



بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

∞∞∞∞

تم رفع هذه الرسالة بواسطة /صفاء محمود عبد الشافي

بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون

أدنى مسئولية عن محتوى هذه الرسالة.

ملاحظات: لا يوجد





# **Cord Blood levels of Brain-Derived Neurotrophic Factor (BDNF) In Full Term Neonates at Risk for Iron Deficiency**

*Thesis*

*Submitted for Partial Fulfillment of Master Degree in Pediatrics*

*By*

**Sara Helmy Abd Elaziz Rezk**

*M. B., B. Ch., Azhar University, 2014*

*Under supervision of*

**Prof. Dr. Ola Galal Bader El-Deen El-Farghali**

*Professor of Pediatrics*

*Faculty of Medicine, Ain Shams University*

**Prof. Dr. Mortada El-Sayed Ahmed**

*Assistant Professor of Obstetrics and Gynecology*

*Faculty of Medicine, Ain Shams University*

**Dr. Nesmahar Tark Abdel Hamed Azzam**

*Lecturer of Pediatrics*

*Faculty of Medicine, Ain Shams University*

**Dr. Marwa Adham El-Mohamdy Hasb El-Nabi**

*Lecturer of Clinical Pathology*

*Faculty of Medicine, Ain Shams University*

*Faculty of Medicine*

*Ain Shams University*

*2022*

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

# قَالَ

سَبَّحَانَكَ لَا إِلَهَ إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ  
الْعَلِيمُ الْعَظِيمُ

صدق الله العظيم

سورة البقرة الآية: ٣٢

# Acknowledgment

*First and foremost, I feel always indebted to **ALLAH**, the  
Most Kind and Most Merciful.*

*I'd like to express my respectful thanks and profound  
gratitude to **Prof. Dr. Ola Galal Bader El-Deen El-  
Farghali**, Professor of Pediatrics, Faculty of Medicine, Ain  
Shams University for her keen guidance, kind supervision,  
valuable advice and continuous encouragement, which made  
possible the completion of this work.*

*I am also delighted to express my deepest gratitude and  
thanks to **Prof. Dr. Mortada El-Sayed Ahmed**, Assistant  
Professor of Obstetrics and Gynecology, Faculty of Medicine, Ain  
Shams University, for his kind care, continuous supervision,  
valuable instructions, constant help and great assistance  
throughout this work.*

*I am deeply thankful to **Dr. Nesmahar Tark Abdel  
Hamed Azzam**, Lecturer of Pediatrics, Faculty of Medicine,  
Ain Shams University, for her great help, active participation and  
guidance.*

*I wish to introduce my deep respect and thanks to **Dr.  
Marwa Adham El-Mohamdy Hasb El-Nabi**, Lecturer of  
Clinical Pathology, Faculty of Medicine, Ain Shams University, for  
her kindness, supervision and cooperation in this work.*

*Sara Helmy*

# **Cord Blood Hemoglobin (Hb) Levels In Full Term Neonates Of Mothers With Iron Deficiency**

**Anemia (IDA)**

**<sup>1</sup>Ola Galal Bader El-Deen El-Farghali, <sup>2</sup>Mortada El-Sayed Ahmed, <sup>1</sup>Nesmahar Tark Abdel**

**Hamed Azzam, <sup>3</sup>Marwa Adham El-Mohamdy Hasb El-Nabi, <sup>1</sup>Sara Helmy AbdElaziz Rezk**

Department of pediatrics, Faculty of Medicine, Ain Shams University 2

Department of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University  
Department of clinical and clinical pathology, Faculty of Medicine, Ain Shams University

**Corresponding author:** Sara Helmy AbdElaziz Rezk, **Mobile:** 01032237561; **Email:**

saratabiba@gmail.com.

## **Abstract**

**Background** Iron is a critical micronutrient for tissue oxygenation, cellular metabolism, energy generation, and the metabolism of toxins. Iron transfer from mother to fetus is a regulated process involving iron status in the maternal circulation, its transport across the placenta and subsequent transfer into the fetal circulation.

**Objective:** To evaluate cord blood Hemoglobin (Hb) levels in neonates of mothers with iron deficiency anemia (IDA).

**Patients and Methods:** This prospective case-control study was conducted at Ain Shams University Hospitals. It included 60 full terms newborn who were born at Obstetrics and Gynecology Hospital. An informed consent was taken from the mother or case giver before enrollment in the study.

**Results:** In comparison between cases and controls as regard RBCS parameter, there was no significant difference between cases and controls regarding neonatal Hemoglobin and MCH, but there was significantly lower MCV in cases compared to controls.

**Conclusion:** There was no relation between the maternal Hb deficient levels and neonatal Hb. The first sign of iron deficiency in neonates reflected in lower MCV in cases, but not reached to decrease Hb levels in neonates.

**Keywords:** Cord, Blood, Hemoglobin (Hb), Full-Term Neonates, Mothers Iron Deficiency, Anemia (IDA)

# *List of Contents*

Title	Page No.
List of Abbreviations.....	i
List of Tables .....	iii
List of Figures .....	v
Introduction .....	1
Aim of the Work.....	3
Review of Literature	
Iron Deficiency Anemia in Neonates .....	4
Maternal Risk Factors.....	16
Brain Derived Neurotrophic Factor (BDNF).....	22
Patients and Methods.....	26
Results .....	34
Discussion .....	54
Summary .....	61
Conclusion .....	63
Recommendations .....	64
References .....	65
Arabic Summary .....	—

# *List of Abbreviations*

Abb.	Full term
BDNF .....	Brain-Derived Neurotrophic Factor
CBC .....	Complete blood count
CDC .....	Centers for Disease Control and Prevention
CNS .....	Central nervous system
CS .....	Cesarean Section
DCV .....	Dense core vesicle
DMT1.....	Divalent metal transporter 1
ELISA.....	Enzyme-linked immunosorbent assay
ER.....	Endoplasmic reticulum
F2.....	Ferrous
F3.....	Ferric
FPN .....	Ferroportin
Hb .....	Hemoglobin
HCP-1 .....	Heme carrier protein 1
Hct .....	Hematocrit
ID.....	Iron Deficiency
IDA .....	Iron Deficiency Anemia
IDMs.....	Infants of diabetic mothers
IUFD.....	Intra uterine fetal death
LTF .....	Lactoferrin
MCH .....	Mean corpuscular hemoglobin
MCV.....	Mean corpuscular volume
MMP .....	Matrix metalloproteinases
NGF .....	Neural growth factor
NICE.....	The National Institute for Health and Care Excellence

## *List of Abbreviations Cont...*

Abb.	Full term
NVD.....	Normal Vaginal Delivery
SD .....	Standard deviations
SG .....	Spiral ganglion
TGN .....	<i>Trans</i> -Golgi network
TrkB .....	Tyrosine kinase b receptor
UTI .....	Urinary tract infection
WBC .....	White Blood Cell
WHO .....	World Health Organization



# *List of Tables*

Table No.	Title	Page No.
<b>Table (1):</b>	Risk factors for iron deficiency anemia in infants .....	6
<b>Table (2):</b>	Laboratory findings during the evolution of iron deficiency anemia.....	12
<b>Table (3):</b>	Normal reference values for hemoglobin and mean corpuscular volume .....	13
<b>Table (4):</b>	Estimated iron requirements, absorption and changes in plasma volume and iron status parameters according to pregnancy trimester .....	17
<b>Table (5):</b>	Comparison between cases and controls as regard maternal clinical characteristics.....	34
<b>Table (6):</b>	Comparison between cases and controls as regard neonatal clinical characteristics .....	35
<b>Table (7):</b>	Comparison between cases and controls as regard APGAR Score in 1 min and APGAR Score in 5 min .....	36
<b>Table (8):</b>	Comparison between cases and controls as regard maternal laboratory characteristics.....	37
<b>Table (9):</b>	Comparison between cases and controls as regard neonatal laboratory characteristics.....	39
<b>Table (10):</b>	Correlations between maternal clinical characteristics and BDNF among cases .....	42
<b>Table (11):</b>	Correlations between maternal clinical characteristics and BDNF among controls .....	43
<b>Table (12):</b>	Correlations between maternal clinical characteristics and BDNF among both groups .....	44
<b>Table (13):</b>	Correlations between neonatal clinical characteristics and BDNF among cases .....	45

## *List of Tables Cont...*

Table No.	Title	Page No.
<b>Table (14):</b>	Correlations between neonatal clinical characteristics and BDNF among controls .....	46
<b>Table (15):</b>	Correlations between neonatal clinical characteristics and BDNF among both groups .....	47
<b>Table (16):</b>	Correlations between maternal laboratory characteristics and BDNF among cases .....	48
<b>Table (17):</b>	Correlations between maternal laboratory characteristics and BDNF among controls .....	49
<b>Table (18):</b>	Correlations between maternal laboratory characteristics and BDNF among both groups .....	50
<b>Table (19):</b>	Correlations between neonatal laboratory characteristics and BDNF among cases .....	51
<b>Table (20):</b>	Correlations between neonatal Laboratory characteristics and BDNF among controls .....	51
<b>Table (21):</b>	Correlations between neonatal laboratory characteristics and BDNF among both groups .....	52
<b>Table (22):</b>	ROC curve using BDNF to discriminate between cases and controls.....	53

# *List of Figures*

Fig. No.	Title	Page No.
<b>Figure (1):</b>	Turnover of iron in the human body. Given values indicate amounts of absorbed, used, stored and expelled iron .....	8
<b>Figure (2):</b>	Processes of iron absorption in small intestine enterocytes and release from hepatic/spleen macrophages.....	9
<b>Figure (3):</b>	The fetal and neonatal events attributable to maternal diabetes mellitus .....	20
<b>Figure (4):</b>	Synthesis of BDNF .....	23
<b>Figure (5):</b>	Comparison between cases and controls as regard maternal MCV and MCH. ....	38
<b>Figure (6):</b>	Comparison between cases and controls as regard maternal ferritin and transferrin. ....	38
<b>Figure (7):</b>	Comparison between cases and controls as regard BDNF. ....	40
<b>Figure (8):</b>	Comparison between cases and controls as regard haemoglobin.....	40
<b>Figure (9):</b>	Comparison between cases and controls as regard MCV.....	41
<b>Figure (10):</b>	ROC curve using BDNF to discriminate between cases and controls.....	53

## **Cord Blood Hemoglobin (Hb) Levels In Full Term Neonates Of Mothers With Iron Deficiency**

### **Abstract**

**Background** Iron is a critical micronutrient for tissue oxygenation, cellular metabolism, energy generation, and the metabolism of toxins. Iron transfer from mother to fetus is a regulated process involving iron status in the maternal circulation, its transport across the placenta and subsequent transfer into the fetal circulation.

**Objective:** To evaluate cord blood Hemoglobin (Hb) levels in neonates of mothers with iron deficiency anemia (IDA).

**Patients and Methods:** This prospective case-control study was conducted at Ain Shams University Hospitals. It included 60 full terms newborn who were born at Obstetrics and Gynecology Hospital. An informed consent was taken from the mother or case giver before enrollment in the study.

**Results:** In comparison between cases and controls as regard RBCS parameter, there was no significant difference between cases and controls regarding neonatal Hemoglobin and MCH, but there was significantly lower MCV in cases compared to controls.

**Conclusion:** There was no relation between the maternal Hb deficient levels and neonatal Hb. The first sign of iron deficiency in neonates reflected in lower MCV in cases, but not reached to decrease Hb levels in neonates.

**Keywords:** Cord Blood Hemoglobin (Hb) Levels In Full Term Neonates Of Mothers With Iron Deficiency, Anemia (IDA)

# INTRODUCTION

Iron is a critical micronutrient for tissue oxygenation, cellular metabolism, energy generation, and the metabolism of toxins (*Crichton et al., 2001*). Iron and iron-containing enzymes in the brain are involved in neuronal energy metabolism, myelination, and neurotransmission (*Lozoff and Georgieff, 2006*).

For over 25 years, Iron Deficiency Anemia (IDA) in early life was found to affect brain iron content and cause cognitive and behavioral deficits in early childhood (*Walter, 1994*). Later work found that IDA during the fetal or early postnatal period leads to persistent deficits in learning and memory, emotional regulation, social behavior, and overall neurophysiologic development (*Christian et al., 2010; Chang et al., 2013*). Additionally, early-life ID is associated with increased risk of developing neuropsychiatric disorders (*Insel et al., 2008; Doom et al., 2018*). Despite the identification and correction of ID, these deficits persist into adulthood (*Lukowski et al., 2010*), indicating early life as a critical window for brain development when adequate iron supply is required for proper growth and development. However, screening for and treatment of ID, per clinical practice, is not performed until 9–12 months of age, a time when it may be too late for some infants (*Phillips et al., 2020*).

Therefore, by the time anemia is detected, the brain may have already been iron deficient for some time, particularly during critical periods of neurodevelopment. In this regard, recent research has turned to exosomes as carriers of potential molecular markers (*Properziet et al., 2013*).

Exosomes are small, cell-derived vesicles that shuttle proteins and nucleic acids between cells and play an important role in intercellular communication (*Van Nile et al., 2006; Schory and Bhandngar, 2008*). Prenatally, BDNF has important roles in axon growth, morphologic Differentiation, and neurotransmitter expression (*Huang and Reichardt, 2001*). Postnatally, BDNF supports neuron survival, promotes synaptogenesis, and is important for learning and memory (*Bekinschtein et al., 2008*).

BDNF can be found in blood Exosomes, providing an opportunity to non-invasively assess the state of brain development (*Mustapic et al., 2017*).

## **AIM OF THE WORK**

**T**he objective of this study: is to evaluate cord blood-derived Levels of exosomal Brain-Derived Neurotrophic Factor (BDNF) in neonates at risk for Iron Deficiency (ID).