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Comparison of growth indices in breast-fed and formula-fed infants and their correlation with zinc status

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ABSTRACT

Introduction: Zinc has many effects on human's multiple systems in the body, including gastrointestinal tract. It is essential for normal development, immune system and growth of an infant. Zinc deficiency increases the chances and severity of gastrointestinal tract and respiratory infections. Children are at high risk of zinc deficiency as their requirements increases with growth. The amount of zinc absorbed from infant formulae is considerably lesser than that absorbed from mother's milk. The aim was to study the differences in the growth indices of breast-fed and formula-fed infants and also to look for the association of zinc, if any, with these indices.

Methodology: This cross-sectional study was performed from October 2017 to March 2018 in Peshawar, on 50 healthy infants {25 breast-fed infants (BFI) and 25 formula-fed infants (FFI)}. The infants' weight, height, BMI, head circumference and skinfolds (biceps and triceps) were recorded. Blood samples of all the infants were collected for zinc assay. Data were collected in an MS Excel sheet and descriptive data analysis was done by Minitab version 16.

Results: It was observed that the head circumference (cm) of FFI was significantly higher (40.32± 2.34) in comparison to BFI (38.12±4.46) whereas SDS weight, SDS BMI, biceps and triceps measurements did not reveal any significant difference in the two groups. The variables showing a significant positive correlation with zinc were age ($r = 0.328$, $p=0.02$) and SDS height ($r= 0.274$, $p= 0.05$) while SDS weight, SDS BMI, biceps and triceps measurements were not correlated with zinc status.

Conclusion: All the growth indices except head circumference of both breast-fed and formula-fed infants were comparable. Similarly, all these indices except SDS height were not associated with the levels of zinc during early infancy showing that zinc status does not affect the growth of infants at least in the early phase of life.

Keywords: Zinc, Growth indices, Breast-feeding, Formula feeding

The authors declared no conflict of interest. All authors contributed substantially to the planning of research, data collection, data analysis, and write-up of the article, and agreed to be accountable for all aspects of the work.

INTRODUCTION

Mother and infant health are influenced by the dietary habits of breastfeeding females and impact the overall health conditions of an infant and mother. Malnutrition is one of the major causes of childhood mortality in early infancy.[1-3] Infants up to the age of 6 months get most of their essential macronutrients (carbohydrates, proteins and lipids) from mother's milk in majority of cases. Recent literature revealed that oligosaccharides of breast milk, even non-nutritive, contribute to infant health and infant body composition in early years of life. For instance, levels of glucose and insulin in mother's milk are positive predictors for adiposity in infants who are born to non-diabetic mothers.[4]

Body Mass Index (BMI) is a better indicator of infant body composition at age one month. Prompt weight gain during infancy has been related to childhood obesity. In 2006, WHO published BMI-for-age growth charts for children aged less than two years which are now obsolete for pediatric use.[5] When growth indices (weight for age, length for age, and weight for length) of both formula-fed and breast-fed infants were compared, it was observed that in breast-fed infants at one, two and three month of life, these were significantly higher whereas in formula-fed infants only weight for age was significantly higher at one month interval up to 6 months. An Italian study showed that during first 12 months of life both formula-fed and breast-fed infants exhibit different growth patterns.[6,7] Reported evidence suggest that breast feeding reduces risk of obesity in infants, but on the other hand there is research-based evidence pointing out that babies fed with mother's milk exhibit significant weight gain in first month and maintain it for the whole period of lactation, an aspect that has to be thoroughly investigated.[8,9]

Zinc is stored in the liver during intra uterine life which is sufficient for 4–6 months. Afterwards, it is supplied from daily diet; therefore at age six months, zinc becomes a nutritionally essential micro-nutrient. During this period, breast milk is considered to be a complete diet. According to WHO recommendation, breast milk is adequate for infants during first six months of life and continues along with appropriate weaning diet for initial two years of life.[10,11]

Metallothionein, a zinc-binding protein, is present in liver. The complex of metallothionein with zinc starts accumulating during the third trimester of pregnancy. At 4 months after birth, zinc levels become stable.[12] Breast milk is the only source of zinc in infancy. Colostrum, the richest source of zinc for neonates,[13,14] provides approx. 8mg/L of zinc. This level starts declining and reaches up to 50% of the initial concentration within seven days. At age 2 months, it reduces further to 2mg/L, but this process is very slow as compared to first week of decline. At age one year, the infant is only able to extract 0.5mg/L from mother's milk despite the increase in volume of breast milk with passage of time.[13-15]

Zinc storage in premature infants is very low as they have small livers and very short gastrointestinal tracts. Therefore, mothers require zinc supplementation for proper functioning of their body at the time of birth so as to avoid the complications of zinc deficiency.[13,16] Eighty two percent of lactating or pregnant women have enough zinc intake.[17] Zinc is said to be the first nutrient that starts limiting in breast milk, as its concentration is highest at commencement of lactation, then declines very rapidly during the initial three months.[11] Keeping in view the significance of feeding modalities and role of zinc in infants, this study was designed to compare the growth indices between the feeding groups and their relationship with zinc level in early infancy.

MATERIALS & METHODS

Study design, ethics and sample size

This was a cross-sectional study, carried out in Peshawar, Khyber Pakhtunkhwa from October 2017 to March 2018. The study was approved by the Khyber Medical University Ethics Board (KMU-Ethics Board). Based on median difference of 14.3 mmol/kg total short-chain fatty acids between breast fed and formula fed infants at 2 months of age from the study of Siigur et al 1993[18] and considering margin of error of 5%, total of 25 infants are required in each group (total n=50). Each participant was screened using a health check questionnaire to rule out any co-morbid conditions. Informed written consents were obtained from the mothers/guardian of the participants.

Anthropometric assessment of infants

Weight and length measurement of an infant was performed once. Infant crown-heel length was measured once by using headpiece and foot piece both applied perpendicular to the hard surface and non-stretch tape was used to measure the length in centimeters. Head circumference was measured at a level passing from supraorbital protuberance anteriorly and occipital protuberance posteriorly using non-stretch tape to the nearest 0.1cm. Each infant was weighed in Beurer digital baby scale (BY-80) in kilograms. Skin folds (biceps and triceps) were measured with the help of skinfold caliper (Holtain Ltd, Crosswell, UK). Height of the mothers was determined using a portable stadiometer with the head in horizontal Frankfort plane. Mid upper arm circumference was measured to the nearest 0.1cm using a plastic measuring tape. Weight of the mother was taken by Beurer digital scale "GS 200 Allium" to the nearest 100 g.

Skinfold thickness measurement of enrolled subjects (infants and mothers)

Skinfold thickness is used to measure total body fat and hence the distribution of fat to body mass.[19] It measures the thickness of subcutaneous fat at various sites. The skinfold thickness of the enrolled participants was measured after informing the mothers about the skin fold measuring procedure. They were reassured by demonstrating the action of the caliper on their index figure that there will be no pain and the infant will feel a little discomfort. The biceps and triceps skin folds of both the formula-fed infants as well as breast-fed infant along with their mothers were measured. "Holtain skin-fold caliper (Holtain Ltd, Croswell, UK)" was used for this purpose. Skin fold thickness was measured at the nearest 0.1mm.

Triceps skin fold

The participant skin was firmly clenched with index finger and thumb in order to hold the two thickness layers of skin and subcutaneous fat but not the muscles. The caliper was then placed over the skinfold with 90-degree angle. The caliper was held for five seconds and the reading was noted.

Biceps skin fold

For measuring the biceps, upper arm midline anteriorly, 1cm above the mark used for triceps reading was taken by the caliper.

Collection of blood samples, plasma zinc extraction and analysis

Blood samples of infants and their mothers were collected in Li-heparinized tubes (Yaohua Medical). Plasma was separated and stored at -80°C until analysis. All the glassware was soaked in 10% HNO_3 for 24hrs, then rinsed three times with deionized water. Hemolyzed samples were excluded; 0.4 ml of plasma sample and 3 ml of Nitric acid (65%) were added into a 25 ml beaker and digested at 70-80°C on an electric hot plate for 90 minutes. Thereafter, 1.5ml of hydrogen peroxide (30%) was added into the beaker and the digestion was continued. When the remaining volume was reduced to about 0.5-1ml, the liquid was transferred into a 5.0 ml volumetric flask after cooling, followed by the addition of nitric acid stock standard solution to obtain a final volume of 5ml. Samples were then taken for zinc analysis to the Center of Research laboratory at Peshawar University. Atomic absorption Spectrophotometry technique was used for zinc assay.

Statistics

All data collected during the study span were arranged and organized on Excel sheet. Anthropometric data were then copied to statistical tool Minitab version 16® for descriptive statistics. Normality of data was assessed by Anderson-Darling test for continuous variables like SDS height, SDS weight, SDS BMI and BMI. Probability plots signified that anthropometric data were normally distributed hence parametric statistics were applied. Data were expressed as mean ± SD; p values ≤0.05 were considered significant.

RESULTS

Demographic and anthropometric data consisted of family size, number of siblings, age of infant at the time of assessment, SDS height, SDS weight and SDS BMI (Table1); Two-sample T-test was applied to calculate p value.

Table 1: Anthropometric and demographic characteristics of infants

Variables	Mean	SD
Height (cm)	53.42	5.84
Weight (kg)	5.37	1.01
SDS Height	-2.75	3.10
SDS Weight	-0.53	2.05
BMI (kg/m2)	19.17	4.11
SDS BMI	1.59	2.30
Age at Assessment (days)	78.40	35.88
Family Size (n)	6.78	3.30
No. of siblings (n)	2.00	2.07

Plasma zinc levels (mg/L) in breast-fed group were 0.185 ± 0.219 (mothers) and 0.138 ± 0.118 (infants) while in formula-fed group the levels were 0.091 ± 0.010 (mothers) and 0.120 ± 0.026 (infants). The zinc levels were comparable in the infants of both groups whereas, the level was significantly higher (p=0.045) in the mothers of breast-fed group as compared to formula-fed group (Table 2).

Table 2: Plasma zinc status of mothers and infants

Variables	Normal reference levels mg/L	Breast-fed infants		Formula-fed infants		p value
		Mean	SD	Mean	SD	
Plasma zinc of mothers' mg/L	0.66-1.10	0.185	0.219	0.091	0.0100	$0.045^{\dagger}$
Plasma zinc of infants' mg/L	0.60-1.20	0.138	0.118	0.120	0.026	0.482

Reference Values; for 0-10 years: 0.60-1.20 mcg/mL and > or =11 years: 0.66-1.10 mg/L (19, 20).

Individual anthropometric parameters between the two groups formula-fed infants (FFI) and breast-fed infants (BFI) were evaluated using paired t-test. The mean anthropometric measurements between the two groups did not show any significant difference. However, it was noted that the head circumference of FFI was significantly higher (40.32± 2.34) as compared to BFI (38.12 ± 4.46), p < 0.05 (Table 3).

Table 3: Mean differences in anthropometric parameters between the groups

Variables	Breast-fed infants		Formula-fed infants		P-value
	Mean	**SD**	**Mean**	**SD**	
Head Circumference (cm)	38.12	4.46	40.30	2.36	$0.03^{\dagger}$
Biceps (mm)	0.14	0.05	0.14	0.05	0.78
Triceps (mm)	0.15	0.06	0.14	0.05	0.63
BMI SDS	1.25	2.41	1.94	2.19	0.29
SDS height (cm)	-0.65	3.67	-0.86	2.49	0.81
SDS weight (kg)	-0.76	2.49	-0.31	1.53	0.44

Significant p value ($^{\dagger}P<0.05$, $^{\dagger\dagger}P=<0.01$, $^{\dagger\dagger\dagger}P<0.0001$)

Correlation of anthropometric and demographic variables with plasma zinc of infants

Pearson correlation was applied to assess the correlation of infants' zinc with age, number of siblings, family size, BMI SDS and SDS height and SDS weight. Variables showing significant positive correlation were age (r=0.328, p=0.021) and SDS height (r=0.274, p=0.056). All other variables like number of siblings (r=-0.050, p=0.425), family size (r=-0.117, p=0.735) and BMI SDS (r=-0.222, p=0.125) showed negative but insignificant correlation (Table 4).

Table 4: Correlation of plasma zinc of infants with anthropometric and demographic variables

Variables	Pearson correlation	p value
Age (days)	0.32	0.02†
No of siblings	-0.05	0.42
Family Size (n)	-0.11	0.42
SDS BMI	-0.22	0.12
SDS height	0.27	0.05†
Biceps	0.23	0.11
Triceps	0.17	0.22

Significant p value ($^{\dagger}P<0.05$, $^{\dagger\dagger}P=<0.01$, $^{\dagger\dagger\dagger}P<0.0001$)

DISCUSSION

It is well established that the breastfeeding is an excellent source of nutrients for the infants.[20,21] It is considered and recommended the "only" source of nutrition in the early six months of infancy. It has been reported that human milk has the ability to protect infants against excessive weight gain and later on obesity in adulthood. Our findings in this study support the later notion, as we found that the mean BMI SDS in breast-fed infants was lower than the formula-fed infants, but the difference could not attain the level of significance (p=0.295). Traditional formula milk contains higher contents of protein than breast milk.[8] Protein-rich formulae are known to enhance plasma insulin levels which, in turn, lead to release of insulin-like growth factor-1 and may lead to weight gain initially and later obesity in the adulthood.[8,22] Contrary to this, some studies have reported that the in formula-fed infants the mean SDS weight were lower as compared to breast-fed infants, the observation attributed the authors to the prevalence of diarrhoea in the formula infants.[3]

Recent studies support that the human milk contains more contents of non-nutritive carbohydrates like human milk oligosaccharides (HMOs) which can potentially contribute to body composition and infants' growth. This interesting area requires further investigations which may help to identify the potential contributors of infant's growth and body mass composition during early and late infancy.[4,9,23] The means of SDS height when compared between the breast fed and formula fed infants didn't show any major differences. Interestingly, the formula-fed infants increase in mean length was higher than breast fed infants endorsing the findings of earlier reports.[24-26]

The mean measurement of the head circumference was significantly higher in formula-fed infants when compared to breast-fed infants. This was in contrast to the observation in a study conducted by Michaelsen KF et al[27] who didn't find any differences in the mean measurement of both the groups this might be due to fact that their study population was older than the infants included in our study. The indices of adiposity like biceps and triceps skin fold measurement in our study did not vary significantly between the groups as has been reported previously by various authors.[28,29] However, Salmenpera L et al[30] have reported that adiposity indices were relatively higher in formula-fed infants than breast-fed infants which they attributed to the early weaning in addition to the formula milk.

Analysis of the plasma zinc levels showed inverse significant correlation with age of infants and agree with the observations of Okolo SN et al.[31] We also explored the relationship of infant zinc with the growth rate of infants. No significant correlation was observed with the weight, height SDS, and adiposity indices. Similar observations have been reported by Salmenperä L et al.[32] These findings indicate that low zinc levels may not influence the aforementioned parameters.

CONCLUSION

All the growth indices except head circumference of both breast-fed and formula-fed infants were not significantly different revealing a comparable effect of the two modes of feeding on infant growth. Similarly, all these indices except SDS height were not associated with the levels of zinc during early infancy showing that zinc status does not affect the growth of infants at least in the early phase of life

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