DOI: https://doi.org/10.53555/nnmhs.v9i5.1681 Publication URL: https://nnpub.org/index.php/MHS/article/view/1681

COGNITIVE OUTCOMES IN CHILDREN WITH CONDITIONS AFFECTING THE SMALL INTESTINE : A SYSTEMATIC REVIEW

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Abstract

It is possible that children who suffer from gastrointestinal (GI) disorders have a less-than-ideal nutritional status, particularly as a result of malabsorption and symptoms that are brought on by a restricted food intake. A cognitive function is any conscious mental action, including thinking, remembering, learning, or utilizing language. Examples of cognitive functions include these. Attention, memory, consideration, the ability to solve problems, and executive abilities such as planning, assessing, supervising, and evaluating are all aspects of cognitive function. Neurodevelopment issues in intestinal failure (IF) children have surfaced. The researchers Hukkinen et al. reviewed the existing research and came to the conclusion that children with IF are at a high risk of delayed psychomotor and cognitive development. However, this conclusion was drawn from a small number of studies that used a variety of research methods. This study reveals that children with IF and surgical NEC are at a greater risk of having bad cognitive outcomes in patients with illnesses affecting the small intestine who require PN. These patients include individuals with conditions such as Crohn's disease and ulcerative colitis.

Katakunci: *Cognitive; Gastrointestinal; Intestine Failure; Parenteral Nutrition; Small intestine*

INTRODUCTION

Gastrointestinal (GI) disorders may be associated with suboptimal nutritional status in children, particularly due to malabsorption and symptoms caused by restricted food intake.[1,2] When an infant has a disease that affects the small intestine, the gut is unable to absorb the nutrients and fluids necessary for growth to the extent that it should. Because of this, these infants are dependent on parenteral nourishment, also known as parenteral nutrition (PN).[3]

Some of them, which ranged from 23–35 percent of babies who had necrotizing enterocolitis (NEC) that was treated surgically, 10% to 34% of infants born with abnormalities in the abdominal wall; 12% of newborns born with intestinal atresia.[4,5] The prevalence of any FGID in newborns aged 0-12 months was 24.7%, while the prevalence of any FGID in infants aged 13-48 months was 11.3%. In babies, the most prevalent disorder was baby regurgitation (13.8%), and in toddlers, the most common disorder was functional constipation (9.6%).[6,7]

Nutritional support has an important role in maintaining growth and improving clinical outcomes in these children. There are several conditions that are motility disorders, for example gastroesophageal reflux disease, esophageal motility disorders, gastroparesis, chronic intestinal pseudo-obstruction, and constipation. Several approaches including diet modification, enteral nutrition, and parenteral nutrition need to be adjusted based on the patient's nutrition and clinical judgment.[8]

Cognitive function is a conscious mental activity, such as thinking, remembering, learning and using language. Cognitive function is also the ability of attention, memory, consideration, problem solving, and executive abilities such as planning, assessing, supervising and evaluating.[9,10] Neurodevelopment difficulties in intestine failure (IF) children have emerged. Hukkinen et al. evaluated the literature and concluded that children with IF are at high risk of delayed psychomotor and cognitive development, but this was based on few and small studies with varied methodologies.[11]

It is unknown whether neurodevelopmental deficits are caused by prolonged PN administration, disease-specific factors, or more general factors. This article provided about cognitive outcomes in children with conditions affecting the small intestine.

METHODS

This systematic review followed the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 reporting guidelines. This extensive evaluation was conducted to investigate the cognitive outcomes in children with small intestine-related conditions. The research that is currently being considered is centered on the subject being investigated. In order to conduct an accurate evaluation of previously conducted studies, it is necessary that the research meet specific requirements.

The following constitutes fulfillment of these prerequisites: 1) Articles need to be readily available online; 2) Articles written in English are given preference; and 3) The systematic review will only evaluate articles published in the years 2015 and later.

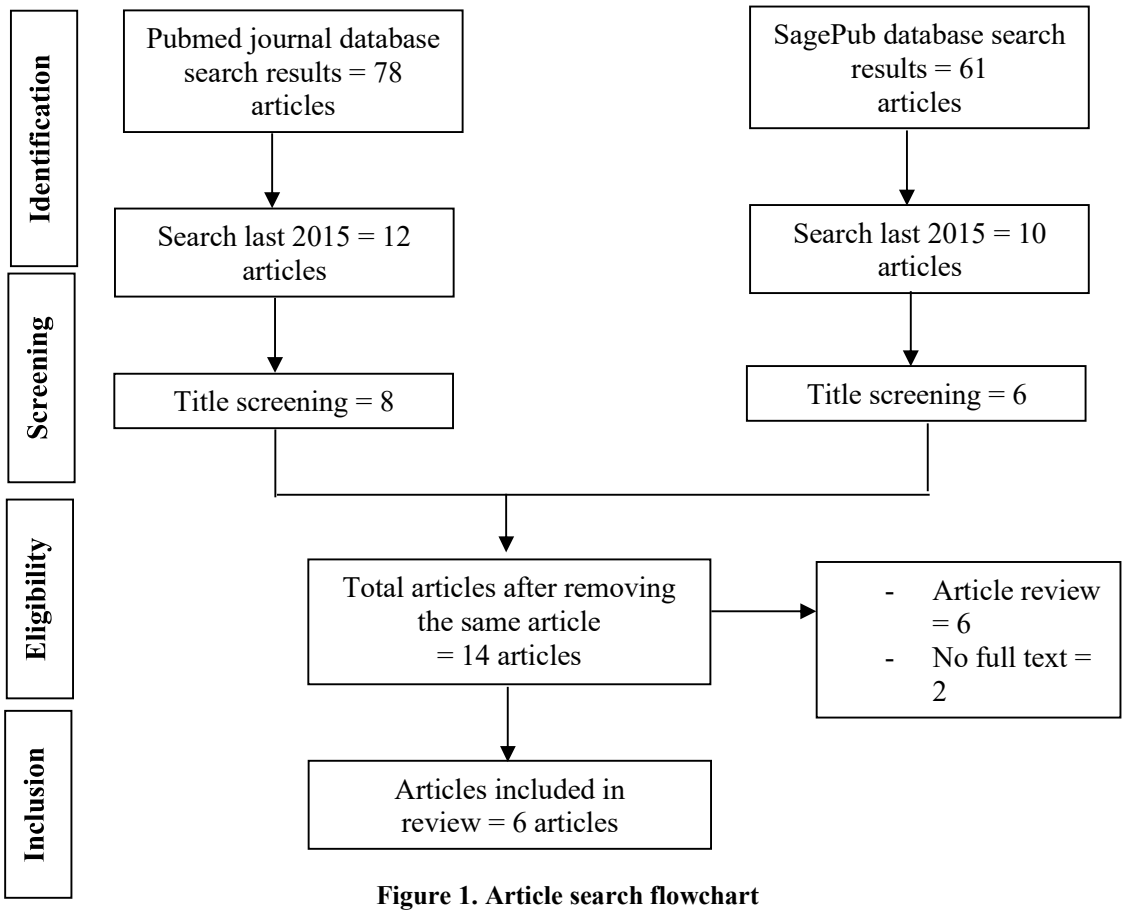

Figure 1. Article search flowchart

The search for studies to be included in the systematic review was carried out from May 14th, 2023 using the PubMed and SagePub databases by inputting the words: "cognitive outcomes", "children", and "small intestine condition". Where *("cognition"[MeSH Terms] OR "cognition"[All Fields] OR "cognitions"[All Fields] OR "cognitive"[All Fields] OR "cognitively"[All Fields] OR "cognitives"[All Fields]) AND ("outcome"[All Fields] OR "outcomes"[All Fields]) AND ("child"[MeSH Terms] OR "child"[All Fields] OR "children"[All Fields] OR "child s"[All Fields] OR "children s"[All Fields] OR "childrens"[All Fields] OR "childs"[All Fields]) AND ("intestine, small"[MeSH Terms] OR ("intestine"[All Fields] AND "small"[All Fields]) OR "small intestine"[All Fields] OR ("small"[All Fields] AND "intestine"[All Fields])) AND ("condition"[All Fields] OR "condition s"[All Fields] OR "conditions"[All Fields])* is used as search keywords.

After conducting a comprehensive literature review that included an analysis of the titles and abstracts of previously published research, the inclusion and exclusion criteria for the study were modified to reflect the investigation's findings. Only research projects that satisfied all of the inclusion criteria were considered for the systematic review. When comparing two research studies, it is essential to consider the study's title, author, publication date, country of origin, research design, and investigated variables.

To facilitate your evaluation and analysis of this content, it has been presented in a particular format. In order to determine whether the research studies could be included, the authors of the publications conducted objective evaluations of a selection of the research projects described in the titles and abstracts of the articles. Then, the full texts of the studies that satisfy the systematic review's inclusion criteria will be evaluated to determine which publications are eligible for categorical inclusion in the review. This will be performed so that the evaluation is as accurate as feasible.

RESULT

Hijkoop, et al (2018)[12] conducted a study woth 61 children (82% of eligible cases). Extra-abdominal bowel dilatation was substantially linked with complex gastroschisis at 30 weeks of gestation (*odds ratio* [OR] = 5.0; 95% CI = 1.09-22.98), with a high negative (88%) but modest positive (40%) predictive value. Height SDS at 12 months (OR = -0.46; 95% CI = -0.82 to -0.11) and weight SDS at 12 and 24 months (OR = -0.45; 95% CI = -0.85 to -0.05 and OR = -0.44; 95% CI = -0.87 to -0.01, respectively), were substantially lower than 0 SDS. The PDI of children with complex gastroschisis was considerably lower (OR = 76; 95% CI = 68-84)) than that of children with simple gastroschisis (OR = 94; 95% CI = 90 - 97) (p <0.001).

Hijkopp, et al (2018)[13] included 145 fetuses and neonates. At 24 months, mean (95% CI) height and weight standart deviation scores (SDS) were significantly below 0 in both minor (height: -0.57 (-1.05 to -0.09); weight: -0.86 (-1.35 to -0.37)) and giant omphalocele (height: -1.32 (-2.10 to -0.54); weight: -1.58 (-2.37 to -0.79)). Mental development was comparable with reference norms in both groups. Motor function delay was found significantly more often in children with giant omphalocele (82%) than in those with minor omphalocele (21%, P=0.002).

Table 1. The litelature include in this study

Author	Origin	Method	Sample Size	Result
Hijkoop, 2018[12]	Netherland	Prospective cohort study	61 children with gastroschisis	It was not possible for prenatal ultrasonography indicators to differentiate between simple and complicated gastroschisis in a reliable manner. Children who have complex gastroschisis may have a greater risk for delayed psychomotor development; hence, these children should be examined more closely and given appropriate intervention if necessary.
Hijkoop, 2018[13]	Netherland	Prospective cohort study	145 fetuses and neonates	The prenatal and postnatal frames of reference of omphalocele are very different from one another; therefore, it is recommended that parental counseling involve a multidisciplinary approach. We advocate vigilant surveillance of these children and early referral to physical therapy because many children with large omphalocele had delayed motor development.
Zozaya, 2021[14]	Canada	Retrospective cohort study	2,019 infants	In extremely premature infants, having any type of bowel perforation, necrotizing enterocolitis, or spontaneous intestinal perforation are all variables that increase the likelihood of the infant passing away or having major neurological impairment.
Kuik, 2020	Netherland	Prospective observational cohort study	44 children	Children who were born prematurely and survived neonatal encephalopathy are more likely to have lower cognitive and motor composite scores at the age of two to three years

				if their full enteral feeding (FEFt) following NEC was prolonged. These findings highlight how critical it is to shorten the duration of the nil by mouth treatment protocol whenever and wherever it is feasible to do so.
Burnett, 2018[15]	Australia	Prospective observational cohort study	876 infants	Depending on the reference group, individuals who survived gastroschisis and exomphalos may be at risk for impaired neurodevelopment in toddlerhood. Furthermore, children who were born with gastroschisis may be particularly at risk for difficulties with executive functioning while having an IQ that is within normal norms.
Humberg, 2020[16]	Germany	Prospective observational cohort study	2,241 infants	The findings suggest that the varied etiologies and degrees of inflammation caused by NEC and SIP may result in distinct patterns of neurodevelopment in the affected individuals. As a result, our findings point to the possibility of an early gut-brain axis distortion being involved in the development of NEC in infants, which is something that needs to be investigated further.

Zozaya, et al (2021)[14] conducted a study with total of 2,019 infants, and 39 (1.9%) of them had spontaneous intestinal perforation. 61 (3%) of them had necrotizing enterocolitis that was perforated, while 115 (5.7%) had necrotizing enterocolitis that was not perforated. Infants who did not have any of these bowel diseases had a lower risk of death or significant neurodevelopmental impairment when compared to infants who had spontaneous intestinal perforation (aOR = 2.11; 95% CI = 1.01-4.42), necrotizing enterocolitis (aOR = 2.58; 95% CI = 1.81-3.68), or any bowel perforation (aOR = 3.97; CI = 2.43-6.48). This was the case regardless of which bowel disease the infant had.

Kuik, et al (2020)[17] included 44 children, median gestational age of 27.9 (IQR= 26.7-29.3] weeks, birth weight 1148 (IQ =: 810-1461) grams. Median FEFt after NEC was 20 [IQR = 16-30] days. Median follow-up age was 25.7 [IQR: 24.8-33.5] months. FEFt > 20 days was associated with lower cognitive and lower motor composite scores of the Bayley-III (B: -8.6, 95% CI -16.7 to -0.4, and B: -9.0, 95% CI, -16.7 to -1.4). FEFt was not associated with CBCL scores. Post-NEC complications (n = 11) were not associated with Bayley-III scores nor with CBCL scores.

Other study conducted by Burnett[15] showed neurodevelopment in two-year-olds with gastroschisis and exomphalos was consistent with test normative data, but below the level of local normative data for all domains (effect sizes ranging from -0.4 to -1.4 standard deviations). At five years of age, children with gastroschisis performed similarly to the normative mean for IQ, but their parents reported elevated rates of executive functioning problems (18-41% versus the expected 7%). In addition, there was a trend toward an increase in the frequency of internalising concerns (33% versus the normative expectation of 16%). Exomphalos-affected five-year-olds performed similarly to the normative mean for IQ and had low rates of executive and behavioral difficulties.

Humberg, et al (2020)[16] conducted a study with a surgical diagnosis of NEC (n = 43) or SIP (n = 41) to NEC (n = 43) or SIP (n = 41) negative controls (n = 43). Infants with a history of NEC had a threefold increased risk of developing IQ scores 85 (RR 3.0 [1.8–4.2], p <0.001), whereas a history of surgical SIP did not increase the relative risk of developing reduced IQs at school age (RR 1.0 [0.4–2.1], p = 1.000). In a matched-cohort analysis, we confirmed that neonates with surgical NEC had lower mean IQ scores than unaffected controls (SD) (8517 vs. 9414, p = 0.023), whereas there were no significant differences for SIP history.

DISCUSSION

A child's ability to think and comprehend new information is referred to as their cognitive development. It is essential to have early detection methods for changes in cognitive functioning in order to promote development as quickly as is humanly possible. Most of the time, only medical predictors are examined, despite the fact that we are aware that psychological elements, such as bonding between parents and children and emotional functioning, are connected with intellectual growth.[18]

Cognitive function is a conscious mental activity, such as thinking, remembering, learning and using language. Cognitive function is also the ability of attention, memory, consideration, problem solving, and executive abilities such as planning, assessing, supervising and evaluating.[9,10] Study observed in a significantly lower frequency among children who had abnormalities in the abdominal wall or midgut. It was found that characteristics connected to an early hospital admission were more predictive of developmental outcome than the duration of PN reliance.[16,17,19]

Accumulating evidence suggests that early nutrition influences later cognitive performance. The possibility that the diet of mothers, infants, and children could influence later mental performance has significant implications for public health

practice and policy development, our comprehension of human biology, the development of food products, economic progress, and future wealth creation. To date, however, the majority of evidence comes from animal studies, retrospective studies, and human studies of short-term nutritional intervention.[17,20]

The severity of the condition could be to blame for the difference. For instance, in one of the studies, children who had complicated gastroschisis (which was accompanied by intestinal atresia, necrosis, perforation, and/or volvulus) had worse outcomes compared with simple gastroschisis patients; and complex gastroschisis patients are also the ones who are more prone to develop IF. It was found that having a lower gestational age, a longer length of hospital stay, and a higher number of surgical procedures were all risk factors for having a lower DQ or IQ.[12,13]

A significant percentage of people in IF are born before their due date. The human brain expands at an exponential rate during the fetal and infant stages of development. The disruption of brain organization that occurs when a neonate is born prematurely can have an effect on the subsequent development of cognitive abilities.[14,21,22] According to the findings of a number of research, preterm children have poorer outcomes in terms of their neurodevelopment as compared to term-born children.[14,23]

In recent decades, treatment outcomes for pediatric intestinal failure have improved significantly. With enhanced survival, the focus is now shifting to other vital outcomes, such as life quality and neurodevelopment. Until now, relatively few studies with limited patient numbers and variable methodologies have addressed these issues. On the basis of these studies employing generic health-related quality of life instruments, children with intestinal failure have poorer physical health, while PN-dependence is also associated with diminished emotional functioning.[11,24]

Older children and parents often have social impairments. Despite small sample sizes and short follow-up periods, new neurodevelopment studies suggest motor and mental skills are impaired in children with intestinal failure. A juvenile intestinal failure-specific survey could better identify health concerns that affect quality of life. Neurodevelopment in infant intestinal failure needs robust, well-designed research with long follow-ups. Medical experts treating intestinal failure children must prioritize quality of life and neurodevelopment.[11,24]

CONCLUSION

This study reveals that children with IF and surgical NEC are at a greater risk of having bad cognitive outcomes in patients with illnesses affecting the small intestine who require PN. These patients include individuals with conditions such as Crohn's disease and ulcerative colitis.

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