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Early neurodevelopmental outcomes of infants with intestinal failure

Stephanie So [a,g,*], Catherine Patterson [a,g], Anna Gold [b,g], Alaine Rogers [a,g], Christina Kosar [c,g], Nicole de Silva [d,g], Karolina Maria Burghardt [e,g], Yaron Avitzur [e,g], Paul W. Wales [f,g]

[a] Department of Rehabilitation Services, The Hospital for Sick Children, Toronto, Ontario, Canada
[b] Department of Psychology, The Hospital for Sick Children, Toronto, Ontario, Canada
[c] Transplant and Regenerative Medicine Centre, The Hospital for Sick Children, Toronto, Ontario, Canada
[d] Department of Neonatology, The Hospital for Sick Children, Toronto, Ontario, Canada
[e] Division of Gastroenterology, Hepatology and Nutrition, The Hospital for Sick Children, Toronto, Ontario, Canada
[f] Division of General and Thoracic Surgery, The Hospital for Sick Children, Toronto, Ontario, Canada
[g] Group for Improvement of Intestinal Function and Treatment (GIFT), The Hospital for Sick Children, Toronto, Ontario, Canada

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ABSTRACT

Background: The survival rate of infants and children with intestinal failure is increasing, necessitating a greater focus on their developmental trajectory.
Aims: To evaluate neurodevelopmental outcomes in children with intestinal failure at 0–15 months corrected age.
Study design: Analysis of clinical, demographic and developmental assessment results of 33 children followed in an intestinal rehabilitation program between 2011 and 2014. Outcome measures included: Prechtl's Assessment of General Movements, Movement Assessment of Infants, Alberta Infant Motor Scale and Mullen Scales of Early Learning. Clinical factors were correlated with poorer developmental outcomes at 12–15 months corrected age.
Results: Thirty-three infants (17 males), median gestational age 34 weeks (interquartile range 29.5–36.0) with birth weight 1.98 kg (interquartile range 1.17–2.50). Twenty-nine (88%) infants had abnormal General Movements. More than half had suspect or abnormal scores on the Alberta Infant Motor Scale and medium to high-risk scores for future neuromotor delay on the Movement Assessment of Infants. Delays were seen across all Mullen subscales, most notably in gross motor skills.
Factors significantly associated with poorer outcomes at 12–15 months included: prematurity, low birth weight, central nervous system co-morbidity, longer neonatal intensive care admission, necrotizing enterocolitis diagnosis, number of operations and conjugated hyperbilirubinemia.
Conclusion: Multiple risk factors contribute to early developmental delay in children with intestinal failure, highlighting the importance of close developmental follow-up.

1. Introduction

Intestinal failure (IF) is defined as the inability to maintain fluid, electrolyte and nutrient balance due to obstruction, dysmotility, surgical resection, congenital defect or disease-associated loss of absorption. IF often results in dependence on parenteral nutrition (PN) to maintain growth and hydration [1]. A common cause of IF in children is short bowel syndrome, resulting from conditions such as: necrotizing enterocolitis (NEC), gastroschisis, intestinal atresia or mid-gut volvulus [2]. The survival rate of infants with IF is increasing, largely due to advancements in neonatal care, medical and surgical management, and the introduction of multidisciplinary intestinal treatment teams [3–6].

Exponential brain growth occurs during fetal and infant maturation, during which time any illness may have deleterious effects on subsequent neurodevelopment [7]. Additionally, since environmental influences and nutrition play an important role in brain development, complications commonly associated with IF such as prematurity, malabsorption, potential effects of PN, sepsis, surgery and prolonged hospitalization [4,5,8,9] may contribute to neurodevelopmental deficits.

Abbreviations: IF, intestinal failure; PN, parenteral nutrition; NEC, necrotizing enterocolitis; PT, physiotherapy; OT, occupational therapy; SLP, speech and language pathology; GA, gestational age; ELBW, extremely low birth weight; NICU, neonatal intensive care unit; MRI, magnetic resonance imaging; CNS, central nervous system; CP, cerebral palsy; NDI, neurodevelopmental impairment; SD, standard deviation; IQR, interquartile range; GM, Prechtl's Assessment of General Movements; AIMS, Alberta Infant Motor Scale; MAI, Movement Assessment of Infants; CA, corrected age.

* Corresponding author at: Department of Rehabilitation Services, The Hospital for Sick Children, 555 University Ave., Toronto, Ontario M5G 1X8, Canada.
E-mail address: stephanie.so@sickkids.ca (S. So).

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Previous research examining the effects of IF on neurodevelopment has focused primarily on children with NEC, and has shown a consistent link between NEC and neurodevelopmental delay [10–16]. Newborn surgery for NEC or intestinal defects has been shown to increase the risk of adverse neurodevelopmental outcomes [11,13,16–18].

Little research to date has focused on neurodevelopmental outcomes of the medically complex children followed in intestinal rehabilitation programs. The objective of this study was to explore early developmental outcomes and examine specific demographic and medical factors that may be predictive of impairment; thus highlighting areas warranting increased education, rehabilitation and community supports.

2. Material and methods

2.1. Study population

The Group for Improvement of Intestinal Function and Treatment at The Hospital for Sick Children in Toronto, Canada is a multidisciplinary intestinal rehabilitation program that manages the treatment of patients with IF. The team is comprised of health care providers from general surgery, gastroenterology, neonatology, transplantation, clinical nutrition, nursing, social work, physiotherapy (PT), occupational therapy (OT), psychology and speech language pathology (SLP). Criteria for admission to the program includes: children who are dependent on PN support for nutrient or hydration for a duration of >6 weeks due to primary IF or after intestinal resection/loss, or children with a residual small intestinal length of <25% of that expected for age [19]. Within the program, there is a clinical protocol to monitor neurodevelopment, utilizing validated assessment tools administered by physiotherapists, occupational therapists and psychologists.

In order to assess early developmental outcomes, the study sample included children admitted to the program at <4 months of age between January 1, 2011 to December 31, 2013; with developmental assessments occurring prospectively until December 31, 2014. Children missing more than one test point were excluded.

The study sample received similar developmental intervention during their hospitalization including: individualized developmental care in the Neonatal Intensive Care Unit (NICU) [20] and developmentally focused care with weekly PT and/or OT on the ward [21]. Upon discharge home, children received therapy through early intervention or community care programs, which varied in frequency and delivery depending upon clinical need and availability of local resources. Additionally, developmental progress was monitored during out-patient clinic visits by PT, OT, SLP and psychology.

2.2. Demographic and medical data

Following research ethics board approval, data was collected from hospital records by a neonatology nurse practitioner with extensive clinical experience. Gender, gestational age (GA), birth weight, etiology of IF and percentage small bowel length after initial surgery was noted. Prematurity was defined as infants <37 weeks GA with further stratification of moderate to late preterm (32–<37 weeks GA), very preterm (28–<32 weeks GA) and extremely preterm (<28 weeks GA). Low birth weight categories included low birth weight (1.5–2.5 kg) and extremely low birth weight (ELBW, <1.5 kg). Total length of stay in the NICU and length of initial hospitalization in the first year of life was recorded. Magnetic resonance imaging (MRI) results were reviewed and central nervous system (CNS) co-morbidity defined as severe intraventricular hemorrhage grade 3/4, periventricular leukomalacia or microcephaly. Visual and auditory co-morbidities were defined as a diagnosis of retinopathy of prematurity and failure to pass the newborn hearing screen in at least one ear. A documented diagnosis of cerebral palsy (CP) was noted. Neurodevelopmental impairment (NDI) was defined as the presence of one or more of the following; CP, severe vision or hearing loss or scores of <70 (≥2 standard deviation (SD) below the mean) on the early learning composite of the Mullen Scales of Early Learning (Mullen).

Within the first year of life, the number of septic episodes (positive blood culture with a change in clinical status), number of abdominal operations (including liver and/or small bowel transplant), total PN days and evidence of enteral autonomy (ability to reach and sustain 100% of enteral feeds for minimum 2 months) was noted. Advanced liver cholestasis was defined as a serum-conjugated bilirubin level of >100 μmol/L sustained for at least 2 weeks, and not related to an episode of sepsis.

2.3. Developmental assessments

Developmental assessments included: Prechtl's Assessment of General Movements (GM), Alberta Infant Motor Scale (AIMS), Movement Assessment of Infants (MAI) and the Mullen. Assessment time points occurred between 0 and 15 months corrected age (CA), adjusting for prematurity.

The GM classifies the quality of spontaneous movement in infants from preterm to 4 months as normal-optimal, normal-suboptimal, abnormal-mild, or abnormal-definite [22]. AIMS assessments occurred at 4, 8 and 12–15 months and examine motor skills in prone, supine, sitting, and standing [23]. Scores ≥10th percentile were classified as normal, 5-10th percentile as suspicious and ≤5th percentile as abnormal development. The MAI identifies motor dysfunction in four domains: muscle tone, primitive reflexes, automatic reactions, and volitional movement. Each domain item is scored independently according to a normal 4 and 8-month profile, generating a total risk score [24]. Scores were classified as low (0–7), medium (8–13) and high (>13) risk for neuromotor delays. The Mullen, conducted at 12–15 months, is a norm-referenced assessment for children from birth to 68 months of age, consisting of a gross motor scale and four cognitive scales: visual reception, fine motor, expressive and receptive language. An early learning composite score is derived from the four cognitive scales. Normative scores for each scale are converted from T-scores to standard scores with a mean of 100 and SD of 15 [25]. Children with a score of ≤85 (>1 SD below mean) were classified as having mild/moderate delays (below average) while those with a score of ≤70 (>2 SD below mean) as showing significant delays (very low average).

2.4. Statistical analysis

Population characteristics were summarized with median and interquartile range (IQR) for continuous variables, and frequencies and proportions for categorical variables. Developmental assessment results were reported as per test criteria including: categories or risk points placing children at risk for future neuromotor delay, or percentiles or standard scores compared to published norms. Additionally, developmental outcomes with published population norms were stratified and compared with respect to clinical factors that impact outcome at 12–15 months, using a Mann Whitney U, Chi-Square or Fishers Exact test where appropriate. An alpha of <0.05 was considered significant.

3. Results

Thirty-seven infants <4 months of age were admitted between January 1, 2011 and December 31, 2013. Four children were excluded due to being transferred out of the program ($n = 3$), or followed in a peripheral centre ($n = 1$). Demographic and clinical characteristics are summarized in Table 1.

Common diagnoses included NEC and gastroschisis. The majority of infants (82%) were premature; however of these 16 (59%) were moderate to late preterm. NEC was the underlying etiology in all infants who were extremely preterm ($n = 6$) and who had CP ($n = 2$). Additionally 10/12 (83%) of those diagnosed with NEC were ELBW.