

Evaluation of Insulin Resistance among Full Term and Preterm Newborn Infants using Homeostasis Model Assessment - Insulin Resistance

DINA M. AKMAL, M.D.*; HEBATALLAH ABOU HUSSIEN, M.D.*; NERMINE M. RIAD, M.D.**;
MOHAMED MAHMOUD, M.Sc.***; RASHA H. SAYED, M.D.** and IRENE E. BISHAI, M.D.**

The Departments of Pediatrics & Neonatology, Clinical & Chemical Pathology**, Faculty of Medicine, Cairo University and Department of Pediatrics & Neonatology***, Portfouad Emergency Hospital, Portfouad, Portsaid*

Abstract

Background: Insulin resistance (IR) is a key factor in the etiology of type 2 diabetes mellitus, dyslipidemia, hypertension, vascular diseases and may have a role as well in stroke and coronary heart disease. Poor nutrition in fetal and early infant life and prematurity affects the development and activity of β cells of islets of Langerhans. Early changes in insulin and cortisol hormones levels affect glucose homeostasis and may later lead to IR and obesity.

Aim of Study: The purpose of this study is to evaluate IR using homeostasis model assessment-insulin resistance (HOMA-IR) and its relation to gestational age among full term (FT) and preterm infants (PT).

Patients and Methods: Eighty newborn infants between 28 and 41 gestational weeks delivered by vaginal delivery (VD) or Caesarian Section (CS) were enrolled in this study. Three milliliters of umbilical venous blood were obtained immediately after birth to measure both insulin and cortisol levels by Enzyme-linked Immunosorbent Assay and glucose level, HOMA-IR and glucose insulin ratio (GIR) were calculated.

Results: In this cross-sectional study, cord blood insulin and HOMA-IR levels were significantly higher in PT groups than FT groups with p -value <0.001 . Other biochemical tests such as cord blood glucose, cortisol levels and GIR were higher in FT groups than PT groups with p -value: 0.01, <0.001 and <0.001 respectively. In the study population, An inverse relation was found between gestational age with insulin and HOMA-IR while a positive one was observed between gestational age with cortisol and glucose levels. Vaginal delivered FT and PT neonates had higher levels of cord blood cortisol than delivered by CS. Anthropometric measurements revealed highly statistically significant differences between FT and PT newborns with p -value <0.001 .

Conclusion: Increased levels of insulin and HOMA-IR in PT newborns signify its role as a risk factor for development of diabetes in these newborns later. Elevated level of cortisol in FT newborns more than PT reflects its role in fetal matu-

ration and neonatal adaptation after birth. Cortisol was higher in VD newborns as it has a direct relationship with the maternal and fetal stress witnessed during delivery as compared to CS. The inverse relationship between cortisol and insulin suggests the former being responsible for impaired β cell function and insulin sensitivity.

Key Words: Cord blood – Cortisol – Glucose – Insulin – Insulin resistance – HOMA-IR – Gestational age.

Introduction

TYPE 2 diabetes, vascular diseases, metabolic disturbances of lipids have always been strongly linked to insulin resistance (IR) [1]. To illustrate, insulin sensitivity is always defined as the insulin role in decreasing plasma glucose level either by decreasing its formation in liver or by increasing its uptake by adipocytes and muscles. IR is the disturbance in this physiological mechanism or other nutrient metabolism such as lipids, protein or carbohydrates [2].

IR can be assessed by various methods, such as the HOMA-IR which is the homeostasis model assessment-insulin resistance that evaluates the β -cell function on one hand and the glucose-insulin homeostasis on the other hand [3]. Insulin level and basal plasma glucose level are used to find out HOMA-IR [4]. Researches too have found an association between stage of immaturity and plasma insulin level. In other words, in premature infants, there is disruption in the insulin signal transduction pathway, hence insulin demand rises and the probability of developing hyperinsulinemia and IR is elevated [5].

Cortisol, as an adrenocortical hormone, may play a big role in the development of IR cause it

Correspondence to: Dr. Irene E. Bishai
[E-Mail: irir@aucegypt.edu](mailto:irir@aucegypt.edu)

not only disrupts the insulin release in response to an elevated plasma glucose stimulus but also impairs β cell function [6]. In contrast, cortisol level starts to progressively increase only after the thirty's of week of gestation cause of its role in terminal fetal development and neonatal adapting at birth [7,8]. In addition, cortisol is used a stress maker denoting any stress condition including mode of delivery [9].

The aim of the present study is to detect the following items:

- The frequency of IR among enrolled full term (FT) and preterm (PT) newborn infants.
- The correlation between IR and gestational age.
- The impact of the mode of delivery on development of IR.
- The correlation between cord plasma cortisol with HOMA-IR.

Patients and Methods

This cross-sectional study was conducted in the Obstetrics and Gynecology, Pediatrics and Clinical Pathology Departments from November 2017 to June 2018; Faculty of Medicine, Cairo University. All data regarding mother and newborn were collected from the files of the hospital. Approval of the study was obtained from The Ethical Committee at the Faculty of Medicine, Cairo University and an informed consent was obtained from parents prior to data collection.

Eighty newborn infants between 28 and 41 gestational weeks were included in this study and were divided into 4 groups: [Group 1 (G1): 20 term newborn infants delivered by normal vaginal delivery, Group 2 (G2): 20 term newborn infants delivered by cesarean section, Group 3 (G3): 20 preterm newborn infants delivered by normal vaginal delivery and Group 4 (G4): 20 preterm newborn infants delivered by cesarean section]. Infants of mothers suffering from any infectious diseases or having obstetric complications or on dexamethasone before delivery are not included. FT and PT newborns with a 5th-minute Apgar score less than 8 are also excluded.

Systemic examination and vital signs and gestational age were assessed after birth. Resuscitation was done according to the guidelines of neonatal resuscitation program, published by the American Academy of Pediatrics and American Heart Association [10]. Finally, Apgar score was done at 1st minute and 5th minute Postpartum [11] and anthropometric measurements of babies were recorded.

Sample collection:

Venous cord blood (VCB) was collected under aseptic conditions from the umbilical cords of all 80 newborns immediately after delivery, but prior to expulsion of placenta. Three mL blood were drawn from the umbilical cord veins and were divided into 1 ml on a fluoride vacutainer for measuring plasma glucose level (within 4 hours of collection) and 2ml on a plain vacutainer for measuring insulin and cortisol levels.

Samples were taken to determine blood Glucose level (mg/dL) by AU 680 Beckman in addition to Insulin (μ IU/mL) (DRG catalog number: EIA-2935, Germany) as well as Cortisol (ng/mL) levels (DRG catalog number: EIA-1887, Germany) by Enzyme-linked immunosorbent assay (ELISA).

HOMA-IR Calculation represents insulin resistance (IR) which is $HOMA-IR = \text{Fasting insulin } (\mu\text{U/mL}) \times \text{fasting glucose (mg/dL)} / 405$. Glucose insulin ratio (GIR) Calculation represents insulin sensitivity (IS), $GIR = \text{Fasting glucose} / \text{fasting insulin}$.

Statistical analysis:

Version 20.0 (SPSS Inc., Chicago, Illinois, USA) was used to analyze the recorded data. While mean \pm standard deviation is used to analyze quantitative data, percentage and frequency express qualitative ones. This research uses more than one test of significance such as Chi-square (X^2) test of significance and Pearson's correlation coefficient (r) and the t -test of significance. Another tool was used to detect the optimum cut off, Receiver operating characteristic (ROC curve) analysis, this analytical curve includes both sensitivity and specificity.

p -value was determined, it was considered significant if less than 0.05 and highly significant if less than 0.001, this conclusion is based on confidence interval set to 95% and error margin of error set to 5%.

Results

Demographic data and Anthropometric measurements for full-term (FT) and preterm (PT) newborns showed highly statistically significant differences with p -value less than 0.001 (Table 1). On the other hand, neither demographic data nor Anthropometric measurements showed statistically significant differences between G1 & G2 or between G3 & G4 groups regarding sex, gestational age (GA) and anthropometric measurements (p -value >0.05 for all parameters).

Table (1): Comparison between FT (G1 & G2) and PT (G3 & G4) newborns according to sex, gestational age and anthropometric measurements.

	FT (N=40) (G1 & G2)	PT (N=40) (G3 & G4)	p-value
<i>Sex:</i>			
Male	16 (40%)	19 (47.5%)	0.499
Female	24 (60%)	21 (52.5%)	
	Mean ± SD	Mean ± SD	
GA/weeks	38.50±0.96	32.65±2.46	<0.001**
Birth weight (kg)	3.32±0.42	1.95±0.46	<0.001**
Length (cm)	49.74±1.76	46.01±1.82	<0.001**
Head circumference (cm)	35.74±1.34	32.58±2.04	<0.001**
Chest circumference (cm)	35.26±1.37	30.84±1.43	<0.001**
Mid arm circumference (cm)	12.21±0.68	9.30±0.79	<0.001**

*p-value <0.05 Significant.

**p-value <0.001 Highly Significant.

cm : Centimeter.

GA : Gestational age.

kg. : Kilogram.

N : Number.

SD : Standard deviation.

With respective to biochemical parameters and insulin resistance (IR) markers; Glucose level, cortisol level and Glucose insulin ratio (GIR) were significantly higher in FT groups compared to PT groups (*p*-value 0.010, <0.001 and <0.001 respectively) (Table 2). On the other hand, the insulin level and HOMA-IR were significantly higher in PT groups than FT groups (*p*-value: <0.001 for both), the mean values of the former were almost double those of the latter group (Table 2).

Table (2): Comparison between FT (G1 & G2) and PT (G3 & G4) newborns according to biochemical parameter and IR markers.

Biochemical parameters & IR markers	FT (N=40) (G1 & G2)	PT (N=40) (G3 & G4)	p-value
	Mean ± SD	Mean ± SD	
Glucose (mg/dL)	84.08±17.36	74.00±16.80	0.010*
Insulin (mIU/mL)	9.56±5.11	18.01±5.84	<0.001**
Cortisol (ng/mL)	362.15±91.57	218.65±37.59	<0.001**
HOMA-IR	1.97±1.14	3.16±0.98	<0.001**
GIR	11.49±6.56	4.82±2.45	<0.001**

*p-value <0.05 S.

**p-value <0.001 HS.

GIR : HOMA-IR, Homeostasis model assessment-insulin resistance.

N : Number.

SD : Standard deviation.

FT : Full term.

PT : Pre-term.

In FT, comparison between (G1) VD and (G2) CS regarding the biochemical parameters and IR markers, there were statistically significant differences between them in glucose and cortisol levels. The former levels were higher in (G1) than (G2), with *p*-value: 0.022 and the latter levels were

markedly higher in (G1) than (G2), with *p*-value <0.001 as per Table (3). However, there were no statistically significant differences between (G1) and (G2) neither in Insulin levels, HOMA-IR and GIR nor with sex, GA and anthropometric measurements (*p*-value >0.05 for all parameters).

Table (3): Comparison between FT, VD (G1) and FT, CS (G2) according to biochemical parameters and IR markers.

Biochemical parameters & IR markers	FT, VD (N=40) (G1)	FT, CD (N=20) (G2)	p-value
	Mean ± SD	Mean ± SD	
Glucose (mg/dL)	90.25±13.57	77.90±18.81	0.022*
Insulin (mIU/mL)	9.73±5.23	9.39±5.13	0.837
Cortisol (ng/mL)	424.65±85.14	299.65±41.72	<0.001**
HOMA-IR	2.20±1.33	1.73±0.89	0.198
GIR	11.86±6.13	11.12±7.11	0.726

p-value >0.05 NS.

**p*-value <0.05 S.

***p*-value <0.001 HS.

GIR: Glucose insulin ratio.

HOMA-IR: Homeostasis model assessment-insulin resistance.

N : Number.

SD: Standard deviation.

FT : Full-term.

G : Group.

GA : Gestational age.

In PT, comparison between VD (G3) and CS (G4), there were statistically significant differences between them according to cord blood cortisol levels and HOMA-IR. Cortisol levels were markedly higher in (G3) than (G4) with *p*-value <0.001 and HOMA-IR was higher in (G4) than (G3) with *p*-value 0.003 (Table 4). Nevertheless, there were no statistically significant differences between (G3) and (G4) regarding neither glucose, Insulin levels and GIR nor sex, GA and anthropometric measurements (*p*-value >0.05 for all parameters).

Table (4): Comparison between PT, VD (G3) and PT, CS (G4) according to biochemical parameters and IR markers.

Biochemical parameters & IR markers	PT, VD (G3) (N=20)	PT, CS (G4) (N=20)	p-value
	Mean± SD	Mean± SD	
Glucose (mg/dL)	71.80±18.84	76.20±14.63	0.415
Insulin (mIU/mL)	16.58±6.38	19.45±5.00	0.122
Cortisol (ng/mL)	247.05±28.21	190.25±20.16	<0.001**
HOMA-IR	2.72±0.74	3.61±1.01	0.003*
GIR	5.38±2.99	4.26±1.65	0.152

p-value >0.05 NS.

**p*-value <0.05 S.

***p*-value <0.001 HS.

GIR : Glucose insulin ratio.

HOMA-IR: Homeostasis model assessment-insulin resistance.

N : Number.

SD: Standard deviation.

FT : Full-term.

G : Group.

GIR : Glucose insulin ratio.

VD: Vaginal delivery.

CS : Cesarean section.

In agreement, Bagnoli et al.'s research revealed that both insulin levels and HOMA-IR were higher in PT than FT infants [16]. This can be explained by the anabolic role of insulin and its increase need in PT newborns for fetal growth and development

[17].

While Insulin has a direct relation with HOMA-IR, cortisol was negatively associated with HOMA-IR in both FT and PT newborns. In agreement to our research, Ahmad et al., noticed that the mean cord blood glucose and cortisol levels in FT newborns were significantly higher than those in PT infants, while HOMA-IR and Insulin levels were found more in PT newborns than in FT newborns [18]. Therefore, the disruption of the insulin signal transduction leads to hyperinsulinemia and insulin resistance [5,19].

On the other hand, in our research the high levels of cortisol in FT groups than PT groups can be explained by cortisol regulatory action for fetal terminal maturation and eventually adaptation at birth [9,20]. By the second trimester, the activity of 11 β -hydroxy steroid oxidoreductase increases, therefore lower level of cortisol detected in PT newborns in comparison to FT [21]. Bagnoli et al., found positive significant correlation between GA with ACTH and cord blood cortisol [7]. He also noticed that cord blood cortisol level was higher in FT and PT groups that delivered vaginally than delivered by CS. The higher cord blood glucose levels observed in our study in FT can be explained by the inverse correlation between insulin and cortisol and reduced insulin release in response to a glucose stimulus [6].

Receiver operating characteristics (ROC) curve was used to define the best cut off value of HOMA-IR, over preterm and full-term newborns, which was 1.81, with sensitivity of 95%, specificity of 65%. Another ROC curves were used to define the best cut off value of HOMA-IR at different gestational ages which showed increasing cut off values with decreasing GA till 30 weeks of gestation where the highest cut off value of HOMA-IR >4.28. The cut off values decreased in 28 and 29 weeks of gestation but still more than the cut off value 1.81 that diagnose IR. This relatively decreased values can be explained by the limited number of cases at this age included in our study hence further studies is needed to evaluate cut off value of HOMA-IR in newborns delivered at 28 and 29 weeks of gestation. Bagnoli et al., noticed that the cord blood insulin and HOMA-IR values were highest at very PT neonates with GA less than 30 weeks, but cut off value of HOMA-IR at this age group wasn't defined [16].

In our study, comparison between full term groups G1 (VD) and G2 (CS) revealed statistically significant differences between them in cortisol levels. Cortisol levels were markedly higher in G1 than G2, with p -value less than 0.001. In agreement to our study, Vogl et al., detected an association between the mode of delivery and maternal & fetal endocrine stress response in 103 FT neonates [22]. His research revealed lower levels of CS cord blood epinephrine, norepinephrine and cortisol than those delivered by simple VD, VD with epidural anesthesia and ventouse extraction. Furthermore, in a prospective study with 280 newborns enclosed at 3 Swiss university hospitals by Schuller et al., he found that newborns delivered vaginally show higher levels of cord blood cortisol than those delivered by elective CS [23]. In agreement, Sano et al., showed significant positive correlations between cord blood cortisol level and delivery duration being higher during VD [24]. Therefore, the relatively high stress in VD than CS explains the elevated cord blood cortisol in G1 than G2 in our research [25].

In our study, another comparison was done between G1 and G2 that revealed statistically significant differences between them with respective to glucose levels. Glucose levels were higher in G1 than G2, with p -value 0.022. Hussein et al., at Khartoum Hospital, and Marom et al. and Melkie et al., found that cord blood glucose level was significantly higher in vaginally delivered than cesarean delivered neonates [26-28]. These results can be explained by the negative relation that was noticed between insulin and cortisol, which indicate an association between high cortisol with a decrease in β cell function and decrease insulin release in response to a glucose stimulus [6]. Alternatively, the elevated cord blood glucose concentration among VD could also be due to glycogenolysis aggravated by stress hormones such as cortisol and catecholamines [29]. Hence, glycogen stores might be rather decreased in VD infants when compared to those of CS infants resulting in the blood glucose differences observed at 2h of life between these two groups of babies [30,31]. Finally, there were no statistically significant differences between (G1) and (G2) in sex, GA and anthropometric measurements (p -value >0.05 for all parameters).

In our study, we further analyzed and compared the HOMA-IR and cortisol levels with respective to mode of delivery in PT groups. To start with, for PT infants delivered by VD (G3) and CS (G4), HOMA-IR was statistically significantly higher in (G4) than (G3) with p -value 0.003. In contrast, there was no correlation between mode of delivery

and HOMA-IR in FT groups. Cortisol levels were markedly higher in (G3) than (G4) with p -value less than 0.001, denoting a significant difference between them due to the stress of labor that increases both the maternal and fetal cortisol and catecholamines. Scientists believe that at full term, there is full maturation in the hypothalamic pituitary axis, however, PT newborns response to different stressful conditions is quantitatively less, hence denoting immaturity [32]. Nevertheless, there were no statistically significant differences between (G3) and (G4) regarding sex, GA and anthropometric measurements (p -value >0.05 for all parameters).

Conclusion and Recommendation:

In conclusion, our study describes the trend of glucose, insulin, cortisol, HOMA-IR and GIR levels in cord blood of newborns with different gestational ages and different modes of delivery. Higher insulin and HOMA-IR levels were found in PT newborns as compared to FT newborns that could be responsible for development of metabolic diseases like diabetes and its complications in adult life due to high IR in this group of infants.

Higher cortisol level was found in FT than PT newborns as a result of its major regulatory action in terminal maturation of the fetus and neonatal adaptation at birth. In addition, higher cortisol level was found in groups that delivered vaginally than delivered by CS as the former exhibits high maternal and fetal stress during delivery. However, Sex, GA and anthropometric measurements were not affected by mode of delivery. On the other hand, although HOMA-IR is not affected by the mode of delivery in FT groups, we noticed that it was higher in PT infant born by CS, who may have higher IR. This phenomenon requires more investigation to explain this relation.

Finally, Since PT are at higher risk of developing hyperglycemia due to high IR, close monitoring is needed for blood glucose level and follow-up for development of metabolic diseases. Further studies are needed with larger population to determine the cut off value of HOMA-IR in the population at 28, 29 weeks of pregnancy.

Conflict of Interest:

Authors declare no conflict of interest.

Author contributions:

- Conceptualization and study design: Hebatallah Abou Hussien, Dina M. Akmal, Mohamed Mahmoud

- Methodology and technique: Hebatallah Abou Hussien, Dina M. Akmal, Nermine M. Riad, Mohamed Mahmoud, Irene Bishai.
- Acquisition, analysis, and interpretation of the data: Hebatallah Abou Hussien, Dina M. Akmal, Nermine M. Riad, Mohamed Mahmoud, Rasha H. Sayed, Irene Bishai.
- Writing - original draft preparation: Dina Akmal, Nermine M Riad, Mohamed Mahmoud.
- Writing - review and editing: Hebatallah Abou Hussien, Dina M. Akmal, Nermine M. Riad, Mohamed Mahmoud, Rasha H. Sayed, Irene E. Bishai.
- Supervision: Hebatallah Abou Hussien.

References

- 1- PATEL T.P., RAWAL K., BAGCHI A.K., AKOLKAR G., BERNARDES N., DIAS D. DA S., et al.: Insulin resistance: An additional risk factor in the pathogenesis of cardiovascular disease in type 2 diabetes. *Heart Fail Rev.*, Jan. 1; 21 (1): 11-23, 2016.
- 2- DIAMANTI-KANDARAKIS E. and DUNAIF A.: Insulin resistance and the polycystic ovary syndrome revisited: An update on mechanisms and implications. *Endocr. Rev.*, Dec. 33 (6): 981-1030, 2012.
- 3- MATTHEWS D.R., HOSKER J.P., RUDENSKI A.S., NAYLOR B.A., TREACHER D.F. and TURNER R.C.: Homeostasis model assessment: Insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia.*, Jul. 28 (7): 412-9, 1985.
- 4- KURTOĞLU S, HATIPOĞLU N., MAZİCİOĞLU M., KENDİRİCİ M., KESKİN M. and KONDOLOT M.: Insulin resistance in obese children and adolescents: HOMA-IR cut-off levels in the prepubertal and pubertal periods. *J. Clin. Res. Pediatr. Endocrinol.*, 2 (3): 100-6, 2010.
- 5- SAHASRABUDDHE A., PITALE S., RAJE D. and SAGDEO M.M.: Cord blood levels of insulin and glucose in full-term pregnancies. *J. Assoc. Physicians India*, Jun. 61 (6): 378-82, 2013.
- 6- ADAM T.C., HASSON R.E., VENTURA E.E., TOLEDORCORRAL C., LE K.A., MAHURKAR S., et al.: Cortisol is negatively associated with insulin sensitivity in overweight Latino youth. *J. Clin. Endocrinol. Metab.*, Oct. 95 (10): 4729-35, 2010.
- 7- BAGNOLI F., MORI A., FOMMEI C., CORIOLANI G., BADI S. and TOMASINI B.: ACTH and cortisol cord plasma concentrations in preterm and term infants. *J. Perinatol Off J. Calif Perinat Assoc.*, Jul. 33 (7): 520-4, 2013.
- 8- KİRİMİ E., CESUR Y. and GÜL A.: Normal levels of insulin, growth hormone and cortisol levels in venous cord blood of healthy full-term infants: Correlation with birthweight and placental weight. *East J. Med.*, 6 (1): 14-7, 2001.

- 9- HILLMAN N.H., KALLAPUR S.G. and JOBE A.H.: Physiology of transition from intrauterine to extrauterine life. *Clin. Perinatol.*, Dec. 39 (4): 769-83, 2012.
- 10- ZAICHKIN J., MCCARNEY L. and WEINER G.: NRP 7th Edition: Are You Prepared? *Neonatal Netw NN*, 35 (4): 184-91, 2016.
- 11 - VAHABI S., HAIDARI M., AKBARI TORKAMANI S. and GORBANI VAGHEI A.: New assessment of relationship between Apgar score and early neonatal mortality. *Minerva Pediatr.*, Jun. 62 (3): 249-52, 2010.
- 12- LI X., ZHANG M., PAN X., XU Z. and SUN M.: "Three Hits" Hypothesis for Developmental Origins of Health and Diseases in View of Cardiovascular Abnormalities. *Birth Defects Res.*, 109 (10): 744-57, 2017.
- 13- CHARLES M.A., DELPIERRE C. and BRÉANT B.: [Developmental origin of health and adult diseases (DO-HaD): Evolution of a concept over three decades]. *Med. Sci.*, Jan. 1; 32 (1): 15-20, 2016.
- 14- MATHAI S., CUTFIELD W.S., DERRAIK J.G.B., DALZIEL S.R., HARDING J.E., ROBINSON E., et al.: Insulin Sensitivity and β -Cell Function in Adults Born Preterm and Their Children. *Diabetes*, Oct. 61 (10): 2479, 2012.
- 15- HALES C.N. and BARKER D.J.P.: Type 2 (non-insulin-dependent) diabetes mellitus: The thrifty phenotype hypothesis. 1992. *Int J Epidemiol.*, Oct. 42 (5): 1215-22, 2013.
- 16- BAGNOLI F., VODO F., VODO S., CONTE M.L., TOMASINI B., VODO Z., et al.: Glucagon and insulin cord blood levels in very preterm, late preterm and full-term infants. *J Pediatr Endocrinol Metab JPEM*, May 27 (5-6): 419-23, 2014.
- 17- FaBRICIUS-BJERRE S., JENSEN R.B., FÆRCH K., LARSEN T., MØLGAARD C., MICHAELSEN K.F., et al.: Impact of Birth Weight and Early Infant Weight Gain on Insulin Resistance and Associated Cardiovascular Risk Factors in Adolescence. *PLOS ONE*, Jun. 2; 6 (6): e20595, 2011.
- 18- AHMAD A., RUKMINI M.S., YADAV C., AGARWAL A., MANJREKAR P.A. and HEGDE A.: Indices of Glucose Homeostasis in Cord Blood in Term and Preterm Newborns. *J. Clin. Res. Pediatr. Endocrinol.*, Sep. 1; 8 (3): 270-5, 2016.
- 19- Blanco C.L., Liang H., Joya-Galeana J., DeFronzo R.A., McCurmin D., Musi N.: The Ontogeny of Insulin Signaling in the Preterm Baboon Model. *Endocrinology*, May 151 (5): 1990, 2010.
- 20- R.C., AP M.N., DB D., AC R.: Effects of antenatal glucocorticoids on the developing brain. *Steroids [Internet]*. Oct [cited 2022 Dec 2]; 114. Available from: <https://pubmed.ncbi.nlm.nih.gov/27343976/>, 2016.
- 21- HINDE K., SKIBIEL A.L., FOSTER A.B., DEL ROSSO L., MENDOZA S.P. and CAPITANIO J.P.: Cortisol in mother's milk across lactation reflects maternal life history and predicts infant temperament. *Behav. Ecol.*, 26 (1): 269-81, 2015.
- 22- VOGL S.E., WORDA C., EGARTER C., BIEGLMAYER C., SZEKERES T., HUBER J., et al.: Mode of delivery is associated with maternal and fetal endocrine stress response. *BJOG Int. J. Obstet. Gynaecol.*, Apr. 113 (4): 441-5, 2006.
- 23- SCHULLER C., KÄNEL N., MÜLLER O., KIND A.B., TINNER E.M., HÖSLI I., et al.: Stress and pain response of neonates after spontaneous birth and vacuum-assisted and cesarean delivery. *Am. J. Obstet. Gynecol.*, Nov. 207 (5): 416.e1-6, 2012.
- 24- SANO Y., DOI T., KIKUCHI S., KAWAI K. and TANAKA M.: Correlations between stress hormone levels in umbilical cord blood and duration of delivery. *JPMA J. Pak. Med. Assoc. Jul.* 65(7):782-4, 2015.
- 25- BENFIELD R.D., NEWTON E.R., TANNER C.J. and HEITKEMPER M.M.: Cortisol as a biomarker of stress in term human labor: Physiological and methodological issues. *Biol. Res. Nurs.*, Jan. 16 (1): 64-71, 2014.
- 26- HUSSEIN S.M., SALIH Y., RAYIS D.A., BILAL J.A. and ADAM I.: Low neonatal blood glucose levels in cesarean-delivered term newborns at Khartoum Hospital, Sudan. *Diagn Pathol.*, Jun. 9; 9: 112, 2014.
- 27- MAROM R., DOLLBERG S., MIMOUNI F.B., BERGER I., MORDECHAYEV N., OCHSHORN Y., et al.: Neonatal blood glucose concentrations in caesarean and vaginally delivered term infants. *Acta Paediatr Oslo Nor.*, 20 10 Oct. 99 (10): 1474-7, 1992.
- 28- MELKIE M., YIGEREMU M., NIGUSSIE P., TEKA T. and KINDE S.: Is the difference in neonatal blood glucose concentration of caesarian and vaginally delivered term infants requiring separated reference intervals? *BMC Res. Notes.*, Sep. 24; 5 (1): 519, 2012.
- 29- THOMPSON-BRANCH A. and HAVRANEK T.: Neonatal Hypoglycemia. *Pediatr Rev.*, Apr. 38 (4): 147-57, 2017.
- 30- CHO W.I. and CHUNG H.R.: Glucose Homeostasis during Fetal and Neonatal Period. *Korean. J. Perinatol.*, Jul. 20; 27 (2):9 5-102, 2016.
- 31 - E P., S S., C G, LH P., N M. and MJ H.: Breastfeeding after cesarean delivery: a systematic review and meta-analysis of world literature. *Am. J. Clin. Nutr. [Internet]*. May [cited 2022 Dec 3]; 95(5). Available from: <https://pubmed.ncbi.nlm.nih.gov/22456657/>, 2012.
- 32- GESTEIRO E., RODRÍGUEZ BERNAL B., BASTIDA S. and SÁNCHEZ-MUNIZ F.J.: Maternal diets with low healthy eating index or Mediterranean diet adherence scores are associated with high cord-blood insulin levels and insulin resistance markers at birth. *Eur. J. Clin. Nutr.*, Sep. 66 (9): 1008-15, 2012.

تقييم مستوى مقاومة الأنسولين في حديثي الولادة كاملي وناقصي النمو باستخدام نموذج التوازن لتقييم مقاومة الأنسولين

تعتبر مقاومة الأنسولين إحدى كبرى عوامل الخطورة المساعدة في حدوث كثير من الأمراض مثل مرض السكري النوع الثاني ومرض ارتفاع ضغط الدم وارتفاع مستوى الدهون بالدم وتصلب الشرايين وحوادث مضاعفاتها مثل الجلطات الدماغية وجلطات الشرايين التاجية.

ويمكن تجنب هذه الأمراض ومضاعفاتها بالتشخيص المبكر لمقاومة الأنسولين والتعرف على الفئة الأكثر عرضة لها وسرعة علاجها.

إن نقص العمر الرحمي ونقص التغذية الجنينية والتغذية في الفترة الأولى بعد الولادة أحد الأسباب المؤثرة على تكوين ونمو خلايا البنكرياس المسؤولة عن إفراز الأنسولين مما يؤدي إلى زيادة نسبة حدوث مقاومة الأنسولين.

ويعتبر اختلال مستوى الكورتيزول والأنسولين في هذه المرحلة العمرية أحد أسباب اختلال أيض الجلوكوز وبالتالي يزيد من معدل حدوث مقاومة الأنسولين والسمنة في مرحلة ما بعد البلوغ.

الهدف من الدراسة : تقييم مستوى مقاومة الأنسولين في حديثي الولادة كاملي وناقصي النمو باستخدام نموذج التوازن لتقييم مقاومة الأنسولين. ومعرفة العلاقة بينها وبين العمر الرحمي وطريقة الولادة لحديثي الولادة.

المرضى وطرق البحث : أجريت هذه الدراسة المقطعية في أقسام أمراض النساء والتوليد وطب الأطفال والباطو لوجيا الإكلينيكية، كلية الطب، جامعة القاهرة. تم الحصول على الموافقة لبروتوكول الدراسة من اللجنة الأخلاقية في كلية الطب، جامعة القاهرة. لكل مريض موجود في الدراسة، تم الحصول على الموافقة المسبقة من الأباء قبل جمع البيانات وبعد شرح أهداف الدراسة.

شملت الدراسة ٨٠ رضيعاً يتراوح عمرهم الرحمي بين ٢٨ و ٤١ أسبوعاً وتم تقسيمهم إلى ٤ مجموعات :

- ١- عشرون رضيع كامل النمو ومولود ولادة مهبلية طبيعية.
- ٢- عشرون رضيع كامل النمو ومولود ولادة قيصرية.
- ٣- عشرون رضيع ناقص النمو ومولود ولادة مهبلية طبيعية.
- ٤- عشرون رضيع ناقص النمو ومولود ولادة قيصرية.

كان متوسط العمر الرحمي للمواليد في المجموعتين كاملي النمو (0.96±38.50) أسبوعاً، ومتوسط أوزانهم (0.42±3.32) كجم، وعدد الذكور ١٦ بنسبة ٤٠٪، وعدد الإناث ٢٤ بنسبة ٦٠٪.

بينما كان متوسط العمر الرحمي للمواليد في المجموعتين ناقصي النمو (2.46±32.65) أسبوعاً، ومتوسط أوزانهم (0.46±1.95) كجم، وعدد الذكور ١٩ بنسبة (٤٧.٥٪)، وعدد الإناث ٢١ بنسبة (٥٢.٥٪).

وقد أظهرت الدراسة النتائج الآتية : ارتفاع مستوى الجلوكوز والكورتيزول والنسبة بين الجلوكوز والأنسولين في مجموعات المواليد كاملي النمو عن مجموعات ناقصي النمو ووجود دلالات إحصائية بين المجموعتين (p -value <0.001). ارتفاع مستوى الأنسولين ونسبة نموذج التوازن لتقييم مقاومة الأنسولين في المجموعات ناقصي النمو عن كاملي النمو ووجود دلالات إحصائية بين المجموعتين (p -value <0.001). في المجموعات كاملي النمو وجد دلالات إحصائية وارتفاع مستوى الكورتيزول (p -value <0.001) والجلوكوز (p -value :0.022) بالمجموعة المولودة ولادة مهبلية عن المجموعة المولودة ولادة قيصرية. في المجموعات ناقصي النمو وجد دلالات إحصائية وارتفاع بمستوى الكورتيزول (p -value <0.001) بالمجموعة المولودة ولادة مهبلية عن المجموعة المولودة ولادة قيصرية، بينما وجد ارتفاع في نسبة نموذج التوازن لتقييم مقاومة الأنسولين في المجموعة المولودة ولادة قيصرية عن المجموعة المولودة ولادة مهبلية (p -value :0.003).

ونستنتج من هذه النتائج : يعاني حديثي الولادة ناقصي النمو من ارتفاع نسبة مقاومة الأنسولين لديهم مما قد يكون سبباً في ارتفاع احتمالية إصابتهم بأمراض التمثيل الغذائي مثل مرض السكري النوع الثاني ومضاعفاته. ارتفاع نسبة مقاومة الأنسولين لناقصي النمو ذو الولادة القيصرية عن الولادة المهبلية يحتاج لدراسات أخرى لتأكيد وشرح هذه النتائج. الكورتيزول واحد من الهرمونات المسؤولة عن نضج واكتمال تكوين الجنين في الأشهر الأخيرة من الحمل ويساعد الجنين في مرحلة التكيف الفسيولوجي بعد أثناء وبعد الولادة. يمكن استخدام مستوى الكورتيزول في دم المواليد كأحد الدلالات على الضغط والتوتر الذي تعرض له الجنين ما قبل وأثناء الولادة.