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Short Bowel Syndrome in neonates and early infancy

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ABSTRACT

Short bowel syndrome (SBS) is the commonest cause of intestinal failure in neonates. SBS results from widespread damage to the small intestine, leading to loss of functional capacity of this organ. This is generally secondary to conditions like necrotizing enterocolitis, gastroschisis, intestinal atresia, and midgut volvulus. The small bowel usually adapts to this damage in due course of time. The clinician's role usually entails the management of parenteral nutrition and the fluid and electrolyte balance to tide over this phase. The management should be initiated as soon as the diagnosis is suspected, especially post-surgical resection of the bowel. This should comprise enteral nutrition, with proactive monitoring and supplementation of electrolytes and micronutrients. Intestinal lengthening procedures like the Serial transverse enteroplasty (STEP), and Longitudinal intestinal lengthening and tailoring (LILT) may be considered in infants, where medical therapy fails to correct the pathology. The intricate nature of the condition warrants a multi-disciplinary approach, involving clinicians, intensivists, and surgeons, which ensures the best neonatal outcomes, in terms of the survival rates in these babies.

INTRODUCTION

Short bowel syndrome (SBS) is a malabsorptive condition, characterized by an extensive loss of intestinal mass, secondary to a congenital or acquired disease. The intestine usually adapts to this loss, typically after surgical resection. This involves alterations, both at the macro and microscopic levels, basically targeted at increasing the absorptive potential of the remaining portion of the small bowel. However, this adaptogenic response takes time to get established, and the intervening period becomes critical. Parenteral nutrition (PN) is the cornerstone in wading off this period, by providing sufficient time for the body to adapt and recalibrate its functional capacity. There are several studies that prove that PN is critical in achieving enteral autonomy. [1,2] Advances in medical and surgical management have resulted in reduced mortality and better outcomes in neonates with SBS. [3] These include corrective steps like adding several micronutrients to feeds for neonates and infants and precise calculation and reconstitution of parenteral nutrition using aseptic techniques like the laminar flow chamber. Advances in neonatal critical care have changed the scenario for babies with short bowel even in LMICs and resource-challenged nations. Better anesthesia techniques and perioperative advances have encouraged surgeons to perform bowel restoration and bowel lengthening procedures more frequently.

Definition of SBS

Pediatric intestinal failure (PIF) has been defined by the American Society for Parenteral and Enteral Nutrition (ASPEN) as "The reduction of functional intestinal mass below that which can sustain life, resulting in dependence on supplemental parenteral support for a minimum of 60 days within a 74 consecutive day interval". [4] Intestinal failure encompasses various disorders including surgical short-bowel syndrome, as well as gastrointestinal motility disorders (Long segment Hirschsprung disease, Intestinal pseudo-obstruction) and congenital mucosal abnormalities (Microvillus inclusion disease, Tufting enteropathy).

There are multiple SBS definitions in vogue in the literature, and this lack of a uniform definition renders the comparison and compilation of various studies a particularly arduous task. SBS may be defined anatomically based on the amount of residual small intestine remaining or by the duration of PN dependency. The recommended definition of SBS as per the

North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) is the need for PN for >60 days after intestinal resection or a bowel length of less than 25% of expected (Table 1). [5,6]

Table 1: Small bowel length and post conceptional age.

SMALL BOWEL LENGTH		
Postconceptional age	**Mean (cm)**	**SE**
24-26 wk	70.0	6.3
27-29 wk	100.0	6.5
30-32 wk	117.3	6.9
33-35 wk	120.8	8.8
36-38 wk	142.6	12.0
39-40 wk	157.4	11.2
0-6 mo	239.2	18.3
7-12 mo	283.9	20.9
13-18 mo	271.8	25.1
19-24 mo	345.5	18.2
25-36 mo	339.6	16.9
37-48 mo	366.7	37.0
49-60 mo	423.9	5.9

The functional definition has been stated as Short-bowel syndrome can be described as intestinal failure resulting from surgical resection, a congenital defect, or disease-associated loss of absorption and is characterized by the inability to maintain protein-energy, fluid, electrolyte, or micronutrient balances when on a conventionally accepted, normal diet. [7]

On the basis of length, a subgroup has also been defined as ultrashort bowel syndrome (USBS)-defined as bowel length less than 10 cm or less than 10% of the expected length for age. This has historically been considered a separate subgroup, as it has been associated with poorer outcomes, including the potential for palliative care in the immediate postnatal period. [8]

Etiology

Congenital malformations, like intestinal atresias, gastroschisis and volvulus comprise the most common group of conditions responsible for SBS. [9] Acquired causes like necrotizing enterocolitis too may lead to SBS. A study has shown necrotizing enterocolitis to be the most common cause (35%) of SBS in neonates and infants. Other etiologies included complicated meconium ileus (20%), abdominal wall defects (12.5%), intestinal atresia (10%), and volvulus (10%). [10]

Pathophysiology and Predictors of Enteral Autonomy

The clinical course of SBS patients can be described in the following three stages (Fig. 1). Enteral autonomy has been defined as "The maintenance of normal growth and hydration status by means of enteral support without the use of parenteral support for a period of more than 3 consecutive months." [4] There are various risk factors that affect this enteral autonomy and predispose to SBS: The residual length of the small intestine, post-surgical resection, is one of the most important predicting factors. A study by Fallon et al. demonstrated that 78% of infants with a small intestinal length of less than 30cm were ultimately weaned off, although after prolonged PN support. [1] Loss of the ileocecal valve too has been shown to be important. It has been shown to specifically alter the small bowel bacterial balance, thus predisposing the infant to SBS. [11] The role of the loss of the colon is a well-known risk factor in adults, but its relative importance in children is still controversial, though some studies have suggested that it may play a less important role in children. [12]

Plasma citrulline has been proposed to be a non-invasive marker of prediction of functional intestinal capacity, as it is believed to be produced almost exclusively by the enterocytes. SBS or intestinal mucosal injury leads to a reduction in the citrulline levels in the plasma, and, consequently, some studies have shown a correlation between the plasma citrulline levels and the residual small bowel length, thus predicting the severity of the intestinal injury.

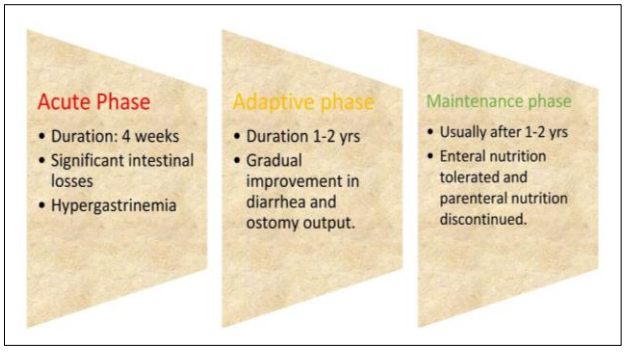

Figure 1: Clinical course of patients with SBS.

However, the actual length of the residual small bowel, as expounded upon previously, is definitely a better predictor of the severity of the disease and the expected duration of the PN. [15]

The prognosis also depends upon the level of the anastomosis. Post resection, three groups of anastomoses have been defined:

1. Jejuno-colic anastomosis: This is the most common. The complete ileum, including the ileocecal valve and parts of the jejunum and colon, is resected.

The prognosis largely depends upon the length of the residual jejunum.

2. Jejuno-ileal anastomosis: This has the best prognosis, as only a part of the ileum is removed, and importantly, the ileocecal valve is preserved.

3. End-jejunostomy: This group has the worst prognosis due to the resection of the entire ileum and colon. Colon, even if preserved, is disconnected and not available for absorptive areas. [13]

Post-surgical resection, the intestine undergoes a series of anatomical and physiological alterations, a process termed "Adaptation". These changes are targeted at enhancing the absorptive capacity of the surviving segment of the intestine. This process of adaptation starts within 48 hours of the resection and may continue for 12-18 months. It involves various adaptogenic changes like dilation and lengthening of the remaining segment. [16] Physiological changes include increased crypt cell proliferation and hypertrophy of the villi. Humoral mediators, like growth hormones, insulin-like growth factors, epidermal growth factors, etc. are the cornerstone to the development of intestinal adaptation, though many other factors are partly also responsible. [17] The ileum has the maximum plasticity in terms of structural adaptogenic transformation, the jejunum has more modest capabilities in comparison, and it is mainly limited to functional changes. [18]

Complications

A) Fluid and electrolyte disturbances

Typically, post-surgical resection, the infant experiences an immediate paralytic ileus stage. This is followed by the phase of diarrhea, characterized by massive fluid and electrolyte losses. The etiology of this diarrhea is multifactorial: i) Increased GI motility; ii) GI mucosal hypersecretion; iii) Bile dysfunction leading to fat malabsorption and bile acid-induced secretomotor diarrhea; iv) Loss of probiotic bacteria, leading to increased pathogenic bacterial growth; v) Hypergastrinemia secondary to the parietal cell hyperplasia (up to 25% of patients develop this complication).

B) Central line-associated bloodstream infections (CLABSI)

Children with SBS almost always require venous access for long-term parenteral nutrition fulfillment. A central venous catheter (CVC), though convenient, is fraught with the risk of CLABSI and venous thrombosis. Peripherally inserted central catheters (PICC) are comparatively safer and often preferred in the setup of resource-challenged settings for administering PN. [19]

C) Intestinal Failure associated liver disease (IFALD)

IFALD is defined as "hepatobiliary dysfunction as a consequence of medical and surgical management strategies for intestinal failure, which can variably progress to end-stage liver disease, or can be stabilized or reversed with the promotion of intestinal adaptation". IFALD is a dreaded complication, often leading to mortality in these patients with intestinal failure. Pathogenesis of IFALD is poorly understood, and possibly includes lack of oral intake, sepsis, deranged intestinal flora, and prematurity. Lipid emulsions too have been implicated in its pathogenesis, especially some components of commercially available emulsions like omega-6 FAs, omega-3 Fats, and sterols. [20]

D) Bacterial overgrowth

The intestinal microflora exists in a delicately balanced environment. Pathogenic bacterial overgrowth may occur as a result of stasis, which follows intestinal motility abnormalities. This microflora dysrhythmia further exacerbates the extant malabsorption and diarrhea, thus forming a vicious, progressive cycle. In adults, the culture of direct aspirates of small bowel contents and hydrogen breath testing (HBT) may be employed to diagnose small intestinal bacterial overgrowth. [21] However, such interventions are relatively arduous in infants. Thus, a course of antibiotics is often utilized in the setting of SBS with symptoms like abdominal pain, bloating, and diarrhea. [22] D-lactic acidosis is a rare complication in children with SBS, which results from the fermentation of dietary carbohydrates by intestinal bacteria. [23]

E) Malabsorption and micronutrient deficiency

Malabsorption of fat-soluble vitamins (A, D, E, and K) is a characteristic of SBS. A deficiency of minerals like iron, vitamin B12, copper, iodine, and zinc too may manifest. [24] Generally, ileal resection is associated with the maximum abnormalities- vitamin B12 deficiency, for example, is typically associated with the resection of the terminal ileum. The distal ileum is the site for the absorption of fat and fat-soluble vitamins. Micronutrient deficiencies may be present even with minimal systemic symptoms. [25]

Management

1. Fluid and electrolyte supplementation

Dyselectrolytemia and blood pressure fluctuations are very common in the acute phase of SBS, especially when the stoma output is greater than 20-30 ml/kg/day. Careful monitoring of the patient's hemodynamic parameters, weight, and fluid and electrolyte balance is imperative at this stage. [26] Poor somatic growth has been shown to be associated with urine

sodium less than 30 mEq/L (30 mmol/L), and corrective measures are like adding salt to feeds, etc. [27]

2. Parenteral nutrition

Post-surgical resection, the remnant bowel requires time to recover and adapt. This transition phase is managed by parenteral nutrition, with the aim of providing essential nutrients for adequate growth, until the gut recovers. Various strategies have been studied for the prevention of IFALD in post-surgery infants, prone to SBS-lipid minimization and the use of Fish oil lipid emulsions are two strategies that have shown to be particularly useful. [28] In fact, lipid restriction, especially in the initial stages, has been shown to circumvent the development of parenteral nutrition-associated liver disease (PNALD) too. Similarly, the restriction of intravenous soy-based lipids to 1g/kg/day has been shown to reduce the likelihood of the development of Liver disease in these infants. [29]

There are limited data on the nutritional adequacy of intravenous fish oil lipid emulsion (FOLE) compared with standard soybean oil lipid emulsion (SOLE) in the setting of intestinal failure, however growth data comparison in a large cohort of infants showed comparable somatic growth to those treated with SOLE in early infancy, and improved somatic growth up to 24 months of age, supporting its wider use in this patient population. [30]

As enteral feeds are better tolerated, PN should be regimentally tapered off. [31] There may be a potential benefit of initiating cyclic PN prior to the development of hyperbilirubinemia in surgical neonates. [32]

3. Enteral nutrition (EN)

Multiple studies have been published, suggesting the beneficial role of early initiation of enteral feeding in post-bowel resection surgery. [33] In a multicentre prospective trial, early postoperative (starting a mean of 12 h) initiation of breastfeeding, in small quantities, was found to be useful. This held true even in patients in which intestinal anastomoses were performed. [34] Human milk may assist in the early adaptation of the gut, owing to the presence of growth-promoting factors like the growth hormone, epidermal growth factor, and Glutamine. Thus, human milk should always be the preferred choice of feed postoperatively. Cow's milk may be tried in case the aforementioned is not available. Amino-acid-based formulae may be given a shot in cases of intolerance to milk. [35] It is also reasonable to start with an elemental formula, in the absence of milk, switching to extensively hydrolyzed polymeric feeds, particularly if the patient is older than 1 year. [31] However, no clear recommendations exist for the choice of feeds, immediate postoperative, in neonates and young infants.

Formulae with medium chain triglyceride content in the excess of 40% are preferred, as they are directly absorbed into the portal system, obviating the need for bile acids. This leads to much better absorption in the small intestine, as compared to the formulae with a preponderance of long-chain fatty acids. Long-chain fatty acids, too, however, are essential, as they have a role to play in intestinal adaptation. Therefore, ideally, a combination of long-chain and medium-chain triglycerides, along with a low total fat content should be employed. [36]

In the postoperative period, in patients of SBS, two feeding strategies may be utilized- continuous tube feed, which has the advantage of an overall increased absorption of nutrients, [38] and intermittent feeding may be employed, which is more physiological leading to a better stimulus for the secretion of the various GI enzymes and hormones, including gall bladder draining. Generally, in the postoperative period, continuous enteral feed is started swiftly. Small, oral bolus top-ups are attempted as soon as possible thereafter. [30] The further progression of these feeding strategies is individualized, mainly depending upon the stool and stoma output of the patient. It is also noteworthy to add that SBS infants are highly prone to cow milk allergy, and hence, should be carefully monitored for the same. [37]

Pharmacological Interventions in SBS (Table 2)

1. Antisecretory agents

Acid suppression: Patients with SBS are prone to hypergastrinemia, especially for the first six months after surgery. Either H2-receptor blockers or proton pump inhibitors are often used to suppress gastric acid secretion. In general, H2 antagonists are considered second-line treatment because of their decreased efficacy relative to PPIs. [39] The risk of bacterial overgrowth and vitamin B12 malabsorption is associated with their long-term use.

Bile acid sequestrants: Cholestyramine may be appropriate for patients with diarrhea due to malabsorbed bile acids entering the colon following extensive resection of the distal ileum. Should be used with caution because they may impair fat-soluble vitamin absorption and cause gastrointestinal irritation.

Octreotide: is a somatostatin analog that may be considered an option for watery diarrhea that does not respond to other measures. Octreotide can decrease secretory losses due to a high jejunostomy but has not been recommended uniformly because of its interference with the adaptation process after intestinal resection.

2. Drugs for motility disorder

Loperamide and diphenoxylate-atropine are the first-line drugs for antimotility agents. Loperamide, which

is a peripherally restricted μ-opioid receptor agonist, does not cause undesirable central nervous systems (CNS) effects, such as sedation, euphoric effects, or addiction. In SBS with bowel motility disorders, the use of prokinetic agents may be indicated. Erythromycin improves antro-duodenal coordination and increases gastric emptying. Azithromycin, which is a longer-acting analog, may be utilized for the same purpose. Cisapride is another potentially useful therapy for gastrointestinal dysmotility. Studies have shown modest improvement in feeding tolerance; however, patients treated with Cisapride require careful cardiac monitoring because of the risk of QT prolongation. [40]

3. Ursodeoxycholic acid

Ursodeoxycholic acid (UDCA) is frequently used in the management of Parenteral nutrition-associated cholestasis. It is administered at a dose of 20-30 mg/kg/day divided into two or three doses once patients are tolerating EN. Animal studies and human studies have concluded that UDCA administration is beneficial in SBS treatment by enhancing the natural adaptive response of the intestinal remnant following massive jejunoileal resection. [41,42]

Table 2: Drugs used in the management of SBS.

Drug class and mechanism	Drugs	Doses
Histamine H2 receptors / Proton-pump inhibitors Decrease acid production	Ranitidine Famotidine Pantoprazole Omeprazole Lansoprazole Esomeprazole	5–10 mg/kg/day PO/IV BID 1 mg/kg/day PO/IV BID 1–2 mg/kg/day PO/IV QD 1–4 mg/kg/day PO QD/BID 1–2 mg/kg/day PO QD/BID 10 mg PO/IV QD (<20 kg), 20 mg PO/ IV QD (> 20 kg)
Bile acid sequestrants Decrease malabsorption due to bile acids	Cholestyramine	240 mg/kg/day PO BID/TID
Somatostatin analog Decreases intestinal secretions	Octreotide	4-10 mic/kg/hr
Antimotility agents Decrease transit time	Loperamide	0.4–0.8 mg/kg/day PO QID 15–60 mg PO QID
Prokinetic agents		
Improve intestinal dysmotility	Metoclopramide Erythromycin	0.1-0.3 mg/kg/dose 3-4 times/day 10 to 20 mg/ kg per day in 3 divided doses.
Antibiotic Decrease Small intestinal bacterial overgrowth	Metronidazole Rifaximin Neomycin Clindamycin Ciprofloxacin	21–30 mg/kg/day PO TID for 7–14 days 200–550 mg PO TID for 7–14 days 50–100 mg/kg/day PO TID/QID for 7–14 days 10–25 mg/kg/day PO TID for 7–14 days 15–20 mg/kg/day PO BID for 7–14
Growth factors: glucagon-like peptide 2 analogs	Teduglutide	0.05 mg/kg/day SQ QD

4. Antibiotics

Aggressive management of small intestinal bacterial overgrowth (SIBO) includes treatment with antibiotics such as oral gentamicin, metronidazole, rifaximin, neomycin, clindamycin, and ciprofloxacin for 7–14 days. Cyclical use (1 week per month) of broad-spectrum antibiotics (e.g., Metronidazole or Ciprofloxacin) is the mainstay of therapy for SIBO at many centers. [43] Antibiotic rotation policy can reduce the development of drug resistance.

5. Probiotics

Patients with SBS have a significant change in the intestinal microbiota. There is a paucity of clinical studies of probiotic supplementation in children with SBS. However, the evidence from animal studies and clinical case reports indicates that probiotics do have a potential for benefit in this population of patients. This needs validation and evaluation in large trials. [44]

6. Glutamine

Controversy surrounds supplemental enteral glutamine. Beneficial effects of isonitrogenous and isocaloric glutamine supplementation of parenteral nutrition have not been identified in newborns and infants after major digestive-tract surgery. [45] The available data from randomized controlled trials do not suggest that glutamine supplementation has any important benefits for young infants with severe gastrointestinal disease. [46]

7. Hormonal therapy

Therapy with gastrointestinal hormones to induce intestinal adaptation shows promise as a medical therapy for intestinal failure. Two recent medical therapies have emerged recently: glucagon-like peptide 2 (GLP-2) and somatropin (human growth hormone).

Glucagon-like peptide 2 (GLP-2) is a naturally occurring hormone secreted by enteroendocrine cells in the distal ileum and colon. Seventeen pediatric patients with intestinal failure associated with SBS were treated with teduglutide. Patients received 0.05 mg/kg/day of subcutaneous teduglutide. Teduglutide seems to be a safe and effective treatment in the pediatric SBS population with better results than in the pivotal study as well as in the adult population. [47] In another analysis, combined safety data of 89 pediatric patients from 4 clinical studies of teduglutide in children with short-bowel syndrome-associated intestinal failure (SBS-IF) was assessed. Three serious acute events in 3 patients (3.4%) were considered related to teduglutide treatment: ileus, d-lactic acidosis, and gastrointestinal obstruction due to hard stools. [48] There is a lack of neonatal studies to support the efficacy and adverse effect profile of this new treatment modality. Growth hormone (GH) has not been shown to improve the weaning off of PN in PN-dependent children with SBS. [49]

8. Micronutrient supplementation

Regular monitoring and aggressive supplementation of micronutrients in children with intestinal failure are warranted. In a retrospective analysis of children with severe intestinal failure, multivariate analysis identified regular use of a multivitamin supplement (P=.004) and intact ileocecal valve (P=.02) as protective against the development of vitamin deficiencies, independent of bowel length, gestational age, and PN days. [50]

The most common deficiency seen in SBS is Iron deficiency. Due to the malabsorption of vitamin D and calcium, patients with SBS are at risk for metabolic bone disease. Suboptimal 25-OHD levels are common in children with intestinal failure on home PN. This emphasizes the critical importance of routine surveillance of serum vitamin D levels and consideration of oral supplementation when indicated. [51] Magnesium deficiency is also common and occurs most severely in those with resection of the distal small bowel.

Prevention and Treatment of CLABSI

Each center should have an individualized protocol for the prevention, recognition, and prompt treatment of CLABSI. Ethanol lock therapy is emerging as a promising therapy in prevention. It has been shown to reduce both CLABSI and central line complication rates in children with Intestinal failure. [52]

Surgical Aspects

The preservation of as much bowel length as possible during the initial surgical management may help in decreasing SBS. If bowel viability is a concern, the abdomen can be left open or temporarily closed, with a planned second-look operation in 24 to 48 hours. In some patients who are critically unstable, the abdomen may be opened and the entire bowel contents placed in a silo until a more definitive operation can be performed when the patient stabilizes. [53]

Intestinal lengthening procedures like the Serial transverse enteroplasty (STEP), and Longitudinal intestinal lengthening and tailoring (LILT) are both accepted procedures for the surgical management of SBS in children. Both procedures have a similar extent of intestinal lengthening (approximately 70%) and result in improvement of enteral nutrition and reversal of complications of parenteral nutrition. The outcome after STEP seems to be more favorable, but larger series are needed to estimate the effectiveness of procedures and also assess an accurate selection of eligible patients. [54]

Mucous Fistula Refeeding (MFR)

Mucous fistula refeeding involves the instillation of proximal stoma contents into a distal enterostomy/ mucous fistula. Bhat et al systematically evaluated the existing literature on chyme recycling (CR) in neonatal and Pediatric populations. Clinical benefits included weight gain, PN reduction or cessation, normalization of fluid balance, improvement in liver function tests, and distal gut maturation. [55] Neonates who underwent MFR had a lower chance of an anastomotic leak and quicker progression to full feed after reversal versus controls. However, significant complications associated with MFR have been described including perforation and bleeding. Current evidence suggests the benefits of MFR; however, an international consensus is yet to be reached on the optimal method. [56]

Stoma Reversal

The prompt restoration of bowel continuity through stoma closure is associated with more rapid weaning from PN. In various surgical conditions like ileal atresias patients may be readmitted or not discharged after primary surgery. It may be challenging for caregivers to manage the high output stomas in the absence of trained healthcare professionals. These patients may be started on TPN and MFR followed by an early reversal of the stoma. At times, diagnoses like total colonic aganglionosis or Hirschsprung may be entertained before stoma reversal. These patients will require a high level of neonatal care in balancing the

electrolytes and nutrition. An aggressive trend in weight gain, even though slow is essential before restoring bowel continuity.

Prognosis and Long-term Outcomes

Enteral autonomy, sepsis, development of IFALD, and participation in a multidisciplinary intestinal rehabilitation program have been identified as significant predictors of survival in children with SBS. Residual small bowel length has been found to be a significant independent predictor of the duration of PN. [57] Necrotizing enterocolitis (NEC) which is the most common underlying diagnosis of short bowel syndrome (SBS) has a significantly higher likelihood of fully weaning from parenteral nutrition compared to children with other causes of SBS. [58] In a study, the long-term impact of infantile short bowel syndrome on nutritional status and growth was assessed. SBS results in shorter stature than was expected from their calculated target height. Bone mineral content was lower than reference values, but the subjects had normal weight for height and body fat percentage. [59] Preterm infants with SBS have been found to be at an increased risk of impaired growth and adverse neurodevelopmental outcomes at 18-26 months of corrected age. [60]

The advancement of neonatal care and provision of long-term parenteral nutrition support has improved the outcomes of this entity. Long-term outcomes and disease burden of neonatal onset short bowel syndrome were studied in adolescents. Of the cohort studied, there was no mortality, and more than 75% achieved enteral autonomy. The disease burden remains high for adolescents who remain dependent on PN. [61] With the advancement in medical and surgical management, the need for intestinal transplantation in patients with SBS has decreased drastically. [62] Management of SBS patients in a multidisciplinary intestinal rehabilitation program has led to improved survival, higher rates of weaning from PN, and other important outcomes.[63]

CONCLUSION

Management of SBS involves a multidisciplinary approach. Survival and quality of life have improved in these neonates with better PN strategies and the implementation of rehabilitation programs. The management of these patients involves nutritional, pharmacologic, and surgical interventions to achieve enteral autonomy while minimizing the complications of PN therapy. The use of hormonal modulation like GLP2 analogues to facilitate intestinal adaptation needs further research, especially in early infancy. Bowel lengthening and tapering procedures may be beneficial in a selected group of patients.

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