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Evaluation of Oxidative Stress Markers in Relation APGAR Scores to in Egyptian Newborns with Intrauterine Growth Retardation

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The study aimed to estimate the status of oxidative stress markers in neonates of both sexes born 37- 41with intrauterine growth restriction (IUGR) comparing them to healthy convenient for gestational. The study included 44 Egyptian neonates with IUGR of both sexes and 45 neonates of both sexes with appropriate for gestational age. In both groups the neonates were delivered vaginally without any assisted vaginal delivery to mothers without known medical conditions affecting placental sufficiency. Malondialdehyde (MDA, total antioxidant capacity (TAC) and paraoxonase-1(PON1) were measured. Obstetric data including mode of delivery, instrumental delivery and gestational age at delivery by ultrasound Neonatal assessment including gestational age by new Ballard, sex of neonate, weight, head circumference, APGAR score at 1 and 5 minutes, length, full general & systemic examinations of newborn. The activity of MDA was increased, whilelevels of TAC and PON1 were significantly lower in IUGR than controls. APGAR score at both 1 min and 5 min and Ballard were significantly decreased in the IUGR group. Mean birth weight, length, maternal gestational age and head circumference of IUGR cases were decreased than control. APGAR scores were negatively correlated with MDA. In conclusion oxidative stress associated with IUGR newborns and antioxidants during pregnancy may be advised. Oxidative stress markers might have early prediction value for diagnosis of these conditions and probable pharmacological intervention with antioxidants may improve the pregnancy conditions.

Keywords: APGAR score; Intrauterine growth retardation; malondialdehyde; Total Antioxidant Capacity; paraoxonase-1.

IUGR is of distinctive disquiet in developing countries where30% of the neonates are growth retarded. These infants are liable to early neonatal mortality because of complications as birth asphyxia, shock, hyperbilirubinemia, thrombocytopenia, hypoglycaemia, acidosis, septicaemia and hypoxia [1].Oxidative stress has been detected in both newborn in IUGR and pregnant mother [2]. Also,it has been found to respond to antioxidants treatment [3].In newborns, maturation in

expressions of gestational agemight be a chieffactor in the infant's toleranceagainst the deleterious impacts of free oxygen radicals. It has been found that disability of maturation ofantioxidant defense system in premature infants implicatesto the onset and development of bronchopulmonary dysplasia. Oxygen free radicals are highly reactive and able to destruct macromolecules as polyunsaturated fatty acids, proteins, carbohydrates and DNA[45]. APGAR scoring system based on easily five recognizable discriminators, irritability color, respiratory effort, reflex, muscletone and heart-rateis apremium techniqueto evaluate a condition of newborn. Low Apgar scores are significantlyrelated with neonatal mortality[6]. The IUGR rate in developing countries according to estimates is about six times higher than that in developed countries [7].

Therefore, we carried out the present work to evaluate oxidative injury in IUGR in Egyptian newborns**.**

Subjects

This prospective cohort study was performed in the department of obstetrics and gynecology in Kasr El Ainy hospital and El Galaa teaching hospital from May 2017 to January 2018. The research ethics was approved by the scientific ethical committee of the Department of Pediatrics, Faculty of Medicine, Cairo University. The study was conducted on 89 neonates divided into 2 groups Group 1 (intrauterine growth restriction group): included 44 neonates of both sexes born 37- 41with intrauterine growth restriction. Group 2 (appropriate for gestational age group): included 45 neonates of both sexes born 37-41and appropriate for gestational age. In both groups the neonates were delivered vaginally without any assisted vaginal delivery to mothers without known medical conditions affecting placental sufficiency e.g. diabetes, hypertension and preeclampsia. Neonates with congenital anomalies were eliminated from our study**.**

Methods

All neonates were subjected to the following

Full maternal data was taken including age of mother, gravidity, parity, abortions, gestational age by early ultrasound and maternal illnesses as pre-eclampsia, hypertension, gestational diabetes, premature rupture of membrane. Obstetric data including mode of delivery, instrumental delivery and gestational age at delivery by ultrasound. Neonatal assessment including gestational age by new Ballard, sex of neonate, head circumference, length, APGAR score at 1 and 5 minutes, weight and full general & systemic examinations of newborn. All the infants were born at term. Gestational age was evaluated from the of last menstrual period date and simultaneous clinical evaluation was done using the New Ballard score[8]

Biochemical Analysis

Lipid peroxides determination

Malondialdehyde was assessed by measuring thiobarbituric reactive species according to Ruiz-Larrea et al. 1994 method in which the thiobarbituric acid reactive sub-stances react with thiobarbituric acid to generate a red colored complex having absorbance peak at 532 nm [9].

Total antioxidant capacity determination

Serum total antioxidant activity was measured through the reaction of antioxidants with a definite quantity of hydrogen peroxide ($H_2 O_2$). The antioxidants eliminate a definite quantity of the provided H_2O_2. The residual H_2O_2 is measured colorimetric ally by an enzymatic reaction in which the 3, 5, dichloro-2-hydroxy benzensulphonate is converted to a colored product[10].

Paraoxonase-1 (PON-1) activity determination

The activity of arylesterase of PON-1 was assessed via a colorimetric method using substrate phenyl acetate. PON1 catalyzes the phenyl acetate cleavage forming phenol. The phenol formation rate was assessed through observing the absorbance increase at 270 nm. [11].

Statistical analysis

Data were analyzed using the statistical SPSS program for Windows, release 20.0 (SPSS,USA). Results are given as means ± standard deviation (SD). Independent sample t test was used for comparison of unpaired data**.** APGAR score is given as median (range). Mann–Whitney U test was used for comparisonof Apgar scores (non-parametric data). P-valueless than 0.05 was considered significant.

RESULTS

APGAR score both at 1 min and 5 min were significantly lower in the IUGR group compared to control group (Table 1). There was no significant difference of each of maternal age, gravity, parity, abortion and early gestation of

IUGR cases compared to control group. Mean Ballad score, birth weight, length and head circumference of IUGR cases were significantly decreased compared to control group.

MDA levels was significantly elevated in the IUGR group than control group (Table 2). Both TAC and PON1 were significantly lower in IUGR cases than control group**.** Significant negative correlation was observed between MDA and APGAR scores (Table 3).

DISCUSSION

It was hypothesized that oxidative stress, expressed as imbalance inoxidant-antioxidant, has a crucial role in the placental-related disorders

Table 1. Maternal and newborns characteristics in cases with IUGR and controls

	Group	Mean ± Std. Deviation	*P- value**
Maternal-age	IUGR	27±4.86	0.927
	Controls	27.11±6.19	
Maternal-gravity	IUGR	2.77±1.67	0.232
	Controls	3.3±2.43	
Maternal-parity	IUGR	1.26±1.36	0.505
	Controls	1.46±1.45	
Maternal-abortion	IUGR	0.53±1.26	0.425
	Controls	0.85±2.25	
Gestational-early (*weeks)*	IUGR	38.28±1.16	0.625
	Controls	38.67±2.16	
Gestational-Late(weeks)	IUGR	33.60±1.19	0.001
	Controls	38.67±1.51	
Ballard score	IUGR	38.12±1.02	0.004
	Controls	38.83±1.21	
Birth weight (kg)	IUGR	2.11±0.48	0.004
	Controls	3.14±0.22	
Length (cm)	IUGR	42.91±1.96	0.001
	Controls	48.33±2.181	
Head circumference(cm)	IUGR	31.07±0.66	0.001
	Controls	34.21±1.48	
1 min APGAR score	IUGR	7 (1-8)	0.001
	Controls	8(5–8)	
5 min APGAR score	IUGR	9 (5-8)	0.001
	Controls	10 (5-10)	

**P* for the comparisons between IUGR newborns vs. controls

Table 2. Oxidative stress markers in IUGR newborns

	Group		Mean ± Std. Deviation	*P*-value*
MDA	IUGR	1.71±0.456	0.001	
	Controls	1.37±0.394		
TAC	IUGR	1.45±0.42	0.001	
	Controls	1.71±0.39		
PON1	IUGR	48.60±14.04	0.001	
	Controls	56.61±21.65		

**P* for the comparisons between IUGR newborns vs. controls

Table 3. Results from the correlation analysis that evaluated the relationships between oxidative stress markers and 1 min and 5 min APGAR scores

	Pearson Correlation	MDA	TAC	PON1
5 min APGAR score	r	-0.477	-0.017	0.120
	Sig. (2-tailed)	0.017	0.874	0.261
1 min APGAR score	r	-0.457	0.030	0.049
	Sig. (2-tailed)	0.015	0.783	0.649

development, as disorders ofhypertension of IUGR and pregnancy [12,131415].

Prematurity is a significant public health issue. The main reason for death in children under the age of five is complications from premature birth. It has been suggested that oxidative stress may be a pathophysiological condition that contributes to this undesirable condition. Premature neonates are especially vulnerable to oxidative stress injury because they lack well-developed antioxidant and immunological defense mechanisms. The transmission from intrauterine to the extrauterine environment impressively upsurges production of free radical, which is usually downregulated by the antioxidant defense system[17]. Excessive reactive oxygen species (ROS), which are produced when there is an imbalance in this control, lead to oxidative stress. The antioxidant defense system is unable to reverse ROS damage under oxidative stress[17,18] either as a result of an excessive ROS production, a poor ROS inactivation, or both. The majority of the researchers examined in this review demonstrated a connection between higher risk of clinical outcomes, such as neonatal illnesses and morbidity, and elevated levels of oxidative stress biomarkers and/or decreased antioxidant levels in cord blood. IUGR was one of the disorders that shown a stronger correlation with elevated oxidative stress and/or decreased antioxidant levels [19]. Silva and his colleagues conducted an analysis of the vitamin E concentration in umbilical cord serum in 140 newborns (64 premature and 76 term) to examine an association between the biomarker and intrauterine growth, which was one of the studies that evaluated IUGR[19]. The findings revealed that premature neonates were more likely to experience IUGR, and the majority of them had low vitamin E levels. Pregnancy complications like as IUGR, which have a prevalence of between 3 and 7% of deliveries, are frequently mentioned when the fetus is thought to be too small for the GA. A relationship between MDA and ROS levels and a higher probability of a poor Apgar score was reported by another studies [20]. The research also used antioxidant activity levels as additional indicators. In general, measuring antioxidant activity may be more beneficial than measuring oxidative stress levels since the data provide a better knowledge of potential processes and therapy options. [21].

The reason of maternal oxidative stress in IUGR is not obvious yet. Nevertheless, insufficient exudation causes placental hypoxia at the intervillous space and might share in both fetal and maternal oxidative stress. Significant remodeling of the placenta is monitored at the start of the second trimester or at the end of the first trimester that commonly is the starting point of IUGR. Slight insufficiency in diversion of arteries might cause low-grade fluctuations in villous oxygenation that lead to homeostatic responses in the form of protein synthesis inhibition and mild endoplasmic reticulum stress that leads to the reduced functional capacity and the small size of the placenta [22,23]. Oxidative stress represses nitric oxide (NO) bioavailability as it is quickly degenerated by the oxygen-derived free radical superoxide anion. This anion operates as a vasoconstrictor and is a chief determinant of nitric oxide (NO) bioavailability and biosynthesis. Numerous researches have elucidated that hypertension in human is correlated with a decreased bioavailability of NO and an exaggerated ROS amount [24,2526]. The IUGR pathophysiology is multifactorial and in the majority of cases associated with either infectious, fetal, genetic, maternal, or placental pathology[27]. The increased level of oxidative stress markers as 8-hydroxy-2-deoxyguanosine (8-OHdG) and MDA and the diminished total antioxidant capacity level were illustrated by numerousstudies[13,28–30].

CONCLUSION

In conclusion, oxidative stress associated with IUGR newborns and antioxidants during pregnancy may be advised. Oxidative stress markers might have early prediction value for diagnosis of these conditions and probable pharmacological intervention with antioxidants may improve the pregnancy conditions.

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Conflicts of Interest

There is no conflict of interest.

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