

Acknowledgment

First and foremost, praise and thanks be to the Almighty (ALLAH) for his limitless help and guidance and peace be upon his prophet.

I wish also to express my sincere and deep appreciations to Prof. Dr. Eman Ahmed Zaky, Professor of pediatrics, Ain Shams University for her continuous guidance, support and constructive criticism through the whole work. She has generously devoted much of her time and her effort for planning and supervision of this study.

I would like to express my deepest gratitude to Prof. Dr. Howida Hosny El Gebaly, Professor of Pediatrics in Institute of Postgraduate Childhood Studies for her great help, valuable guidance, and continuous encouragement through the whole research. I am deeply affected by her care and consideration. I am much honored to have her as my supervisor.

I am also deeply grateful and would like to express my deepest thanks to Prof. Dr. Eman Abd El Wahab El Ashmawy, Professor of Child Health, National Research Centre for her sincere effort, valuable remarks, and constant support which have contributed a lot to the delivery of this work.

And I am also deeply grateful and would like to express my deepest thanks to Prof. Dr. Eman El Gorory, Prof. of Clinical Pathology, National Research Centre for her great help, contribution and precious effort throughout this work.

I could not forget the great help of Dr. Amal Ibrahim Hassanin, assistant professor of Child Health, National Research Centre and her effort throughout this work.

Last and not least special thanks are dedicated to all infants and their parents who participated in this work.

Ghada M. El- Kassas

Dedication

*My heartily thanks and deepest gratitude to
my parents,
my mother & father-in-law,
my lovely daughter Noran and son Omar.*

*A SPECIAL DEEP THANKS TO MY
KINDHEARTED HUSBAND FOR HIS SUPPORT,
HELP, UNDERSTANDING AND TOLERANCE
ALL THE TIME*



Table of Content

Titles	Page
List of Abbreviation	i
List of Tables	iv
List of Figures	viii
Introduction and aim of work	1
Review of literature	4
Chapter 1: Low Birth Weight	
Chapter 2: Ghrelin Hormone	71
Subject and methods	124
Results	134
Discussion	178
Summary	192
Conclusion	195
Recommendation	196
References	197
Appendix	—
Arabic summary	—

List of abbreviations

- ABW: Appropriate birth weight
- AGA: Appropriate for gestational age
- AN: Anorexia nervosa
- ACTH: adrenocorticotropin hormone
- AgRP: Arginine releasing peptide
- AIDS: immune deficiency syndrom
- AMPK: AMP-activated protein kinase
- ARC: Arcuate nucleus
- Arg: Arginine
- BPD: Bronchopulmonary dysplasia
- CAD: Coronary artery disease
- CHF: Chronic heart failure
- CNS: Central nervous system
- CP: Cerebral palsy
- CRH: Corticotrophin releasing hormone
- Des-Gln14: Des-Glutamine14
- DM: Diabetes mellitus
- DNA: Deoxy Ribonucleic acid
- DWMI: diffuse white matter injury
- ELBW: Extremely low birth weight
- GA: Gastetional age
- GABA: -aminobutyric acid
- GH: Growth hormone

- GHD: Growth hormone deficient
- GHRH: Growth hormone releasing hormone
- GHRP-6: Growth hormone releasing peptide-6
- GHSs: Growth hormone secretagogues
- GHS-R: Growth hormone secretagogue receptor
- GIT: Gastro-intestinal tract
- Gly-Ser-Ser- Phe: Glycine- Serine-Phenylalanine
- GM-IVH: Germinal matrix intraventricular hemorrhage
- GORD: Gastroesophageal reflux disease
- HDLs: High-density lipoproteins
- I.CV: Intracerebroventricular
- IGF-1: Insulin-like growth factor-1
- IgG: Immunoglobulin G
- IL-1: Interleukin-1
- IP3: Inistol triphosphate
- IUGR: Intrauterine growth retardation
- IV: Intravenous
- IVH: Intraventricular hemorrhage
- Leu: Leucine
- LBW: Low birth weight
- L-S ratio: Lecithin-sphingomyelin ratio
- MCFAs: Medium-chain fatty acids
- MCTs: Medium chain triacylglycerols
- Met: Methionine
- NBW: Normal birth weight

- NEC: Necrotizing enterocolitis
- NICU: Neonatal intensive care unit
- NPY: Neuropeptide Y
- OGTT: Oral glucose tolerance test
- PDA: Patent ductus arteriosus
- PHI: Periventricular hemorrhagic infarction
- PKA: Protein kinase A
- PKC: Protein kinase C
- PP: Pancreatic polypeptide
- PRL: Prolactin
- PVL: Periventricular leukomalacia
- PVN: Paraventricular nucleus
- PWS: Prader-willi syndrome
- RDS: Respiratory distress syndrome
- RIA: Radioimmune assay
- RNA: Ribo-deoxynucleic acid
- ROP: Retinopathy of prematurely
- SDS: Standard deviation score
- SGA: Small for gestational age
- SRIF : Somatostatin
- T.H: Thyroid hormones
- UNICEF: United Nations Children's Fund
- VLBW: Very low birth weight
- VMN: ventromedial nuclei
- WHO: World health organization

List of Tables

Table No.	Titles	Page
Tables of Review		
(1)	Risk factors for low birth weight	8
(2)	Characteristics and examples of intrauterine growth restriction	11
(3)	Physical maturity scores	15
(4)	Suggested feeding regimen for preterm infants	36
(5)	Genetic disorders characterized by prenatal growth deficiency	48
(6)	growth factors and fetal growth	54
(7)	biological activities of ghrelin	89
(8)	Possible clinical applications of ghrelin	114
Tables of Results		
(9)	Statistical comparison of demographic data between group I (LBW) and group II (controls) included in the study	134
(10)	Maternal risk factors of studied group	134
(11)	Descriptive statistics of gestational age and anthropometric data of group I (LBW) at onset of the study	139
(12)	Descriptive statistics of anthropometric data of group I (LBW) included in the study at 6th month	139
(13)	Descriptive statistics of anthropometric data of group I (LBW) included in the study at 12th month	140
(14)	Descriptive statistics of serum ghrelin of group I (LBW) included in the study	140
(15)	Catch up growth distribution in studied LBW infants at the age of 12th months	141

(16)	Descriptive statistics of gestational age and anthropometric data of group II (controls) at onset of the study	142
(17)	Descriptive statistics of anthropometric data of group II (controls) included in the study at 6th month	142
(18)	Descriptive statistics of anthropometric data of group II (controls) included in the study at 12th month	143
(19)	Descriptive statistics of serum ghrelin of group II (controls) included in the study	143
(20)	Statistical comparison of anthropometric parameters of group I (LBW infants) at onset of study, at 6th, and at 12th month of age	144
(21)	Statistical comparison of serum ghrelin of group I (LBW infants) at onset of study, at 6th, and at 12th month of age	145
(22)	Comparison between males and females LBW infants at onset, at 6th and at 12th month of age regarding their anthropometric measurements	147
(23)	Statistical comparison between males and females LBW infants at onset of study, at 6th, and at 12th month of age regarding their serum ghrelin	147
(24)	Statistical comparison between LBW infants who delivered normally and those who delivered by CS at onset of study, at 6th, and at 12th month of age regarding their anthropometric measurements	148
(25)	Statistical comparison between LBW infants who delivered normally and those who delivered by CS at onset of study, at 6th, and at 12th month of age regarding their serum ghrelin	150
(26)	Comparison between (SGA) and (AGA) LBW infants at onset of study, at 6th, and at 12th month regarding their anthropometric measurements	151
(27)	Comparison between LBW infants who were born (SGA) and those who were born (AGA) at onset, at 6th and 12th month regarding serum ghrelin	152

(28)	Statistical comparison between LBW infants who attained catch up growth and those who didn't attain catch up at onset of study, at 6 th , and at 12 th month of age regarding their anthropometric measurements	153
(29)	Statistical comparison between LBW infants who attained catch up growth and those who didn't attain catch up at onset of study, at 6 th , and at 12 th month of age regarding their serum ghrelin	155
(30)	Statistical comparison of anthropometric parameters of group II (controls) at onset of study, at 6 th , and at 12 th month of age	156
(31)	Statistical comparison of serum ghrelin of group II (controls) at onset of study, at 6 th , and at 12 th month of age	157
(32)	Statistical comparison between males and females of group II (controls) at onset of study, at 6 th , and at 12 th month of age regarding their anthropometric measurements	159
(33)	Statistical comparison between males and females of group II (controls) at onset of study, at 6 th and 12 th month regarding their serum ghrelin	160
(34)	Statistical comparison between infants who delivered normally and those who delivered by CS of control group at onset of study, at 6 th , and at 12 th month of age regarding their anthropometric measurements	161
(35)	Statistical comparison between infants of group II (controls) who delivered normally and those who delivered by CS at onset of study, at 6 th , and at 12 th month of age regarding their serum ghrelin	162
(36)	Statistical comparison between infants of group II (controls) who delivered normally and those who delivered by CS at onset of study, at 6 th , and at 12 th month of age regarding their serum ghrelin	162
(37)	Comparison between studied LBW and controls at 1 yr regarding height velocity and height velocity SDS	163
(38)	Statistical comparison between LBW and control infants at onset of study, at 6 th , and at 12 th month	164

	of age regarding their anthropometric measurements	
(39)	Statistical comparison of delta change (changes = difference) in anthropometric data between low birth weight and controls subtracting the values at the study onset from those recorded at 6 th month and 12 th month of age	165
(40)	Correlation between serum ghrelin and different anthropometric measurements in LBW infants at onset of study, 6 th and 12 th month of age	168
(41)	Statistical correlation between delta changes (changes) in serum ghrelin with delta changes (changes) in anthropometric data of group I (LBW infants) from 6 th month - Onset of the study, 12 th month – Onset of the study and 12 th month – 6 th month	172
(42)	Correlation between serum ghrelin and different studied anthropometric measurements in group II (controls) at onset of study, 6 th month, and 12 th month of age	173
(43)	Statistical correlation between delta changes (changes) in serum ghrelin with delta changes (changes) in anthropometric data of group II (controls) from 6 th month - Onset of the study, 12 th month – Onset of the study and 12 th month – 6 th month	176

List of Figures

Figure No.	Titles	Page
Figures of Review		
(1)	Neuromuscular criteria for maturity	15
(2)	selected risk factors associated with impaired growth	43
(3)	Schematic diagram showing the effect of cortisol on the activation of the GH-IGF axis in ovine hepatocytes	54
(4)	Intrauterine growth curves	58
(5)	Fetal-infants growth chart of preterm infants	68
(6)	Typical growth chart of LBW AGA infant	70
(7)	Typical growth chart of LBW SGA infant	70
(8)	Chemical structure of acylated and non-acylated ghrelin	77
(9)	Difference between human and rat ghrelin	80
(10)	Dendrogram of ghrelin receptor (GHS-R) and other GPCRs	82
(11)	Pattern of ghrelin secretion through the day	85
(12)	Known biological activities of ghrelin	90
(13)	Effects of ghrelin on pituitary hormone secretion	91
(14)	Schematic model of the possible interactions between GHRH, ghrelin/GHS and SRIF	93
(15)	Hypothalamic neural networks involving appetite-regulating peptides	100
(16)	The regulation of secretion and actions of ghrelin on the gut-brain axis	102
Figures of Results		
(17)	Classification of newborns (both sexes) by intrauterine growth and gestational age	126

(18)	Sex distribution of group I (LBW infants) included in the study	135
(19)	Sex distribution of group II (controls) included in the study	135
(20)	Percentage of mode of delivery of group I (LBW infants) included in the study	136
(21)	Percentage of mode of delivery of group II (controls) included in the study	136
(22)	Percentage of appropriate and small for gestational age infants of group I (LBW) included in the study	137
(23)	Percentage of consanguinity of group I (LBW infants) included in the study	137
(24)	Percentage of consanguinity of group II (controls) included in the study	138
(25)	Percentage of infants who attained (positive) and those who didn't attain (negative) complete catch up growth at end of 1st year	138
(26)	Maternal risk factors of group I (LBW infants) included in the study	138
(27)	Statistical comparison of serum ghrelin of group I (LBW) at onset of the study and 6th months	145
(28)	Statistical comparison of serum ghrelin of group I (LBW) at onset of the study and 12th months	146
(29)	Statistical comparison of delta changes in serum ghrelin of group I (LBW) from 6th month – onset of the study and 12th month - onset of the study	146
(30)	Statistical comparison of lengths at onset of the study of group I (LBW infants) in relation to mode of delivery	149
(31)	Statistical comparison between head circumference at onset of the study of group I (LBW infants) in relation to mode of delivery	149

(32)	Statistical comparison between weights at onset of the study of group I (LBW infants) in relation to mode of delivery	150
(33)	Statistical comparison of length at 6 th month of group I (LBW infants) included in the study in relation to catch up growth	154
(34)	Statistical comparison of length at 12 th month of group I (LBW infants) included in the study in relation to catch up growth	154
(35)	Statistical comparison of weights at 12 th month of group I (LBW infants) included in the study in relation to catch up growth	155
(36)	Statistical comparison of serum ghrelin at 6 th month of group I (LBW infants) included in the study in relation to catch up growth	156
(37)	Statistical comparison of serum ghrelin of group II (controls) at onset of the study and 6 th months	157
(38)	Statistical comparison of serum ghrelin of group II (controls) at onset of the study and 12 th months	158
(39)	Statistical comparison of delta changes in serum ghrelin of group II (controls) from 6 th month – Onset of the study and 12 th month - Onset of the study	158
(40)	Statistical comparison of serum ghrelin between group I (LBW) and group II (controls) at onset of the study	163
(41)	Statistical comparison of delta weight between group I (LBW) and group II (controls) from 6 th month – onset of the study	165
(42)	Statistical comparison of delta skin fold thickness from 6 th month - beginning of the study between group I (LBW) and group II (controls)	166
(43)	Statistical comparison of delta weight from 12 th month- beginning of the study between group I (LBW) and group II (controls)	166
(44)	Statistical comparison of delta head circumference from 12 th month- beginning of the study between group I (LBW) and group II (controls)	167

(45)	Statistical comparison of delta body mass index from 12th month- beginning of the study between group I (LBW) and group II (controls)	167
(46)	Statistical correlation between serum ghrelin and weight of group I (LBW infants) at onset of the study	168
(47)	Statistical correlation between serum ghrelin and head circumference of group I (LBW infants) at onset of the study	169
(48)	Statistical correlation between serum ghrelin and weight of group I (LBW infants) included in the study at 6th month	169
(49)	Statistical correlation between serum ghrelin and length of group I (LBW infants) included in the study at 6th month	170
(50)	Statistical correlation between serum ghrelin and head circumference of group I (LBW infants) included in the study at 6th month	170
(51)	Statistical correlation between serum ghrelin and mid arm circumference of group I (LBW infants) included in the study at 6th month	171
(52)	Statistical correlation between serum ghrelin and length of group I (LBW infants) included in the study at 12th month	171
(53)	Statistical correlation between serum ghrelin and weight at onset of the study of group II (controls)	174
(54)	Statistical correlation between serum ghrelin and weight of group II (controls) included in the study at 6th month	174
(55)	Statistical correlation between serum ghrelin and body mass index of group II (controls) included in the study at 6th month	175
(56)	Statistical correlation between serum ghrelin and head circumference of group II (controls) included in the study at 6th month	175
(57)	Statistical correlation between serum ghrelin and weight of group II (controls) included in the study at 12th month	176
(58)	Statistical correlation between delta changes in serum ghrelin and delta weight from 6th month – Onset of the study of group II (controls)	177