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HIRSCHSPRUNG'S DISEASE: OUR INSTITUTIONAL EXPERIENCE

Dr. Arka Chatterjee	Mch Resident, Department of Paediatric Surgery, Sir Padampat Mother and Child Health Institute, S.M.S. Medical College, Jaipur, Rajasthan, India.
Dr. Neeraj Tuteja	Assistant Professor, Department of Paediatric Surgery, Sir Padampat Mother and Child Health Institute, S.M.S. Medical College, Jaipur, Rajasthan, India.
Dr. Ramesh Chand Tanger	Associate Professor, Department of Paediatric Surgery, Sir Padampat Mother and Child Health Institute, S.M.S. Medical College, Jaipur, Rajasthan, India.
Dr. Pradeep Gupta	Assistant Professor, Department of Paediatric Surgery, Sir Padampat Mother and Child Health Institute, S.M.S. Medical College, Jaipur, Rajasthan, India.
Dr. Arvind Kumar Shukla*	Senior Professor, Department of Paediatric Surgery, Sir Padampat Mother and Child Health Institute, S.M.S. Medical College, Jaipur, Rajasthan, India. *Corresponding Author

ABSTRACT **BACKGROUND:** Hirschsprung's disease is one of the most important causes of functional intestinal obstruction in the paediatric age group. The clinical characteristics of patients with Hirschsprung's disease at a tertiary referral centre were studied over a 22-month period.

Aims and Objectives: To study the demography, including Age, Sex, various clinical presentations, types, segment involved, surgery, complications and survival in patients with Hirschsprung's disease at a tertiary care referral centre in Rajasthan, India.

Materials and methods: This was a prospective observational study between October 2018 and June 2020, over 22 months, at tertiary referral centre in North-Western India. Clinical data were tabulated, various presentations of the disease were studied, intra-operative findings were noted and post-operative course was studied.

Results: 82 cases of Hirschsprung disease were admitted, of which 66 were male and 16 were female.

Of these, 10 presented in the neonatal age group, 25 during infancy (1 month to 1 year of age) and the rest – 47 patients presented beyond infancy.

The commonest symptoms in infants and older children was chronic constipation, whereas delayed passage of meconium, abdominal distension and bilious vomiting were among the common symptoms in neonates.

The patients underwent exploratory laparotomy with multiple biopsies and diversion colostomies. 43 patients underwent the definitive procedure. In all the 43 patients, Martin's modification of Duhamel's procedure, was the surgery performed.

Complications included persistence of constipation, enterocolitis, and a few cases of anastomotic leak.

KEYWORDS : Hirschsprung's Disease, Demography, Clinical symptoms, Management, Anganglionosis.

INTRODUCTION

Hirschsprung disease (HD) is a developmental disorder of the intrinsic component of the enteric nervous system that is characterized by the absence of ganglion cells in the myenteric and submucosal plexuses of the distal intestine. Because these cells are responsible for normal peristalsis, patients with Hirschsprung disease present with functional intestinal obstruction at the level of aganglionosis (1).

Its incidence is approximately 1 in 5000 live-born infants (1). However, it varies significantly between different ethnic groups, with the highest being in Asia (2.8/10,000 live births) (2).

Hirschsprung's disease is a result of the failure of migration of ganglion cells, cephalocaudally through the neural crest during fourth to 12 weeks of gestation, causing an absence of ganglion cells in all or part of the colon (3). The aganglionic segment usually begins at the anus and extends proximally (4). The most common segment involved is the recto-sigmoid region which is known as short segment Hirschsprung's Disease. When the portion of the colon involved extends beyond this, it becomes long segment Hirschsprung's Disease, and it can involve the entire colon. The small intestine being involved in addition to the large intestine is quite rare (5). Majority of the cases are sporadic, however, familial incidence has been reported up to 20% (6, 7). HD is a heterogeneous condition with multiple genetic causes and etiologic mechanisms. The heterogeneous nature of Hirschsprung disease is supported by increasing evidence that mutations in a variety of genes may be responsible. (1). Around 15 genes have been identified, among which, the RET proto-oncogene is the most commonly identified (8).

RET abnormalities are more commonly found in familial and long-segment disease (1). A suspicion regarding the association of environmental or epidemiological factors such as Vitamin A deficiency, exists (9). However, this is not well-characterized yet.

HD has various presentations, ranging from neonatal intestinal obstruction, to chronic progressive constipation in older children. Around 80% of the patients present in the early months of life with difficult bowel movements, poor feeding, bilious vomiting and progressive abdominal distension (1, 10, 11). Delayed passage of meconium beyond the first 24 hours is characteristic, and is present in 90% of children with Hirschsprung's Disease (1).

Diagnosis of HD is mainly done by radiographic studies, anorectal manometry and histological examination of rectal wall biopsies (12). In any neonate who presents with the features of obstruction, a water-soluble contrast enema is the first step in the diagnostic pathway (1).

HD was first successfully treated by Orvar Swenson about 60 years ago (13). In this surgery – the Swenson procedure, the distal aganglionic colon was freed up to 2 cm above the dentate line and end to end anastomosis was performed. Currently, there are many other surgeries including the Duhamel retro-rectal pull through (14), and its modifications – such as the Martin's modification (15) of the Duhamel pull through, which was the surgery performed in the nearly all the patients in this study that underwent the definitive procedure. Other surgeries are endorectal pull-through of Soave procedure and its various modifications (16).

The objectives of this study were to explore the demography, including Age, Sex, various clinical presentations, types, segment involved, surgery, complications and survival in patients with Hirschsprung's disease at a tertiary care referral centre in Rajasthan, India.

MATERIALS AND METHODS

This was a prospective observational study, conducted between October 2018 to June 2020, in the department of Paediatric Surgery, at a tertiary care centre in Rajasthan, India.

The study included all cases of Hirschsprung disease that presented at the hospital.

The patients presented either in the neonatal age group with features of intestinal obstruction, such as abdominal distension, bilious vomiting and, also with delayed passage of meconium beyond the first 24 hours. Blast sign on rectal examination was present in all the neonates.

The older children presented with chronic progressive constipation. The earliest age of presentation in this study was 2 days and the oldest age was 12 years.

The neonates who presented with the symptoms of intestinal obstruction were first resuscitated, with adequate intravenous fluids, antibiotics, nasogastric tube drainage. Erect x ray abdomen usually revealed dilated large bowel loops. Contrast enema study usually revealed dilated sigmoid colon and dilatation of colon proximal to the transition zone, characterized by an obvious change in diameter from narrow to dilated. Retention of contrast beyond 24 hours was also an indicator of the disease.

Once the patients were adequately resuscitated, after obtaining proper consent, the patients were taken up for exploratory laparotomy. At laparotomy, the transition zone was identified, most often at the rectosigmoid junction. The transition zone found at surgery correlated with the radiological transition zone in most of the cases. A colostomy, 5 cms proximal to the transition zone, was done with resection of the transition zone in most cases, in order to decompress the bowel. The colostomy was most commonly an end colostomy with a Hartman's pouch creation. In other cases, a loop colostomy or a divided colostomy was performed. Biopsies were taken from the transition zone, the colostomy site and the rectosigmoid junction. Hematoxilin and Eosin (H and E) staining, Acetylcholinesterase staining (AChE) are used. The biopsy reports usually revealed absence of ganglion cells in the rectosigmoid and rectum, along with the presence of hypertrophic nerve fibers. The functioning colostomy site had presence of ganglion cells. In older children presenting with chronic constipation, a rectal biopsy was taken which had the same histological findings as mentioned above. An elective levelling colostomy was done in these cases, following the rectal biopsy, with further biopsies being taken of the transition zone and the colostomy sites.

Definitive surgery

After obtaining all the biopsy reports, the definitive surgery was planned. Prior to the definitive surgery, thorough rectal washes were given, in order to evacuate feculomas. A complete bowel wash was given either through normal saline via a nasogastric tube, or polyethylene glycol solution orally.

After satisfactory preparation of the bowel, the definitive surgery was performed, following a proper informed consent, detailing the risks and complications of the procedure and after obtaining fitness for surgery.

In all the patients who underwent the definitive surgery, Martin's modification of Duhamel pull through was performed.

The surgery was done with the patient in semi-lithotomy position, with the lower limbs abducted, flexed at the knee, and the anus exposed adequately, placing a bolster below the sacrum of the patient.

The abdominal exposure was done with a left sided hockey stick incision, incorporating the colostomy within the incision. If the previous colostomy was a loop or divided colostomy, the distal limb was resected partially, leaving behind adequate length of the distal sigmoid and rectum for the anastomosis. In the majority of the patients, an end colostomy with Hartman's pouch creation had been performed in the previous surgery. In these patients, the Hartman's pouch was identified at the definitive surgery. The pouch was dissected, freeing the posterior attachments, creating an adequate recto-rectal space. This space was created by using blunt dissection. Extra care was taken in order to avoid damage to both ureters and pelvic vessels and plexus of nerves.

Once the space was created, a “smiling” incision was made on the posterior wall of the rectum, around 2 cms, from the dentate line. The proximal function colostomy segment was freshened, and sent for biopsy in order to assure that the segment pulled through contains ganglion cells, and adequate length of the colon was mobilized, in order to form the pull through segment. This segment was “pulled-through” the incision in the posterior wall of the rectum, and the anterior and posterior lips of the pulled through segment was anastomosed to the upper and lower lips of the incised posterior wall of the rectum, respectively. This “end-to-side” anastomosis was fashioned using absorbable polyglycolic acid sutures, in an interrupted manner, in order to facilitate the firing of the linear gastro-intestinal stapler. A transverse incision was made on the ante-mesenteric wall of the pulled through colon, corresponding to the site of the second anastomosis. A part of the aganglionic bowel was resected and the two limbs of the gastro-intestinal stapler inserted, from the caudal end, one into the pulled through segment, and one limb into the native rectum. The stapler was fired, thus creating a common chamber between the two segments. Any remaining “spur” was inspected for, and if it was found to be of a significant length, another linear gastro-intestinal stapler was fired, this time with one limb placed within the transverse incision which was made over the ante-mesenteric wall of the pulled through segment and the other limb within the proximal end of the aganglionic segment. The second hand-sewn anastomosis was fashioned between the two limbs in two layers, with interrupted polyglycolic acid sutures, for the first layer, and silk sutures for the second layer. After checking for haemostasis, the abdomen was closed in layers.

The clinical data were tabulated, the segments involved were noted, the type of surgery with the complications were evaluated.

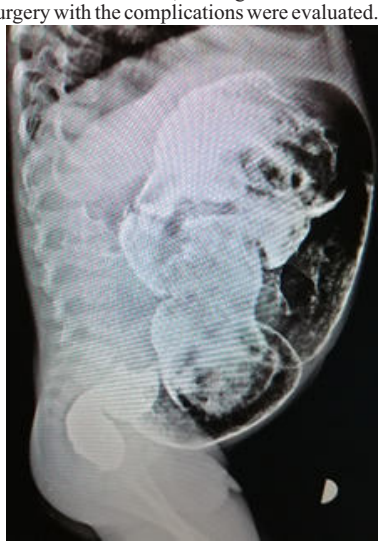

Figure 1 – Barium enema showing transition zone at the descending-sigmoid region

RESULTS

There were 82 cases of Hirschsprung's Disease, that presented between the age of 2 days and 12 years, between September 2018 and June 2020. Of these, 66 were male and 16 were female.

10 patients presented in the neonatal age group (1 day to 1 month), 25 patients during infancy (1 month to 1 year), and the rest of the patients – 47, presented beyond infancy.

History of delayed passage of meconium was present in all the neonates, and in majority of the children presenting later, as well. Apart from this symptom, among neonates, signs of intestinal obstruction were present, including abdominal distension and bilious vomiting.

3 of the 10 neonates presented with intestinal perforation, as evidenced by gas under the diaphragm on their erect abdominal x rays. The other 7 neonates that underwent water soluble contrast enema, following plain abdominal x rays, had dilated distal bowel loops, with a transition zone visible, most commonly at the rectosigmoid junction. 3 of these 7 neonates had the transition zone at the rectosigmoid junction. Another 3 of the 7 neonates had a transition zone at the splenic flexure of the transverse colon. 1 neonate had entire large bowel involved, on contrast enema. On surgical exploration the transition zones correlated with their contrast studies in each of the neonates.

4 of the remaining 72 patients underwent rectal biopsy, alone. The rest of the patients belonging to infancy and older age groups, underwent colostomies, proximal to the transition zone with either a Hartman's

pouch formation or loop colostomy or a divided colostomy, or ileostomy. In 43 among the 82 patients, a Hartman's pouch was created. In 3 patients, an ileostomy was made.

43 among 82 patients underwent the definitive procedure. Martin's modification of Duhamel's procedure, was the surgery performed in all the 43 patients.

One patient, who had total colonic aganglionosis, underwent ileo-anal pull through. Stoma site diarrhoea were seen in 12 patients. Skin excoriation was seen in 15 patients.

Non-function of stoma was seen in 2 patients.
Enterocolitis was the complication present in 10 of the 43 patients who underwent definitive surgery. 4 patients had persistence of constipation. 2 patients had anastomotic leak, both of whom underwent diverting colostomies. In one patient, perforation of the sigmoid colon had developed, which was primarily repaired. Surgical site infection was seen in 6 patients. Wound dehiscence was seen in 2 patients.

81 out of 82 patients survived. 1 patient had expired as a result of sepsis.

Table 1 – Sex distribution among the patients

MALE	66 patients
FEMALE	16 patients
RATIO	4.1:1

Table 2 – Different ages of presentation

AGE GROUP OF PRESENTATION	NUMBER OF PATIENTS	PERCENTAGE
NEONATES (1 DAY TO 1 MONTH)	10	12.2%
INFANTS (1 MONTH TO 1 YEAR)	25	30.5%
BEYOND INFANCY	47	57.3%

Table 3 – various clinical presentations in neonates

CLINICAL PRESENTATION AMONG NEONATES	NUMBER OF PATIENTS
INTESTINAL PERFORATION	3 OUT OF 10
ABDOMINAL DISTENSION, BILIOUS VOMITING	7 OUT OF 10
DELAYED PASSAGE OF MECONIUM	10 OUT OF 10

Table 4 – various clinical presentations beyond neonatal age group

CLINICAL PRESENTATION BEYOND NEONATAL AGE GROUP	NUMBER OF PATIENTS
CHRONIC CONSTIPATION	72 OUT OF 72
ABDOMINAL DISTENSION	60 OUT OF 72

Table 5 – Primary surgery performed

SURGERY PERFORMED	NUMBER OF PATIENTS
DIVERSION COLOSTOMY	75
ILEOSTOMY	3
RECTAL BIOPSY ALONE	4

Table 6 - Definitive surgery performed

SURGERY PERFORMED	NUMBER OF PATIENTS
MARTIN'S MODIFICATION OF DUHAMEL PULL THROUGH	43 patients

Table 7 – Protective stoma given

PROTECTIVE STOMA	NUMBER OF PATIENTS
ILEOSTOMY	3
COLOSTOMY	1

Table 8 – Length of segment involved

SEGMENT INVOLVED	NUMBER OF PATIENTS
SHORT SEGMENT – RECTOSIGMOID	76
LONG SEGMENT – UP TO TRANSVERSE COLON	5
TOTAL COLONIC AGANGLIONOSIS	1

Table 9a – Complications of Surgery

COMPLICATIONS RELATED TO STOMA	NUMBER OF PATIENTS
SKIN EXCORIATION	15
STOMA DIARRHOEA	12
ENTEROCOLITIS	10
NON-FUNCTION OF STOMA	2

Table 9b – Complications of Surgery

COMPLICATIONS RELATED TO DEFINITIVE PROCEDURE	NUMBER OF PATIENTS
SURGICAL SITE INFECTION	6
PERSISTENCE OF CONSTIPATION	4
ANASTOMOTIC LEAK	2
WOUND DEHISENCE	2
SIGMOID COLON PERFORATION	1

DISCUSSION

This study was a prospective observational study.
Hirschsprung's disease is an important cause of intestinal obstruction in the paediatric age group.

There were 82 patients of Hirschsprung disease that presented between October 2018 and June 2020.

The male to female ratio in this study was 4.1:1 which is comparable to the worldwide ratio of 2.9:1 to 4.5:1 (17, 18, 19, 20). In this study, 12.2% of patients presented in the neonatal age group. Most of the patients (87.8%) patients presented beyond neonatal age group with 57.3% patients presenting beyond the age of 1 year. This is in accordance with many studies in developing countries such as the one conducted by Mabula et al (10). However, it is in variance with other such studies in developing countries, such as the one conducted by Karim et al (21). This is also in variance with the presentation in developed countries, where majority of the patients – up to 90%, present during the neonatal age group (22).

The clinical presentation which was most common in this study was of chronic constipation and abdominal distension. This is similar to those in other studies (17, 23, 24).

Many patients present late as described in studies conducted in many developing countries (17, 23, 24), usually when regular administration of enemas no longer relieve the symptoms.

The gold standard in the diagnosis of Hirschsprung's disease is rectal biopsy. The definitive finding of HD is the absence of ganglion cells in the submucosal and myenteric plexuses, identified after hemotoxilin and eosin (H and E), and acetylcholine esterase. The patients underwent full thickness rectal biopsy, either from the posterior wall or the lateral wall of the rectum about 1 – 1.5 cms above the dentate line. In this study, it was found that the posterior rectal wall biopsy causes fibrosis of the rectum and may cause difficulty during the posterior dissection done during the pull through surgery, in the retro-rectal space. In one patient, a protective ileostomy was made during the definitive surgery, as a result of the severe fibrosis encountered at the site of the posterior rectal biopsy. Therefore, the lateral rectal biopsy may be a better option, to avoid the fibrosis.

Full thickness biopsies were taken in our study due to the lack of a suction biopsy device.

A water-soluble contrast enema was performed in neonates and a barium enema in older children. This helps to delineate the transition zone and also aids in the diagnosis of Hirschsprung's disease, however, the transition zone may not be apparent below the age of 3 months (25). In neonates, the contrast enema also helps in ruling out and as a potential definitive treatment of other differential diagnosis for Hirschsprung's disease, such as meconium ileus and meconium plug syndrome (1).

Anorectal manometry was not performed in any of the patients as it was not available at our centre.

The surgery that was done in neonates were either in cases of those that presented with neonatal intestinal obstruction such as abdominal distension and vomiting – in 7 out of 10 neonates. In these patients, an exploratory laparotomy and a diverting stoma with multiple biopsies,

was performed. In the other 3 neonates, that presented with bowel perforation, an exploratory laparotomy and stoma with multiple biopsies, was performed. The stomas created in these cases was either at the perforation site or proximal to it.

In older children, a rectal biopsy and an elective diversion colostomy with multiple biopsies, were performed in most cases.

The stomas were created 5 cms proximal to the transition zone found at surgery, which correlated with the radiological transition zone in most of the cases.

This was in accordance with a study by Chen et al in 2017. They had concluded that the level of radiological transition zone is a useful predictor for actual disease involvement in older patients as well as in infants affected with HD (26).

Short segment HD – involving the rectosigmoid was seen in 76 patients, long segment – up to transverse colon – in 5 patients, and total colonic aganglionosis in one patient.

43 patients underwent definitive surgery - Martin's modification of Duhamel's pull-through. These were performed with the help of linear gastro-intestinal staplers.

One patient who had total colonic aganglionosis, underwent ileo-anal pull-through.

In 4 cases, a protective stoma was created, 3 of these ileostomies and one colostomy.

Although Soave's, Swenson's and transanal (perineal) pull-through procedures have been performed at our centre earlier, they were not performed during the course of this study.

Laparoscopic TERPs have also been performed at our institute, prior to the period of this study.

The staged management of this disease, as was performed in this study, entails either 2 or 3 stages – the first being the diverting colostomy, the second – the definitive pull-through procedure, which is usually performed after around 6 to 12 months of the diverting stoma procedure, upon improvement of the nutritional status. The third stage involves stoma closure, if applicable, as was the case in 4 of the patients in this study. This staged management has various drawbacks, such as increased duration of hospital stay, problems associated with stomas, and multiple exposures to anaesthesia (27, 28, 29, 30). In various centres, a single stage approach is being used (27, 29, 30), to avoid these various problems.

In our centre, most of the patients present late, with grossly dilated bowels, which is not suitable for a primary pull-through surgery. The added advantage of stomas in this disease, include adequate decompression of the bowel, relief of the acute obstruction, and also facilitating bowel washes prior to the definitive surgery.

Most of the patients were found to be continent, clinically.
The complications included - stoma site diarrhoea, which was seen in 12 patients, skin excoriation in 15 patients, non-function of stoma in 2 patients.

The complications of the definitive pull through that were encountered in this study include enterocolitis, seen in 10 of the 43 patients, while 4 patients had persistence of constipation.

2 patients had an anastomotic leak for which diversion colostomies were performed. 1 patient developed a sigmoid colon perforation which was primarily repaired. Surgical site infection was seen in 6 patients. Wound dehiscence was seen in 2 patients.

There are a number of problems that are encountered in the management of Hirschsprung's Disease. Late presentation of the patients with gross abdominal distension is a major challenge in this disease.

A lack of anorectal manometer, frozen section and the late presentation of the patients to the hospital are the main limitations of this study.

CONFLICTS OF INTEREST

None

CONCLUSION

To conclude, Hirschsprung's disease with its various presentations poses a major challenge, especially as most of the patients present late to the hospital.

Spreading awareness regarding this disease with its various clinical symptoms, may help in facilitating early presentation and early referral to the hospital.

Single stage surgery and laparoscopic pull through procedures would be feasible to be attempted only if the patients arrive early in the course of this disease without grossly dilated bowels, and with adequate expertise.

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