

# Study of Short-Term Outcomes of Targeted Therapy in Operated Patients of Hirschsprung Disease Who Were Found To Have Poor Functional Outcome at Initial Assessment

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## Keywords

Hirschsprung Disease  
Bowel Function Scoring  
Fecal Incontinence  
Constipation

## Abbreviations

**BFS** - Bowel function score  
**DPT** - Duhamel pull-through  
**EUA** - Examination under anesthesia  
**HD** - Hirschsprung Disease  
**HIC** - High income countries  
**LMIC** - Low- middle- income countries  
**QoL** - Quality of life  
**TCA** - Total colon aganglionosis

## Abstract

**Background:** Long-term morbidity and functional bowel problems after surgical treatment of HD are significant. There is no consensus regarding the most appropriate scoring system for the assessment of functional outcomes. Also, there is a paucity of data from low- and middle-income countries (LMIC).

**Materials and Methods:** This prospective interventional study included 31 children, aged 4 to 18 years, who had undergone definitive surgery for Hirschsprung disease (HD) between 2011 and 2020. Among the cohort, those with low bowel function score BFS (<17) were selected for targeted therapy of constipation, soiling, or both.

**Results:** There were 19 patients with BFS < 17. Male-female ratio was 17:2. The mean age at enrollment was 6 yrs (range 4.3 - 12 yrs). Fifteen (79%) of them had classical HD, while 4 (21%) had long-segment HD. The mean time elapsed since surgery was  $3.86 \pm 2.37$  years. Twelve (63%) of them had constipation, while 7 (37%) had both constipation and soiling and none had exclusive soiling. The mean BFS before and after targeted therapy was  $15 \pm 1.05$  (range 13-16) and  $18.21 \pm 0.63$  (range 17-19) respectively. After intervention, in all of them BFS improved  $\geq 17$ .

**Conclusions:** HD has significant problems for many years after definite surgery. Using BFS, we can identify patients who need early targeted interventions including medical and surgical therapy. The extent of aganglionic bowel, age at the initial presentation and gender do not appear to affect the final outcome. Short-term 3-month targeted therapy was beneficial in those with BFS<17.

## INTRODUCTION

Hirschsprung disease (HD), congenital absence of ganglion cells of the distal bowel, is one of the most common surgical conditions in the pediatric age group.<sup>(1,2)</sup> Surgical resection of poorly functioning aganglionic segment and an anastomosis of a normally innervated proximal bowel to the distal rectum is the definitive treatment of HD. Final outcome and long-term function do not differ significantly between various surgical operations such as the Swenson's procto-colectomy, Duhamel pull-through (DPT), Soave's operation and laparoscope-assisted endorectal pull-through.<sup>(3)</sup>

Jarvi et al. found that long-term morbidity and functional bowel problems are significant after definitive treatment of HD. Fecal incontinence and constipation are troublesome postoperative complications. Obstructive symptoms may be due to residual aganglionic segment, stricture, or dysmotility, whereas fecal incontinence may be due to operative injury to anal sphincter, inappropriately low colo-anal anastomosis or overflow soiling.<sup>(4)</sup>

Various factors that may affect the quality of life (QoL) including the age at surgery, sex, type of surgery operation, level of aganglionosis, initial stoma diversion, enterocolitis episodes, and bowel dysfunction have been studied. None of them other than bowel dysfunction was found to impact the QoL.<sup>(5)</sup>

Although HD is a disease of childhood, its final outcome continues to evolve well into adolescence and adulthood. A combination of several parameters must be carefully assessed at specified intervals to identify patients who are liable to have mid-and long- term complications and those who will benefit significantly from early intervention.

To date, there is no consensus regarding the most appropriate scoring system for assessing the

functional outcomes in these patients. Some authors like Hartman<sup>(6)</sup> use generic questionnaires while others like Meinds use Rome- IV criteria of constipation.<sup>(7)</sup> Some authors like Moore et al<sup>(8)</sup> from South Africa and Gabriella et al<sup>(9)</sup> from Indonesia have used anthropometric data as an index to compare the long-term effect of HD surgeries on the child's growth and development by comparing them with standardized growth charts. However mere physical growth is an insufficient indicator of overall development.

Another important point is that most of these studies were done in high-income countries (HIC) where the standards of ancillary services are excellent. A study by Kumar et al from Vellore, India examined the functional outcomes and QOL in HD; but did not find significant differences between the patient cohort and healthy controls. This was a cross-sectional study and it did not evaluate the long-term result of targeted interventions.<sup>(10)</sup>

Thus, a critical assessment of mid- and long-term complications in patients operated for HD in LMIC is lacking. We hypothesized that patients with low bowel function score (BFS) during initial assessment, if provided with targeted intervention without delay, can lead near-normal lives well into adulthood. This study was conducted to examine this hypothesis.

## MATERIAL AND METHODS

A prospective interventional study of children treated for HD was performed after receiving clearance from the institutional ethical committee. The patients aged 4 to 18 years who had undergone definitive surgery for HD at the Pediatric Surgery Department of our tertiary center from 2011 to 2020 were recruited for the study after due approval of Institutional Ethics Committee. Those who underwent definitive surgery within 6 months of study enrollment and those who were not willing were excluded from the study. Some of them had temporizing diverting

colostomy done elsewhere. Patients having total colonic aganglionosis (TCA), ultra-short HD (anal achalasia), severe neurological deficit, permanent stoma or hypothyroidism were excluded from the study. Of the patients were re-operated for HD over seven years (July 2016- November 2022), 56 could be contacted and only 31 patients agreed to be enrolled in the study. Previous records of operated patients were retrieved and reviewed. Patients were convened to the hospital for physical examination. Those who could not visit the hospital were contacted by phone and the conversation was recorded. Those who experienced problems related to surgery were encouraged to visit the hospital. Written informed consent was obtained from each participant. Details regarding the length of aganglionic bowel, nature of surgical treatment, episodes of enterocolitis, complications, and any additional surgical interventions needed were noted from previous records.

HD was classified as: (a) classical - if the aganglionic region was limited to the rectum and sigmoid colon; (b) long segment - if it extended proximal to the sigmoid colon but not the entire colon. The definition of constipation used was according to the criteria proposed by Drossman et al.<sup>(19)</sup> Constipation was defined as straining at the stools more than 25% of the time or less than 3 stools per week. Fecal soiling was defined as small amounts of feces having to be scrubbed off the underclothing at least once a month.<sup>(20)</sup> Incontinence was defined as the inability to control bowel movements causing the child of age  $\geq 4$  yrs to repeatedly pass stools in inappropriate places.<sup>(21)</sup> Enterocolitis was diagnosed by the combination of abdominal distension, diarrhea or bloody stools, vomiting, and fever. Mid-term complications were defined as those occurring between 6 months - 2 years following definitive surgery. Long-term complications included those occurring after 2 years of surgery.

All patients were assessed using Bowel Function Score (BFS) questionnaire (Appendix-1). BFS is a 20-point score which includes various parameters like constipation, soiling, urgency, frequency of defecation, fecal accidents, and social problems. All those with BFS < 17 (n=19) were categorized as poor outcome patients and labeled as 'index cases'. Among these, 16 (84%) developed symptoms after 6 months of surgery and 3 (15%) after 2 years of surgery.

All the index cases underwent barium enema imaging of colon. (Fig 1) Those presented with exclusive constipation had examination under anesthesia (EUA), while those with both constipation and soiling had both EUA as well as anorectal manometry. All were offered with targeted therapy for the condition diagnosed on investigations. (Fig 2 and 3) The effect of the targeted therapy was studied after 3 months and the improvement in BFS, if any, was recorded.

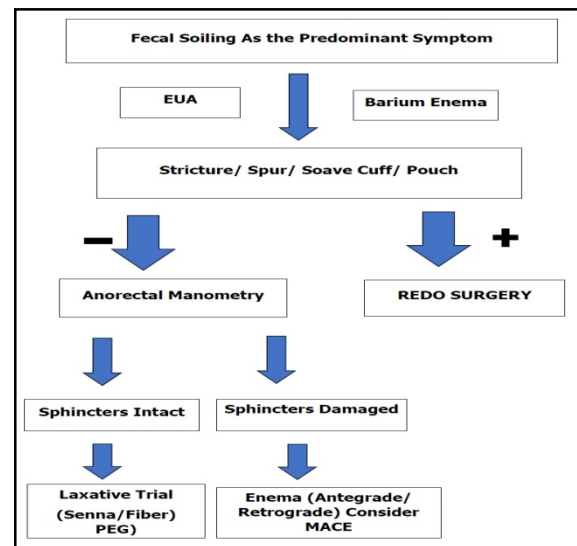
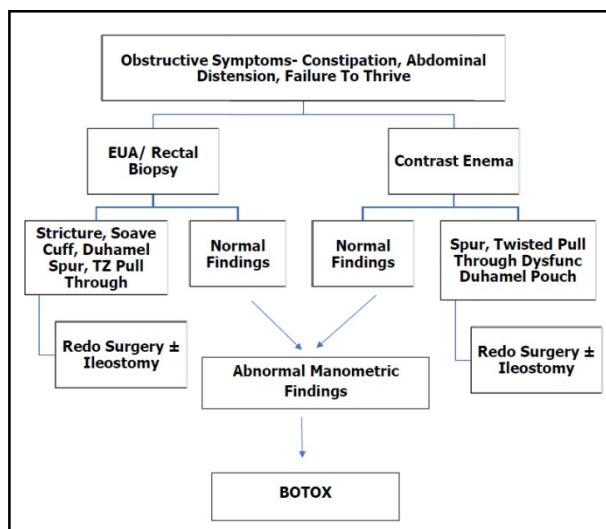


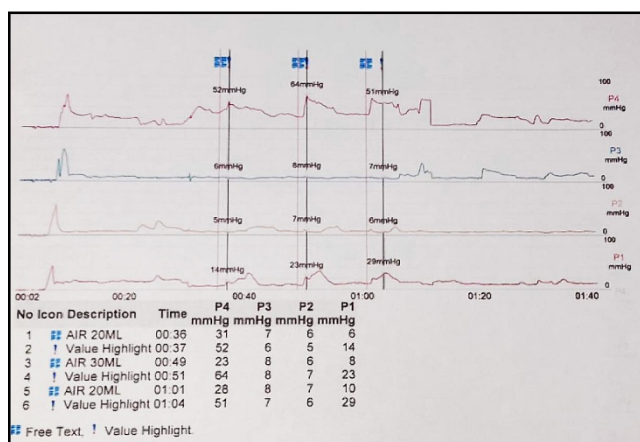
Fig 1. Scheme of evaluation

## RESULTS

Of the 31 enrolled patients, 90% (n=28) were males and 10% (n=3) were females. The average age at enrolment was 7.4 years in males and 6.3 years in females. The mean age at initial contact for definitive treatment was  $3.6 \pm 3.5$  yrs (range: 4 mo to 11 yrs). Of them, 23 (74%) had classical HD, while 8 patients (26%) had long-segment HD.



**Fig 2.** Algorithm of targeted therapy for Bowel Function Score <17 with constipation



**Fig 3.** Anorectal manometry of 12 year male patient (Pre-treatment BFS - 16)

The mean time elapsed since definitive surgery was  $5.8 \pm 2.4$  yrs.

The mean BFS of 31 enrolled patients at presentation was  $18.8 \pm 0.8$ . Among them 19 had BFS <17. There was no difference in BFS of males and females ( $14.94 \pm 1.09$  vs.  $15.50 \pm 0.71$ ); however meaningful analysis was not possible as there were only 3 girls.

The mean BFS of the 19 'index cases' before giving targeted therapy was  $15 \pm 1.05$  (range 13-16). The mean age of symptomatic presentation of the index cases was 1.42 yrs. Fifteen (79%) of the index cases had classical HD, while 4 (21%) had

long-segment HD. BFS of classical versus long-segment disease ( $15.07 \pm 0.96$  vs.  $14.75 \pm 1.50$  respectively) did not differ significantly. All 19 patients had undergone DPT as the definitive surgery. The mean time elapsed since surgery was  $3.86 \pm 2.37$  years. Twelve (63%) of the index cases had exclusive constipation, 7 (37%) had both constipation and soiling and none had exclusive soiling.

Barium contrast enema in all 19 index cases was normal. (Fig.4) Seventeen (89.5%) of the index cases had normal EUA findings, while 2 (10.5%) were found to have spur-on EUA; these 2 patients underwent 'spur division' at the same sitting. The other 17 patients (89.5%) were managed medically with dietary modifications (fiber rich diet such as salad, green vegetables), adequate fluid intake, laxatives, and water-soluble fibers to increase the bulk of the stool. The mean BFS after targeted therapy was  $18.21 \pm 0.63$  (range 17-19). All the index cases improved after targeted therapy with a BFS  $\geq 17$ .



**Fig 4.** Barium enema in 5-yr-old boy (Pre-treatment BFS 16)

## DISCUSSION

Duhamel introduced a new operative technique for Hirschsprung's disease in infants in 1956, his

procedure has gained worldwide acceptance. Heij et al. performed a systematic follow-up after DPT and confirmed a considerably high incidence of mid- and long-term complications. They observed that 17 out of 63 suffered some degree of incontinence, and 22 experienced soiling and/or constipation.<sup>(11)</sup>

Constipation is a major problem after DPT due to a large capacity reservoir partially consisting of the aganglionic bowel. Rescorla et al showed that 27% of DPT patients used enemas or stool softeners, and 8% had severe constipation.<sup>(12)</sup> In the current study also 61% of patients had significant problems after DPT.

Among the 19 index patients with low BFS, the mean pre-therapy BFS was 15.05 (range 13-16). This implies that patients who had undergone DPT have significant problem several months after the operation.

All index cases were evaluated for improvement, after 3 months of targeted therapy. It was heartening to note that the targeted therapy was effective in managing mid- and long-term complications in all of them.

Considerable literature is available for short- and mid-term complications of HD, but there is very little literature regarding long-term complications especially from LMIC. Ying et al found the prevalence of fecal incontinence, constipation, and bladder dysfunction after 10 yrs of definitive surgery was 20%, 14%, and 7% respectively.<sup>(13)</sup> Overall pooled BFS and QoL scores showed satisfactory results.

When analyzing the outcomes definitive treatment of HD, various surgical techniques must be taken into consideration. Various studies have compared outcomes with respect to DPT, Swenson, Soave, Laparoscopic endorectal pull through (LERPT), and transanal endorectal pull through (TERPT). However, there is no clear advantage of one

procedure over the other. Different risks and benefits are associated with these surgeries.

Since most of the surgeries performed at our center were DPT, we had no opportunity to study the outcomes of other surgical techniques. As regard to DPT in this study, 12 patients had constipation while 9 had constipation with soiling, and none had soiling alone. The symptom of only soiling (called true incontinence) signifies sphincter damage during surgery. Probably no other complication has a greater impact on the QoL than the incontinence. Unfortunately, incontinence rates are often not reported in many of the larger series. Others failed to make a distinction between occasional soiling and significant incontinence.

It is difficult to attribute a cause of high incontinence rates in some series. Comparison of series is difficult as the technique, expertise and meticulousness of stool history vary considerably between them.<sup>(14)</sup> Since none of our patients had 'true incontinence' it can be said the DPT is a relatively a safe procedure to be done by experienced surgeons.

In our study, the final functional outcome after DPT for HD was independent of the length of aganglionosis. Contrary to this, Shu et al<sup>(15)</sup> found that among the 12 out of 58 (21%) patients who were symptomatic, one-third had aganglionic segment less than 30 cm and two-third had aganglionic bowel more than 30 cm, whereas in the 46 asymptomatic patients, 91% (n=42) had less than 30 cm aganglionic segment, and 4 had 30 cm or longer aganglionic segment. This difference was statistically significant thereby suggesting that the extent of HD has an impact on the outcome. Similarly, Moore et al<sup>(16)</sup> also found a significant difference in outcomes of patients with classical HD versus long-segment HD versus TCA. Of the 178 responders, 123 (69%) had a classical HD, 41 (23%) had a long segment HD, and 14 (8%) had TCA. In 29 patients with postoperative

complications, 14 had long segments HD (48.2%), and 5 (17.2%) had TCA. This patient segment (with complications) represents 34% of those with long colonic aganglionosis and 62% of those with TCA in the study sample. Catto-Smith et al<sup>(17)</sup> reported that a substantial proportion of the interviewees limited their physical or social activity because of soiling or odor. Patients with a history of long-segment disease had overnight soiling more frequently than those with short segment disease (often/ always: long segment 9/18; short segment 8/53;  $P < 0.01$ ). Soiling stool was more loose in consistency (long segment 12/13; short segment 10/13;  $p < 0.05$ ). This difference could be explained by the following findings. First, our sample size of the study is small. Second, all of our patients underwent DPT as the definitive surgery, while in the study by Moore et al, different surgical procedures have been done. Also, we have excluded cases of TCA in our study.

The timing of pull-through surgery is a controversial issue and the current trend is to do the pull-through operation early. However, Gunnarsdottir et al<sup>(18)</sup> could not find any statistical difference in the QoL in the adults who underwent surgery before 6 months of age as compared with those who were operated on later.

The benefit of early diagnosis and treatment is that most of the mid-term complications can be managed well before the child starts going to school, thus preventing any social embarrassment and loss of school days. Most of the pediatric surgeons can perform pull through operation in infants without much difficulty hence one must try to diagnose and treat HD at the earliest. It is worth mentioning that with improved diagnostic availabilities and better access to healthcare for more populations, now children are presenting at a younger age than before. In our study, the youngest patient to have presented was 4 months old. In contrast, a few years ago, the patients used to first present as late as 7-8 years. On comparing BFS among index cases no statistically significant

difference was found concerning the age at which the patient first presented with symptoms. Thus, it is concluded that the age at presentation has no impact on the final outcome.

Gunnarsdottir et al<sup>(18)</sup> found that females had significantly lower mean scores for general health and mental health than the age and sex-matched controls in Swedish general population. Females had also lower mean scores than males in all subgroups. Women with HD had a lower QoL in adulthood and needed special consideration in their follow-up. Reviewing their medical records did not reveal any plausible explanation.

The unique feature of this study is that unlike most of the previous studies, it is a longitudinal study wherein we have assessed the efficacy of targeted therapy in improving BFS. The studies available in the literature provided only a cross-sectional evaluation of QoL.

There are few demerits of the current study. The cohort studied was retrospective; the operative notes of patients did not specifically mention if it was Martin's modification or otherwise. Small sample size with a limited period of study is another demerit. The relationship between the outcome versus the type of HD and sex of patients needs to be interpreted with caution due to fewer cases of long-segment HD and number of females in the study. It was not possible to assess the outcome of different surgical procedures as DPT is the predominant surgery done at our institute. The BFS questionnaire does not take into account episodes of enterocolitis which is a catastrophic complication of HD. So, its impact on the overall outcome could not be assessed. The study design does not take into account urinary dysfunction which according to some studies is quite prevalent following DPT. This study excluded cases of TCA and HD patients with associated Down syndrome. These patients are generally expected to have more problems related to bowel control. To test



the efficacy of BFS, the study must include these patients as well.

To conclude, this study showed that a significant number of HD patients continue to have bowel problems for many years after definite surgery. Parents or caretakers of patients must be counseled regarding the need of long-term follow up which extends to many years after definitive surgery. These patients face significant gastrointestinal problems (constipation with or without soiling). Using bowel function scores, we can identify patients who need early targeted interventions including medical and surgical therapy. Most patients present with mid-term complications, while few patients have long-term complications, though the functional outcome among both these groups of patients is similar. The residual spur seen in a few patients, suggests that the use of appropriate size staplers and Martin's modification of Duhamel pull-through at initial surgery might avoid this complication. Extent of HD, age at the initial presentation and gender do not affect the final outcome. Short-term targeted therapies for 3-month appears to have favorable results.

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## APPENDIX -1

### Box 1: Bowel Function Score Questionnaire

Factors	Score
<b>Ability to hold back defecation</b>	
❖ Always	3
❖ Problems < 1/week	2
❖ Weekly problem	1
❖ No voluntary control	0
<b>Urge to defecate</b>	
❖ Always	3
❖ Most of the time	2
❖ Uncertain	1
❖ Absent	0
<b>Frequency of defecation</b>	
❖ Every other day or twice a day	2
❖ More often	1
❖ Less often	0
<b>Soiling</b>	
❖ Never	3
❖ Straining<1/week, No change of underwear required	2
❖ Frequent staining, change of underwear often required	1
❖ Daily soiling requiring protective aids day and night	0
<b>Fecal accidents</b>	
❖ Never	3
❖ < 1/week	2
❖ Weekly requiring protective aids	1
❖ Daily requiring protective aids	0
<b>Constipation</b>	
❖ None	3
❖ Manageable with diet modification	2
❖ Manageable with laxatives	1
❖ Manageable with enemas	0
<b>Social problems</b>	
❖ None	3
❖ Sometimes	2
❖ Problems restricting social life	1
❖ Severe social / psychological problems	0