PITUITARY GONADAL ABNORMALITIES IN EGYPTIAN CHILDREN AND ADOLESCENTS WITH CHRONIC RENAL INSUFFICIENCY

Thesis

submitted for partial fulfillment of MD Degree in Paediatrics

By

Ihab Zaki F. El Hakim

M.B., B. Ch., MS Paediatrics

Assistant lecturer of Paediatrics,

Faculty of Medicine, Ain Shams University.

Supervised by

Prof. Dr. Farida Ahmad Farid

Professor of Paediatrics,

Faculty of Medicine, Ain Shams University.

Assistant supervisors

Dr. Khaled Salah Awwad

Assistant professor of Paediatrics,

Faculty of Medicine, Ain Shams University.

Dr. Mohammed S. El Din Faheem

Lecturer of Paediatrics,

Faculty of Medicine, Ain Shams University.

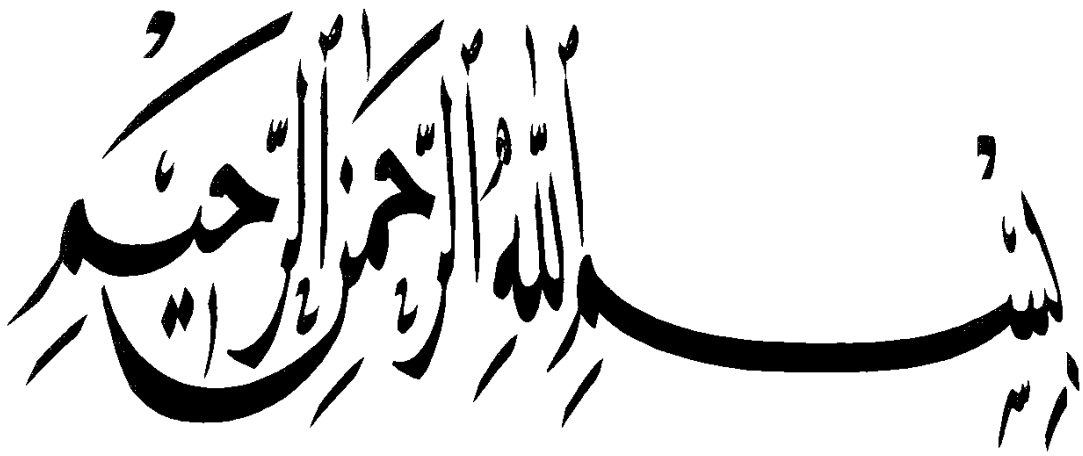
Dr. Taher Mohammed Farid

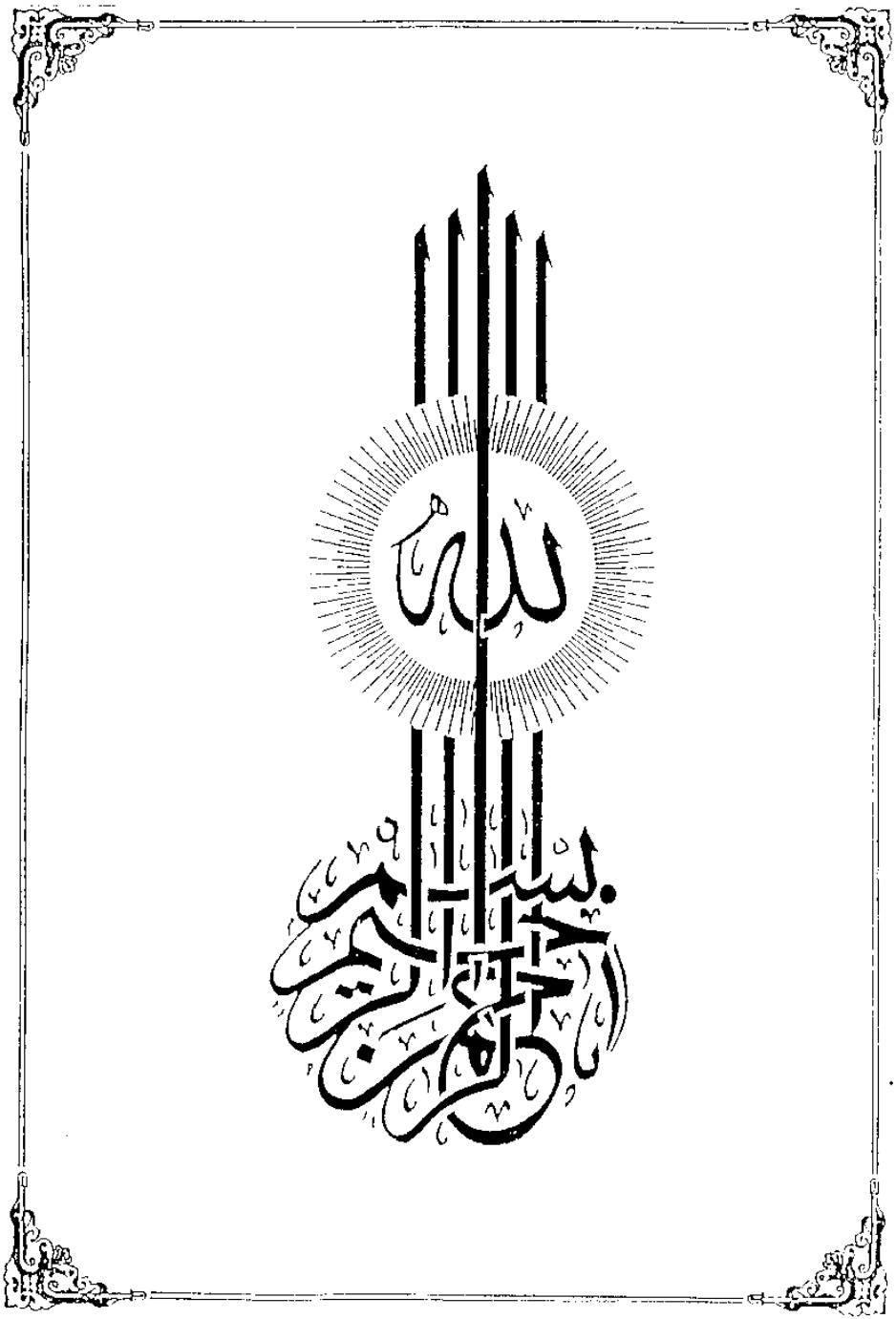
Lecturer of Biochemistry,

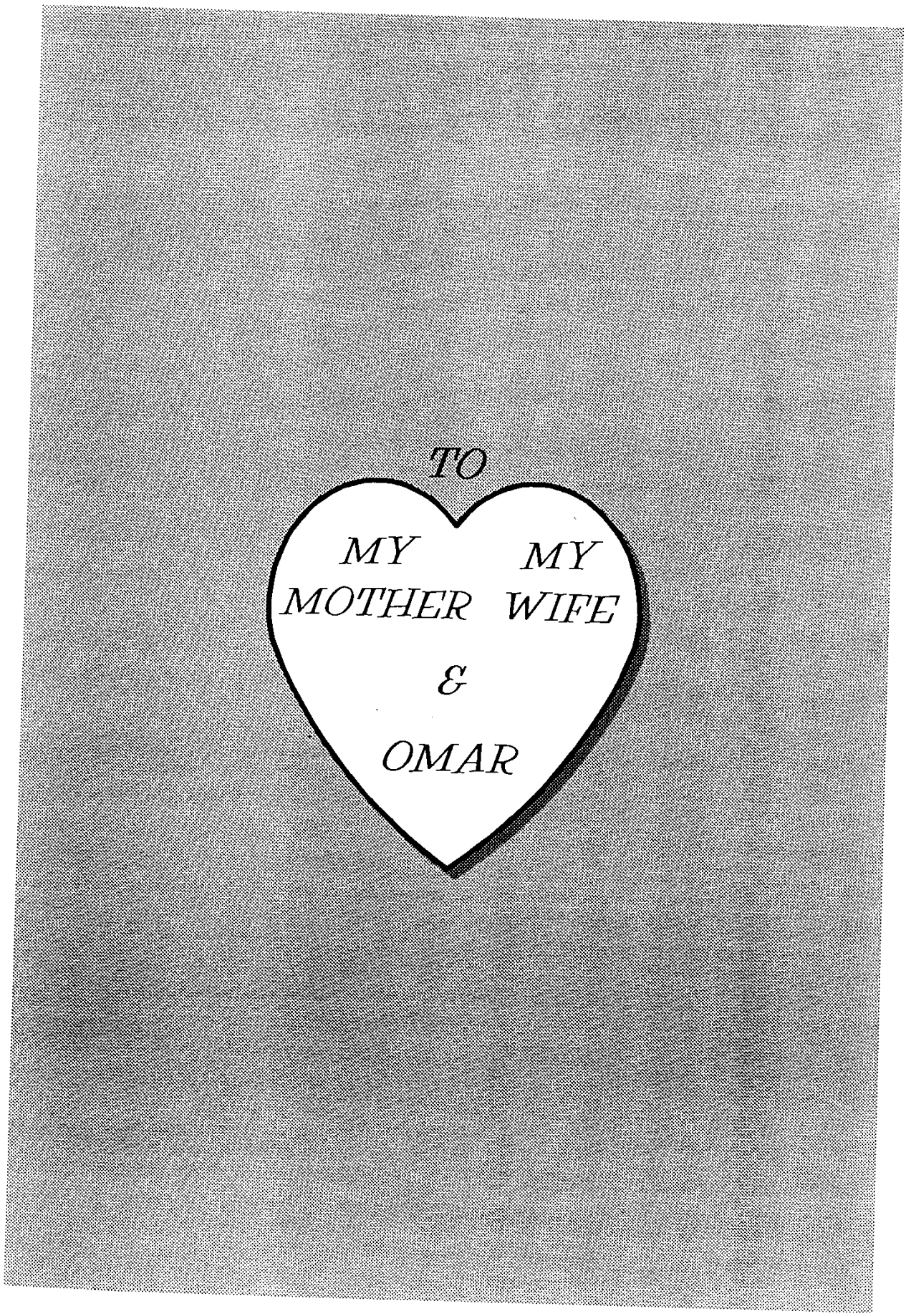
Faculty of Medicine, Ain Shams University.

Cairo

1995







Acknowledgment

First and foremost thanks are to Allah, The Most Beneficent and Merciful.

I must state here the debt I owe to Dr. Farida Ahmad Farid, Professor of Paediatrics, Ain Shams University, for her constructive remarks and valuable advice. Working under her supervision is all at once both pleasurable and educational. Her motherly attitude towards her patients and her team is unique and memorable.

To Dr. Khaled Salah Awwad, Assistant professor of Paediatrics, Ain Shams university I would like to express my cordial thanks and sincere gratitude; he gave me an excellent example of how a true scientist should guide and supervise his student's work.

I would like also to extend my deep appreciation to Dr. Mohammed S. El Din Faheem, Lecturer of Paediatrics, Ain Shams University, for his endless encouragement and constructive criticism with the spirit and capacity of a true scholar.

This work would have never been completed without the great help, close supervision and meticulous lab work offered by Dr. Taher Mohammed Farid, Lecturer of Biochemistry, Ain Shams University.

Any expression of thanks would fail to give the team of the Paediatric Dialysis Unit, Ain Shams university, its worth of gratitude for its practical and moral support throughout this work. Also the team of the Oncology Diagnostic Unit deserves a special thank for the help given during the practical part of this thesis.

Last but by no means least, I acknowledge my courageous patients and their brave parents for their cooperation and their sincere feelings. I also acknowledge all my senior and junior colleagues who helped me in one way or another in achieving this work.

Ihab El Hakim

CONTENTS

LIST OF ABBREVIATIONS

µl	microlitre
^{51}Cr-EDTA	chromium 51-ethylene diamine tetracetate
^{99}Tc-DTPA	technitium 99-diethylene triamine pentacetate
A-V	arterio-venous
ABP	arterial blood pressure
ACE	angiotensin converting enzyme
ACTH	adrenocorticotropic hormone
ADH	antidiuretic hormone
ANP	atrial natriuretic peptide
B	bromocriptine
BP	blood pressure
C	clomiphene citrate
CAPD	continuous ambulatory peritoneal dialysis
CCB	calcium channel blocker
CCPD	continuous cycler-assisted peritoneal dialysis
Ccr	creatinine clearance
CGN	chronic glomerulonephritis
CNS	central nervous system
CO	cardiac output
CRF	chronic renal failure
DHEA	dehydroepiandrosterone
DHEAS	dehydroepiandrosterone sulfate
DHT	dihydrotestosterone
e.g.	for example
ELISA	enzyme-linked immunosorbent assay
ESRD	end stage renal disease
ESTR	estradiol
F	female
FSH	follicle-stimulating hormone
GFR	glomerular filtration rate
GH	growth hormone
H_2SO_4	sulfuric acid
HCG	human chorionic gonadotropin
HCl	hydrochloric acid
HD	haemodialysis
HDL	high density lipoprotein

HRP	horseradish peroxidase
HS	highly significant
HSP	Henoch-Shoenlein purpura
Ht.	height
i.e.	that is to say
IGF I	insulin-like growth factor I
IU	international unit
K	potassium
Kg	kilogram
LBW	low birth weight
LDL	low density lipoprotein
LH	leuteinizing hormone
LHRH	leuteinizing hormone-releasing hormone
M	male
MEIA	microparticle enzyme immunoassay
MENS	menstruation
mEq	milliequivalent
mg	milligram
min.	minute
mIU	milli-international unit
ml	millilitre
MRI	magnetic resonance imaging
Na	sodium
NB	neurogenic bladder
ng	nanogram
nm	nanometer
NS	not significant
OD	optical density
OH	hydroxy
PCK	polycystic kidney
pg	picogram
PG	prostaglandin
PHI-27	peptide-histidine-isoleucine-27
PRL	prolactin
PTFE	poly-tetra-fluoro-ethylene
PTH	parathyroid hormone
RLU	relative light unit
S	significant
Scr	serum creatinine
SD	standard deviation
sec.	second

SMR	sexual maturity rating
SN	serial number
T_3	triiodothyronine
T_4	thyroxin
TEST	testosterone
TMB	tetramethylbenzidine
TMP	trans-membrane pressure
TPR	total peripheral resistance
TRH	thyrotropin-releasing hormone
TRH	thyrotropin-releasing hormone
TSH	thyroid-stimulating hormone
TTP	thrombotic thrombocytopaenic purpura
USA	The United States of America
UTI	urinary tract infection
VIP	vasoactive intestinal peptide
vs	versus
WHO	world health organization
y	year

List of tables

Tables of results:

List of Figures

Introduction

The kidney is an important organ by which human life can adjust and maintain its own homeostasis. Kidney performs this job, not only by removal of waste and toxic by-products, but also through its hormonal and haemopoietic functions. So, homeostatic mal-adjustment is expected in case of renal insufficiency (Rees et al., 1989).

Chronic renal insufficiency is one of the serious problems in paediatric age group which was ultimately fatal. However, with the advent of maintenance haemodialysis for treatment of end-stage renal disease has resulted in a large population of survivors with chronic renal failure. Since the artificial kidney is at best a poor substitute for the real organ, not all symptoms of renal insufficiency are corrected. These residual symptoms together with the abnormalities iatrogenically created by dialysis, constitute the syndrome of chronic uraemia, characterized by anaemia, neuropathy, renal osteodystrophy, hyperlipidaemia and a number of endocrinopathies (Henning et al., 1988).

Although there is a few data documenting the hormonal status of uraemic children in the pubertal age, chronic renal failure is known to cause delayed sexual maturation. Several possibilities could theoretically account for this abnormality: a) Primary gonadal damage by uraemic toxins, b) Extreme sensitivity of the hypothalamo-pituitary axis to the inhibitory effect of gonadal steroids (Belgorosky et al., 1990).

Hyperprolactinaemia among patients with chronic renal failure, even among those on maintenance haemodialysis has a high incidence and is positively correlated to serum creatinine (Cowden et al., 1978). It seems to be caused by the progressive loss of the ability of the kidney to remove prolactin whether through urinary clearance or by tubular resorption and catabolization (Gomez et al., 1980). It may have a role in the problem of pubertal delay by interfering with leuteinizing hormone secretion (Rigden et al., 1990).