Clinico-pathological Outcomes of Hirschsprung Disease in Pediatric Population: A Retrospective Cohort Study and Brief Review of Literature

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ABSTRACT

Introduction: Hirschsprung disease is a common cause of intestinal obstruction during the neonatal period. The clinical picture can be quite varied. The current study is one of the large case series describing the clinic-pathological features, course and outcomes of Hirschsprung disease in paediatric population admitted in a larger Tertiary care paediatric surgery unit in the eastern part of India.

Material and Method: This retrospective cohort study was conducted in the Department of Paediatric Surgery at Nilratan Sircar Medical College & Hospital, Kolkata. The clinical data from paediatric Patients diagnosed with Hirschsprung disease who have undergone surgical procedures were collected from August 2011 to April 2013. Patients were excluded if surgical procedures could not be done or in case of death before the procedure. Data related to Clinical presentation, various outcomes following Operative procedures and post-operative complications were retrieved and analysed.

Result: One hundred and forty-eight patients with Hirschsprung Disease were included in the study. About 52% of all patients were neonates and nearly 80% of all patients presented before infancy. Nearly three fourth of patients were male. Acute intestinal obstruction was the most common clinical presentation (58.1%). About 60% of all cases were found to have classical rectosigmoid involvement on pathological examination. Exploratory laparotomy with stoma during infancy followed by Duhamel procedure during the later period was the surgical procedure performed in the majority of cases. Intestinal perforation was found in 12 cases before surgical procedure, with Caecum being the commonest site of perforation (33.3%) followed by the transverse colon (16.6%).

Conclusion: Clinical presentations of Hirschsprung disease are quite varied, sometimes may be nonspecific. Bowel perforation can be a rare but life-threatening presentation. Duhamel procedure is a safe and effective surgical approach and associated with few complications.

Key Words: Hirschsprung disease, Intestinal Obstruction, Chronic Constipation, Bowel Perforation, Laparotomy, Duhamel procedure

INTRODUCTION

Hirschsprung disease represents a group of conditions characterized by the absence of ganglion cells in myenteric and submucosal plexuses of the distal rectum and extending proximally to a variable extent which causes a functional intestinal obstruction.¹ The clinical presentation depends on the extent of the aganglionic segment. The condition results from the failure of migration of neural crest cells into the gut during the period of embryogenesis. It is postulated that the earlier the arrest of migration occurs, the longer the agangli-

onic segment results.² The number of genes that regulate the migration of neural crest cells have been identified. These genes, which includes RET, GDNF, GFR α 1, NRTN, ED-NRB, ET3, ZFHX1B, PHOX2b, SOX10, and SHH were thought to have a role in the pathogenesis of Hirschsprung disease.³ But a mutation in these genes accounts for only half of all cases. Thus, the mutation in other genes or a combination of genetic mutations might contribute to the pathogenesis of Hirschsprung disease.

Incidence of HD is around 1 per 5000 live births.^{4,5} Inheritance of the disease is non-mendelian and complex. The

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risk of recurrence of HSCR is almost 200 times higher in a sibling compared to the general population (4% vs 0.02%)³. There is a male predominance of about 4 to 1 in HD, 4 boys versus each girl.^{4,5,6} Clinical presentation can vary from an acute abdominal emergency in the neonatal period to chronic nonspecific constipation during childhood.⁶ Up to 30% of cases may have associated anomalies like cardiac defects, velocardiofacial abnormalities, malformations of the gastrointestinal tract, central nervous system abnormalities, genitourinary problems, craniofacial abnormalities, spinal Bifida.³

The current study was planned to describe the Clinico-pathological profile and outcome of cases with Hirschsprung disease in the paediatric population admitted in a tertiary care hospital in West Bengal.

MATERIALS AND METHODS

The study was a retrospective cohort study conducted in the Department of Paediatric Surgery at Nilratan Sircar Medical College & Hospital, Kolkata. Cases confirmed by histopathological examination and clinically diagnosed cases of Hirschsprung disease were included in the study. The latter scenario was used for case definition in cases where histopathology could not be done or in case of non-availability of histopathology report. Clinical diagnosis was based on the presence of clinical features and radiological evaluation consistent with the diagnosis of Hirschsprung disease and exclusion of other diseases during laparotomy. Both inpatient and outpatient medical records were reviewed for inclusion in the study. Paediatric patients admitted to the Paediatric surgery unit, paediatric unit, as well as neonates from neonatal units were included in the study. Cases referred from other health facilities were also included. Patients with a clinical diagnosis who could not undergo the surgical procedures due to any reason or died before planned surgical intervention were excluded. During the process, 148 cases with Hirschsprung Disease could be included. Data were retrieved from the medical record, collected and documented from August 2011 to April 2013.

The baseline demographic data, clinical features, Course of disease, surgical procedure and postoperative morbidities were documented. Patients were managed as per the standard guidelines. The data was collected in a predesigned structured proforma.

Collected data were entered into an electronic database prepared in Microsoft Excel® in 2007 (Microsoft, Redmond, CA, USA). Baseline variables were documented using descriptive statistics. Mean and standard deviation was calculated for continuous data. The incidence of associated complications was calculated as the percentage of total cases.

All statistical analysis was done by using statistical software SPSS version 22.0.

RESULT

A total of 148 patients with the diagnosis of Hirschsprung Disease were included during the study period. The baseline characteristics of the study subjects are depicted in table 1. The majority of cases were presented during the neonatal period. Nearly 80% of all cases presented before their first birthday. Almost three fourth are male with a male to female ratio of 3:1 (Table 1).

The most common clinical presentation was features of acute intestinal obstruction. All neonates presented with features of acute intestinal obstruction with abdominal distension and vomiting. History of delayed passage of meconium was present in almost all (90.4%) cases. Chronic constipation as the presenting symptom was noted in about 44% of cases. One-fifth of cases (n=30) had features of enterocolitis during the clinical course. Twenty-two (73.3%) patients developed features of enterocolitis before surgery and the remaining 8 patients (26.7%) developed features of enterocolitis as a postoperative complication. Abdominal distension was present in around 70% of cases at the time of admission. Nearly 36% of patients had a history of recurrent vomiting and bilious vomiting was present in 12% of all cases (Table 2).

Exploratory laparotomy was done in 138 (93.2%) cases. All neonates with features of acute intestinal obstruction had undergone exploratory laparotomy. Rectal biopsy was done in 21 children and anorectal manometry was done in 13 children. A contrast enema study was performed in 75 (50.6%) cases.

During laparotomy, almost 60% of total cases were found to have features of classical Hirschsprung Disease with a transition zone found at the distal part of the sigmoid colon and rectum. Long segment disease with an aganglionic segment extending up to splenic flexure was observed in 11 (8.3%) cases. Total colonic variety with a more extensive aganglionic segment was found in 23 (17.3%) cases. Almost three fourth of the cases were male, but the male: female ratio was found to be lesser with total colonic variety. A definite transition zone could not be identified in 18 cases and these cases diagnosis was confirmed by histopathological examination from levelling biopsy (Table 3).

Perforation of the bowel was observed in 12 (8.1%) cases during laparotomy. All cases of bowel perforation were observed in non-classical varieties with an incidence of 54.5% (6 out of 11) and 26% (6 out of 23) in the long segment and total colonic variety respectively. Two cases had bowel perforation at multiple sites. Caecum was the most common site of perforation observed in the study and was found in one in

every third patient with bowel perforation. Ascending colon, Transverse and Descending Colon, Appendix were the other sites of perforation documented in the study (Table 4). Various short term and long-term complications following surgical intervention are depicted in table 5. Long term follow-up data with at least two follow-up visits after the definitive procedure was available for 93 cases. Wound infection at the site of stoma was the commonest short-term complication (Table 5). As many as 20% of cases continued to have constipation following surgery which was managed conservatively in the majority of cases. Some minor surgical procedure (Spur excision) was performed in 3 cases to relieve constipation.

DISCUSSION

Hirschsprung disease represents a cluster of conditions characterised by failure of migration of neuroblasts to the enteric nervous system in distal bowel, leading to aganglionosis in intermyenteric plexuses of intestine.⁸ This abnormal migration results from defective signalling during normal development. Several genes that regulate the migration of neuroblasts are known and a mixture of those genes determines the phenotypical expression.^{9,10}

Presentation during infancy with functional intestinal obstruction is the commonest clinical presentation. The reported incidence of the disease is 1 in 5000 live births.¹¹ A significant male predominance has been reported in the literature, with a male to female ratio of 4:1, except in cases with total colonic involvement where the ratio is around 0.8-1:1.⁴⁻⁸ The majority of the cases were male in the present study with a male to female ratio of around 3:1. However, contrary to the reported kinds of literature, a tendency towards higher male involvement was observed in cases with total colonic aganglionosis in the present study. The male to female ratio in these cases was 1.5:1.

As many as 50% to 90% of cases of Hirschsprung disease are present during the neonatal period.^{7,13} This percentage has increased in recent years owing to greater awareness of the condition. The disease should be suspected if there is a history of failure to pass meconium within the first 48 hours of life.⁷ These neonates present with abdominal distension, feeding intolerance, vomiting which may be bilious.¹³ Abdominal distension is seen in around 63-91% of neonates with Hirschsprung disease, and bilious vomiting in 19-37% of children.¹² The children beyond the neonatal period often present with chronic constipation, which is usually confused with habitual constipation. This is common among breast-fed infants, who may develop constipation around the time of weaning.¹³ Although the majority of patients who presented beyond the neonatal period have the short segmented disease,^{13,14} recent studies have reported a significant incidence of long segment or total colonic involvement with

the later presentation.¹³ More than 50% of the cases in the present study were diagnosed during the neonatal period. Almost 76% of cases were identified before the age of 1 year. Around one-fifth of the patients presented beyond infancy. The reported incidence of Hirschsprung-associated enterocolitis (HAEC) varies from 17% to 50% in various published series.¹⁸ Almost 20% of the total cases had features of enterocolitis during the disease in the current study. The majority of them (around two-third) presented beyond infancy. Enterocolitis during the post-operative period was observed in 8 cases.

The proximal extent of the aganglionic segment helps to classify various types of disease. The classical disease involves the rectosigmoid area. In long-segment Hirschsprung disease, the aganglionic portion extends more proximal to the sigmoid up to the splenic flexure. An ultra-short segment disease, also referred to as internal sphincter achalasia involves only the internal anal sphincter.^{7,26} Total colonic aganglionosis involving part of the small intestine in addition to the large bowel has been also described as a variant of Hirschsprung disease.²⁶ Classical HD accounts for almost 74% to 80% of all cases. The relative frequency of long-segment disease and total colonic involvement has been described to be around 12-22% and 4-13% respectively.⁴ We observed a slightly higher incidence of total colonic aganglionosis in the current study as compared to the reported literature.¹⁵⁻¹⁹

A rare, however vital complication of the disease is bowel perforation. A literature review by Newman et al identified bowel perforation to occur in around 4% of cases.¹⁹ Bowel perforation is common during the neonatal period but is rarely the initial presentation. Perforations most typically occur within the proximal colon (68%), the appendix (17%), or the distal small intestine (6%); in addition, bowel perforations could occur in each of the aganglionic and ganglionic portion of the bowel in HD.²⁰ It was reported that this complication is most commonly associated (62%) with total aganglionosis.²¹ In the present study, Caecum was noted to be the commonest site of perforation, followed by the transverse colon. All viscus perforation within the current study has occurred in the non-classical types of disease, which was observed in almost 30% of such cases. Although the pathogenesis of intestinal perforation in HD is still unknown, most studies have proposed that inflammation could play a significant role in its development. Progressive dilatation of bowel loop and inflammation results in bowel loops filled with fibrinous exudates which heighten the risk of perforation.

A two-stage surgical approach with Preliminary Colostomy followed by definitive repair was the most common procedure performed in the study group. The primary repair could be done in 6.7% of all cases. Duhamel procedure was done in all these cases. Duhamel procedure has been widely used

around the world, and a favourable long-term result has been reported.²⁰ A single-stage trans-anal pull-through procedure may have the advantage of being cost-effective, shorter hospital stays and avoiding the known morbidity related to stomas.^{21,22} Despite the move towards single-stage surgery in recent years, a stoma may be indicated for children with severe enterocolitis, perforation, malnutrition, or massively dilated proximal bowel, and in situations where there are inadequate pathologic findings to reliably identify the transition zone on frozen section. Recently laparoscopic techniques have been described with almost equivalent results but may have a shorter hospital stay.²² As regards Duhamel and trans anal pull-through the procedure, evidence is not sufficient to recommend one procedure over the other and the experience of the surgeon remains a key factor to determine the choice of procedure.¹⁷ No studies have compared the outcomes following trans-anal and laparoscopic approaches. Trans-anal pull through might have a lower complication rate, minimal analgesia, and might allow early feeding and discharge.^{23,24} Laparoscopic-assisted colonic pull-through procedure is gaining popularity in recent times and few studies have concluded that laparoscopic-assisted colon pull-through may reduce perioperative complications and postoperative recovery time.^{26,27,28} Although laparoscopic pull-through is relatively simple, the trans-anal approach has the advantage that it can be performed by any paediatric surgeon, including those without laparoscopic skills, and by paediatric surgeons in parts of the world with limited access to laparoscopic equipment.^{27,28}

CONCLUSION

In addition to the usual clinical features, bowel perforation can be a presenting feature in Hirschsprung disease. Unexplained bowel perforation in the neonate may raise a suspicion of Hirschsprung disease, which tend to occur more frequently in the non-classical type of disease. Though a favourable surgical outcome following the Duhamel procedure was documented in the present study, comparison with alternative surgical techniques was lacking. Future studies comparing the outcomes following various surgical techniques in Indian setup may be needed to determine the most suitable surgical approach in Hirschsprung disease.

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Author Contributions

AP: Conceptualized, designed the study and collected data.

BM: Collected data and critical input in the preparation of the draft.

DN: Analysed data and prepared the initial draft.

All authors approved the final manuscript.

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Table 1: Baseline Characteristics of the study population (n=148)

	Number (n,%)
Total number of cases	148 (100%)
Sex distribution	
Male	109 (73.6%)
Female	39 (26.4%)
Age at presentation	
Neonatal period	77 (52.0%)
Infancy	39 (26.4%)
Childhood	32 (21.6%)
Initial presentation	
Acute intestinal obstruction	86 (58.1%)
Chronic Constipation	62 (41.9%)
Total surgery done	148
Exploratory laparotomy, stoma	138 (93.2%)
Duhamel Procedure	111 (75.0%)
Transanal Pull Through	9 (6.1%)
Anorectal myectomy	1 (0.7%)

Table 2: Clinical features of the study population (n=148)

Clinical feature	Frequency (n,%)
Delayed passage of meconium	133 (90.4%)
Vomiting	54 (36.5%)
Bilious Vomiting	18 (12.1%)
Abdominal Distension	103 (69.6%)
Constipation	65 (43.9%)
Diarrhoea	30 (20.3%)

Table 3: Pathological features of the study population (n=133)

	Frequency of cases (n,%)	Male (n)	Sex Female (n)	Number with Perforation (n,%)
Classical HD	81 (60.9%)	58	23	0 (0%)
Long segment HD	11 (8.3%)	9	2	6 (54.5%)
Total colonic HD	23 (17.3%)	14	9	6 (26%)
No definite Transition zone	18 (13.5%)	11	7	0 (0%)

Table 4: Site of Perforation among the study subjects (n=12)

Site of Perforation	Frequency (n,%)
Caecum	4 (33.3%)
Appendix	1 (8.3%)
Ascending colon	1 (8.3%)
Transverse colon	2 (16.6%)
Sigmoid colon	1 (8.3%)
Multiple	2 (16.6%)
Site not found	1 (8.3%)

Table 5: Short term and Long term Complications (n=148)

Short term complications (n=148)	
Complications	Frequency (n,%)
Wound infection	17 (11.5%)
Wound Dehiscence	6 (4.1%)
Enterocolitis	8 (5.4%)
Bleeding at anastomosis	2 (1.4%)
Long term Complications (n=93)	
Remnant Spur	5 (5.4%)
Prolapse	2 (2.1%)
Constipation	19 (20.4%)
Incontinence	1 (1.1%)
Adhesion band	4 (4.3%)