STUDY COMPARING ANTHROPOMETRIC MEASUREMENTS BETWEEN TRANSFUSION DEPENDANT AND TRANSFUSION NON-DEPENDANT THALASSEMIA CHILDREN AT PENANG HOSPITAL

BY

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ABSTRAK DALAM BAHASA MALAYSIA

Beberapa kajian telah dijalankan mengenai masalah thalassemia di kalangan kanak-kanak di Malaysia. Ini merupakan suatu kajian keratan lintang prospektif yang dikendalikan di Jabatan Pediatrik, Hospital Pulau Pinang dari bulan September 1999 sehingga bulan Ogos 2002. Seramai 45 orang kanak-kanak yang mengidapi penyakit thalassemia dipilih untuk kajian ini. Objektif pertama adalah untuk membandingkan perkembangan antropometrik di antara kanak-kanak yang mengalami thalassemia dan memerlukan penambahan darah secara kerap (kumpulan 1) dan mereka yang tidak (kumpulan 2). Objektif kedua adalah untuk menilai korelasi diantara kadar kenaikkan tinggi dengan air darah ferritin, tahap darah sebelum dan selepas penambahan darah dan chelation pada kanak-kanak di kumpulan 1. Ukuran antropometrik tinggi, berat, ukur lilit pergelangan lengan atas, ketebalan lipatan kulit trisep dan bisep diambil pada kumpulan 1 dan 2. Kadar kenaikkan tinggi dan berat juga diperolehi untuk kedua-dua kumpulan. Ukuran tersebut dibandingkan diantara dua kumpulan ini. Selain daripada itu, ukuran carta ketumbesaran berdasarkan tinggi dan berat juga diperolehi untuk kedua-dua kumpulan. Keputusan antropometrik bila dibanding di antara kedua kumpulan, adalah tidak signifikan. Ketumbesaran terbantut pada kedua-dua kumpulan tersebut dari umur dua belas tahun keatas. Air darah ferritin, chelation, tahap darah sebelum dan selepas penambahan darah tidak mempunyai kaitan yang baik dengan kadar kenaikkan tinggi pada kanak-kanak di kumpulan 1. Kesimpulannya, kanak-kanak daripada kumpulan 1 dan kumpulan 2 didapati mengalami ketinggian yang terbantut dari umur 12 tahun keatas. Selain daripada itu, kadar kenaikkan tinggi tidak mempunyai kaitan yang baik dengan air darah ferritin, chelation, tahap darah sebelum dan selepas penambahan darah pada kanak–kanak di kumpulan 1.

ABSTRACT IN ENGLISH

Several studies have been conducted on the various problems in thalassemic children in Malaysia. This was a cross-sectional prospective study of 45 thalassemic children at Penang Hospital from September 1999 till August 2002. The first objective of this study was to assess whether there were any differences in anthropometric measurements between transfusion dependant (group 1) and transfusion non-dependant thalassemia children (group 2). The second objective was to identify if there were any correlations between height velocity with respect to serum ferritin levels, pre and post transfusion hemoglobin levels and chelation in group 1 children. Anthropometric measurements which include height, weight, mid-arm circumference, triceps and biceps skin fold thickness were measured in both groups. These anthropometric measurements were then compared between the 2 groups. Height velocity and weight velocity was measured in group 1 and group 2 children. The height and weight percentiles were plotted for both groups. The anthropometric measurements for group 1 and group 2 were not significantly different. There was growth retardation in both groups of children with thalassemia above 12 years of age. Serum ferritin levels, chelation, pre and post transfusion hemoglobin levels showed a poor correlation to height velocity in group 1 children. It was concluded that children in group 1 and group 2 have short stature at a later age with poor correlation of height velocity to serum ferritin levels, chelation, pre and post-transfusion hemoglobin levels in group 1 children.

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INTRODUCTION

1 INTRODUCTION

Thalassemia may have originated over 50,000 years ago in a valley south of Italy and Greece now covered by the Mediterranean Sea. The name thalassemia was first used in 1932. It originates from the Greek word *"thalassa"* meaning "the sea" and anemia, translating to "anemia by the sea". [1,2]

Dr. Thomas Cooley and Dr. Pearl Lee who described five cases of thalassemia in 1925 first recognized thalassemia as a clinical entity. [2]

It is most commonly found in people of Southern Europe (most notably Italian and Greek), East Indian, North African, Middle Eastern, Southern Chinese and some parts of South East Asia. Due to global migration patterns, there has been an increase in thalassemia in North America in the last 15 years. [1]

Thalassemia is the most common single gene disorder in Malaysia. It is mostly seen among the Chinese and Malays and only in a small percentage of Indians. Thalassemia occurs as a result of imbalance in the globin chain production. This results in mutations, deletions or point mutations within the α or β–globin chains located on chromosomes 16 and 11 respectively. Homozygous β thalassemia results from reduced or absent β–globin chain production. Alpha thalassemia results from impaired α–globin chain production which can lead to five types of alpha thalassemia depending on the number and location of the abnormal genes.[3] In a silent carrier type there is one gene deletion, in alpha thalassemia minor there are two gene deletions, in hemoglobin H

disease there are three gene deletions and in hemoglobin Barts there are four gene deletions. [3]

More than 23 different molecular defects have been identified for alpha thalassemia to date, while over 150 various mutations have been identified in beta thalassemia. Some of the common types of mutations in beta thalassemia, along with their severity and ethnic distribution are – 619 del (β^{o}, Indian), - 101 (β^{++} Mediterranean), - 88 (β^{++} Black), IVS2 - nt654 (Chinese), AATAAA- >AATAGA (β^{+}, Malay). The treatment is still difficult in many cases. [4,5,6]

One of the common problems associated with thalassemia is short stature. Many causes have been implicated as to the etiology of short stature in these children.[7] Study by S. Pantelakis et al (1994) [3] showed that patients who have regular blood transfusion and receiving chelation therapy tend to have short stature after the age of 10 to 12 years. The authors concluded that more studies would be required to clarify whether height reduction is due to the toxic effects of iron overload, the chelating agent itself, to growth hormone deficiency or to a deficiency in insulin like growth factor I.

The introduction of regular blood transfusion, maintaining hemoglobin level above 10 gm/dl and subcutaneous desferrioxamine chelation therapy has improved the long-term prognosis in these children. In the last three decades various transfusion regimens have been used in the treatment of children with thalassemia. Julia A Mcmillan et al (3rd edition) [8], Berhman and Vaughn (13th edition) [9] and Elias Schwartz et al (1980) [10] defined regular blood transfusion as those children receiving blood transfusion at every 2-6 weeks intervals. No studies have been done looking at the

growth patterns in thalassemic children receiving regular blood transfusion at Penang hospital so far. My study was undertaken to look at the growth patterns of thalassemic children at Penang hospital.

This study would also help to determine if the current transfusion regimen and chelation therapy used in thalassemic children at Penang hospital show growth patterns similar to those in other studies. If the study indicated that growth retardation occurred at an earlier age in the thalassemic children at Penang hospital, it may be necessary to change the transfusion regimen or the chelation therapy in order to obtain better results. However, if the growth patterns were similar to other studies then, it would be necessary to look at other causes of short stature in these children such as iron overload, endocrine causes and growth hormone deficiency. P.C.W. Lyn et al. (1985) [11] studied the management of beta thalassemia in an urban district hospital at Sabah. They found that hypertransfusion regimen improves the quality of life of these children. Similar studies could also be done in order to decide which transfusion regimen is better for the thalassemia children.

Studies to determine growth most frequently use data of height-for-age and weight-for-age. They are good indicators of morbidity and mortality.[7, 12]

In the late 1960s, it was shown that there was a good correlation between total mid–upper arm circumference and the muscle circumference (obtained by correcting for the layer of subcutaneous tissue). However, the lack of any suitable well–known, easily available standard had discouraged the use of this measurement as a clinical or survey tool. [13]

By the 1980s, mid-upper arm circumference and muscle circumference measurements were more established methods of anthropometrical assessment. This method of measurement represents the summation of the bone, muscle and fat components of the arm. A study by Ng et al [16], suggested that a mid-arm circumference reading of 13.0 to 13.7 cm may be used for identifying moderate to severe protein energy malnutrition and under 13 cm for severely malnourished children requiring immediate rehabilitation. [14]

The World Health Organization (WHO) convened an expert committee to re-evaluate the use of anthropometry at different ages for assessing health, nutrition and social well being. The committee identified reference data for anthropometric indexes when appropriate and provided guidelines on how the data should be used. For fetal growth they recommended an existing sex–specific multiracial reference. To evaluate adolescent height-for-age they recommended the current use of National Center for Health Statistics, WHO reference. It was noted that the most commonly used indexes for assessing child growth were height-for-age, weight-for-age and mid-upper arm circumference.[15]

Survival alone is not the solution for the victims of thalassemia. We have to find ways to provide quality of life for these patients and to support their families who become easily devastated morally and financially. Our task is to provide hope and compassion to these children and their parents until a cure is found. A better understanding of the demographics of thalassemia has a potential to aid in more efficient utilization of health care resources, improved planning and provision of health care services. [5]

OBJECTIVE

2 OBJECTIVE OF STUDY

The objectives of this study were:

1. To determine if there were any differences in anthropometric measurements such as height, weight, mid-arm circumference, biceps and triceps skin-fold thickness between thalassemia children who are transfusion dependant (group1) and transfusion non-dependant (group 2).

2. To determine the correlation of height velocity with respect to serum ferritin levels, chelation, pre and post transfusion hemoglobin levels in group 1 children.

METHODOLOGY

3 MATERIALS AND METHOD

3.1 General Descriptions

This was a cross-sectional prospective study carried out at Penang Hospital from September 1999 till August 2002. Children diagnosed with thalassemia were selected. They were divided into 2 groups:

1) Transfusion dependant (group 1) [8, 9, 10]

2) Transfusion non-dependant (group 2).

The sample size calculation was achieved by applying the following parameters of height, weight, mid-arm circumference (MAC), biceps skin-fold and triceps skin-fold thickness based on objectives 1 and 2. The required sample size was 17 children in each group. Software computer programme was used to calculate the sample size. There were a total of 45 children in the study. Group 1 consisted of 28 children, while group 2 consisted of 17 children.

Transfusion dependant thalassemic children (group1) received regular blood transfusion every 6 to 8 weeks. The hemoglobin levels were maintained above 8.5 gm/dl. The seventeen transfusion non-dependant children (group 2) received blood transfusion only occasionally. Two of the children received six monthly transfusions, 1 child received 7 monthly, 1 child received 10 monthly and 2 children received yearly transfusions. The remaining 11 children did not receive any blood transfusion. Children in group 2 were from a heterogeneous group consisting of HbE/Beta thalassemia, HbE

thalassemia, thalassemia intermedia, beta thalassemia trait and Constant Spring. The diagnosis of thalassemia was based on hemoglobin analysis result. Their ages ranged from 1 till 15 years old. [7, 16, 17, 18]

Informed verbal consent was obtained from the parents/guardians of the children involved in the study. The anthropometric measurements as well as blood investigations for serum ferritin levels, pre and post transfusion hemoglobin levels were taken.

3.2 Inclusion Criteria.

Children from ages 1 to 15 years, [7, 16, 17, 18, 19] with confirmed diagnoses of thalassemia by hemoglobin electrophoresis were selected. The youngest child was 1 year old and the oldest was 15 years old. The children in group 1 were transfusion dependant and received iron chelation. The iron chelating agent used was subcutaneous desferrioxamine, infused over 8 to 10 hours, five times per week. [20] Chelation was started at a mean age of 6.5 years (6.5 ± 3.4). The dose of chelating agent used was calculated from September 1999 till August 2002. The children in group 2 were transfusion non-dependant and did not require iron chelation therapy.

3.3 Exclusion Criteria.

Transfusion dependant thalassemia children who did not receive chelation therapy were excluded from this study. Children who had complications of thalassemia were excluded from this study. Children with organ failure such as cirrhosis of the liver and liver failure, cardiac failure caused by anemia, increased plasma volume, and myocardial iron overload, arrhythmias, pericarditis and spinal cord compression caused by epidural extramedullary hematopoiesis were also excluded from this study. [21]

3.4 Anthropometric measurements

Anthropometric measurements such as height, weight, mid-arm circumference (MAC), biceps and triceps skin-fold thickness were taken from both the groups of children. The author did all of these measurements. The first measurement was taken at the beginning of the study. The second measurement was taken thirty four months later. Three measurements were taken for each parameter and a mean of the three readings was used. The same Pediatric Clinic staff nurse reconfirmed all the measurements taken.

3.4.1 Height.

The supine length was recorded for children younger than 2 years old, using an infantometer. The head was held against the headboard with the face in the horizontal plane. The infant's hips and knees were gently extended while keeping the pelvis "fixed. The movable footboard was brought up to touch the sole of the feet, which was kept at 90 degrees. The measurements were taken to the nearest 0.1 cm.

The standing height was measured in older children using a height attachment to the Seca weighing scale. The height was measured to the nearest 0.1 cm. The children were measured barefoot, heel in the same vertical plane as the measuring instrument. The arms were kept at the side and face held in such a way, that the outer canthus of the eye and the external auditory meatus were horizontal. The accuracy of the Seca weighing scale and the height attachment to the Seca weighing scale were checked periodically during the surveys.

3.4.2 Weight.

A standing weight was obtained to the nearest 100 grams using a Seca weighing scale with a height attachment. The accuracy of the Seca weighing scale with the height attachment was checked periodically and calibrated regularly during the survey. The children were barefoot and had minimum clothing of shirt and short pants before the measurements were taken. [11, 12]

3.4.3 Mid-Arm Circumference (MAC).

Mid-arm circumference (MAC) was taken as the mid-point of the upper arm between the acromian and olecranon process. With a non-stretchable measuring tape the determined mid-point was carefully measured. All measurements were recorded to the nearest 0.1 cm. [12]

3.4.4 Triceps-Skin Fold Thickness.

A Harpenden skin fold caliper was used. The examinee's right arm was flexed 90 degrees at the elbow, and the mid-point between the acromian and olecranon on the posterior aspect of the arm was determined. Then, with the examinee's arm hanging freely at his/her side, the examiner measured the thickness of a fold of skin and the underlying subcutaneous tissue with the skin-fold caliper at the mid-point of the arm. Care was taken to ensure that the measurement was made in the mid line posteriorly, the crest of the fold being parallel to the long axis of the arm. Care must be taken to ensure that the muscle tissue was not included in the fold. [22] The examiner grasped the fold between the thumb and the forefinger and maintained pressure on the fold until the measurement was complete. The caliper was applied to the fold about 1cm distal to the

examiner's thumb and forefinger. Measurements to the nearest 0.1 mm were made. [14, 22, 23]

3.4.5 Biceps Skin-Fold Thickness.

The procedure was similar to that of triceps skin-fold thickness measurement but performed at the anterior aspect of the arm.

3.4.6 Height and weight velocity.

The height and weight velocity was calculated over a period of thirty four months.

3.4.7 Height and weight percentile.

Height and weight percentiles of the children in the study were plotted on the growth chart developed by the National Center for Health Statistics in collaboration with National Center for Chronic Disease Prevention and Health Promotion. [24]

3.4 Statistical Analysis.

Chi square test and applied Fisher's Exact Test were used for age, sex, race, height and weight percentile analysis. The confounders for age, sex and race were not matched but controlled statistically by using the multivariate analysis from the SPSS programme. General linear model method was applied to analyze the data of height, weight, mid-arm circumference, triceps and biceps skin-fold thickness. Pearson's Correlation coefficient and linear regression were used to identify the correlation of height and weight with respect to serum ferritin levels, pre-transfusion hemoglobin levels, post-transfusion hemoglobin levels and chelation (desferrioxamine). There were no missing data during the conduct of the study.

3.6 Null Hypothesis (H_0).

There are no differences in anthropometric measurements (height, weight, mid-arm circumference, triceps and biceps skin-fold thickness measurements) between group 1 and group 2.

3.7 Alternate Hypothesis (H_1).

There are definite differences in anthropometric measurements (height, weight, mid-arm circumference, triceps and biceps skin-fold thickness measurements) between group 1 and group 2.

RESULTS

4 RESULTS

There were a total of 45 children in the study. There were 16 children in 1 to 5 years, 13 children in >5 to 10 years and 16 children in >10 to15 years age group (Fig 4.1). There were twenty six (57.8%) boys and 19 (42.2%) girls. The youngest child was 1 year old and the oldest was 15 years. These children were divided into transfusion dependant (group 1) and transfusion non-dependant (group 2). In group 1, there were 28 children who were further divided according to the age groups of 1 to 5 years, >5 to 10 years and >10 to15 years (Figure 4.2). In group 2, there were 17 children who were also divided according to the age groups as in group 1. (Fig 4.3)

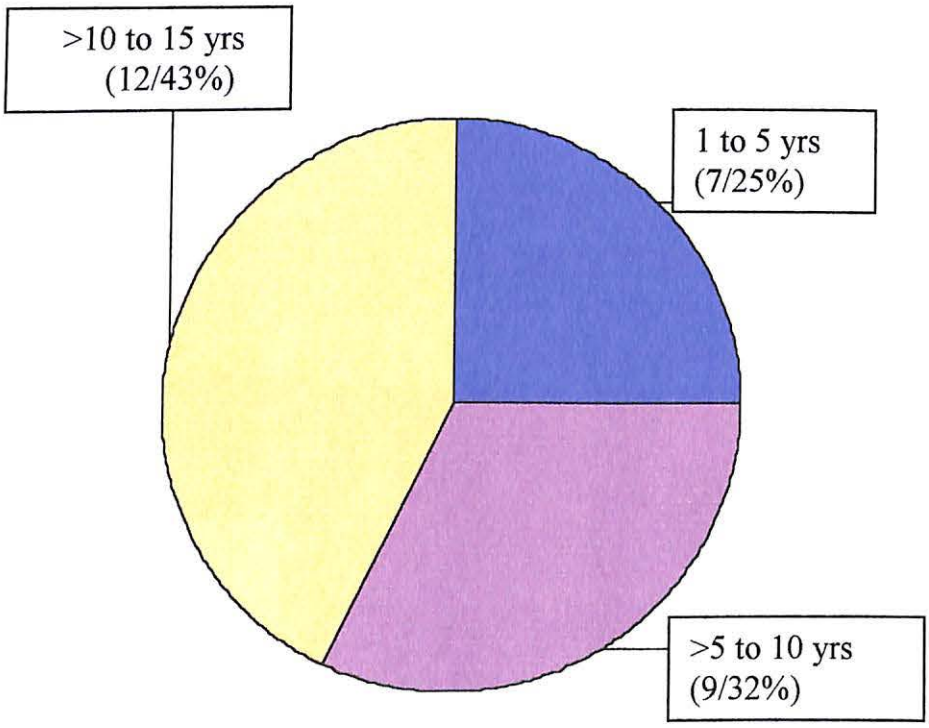

Figure 4.2: Diagram showing the different ages of children in group 1.

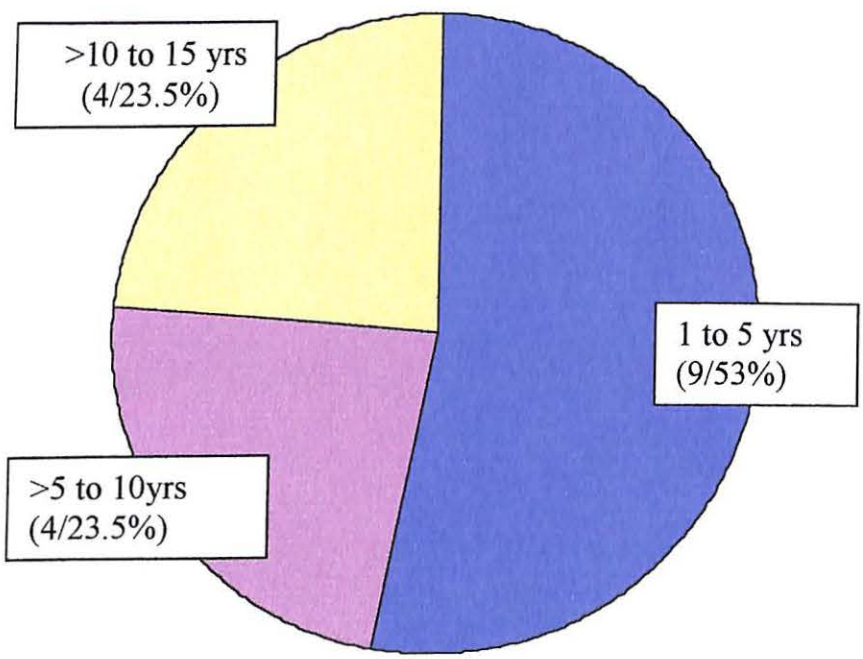

Figure 4.3: Diagram showing the different ages of children in group 2.

The children in this study had different types of thalassemia, which were beta thalassemia major, hemoglobin E/Beta thalassemia, hemoglobin E thalassemia, Constant Spring, thalassemia intermedia and beta thalassemia trait. (Table 4.1)

Table 4. 1 Different types of thalassemia in the study

Types of Thalassemia	Group 1	Group 2
Beta thalassemia major	20	0
HbE/Beta thalassemia	6	11
HbE thalassemia	1	3
Beta thalassemia intermedia	0	1
Constant Spring	1	1
Beta thalassemia trait	0	1
Total	28	17

4.1 Anthropometric measurment comparison between group 1 and group 2

The height, weight, mid-arm circumference, biceps skin-fold thickness and triceps skin-fold thickness measurements were taken at the beginning (first measurement) and at the end of the study (second measurement) for the two groups. (Tables 4.2, 4.3).

The growth appeared to be more in group 1 when compared to group 2 especially, in terms of height and weight. However, there were no significant differences in height, weight, mid-arm circumference, triceps and biceps skin-fold thickness between the two groups.

Similarly, height and weight measurements according to the different age groups of 1 to 5 years, > 5 to 10 years and > 10 to 15 years too, did not show any significant differences. (Table 4.4, 4.5) There were also no significant differences in the height and weight velocity between the two groups over a period of 34 months. (Table 4.6)

Table 4.2: Anthropometric parameters of first measurements in group 1 and 2 children.

Variable	Sex	Group 1	Group 2	p value
Height (cm)	Male Female	121.73 ± 21.60 117.14 ± 16.58	103.00 ± 22.37 109.50 ± 32.64	NS
Weight (kg)	Male Female	23.58 ± 9.36 21.86 ± 6.01	15.88 ± 6.59 20.36 ± 11.33	NS
Mid arm Circumference (cm)	Male Female	16.91 ± 3.66 17.14 ± 1.92	15.28 ± 1.87 15.48 ± 5.14	NS
Triceps skin fold thickness (mm)	Male Female	8.76 ± 2.53 10.51 ± 1.51	8.36 ± 2.13 9.78 ± 4.46	NS
Biceps skin Fold thickness (mm)	Male Female	5.53 ± 1.74 5.81 ± 1.00	4.54 ± 0.90 6.38 ± 3.21	NS

Table 4.3: Anthropometric parameters of second measurements in group 1 and 2 children.

Variable	Sex	Group 1	Group 2	p value
Height (cm)	Male	135.10 ± 19.52	117.93 ±18.22	NS
	Female	128.68 ± 15.35	124.85 ± 31.00	
Weight (kg)	Male	30.25 ± 11.36	21.96 ± 7.51	NS
	Female	27.68 ± 8.25	27.90 ± 16.18	
Mid arm Circumference (cm)	Male	19.99 ± 3.35	17.76 ± 2.27	NS
	Female	19.90 ± 2.82	20.19 ± 5.28	
Triceps skin fold thickness (mm)	Male	12.48 ± 3.92	9.02 ± 1.85	NS
	Female	12.49 ± 3.12	12.50 ± 6.38	
Biceps skin Fold thickness (mm)	Male	7.76 ± 3.34	5.38 ± 1.71	NS
	Female	8.48 ± 3.05	7.66 ± 4.87	

Table 4.4: Showing height (cm) and weight (kg) parameters of first and second measurements in group 1 children according to different age groups.

Age group (years)	Variable	First measurement	Second measurement	Velocity (Height & weight)
1-5	Height (cm) Male	91.50 ± 14.06	108.64 ± 11.31	17.14
	Female	95.50 ± 5.22	111.17 ± 4.48	15.7
	Weight (kg) Male	12.75 ± 2.99	16.75 ± 2.53	4.0
	Female	14.83 ± 1.15	18.33 ± 0.76	3.5
>5-10	Height (cm) Male	124.00 ± 8.88	138.13 ± 10.61	14.1
	Female	119.10 ± 5.88	128.40 ± 8.36	9.3
	Weight (kg) Male	22.00 ± 5.08	30.37 ± 9.39	8.4
	Female	21.80 ± 3.30	27.40 ± 4.87	5.6
>10-15	Height (cm) Male	134.17 ±13.99	145.52± 13.96	11.4
	Female	135.50 ± 7.70	146.67 ± 8.50	11.2
	Weight (kg) Male	29.06 ± 8.29	36.18 ± 9.59	7.1
	Female	29.00 ± 2.65	37.50 ± 4.09	8.5

Table 4.5: Showing height (cm) and weight (kg) parameters of first and second measurements in group 2 children according to different age groups.

Age group (years)	Variable	First measurement	Second measurement	Velocity (Height & weight)
1-5	Height (cm) Male	85.20 ± 9.36	103.50 ± 7.87	18.3
	Female	80.38 ± 8.77	97.70 ± 12.08	17.3
	Weight (kg) Male	10.50 ± 1.88	16.20 ± 2.16	5.7
	Female	10.38 ± 2.29	13.92 ± 2.67	3.5
>5-10	Height (cm) Male	121.25 ±1.77	134.30 ± 3.25	13.1
	Female	139.25±20.86	155.00 ±18.38	15.8
	Weight (kg) Male	21.25 ± 0.35	30.85 ± 5.44	9.6
	Female	29.20 ± 8.20	42.00 ± 4.24	12.8
>10-15	Height (cm) Male	129.25 ±4.60	137.65 ± 6.58	8.4
	Female	138.00 ± 1.41	149.00 ± 4.24	11.0
	Weight (kg) Male	23.95 ± 0.78	27.50 ± 4.24	3.6
	Female	31.50 ± 3.53	41.75 ± 15.20	10.3

Table 4.6: Height (cm) and weight (kg) velocity (per year) over 34 months in group 1 and 2 children according to different age groups.

Age group (years)	Parameters	Group 1 (per year)	Group 2 (per year)	p value
1 – 5	Height (cm) Male	6.0	6.5	NS
	Female	5.5	6.1	
	Weight (kg) Male	1.4	2.0	NS
	Female	1.2	1.2	
>5 – 10	Height (cm) Male	5.0	4.6	NS
	Female	3.3	5.6	
	Weight (kg) Male	3.0	3.4	NS
	Female	2.0	4.5	
>10 - 15	Height (cm) Male	4.0	3.0	NS
	Female	3.9	3.9	
	Weight (kg) Male	2.5	1.3	NS
	Female	3.0	3.6	