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A Preliminary Study of Levels of Selected Nutrients for Neonates Born to Diabetic and Non-Diabetic Mothers in Bangladesh

SHAHANA AFROSE CHOWDHURY[1], MOHAMMAD ARIFUR RAHMAN[1], **A. M. SHAFIQUL ALAM***[1], SHAH MOHAMMAD KERAMAT ALI[2] AND SYED NAZMUL HUDA[2]

[*1] Department of Chemistry, University of Dhaka, Dhaka-1000, Bangladesh.
[2]Institute of Nutrition and Food Science, University of Dhaka, Dhaka-1000, Bangladesh.

Abstract

To investigate some selected nutrients status in the neonates born to diabetic and non-diabetic mothers a prospective study was carried out. From the Obstetric Unit of Bangladesh Institute of Rehabilitation in Diabetes, Endocrine and Metabolic disorder (BIRDEM) Hospital, Dhaka, Bangladesh, 236 newborns were recruited; 74 from diabetic, 59 from gestational diabetic and 103 from non-diabetic mothers group for this study. Cord-serum levels of Cu, Zn, Fe, Mg, Ca and ascorbic acid were investigated, and some anthropometric measurements were recorded to correlate with the nutrient levels. Fe was found significantly higher ($p<0.05$) whereas, ascorbic acid was found significantly lower ($p<0.05$) in diabetic group compared with other two groups. However, Mg and Ca levels were found significantly higher ($p<0.05$) in non-diabetic group. There was no significant difference observed in Cu, Zn levels for the 3 groups. Ca level was significantly correlated with birth weight and length of the neonates. These data suggests that diabetes has some effects on fetal growth and its nutritional status that also reflect the socio-economical status of the families of the neonates.

Introduction

Human development starts from conception; therefore, in all respects, fetal life is very important. The fetus is a separate physiological entity, relying on the mother to supply nutritional requirements even at the cost of reducing resources of the mother [1]. In the tissues of living organisms a number of inorganic nutrients are present in very small amounts and these are referred to as trace elements [2]. Those which are essential for life act as cofactors of enzymes and organizers of the structures of the cells (for example, mitochondria) and their membranes [3]. Certain trace elements, including zinc (Zn), copper (Cu), iron (Fe), magnesium (Mg) are known to play key physiological roles [2-5].

Ascorbic acid (Vitamin C) serves as a reducing agent in a number of important hydroxylation reactions in the human body [6]. However, it appears to have additional metabolic roles [7]. Ascorbic acid participates in the synthesis of adrenal hormones and vasoactive amines. It is also involved in microsomal drug metabolism, wound healing, leukocyte functions, tyrosine and folate metabolism [8-11] and may have cancer-prevention properties [12]. It is oxidized readily and the presence of Fe, Zn and Cu enhances the reaction rate [13].

Diabetes Mellitus (DM) is a chronic metabolic disorder, which has a profound effect on different metabolic processes. DM is caused by the inability of the pancreatic beta cells to produce sufficient insulin to utilize and store body glucose [14]. A decrease in insulin alters the nutritional status of the individual for both macro and micro-nutrients [15]. When associated with pregnancy,

*[1]Author for Correspondence

diabetes places the mother at an increased risk for hypoglycemia, hypocalcemia, hyperbilirubinemia, polycythemia and hyperinsulinemia [16,17]. Long-standing and severe diabetes associated with vasculopathy is responsible for retardation of intrauterine growth [18]. During pregnancy various minerals including calcium (Ca), Mg, Zn, Cu, are essential for fetal growth [19]. Diabetic subjects were reported to have elevated serum levels of dehydroascorbic acid [20].

The present study was designed to measure the levels of Cu, Zn, Fe, Ca, Mg and ascorbic acid in the cord-serum of neonates from diabetic, Gestational Diabetes Mellitus (GDM) and non-diabetic (ND) mothers in Bangladesh. The purpose has been to investigate the nutrient levels among the groups and to determine the relationship of the anthropometric measurements of neonates with the nutrient levels in cord-serum.

Subjects and methods

The neonates studied here were born in the Obstetric Unit of Bangladesh Institute of Rehabilitation in Diabetes, Endocrine and Metabolic disorder (BIRDEM) Hospital, Dhaka, Bangladesh. Consent from the hospital authority was provided prior to the commencement of the study. The mothers (n=236) were categorized into three groups:

Group I: pre-existing diabetic (n=74); including type 1 and 2 both [*WHO criteria*] [21]

Group II: gestational diabetic (n=59); [*WHO criteria*] [21]

Group III: non-diabetic (n=103) or the control group selected from babies born to mothers without diabetes at the same hospital and at the same time.

Gestational diabetic mothers were diagnosed for gestational diabetes mallitus (GDM) at 24-28 weeks of their gestational period. Blood and urine samples were collected and analysed to detect GDM at the diabetic center. 87% of the diabetic mothers were insulin dependent and the rest were non-insulin dependent. In this project, both of the diabetes types were considered as one group.

All neonates were full-term, of normal birth weight and were taken randomly during 1998-9. No other selection criteria were applied. Basic data obtained for the mothers of three groups included age, body mass index (BMI), recent blood pressure (BP) both systolic and diastolic, hemoglobin alpha 1 (HbA_1c), after 8-10hours of overnight fasting blood was collected for the measurement of fasting blood glucose (FBG), and gestational age. At birth, the weight and height of the neonate were recorded. Information was obtained by reviewing medical records and direct interview with the mother’s consent. During the visit to the medical center, blood was collected from the mothers. HbA_1c was done by high performance liquid chromatography (HPLC) using Shimadzu (Japan) instrument model LC-10AD and reversed-phase C_{18} column (Merck, Germany). Mixed venous-arterial blood (about 10mL) from the clamped umbilical cord (placental line) was collected immediately after the delivery (prior to expulsion of the placenta). Before hemolysis, all blood samples were centrifuged at 2,000 revolutions per minute (rpm) for 10-15 minutes. The clear serum was separated immediately and stored below – 40°C.

The concentrations of Zn, Cu, Fe, Ca and Mg in cord-serum samples were determined by Atomic Absorption/ Flame Emission Spectrophotometry, using a Shimadzu (Japan) instrument model AA- 680. The levels of ascorbic acid were estimated by UV-visible spectroph-otometry using dinitrophenyl hydrazine and the method of Washko *et al* (20) with a Shimadzu instrument, model 160-A. Standard Reference Materials (SRM) for Cu, Zn, Ca and Mg were analyzed for testing the accuracy of the method. These were Trace Elements Serum, from Nycomed Pharma AS, Oslo, Norway.

Statistical analysis

Student’s *t*-test was used to compare mean values. Values were expressed as mean ± SD or mean (95% Confidence Intervale), for all evaluations, $p < 0.05$ was considered significant.

Univariate and multiple logistic regression analyses were performed to determine associative relationship between variables. Statistical Package for Social Sciences (SPSS) for Windows version 7.5 was used for statistical analysis.

Results

The data regarding the socio-economic status of the parents of each group were presented in Table 1. Data showed for all groups of parents almost half of them were low income and low educational level.

Main clinical characteristics for the mothers of three neonatal groups and the anthropometric measurements and the corresponding lengths of gestation for the neonates of these groups were shown in Table 2. Significant difference was found for maternal age between group I, II and III. Significant differences were observed in neonatal mean weight and height of groups I and II related to group III.

The cord blood levels of selected micronutrients in the three groups are compared in Table 3. The mean levels for Cu and for Zn of the two groups were similar with no significant differences. However, the mean level of Fe was significantly higher ($p<0.05$) in group I than in group III. There was also a significant difference ($p= 0.05$) in Ca levels and for Mg was found to be highly significant ($p<0.05$). The ascorbic acid level was also significantly higher ($p< 0.05$) in group III.

The comparison of trace metals and ascorbic acid between group II and III and the interrelationships between these two groups were also presented in Table 3. No significant differences were found in Cu, Zn, Fe, Ca and ascorbic acid levels for these groups. Mean concentrations of these nutrients were found to be similar.

Only the Mg level of group II was found highly significant ($p< 0.05$) than group III.

The mean levels for Cu and for Zn of the three groups were similar with no significant differences. However, for Fe, significant differences were observed between groups II and III, and groups I and III. Similar results were found for Mg and ascorbic acid. The levels of Ca showed significant differences between all the three groups studied in this project.

The correlations between nutrient levels of cord-serum and anthropometrical indices are presented in Table 4. There was no significant correlation between gestational age and any nutrient level. Calcium level was significantly correlated with both birth weight and length of the newborns.

Table 1. Socio-economic status of the parents by groups

Socio-economic status		Percentage (%)		
		Group I (n=74)	*Group II (n=59)*	*Group III (n=103)*
Father's Education	Below Graduate	32.43	32.20	23.30
	Graduate	40.54	44.07	47.57
	Above Graduate	27.03	23.73	29.13
Mother's Education	Below Graduate	62.16	69.49	61.17
	Graduate	37.84	30.51	38.83
Father's Occupation	Service	64.86	79.66	65.05
	Worker	35.14	20.34	34.95
Mother's Occupation	Service	32.43	27.12	46.60
	Housewife	67.57	72.88	53.40
Family Income (per month)	> Tk. 10,000 (US$ 200)	59.46	59.32	64.08
	< Tk. 10,000 (US$ 200)	40.54	40.68	35.92

Table 2. Main maternal and neonatal characteristics in the three different groups

Characteristics	Group I (n=74)	Group II (n=59)	Group III (n=103)	p- value
Maternal:				
Age (years)	29.47 ± 4.08	28.52 ± 4.26	25.41 ± 4.16	<0.002
Weight (kg)	65.36 ± 5.92	64.87 ± 6.18	64.58 ± 5.23	NS
Pregnancy BMI (kg/m^2)	24.87 ± 3.73	24.76 ± 3.87	24.21 ± 3.18	NS
Blood Pressure (mmHg)	>140/90	>130/90	<140/90	NS
Duration of diabetes (years)	≥ 10	-	-	-
Gestation (weeks)	38.42 ± 0.76	38.91 ± 0.82	38.84 ± 0.75	NS
Neonatal:				
Birth Weight (kg)	3.45 ± 0.67	3.38 ± 0.63	3.06 ± 0.58	<0.001
Height (cm)	47.53 ± 2.88	48.00 ±2.37	46.82 ± 2.42	<0.001
Sex:				
Male	39	28	50	NS
Female	35	31	53	NS

*Values are presented as mean ± SD, NS, indicates not significant for $p < 0.05$

Table 3. Comparison of the micronutrient levels for the neonate group

	Cu	Zn	Fe	Mg	Ca	Ascorbic acid
Group I (n=47)	65.7 ± 12.6	124.8 ± 43.7	581 ± 175	8.1 ± 1.4	1.4 ± 0.3	0.2 ± 0.1
Group II (n=54)	64.8 ± 12.5	143.1 ± 38.9	393 ± 200	8.7 ± 1.2	1.5 ± 0.3	0.4 ± 0.2
Group III (n=52)	65.8 ± 17.3	132.3 ± 44.4	423 ± 175	9.2 ± 1.4	1.7 ± 0.2	0.4 ± 0.1
p- value	0.5	0.4	0.001	0.000	0.000	0.000
95% confidence intervals for the differences						
Group I-Group II	(-5.4,11.0)	(-37.8,12.0)	(18.2,205.0)	(-1.4,-0.1)	(-0.3,0.0)	(-0.3,-0.2)
	NS	NS	S	S	S	S
Group I-Group III	(-9.1,7.5)	(-35.7,14.6)	(50.6,239.1)	(-1.9,-0.7)	(-0.4,-0.2)	(-0.2,-0.1)
	NS	NS	S	S	S	S
Group II-Group III	(-11.6,4.4)	(-21.9,26.6)	(-57.8,124.2)	(-1.2,0.0)	(-0.3,0.0)	(0.0,0.1)
	NS	NS	NS	NS	S	NS

*Units for Cu, Zn, Fe are are μg/dL and for Mg, Ca and ascorbic acid mg/dL. NS, not significant and S, significant for $p < 0.05$.

Table 4. Correlation coefficients (r) between anthropometric measurements and nutrient levels of neonates

Anthropometric measurement	Cu	Zn	Fe	Mg	Ca	Ascorbic acid
Birth weight	r= 0.1 p= NS	r= 0.1 p= NS	r= 0.2 p= NS	r= 0.1 p= NS	r= 0.6* p= 0.00	r= 0.1 p= NS
Height	r= 0.1 p= NS	r= 0.2 p= NS	r= 0.0 p= NS	r= 0.1 p= NS	r= 0.4* p= 0.00	r= 0.1 p= NS
Gestational age	r= 0.0 p= NS	r= 0.2 p= NS	r= 0.0 p= NS	r= 0.2 p= NS	r= 0.1 p= NS	r= 0.0 p= NS

*p- value is significant when r > 0.25 and NS, not significant.

Discussion

To the best of our knowledge this study is the first of its kind in Bangladesh, where newborns of three groups of mothers were investigated for selected nutrients and relationships of the nutrient levels with neonatal characteristics were examined and also parental socio-economic status were evaluated. As their level of income was low (Table 1), most of the pregnant mothers did not get sufficient nutrition and medical care during their pregnancy. Furthermore, their knowledge about diabetes related complications during gestation and its effects on the neonates were comparably very low. Most of them were not aware of the consequences of the disease. The results of this study (Tables 2 and 3) have been compared with data from some other countries and the neonates of Bangladesh studied here had lower nutrient levels and mean birth weights [22-24].

The cord- blood situation is known to reflect the status of the micro and macro nutrients including Cu, Zn, Fe, Ca, Mg and ascorbic acid [24]. In the current study, no significant difference in Cu and Zn levels were found for the three groups. The concentration for Fe was found higher whereas for ascorbic acid, it was lower in the diabetic group than the other two groups. It is unlikely that this increase is due to possible oral iron supplementation during pregnancy. The modest decrease in ascorbic acid in diabetic group does not allow any conclusion about the biologic significance, remains unclear. As we know, no sound results have been produced in previous studies about this issue. It has also been reported that the fetal content of Ca is directly related to the fetal weight, but is unaffected by the length of gestation [23]. The data obtained here showed a similar result with a significant correlation between Ca level, birth weight and length of the newborn. In a study undertaken in India, neonates of diabetic mothers were reportedly of greater length and weight [22, 24]. The lack of confirmation of this trend in the current study may reflect socioeconomic factors and their effect on maternal nutrition and hence on neonatal nutrition. Enhanced dietary status of mothers during gestation might help to improve the levels of minerals and vitamins potentially benefiting the development of the unborn child, particularly for chronic diabetic mothers.

In conclusion, it is necessary to pay prior attention to the future development of children born to mothers with diabetes. Our findings justify further studies to investigate the biologic significance of the relationship between the nutrient status of neonates and diabetic condition of their mothers.

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