9) :	Important prognostic factors of HD.....35
Table(10):	Histologic classification , relative frequency.....40 and common anatomic sites of NHL
Table(11):	NCI Working Formulation and its relation42 to the Rappaport Classification of NHL .
Table(12):	Clinical staging of NHL45
Table(13):	Clinical and pathologic features affecting.46 treatment outcome in NHL
Table(14):	Disease states associated with activation.....57 of cellular immunity
Table(15):	Reagents supplied with the kits.....72
Table(16):	Clinical and laboratory data of ALL patients.....77 at diagnosis (group Ia)
Table(17):	Clinical and laboratory data of ALL patients.....78 in remission (group Ib)
Table(18):	Clinical and laboratory data of ALL patients.....79 at relapse (group Ic)
Table(19):	Clinical and laboratory data of ANLL patients....80 (group II)
Table(20):	Clinical and laboratory data of NHL and HD.....81 patients (group III)
Table(21):	Clinical and laboratory data of the controls.....82 (group IV)

Table(22):	Comparison of the clinical findings of.....83 group(Ia , Ib , Ic), group II and group III to the control group IV
Table(23):	Comparison of serum level of neopterin.....83 among ALL patients (at diagnosis , remission and relapse)
Table(24):	Comparison of serum level of neopterin.....84 between NHL and HD patients
Table(25):	Comparison of serum level of neopterin84 between NHL I-II and NHL III-IV
Table(26):	Comparison of serum level of neopterin.....85 among the , three studied groups

List of Figures

	Pages
Figure (1) : Chemical structure of neopterin.....	49
Figure (2) : Biosynthetic pathway for neopterin.....	51
Figure (3) : The mean serum level of neopterin in the three studied groups and the control group.....	86
Figure (4) : Comparison of the mean serum level of neopterin in ALL patients with isolated BM relapse and ALL patients with BM and CNS relapses	87
Figure (5) : A negative correlation between serum..... neopterin and Hb % in group Ia ,Ic	88
Figure (6) : A negative correlation between serum neopterin and Hb % in group II	89
Figure (7) : A negative correlation between serum. neopterin and Hb % in groups III	90
Figure (8) : A positive correlation between serum neopterin and TLC in group Ia,Ic	91
Figure (9) : A positive correlation between serum neopterin and TLC in group II.	92
Figure (10) : A positive correlation between serum..... neopterin and TLC in group III	93
Figure (11) : A negative correlation between serum..... neopterin and platelets count in group Ia ,Ic	94
Figure (12) : A negative correlation between serum neopterin and platelets count in groups III	95
Figure (13) : A positive correlation between serum..... neopterin and % of blasts in bone marrow in group Ia , Ic	96
Figure (14) : A positive correlation between serum..... neopterin and % of blasts in bone marrow in group II	97

Introduction

Introduction

Acute leukemia is a primary malignant disease of blood forming organs characterized by predominance of immature myeloid or lymphoid precursors (blasts). (**Weinstein , 1988**).

In Egypt, **Khalifa et al., (1993)** reported a prevalence of leukemia of 56.3% among pediatric malignant diseases.

The term lymphoma embraces a heterogenous group of disorders persumed to be malignant, that originates in one or other of the lymph nodes or other lymphatic tissues of the body. (**Goldman, 1989**).

Neopterin is an intermediate product in the metabolic pathway of pteridines released in vitro from non proliferating activated cells such as macrophages stimulated with interferons.

Increased serum levels of ^{neopterin} cell mediated immune activation and in neoplastic diseases, including haemopoietic tumors. (**Kelsey et al.,1994**).

Davies et al.,1992 suggested that neopterin concentrations may be useful for assessment of tumor activity in adult haematological malignancies.

Recently, **Motyl et al., 1994** described increase in serum and urinary neopterin levels in Hodgkin and non Hodgkin lymphoma in adults.

