

URINARY NEOPTERIN IN CHRONIC ACTIVE HEPATITIS C

Thesis

Submitted for Partial Fulfillment of
Master Degree of
Internal Medicine

Presented by

Nagwa Mahmoud Khalil Abu Eita
M.B., B. Ch.

Supervisors

Prof. Dr. Mohamed Kamel Sabri

Prof. of Internal Medicine
and Immunology
Ain Shams University

Prof. Dr. Mona Mohamed Rafil

Prof. of Clinical Pathology
and Immunology
Ain Shams University

Dr. Abd El-Rahman Abd El-Hamid Soliman

Assis. Prof. of Internal Medicine and Immunology
Ain Shams University

**Faculty of Medicine
Ain Shams University**

1997



بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

"سَنُرِيهِمْ ءَايَاتِنَا فِي الْأَفَاقِ وَفِي أَنْفُسِهِمْ
حَتَّىٰ يَتَبَيَّنَ لَهُمْ أَنَّهُ الْحَقُّ ۖ أَوَلَمْ يَكْفِ
بِرَبِّكَ أَنَّهُ عَلَىٰ كُلِّ شَيْءٍ شَهِيدٌ"

صدق الله العظيم

سُورَةُ فَصَّلَتْ

آيَةُ "٥٣"

***To my
Family***

***To my
Supervisors***

ACKNOWLEDGEMENT

I would like to express my sincere thanks, deepest gratitude and appreciation to ***Prof. Dr. Mohamed Kamel Sabri, Professor of Internal Medicine and Immunology, Ain Shams University*** who offered me the generous support and many useful criticisms and suggestions throughout this work. His precious guidance and continued supervision which were kindly given are far beyond acknowledgement.

I wish to express my deepest gratitude to ***Prof. Dr. Mona Mohamed Rafik, Professor of Clinical Pathology & Immunology, Ain Shams University***, for her great help in offering me all the facilities, true assistance in fulfilling the practical part of this work and for her kind supervision.

I am honored to express my sincere thanks and deepest gratitude to ***Dr. Abd-El-Rahman Abd-El Hamid Soliman, Assis. Prof. of Internal Medicine and Immunology, Ain Shams University*** for his kind supervision, cordial support, most appreciable advice and great help that have contributed a lot to conduct this work to that term. His close continued supervision is beyond acknowledgement.

I am deeply grateful to ***Dr. Shahira Mohamed Fathy El-Fedawey, Lecturer of Clinical Pathology and Immunology, Ain Shams University*** for her kind great help, cooperation and close guidance in the practical part of this work.

I wish to express my sincere thanks to ***Dr. Maged Abd-El Kariem, Lecturer of Community and Statistical Medicine, Ain Shams University*** for his valuable kind help in the statistical part of this work.

To all my respectable colleagues and members of Internal Medicine Department in Dar El-Shifa Hospital [Ministry of Health], to whom I belong, I'm deeply grateful.

To all the nursing staff in Dar El-Shifa Hospital, who did help in collecting samples for performance of this work, as well as my patients, I am quiet grateful.

LIST OF CONTENTS

	<u>Page</u>
- INTRODUCTION AND AIM OF THE WORK	1
- REVIEW OF LITERATURE	
Chapter I:	
Virus C Hepatitis	3
Epidemiology and transmission	4
Virology	9
Immune mediated liver damage	19
Clinical features	25
Complications	27
Diagnosis	32
Treatment	34
Vaccination	53
Chapter II:	
Neopterin.....	54
Historical aspect	54
Chemistry	55
Biosynthesis	56
Sources	58
Clinical significance	66
Neopterin and different pathological disorders..	67
- PATIENTS AND METHODS	83
- RESULTS	88
- DISCUSSION	110
- SUMMARY AND CONCLUSION	118
- REFERENCES	122
- ARABIC SUMMARY.	

LIST OF TABLES

	<u>Page</u>
Table [1-1]: HCV Genotyping Methods	18
Table [1-2]: Extrahepatic manifestations of HCV infection	31
Table [2-1]: The production of neopterin by PBMC in response to different mitogens and antigens	63
Table [3-1]: Incstar neopterin assay procedure and flow table	86
Table [4-1]: Age and sex distribution of the four studied groups	91
Table [4-2]: Age and sex distribution of the control group [V]	92
Table [4-3]: Liver and kidney function tests for patients of group I	93
Table [4-4]: Liver and kidney function tests for patients of group II	94
Table [4-5]: Liver and kidney function tests for patients of group III	95
Table [4-6]: Liver and kidney function tests for patients of group IV	96
Table [4-7]: Urinary neopterin levels [μ mols/mol creatinine] for patients of group I & II	98
Table [4-8]: Urinary neopterin levels [μ mols/mol creatinine] for patients of group III & IV	99
Table [4-9]: Urinary neopterin levels [μ mols/mol creatinine] for the control subjects [group V]	100
Table [4-10]: Comparison between the mean value of urinary neopterin [μ mols/mol creatinine] of group I and group [V] [the controls]	103
Table [4-11]: Comparison between the mean value of urinary neopterin [μ mols/mol creatinine] of group II and group V [the controls]	103

	<u>Page</u>
Table [4-12]: Comparison between the mean value of urinary neopterin [$\mu\text{mols/mol}$ creatinine] of group III and group V [the controls]	104
Table [4-13]: Comparison between the mean value of urinary neopterin [$\mu\text{mols/mol}$ creatinine] of group IV and group V [the control]	104
Table [4-14]: Comparison between the mean values of urinary neopterin of group [I] and the other patients groups [$\mu\text{mols/mol}$ creatinine]	105
Table [4-15]: Comparison between the mean values of urinary neopterin $\mu\text{mols/mol}$ creatinine of group II and group III and IV	106
Table [4-16]: Comparisons between The mean values of urinary neopterin [$\mu\text{mols/mol}$ creatinine] in all patients of both sex	107
Table [4-17]: Correlation between liver enzymes and urinary neopterin levels in all patients groups	107

LIST OF FIGURES

	<u>Page</u>
Fig. [1-1]: The identification of a viral clone of the hepatitis C virus from chimpanzee liver infected with 'non-A, non-B' virus	10
Fig. [1-2]: HCV genome and recombinant antigens, as elucidated by commercially available assays	12
Fig. [1-3]: HCV replication	14
Fig. [1-4]: Approach to treatment if hepatitis C virus RNA testing is not available	38
Fig. [1-5]: Approach to treatment if hepatitis C virus RNA testing is available	40
Fig. [1-6]: Approach to treatment if hepatitis C virus RNA measurement and genotyping or serotyping are available	42
Fig. [2-1]: Chemical structure of neopterin	55
Fig. [4-1]: Mean levels of ALT & AST [IU/L] for all patients' groups	97
Fig. [4-2]: Individual distribution of urinary neopterin levels [μ mols/mol creatinine] for all patients' groups & the control group	101
Fig. [4-3]: Showing mean levels of urinary neopterin [μ mols/mol creatinine] for all patients' groups & the control group	102
Fig. [4-4]: Correlation between urinary neopterin levels [μ mols/mol creatinine] & ALT [IU/L]	108
Fig. [4-5]: Correlation between urinary neopterin levels [μ mols/mol creatinine] & AST [IU/L]	109

