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CORD BLOOD OXIDATIVE STRESS MARKERS CORRELATE WITH BIRTH AND PLACENTA WEIGHT

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ABSTRACT

Background: *Oxidative stress injury has been linked with some clinical conditions in newborn. This cannot be readily measured. Measuring placenta and birth weight along with other features may help in predicting likelihood of oxidative stress injury babies have suffered.* ***Aim :*** *to measure birth and placenta weight of new born babies as well as determining cord blood total antioxidant status and malondialdehyde (product of oxidant injury)* ***Methods****: Study site was labour ward of Ladoke Akintola University of Teachnology Teaching Hospital, Osogbo, Nigeria. Sixty four term newborn babies were recruited into the study. Plasma extracted from cord blood of subjects was used for the laboratory determination of total antioxidant status, malondialdehyde and uric acid. Total antioxidant status and malondialdehyde were measured using methods of Koracevic et al and Satoh et al respectively. Uric acid was measured by enzymatic method.* ***Results****: There were positive correlations between placenta weight and TAS($r=0.115;p>0.05$), between placenta weight and Uric acid($r=0.075;p>0.05$), between birth weight and TAS($r= 0.233,p=0.064$), between birth weight and Uric acid($r=0.172;p>0.05$). There were significant negative correlations between placenta weight and MDA($r=-0.25;p<0.05$),between birth weight and MDA($r=-0.56;p<0.05$).* ***Conclusion:*** *The birth weight of the baby as well as weight of the placenta is negatively correlated significantly with cord blood oxidative stress*

Keywords: Total antioxidant status (TAS), Malondialdehyde (MDA), Uric acid, Oxidative stress, Free radicals.

INTRODUCTION

Pregnancy is a stressful physiological condition and it has been associated with oxidative stress injury (Fidelis *et al.*, 2004; Sharma *et al.*, 2006). Oxidative stress in pregnancy has been linked with some complications; preeclampsia (Theresa *et al.*, 2005; Bernardi *et al.*, 2008), intrauterine growth retardation (Kressig *et al.*, 2008; Mert *et al.*, 2012), intrauterine fetal death (Hracsko *et al.*, 2008) as well as perinatal death (Rashidul and Mannan, 2006). With all that have been said in the literatures about oxidative stress injury, it cannot still be readily measured in our day-to-day practice. The search for readily measured parameters may help in predicting oxidative stress injury.

Weight of the baby and its placenta are measured almost immediately after first minute Apgar score is taken. Pregnant women gain weight appropriately as the pregnancy advances and one of the contributory factors is the growth of the baby. Inability of pregnant women to gain weight appropriately has been associated with an increase oxidative stress injury (Mert *et al.*, 2012). However, (Violeta *et al.*, 2005) reported increasing product of free radical injury in women that significantly gained weight during pregnancy Oxidative stress occurs when there is an imbalance in oxidant (free radical) and antioxidant in excess of oxidant. The attack of free radicals on membrane lipid starts a chain of reactions that has malondialdehyde (MDA) as one of the intermediate products (Schroeder *et al.*, 1990). This is being measured widely to show the evidence of oxidant (free radical injury) in biological samples. Glutathione peroxidase, superoxide dismutase, vitamins as well as uric acid are antioxidants expected to counteract the effects of free radical injury. In view of what has been said in the literatures concerning oxidative stress injury and its difficulty in measurement from biological samples in our day-to-day practice, this study was designed to correlate product of free radical injury (MDA), total antioxidant status (TAS) and uric acid (UA) with placenta and birth weight.

MATERIALS AND METHODS

Study site and population

Study site was labour wards of Ladoke Akintola University of Teachnology Teaching Hospital, Osogbo, Nigeria. Sixty four term newborn babies were recruited into the study. These babies were delivered through spontaneous vertex delivery. Each mother was certified of not being a known hypertensive, diabetic, active smokers and none had preeclampsia. Babies of women with prolong labour were also excluded. None of the babies was among a set of multiple gestations and those with obvious congenital malformation were excluded.

Ethical clearance was gotten from ethical and research committee of Ladoke Akintola University of Technology Teaching hospital, Osogbo, Nigeria

Sample collection and processing

Cord blood sample was collected from new born babies immediately after delivery. Immediately after delivery, the umbilical cord was clamped at two points. Sterile needle was inserted into a superficial umbilical artery in between the two clamps and 10mls of blood was drawn. This was dispensed into lithium heparine containing specimen bottles. The sample was however, centrifuged at 3000g for 10minutes and supernatant was extracted into plain screw cap specimen bottle. The plasma was therefore kept frozen until laboratory analysis. This plasma was used for the laboratory determination of TAS, MDA and Uric acid. Baby and placenta were also weighed in kilogram

Biochemical Analysis

Total antioxidant status was measured using method of (Koracevic *et al.*, 2001). It is based on the principle that a standardised solution of Fe-EDTA complex reacts with hydrogen peroxide (Fenton reaction) to give hydroxyl radical, a reactive oxygen species. This reactive oxygen species degrades benzoate to produce thiobarbiturate reacting substances (TBARS). The antioxidant from added sample causes suppression of the production of TBARS. Therefore the decrease in the concentration of TBARS as a result of antioxidants is measured spectrophotometrically and serves as concentration of antioxidants present in the biological sample added. Plasma MDA was measured using method by Satoh et al, 1978. The principle is based on malondialdehyde in the plasma reacting with thiobarbituric acid (TBA) in acidic medium to form a pink colour complex measured spectrophotometrically. The deeper the colour generated the higher the concentration of malondialdehyde. Plasma uric acid was measured using ready to use commercially manufactured kit by Fortress Diagnostics Limited, Unit 2C Antrim Technology Park, Antrim NT41 IQS, United Kingdom. This is based on the principle that uric acid in plasma is converted to allantoin and hydrogen peroxide in the presence of uricase. Hydrogen peroxide, in the presence of peroxidase enzyme is converted to a dye called Quinone-dimine dye . This colour complex is measured spectrophometrically.

Statistical Analysis

Statistical analysis was done by the aid of SPSS 16. Correlation analysis was performed using Pearson's correlation coefficient (r). P-value <0.05 was regarded as significant.

RESULTS

The age of all the pregnant women was between 22 and 31 years. They all delivered at gestational age of between 36 and 40 weeks. The mean average weight of placenta was 0.53±0.18 and that of birth weight was 3.15±1.05. Mean values of plasma total antioxidant status (TAS), malondialdehyde (MDA) and Uric Acid were 2.13±1.10mmol/l, 4.87±1.6 µmol/l and 0.22±0.09mmol/l respectively. All these are shown in table 1

Table 2 grouped subjects in their various ranges of measured variables. Subjects with birth weight less than 2.20kg had mean plasma MDA to be 6.3 µmol/l, TAS to be 1.21mmol/l and uric acid to

be 0.12mmol/l. Those subjects that had placenta and birth weight to be 2.21-3.5kg were found to have mean plasma MDA to be 5.0µmol/l, TAS to be 2.9mmol/l and uric acid to be 0.20. Similarly those subjects that had birth weight greater than 3.6kg were observed to have mean plasma values of MDA to be 3.5µmol/l, TAS 3.1mmol/l and uric acid to be 0.28mmol/l. Similar trend was observed when different ranges of placenta weight was related to mean values of biochemical parameters. This is as shown in table 3

Table 4 showed correlation among the measured variables. There were positive correlations between placenta weight and birth weight ($r=0.57;p<0.001$), TAS and Uric acid ($r=0.250;p<0.05$), between placental weight and TAS ($r=0.115;p>0.05$), between placenta weight and Uric acid ($r=0.075;p>0.05$) between birth weight and TAS ($r= 0.233,p=0.064$), between birth weight and Uric acid ($r=0.172;p>0.05$). Furthermore, there were negative correlations between placenta weight and MDA ($r=-0.25;p<0.05$),between birth weight and MDA ($r=-0.56;p<0.05$), between TAS and MDA ($r=-0.310;p<0.05$) and between uric acid and MDA ($r=-0.11;p>0.05$).

DISCUSSION

All subjects were born at term. This has helped to remove the effect gestational age has on oxidative stress. Oxidative stress has been observed to be increasing as pregnancy advances (Idogun *et al.*, 2008; Luqman *et al.*, 2008). The age range of mothers of recruited babies were also considered, none was above 40years. The effect of ageing on our selected biochemical parameters was also removed (Clarissa *et al.*, 2013). All babies were born through spontaneous vertex delivery bearing in mind the effect that different mode of deliveries could have on oxidative stress. It has been reported that babies born through elective ceasarian section have less oxidative stress than those born through spontaneous vertex delivery (Calderon *et al.*, 2008). This has been attributed to the stress of labour the baby passes through and some labour may even be prolonged.

Oxidative stress in babies develops the same way it develops in adult. This is as a result of generation of free radical in excess of the available antioxidants. Free radicals like reactive oxygen species when they attack cellular polyunsaturated membrane lipid, a stepwise reaction comes into play. These set of dangerous reactions go on until when antioxidant defence comes into play. Majority of available and infact widely studied antioxidants stop the damaging effect of reactive oxygen species (Mittler *et al.*, 2004; Gratao *et al.*, 2005). This study considered the measurement of plasma malondialdehyde to access the extent of free radical injury (lipid peroxidation). Plasma uric acid and total antioxidant status were also measured to show newborn antioxidant capacity. All these were correlated with placenta and birth weight. The positive correlation of placenta and baby weight to TAS and UA as well as negative correlation with MDA observed in this study shows negative correlation with oxidative stress. That is, low birth weight baby might have suffered more oxidative stress than normal birth weight baby. The report of this finding is scarce in the literature. However, oxidative stress has been observed to be a suggested pathogenesis for intra uterine growth retardation (Kressig *et al.*, 2008; Mert *et al.*, 2012) and fatal death (Hracsko et al., 2008).

Also, it has been observed that newborn baby suffers oxidative stress (Mohd *et al.*, 2009; Sayat *et al.*, 2011). This was also observed in our study. Plasma MDA was negatively correlated with TAS and UA. This could mean that the free radicals being generated overwhelm the available antioxidants. Antioxidants might not also being supplied enough to counteract the little free radicals (oxidant) being generated.

Table 2 divides placenta and baby weight into different categories and the corresponding mean plasma biochemical parameters were obtained. With increasing weight of the baby and placenta the plasma levels of total antioxidant status and uric acid increase. There was corresponding decrease in plasma malondialdehyde . A hypothesis may be formulated that the placenta and baby weight are directly proportional to oxidative stress. This may be as a result of remnant oxidative stress of pregnant women has been found in the new born. It has been reported that oxidative stress in pregnant women is well correlated with that of the newborn (Arikan *et al.*, 2001; Erdem *et al.*, 2012; Şahinli *et al.*, 2012). Also that newborn through the stress of labour also may have their internal generated free radical to cause oxidative stress. Furthermore, antioxidant capacity may not have been fully developed in them.

CONCLUSSION

The birth weight of the baby as well as weight of the placenta is negatively correlated significantly with cord blood oxidative stress. Low birth weight babies have more oxidative stress than babies with normal birth weight Measuring baby's birth and placenta weight along with other clinical features may compliment suspicion of oxidative stress. Antioxidant supplement may be more considered in babies with low birth weight

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Table-1. Mean±Sd of Variables

Variables	Mean±SD
Mothers' Age /years	27.28±4.5 (22-31)
Placenta weight/kg	0.53±0.18 (0.35-0.71)
Birth weight/kg	3.15±1.05 (2.10-4.2)
MDA/µmol/l	4.87±1.60 (3.27-6.47)
TAS/mmol/l	2.13±1.01 (1.12-3.14)
Uric Acid/mmol/l	0.22±0.09 (0.13-0.31)

Table-2. Different Ranges Of Birth Weight With Their Corresponding MDA,TAS And Uric Acid Values

Birth weight/kg	MDA/ µmol/l	TAS/ mmol/l	Uric Acid/ mmol/l
<2.20	6.30	1.21	0.12
2.21-3.50	5.00	2.90	0.20
>3.60	3.50	3.10	0.28

Table-3. Different Ranges of Placenta Weight with their Corresponding Mda,Tas and Uric Acid Values

Placenta weight/kg	MDA/ µmol/l	TAS/ mmol/l	Uric Acid/ mmol/l
<0.45	5.90	1.23	0.13
0.46-0.55	5.03	2.60	0.24
>0.56	3.69	3.33	0.26

Table-4. Correlations among Variables

	Placenta weight/kg	**Birth weight/kg**	**TAS/mmol/l**	**MDA/μmol/l**	**Uric Acid/mmol/l**
Placenta weight/kg	1	R=0.572 P<0.001	R=0.115 P>0.05	R=-0.247 P<0.05	R=0.075 p>0.05
Birth weight/kg	R= 0.663 P<0.001	1	R=0.233 P=0.064	R=-0.561 P<0.05	R=0.172 p>0.05
TAS/mmol/l	R=0.115 P>0.05	R=0.233 P=0.064	1	R=-0.310 P<0.05	R=0.250 P<0.05
MDA/μmol/l	R=-0.247 P<0.05	R=-0.561 P<0.05	R=-0.310 P<0.05	1	R=-0.11 p>0.05
Uric Acid/mmol/l	R=0.075 p>0.05	R=0.172 p>0.05	R=0.250 P<0.05	R=-0.11 p>0.05	1