Liver Dysfunction in the Pediatric Emergency Room: The Role of Infection

Thesis

Submitted for Fulfillment of Master Degree (M.Sc.) in
Pediatrics

Presented by

Yasser Ahmed Rashed
(M.B.B.Ch.)

Under Supervision of

Prof. Dr. Hala Mohamed Fouad
Professor of Pediatrics
Faculty of Medicine, Cairo University

Prof. Dr. Mona El Said El-Raziky
Professor of Pediatrics
Faculty of Medicine, Cairo University

Prof. Dr. Eman Fawzy Halawa
Assistant Professor of Pediatrics
Faculty of Medicine, Cairo University

Faculty of Medicine
Cairo University
2012

بسم الله الرحمن الرحيم

"وقل رب زدني علما"

صدق الله العظيم
(سورة طه، الآية ١١٤)

ABSTRACT

Sepsis is the leading cause of death in patients admitted in intensive care units (IUCs). Hepatic dysfunction represents a common manifestation during the sepsis process, ranging from a mild elevation of serum bilirubin and/or liver enzymes to severe hepatic failure.

The aim of current study was to investigate the relation between sepsis in (PICU) and hepatic dysfunction in children admitted to Pediatric Emergency Department of Cairo University Children Hospital, our results showed that the 50 studied children showed elevated liver enzymes (the mean ALT was 167.32±176.74), (mean AST was 140.72±105.65) with elevation of CRP (the mean CRP was 26.76±19.21 mg/l) and TLC (mean TLC was 13.77±7.43/cmm) (mean Hb% was 10.13±2.33 gm/dl) and (mean platelets count was 216.07±141.21/cm) denoting role of infections in hepatic dysfunction in (PICU), the mean age of the studied children was 10.80±16.42 months. Sepsis represented 70% of the children with elevated liver enzymes; where Klebsiella was the commonest organism detected in blood cultures (50%). Among all the children who showed elevated liver enzymes, jaundice was commonest detected sign of liver dysfunction (56%). Improvement of infection was associated with improvement of liver dysfunction.

Keywords: Sepsis, Liver Dysfunction, Pediatric Intensive Care Unit.

Acknowledgement

*First, thanks are all due to **Allah** for Blessing this work until it has reached its end, as a part of his generous help throughout our life.*

It was an honor to work under the supervision of eminent professors, who lent me their whole hearted support and immense facilities as is their usual with their juniors. To them, I owe more than I can record.

*I would like to express my deepest gratitude and highest appreciation to **Professor Dr. Dawlat Abdel hamid Belal,** professor of internal medicine and nephrology, faculty of medicine, Cairo University, for her continuous encouragement, generous support and unlimited help, no word can express my gratitude.*

*I would like to express my sincere gratitude to **Dr. Bahaa ElDin Mostafa Zayed**, Lecturer of Internal Medicine and Nephrology, Cairo University, who supervised this work with great interest and who gave me unlimited support throughout the work.*

*Many thanks to **Dr. Malak Nabil Amin**, Lecturer of Internal Medicine and Nephrology, Theodor Bilharz Research Institute,for her continuous help, valuable suggestions, guidance and encouragement during the progress of this work.*

I am greatly honored to express my deep gratitude and faithfulness to ***Prof. Dr. Afaf abdelhady,*** *Professor of biochemistry, Theodor Bilharz Research Institute, for her continuous help and kind sympathy.*

I am extremely grateful to ***dr. Ashraf abdel Khalek*** *, Lecturer of Intensive Care , Theodor Bilharz Research Institute for his unlimited efforts in the echocardiographic examination , he gave me much of her time, advise and effort throughout this work.*

Special thank and gratitude to my Mother ***Prof. Dr. Azza el Shamaa*** *, professor of internal Medicine and nephrology, Theodor Bilharz Research Institute , for her great support and help for the completion of this work.*

Finally, No words can express my deepest appreciation andgratitude to ***my family and my wife*** *for their never ending support and care.*

CONTENTS

Page

List of Abbreviations ……..……..... V

List of Figures…….……... VIII

List of Tables ……..…… IX

INTRODUCTION AND AIM OF THE WORK ……... 1

REVIEW OF LITERATURE:

- **Chapter I:** Cardiovascular Disease in ESRD …… 4
- **Chapter II:** Disorders of Calcium and Phosphorus in ESRD …… 25
- **Chapter III:** Dialysate Composition ……. 52

SUBJECTS AND METHODS …….……..…… 75

RESULTS …….…….……..... 81

DISCUSSION 97

SUMMARY AND CONCLUSIONS 111

RECOMMENDATIONS ……...……...…... 116

REFERENCES ……..……..……. 117

ARABIC SUMMARY ……..

List of Abbreviations

ABD	:	adynamic bone disease
ACE-I	:	Angiotensin Converting Enzyme Inhibitor
ALP	:	Alkaline phosphatase
AMI	:	Acute myocardial infarction
ARBS	:	Angiotensin receptor blockers
AVC	:	Aortic valve calcification
BAPTA	:	bis(o-aminophenoxy)ethane-N, tetraacetic acid
BB	:	Beta blockers
BP	:	Blood Pressure
Ca	:	Calcium
Ca MB	:	Ca mass balance
Ca x P	:	Calcium Phosphorus product
CAD	:	Coronary Artery disease
CaR	:	calcium sensing receptor
CHD	:	Coronary heart disease
CHF	:	Congestive heart failure
CI	:	Collapse Index
CKD	:	Chronic Kidney Disease
CKD-MBD	:	Chronic kidney disease –mineral bone disorder
CRP	:	C-reactive protein
CV	:	Cardiovascular
CVD	:	Cardiovascular disease
dCa	:	Dialysate calcium
DCOR	:	Dialysis Clinical Outcomes Revisited
ECG	:	Electrocaodiography
ESRD	:	End stage renal disease
FDA	:	Food and drug association
FGF 23	:	Fibroblast growth factor 23
GFR	:	Glomerular Filtration Rate
gm	:	Gram
HD	:	Hemodialysis
HdCa	:	High calcium dialysate
HDF	:	Haemodiafiltration
HMG-CoA	:	Hydroxy-3-methylglutaryl coenzyme A

I ca	:	Ionized Calcium
IDH	:	Intradialytic Hypotension
IDWG	:	Interdialytic weight gain
IDWG	:	Interdialytic weight gain
IU	:	International unit
K	:	Potassium
K/DOQI	:	Kidney Disease Outcomes Quality Initiative
KDIGO	:	Kidney Disease: Improving Global Outcomes
Kg	:	Kilogram
LdCa	:	Low calcium dialysate
LDL	:	Low density lipoproteins
LHD	:	Long haemodialysis
LV	:	Left ventricle
LVH	:	Left ventricular Hypertrophy
MAC	:	Mitral annular calcification
Mg	:	Magnesium
Mg/L	:	Milligrams/Litre
MGP	:	Matrix Gla protein
ml	:	milliliter
Mmol/l	:	Millimolar/liter
Na	:	sodium
NDHD	:	nocturnal daily haemodialysis
NSAIDs	:	Non steroidal anti inflammatory drugs
Po4	:	Phosphours
PTH	:	Parathyroid hormone
PVD	:	Peripheral vascular disease
QB	:	Pump speed
rHuEpo	:	recombinant human erythropoietin
SBP	:	Systolic blood pressure
SD	:	Standard deviation
SDHD	:	Short daily haemodialysis
SHD	:	Standard haemodialysis
SHPT	:	Secondary hyperparathyroidism
SMC	:	Smooth muscle cell
SPSS	:	Statistical Package for the Social Science
T ca	:	Total Calcium

TPN	:	Total parentral nutrition
US	:	United States
USRDS	:	United States renal data system
VDR	:	Vitamin D receptor
VDRAs	:	vitamin D receptor activators
VSMCs	:	vascular smooth muscle cells
%	:	Percentage
$1,25(OH)_2D_3$	:	1,25-dihydroxy vitamin D

LIST OF FIGURES

Fig. No.	*Title*	*Page*
1.	Theories for vascular calcification	17
2.	Possible roles of elevated Calcium and Phosphorus on vascular smooth muscle calcification	20
3.	Mineral metabolism and bone disease in CKD	27
4.	Mechanisms by which Phosphorus induces PTH secretion	30
5.	The homeostasis of calcium and phosphorus	31
6.	A comparison of serum phosphate relative reduction kinetics during three sequential dialysis prescriptions	42
7.	Approach to Management of bone metabolism and disease in CKD patients on dialysis (stage 5)	46
8.	Mechanism of hypotension when using low-sodium dialysate	54
9.	Effects of high - sodium dialysate	55
10.	Examples of sodium profiling regimens	57
11.	Individualization of Dilysate Calcium	68
12.	Serum calcium during and after dialysis with a high dialysate calcium bath	72
13.	Gender of patients in Group A & Group B	81
14.	Aetiology of chronic renal failure in studied patients.	82
15.	Comparison between group A and group B regarding hemodialysis duration , systolic and dystolic blood pressure	85
16.	Comparison between valvular calcification between group A and group B	87
17.	Comparison between valvular calcification and non valvular calcification patients within group A	88
18.	Comparison between valvular calcification and non valvular calcification patients within group B	89
19.	comparison between group A and group B regarding calcium and Alphacalcidol treatment	91
20.	Comparision between laboratory data between group A and Group B	92
21.	Comparison between echocardiographic data of (Group A) and (Group B)	95

List of Tables

Table No.	*Title*	*Page*
1.	Risk Factors for Cardiovascular Disease in Kidney Disease	5
2.	NKF-K/DOQI treatment targets for the management of iPTH, calcium, phosphorus and Ca×P in patients requiring dialysis	33
3.	A strategy to control hyperphosphataemiain ESRD patients	36
4.	Vitamin D Nomenclature	44
5.	Causes of adynamic renal osteodystrophy	50
6.	Usual composition of dialysate	52
7.	Causes of hyperkalemia in ESRD patients	60
8.	Causes of hypokalemia in ESRD patients	62
9.	Adverse systemic consequences of metabolic acidosis	66
10.	Potential advantages and disadvantages of different dialysate calcium concentrations	73
11.	Potential advantages and disadvantages of different components of the dilysate	74
12.	Descriptive statistics of the mean age of patients included in the study	82
13.	Descriptive statistics of laboratory data of all patients included in the study	83
14.	Descriptive statistics of echocardiographic data of all patients included in the study	84
15.	Descriptive statistics of Hemodialysis Data of all patients included in the study	85
16.	Prevalence of Calcification of patients included in the study	87
17.	Descriptive statistics between Valvular calcification patients compared to non valvular calcification patients within group A	88
18.	Descriptive statistics between Valvular calcification patients compared to non valvular calcification patients within group B	89
19.	Prevalence of Intradialytic Hypotensionin all patients included in the study	90
20.	Comparison between treatment dose with calcium supplement and Alphacalcidol Between Group A and Group B	91
21.	Comparison between laboratory data of Group A and Group B	92
22.	Comparison between echocardiographic data of Group A and Group B	95

INTRODUCTION

Even though calcium is one of the most abundant substances in the body, the plasma concentration of ionized calcium is only about 1.1 to 1.5 mmol/L. The total body calcium ranges from 1.0 to 1.5 kg (or about 1.5% of the total body weight), of which 99% is stored in the bones. Of the calcium in the plasma, 40% is bound to proteins (80–90% of that to albumin), 14% is complexed, and 46% is ionized. The latter 2 fractions are dialyzable. A balanced diet provides about 800–1200 mg of calcium per day, of which varying amounts are absorbed by the intestines **(Popovtzer, 2003)**.

In dialysis clinics in the United States, the concentration of calcium in the dialysate is probably the most varied of all the electrolytes. The most common concentrations used today are 1.25, 1.5, and 1.75 mmol/L (i.e., 2.5, 3.0, and 3.5 mEq/L; or 5.0, 6.0, and 7.0 mg/ dL) **(Sam et al , 2006).**

The choice of dialysate calcium concentration is able to influence many of the most important factors in the successful management of chronic HD patients **(Christopher, 2008).**

Concentrations in the dialysate can be customized depending on the current and targeted serum Ca levels as well as the desire to maintain hemodynamic stability during dialysis **(Palmer, 2001).**

Long-term use of dialysate calcium with 1.25mmol/L would be associated with relatively lower serum calcium concentrations, which

would lead to more rapid elevation of iPTH and progression of secondary hyperparathyroidism**(Hwang et al., 2008).**

In haemodialysis patients with secondary hyperparathyroidism, a dialysate calcium concentration of 1.75 mmol/L results in better control of parathyroid overfunction and high turnover bone disease than with lower dialysate calcium concentrations**(Molina et al., 2008).**

Excessive lowering of serum calcium during the haemodialysis session by a low dialysate calcium concentration may be associated with more frequent episodes of hypotension and cardiac rhythm disturbances. Probably, the most life-threatening episodes are ventricular arrhythmias in association with concomitant hypokalaemia **(Severi et al., 2008).**

Cardiac arrhythmias are also more likely to occur in HD patients with lower dialysate Ca associated with the potential for worsening of QT prolongation **(Nappi et al., 2000).**

AIM OF THE WORK

The aim of this work is to investigate the relative role of Different Dialysate Calcium Concentrations on Parathyroid Hormone Levels and Cardiovascular stability in ESRD patients on regular hemodialysis.

CHAPTER I

Cardiovascular Disease in ESRD

Introduction:

Cardiac disease is the major cause of death, accounting for 41 percent of all-cause mortality in patients receiving hemodialysis ***(Lafrance et al., 2006).***

Cardiac diseases are associated independently with a decrease in kidney function and progression of existing kidney diseases ***(Elsayed et al., 2007,*** In both the acute setting and more long-term phase, even small decreases in GFR are associated with adverse outcome ***(Coca et al., 2007).***

Persons with CKD are predisposed to three types of CVD, atherosclerosis, arteriosclerosis, and cardiomyopathy when compared with age and gender matched persons with normal kidney function ***(Wali et al., 2005).*** In the past cardiovascular death was mainly viewed as the result of accelerated coronary heart disease (CHD). Although CHD is undoubtedly more frequent than in the background population, the importance of the two other, largely unresolved cardiovascular problems, Sudden death and cardiomyopathy ***(Remppis and Ritz., 2008)***.