EVALUATION OF GROWTH IN NEONATAL INTENSIVE CARE UNIT (NICU) INFANTS WITH INTESTINAL FAILURE OR FEEDING INTOLERANCE

A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS

FOR THE DEGREE OF MASTER OF SCIENCE

IN THE GRADUATE SCHOOL OF THE

TEXAS WOMAN'S UNIVERSITY

COLLEGE OF HEALTH SCIENCES

TEXAS WOMAN'S UNIVERSITY

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DECEMBER 2015

ABSTRACT

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EVALUATION OF GROWTH IN NEONATAL INTENSIVE CARE UNIT (NICU) INFANTS WITH INTESTINAL FAILURE OR FEEDING INTOLERANCE

DECEMBER 2015

The purpose of this study was to evaluate growth velocities of infants with intestinal failure or feeding intolerance for the first 84 days of life and determine birth and 40 week post-menstrual age (PMA) percentiles using the Olsen growth curves.

Participants included 167 infants ages 0-3 months followed by the Texas Children's Hospital Neonatal Intensive Care Unit (NICU) Intestinal Rehabilitation Team with intestinal failure or feeding intolerance. Weekly weight, length, and head circumference growth velocities were calculated and growth data were compared to the Olsen growth standards.

Weight, length, and head circumference percentiles significantly decreased from birth to 40 weeks PMA or discharge ($P < 0.001$). Average growth velocities (weight gain 19.97 g/week, length 0.81 cm/week, head circumference 0.52 cm/week) fluctuated and all were below expected norms. Infants with intestinal failure or feeding intolerance were uniquely nutritionally compromised putting them at high risk for extrauterine growth restriction.

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CHAPTER I

INTRODUCTION

Evaluating Growth Patterns in Infants

The Centers for Disease Control and Prevention (CDC) have established growth reference charts, which consist of a series of percentile curves that illustrate the distribution of body measurements in children. The National Center for Health Statistics (NCHS) developed these percentile curves in 1977 (Kuczmarski et al., 2002) with the most recent revision completed in 2000 (Centers for Disease Control and Prevention, 2009). The gender-specific charts for infants birth to 36 months of age include weight-for-age, recumbent length-for-age, head circumference-for-age, and weight-for-length. The data for the CDC growth charts were collected from cross-sectional representative National Health Examination Surveys (NHES II and NHES III), National Health and Nutrition Survey (NHANES I) as well as from the infant population from Fels Longitudinal Growth Study (Centers for Disease Control and Prevention, 2009). The charts can be used to serve as a reference to evaluate physical size and growth, as well as to identify those with greater health risks. These charts evaluate how children in the United States grew during a specific time period (Grummer-Strawn, Reinold, & Krebs, 2010). Infants at the third percentile or below as well as infants at the 97th percentile and above are deemed at health and nutritional risk.

In 2006 the World Health Organization (WHO) released new growth standards for children ages 0-59 months. The WHO growth charts are standards representing how children should grow under optimal environmental and health conditions. Data collected were based on healthy children living under conditions likely to favor achievement of full genetic growth potential. Subjects were recruited from the following six counties: Brazil, Ghana, India, Norway, Oman and the United States (Grummer-Strawn et al., 2010). Longitudinal data were collected at birth, 1 week, and every 2 weeks for the first 2 months after birth, monthly through age 12 months, and bimonthly from age 14 to 24 months. For children 2-5 years of age, data were collected cross-sectionally by measuring groups of children at specific ages and specific points in time. The WHO established the breastfed child as the normative model for growth and development. All infants in the WHO sample were breastfed at least until 12 months of age and solely breastfed for at least 4 months with introduction of complementary foods by at least 6 months. Similar to the CDC growth charts, the WHO growth standard charts are available for weight-for-age, length-for-age, head circumference-for-age, and weight-for-length. The WHO also includes a chart for body mass index (BMI)-for-age starting at birth. BMI charts, however, are not recommended for clinical use before two years of age (Flaherty-Hewitt, 2014). According to the WHO standards, cutoffs of ± 2 standard deviations, corresponding to the 2.3rd and 97.7th percentiles, are used to define abnormal growth (Grummer-Strawn et al., 2010).

The CDC recommends the use of the 2006 WHO international growth reference charts for infants and children ages 0-2 years (Grummer-Strawn et al., 2010). Whereas the WHO charts describe growth of healthy children in optimal conditions, the 2000 CDC growth charts are a growth reference, not a standard, and describe how certain children grew in a particular place and time. Clinicians use these CDC growth charts in practice to assess normative size and growth of maturing infants, children and adolescents.

In the Neonatal Intensive Care Unit (NICU) setting, intrauterine growth curves are the standard for assessing weight, length, and head circumference of preterm infants (Olsen, Groveman, Lawson, Clark, & Zemel, 2010). New intrauterine gender-specific growth curves, known as the Olsen growth curves, were validated and published in 2010. Intrauterine curves, which are based on cross-sectional birth data, differ from longitudinal postnatal curves in that these illustrate ideal fetal growth versus actual growth of preterm infants over time. The Olsen growth curves provide clinicians with updated data drawn from a diverse population within the United States.

High-risk infants are commonly classified as small for gestational age (SGA) or large for gestational age (LGA) in the NICU. Infants who are SGA are at risk for adverse outcomes such as inadequate growth as well as neurodevelopmental delays. LGA infants are at risk for early hypoglycemia and are more likely to develop metabolic syndrome later in life (Olsen et al., 2010). Prior to the development of the Olsen curves, many infants were inaccurately classified as appropriate for gestational age (AGA) when they were in fact SGA or LGA. Therefore, it is possible that some of these infants may not

have been evaluated for further health risks. With the development of the updated Olsen curves, clinicians are now able to appropriately assess the growth of preterm infants in the NICU.

The Olsen growth charts measure gender-specific weight-for-age, length-for-age, and head circumference-for-age in preterm infants ages 22 to 42 weeks at birth. Gestational age is calculated by the date of the last menstrual period but also by examination of the newborn infant using the Dubowitz or Ballard score (Rosenberg et al., 2009). The cutoffs for the Olsen curves are the 10^{th} and 90^{th} percentiles. Infants are classified as SGA, with the Olsen curves, if they are less than the 10^{th} percentile while those that are greater than the 90^{th} percentile are classified as LGA (*Figure 1*). Infants that are between the 10^{th} and 90^{th} percentile are classified as AGA Typically, when an infant is SGA or LGA, this categorization refers to weight-for-age unless otherwise noted. Nevertheless, an infant may be categorized as LGA by weight-for-age but AGA by length-for-age.

Weight and length are important anthropometric measurements in infants to evaluate growth. Weight is an acute marker of nutritional status while longitudinal growth reflects chronic nutritional status and may be associated with the overall health status of an infant (Rogol, Clark, & Roemmich, 2000). According to Rogol et al., “a child’s growth can be compared with that of his or her peers by referring to the norm on an appropriate growth chart. More important, the longitudinal measurements of a child’s growth are a dynamic statement of his or her general condition or health.”

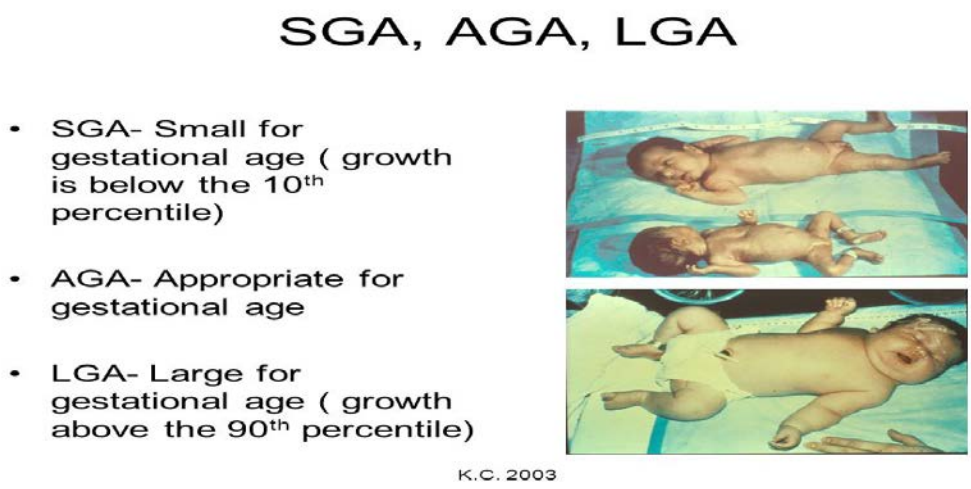

Figure 1: Appropriate, small and large sized infants

K.C. 2003 The Newborn Assessment And The Normal Newborn. www.slideplayer.com

Statement of the Problem

Although nutritional management strategies to promote appropriate growth in infants with intestinal failure or feeding intolerance have been suggested, little is known about the usual growth patterns for this infant population. Growth of the infant, as reflected by normal weight gain and growth velocity for age when orally and/or enterally fed, is one of the best indicators of full recovery of intestinal function (Goulet, 2010). However, no data exists documenting the average growth of neonates with intestinal failure or feeding intolerance. Furthermore, studies have not assessed the growth trends of these infants in comparison to standardized growth reference charts.

The Purpose of this Study

The purpose of this study was to assess the growth patterns of infants with intestinal failure or feeding intolerance. Data on the growth of these infants was obtained to provide clinicians with a resource for future evaluation of infants with intestinal failure or feeding intolerance. With an understanding of actual growth patterns of infants with intestinal failure or feeding intolerance in the future, nutritional care plans could be better tailored to improve outcomes. Infant growth was expected to resemble a normal distribution; however, if curves were positively skewed, the population was below the mean growth for infants therefore, this study was undertaken to establish and mean growth pattern for infants with feeding intolerance or intestinal failure. In the future, these mean daily weight growth patterns would allow clinicians to determine how well an infant with intestinal failure or feeding intolerance was growing and thriving compared to an infant without intestinal complications.

Null Hypotheses

The null hypotheses were: (1) There will be no difference in the growth of infants with intestinal failure and feeding intolerances for the first 3 months of life compared to the growth reference standards. (2) There will be no change in growth percentile at birth and growth percentile at 40 weeks PMA of infants with intestinal failure and feeding intolerances. (3) There will be no relationship between growth velocities and change in growth percentile over the period of hospitalization.

CHAPTER II

LITERATURE REVIEW

History of the Intensive Care Unit

The Intensive Care Unit (ICU) is about 60 years old. Development of the ICU can be attributed to the polio epidemic of 1952 that devastated Copenhagen, Denmark (Kelly, Fong, Hirsch, & Nolan, 2014). During this epidemic, hundreds of people experienced respiratory failure secondary to respiratory muscle paralysis and bulbar palsy. Many of these patients required artificial ventilation for consecutive weeks. During this period, the hospital located in Copenhagen had only one tank respirator along with six cuirass respirators. Without the means to provide proper care, the mortality rate for the polio victims was 85-90%. According to Kelly et al., the chief physician at the Blegdam Hospital, Professor Lassen, strongly desired to provide adequate treatment for every polio victim despite the insufficient supply of respirators. He therefore consulted with Dr. Bjorn Isben, a Copenhagen anesthesiologist. Dr. Isben had the idea of setting aside an entire ward specifically to provide one on one care for all the patients. With a dedicated ward, the polio patients were able to receive manual ventilation and the care they required. The survival rate for the victims more than doubled from 10-25% to a 60% survival rate. Thus, in December 1953, the specialty of the Intensive Care Unit was born.

During the 1960's in the United States (U.S.), Max Harry Weil established a 4-bed shock ward at Los Angeles County University of Southern California Medical Center

(Kelly et al., 2014). Max Henry Weil is known as the father of modern intensive care. Over the next 20 years the intensive care unit began to develop into the multidisciplinary practice that it is today. Most hospitals now have ICUs with dedicated physicians, nurses, physiotherapists, pharmacists, dietitians, technicians, and radiologists. Medical interventions in the ICU are much more intensive than those in the general ward. One of the most notable functions of the ICU that sets it apart from the other wards is the ability to support multiple organ systems due to critical illness both temporarily and in some cases permanently.

With the rise in the aging population, along with a rise in obesity and other co-morbidities, the demanding need of the ICU continues to rise exponentially (Kelly et al., 2014). The development of the ICU has proven to be a vital part of the hospital. Reduced mortality rates, length of stay, and fewer complications are associated with admitting high-risk patents to the ICU. For example, cardiac patients admitted to the ICU rather than regular wards have death rates of less than 2% (Kelly et al., 2014).

History of Neonatal Care

The 1950s proved to be vital part of medical history. Not only was the ICU established in this decade, but also the idea of infant care and assessment began to gain attention in the medical world. According to Lester and Tronick, infants were once viewed as unstructured and lacking in sensory capabilities. During this time, there were no infant examinations because there was ‘nothing’ to exam (Lester, Tronick, 2004). In the 1950s and on into the 1990s, developmental researchers continually demonstrated that

infants are highly complex and functioning. Scientists began extensive research on the infant's reflexes and brain activity. Once scientists discovered that infants function not only on a neurologic level, but that their brain was active, an examination of the infant's neurologic status became a standard of care. Research soon showed that neonates were capable of complex, highly differentiated hand movements, discrimination of sounds, instrumental conditioning, affective behaviors in response to stimuli, detection of odors, coordination of movement and speech, and different cry patterns (Lester, Tronick, 2004). The recognition of infant competence led to the establishment of different infant assessments as a standard of care to evaluate each neonate's individual functional status. With increased sophistication in the care of neonates and the increased ability to assess their functional status, the idea of a specific intensive care unit for infants arose in 1960 (Gartner et al., 2001). With the establishment of the Neonatal Intensive Care Unit (NICU), there has been a steady decrease in infant mortality. Doctors could now save lives of many premature or critically ill newborns who a decade earlier would not have survived.

Because they are deemed as a necessity, today mothers everywhere have access to a NICU. Widespread access to NICUs is based on regionalization. "Under regionalization, centrally situated hospitals maintain one or more NICU available to all babies of high-risk mothers and to critically ill newborns referred from other hospitals located within a certain area" (Gartner et al., 2001). High-risk mothers are those at risk for giving birth prematurely or giving birth to a low birth weight infant. Some examples

of high-risk mothers are: teenage pregnancies, mothers who receive little or no prenatal care, substance abuse including smoking and drinking, as well as a previous premature or low birth weight delivery (Gartner et al., 2001). Regardless of the overwhelming advances in neonatal care, the birth rate of low weight infants has remained virtually constant over the past 20 years. The survival rate however, has continued to increase (Gartner et al., 2001). As the number of NICUs increased, the importance of birth weight and neonatal growth as crucial markers directly related to the health of an infant became apparent. The Olson charts were developed to monitor average growth in infants without intestinal failure; however, tools to monitor growth of infants with intestinal failure and feeding intolerance were lacking.

Intestinal Physiology

The intestines are a complex organ system responsible for absorption of nutrients, which is vital for the growth and development of neonates. The intestines are responsible for metabolizing macronutrients as well as fluid, vitamins, and minerals (Beattie, Barclay, & Wilson, 2010). The primary function of the gastrointestinal tract is to regulate the influx of calories, fluids, and nutrients to provide growth in children and weight maintenance in adults. The small intestine is made up of three distinct sections: the duodenum, jejunum, and ileum. Each section differs in anatomy, motility, secretion, digestion, and absorption (Nelms, Sucher, Lacey, Roth, 2011). The structure of the small intestine results in a highly functional intestine that provides maximum surface area for complete digestion and absorption of most food.

Understanding the specialized physiological functions of the proximal and distal bowel (Figure 2) allows health care practitioners to better treat the biological imbalances that occur when part of the bowel is missing or not functioning properly. The primary organs of the upper digestive tract and digestive functions are illustrated in Figure 2. The duodenum and jejunum are responsible for both carbohydrate and protein digestion (Jeejeebhoy, 2002). Calcium uptake occurs primarily in the duodenum associated with a vitamin D-dependent protein, calbindin, found in duodenal enterocytes (Carlson, Chang, Nandivada, Cowan, Pruder, 2013). The duodenum and jejunum can perform each other's role in digestion and absorption (Nelms et al., 2011). Digestion of fat and absorption of fat-soluble vitamins and vitamin B_{12} takes place in the ileum (Jeejeebhoy, 2002). Most fluids and electrolytes are absorbed in the ileum such as water, sodium, and potassium; however, bicarbonate is secreted (Carlson et al., 2013). The small intestine is very adaptive and efficient. According to Beattie et al., more than 50% of the small intestine must be removed before the absorption, electrolyte balance, and growth of a full term infant are compromised. As mentioned earlier, the duodenum and jejunum are very adaptive and can fill each other's role. The ileum, however, is only adaptive to a certain point. Most nutrients can be absorbed by the ileum if they remain in this part of the intestine long enough. Generally, if only sections of the proximal intestine are removed the ileum will adapt to function as the jejunum and patients are less likely to require prolonged parenteral nutrition (Carlson et al., 2013). On the other hand, the jejunum is not able to absorb bile salts or produce vitamin B_{12} specific receptor sites that exist in the

ileum. This exception to the small intestine's adaptability makes significant ileal resection more difficult to treat and likely to lead to prolonged parenteral nutrition.

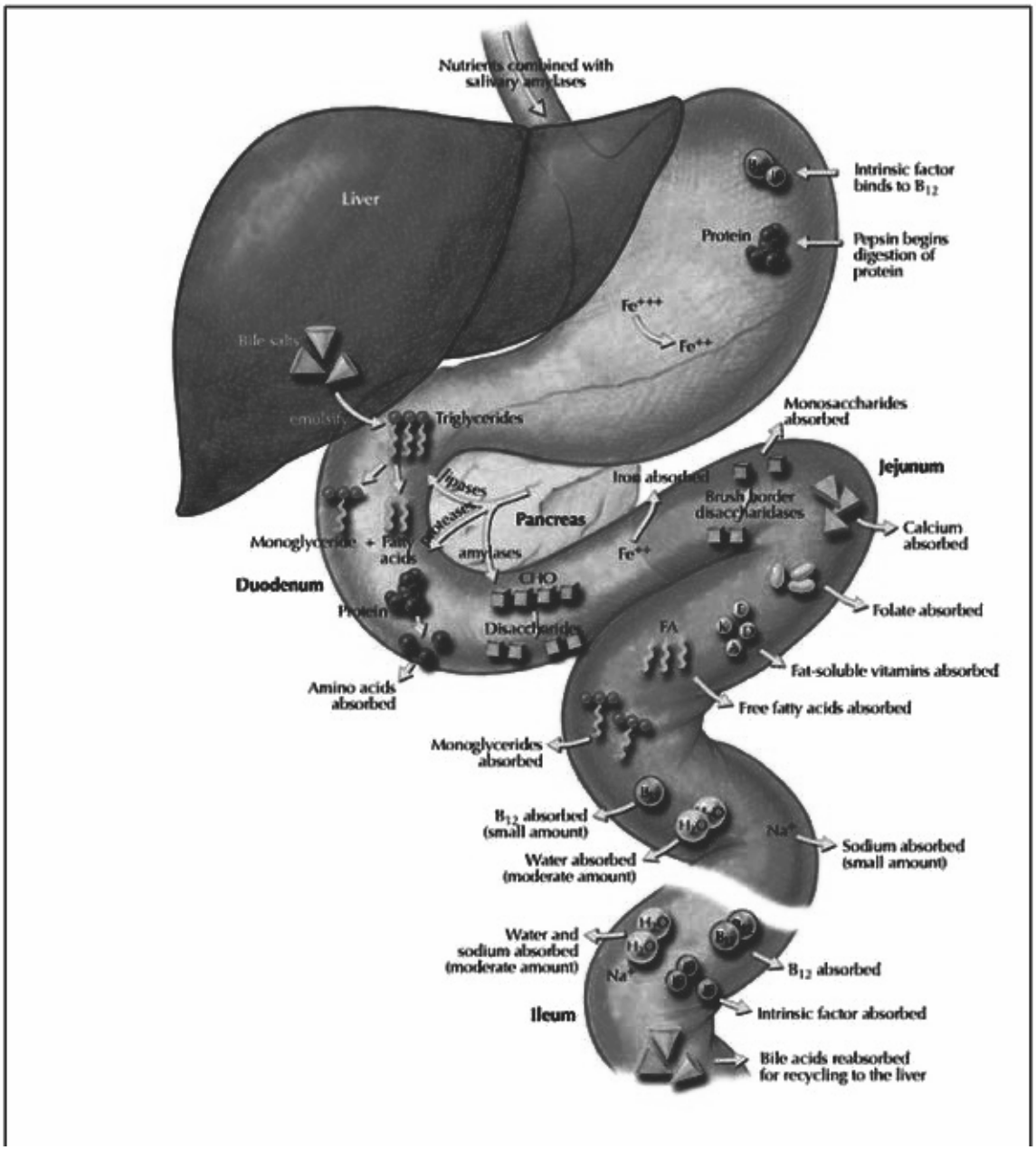

*Figure 2:*The primary organs of the upper digestive tract, including the esophagus, stomach, and small intestine (JeeJeebhoy, 2012)

Intestinal Failure

Intestinal failure is the result of a critical reduction in the gut's ability to digest and absorb nutrients. The term 'intestinal failure' was first coined in 1980 (Carlson et al., 2013). Most practitioners define intestinal failure in neonates as an "inadequate functional gastrointestinal tract to sustain growth and development without supplemental parenteral nutrition" (Carlson et al., 2013, pp. 192). Intestinal failure occurs when a section of the small intestine does not function properly; that is, it is insufficient ability to perform normal function or not present secondary to surgery. Decreased function leads to failure to thrive, restricted growth, and developmental issues in the neonate. Typically, the small intestine can adapt to absorb nutrients but this adaption takes time and may be hindered by infection. When more than 50% of the small intestine is removed, significant reduction in both digestion and absorption occur (Nelms, Sucher, Lacey, & Roth, 2011). A fluctuated of abnormalities can cause intestinal failure including congenital defects, mucosal disease, dysmotility disorders, and maldigestive disorders (Carlson et al., 2013). According to O'Keffe et al., intestinal failure results from "obstruction, dysmotility, surgical resection, congenital defect, or disease associated loss of absorption and is characterized by the inability to maintain protein-energy, fluid, electrolyte, or micronutrient balance when on a conventionally accepted normal diet" (Carlson et al., 2013).

The most common form of intestinal failure is Short Bowel Syndrome (SBS) occurring in about 5 babies per million live births (Goulet, 2010). SBS occurs when a

significant part of the intestine is resected, leading to malabsorption due to functional loss of gut mucosal absorptive surface area (Carlson et al., 2013). The malabsorption state, which results from SBS, requires nutrition and hydration to be supplemented via parenteral nutrition (Beattie et al., 2010). Necrotizing enterocolitis (NEC) is the most common cause of SBS and intestinal failure (Carlson et al., 2013). This inflammatory condition of unknown etiology is infamous for affecting the preterm, low-birth weight infant (Beattie et al., 2010) and often requires significant bowel resection. Other common causes and prevalence of short bowel syndrome in the United States are shown in Figure 3 and include: NEC, resection following intestinal atresia, gastroschisis, or other congenital malformation including midgut volvulus from malrotation (Goulet, 2010).

Infants with SBS and intestinal failure are uniquely nutritionally challenged. These infants often need prolonged parental nutrition. Weaning babies with SBS and intestinal failure from parenteral nutrition to enteral nutrition can take up to 2 years or more and is most dependent on the length of bowel remaining (Beattie et al., 2010).

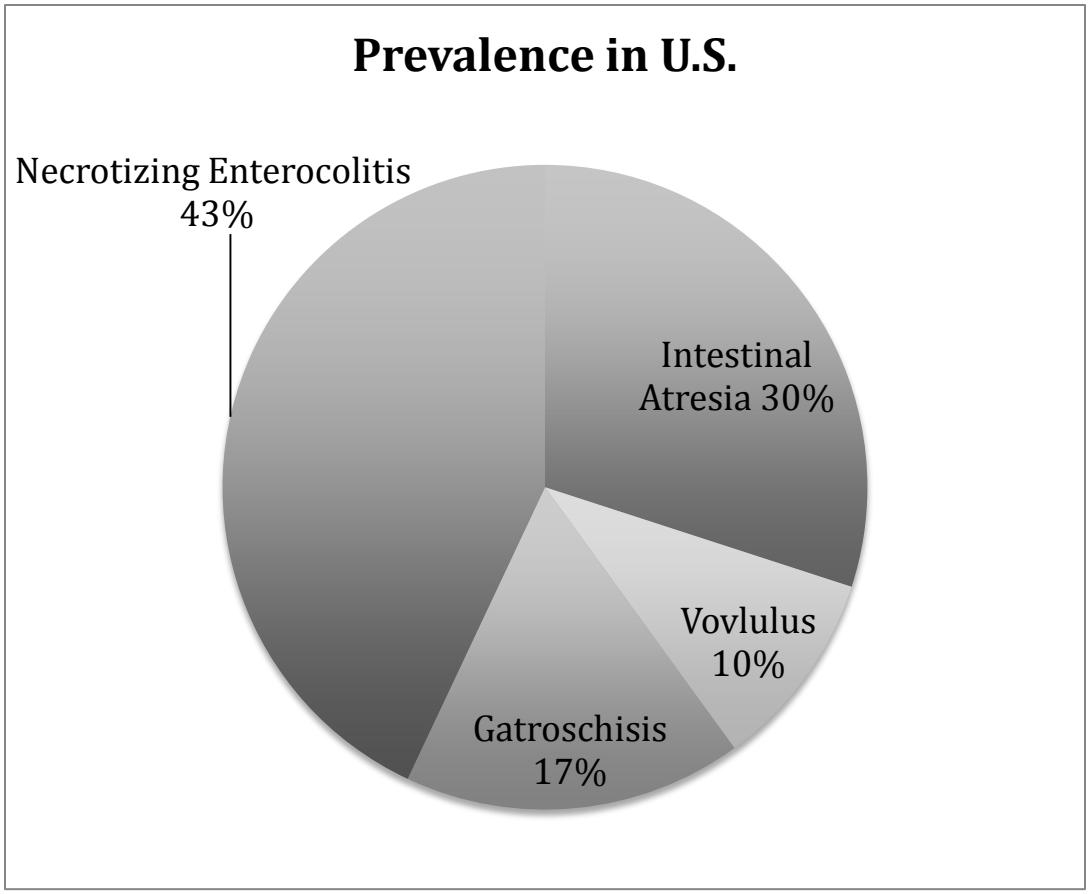

Figure 3: Common causes of Short Bowel Syndrome (SBS)

Feeding Intolerance

According to Surmeli-Onay, Korkmaz, Yigit, and Yurdakok, feeding intolerance is defined as "gastric residual volume of more than 50% of the previous feeding volume, emesis, abdominal distension or both of these symptoms and a decrease, delay or discontinuation of enteral feedings" (Surmeli-Onay et al., 2013, pp 529). Feeding intolerance is the most common gastrointestinal complication seen in preterm infants. This intolerance usually results in withholding enteral nutrition for a period of time,

which may further stunt the growth process unless the infant is supported with parenteral nutrition. The exact pathophysiology of feeding intolerance is multi-factorial in infants and may be due to immature gastrointestinal motility, delayed gastric emptying, or immature digestion and absorption, all of which are exaggerated in intestinal failure (Jadcherla and Lliegman, 2002).

Neonatal Nutritional Care

The current treatment for intestinal failure and feeding intolerance differs by individual and can vary significantly depending on the severity. Almost all cases require total parenteral nutrition (TPN) as the initial treatment (Goulet, 2010). Parenteral nutrition is the administration of nutrition directly into the circulatory system through the veins. This type of nutrition does not stimulate the gut. Parenteral nutrition is mandatory to maintain adequate hydration and nutrition to sustain life in the presence of intestinal failure or feeding intolerance, however, prolonged parenteral nutrition is also associated with severe complications such as sepsis and liver failure. Though the first goal in patient care is to decrease the amount of peripheral or intravenous nutrition while increasing the amount of enteral nutrition, some patients may require parenteral nutrition permanently. Enteral nutrition refers to nutrition given via feeding tube, catheter, or stoma that delivers nutrients into the gastrointestinal tract (Nelms et al., 2011). Enteral nutrition stimulates the gut and clinicians hope that over time the small intestine will adapt to allow for enteral nutrition. Surgery may be required if steady progress is not made towards the decrease in parenteral nutrition and increase in enteral or oral nutrition. Intestinal and or

liver transplantation can be performed for severe forms of intestinal failure or when severe liver disease has resulted from long-term parenteral nutrition.

Historical Research

Since the inception of the NICU scientific investigation on intestinal failure in infants has grown rapidly. The exponential growth pattern in number of scientific research articles regarding intestinal failure in infants is shown in Figure 4. Increasing research on infant intestinal failure is likely to continue as medicine and research advances improve the outcome of this population.

Figure 4: Historical research

CHAPTER III

METHODS

Participants

Participants included infants ages 0-3 months who were followed by the Texas Children's Hospital (TCH) Neonatal Intensive Care Unit (NICU) Intestinal Rehabilitation Team. Infants were enrolled from April 2012 until October 2014. Data were recorded from the electronic medical records of these infants who were consecutively followed during hospital admission. Criteria for assignment to the Intestinal Rehabilitation Team included: SBS, feeding intolerance, prolonged parenteral nutrition, or referral by primary physician Because the same specialized nutrition support team followed all infants using a common protocol, nutrition practices were standardized and were similar among subjects. There were no control subjects or opportunities for randomization. Patient identification was coded, assigning a study identification (ID) number to each subject in order to protect patient privacy. On all data spreadsheets and documents, only the patient's coded ID number was used for identification purposes. The Institutional Review Boards of Baylor College of Medicine and Affiliated Hospitals as well as Texas Woman's University approved this study.

Procedures

The TCH NICU Intestinal Rehabilitation Team was established on April 3, 2012. Data were retrospectively collected on all patients who had been followed by the team

since its inception. All activities involved in this protocol were observational only; there were no interventions. Data collected from the medical records included: medical record number, gender, race, gestational age at birth, date of admission to TCH NICU, date of discharge or death, length of stay, medical and surgical history, primary diagnosis, and anthropometrics. The collected data as well as weekly anthropometrics and growth velocities were recorded on an excel spreadsheet (Appendix A). Some of the collected data were prior to the time the patient was seen by the Intestinal Rehabilitation Team such as birth weight or previous lab values. Outcomes included growth velocities, and percentile ranking at birth, 40 weeks post menstrual age (PMA), and discharge or death. PMA was used for this study because it takes into account gestational age plus time elapsed from birth.

Data Collection

Data on the growth of the participants was obtained from Texas Children's Hospital's electronic medical records. Weight was recorded daily while length and head circumference were recorded weekly. Bedside nurses obtained weight using digital baby scales. Measurements for length and head circumference were obtained using a length board and tape measure, respectively. A cutoff of 3 months, day of life 84, was used when calculating weekly growth velocities.

Growth velocities were calculated by first recording the weight, length, and head circumference of all the subjects every 7 days starting from birth until day of life 84 in order to compare to published standards (Tsang, 1993). Weekly weight, length, and head

circumference velocities were then calculated to determine average growth over the past 7 days. Weekly weight gain velocity was calculated by subtracting the previous week's weight from the current weight and dividing by seven days to determine average g/d weight gain. If the infant was less than two kg in weight, the formula was slightly altered by taking the previous week's weight divided by one thousand to determine g/kg/d weight gain. Then the original velocity formula was divided by the g/kg/d quotient. Length velocities were also calculated weekly by subtracting the prior week's length from the current week's length to determine cm/wk average length gain. Similarly, weekly head circumference was calculated by subtracting the previous week's head circumference from the current head circumference to determine cm/wk average head circumference gain.

Using the infants' date of birth and gestational age at birth, the number of weeks from birth to 40 weeks PMA, number of days from birth to PMA, and the date at which the infant was 40 weeks PMA were calculated. Date of birth plus number of days after birth until the infant was 40 weeks PMA represented the date at which the infant was 40 weeks PMA. This date was used to calculate the growth velocities from birth to 40 weeks PMA. Subtracting the infant's birth weight from weight at 40 weeks PMA and dividing that number by the number of days from birth to 40 weeks PMA was used to calculate weight velocity from birth to 40 weeks PMA. Birth length subtracted from length at 40 weeks PMA and then divided by the number of weeks from birth to 40 weeks PMA represented the infant's length velocity from birth to 40 weeks PMA. Head circumference

growth velocity was calculated by subtracting the head circumference at birth from the head circumference at 40 weeks PMA and then divided by the number of weeks from birth to 40 weeks PMA.

The date of discharge or death was recorded and used to calculate the number of days and weeks from birth to discharge or death. This data was used to calculate each infant's growth velocity from birth until discharge death. Subtracting birth weight from weight at discharge or death, and dividing that number by the number of days from birth to discharge or death, determined the growth velocity in weight from birth until discharge or death (g/d). Length and head circumference were computed using the same formula: subtracting the birth measurement from the measurement at death or discharge and dividing that number by the number of weeks from birth to discharge or death (cm/wk).

A term infant is an infant who is born at 37 weeks gestational age or later (Paterson & Redpath, 2013). Any infant that is born prior to 37 weeks gestational age is considered preterm. The Olsen charts were created specifically for preterm infants but are validated for infants 22-42 weeks gestational age. All participants in this study meet the criteria to be compared to the Olsen curves to obtain percentiles. Each infant's growth percentiles for weight, length, and head circumference were determined by comparison to the Olsen curves.

Rather than estimating an infant's percentile between two percentile rankings, two formulas allowed an exact percentile to be determined by using the upper and lower limits of each percentile group. For example, if a 25 wk gestational age infant's weight of

575g at birth fell between the 3rd and 10th percentiles, the upper limit (626g is 10th %ile) and lower limit (550g is 3rd %ile) of weight would be used in the formula. First, a slope was found by subtracting the lower limit value from the upper limit value and dividing it by the difference found when the lower limit percentile was subtracted from the upper limit percentile. When this quotient was subtracted from the lower limit value and then multiplied by the lower limit percentile, a slope was found. The value of the slope was used to find an exact percentile. Exact percentiles were calculated using the following formula: (anthropometric measurement – slope) / ((upper limit value – lower limit value) / (upper limit percentile – lower limit percentile)). Rather than estimating an infant's percentile to be between the 25th and 50th percentile, this formula allowed an exact percentile, for example 47.7, to be determined.

Each infant's growth percentiles for weight, length, and head circumference were found by comparing them to the growth charts shown in Table 1 and Table 2 created by Olsen et al. Rather than rounding to the nearest percentile, an exact percentile was determined.

Table 1
Male Birth Weight, Length, and Head Circumference Percentiles by Gestational Age

GA, wk	*n*	Birth Size		Percentile						
		Mean	SD	3rd	10th	25th	50th	75th	90th	97th
Weight, g										
23	153	622	74	NA[a]	509	563	621	677	727	NA[a]
24	451	689	96	497	561	623	690	756	813	869
25	722	777	116	550	626	700	780	857	926	992
26	881	888	145	613	704	794	890	983	1065	1145
27	1030	1001	170	680	789	895	1009	1120	1218	1312
28	1281	1138	203	758	884	1007	1141	1271	1385	1496
29	1505	1277	218	845	988	1128	1280	1429	1560	1688
30	1992	1435	261	955	1114	1272	1443	1612	1761	1906
31	2460	1633	275	1093	1267	1441	1631	1818	1984	2147
32	3677	1823	306	1246	1433	1622	1829	2034	2218	2398
33	5014	2058	341	1422	1625	1830	2057	2284	2488	2688
34	7291	2288	364	1589	1810	2035	2285	2536	2763	2987
35	6952	2529	433	1728	1980	2238	2527	2819	3084	3348
36	7011	2798	498	1886	2170	2462	2792	3127	3432	3737
37	6692	3058	518	2103	2401	2708	3056	3411	3736	4060
38	8786	3319	527	2356	2652	2959	3306	3661	3986	4312
39	8324	3476	498	2545	2833	3131	3469	3813	4129	4446
40	7235	3582	493	2666	2950	3245	3579	3919	4232	4545
41	2538	3691	518	2755	3039	3333	3666	4007	4319	4633
Length, cm										
23	153	30.5	1.6	NA[a]	28.0	29.1	30.3	31.4	32.4	NA[a]
24	451	31.5	1.8	27.9	29.1	30.3	31.5	32.8	33.9	34.9
25	722	32.7	2.1	28.8	30.2	31.5	32.9	34.2	35.4	36.5
26	881	34.2	2.2	29.9	31.3	32.8	34.3	35.7	37.0	38.2
27	1030	35.6	2.4	31.0	32.6	34.1	35.7	37.3	38.6	39.8
28	1281	37.2	2.5	32.2	33.9	35.5	37.2	38.8	40.2	41.5
29	1505	38.6	2.5	33.5	35.2	36.9	38.7	40.3	41.7	43.1
30	1992	39.9	2.8	34.8	36.6	38.3	40.1	41.8	43.2	44.6
31	2460	41.5	2.5	36.2	38.0	39.8	41.6	43.3	44.7	46.1
32	3677	42.8	2.7	37.7	39.5	41.2	43.0	44.7	46.1	47.5
33	5014	44.3	2.6	39.1	40.9	42.6	44.4	46.1	47.5	48.9
34	7291	45.6	2.6	40.4	42.2	43.9	45.7	47.4	48.9	50.3
35	6952	46.8	2.7	41.5	43.3	45.0	46.9	48.6	50.2	51.6
36	7011	48.0	2.8	42.7	44.5	46.2	48.1	49.9	51.5	53.0
37	6692	49.2	2.7	44.0	45.7	47.4	49.3	51.1	52.6	54.1
38	8786	50.2	2.7	45.2	46.8	48.5	50.2	52.0	53.5	55.0
39	8324	51.0	2.4	46.1	47.7	49.3	51.0	52.7	54.2	55.6
40	7235	51.6	2.4	46.9	48.4	49.9	51.6	53.2	54.7	56.1
41	2538	52.1	2.4	47.5	49.0	50.5	52.1	53.7	55.1	56.5
HC, cm										
23	153	21.3	1.0	NA[a]	20.0	20.6	21.3	22.0	22.7	NA[a]
24[b]	451	22.2	1.1	20.1	20.8	21.5	22.2	23.0	23.6	24.3
25	722	23.1	1.1	20.9	21.7	22.4	23.2	23.9	24.6	25.3
26	881	24.1	1.3	21.8	22.5	23.3	24.2	25.0	25.7	26.4
27	1030	25.2	1.3	22.6	23.5	24.3	25.2	26.0	26.8	27.6
28	1281	26.1	1.4	23.5	24.3	25.2	26.1	27.1	27.9	28.6
29	1505	27.0	1.4	24.3	25.2	26.1	27.1	28.0	28.8	29.6
30	1992	27.9	1.5	25.1	26.1	27.0	28.0	29.0	29.8	30.6
31	2460	28.9	1.5	26.0	27.0	27.9	28.9	29.9	30.8	31.6
32	3677	29.8	1.5	26.9	27.8	28.8	29.9	30.9	31.8	32.6
33	5014	30.7	1.6	27.7	28.7	29.7	30.8	31.8	32.7	33.6
34	7291	31.6	1.6	28.5	29.5	30.5	31.6	32.7	33.6	34.6
35	6952	32.4	1.6	29.2	30.3	31.3	32.4	33.6	34.5	35.5
36	7011	33.2	1.7	29.9	31.0	32.1	33.2	34.3	35.3	36.3
37	6692	33.8	1.7	30.6	31.7	32.7	33.9	35.0	36.0	36.9
38	8786	34.4	1.7	31.2	32.2	33.2	34.4	35.5	36.4	37.3
39	8324	34.6	1.6	31.5	32.5	33.5	34.6	35.7	36.6	37.6
40	7235	34.8	1.5	31.8	32.8	33.8	34.8	35.9	36.8	37.7
41	2538	35.1	1.5	32.0	33.0	34.0	35.0	36.1	37.0	37.8

Table 2

Female Birth Weight, Length, and Head Circumference Percentiles by Gestational Age

GA, wk	*n*	Birth Size		Percentile						
		Mean	SD	3rd	10th	25th	50th	75th	90th	97th
Weight, g										
23	133	587	80	NA[a]	477	528	584	639	687	NA[a]
24	438	649	89	464	524	585	651	715	772	828
25	603	738	121	511	584	657	737	816	885	953
26	773	822	143	558	645	732	827	921	1004	1085
27	966	934	168	615	719	822	936	1047	1147	1244
28	1187	1058	203	686	807	928	1061	1193	1310	1425
29	1254	1199	226	778	915	1052	1204	1354	1489	1621
30	1606	1376	246	902	1052	1204	1373	1542	1693	1842
31	2044	1548	271	1033	1196	1361	1546	1731	1897	2062
32	3007	1730	300	1177	1352	1530	1731	1933	2116	2297
33	4186	1960	328	1356	1545	1738	1956	2178	2379	2580
34	5936	2194	357	1523	1730	1944	2187	2434	2661	2888
35	5082	2420	440	1626	1869	2123	2413	2711	2985	3261
36	4690	2675	514	1745	2028	2324	2664	3015	3339	3667
37	4372	2946	551	1958	2260	2575	2937	3308	3651	3997
38	5755	3184	512	2235	2526	2829	3173	3525	3847	4172
39	5978	3342	489	2445	2724	3012	3338	3670	3973	4276
40	5529	3461	465	2581	2855	3136	3454	3776	4070	4363
41	1906	3546	477	2660	2933	3214	3530	3851	4142	4433
Length, cm										
23	133	29.9	1.8	NA[a]	27.7	28.7	29.9	31.0	31.9	NA[a]
24	438	31.0	1.7	27.5	28.7	29.8	31.1	32.3	33.3	34.3
25	603	32.3	2.0	28.3	29.7	31.0	32.3	33.6	34.8	35.9
26	773	33.4	2.2	29.2	30.7	32.1	33.6	35.1	36.3	37.4
27	966	35.0	2.3	30.2	31.9	33.4	35.0	36.6	37.9	39.1
28	1187	36.4	2.5	31.4	33.1	34.8	36.5	38.1	39.5	40.8
29	1254	37.8	2.7	32.8	34.6	36.3	38.0	39.7	41.2	42.5
30	1606	39.6	2.6	34.3	36.0	37.7	39.5	41.3	42.7	44.1
31	2044	40.9	2.6	35.7	37.5	39.2	41.0	42.7	44.1	45.5
32	3007	42.1	2.6	37.1	38.9	40.6	42.3	44.0	45.5	46.9
33	4186	43.7	2.6	38.6	40.3	41.9	43.7	45.4	46.9	48.3
34	5936	45.0	2.6	39.8	41.5	43.2	45.0	46.7	48.2	49.7
35	5082	46.0	2.7	40.9	42.6	44.3	46.2	48.0	49.5	51.0
36	4690	47.2	2.8	42.0	43.7	45.5	47.4	49.2	50.8	52.3
37	4372	48.4	2.8	43.2	44.9	46.6	48.5	50.3	51.9	53.4
38	5755	49.5	2.6	44.4	46.1	47.7	49.5	51.2	52.7	54.2
39	5978	50.1	2.5	45.3	46.9	48.5	50.2	51.9	53.3	54.7
40	5529	50.7	2.4	46.1	47.6	49.1	50.8	52.4	53.8	55.1
41	1906	51.3	2.4	46.7	48.2	49.7	51.3	52.8	54.2	55.5
HC, cm										
23	133	20.8	1.2	NA[a]	19.5	20.1	20.9	21.6	22.2	NA[a]
24	438	21.7	1.1	19.6	20.3	21.0	21.8	22.5	23.2	23.8
25	603	22.7	1.2	20.4	21.1	21.9	22.7	23.4	24.1	24.8
26	773	23.5	1.2	21.2	22.0	22.7	23.6	24.4	25.1	25.9
27	966	24.5	1.3	21.9	22.8	23.6	24.5	25.4	26.2	27.0
28	1187	25.5	1.5	22.7	23.7	24.6	25.5	26.5	27.3	28.1
29	1254	26.5	1.5	23.6	24.6	25.5	26.5	27.5	28.4	29.2
30	1606	27.5	1.5	24.6	25.6	26.5	27.5	28.5	29.4	30.2
31	2044	28.4	1.5	25.5	26.5	27.4	28.4	29.4	30.3	31.1
32	3007	29.3	1.5	26.5	27.4	28.3	29.3	30.3	31.2	32.0
33	4186	30.2	1.5	27.3	28.3	29.2	30.2	31.2	32.1	33.0
34	5936	31.1	1.6	28.1	29.1	30.1	31.1	32.2	33.1	34.0
35	5082	31.9	1.6	28.8	29.8	30.8	31.9	33.0	34.0	34.9
36	4690	32.6	1.7	29.4	30.5	31.5	32.7	33.8	34.8	35.8
37	4372	33.3	1.7	30.1	31.1	32.2	33.3	34.4	35.4	36.3
38	5755	33.8	1.6	30.7	31.7	32.7	33.7	34.8	35.7	36.7
39	5978	34.0	1.5	31.1	32.0	33.0	34.0	35.1	36.0	36.9
40	5529	34.2	1.5	31.4	32.3	33.3	34.3	35.3	36.1	37.0
41	1906	34.5	1.5	31.7	32.6	33.5	34.5	35.5	36.3	37.1

When an infant's measurements were off the Olsen growth curves, below the 3rd percentile or above the 97th percentile, a different method was used to compute an exact percentile because either an upper or lower limit was lacking. In these cases, a one-sided z-score was computed using the number of standard deviations the infant was above or below the mean percentile for gestational age. This z-score was then converted to an exact percentile.

Statistical Methods

This study compared the growth of infants' weight-for-age, length-for-age, and head circumference-for-age to the Olsen growth charts. The infant was considered at nutritional risk below the 10th percentile or above the 90th percentile. Infants measured using the Olsen standards were considered SGA if they were less than the 10th percentile weight-for-age while those that were greater than the 90th percentiles were LGA or overweight. Normal growth was also compared to standard goals for extrauterine growth. Normal weight gain velocity should be approximately 15-20 g/kg/day for infants <2kg or 20-30 g/day for infants >2kg. Length and head circumference growth should be approximately 1 cm/wk (Tsang, 1993). In this study relationships among groups were evaluated using general linear modeling in which growth parameters were the primary outcomes. Paired t-tests were calculated to demonstrate the difference in Olsen percentiles at birth and 40 weeks PMA. Statistical significance was defined as $p < 0.05$. Analyses were completed using SPSS for Windows, Version 19.0 (SPSS Inc., Armonk, NY).

CHAPTER IV

RESULTS

One hundred and seventy-six infants were admitted to the Intestinal Rehabilitation Team service at Texas Children's Hospital and enrolled in this study (Figure 5). The average gestational age at birth for this infant population was 31.5 ± 5.4 weeks compared to 40 weeks gestational age, which is considered a full term infant (Table 3). The minimum gestational age was 23 weeks while the maximum was 40 weeks. The mean birth weight was 1723 ± 951.3 g, mean birth length was 39.7 ± 7.3 cm, and mean head circumference was 27.7 ± 4.6 cm. Mean day of life when admitted to the TCH NICU was 17.1 ± 33.2 and the average length of stay was 112.6 ± 79.7 days (Table 3).

Of the 176 participants only 7 met the criteria of being 40 weeks gestational age or greater to be compared to the WHO charts; therefore, for this study only the Olsen growth curves were used to obtain percentiles. One infant, however, died before day of life 7 and 11 were admitted after day of life 84 resulting in 164 participants used for calculating growth velocity (Figure 5). The original 164 participants were used to calculate their birth and 40 week PMA percentiles according to the Olsen charts. One of the infants had no birth anthropometric measurements recorded and was admitted after 40 weeks PMA and therefore was omitted from this part of the study leaving 163 infants used to determine birth anthropometric percentiles. Nine of these infants died before PMA 40, therefore 154 infants were used to determine 40 weeks PMA percentiles.

Gender distribution of participants was primarily males 61.2% (n=102) versus females 37.8% (n=62) (Table 3). The majority of infants were White or Hispanic, followed by Black and Asian (Table 3).

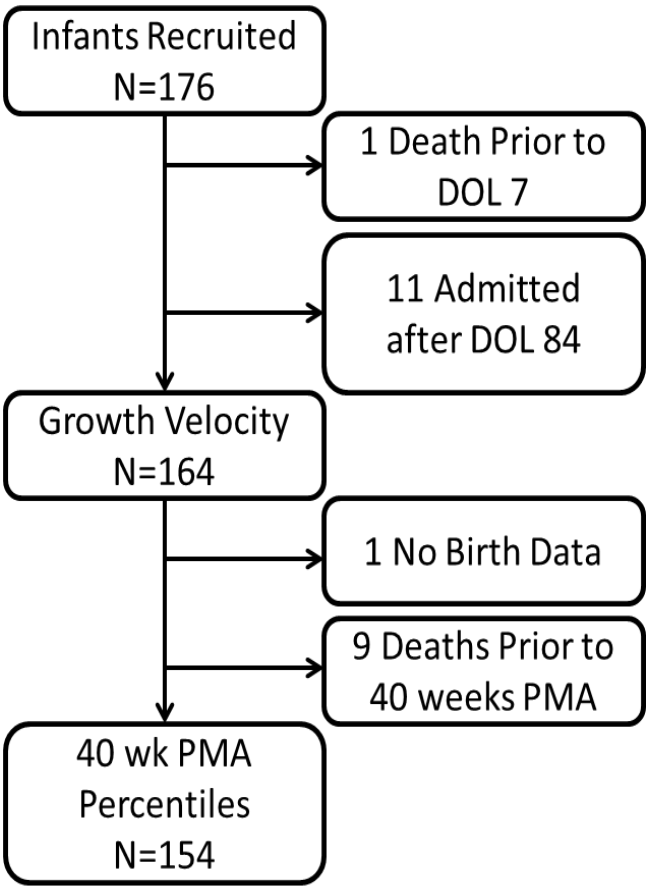

Figure 5: Subject flow

During this study, nine infants died on or before day of life 84. The average age of the infants that died on or before day of life 84 was 49 ± 42 days old. One infant died at one week of age. Two infants died at 5 weeks of age while three died at 7 weeks. One

infant each died at 9 weeks, 10 weeks, as well as 12 weeks of age. One hundred and thirty-two infants remained inpatient after day of life 84.

Table 3

Demographic Characteristics of NICU Infants with Intestinal Failure or Feeding Intolerance [1]

Characteristic	**Data**
Infants	164
Males, n (%)	102 (61.2)
Females, n (%)	62 (37.8)
Ethnicity, n (%)	
White	65 (39.6)
Hispanic	47 (28.7)
Black	37 (22.6)
Asian	12 (7.3)
Other	3 (1.8)
Birth Age (wks)	31.5 ± 5.4
Birth weight (g)	1723 ± 951
Birth length (cm)	39.7 ± 7.3
Birth head circumference (cm)	27.7 ± 4.6
Admission day of life (d)	17.1 ± 33.2
Average length of stay (d)	112.6 ± 79.7

[1] Values are percentage or means ± standard deviations.

Weight-for-age percentile was significantly lower at 40 weeks PMA compared to birth (Table 4) ($p < 0.001$). Length-for-age percentile at 40 weeks PMA was significantly lower than the mean length percentile at birth ($p < 0.001$). Although there was a much smaller decrease in head circumference-for-age percentile as compared to weight and length percentiles, the head circumference-for-age percentile was significantly lower at 40 weeks PMA compared to birth (Table 4) ($p < 0.001$).

Table 4

Growth Measures of Neonatal Intensive Care Unit Infants with Intestinal Failure or Feeding Intolerance from Birth to Post Menstrual Age (PMA) [1]

Variable	**Birth**	**40 Week PMA**	**Change**	**P**
Weight for age percentile	43.3 ± 29.2	17.6 ± 21.1	-25.7 ± 25.6	< 0.001
Length for age percentile	38.1 ± 29.9	12.8 ± 19	- 25.1 ± 27.2	< 0.001
Head circumference percentiles	41.1 ± 28.7	27.1 ± 28.4	-14 ± 30.3	< 0.001

[1] Total sample size of 154 infants

The mean weight-for-age percentile at birth was 43.3 ± 29.2 %ile. This percentile significantly decreased to 17.6 ± 21.1 %ile at 40 weeks PMA ($p < 0.001$) (Table 4). A comparison of infants who were less than the 3rd percentile, less than the 10th percentile, and those between the 10th and 90th percentiles at birth and 40 weeks PMA or discharge is shown in Figure 6. Fourteen infants (9.1%) were below the 3rd percentile weight-for-age at birth while 40 infants (26%) were below the 3rd percentile at 40 weeks PMA or discharge (Figure 6). One-hundred percent of the infants that were below the 3rd percentile at birth remained below the 3rd percentile at 40 weeks PMA or discharge. One-hundred percent of the infants that were below the 3rd percentile at birth remained below the 3rd percentile at 40 weeks PMA or discharge. Similarly, the number of infants below

the 10th percentile increased from 31 (20.1%) to 71 (46.1%). The number of infants less than the 3rd percentile (n=14) and less than the 10th percentile (n=31) more than doubled (n=14 and n=71 respectively) from birth to discharge or 40 weeks PMA. Infants between the 10th and 90th percentile decreased from 132 (85.7%) to 40 (26%) at 40 weeks PMA or discharge. Thirty-one infants were below the 10th percentile and therefore classified as SGA at birth and of these infants 29 (93.5%) remained SGA at 40 weeks PMA or discharge. In all growth parameters, the largest difference between appropriate sized infants at birth versus 40 weeks PMA was seen in weight-for-age.

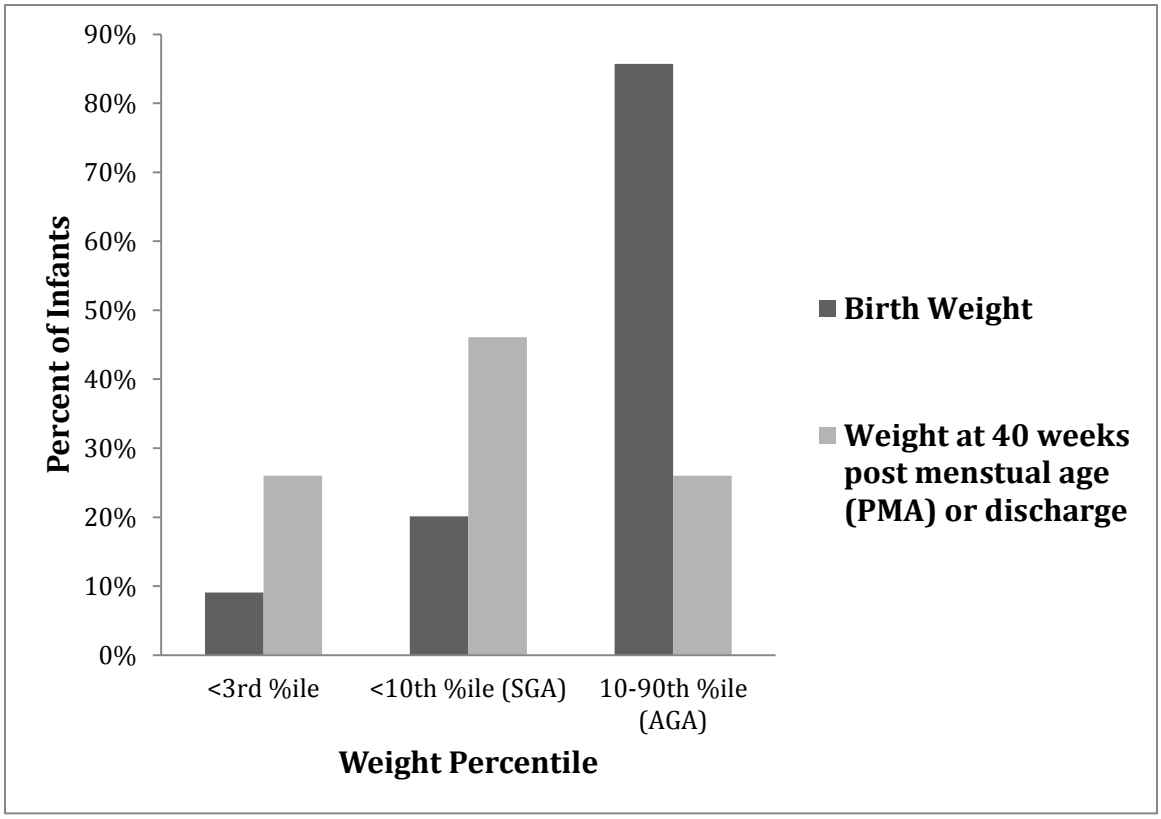

Figure 6: Olsen weight-for-age percentile ranking from birth to 40 weeks PMA or discharge. Note. **The less than 10th percentile includes infants in the less than 3rd percentile*

Mean Length-for-age percentile at birth decreased at 40 weeks PMA or discharge (Figure 7). Twenty-two (14.3%) infants were below the 3rd percentile length-for-age at birth, which increased to 59 (38%) infants below the 3rd percentile at 40 weeks PMA or discharge. This pattern shown for length was similar to the trend weight-for-age percentile changes. Number of infants in the less than 3rd percentile as well as the less than 10th percentile more than doubled from birth to 40 weeks PMA or discharge. Forty-two (27.3%) of infants were classified as SGA at birth. Of these 42 SGA infants, 40 (95.2%) remained SGA at 40 weeks PMA or discharge. At birth 120 (77.9%) of infants

were between the 10th and 90th percentile and therefore categorized as APA. The number of infants between the 10th and 90th percentile significantly decreased to 44 (28.6%) at 40 weeks PMA or discharge.

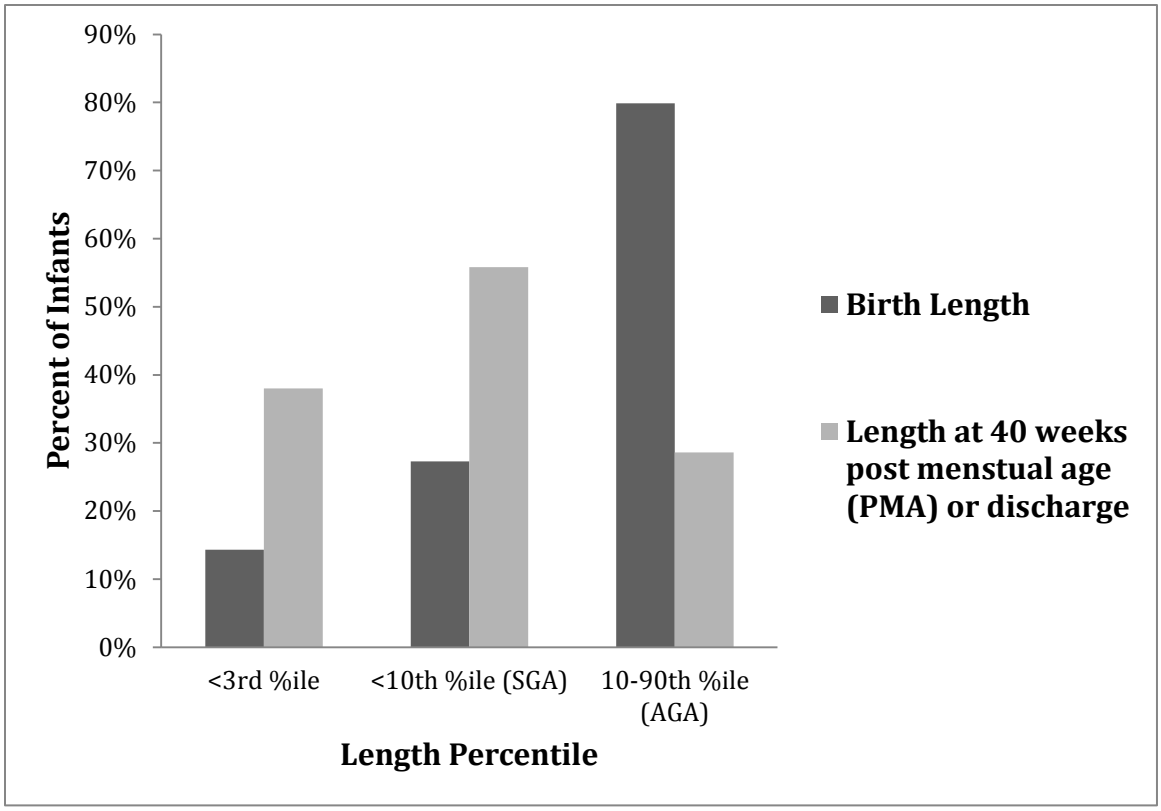

Figure 7: Olsen length-for-age percentile ranking from birth to 40 weeks PMA or discharge. Note. **The less than 10th percentile includes infants in the less than 3rd percentile*

The difference between the mean head circumference-for-age percentiles at birth and 40 weeks PMA were also significant ($P < 0.001$), although the percentile reduction was smaller as compared to weight and length (Table 4). At birth, the mean head circumference-for-age percentile was 41.1 ± 28.7 %ile which decreased to 27.1 ± 28.4 %ile at 40 weeks PMA or discharge. Ten infants (6.5%) were below the 3rd percentile for

head circumference-for-age at birth. At 40 weeks PMA or discharge, 38 infants (24.7%) were below the 3rd percentile for head circumference-for-age. As seen in Figure 8, overall head circumference-for-age percentiles also decreased from birth to 40 weeks PMA or discharge. The number of infants in the 10th to 90th percentile range for head circumference-for-age decreased from 123 (79.9%) at birth to 68 (44.2%) at discharge or 40 weeks PMA. Twenty-eight infants were SGA at birth and 22 (78.6%) of these infants remained SGA at 40 weeks PMA or discharge.

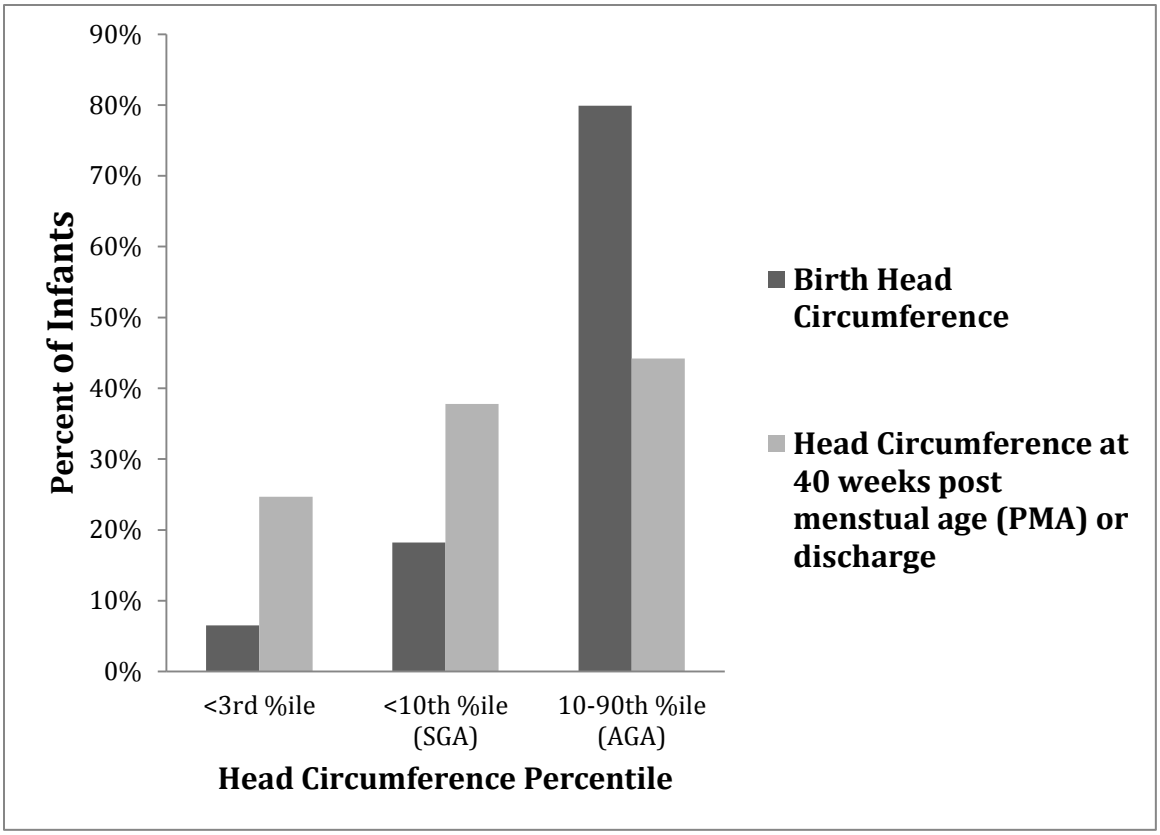

Figure 8: Olsen head circumference-for-age percentile ranking from birth to 40 weeks PMA or discharge. Note. **The less than 10th percentile includes infants in the less than 3rd percentile*

Standard growth curves signifying growth velocities of normal infants represent growth that is maintained consistently over a gradual increasing slope. As seen in Figures 9, 10 and 11, the growth velocities of this infant population for the first 3 months of life do not represent a constant growth over time. At day of life 84, or 3 months, the average weight gain velocity was 19.97g/wk; however, by the discharge, the average weight velocity was just above the low range of the expected norm at 20.56 g/wk. Mean length growth velocity was 0.81 cm/wk but by discharge this had fallen to 0.69 cm/wk. The average head circumference velocity was 0.52 cm/wk at day of life 84 and 0.45 cm/wk by discharge.

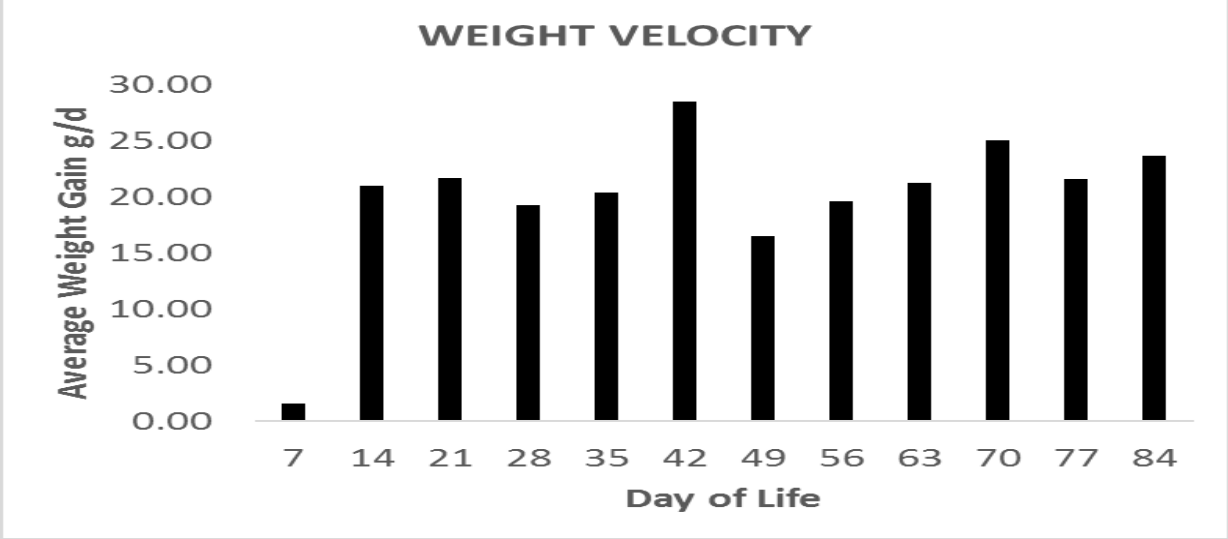

Figure 9: Weight velocity from birth to day of life 84

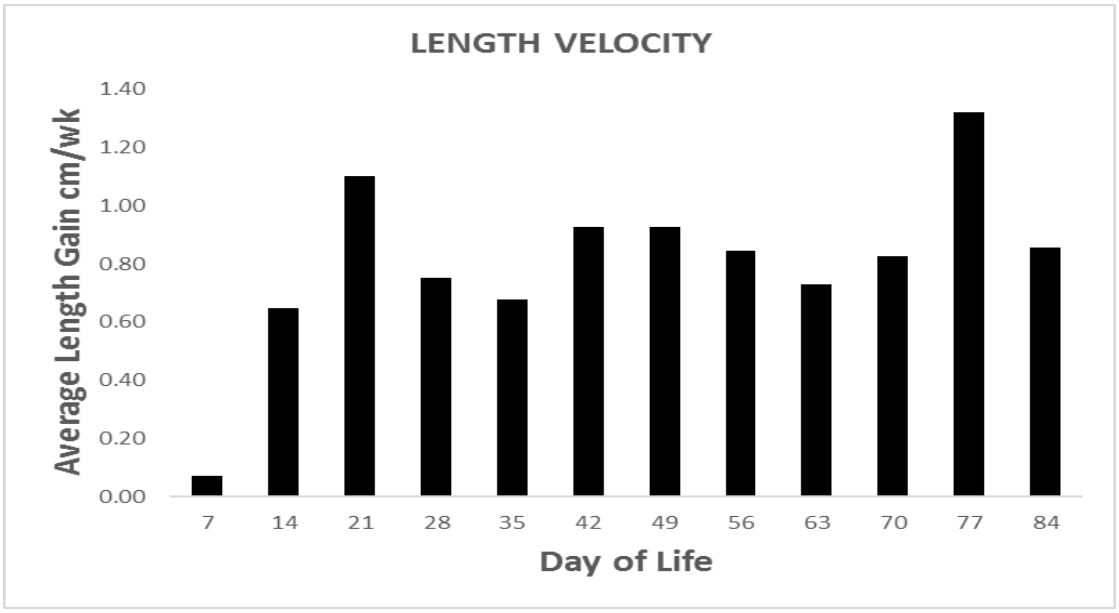

Figure 10: Length velocity birth to day of life 84

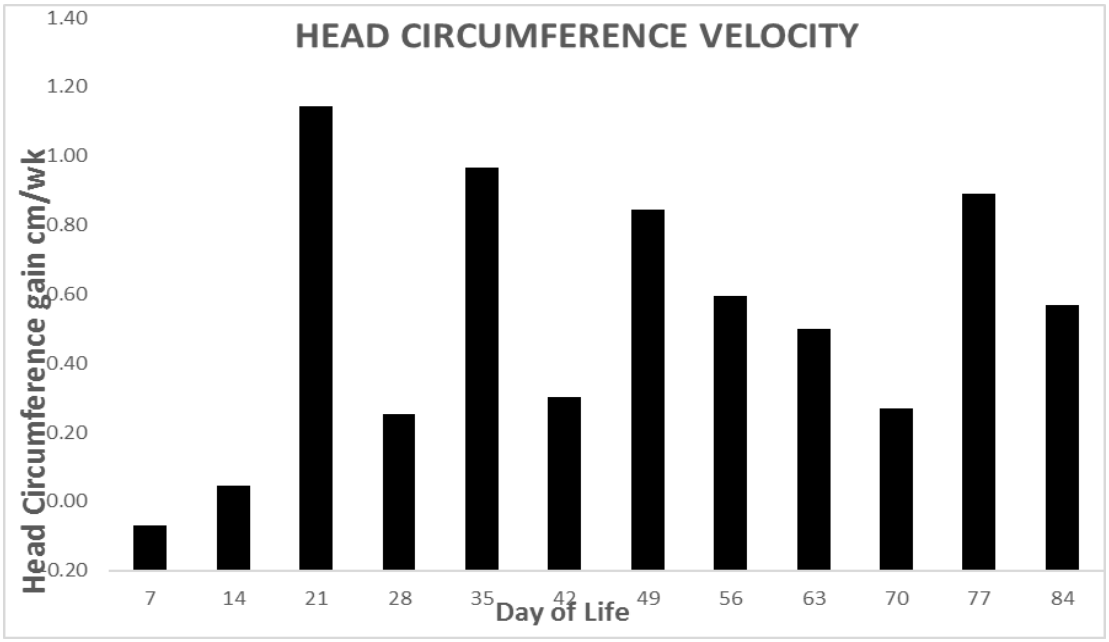

Figure 11: Head circumference velocity from birth to day of life 84

CHAPTER V

DISCUSSION

A majority of the infants in this study with intestinal failure or feeding intolerance demonstrated a substantial decrease in anthropometric measurements from birth to 40 weeks PMA and an even greater decrease of anthropometrics from birth to discharge. Most infants showed a significant decrease of weight, length and head circumference percentiles from birth to 40 weeks PMA or discharge. The smallest change observed was in head circumference-for-age from birth to 40 weeks PMA, though the reduction was still sizeable. More infants were below the 3rd percentile at 40 weeks PMA or discharge than at birth for all anthropometric measurements. Thus, our study found that infants with intestinal failure or feeding intolerance did not match the growth of an infant without intestinal failure or feeding intolerance when compared to the Olsen charts.

Weight, length, and head circumference growth velocities at day of life 84 were below the average of reference infants without intestinal complications. Contrary to the Olsen percentile rankings, the most stunted growth parameter was head circumference. The mean head circumference velocity was approximately half the expected growth rate. Length velocity was also significantly below the growth rate for healthy infants. Mean weight gain was the least effected growth parameter. Only 16 infants were below 2 kg by day of life 84. By discharge, length and head circumference growth velocities had further decreased below the reference growth velocity whereas weight has slightly increased just

above the reference. At discharge, average length velocity was 0.69 cm/wk, head circumference had fallen to 0.45 cm/wk and average weight velocity was 20.56 g.wk. This study found length, which is a longitudinal measurement, to be severely inadequate. The poor growth in length leads this study to conclude that this infant population is at risk for chronic nutrition, growth, and perhaps health complications. According to Rogol et al., weight is an acute marker of nutritional status while length may be associated with the long-term health condition of the infant and reflects chronic nutritional status.

Longitudinal measurements in this study reflected poor overall health in this infant population. The conflicting results on head circumference percentile ranking versus growth velocity may signify that head circumference is the least effective anthropometric measurement to evaluate nutritional status. Unlike the percentile rankings that continually decreased over the period of hospitalization, growth velocities of weight, length, and head circumference demonstrated no consistent pattern over the time of hospitalization (Figures 9, 10, and 11). Growth velocities were tracked weekly. Many factors outside nutrition such as surgery or other complications could have resulted in growth velocities that are adequate one week and poor the next. Infants experiencing a setback in their treatment could result in growth that varied from week to week.

According to Rogol et al., anthropometric measurements are crucial in determining the overall health status of an infant. Growth of infants and children can be compared to their peers when determining appropriate growth parameters and health status. Some charts that are used for such comparison include the CDC growth curves,

WHO growth curves, and the Olsen growth curves. Clinicians can use these percentile curves, along with the results of our study, to assess the appropriate and expected growth parameters for infants with intestinal failure or feeding intolerance. Even with a specialized nutrition focused team monitoring progress closely, growth was still poor in this medical population compared to infants without intestinal complications. Other clinicians may find our results as a confirmation of the importance of nutritional support for this population.

The TCH NICU Intestinal Rehabilitation Team followed all patients included in this study. Weights were tracked daily as the team worked to promote adequate growth. Despite the focused effort of the team to provide proper nutrition, our study found infant's growth was insufficient. Although many factors outside their nutritional intake lead to poor growth, had the infants not been monitored as closely, the outcomes would have been far worse. Incidence of SGA at birth was similar to that reported in very low birth weight (<1250g) infants by Hair et al.; however, they reported a high incidence of SGA (100% of infants who were born SGA) at 40 weeks PMA or discharge (Hair, Hathorne, Chetta, Abrams, 2013).

Strengths

To our knowledge, this is the first study to evaluate the growth of infants with intestinal failure or feeding intolerance. Clinicians can use these findings to better predict growth of infants with intestinal failure or feeding intolerance to better assess nutritional status. Our hope is that this preliminary study will open the door for future studies and

begin to advance our knowledge on how to promote a better quality of life for this infant population. Another strength of this study was the large and diverse infant sample size. At least 5 different races/ethnicity groups were represented. In addition, trained nurses performed all measurements. Furthermore, by including only infants being followed by TCH's NICU Intestinal Rehabilitation Team, standardized nutrition and medical care were provided for infants with intestinal failure and feeding intolerance.

Limitations

By studying the growth of infants at one hospital in Texas, findings may not be generalized to other NICU infant populations. Therefore, this study was limited by a lack of a diverse geographical population. Studying the growth of infants with feeding intolerance or intestinal failure in hospitals not only in Texas, but also nationally, may provide a better picture of the growth patterns for this infant population. There is limited research on this topic and clinicians at other facilities may follow different procedures when caring for infants with intestinal failure or feeding intolerance. Expanding this study could provide useful data. In addition, this study was observational only and used pre-recorded data from medical charts; therefore, we relied on accuracy and timeliness of nurses to chart anthropometrics. Furthermore, this study did not take into consideration the type of care being given therefore we do not know if different care would improve growth. Finally, more studies evaluating the care and growth in infants with intestinal failure or feeding intolerance would provide additional data.

CHAPTER VI

CONCLUSIONS AND IMPLICATIONS FOR FUTURE RESEARCH

A significant difference in the growth patterns of infants with intestinal failure or feeding intolerance was found compared to standard patterns of average growth of infants without intestinal failure or feeding intolerance. The growth of infants with intestinal failure or feeding intolerance did not follow the reference growth standards for the first 3 months of life and therefore the first null hypothesis was rejected. More infants were below the 10^{th} percentile at 4o weeks PMA therefore categorizing them as SGA and at health and nutritional risk. The second null hypothesis was also rejected because the anthropometric percentiles at birth were higher than at 40 weeks PMA. Though both the growth velocities and percentile rankings declined over the period of hospitalization, the third null hypothesis is rejected because no clear relationship was found. While the percentile rankings using the Olsen curves steadily decreased over period of hospitalization and the growth velocities were poor, analysis did not reveal a clear relationship over time.

More studies should be conducted to identify possible reasons for the slower growth rate. Findings would help to target specific interventions to improve growth velocities of this infant population. This study found that infants did not thrive during hospitalization. Future studies should be conducted to calculate specific interventions to improve the growth of infants with intestinal failure or feeding intolerance during hospital admission. Currently, there are limited resources to aid clinicians in caring for

infants with intestinal failure and feeding intolerance. Future studies can improve care and quality of life for these babies.

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APPENDIX A
Data Collection Tool

Intestinal Rehabilitation Rounds, starting 4-3-12							
Number	**Gender M=1, F=2**	**Race (White=1, Black=2, Hisp=3, Asian=4, Other=5)**	**Date of admission**	**DOL when admitted to TCH**	**Date of d/c or death**	**Length of Stay (days)**	**Gestational Age at Birth**
32350-1							
32350-2							
32350-3							
32350-4							
32350-5							
32350-6							
32350-7							
32350-8							
32350-9							
(etc)							
	Males	**RACE**					
	#REF!	**0**		#NUM!		#NUM!	#NUM!
		0		**#DIV/0!**		**#DIV/0!**	**#DIV/0!**
		0		0.0		0.0	0
	Females	**0**		0.0		0.0	0
	#REF!	**0**		**#DIV/0!**		**#DIV/0!**	**#DIV/0!**
		0					
	Total						
	#REF!	**0**					
		0					
		0					
		0					
		0					
		0					
		0					
		0					
		0					
		0					
		0					

Birth Anthropometrics			Diagnosis		
Birth Weight	Birth Length	Birth Head Circumf	All Dx	Primary Dx	PRIMARY DX: 1=gastroschisis; 2=omphalocele; 3=NEC; 4=perf; 5=PDA; 6=obstruction/atresia/volv; 7=Hirschsrungs; 8=other
#NUM!	#NUM!	#NUM!			count1=
#DIV/0!	**#DIV/0!**	**#DIV/0!**			**#REF!**
0	0.0	0.0			
0	0.0	0.0			count2=
#DIV/0!	**#DIV/0!**	**#DIV/0!**			**#REF!**
					count3=
					#REF!
					count4=
					#REF!
					count5=
					#REF!
					count6=
					#REF!
					count7=
					#REF!
					count8=
					#REF!
					TOTAL
					#REF!

Intestinal Rehabilitation Rounds, starting 4-3-12					*different calculations for <2kg and >2kg				
Number	Birth Weight	Birth Length	Birth Head Circumf	Wt at DOL 7	Length at DOL 7	FOC at DOL 7	Wt Velocity at DOL 7	Length Velocity at DOL 7	FOC Velocity at DOL 7
							#DIV/0!	#DIV/0!	#DIV/0!

Wt at DOL 14	Length at DOL 14	FOC at DOL 14	Wt Velocity at DOL 14	Length Velocity at DOL 14	FOC Velocity at DOL 14	Wt at DOL 21	Length at DOL 21	FOC at DOL 21	Wt Velocity at DOL 21	Length Velocity at DOL 21	FOC Velocity at DOL 21
			#DIV/0!	#DIV/0!	#DIV/0!				#DIV/0!	#DIV/0!	#DIV/0!

Wt at DOL 28	Length at DOL 28	FOC at DOL 28	Wt Velocity at DOL 28	Length Velocity at DOL 28	FOC Velocity at DOL 28	Wt at DOL 35	Length at DOL 35	FOC at DOL 35	Wt Velocity at DOL 35	Length Velocity at DOL 35	FOC Velocity at DOL 35
			#DIV/0!	#DIV/0!	#DIV/0!				#DIV/0!	#DIV/0!	#DIV/0!

Wt at DOL 42	Length at DOL 42	FOC at DOL 42	Wt Velocity at DOL 42	Length Velocity at DOL 42	FOC Velocity at DOL 42	Wt at DOL 49	Length at DOL 49	FOC at DOL 49	Wt Velocity at DOL 49	Length Velocity at DOL 49	FOC Velocity at DOL 49
			#DIV/0!	#DIV/0!	#DIV/0!				#DIV/0!	#DIV/0!	#DIV/0!

Wt at DOL 56	Length at DOL 56	FOC at DOL 56	Wt Velocity at DOL 56	Length Velocity at DOL 56	FOC Velocity at DOL 56	Wt at DOL 63	Length at DOL 63	FOC at DOL 63	Wt Velocity at DOL 63	Length Velocity at DOL 63	FOC Velocity at DOL 63
			#DIV/0!	#DIV/0!	#DIV/0!				#DIV/0!	#DIV/0!	#DIV/0!

Wt at DOL 70	Length at DOL 70	FOC at DOL 70	Wt Velocity at DOL 70	Length Velocity at DOL 70	FOC Velocity at DOL 70	Wt at DOL 77	Length at DOL 77	FOC at DOL 77	Wt Velocity at DOL 77	Length Velocity at DOL 77	FOC Velocity at DOL 77
			#DIV/0!	#DIV/0!	#DIV/0!				#DIV/0!	#DIV/0!	#DIV/0!

Wt at DOL 84	Length at DOL 84	FOC at DOL 84	Wt Velocity at DOL 84	Length Velocity at DOL 84	FOC Velocity at DOL 84	Gestational Age at Birth	# of weeks from birth to 40 wks PMA	# of days from birth to 40 wks PMA	Date at DOL 40 wks PMA
			#DIV/0!	#DIV/0!	#DIV/0!				

Wt at DOL 40 wks PMA	Length at DOL 40 wks PMA	FOC at DOL 40 wks PMA	Wt Velocity from BIRTH to 40 wks PMA	Length Velocity from BIRTH to 40 wks PMA	FOC Velocity from BIRTH to 40 wks PMA	Date of d/c or death	Outcome: d/c = 1, death =2	# weeks from birth to d/c or death	# days from birth to d/c or death
			#DIV/0!	#DIV/0!	#DIV/0!				

Wt at DOL d/c or death	Length at DOL d/c or death	FOC at DOL d/c or death	Wt Velocity at DOL d/c or death	Length Velocity at DOL d/c or death	FOC Velocity at DOL d/c or death	Was baby still inpatient after DOL 84? N=0, Y=1	PMA at DOL 84
							#DIV/0!

APPENDIX B
Institutional Review Board Approval Letters

TEXAS WOMAN'S UNIVERSITY
DENTON DALLAS HOUSTON

Institutional Review Board
Office of Research
6700 Fannin, Houston, TX 77030
713-794-2480
mjackson3@twu.edu
http://www.twu.edu/irb.html

DATE: August 27, 2014

TO: Ms. Danielle Morton
Department of Nutrition & Food Sciences - Houston

FROM: Institutional Review Board - Houston

Re: Exemption for Evaluation of growth in Neonatal Intensive Care Unit (NICU) Infants with Intestinal Failure or Feeding Intolerance Issues (Protocol #: 17802)

The above referenced study has been reviewed by the TWU Institutional Review Board (IRB) and was determined to be exempt from further review.

If applicable, agency approval letters must be submitted to the IRB upon receipt PRIOR to any data collection at that agency. Because a signed consent form is not required for exempt studies, the filing of signatures of participants with the TWU IRB is not necessary.

Although your protocol has been exempted from further IRB review and your protocol file has been closed, any modifications to this study must be submitted for review to the IRB using the Modification Request Form. Additionally, the IRB must be notified immediately of any adverse events or unanticipated problems. All forms are located on the IRB website. If you have any questions, please contact the TWU IRB.

cc. Ms. Rose Bush, Department of Nutrition & Food Sciences - Houston
John Radcliffe, PhD, RD, Department of Nutrition & Food Sciences - Houston
Graduate School
Steven A. Abrams

Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals

Protocol Number: **H-32350**
Status: Approved
Initial Submit Date: 1/18/2013
Approval Period: 2/28/2013 - 2/4/2014

Section Aa: Title & PI

A1. Protocol Title

EVALUATION OF NICU INFANTS WITH INTESTINAL FAILURE OR FEEDING INTOLERANCE ISSUES

A2. Principal Investigator

Name:	STEVEN A ABRAMS	Phone:	713-798-7124
Id:	022959	Fax:	713-798-7119
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Center:		Mail Stn:	BCM320

A3. Administrative Contact

Name:	LEJUANA HIMES	Phone:	713-798-7164
Id:	157389	Fax:	713-798-7119
		Email:	lhimes@bcm.edu
		Mail Stn:	BCM320

A3a. Financial Conflict of Interest

Does the investigator have a financial interest in any non-Baylor sponsor or funding source for this research?
No

A3b. Cooperative Agreement

Is this a cooperative agreement protocol?
No

Which institution is the IRB of record?
BCM: Baylor College of Medicine

Section Ab: General Information

A4. Co-Investigators

Name:	BETH ANNE CARTER	Phone:	832-822-3616
Id:	130942	Fax:	
Department:	PEDIATRICS: GASTROENTEROLOGY	Email:	bac@bcm.edu