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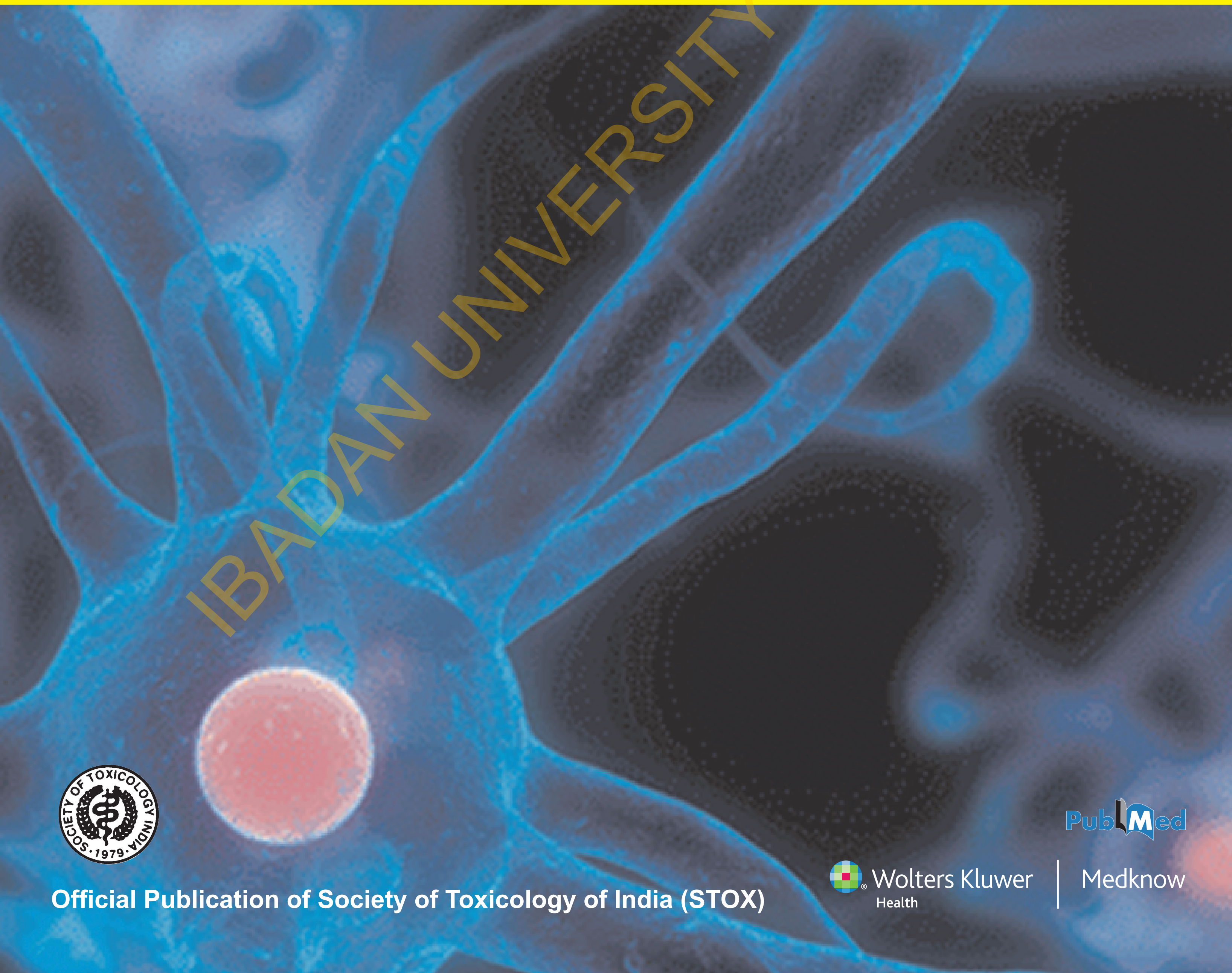

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Original Article

Cadmium Level in Pregnancy, Influence on Neonatal Birth Weight and Possible Amelioration by Some Essential Trace Elements

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ABSTRACT

Cadmium (Cd) is currently of great concern in rapidly industrializing countries-India, China. Their products consumed especially due to increase demand in many developing countries like Nigeria can result in adverse effects. Cd is a ubiquitous environmental pollutant and toxicant and humans are continually exposed to the toxic effects of Cd primarily through food as well as from environmental pollution through industrial activities. Maternal exposure to Cd has been associated with the delivery of low-birth weight babies and an increase incidence of spontaneous abortion. Cd a toxic metal can displace zinc (Zn) an essential element necessary for normal fetal development and growth. With this consideration, 160 subjects comprising of 125 pregnant and 35 non-pregnant subjects as controls were recruited for this study. The pregnant subjects were classified according to the three trimesters of pregnancy as followed; 35, 35, and 55 from the first to the third trimesters respectively. The third trimester subjects were followed-up until after delivery where neonatal parameters (birth weight, head circumference, and length) of babies were measured. 32 (58%) of the women delivered babies with normal birth weight, 19 women (35%) delivered babies with low-birth weight while four women (7%) delivered babies with high- birth weight. Subject who delivered low-birth weight babies had significantly higher Cd concentration and lower Zn concentration and body mass index when compared with those with normal weight babies. These results suggest that Cd indeed has some toxic effects on neonatal birth weight.

Key words: Birth weight, cadmium, selenium, zinc

INTRODUCTION

Neonatal birth weight is one of the best markers of a favorable pregnancy outcome and determinant of prognosis of neonatal mortality and morbidity.[1] Most full-term newborns (born at 37 weeks and 40 weeks) weight between 2,812 g and 4,173 g. Babies weighing less than 2,500 grams are universally defined as low-birth weight babies and are prone to health problems in the neonatal periods and in adulthood.[2] Many of the determinants of birth weight are related to maternal nutritional status[3] and the exposure to toxic pollutants such as cadmium (Cd), malnutrition and deficiency of some essential trace elements such as Zn, iron and copper (Cu) may result in the delivery low-birth weight babies.[4]

Cd is a heavy metal posing severe risks to human health. Up to this day, it could not be shown that Cd has any physiological function within the human body.[5] Exposure to Cd is through ingestion of foods containing Cd; low-levels are found in all foods (highest levels are found

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in shellfish, liver, and kidney meats); smoking cigarettes or breathing cigarette smoke; breathing contaminated workplace air; drinking contaminated water; living near industrial facilities, which release Cd in to the air.[5] Cd is more efficiently absorbed from the lungs than from the gastrointestinal tract.[6]

Zn is an essential trace mineral required by the body for a variety of fundamental biological functions and it plays major roles in the immune system, in reproduction, and in promoting healthy skin and growth. Zn is required for normal fetal development and influences pregnancy outcome.[7] Maternal deficiency of Zn during pregnancy has been associated with the delivery of low-birth weight babies.[8,9] Cd and Zn (both Class II-B transition elements) have similar electronic configuration and valence state, possessing equal affinities for sulphur, nitrogen, and oxygen ligands[10] and hence, similar geochemical and environmental properties.[11] They have an oxidative state of +2 and when ionized, are almost the same in size. Thus, Cd can replace Zn in many biological systems. Cd has been described as an antimetabolite of Zn due to the observed Zn deficiency in most of the Cd-treated systems.[12] Cd toxicity is expressed in the body by Zn binding proteins particularly those containing Zn finger protein structures.[13]

Data from animal studies suggest that maternal iron deficiency during pregnancy leads to lower birth weight and sustained blood pressure elevation in the offspring. In humans, iron deficiency during pregnancy is common and is associated with adverse birth outcomes such as low-birth weight.[14] Iron deficiency can also enhance absorption of divalent metals such as lead, Cd, aluminum, and manganese.[15]

Selenium (Se) is a trace element required in small amounts, but can be toxic in larger amounts. It is necessary for growth and fertility in animals and for the prevention of accumulation of free radicals.[16] It also plays an important role in mitigating the biological damage caused by Cd.[17]

Cu is important for hemopoiesis and it is essential for normal growth and development of human fetuses, infants, and children. Studies have shown that maternal deficiency of Cu during pregnancy can result in the delivery of low-birth weight babies.[18]

The increasing implication of Cd in the derangement of a number of biological and molecular systems especially, genome instability or disturbances makes it instructive to examine the possible effects of Cd where there are instinctive molecular events. This study was, therefore, conducted to examine the effect of Cd on maternal and child health (neonatal birth weight) and evaluate the possible ameliorating effects of macro nutrients such as Zn, Cu and Se; particularly Zn, which plays a pivotal role in the molecular process of reproductin, yet has been insufficiently heralded in the reproductive process.

MATERIALS AND METHODS

A total of 160 subjects with age ranging from 18 years to 45 years, with mean age of 20.1 years ± 6.1 years comprising of 125 pregnant and 35 non-pregnant subjects as controls were recruited for this study from Antenatal Clinic of the Department of Obstetrics and Gynecology, University College Hospital Ibadan and Oluyoro Catholic Hospital Oke Offa, Ibadan, Nigeria, after informed consents were obtained.

The pregnant subjects were classified according to the three trimesters of pregnancy as followed; thirty five (35), thirty five (35) and fifty five (55) from the first to the third trimesters respectively. The third trimester subjects were followed-up until after delivery where neonatal parameters (birth weight, head circumference and length) of babies were measured. Head circumference was measured at the level of occipital protuberance and frontal. The body weight of each subject was measured with a standard scale to an accuracy of 0.1 g.

Demographic characteristics of the subjects were obtained from the administration of a semi-structured questionnaire and anthropometric measurements-weight and height was measured while BMI was calculated. The neonates included in the study were all those who were delivered from participant mothers. The gestational age was measured in terms of weeks from the last menstrual period and accordingly an immature newborn was defined as a newborn with gestational age <37 weeks and a mature newborn as a newborn with gestational age ≥37 weeks. Only babies born at full-term were included in this study.

Subjects with HIV/AIDS, diabetes mellitus, pre-eclampsia, lactating women, and those who did not give consent were excluded from the study.

Blood samples were collected and serum extracted for the measurement of Cd, Zn, iron, Se, and Cu by atomic absorption spectrophotometry[19] while total protein and albumin were determined by Biuret method[20] using reagent kit by DIALAB Laboratory, United Kingdom and bromocresol green (BCG) method[21] using reagent kit produced by Span Diagnostics Limited respectively.

Data were analyzed statistically using SPSS version 15 to determine relationships and associations. Student *t*-test was used to find out significant differences between the means, one-way analysis of variance used to investigate the statistical significance of the association between quantitative variables and Pearson's co-efficient was used to find out associations between quantitative variables. Data are expressed as the mean ± SD, and $P < 0.05$ was considered statistically significant.

RESULTS

Pregnant subjects had significantly lower ($P < 0.05$) serum Zn, iron, and Se levels as compared to non-pregnant subjects while serum Cu level was found to be significantly elevated ($P < 0.05$) [Table 1]. Cd concentration was similar in all the groups except in the third trimester subjects where Cd concentration was significantly higher when compared to the values obtained from the other subjects. Thirty five (35%) of third trimester women delivered babies with low-birth weight, fifty eight (58%) with normal weight babies and seven (7%) with high-birth weight. Subjects who delivered low birth weight babies had significantly higher Cd concentration, lower Zn concentration and body mass index (BMI) when compared with those subjects who delivered normal weight babies [Table 2]. Babies low-birth weight had lower neonatal parameters when compared with those normal birth weight [Table 3]. Only maternal serum levels of Cd, Zn, and Se correlated significantly with neonatal birth weight $P < 0.05$ [Table 4]. Maternal serum Cd ($r = -0.708, P = 0.000$) and Se ($r = -0.305, P = 0.023$) correlated negatively with birth weight were maternal Zn concentration ($r = 0.306$, $P = 0.023$) correlated positively with birth weight.

DISCUSSION

Cd has recently emerged as an important public-health environmental pollutant owing to its continuous release in to the environment as a result of industrial activities particularly, in the rapidly industrializing developing countries. Cd is listed as number 7 (out of 275) in the list of hazardous substances.[6]

Many of the determinants of birth weight are related to maternal nutritional status.[4] Increased exposure to Cd can create derangement in the levels of the micronutrients (Zn, Se, Cu, and iron), which can have a deleterious effect on reproductive outcome.[3]

In this study, pregnancy outcomes (neonatal birth weight, head circumference, and length) and nutritional indices (maternal Zn concentrations, weight, and BMI were inversely and significantly correlated with Cd concentration ($P < 0.05$) in all cases. Neonatal head circumference and length were significantly lower in babies with low-birth weight when compared with normal weight babies ($P < 0.05$). Cd concentrations in the women who delivered low-birth weight babies were significantly higher than those with normal weight babies ($P < 0.05$). These observations suggest adverse effects of Cd, which are consistent with studies implicating Cd as having toxic effects on neonatal growth.[22,23]

Serum Cu concentrations increased progressively with advancement in pregnancy, with serum Cu concentrations being highest in the third trimester. This finding is in agreement with previous observations.[24] However, there was no correlation between maternal Cu concentrations and neonatal birth weight.

Subjects who delivered low-birth weight babies had lower Se concentrations when compared to subjects who delivered normal weight babies. There was a negative correlation between maternal Se concentrations and neonatal birth weight. This inverse correlation may be as a result of the counteracting activity of Se on Cd toxicity suggesting that as Cd level increased there was a decrease in Se concentration probably due to oxidative stress induced by Cd. This finding contradicts the observation that maternal Se concentration had no impact on neonatal birth weight.[25]

Zn concentration in the third trimester subjects who delivered low-birth weight babies were significantly lower

Table 1: Comparison of demographic indices, anthropometric measurements and nutritional parameters of non-pregnant and pregnant subjects in 1st, 2nd and 3rd trimesters

Parameter	NP (*n*=35)	1st TRI (*n*=35)	2nd TRI (*n*=35)	3rd TRI (*n*=55)	*F*-value	*P* value
Cadmium (µmol/l)	0.22±0.1	0.20±0.1	0.21±0.1	0.25±0.2	3.478	0.017*
Zinc (µmol/l)	11.7±4.3	11.4±2.9	11.3±2.7	10.4±2.4	1.407	0.043*
Iron (µmol/l)	26.9±6.5	23.7±6.6	25.9±6.2	23.6±5.6	2.742	0.045*
Copper (µmol/l)	14.5±5.7	14.9±3.3	15.4±2.1	16.8±3.6	3.190	0.023*
Selenium (µmol/l)	3.5±0.8	3.4±0.7	3.5±0.7	3.4±0.8	0.126	0.945
Total protein (g/L)	60.9±1.0	64.0±0.9	58.0±1.2	63.0±1.2	3.487	0.017*
Albumin (g/L)	39.0±0.9	35.0±0.7	32.0±0.7	33.0±0.8	8.097	0.000*
Age (years)	28.6±7.1	28.6±5.7	29.4±4.9	29.5±6.5	0.336	0.871
Parity	2.0±1.6	2.1±1.6	1.9±1.7	2.2±1.5	0.236	0.671
BMI (kg/m^2)	25.3±3.6	26.1±4.9	27.6±5.4	28.7±1.5	0.997	0.039*

*Significant at *P*<0.05, NP=Non-pregnan, TRI=Trimesters, BMI=Body mass index

Table 2: Third trimester maternal indices of women with low and normal weight babies

Parameter	Low birth weight (*n*=19)	Normal birth weight (*n*=32)	*t*-value	*P* value
cadmium (μmol/l)	0.03±0.1	0.02±0.1	7.918	0.017*
Zinc (μmol/l)	8.9±1.8	11.2±2.3	3.706	0.001*
Iron (μmol/l)	22.6±4.9	25.4±6.5	1.784	0.08*
Copper (μmol/l)	16.5±3.1	16.9±3.7	0.420	0.676
Selenium (μmol/l)	3.5±0.7	3.6±0.8	1.628	0.109
Total protein (g/L)	69.0±1.54	60.0±0.8	2.756	0.008*
Albumin (g/L)	32.9±0.6	33.1±0.94	0.088	0.930
Age (years)	28.68±7.5	29.97±5.9	0.487	0.701
Parity	2.4±1.6	2.1±1.5	0.598	0.552
BMI (kg/m^2)	22.8±2.0	28.8±4.1	4.590	0.000*

*Significant at $P<0.05$, BMI=Body mass index

Table 3: Neonatal anthropometric measurements of babies with normal and low birth weight

Parameters	Normal birth weight (*n*=32)	Low birth weight (*n*=19)	*t*-value	*P* value
Birth weight (kg)	3.1±0.4	2.2±0.3	6.952	0.000*
Head circumference (cm)	34.6±3.8	32.3±2.2	2.675	0.010*
Length (cm)	50.1±3.6	46.6±3.4	3.818	0.000*

*Significant at $P<0.05$

Table 4: Correlation of third trimester maternal indices with neonatal parameters

Maternal indices	Neonatal birth weight (kg) (*r*, *P* value) (*n*=55)	Head circumference (cm) (*r*, *P* value) (*n*=55)	Length (cm) (*r*, *P* value) (*n*=55)
Cadmium (μmol/l)	−0.708, 0000*	−0.332, 0.013*	−0.499, 0.001*
Zinc (μmol/l)	0.306, 0.023*	0.225, 0.039*	0.247, 0.036*
Iron (μmol/l)	−0.192, 0.160	−0.161,0.241	0.157, 0.241
Copper (μmol/l)	0.022, 0.872	0.230, 0.901	0.066,0.634
Selenium (μmol/l)	−0.305, 0.023*	−0.116, 0.399	−0.357, 0.058
BMI (kg/m^2)	0.781, 0.000*	0.537, 0.000*	0.488, 0.000*

*Significant at $P<0.05$, BMI=Body mass index

than those with normal weight babies and a positive association was observed between maternal Zn status and neonatal parameters ($P < 0.05$), which is in concordance with previous reports.[9,26]

The significant inverse correlation ($r = -0.270$, $P < 0.05$) observed between maternal Cd and Zn concentrations suggests that as Cd concentration increased there was a decline in maternal Zn concentration. This most probably accounted for the inadequate bioavailability of Zn required for many very fundamental biological activities such DNA and protein syntheses, bone metabolism associated with osteoblastic activities regulated by alkaline phosphatase, which is dependent on Zn. This, therefore, is largely the biochemical basis of the birth outcome observed in this study. The probable mechanism involved is that Cd can displace Zn from metallothionenin, a binding protein that transports Zn since they both have similar configuration and almost the same size when ionized.[13] Thus, in Cd toxicity Zn is displaced from biological systems resulting in the adverse effects observed in this study.

CONCLUSION

Cd was found to have toxic effects on birth weight, head circumference and length of babies. The essential trace elements were significantly lower in women who delivered low-birth weight babies and this suggests that environmental exposure to Cd may have serious effect on the morbidity and mortality of neonates with long-term health consequences. Therefore, it is recommended that environmental pollution be borne in mind particularly in regions with persistent low-birth weight babies and supplements of essential trace micronutrients be given during pregnancy.

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