FUNCTIONAL RESIDUAL CAPACITY IN HEALTHY INFANTS AGED 1-24 MONTHS USING THE BABY BODY PLETHYSMOGRAPHY (CAREFUSION TM)

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ABSTRACT

BACKGROUND: The only lung volume that can be measured reliably in infants is the functional residual capacity (FRC). Published reference values vary, thus, there is a need to determine values for healthy infants using the available equipment.

OBJECTIVES: To determine the normal values of FRC in healthy infants using the baby body plethysmogram (CareFusion) and to determine the correlation between FRC and weight, length, age, and gender.

METHODS: FRC was measured using the CareFusion MasterScreen baby body plethysmogram in 62 healthy infants aged 1-24 months old. FRC was measured after sedation with Chloral hydrate at 50 mg/kg body weight. Three measurements were performed from which the mean (SD) FRC was calculated. To depict the change in FRC with growth, regression analysis between FRC as dependent variable and weight, length, and age as independent variables was done.

RESULTS: Among 62 infants, mean age was 10.97 months (range=1-24 mos), mean weight was 7.93 kg (range=4.5-12 kg) and mean length was 71.91 cm (range=56-90 cm). Thirty-one (50%) are males and 31 (50%) are females. Mean FRC (SD) was 24.56 ml/kg (4.41). Correlation of FRC with age was significant (R=0.820), as well as the weight (R=0.830) and the length (R=0.758). There was no difference in FRC between males and females.

CONCLUSION: The FRC values obtained in this study is 24.56 ml/kg (4.41). There is a direct correlation of FRC with age, weight, and length. The result of this study was comparable to other studies and may be used as a reference value for healthy infants.

KEY WORDS: Baby body plethysmography; Functional residual capacity; Pulmonary function test; Infant

INTRODUCTION

Measurement of lung volumes in infants are important for assessing growth and development of the lungs and for interpretation of volume-dependent lung function parameters. There are various uses of respiratory function tests in infancy. They are used as diagnostic aids to help determine the nature of the lung function disorder; to quantify its magnitude; to assist in determining prognosis or perioperative risk; to assess the effects of medical interventions or diagnostic tests; to evaluate innovative therapies aimed at improving prognosis, quality of life, and lung function; to study the natural course of respiratory disease; and to study the growth and development of the lungs and airways and evaluate early determinants of airway function. (1)

The only lung volume that can be measured reliably and routinely in infants is the resting end-expiratory lung volume or functional residual capacity (FRC). (2) It is important for interpreting volume-dependent pulmonary mechanics such as forced expiratory flows, for defining normal lung growth and for detecting hyperinflation which is a measure of dyspnea or disease state. Published reference data for neonates have been reported, approximately 23 ml/kg when using the helium dilution technique and 32 ml/kg from plethysmographic measurements. (2) In 2001, the American

Thoracic Society and European Respiratory Society (ATS-ERS) task force published recommendations on the methodology and the equipment for infant plethysmography which measures infant lung volumes including FRC. (3) New generation of infant body plethysmographs were developed, making infant lung function readily available. However, meaningful interpretation of results will still depend on the availability of appropriate reference values.

Reference values are a set of values obtained from an individual or group in a defined state of health. Ideally, reference values must be consistent and are those expected for individuals of the same sex, similar stature, age, and other characteristics.

Published reference values for FRC varied among studies on healthy infants. In fact, during the previous years, there has been an unexplained trend toward declining values for plethysmographic assessments of FRC. There is therefore an urgent need to determine normal values for healthy infants using the available equipment, and carefully observe protocols for data collection, analysis, and quality control.

OBJECTIVES

General:

To determine the normal values of functional residual capacity (FRC) in healthy infants using the baby body plethysmogram (CareFusion)

Specific:

To determine the correlation between FRC and body weight, length, age, and gender

METHODOLOGY

This is a cross-sectional study. All healthy infants aged 1-24 months were included in the study. Infants were considered healthy if they fulfill the following criteria:

1. Well nourished based on Z scores (weight for height below Z score 3 and above Z score (-2)

2. Normal physical examination upon enrolment to the study.

Selection of healthy subjects were based on the American Thoracic Society/ European Respiratory Society recommendations.(17) Infants were excluded if they had the following: a) Recent upper respiratory tract infection or acute respiratory tract infection 3 weeks prior to the participation in the study; b) first degree family history or physician diagnosed bronchial asthma, allergic rhinitis,or atopy; c) Two or more episodes of wheezing and coughing in the past relieved by intake of and/or nebulization with B2-agonist; d) history of intake of systemic or inhaled steroids within two weeks; e) premature birth less than 37 weeks AOG, low birth weight (less than 1,500 g), history of bronchopulmonary dysplasia; f) exposure to any household member who smokes inside the house; g) infants with upper airway obstruction; h) facial/oral abnormalities; i) thoracic and chest wall deformities; j) patients on CNS depressants such as opiods, benzodiazepines, or barbiturates which may cause excessive sedation; presence of other conditions supported with laboratory tests, imaging studies, or clinical abstracts from attending physicians who made the diagnosis, such as: k) presence of congenital anomalies involving any organ system; l) cardiopulmonary or other systemic illness such as collagen disease, nephropathies, or any malignancy,; m) neuromuscular disease such as GBS, myasthenia gravis, and muscular dystrophies; n) history of thoracic or abdominal surgery within 3 months prior to participation in the study.

The sample size was calculated using the formula for estimation of population mean.

$$\underline{n= (Z)^2 (SD)^2}$$
$$E^2$$

Where:

Z = 95% confidence level

SD= Standard deviation of the variable of interest, that is, FRC= 3.4

E= measure of effect= 1

$$\underline{n= (1.96)^2 (3.4)^2}$$
$$(1)^2$$

= 44

The number of samples was computed using a 95% level of confidence. With an estimated SD of 3.4 for FRC based on reference (7), at least 44 subjects are needed. This sample size calculation was used to answer the primary objective which is to determine the functional residual capacity in healthy infants aged 1-24 months old.

The formula used for the specific objective was the formula on One Correlation Power Analysis. A sample size of 59 achieves 80% power to detect a difference of 0.1 between the null hypothesis correlation 0f 0.80 and the alternative hypothesis correlation of 0.90 using a two-sided hypothesis test with a significance level of 0.0500. The sample size calculated was at least 59 based on the specific objective, but 62 subjects were included in the study.

Subjects were selected randomly from Barangay PAG-ASA and AGHAM in Quezon City. Subjects were randomly selected from the list of households in the Barangay. Using odd numbers, the first household was selected, then succeeding numbers followed.

An informed consent was obtained by the principal investigator after the selected subjects fully understood the study. A checklist was used to assess the health status of each patient. Physical examination was done and anthropometric measurements were recorded. Infants with normal physical examination were then included in the study.

The infant was then prepared for the procedure. The infant's clothing was loosened so as not to restrict respiratory movements. Feeding was withheld according to the guidelines for monitoring pediatric patients who are sedated. Milk feeding was withheld 4-6 hours prior to the said procedure. (18) Timing of measurement coincided with the infant's normal sleep/waking routine to minimize any need for repeat sedation.

Functional residual capacity (FRC) was measured according to the Care Fusion instruction manual (19) and ERS/ATS recommendations (6). FRC was measured during quiet sleep after sedation with oral chloral hydrate at 50 mg/kg (max dose of 100 mg/kg) which was administered by the principal investigator. Another dose of 25 mg/kg was given in patients who were inadequately sedated. Infants who do not fall asleep after the second dose were rescheduled after a week. Infants who awakened during the procedure were reassessed for need of resedation. A repeat half dose was given to infants who vomited the syrup immediately after administration and observed for recurrence of vomiting. If vomiting persists, the infant will be admitted for hydration and monitoring.

To avoid unnecessary and potentially dangerous transfer of the deeply sedated infants, sedation was administered at the pulmonary laboratory where the procedure was done. Rescuscitation equipments such as bag mask and oxygen, as well as a functioning suction apparatus were available and the principal investigator, as well as the co-investigators, or respiratory therapists who were all trained in pediatric advanced life support were present. The sedated infant was monitored at baseline by the primary investigator. Oxygen saturation and heart rate were monitored. Respiratory rate, blood pressure, and expired CO2 levels were also monitored at every 10-15 minutes. The infant's head position was continuously assessed to ensure airway patency. The sleeping infant was placed inside the plethysmograph and a face mask attached to a pneumotachograph and shutter was sealed around the nose and mouth. The seal was tested by recording at least five tidal breaths before occlusion to establish a stable end-expiratory level and then briefly closing the shutter at end expiration. If the seal is tight, flow will be zero throughout the occlusion and the volume recorded will return to the expiratory baseline after the release of the shutter. The mask was held in place with strapping to support the cheeks and reduce risk of shunting to the upper airways during occlusion. After eliminating leaks, the plethysmograph was closed. A minimum of three end-expiratory occlusions was performed from which the mean FRC was calculated. After the procedure, the infant was monitored and sent home once fully awake for at least 20 minutes and feeding. The infant's skin was evaluated for any rashes after the putty has been applied during the test. The infants were followed up the next day through a phone call for any symptoms such as vomiting and abdominal discomfort after sedation.

Demographic data was described using means and standard deviation. To depict the change in FRC with growth, regression analysis was done using the Pearson's Product Moment Coefficient of Correlation between FRC as dependent variable and weight, length, and age as independent variables.

Since the procedure entails quiet breathing, all subjects were sedated. Chloral hydrate has been the preferred medication for infant pulmonary function test. All existing healthy infant PFT reference data have been derived from studies using Chloral hydrate. It is an oral medication and thus avoids the need for an intravenous catheter. Its duration of action matches well with the duration of the infant pulmonary function test and it provides the appropriate level of sedation. An informed consent from the parents were obtained without coercion. Anonymity and confidentiality of the research correspondents were respected. The hospital's Ethics committee and Investigational Review Board approved the study prior to recruitment of subjects. There is no conflict of interest to disclose as to relationship with the distributor of the equipment.

RESULTS

Demographic Profile of Patients

There were 82 infants randomly recruited from Barangay PAG-ASA and AGHAM in Quezon City. Eighteen (n=18) subjects were excluded due to the following reasons: no consent (n=10), malnourished (n=3), history of recent upper respiratory tract infection (n=2), and failure of sedation (n=3). There were 64 infants who completed the procedure, but 2 were classified as outliers after the preliminary analysis. Sixty-two patients were then included in the final analysis (Figure 1).

Among the 62 subjects who completed the procedure, mean age was 10.97 months (range=1-24 mos), mean weight was 7.93 kg (range=4.5-12 kg) and mean length was 71.91 cm (range=56-90 cm). Thirty-one (50%) are males and 31 (50%) are females. (see Table 1)

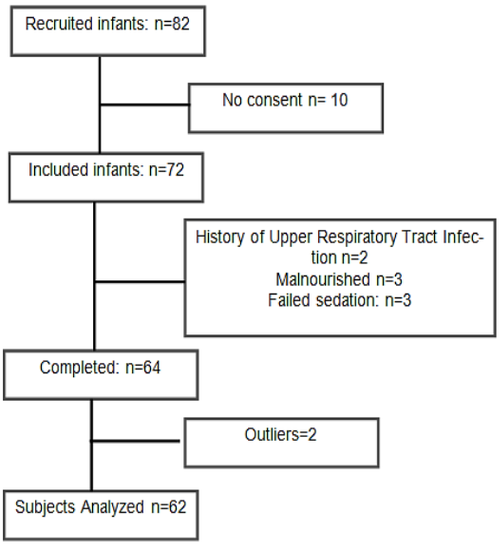

Figure 1. Study Population

Functional Residual Capacity (FRC) Results

In the actual data collection, although the calculated sample size was at least 59, 64 subjects were considered. From the preliminary assessment of the data, 2 observations were classified as outliers and were excluded in the calculation of the normal values inorder to produce a more stable estimate of the normal values. Table 1 summarizes subject details and results. Mean (SD) FRC was 195.89 (58.34) ml and mean (SD) FRC per kg body weight was 24.56 ml/kg (4.41).

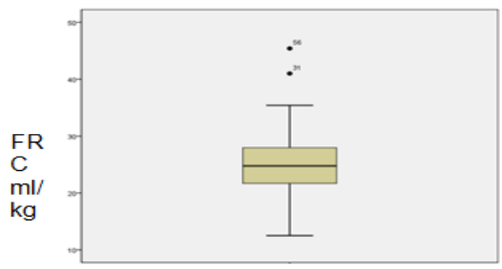

Figure 2. Preliminary graphical description of FRC per kilogram body weight showing 2 outliers

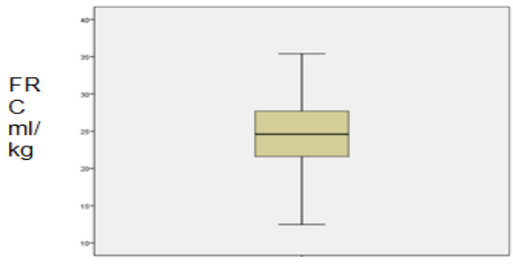

Figure 3. Graphical description of FRC per kilogram body weight after outliers have been eliminated

Table 1. FRC in Healthy Infants: Background Characteristics and Results

Attributes	Mean (sd)	95% CI for Mean	Range	5%ile	95%ile
n	62				
% Male % Female	50 50				
Age, mos	10.97 (6.33)	(9.36, 12.58)	1 – 24	2.00	24.00
Weight, kg	7.93 (1.82)	(7.48, 8.40)	4.5-12	5.00	11.80
Length, cm	71.91 (8.34)	(69.79, 74.03)	56 – 90	60.00	86.85
Mean FRC, ml	195.89 (58.36)	(181.07, 210.71)	75.13 – 349.70	93.85	288.36
Mean FRC, ml/kg	24.56 (4.41)	(23.44, 25.68)	12.5 – 35.4	15.92	31.77

Correlation of FRC with age was found to be significant at the 0.05 level (R=0.820), as well as the weight (R=0.830) and the length (R=0.758). Comparison of mean FRC ml/kg using the T-test showed no difference in FRC between males and females (p=0.49). (See Table 2) Significant correlation between FRC and age, weight, and length was reinforced when regression resulted to the equation:

FRC= 3.9(age in months) + 15.4(wt)- 0.053(length) + k ,where k= 34.32

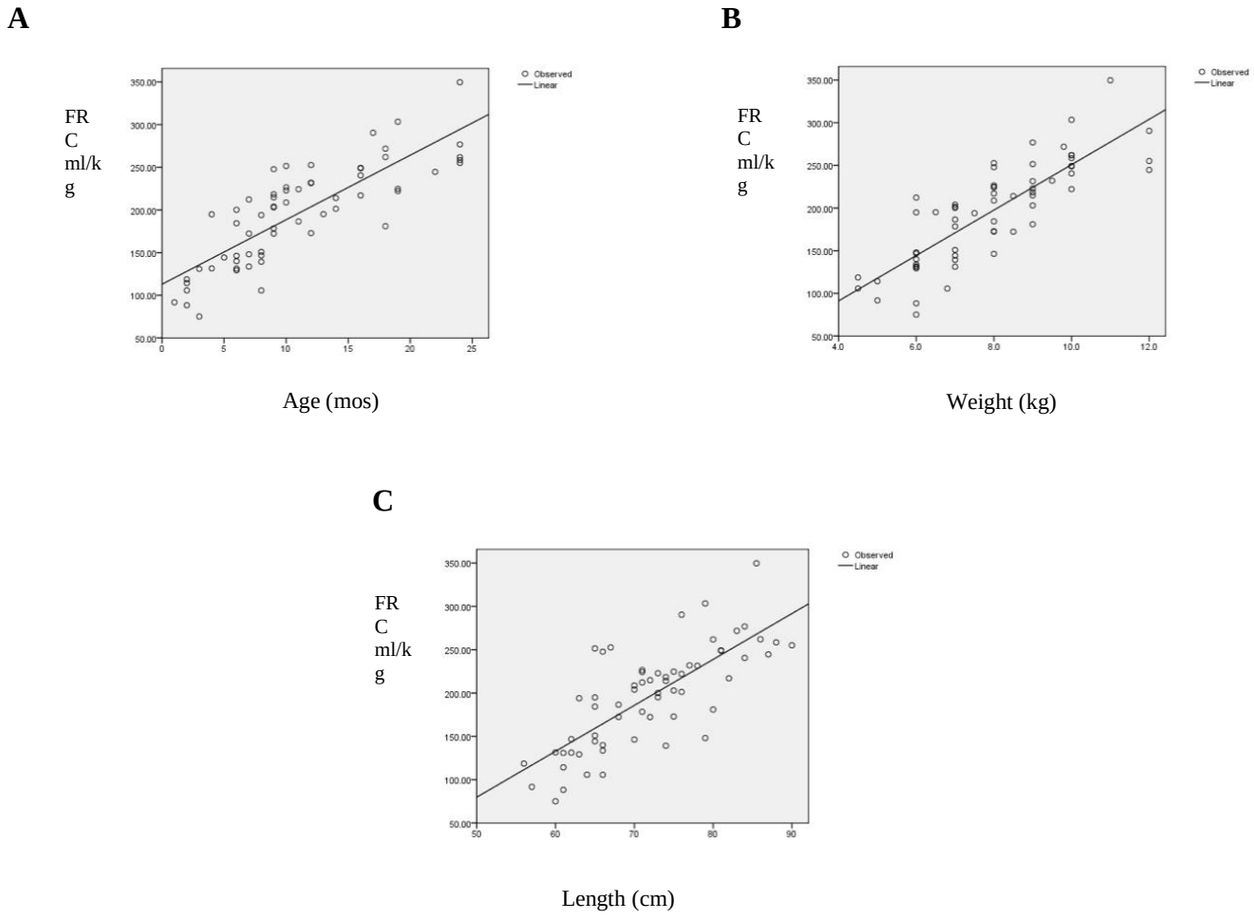

Figure 4.
Scatter plot of FRC against A. Age B. Weight C. Length
Solid line indicating the line of best fit of the scatter of the points

Table 2. FRC in Healthy Infants: Correlation with Background Characteristics

Characteristics		Mean FRC (DS subtracted), ml/kg R‡ or Mean (sd)	p-value
Gender	Male (n = 31)	24.95 (4.58)	0.49¶ (NS)
	Female (n = 31)	24.16 (4.27)	
Age, mos (n = 62)		0.820	0.00§
Weight, kg (n = 62)		0.830	0.00§
Length, cm (n = 62)		0.758	0.00§

‡ – Pearson's Product Moment Coefficient of Correlation
¶ – using t-test for comparing means
§ – using test for the significance of R
[NS] – not significant
* - significant at the 0.05 level of significance
** - significant at the 0.01 level of significance

DISCUSSION

Objective measurement of pulmonary function in infants are very limited since this age group are uncooperative and usually requires sedation. One of the procedures that can be applied in this age group is the determination of Functional Residual Capacity (FRC) which requires infants to be in quiet sleep.

Several studies have reported values for Functional Residual Capacity (FRC) in healthy infants using plethysmography.(2,8) This is the first local data gathered to establish reference values of FRC using the recently available equipment at the Philippine Children's Medical Center and the first in this country.

To produce a reliable data, possible causes of discrepancies between the reported values of FRC as discussed by Hulskamp et al. were considered.(8) Equipment protocol was strictly observed, including subtraction of compressible deadspace according to the ATS-ERS guidelines.(3)

When adjusted for weight, reported mean (SD) FRC was 24.56 ml/kg (4.41), with a range from 12.5-35.4 ml/kg; 95th CI 23.44-25.68 ml/kg. This was comparable to results from previous compilation of reference data. (8) The study by Hulskamp, however had lower values compared to this study which was reported at 19.6 ml/kg (3.4).This discrepancy may be partially attributed to variations in age with relatively few infants being studied during the first few months of life in this present study. Although Hulskamp's study had almost the same age range which is 1-21 months, the scatter of age groups were not reported in detail. In this study, the bulk of the age group falls under ages 9-12 months. Other subject characteristics may be taken into consideration such as the selection of healthy infants. This study recruited subjects from the community and represented an unbiased sample of healthy infants in the Philippines. Inclusion of infants in this study was based on the ATS/ERS guidelines as compared to the study by Hulskamp et al. where infants with history of wheezing were not excluded thus, may explain the difference in the values obtained.

According to the ATS/ERS guidelines on standards for infant respiratory function testing, dead space of the mask should be measured by water displacement and 50% of this value subtracted to take into account the space occupied by the infant's face and the putty film. (3) Compared to the dead space accounted for in the study by Hulskamp, 11.8-14.3 ml were subtracted from the actual FRC compared to the

7.5-10 ml in our study. The higher values of dead space subtracted in their study may explain the lower FRC per kg body weight reported. Dead space from the tubings connecting the pneumotachometer and mouth pressure port to the transducers were all accounted for in the recent software, thus only the dead space from the mask were substracted. Another factor which might have affected the variation in reported values of FRC is feeding prior to sedation. Although the ATS/ERS recommend that the infant may not be placed on NPO since tests tend to be more successful if the infant is fed (9), feeding was witheld 4-6 hours in accordance to the guidelines for monitoring pediatric patients who are sedated. (7) Previous studies have not mentioned withholding feeding prior to sedation. There is limited data that discusses the influence of feeding in pulmonary function tests in infants, but this factor may be considered. A study by Pitcher-Wilmott et al. (20) reported a significant decrease in FRC fifteen minutes after feeding.

Previous studies have established the correlation between FRC and age, weight, and length. Among the mentioned variables, length has been reported to be most correlated with FRC. In this study however, weight (R=0.830) was found to be most correlated compared to age (R=0.820) and length (R=0.758). Previous prediction equations have not included age as a variable, which was found to be the variable more correlated to FRC than length in this study. This study showed that as age, length, and weight increases, FRC also increases. Of all the studies of FRC in infants and preschool children, only those by Taussig et al. (21) and Wall et al. (22) have demonstrated significant differences due to gender where FRC in males exceeded that in females at any given length.

CONCLUSIONS/RECOMMENDATIONS

The FRC values obtained in this study is 24.56 ml/kg (4.41). There is a direct correlation of FRC with age, weight, and length. The result of this study was comparable to other studies and may be used as reference value for healthy infants. The findings support the assumption that decreased values of FRC in healthy infants reflect technological advances and improvement in equipment ptotocols.

Although the computed sample size achieved 80% power, similar studies may be explored in the future using a larger sample size in order to increase the power of the study.

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