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Correlation of low birth weight of neonates to placental levels of Zinc, Copper, Iron, Lipid Peroxidation and Glutathione

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Abstract

This study was conducted to seek association between placental redox (antioxidant/ oxidant) parameters and essential metals status (zinc, copper, iron) with birth weight. Placental tissue of pregnant women was collected and levels of zinc, copper and iron were analyzed by Inductively Coupled Plasma-Mass spectrometry. The level of glutathione (GSH) along with the metals was found to markedly decrease in study group, while MDA concentration was significantly higher as compared to control group. Glutathione was found to be positively associated with the levels of zinc and birth weight inspite of negative correlation being established between birth weight and MDA. Placental iron level was indicated to be constructive association with birth weight and was unlikely related with level of MDA. Our findings from the study group supports that damaged antioxidant defence mechanism status is well linked with elevated level of MDA and decreased concentrations of essential metals rendering lower birth weight in neonates.

Keywords: Birth weight; Metals; Placental tissue;

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Introduction

The weight of newborn babies at birth is an imperative criterion for determining survival, health development status and neonatal mortality. Low birth weight (<2500 g) has many adverse outcome like neurodevelopment disabilities, neonatal mortality, morbidity, hypothermia, and feeding problems [1]. Several causes have been documented as possible confounders to low birth weight including poor nutrition, diseases of the placenta, chromosomal abnormalities and environmental factors etc. [2]. During pregnancy, essential metals (zinc, iron and copper) play an important role in the physical and mental development of the fetus and indicator of maternal dietary status [3]. Iron deficiency during pregnancy is major problem in developing countries and strongly associated with risk of low birth weight since this metal play important role in growth of fetus. [4].

Zinc also as one of the mandatory element, is known as an intelligence component of normal embryogenesis for cellular division and differentiation. Decreased circulating zinc levels between mothers to fetus through placenta are linked to low birth weight, fetal intrauterine growth retardation (IUGR), premature births, and placental ablation [5]. Alike to zinc, insufficiency of copper may be allied to assortment of nutritional and vascular disorders in fetus [6]. Zinc and copper both acts as cofactors in antioxidant enzymatic activities, which shield the fetus from any undue impairment. Therefore, deficiency of these metals in placenta acts as one of the detrimental factor responsible for the depletion of anti-oxidant activities, which may result in oxidative stress and it is now brought in to light that oxidative stress in trophoblastic placental tissue is a curse for fetus growth responsible to early pregnancy and low birth weight. It is well documented that imbalance status of essential metals

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(Zn, Cu and Fe) in childbearing population induces oxidative stress but a relationship between these metals, redox status in placenta with birth weight have not been explored till date simultaneous. Thus, the question of the potential interrelationship of essential metals, oxidant and antioxidant status in placental tissue with growth of fetus during pregnancy is of a great interest and attention in current study.

Materials and Methods

For this study, a total of 85 women were selected i.e 35 women who had delivered low birth weight babies (<2500 gm) serve as study group and 50 women who delivered normal birth weight babies (>2500 gm) serve as control group. This study was approved by the Human Ethics Committee of S.N. Medical College, Agra. Healthy pregnant women who gave birth to clinically healthy babies were selected for this study and subjects suffering from gestational hypertension, congenital malformations, routine clinical and laboratory evidence of infection, fetal distress and any chronic disease were excluded which may be associated with low birth weight of neonates. Approximately 25 gm of placental tissue were taken from each subject for biochemical assays and metals status.

Malondialdehyde (MDA) i.e., end product of lipid peroxidation was measured by the method of Ohkawa et al (1979) [7] while extraction of determination of glutathione (GSH) and metals were done according to the methods of Ellman (1959) [8] and Singh et al. (2009) [9] respectively. Selected metals (iron, zinc and copper) were analysed by ICP-MS (Element XR, thermo Fisher Scientific, Germany).The statistical analysis of data was performed by using IBM-SPSS (version-22) and bivariate Pearson correlation was used to determine correlation coefficient between metals (Zn, Cu, Fe), MDA, GSH and birth weight. A p-value less than 0.05, was accepted as statistically significant for all comparisons and correlations.

Results

Concentrations of placental zinc, copper, iron, GSH and MDA were given in **Table 1**. As shown in table 1 the mean levels of zinc, copper, iron and GSH were lower in study group compared to control group, while elevated level of MDA was recorded in women with low birth weight neonates. Unlike, copper and GSH the levels of zinc, iron and MDA were significantly higher in study group compared to control group. Outcomes of correlation coefficient analysis between the placental metals levels (Fe, Cu and Zn), MDA, GSH, and birth weight as shown in table 2.

Table 1. Levels of essential metals, GSH and MDA in the placenta of the women from low birth weight babies and normal birth weight babies.

Metals	Control Group (Birthweight >2500 g) (n=50)	Study Group (Birth-weight <2500 g) (n=35)
Zn*	23.85±13.33	16.97±12.70
Cu	0.33±0.53	0.29±0.39
Fe*	71.83±40.07	44.40±36.30
GSH	4.87±2.50	3.9±3.08
MDA*	**2.13±1.39**	**3.04±1.73**

Results in µg/dl (metals), µmol /gm protein (GSH), nmol /hr/ gm fresh tissue (MDA)
Values represent mean±SD, ***p<0.05**

Table 2. Bivariate pearson correlation coefficient between essential metals (Zn, Fe, Cu), MDA, GSH and birth weight.

	Zn	Fe	Cu	MDA	GSH	BW
Zn	1					
Fe	**0.27***	1				
Cu	0.02	0.07	1			
MDA	-0.15	**-0.27***	-0.07	1		
GSH	**0.22***	0.05	-0.01	**-0.26***	1	
BW	0.05	**0.21***	0.05	**-0.36***	**0.23**	1

Note: BW= birth weight, statistically significant, *p< 0.05

Discussion

In this study, we determined zinc, copper and iron status in placenta of pregnant women in Agra, metals those play a substantial role in the growth of the fetus throughout pregnancy. However, a disproportion of zinc, copper and iron could be contributed in excessive oxidative stress, which influences fetus development. In this study MDA level was significantly elevated (p<0.05) in study group, while GSH level was lower in study group compared to

control group **(Table 1).**These findings are similar to previous studies suggested that increased MDA level and decreased level of GSH in placental tissue were associated with disproportion of oxidant/antioxidant status, which render low birth weight [10].Increased MDA status in placenta is inversely proportional to birth weight of babies as depicted by a negative significant correlation between MDA and birth weight of babies (**Table 2),** proposes that elevated level of MDA could be concerned with reduction in birth weight. Likewise higher level of per-oxidative stress in low birth weight babies has been described by Manzano et al. 2015 [11]. The effect of oxidative stress depends on the maternal antioxidant level, which potentially shields the maternal–fetal unit**.** A positive and significant correlation between level of GSH and birth weight of neonates **(Table 2),** implies that reduced levels of GSH in study group could be related to birth weight of babies. Alternatively, increased antioxidant status in control group ensure a good birth weight or good health of fetus by terminating reactive oxygen species in normal pregnancy. One of the probable descriptions for this could be that copper and zinc are main components of GSH as a cofactor in enzyme, when zinc and copper levels are high in control group, as reported in present study it may be lead to increased level of GSH in placenta of control group. A significant optimistic correlation between the placental levels of zinc and GSH **(Table 2)**, suggests that elevated zinc level may implicated to GSH and can result shielding against oxidative stress in normal birth weight group. Additionally, in present investigation iron level had significant negative correlation with MDA **(Table 2)** recommends decreased level of iron provoked oxidative stress. Insufficiency of iron in women tends to increases pro-oxidant mechanism in placenta as reported in previous study [12] alike to our finding. Depletion of antioxidants level in iron deficient women cannot terminate free radical species may possibly results in damaging the maternal-fetal entity [13]**.** Our finding are consistent with prior study suggesting that elevated level of MDA and deficiency in activity of antioxidant GSH coupled with the impair micronutrients such as copper, zinc and iron can result in poor pregnancy outcomes, including fetal growth restriction [14].

In developing countries like Tanzania and India, low level of zinc was reported in mothers who delivered low birth weight babies [7] alike to our study. During pregnancy, demand of copper enhances as gestational age proceed, since copper is obligatory in synthesis of ceruloplasmin as well shield the cells from the toxicity of oxidative stress. In the current study, decrease copper level in study group demonstrate a possible affiliation between diminished level of copper and foetal growth, which is in accordance to preceding study that a growing body of fetus had linked to low status of maternal copper [15]. In our study, lower levels of placental iron were recorded in study group than control group thus lower level of iron in placenta may take place in low birth weight and fetal growth as found in number of earlier study [11]. A statistically significant positive correlation between placental iron and birth weight of neonates **(Table 2)**, implies that iron is requisite constituent of foetal growth, whereas its deficiency may concerned with the low birth weight. These data are comparable to an Indian study where level of iron in cord blood and birth weight of neonates was found statistically significantly correlated to each other [16]. In this study lower status of zinc, copper and iron were recorded in study group compared to control group, indicating diminish transfer of these three metals from mother to fetus through placenta, thus inhibiting appropriate transfer of essential metals by placenta in fetus associated to impair redox status and poor growth of fetus. Ultimately we can say that growth of fetus depends on balanced levels of both essential metals and redox status in placenta during pregnancy.

Conclusion

Present study indicates that low birth weight is correlated with placental status of essential metals and redox parameters. Significantly reduced level of zinc and iron in study group may be concerned to imbalance between oxidative stress and antioxidants mechanism with potentially serious complication in pregnancy and growth of fetus. These all factors are plausible causes of low birth weight; but mechanism of low birth weight by redox parameters and essential metals has not yet been clearly understood. Therefore, future research on large scale with molecular studies should be directed confirming possible mechanism of these metals and redox status in growth of fetus for improving health quality of neonates in developing countries.

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Conflict of Interest:

None Declared

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