Growth in Early Childhood of Children who are Born Prematurely and Exclusively Fed With Expressed Breast Milk in the Neonatal Period

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Abstract

The critical period for the growth and the neurodevelopment of a premature infant is the first few weeks of life. The nutritional requirement goes to its highest point during this period and the nutrition should be optimized to baby's needs. We tried to find out whether the exclusive breast feeding is adequate to nourish a neonate during first few weeks of its life by assessing their heights by the age of 2-5 years. We tested fifty children aged 2-5 years who were born prematurely within POA of 26-34 weeks and were exclusively been fed with breast milk during their neonatal period. Data were collected from the clinic records and were analyzed by Descriptive analysis and contingency tables. 74% of the sample achieved the predicted mid parental height by that age, according to the cluster analysis. So, we can conclude that the exclusive breast feeding during the neonatal period is adequate for premature babies to achieve their predicted mid parental heights by the age of 2-5 years

Keywords: Premature Babies; Exclusive Breast Feeding; Mid Parental Height; Expressed Breast Milk

List of Abbreviations: NICU - Neonatal Intensive Care Unit; OFC - Occipito-Frontal Circumference; POA - Period of Amenorrhea

Introduction

The first weeks of life are a critical stage for the growth and neurodevelopment of a very low birth weight (VLBW) infant [1]. This is the phase in which the nutritional requirements for an adequate growth are greater than at any other time in life. The consequences of insufficient nutrition in this critical period have yet to be determined with certainty, but there is considerable evidence that early growth failure has long-term negative effects on childhood growth including height and OFC, and that these effects probably persist into adulthood [2]. The Committee on Nutrition of the American Academy of Pediatrics have recommended a caloric intake of 120 kcal/kg/day for children enterally fed and 80 to 100 kcal/kg/day for those parentally fed, with a protein intake of 3.5 to 4 g/kg/day [3]. However, it is difficult for most VLBW infants to reach this suggested caloric and protein intake in the first two months of age [2]. According to studies done in the western world some time ago showed unfortified EBM will not meet the nutritional needs of infants <1500g [2]. According to them the nutritional needs of premature infants are usually dependent upon parenteral nutrition during early postnatal life, especially for very low birth weight (VLBW) infants. But by present the trend has changed. A study done by Xiao-Ming ben in 2008 has shown that the first choice of nutrition for premature babies is the own mother's breast milk [3]. A meta-analysis done by Dominica A Gidrewicz in 2014 showed that premature breast milk contains higher energy, proteins and fat compared to term breast milk [4]. However, in developing countries early parenteral nutrition cannot be provided due to economic constrains. Thus, we start them on breast milk early, within the first two days. In our follow up clinics, we have observed that most had a satisfactory growth. Thus, we decided to evaluate their height in early childhood.

Objective: The proportion of children who had their height in the range of the mid parental height by the age of 2-5 yrs.
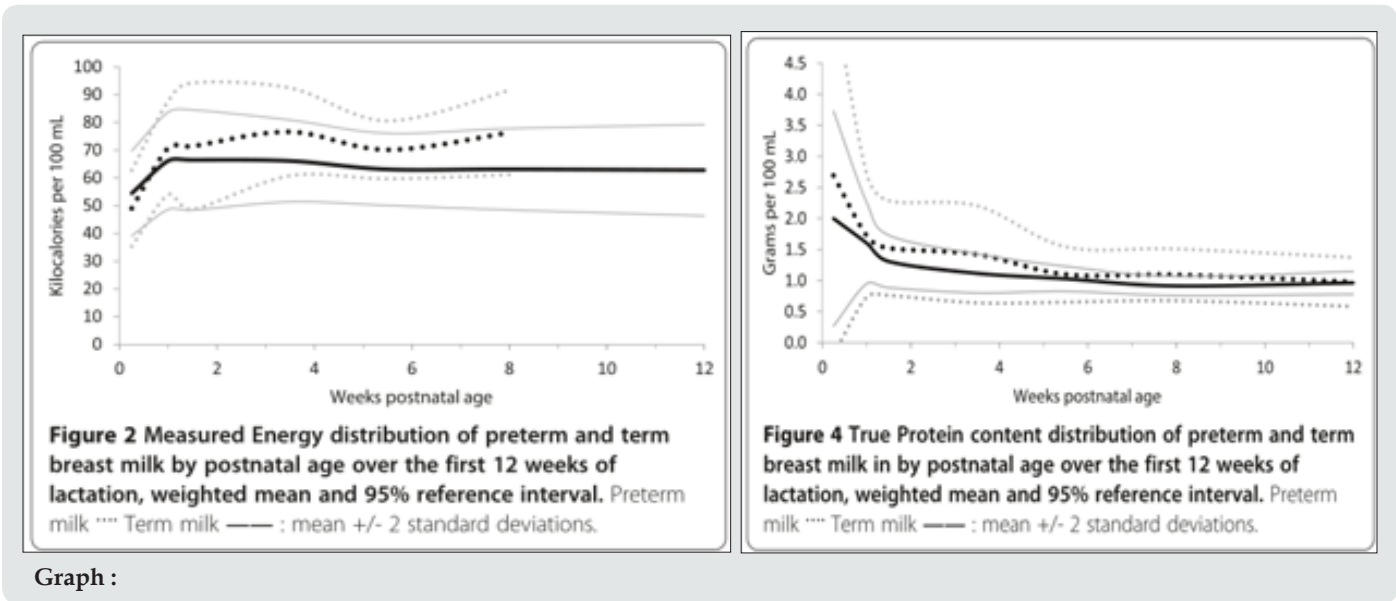
Literature Review

Annals of Ibaden, a post graduate medicine journal recommend that interventions like early commencement of minimal enteral feeds and preference for human breast milk should be practiced optimally. It also emphasizes on both clinical practice as well as research, to reduce nutritional deficits in this vulnerable infants [5]. According to the mea-analysis conducted by Dominica A Gidrewicz and Tanis R Fenton in August 2014, preterm breast milk is higher in energy and most of the nutrients than those of term breast milk [6]. They have proved this by analyzing 41 previous studies. Graphs drawn by them are as follows. By this analysis we can understand that preterm breast milk provides adequate nutrition to the preterm baby, certifying its satisfactory growth. According to research performed in United Kingdom poor weight gain observed in preterm infants who were fed expressed breast milk compared with those fed a cows' milk formula prompted a detailed study of early postnatal growth in preterm infants fed these two milks. 68 infants were divided into two categories by gestational age at birth

a)   28-32 weeks (n=28)

b)   33-36 weeks (n=40).

They were randomly allocated to a feed of expressed breast milk or a milk formula (Ostermilk 1). Rates of weight gain, linear growth, and head circumference growth were evaluated over two periods: birth-1 month, 1-2 months (Graph). The younger group who were fed breast milk showed slower overall growth rates over the first month than those fed formula. In the second month, and for the older infants over both of the 2-monthly periods, growth rates were similar in the two feeding regimens. It is concluded that expressed breast milk is inadequate for the growth of very immature preterm infants during early postnatal life [6]. A retrospective single-center observational study performed on 206 very preterm infantsaimed to investigate the impact of the cumulative intake of fortified human milk on early postnatal growth in a cohort of very low birth weight infants after early transition to full enteral feeds. Full enteral feeds were established at postnatal day 8 (6-10) and adequate postnatal growth was achieved (difference in standard deviation score for weight from birth to discharge -0.105(-0.603 - -0.323)). Standard deviation score for weight from birth to day 28 decreased more in infants with a cumulative human milk intake >75% of all enteral feeds (-0.64(-1.08 - -0.34)) compared to those with <25% human milk intake (-0.41(-0.7 - -0.17); $p = 0.017$). At discharge, a trend towards poorer weight gain with higher proportions of human milk intake persisted. In contrast, no significant difference was observed for head circumference growth. The conclusion was standardized fortification of human milk may not adequately support early postnatal growth [7].

Figure 2 Measured Energy distribution of preterm and term breast milk by postnatal age over the first 12 weeks of lactation, weighted mean and 95% reference interval. Preterm milk ···· Term milk ——— : mean +/- 2 standard deviations.

Figure 4 True Protein content distribution of preterm and term breast milk in by postnatal age over the first 12 weeks of lactation, weighted mean and 95% reference interval. Preterm milk ···· Term milk ——— : mean +/- 2 standard deviations.

Graph :

A systematic review of randomized controlled trials and observational studies was performed in America to determine whether earlier administration of Parenteral Nutrition benefits growth outcomes in preterm infants. Eight Randomizes Control Trials and 13 observational studies met the inclusion criteria (n = 553 and 1796 infants). The meta-analysis was limited by disparate growth-outcome measures. An assessment of bias was difficult because of inadequate reporting. Results are given as mean differences (95% CIs). Early Parenteral Nutrition reduced the time to regain birth weight by 2.2 d (1.1, 3.2 d) for Randomizes Control Trials and 3.2 d (2.0, 4.4 d) in observational studies. The maximum percentage weight loss with early Parenteral Nutrition was lower by 3.1 percentage points (1.7, 4.5 percentage points) for Randomizes Control Trials and by 3.5 percentage points (2.6, 4.3 percentage points) for observational studies. Early PN improved weight at discharge or 36 wk postmenstrual age by 14.9 g (5.3, 24.5

g) (observational studies only), but no benefit was shown for length or head circumference. There was no evidence that early Parenteral Nutrition significantly affects risk of mortality. Conclusions was that early Parenteral Nutrition provides a benefit for some short-term growth outcomes. No evidence that early Parenteral Nutrition increases morbidity or mortality was found [8].

In Indiana a study cohort consisted of 84 premature infants born at less than 30 weeks gestation to test the hypothesis that premature infants would grow adequately when they received more than 50 kcal/kg per day of parenteral nutrition. A computer software program was used to determine parenteral nutrition orders and establish a database. The database provided the nutrition and postnatal growth data. Successful growth was defined as weight greater than the 10th percentile for intrauterine growth. Energy intake exceeded 50 kcal/kg per day after the first day. The cohort weight and head circumference measurements remained above the 10th percentile of intrauterine growth through 36 weeks postmenstrual age. Infants demonstrated successful growth by remaining above the 10th percentile for the following: 4 of 12 (33%) with birth weights 501-750 g, 16 of 26 (62%) with birth weights 751-1,000 g, and 16 of 25 (64%) with birth weights 1,001-1,250 g. These differences were statistically greater than a large reference cohort (P < .0001). Length measurements declined below the 10th percentile of intrauterine growth at 36 weeks postmenstrual age. Conclusion was promptly providing premature infants with parenteral nutrition, including calories greater than the basal energy requirement, can produce postnatal growth that remains above the 10th percentile of intrauterine growth [9].

Methodology

Sample Scheme and Data collection methodology

Simple random sampling is the basic sampling technique where we select a group of subjects (a sample) for study from a larger group (a population). Each individual is chosen entirely by chance and each member of the population has an equal chance of being included in the sample. Therefore, this study we implemented simple random sampling technique [10,11].

Data collection: Data were collected from the clinic records. Height of the child and both parents were measured using the stadiometer by a trained single person at a given time. Each measurement was recorded as the average of three consecutive readings.

Study population: Preterm babies born in between 26 weeks to 34 weeks of POA. Children who were admitted to NICU at teaching Hospital Peradeniya, Children who are currently in the age range of 2yrs to 5yrs and Children who visited the clinic during the period of September to November 2014.

Sample size and Case definition: Fifty babies who are being followed up at the clinic were participated. Children who are born preterm (26 weeks - 34 weeks) who were admitted to NICU at

Teaching Hospital Peradeniya and currently in the age range of 2yrs - 5yrs.

Statistical analysis tool and Descriptive analysis

The data set analysis using R software version 4.1.0 with rcmdr11 packages. Descriptive analysis was used to compare means, variances, range to identify the central tendency and describe the basic features of data. Furthermore, correlation analysis was carried out among variables.

Correspondence Analysis and Contingency Tables

In statistics, a contingency table (also known as a cross tabulation or crosstab) is a type of table in a matrix format that displays the (multivariate) frequency distribution of the variables. They are heavily used in survey research, business intelligence, engineering, and scientific research. They provide a basic picture of the interrelation between two variables and can help find interactions between them.

Pearson's Chi-squared test[12]: Pearson's chi-squared test is a statistical test applied to sets of categorical data to evaluate how likely it is that any observed difference between the sets arose by chance. It is the most widely used of many chi-squared tests (e.g., Yates, likelihood ratio, portmanteau test in time series, etc.)

Single-linkage clustering[13]: In statistics, single-linkage clustering is one of several methods of hierarchical clustering. It is based on grouping clusters in bottom-up fashion (agglomerative clustering), at each step combining two clusters that contain the closest pair of elements not yet belonging to the same cluster as each other.

Dendrogram [14]: A dendrogram is a diagram that shows the hierarchical relationship between objects. It is most commonly created as an output from hierarchical clustering. The main use of a dendrogram is to work out the best way to allocate objects to clusters. The dendrogram below shows the hierarchical clustering of six observations shown on the scatterplot to the left.

Inclusion and Exclusion criteria

Preterm babies born in between 26 weeks to 34 weeks of POA, Babies born as singletons, Babies who didn't suffer from chronic illnesses, and Babies who were exclusively fed with expressed breast milk during the neonatal period were included in the study. Children born as a sibling of a multiple pregnancy, Babies who are not born in between 26 weeks to 34 weeks of POA, Babies who had gastrointestinal complications, Babies who were given parenteral nutrition during the neonatal period, and babies to whom expressed breast milk was not initiated during first two days of life due to surgical reasons were excluded [15,16].

Ethical issues

Ethical clearance was obtained from the Ethical Review committee of Teaching Hospital Kandy - Sri Lanka.

Data Analysis and Discussion

Our Data Set (Data Set)

Patient	Sex	Maturity(POA in weeks)	Birth weight(kg)	Present age(months)	Current wt(kg)	Height(cm)	Mother ht	Father ht	Mid parental height	Predicted ht
1	m	30	1.45	31	2.9	94	154	172	177.7-160.75	168
2	f	32	1.6	60	13.6	98	151	154	156.25-173.26	152
3	m	33	1.43	108	22.3	122	147	163	152.75-169.75	162
4	f	29	0.662	36	9.4	77	146	165	157.75-140.75	140
5	f	29	1.006	26	8.4	73	145	155	135.25-152.25	137
6	m	31	1.1	31	11.6	88.5	149	164	171.25-154.25	164
7	m	31	0.906	27	11.35	90	146	168	154.75-171.75	163
8	m	31	1.4	39	10.1	88	149	161	152.75-169.75	162
9	f	28	1.17	120	24.5	131	150	168	140.25-157.25	158
10	m	32	1.46	62	14	104	155	172	156.25-173.27	171
11	f	34	1.3	36	9.55	77	154	162	161.25-144.25	140
12	f	26	1.15	72	15.7	100.5	151	168	161`.5-144.5	148
13	f	28	1.398	60	16.7	107	155	156	156.25-173.29	160
14	m	30	1.29	132	22.6	130	145	165	152.75-169.75	161
15	m	33	1.05	108	17	120	153	168	158.25-175.25	159
16	f	27	1.3	120	23.3	134	152	175	148.75-165.7	161
17	f	29	1.27	36	11.2	93	158	173	151.25-167.75	161
18	f	28	0.74	60		101	154	175	166.7-149.7	154
19	m	33	1.09	48	9.95	89	141	170	165.75-148.75	158
20	m	30	0.82	43	10.5	92	152	168	157.5-174.5	164
21	f	30	1	39	10.25	93	161	162	159.25-176.25	162
22	m	30	0.845	72	15.85	112	156	172	153.25-170.25	170
23	m	30	0.96	72	13.5	104	146	170	155.75-172.75	164
24	f	31	1.235	29	12.9	87	160	168	166.24-149.25	162
25	m	34	1.68	48	13.3	99	147	163	152.75-169.75	162
26	m	29	1.476	46	14.8	93	141	161	161.25-178.25	163
27	f	32	1.29	59	14.4	104	152	180	156.25-173.28	158
28	m	30	1.1	28	13.4	87	160	178	171.25157.25	163
29	m	28	0.874	66	14.6	106	152	165	156.25-173.25	164
30	f	34	1.35	38	11.8	94	147	163	135,25-151.75	160
31	m	34	1.21	31	10.75	95	149	161	157.25-171	177
32	m	31	1.4	32	13.2	88	156	164	174.75-157.75	168
33	f	29	0.726	50	12	99	156	160	169.74-144.25	161
34	f	30	1.3	79	16.3	114	169	150	147.75-161.75	160
35	f	27	1.18	37	12.55	92	148	167	159.75-142.75	161
36	m	32	1.4	39	12.5	94	155	158	149.25-157.25	156

37	f	31	1.55	29	12	91	160	168	150-166	154
38	f	30	1.06	70	16.05	122	148	154	153.25-136.25	145
39	f	31	1.13	35	14.5	94	155	160	171-154	154
40	m	30	0.832	59	12.7	103	165	173	171-154	154
41	m	32	1.3	31	8.7	85	120	160	138-155	165
42	f	32	1.1	36	12.1	95	152	155	139-156	165
43	m	30	1.25	43	13.4	98	127	132	127.25-144.25	174
44	m	33	1.3	26	11	87	167	170	166.25-183.25	173
45	m	34	1.2	28	13	82	152	157	152.25-169.25	160
46	f	34	1.95	24	9.1	85	152	177	149.75-166.75	162
47	f	26	0.69	72	14.85	90	150	165	142.75-159.75	137
48	f	34	1	26	7	85	150	145	132.75-149.75	158
49	f	27	1.108	45	13.5	110	148	166	142.5-159.25	178
50	f	31	1.6	26	12	78	155	185	155.25-172.25	154

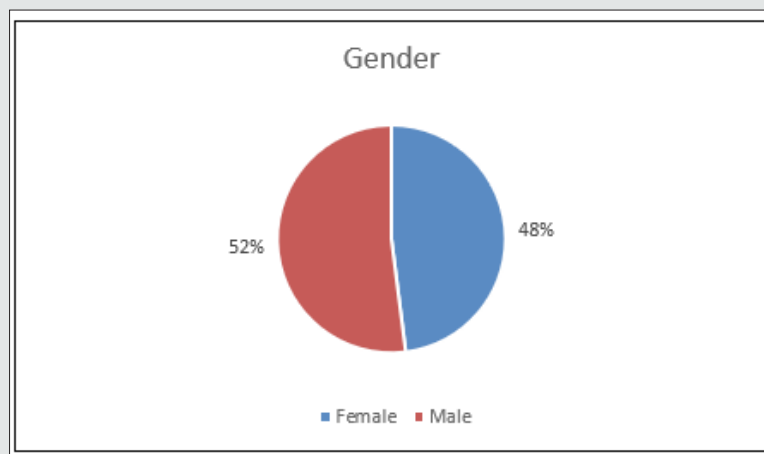## Descriptive Statistics of Variables

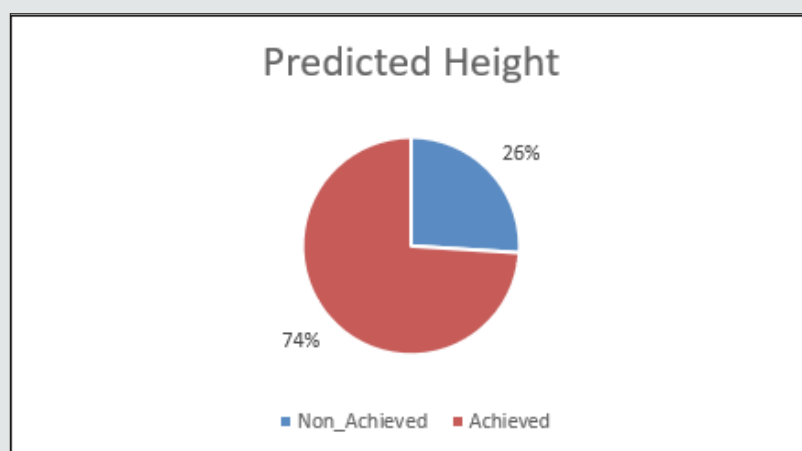**Figure 1:** Gender Representation of Sample.

Figure 2: Mid Parental Height Achievement of Sample.

According to the Table 1, Figure 1 and 2, means and variance of all variables are balanced with the Sample parameters.

Table 1: Descriptive Statistics in Maturity POA & Birth weight.

	Maturity POA(Weeks)	**Birth weight(kg)**
Min	26	0.66
Max	34	1.95
Average	30.59	1.19
Standard Deviation	2.24	0.27

Pearson's product-moment correlation

According to the Table 2, Birth weight and Maturity POA are averagely inter correlated indicating a positive correlation. Positive correlation indicates significant interdependence between variables.

Table 2: Correlation between Birth weight vs maturity (POA).

Variable	**Birth weight**	**Maturity(POA)**
Birth weight	1	0.4245
Maturity POA	0.4245	1

According to the Table 3 and 4, P-value < 0.05, H0 is rejected at 5% significance level and correlation between predicted height and gender is not equal to zero at 5% significance level. Therefore, predicted height and gender indicates significant interdependence relationship.

Table 3: Contingency analysis for Gender vs. Predicted height.

Variable	**Predicted height**			
Gender		Non Achieved	Achieved	Total
	female	10	16	26
	male	3	21	24
	Total	13	37	50

Hypothesis:

H0: True correlation is equal to Zero.
H1: True correlation is not equal to Zero.

Table 4: Pearson's Chi-squared test.

X-squared = 4.3719, df = 1, p-value = 0.0365

Single-linkage clustering Dendrogram

According to the Figure 3, the dendrogram shows 3 main clusters in this study, the task that consists in grouping a set of experiments (observations) in such a way that element belonging to the same group are more similar (in some mathematical sense) to each other than to those in the other groups. Tested 50 children who were born as preterm babies were separated 3 main groups. According to the dendrogram and statistical results, we can prove that there are mid parental height achieved group, mid parental height non-achieved group and extreme outlier case of the sample. Further, babies in mid parental height achieved group represent much closer characteristics to each other clinically and mathematically.
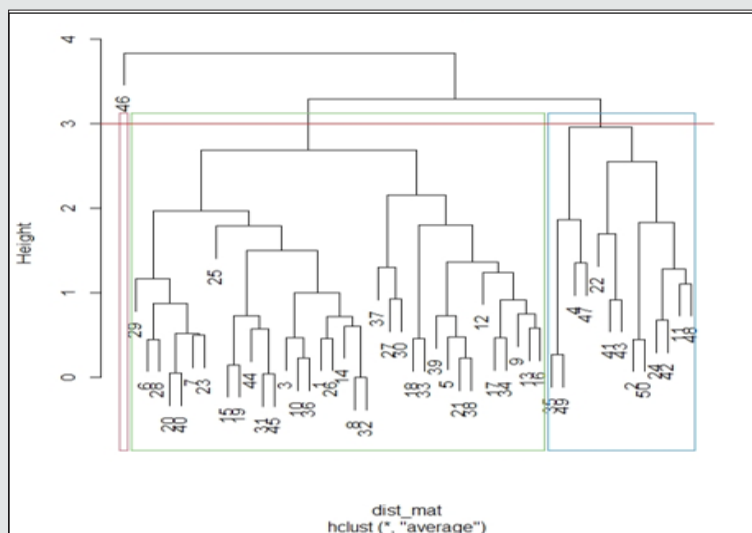

Figure 3: Mid Parental Height Achievement Dendrogram for the sample.

Conclusion

In our statistical analysis we found that 74% of children have achieved a height which is within the predicted mid-parental height range. This shows premature babies achieve their predicted heights even without providing additional nutrition by parenteral route or with fortified formulas during neonatal period. P-value < 0.05, H0 is rejected at 5% significance level and correlation between predicted height and gender is not equal to zero at 5% significance

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level. Therefore, predicted height and gender indicates significant interdependence relationship. Tested 50 children who were born as preterm babies were separated into 3 main groups in cluster analysis. According to the dendrogram and statistical results, we can prove that there are mid parental height achieved group which show 74%, mid parental height non-achieved group and extreme outlier case of the sample. Babies of the predicted mid parental height achieved group, represent much closer characteristics to each other clinically and mathematically. Finally, when considering nutrition of premature babies, we can conclude that statistically significant proportion achieve their predicted mid parental height during the period of 2-5 years. We need to follow this group during pubertal growth spurt and also during adolescence to see whether there is an impact on adult height.

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