Clinical Manifestations of Hirschsprung's Disease: A Six Year Course Review of Admitted Patients in Gilan, Northern Iran

M Izadi[1], F Mansour-Ghanaei[2*], R Jafarshad[2], F Joukar[2], AH Bagherzadeh[2], F Tareh[1]

1. Pediatric Surgery Department,
2. Gastrointestinal and Liver Diseases Research Center, Gilan University of Medical Sciences, Rasht, Iran

*Corresponding Author:
Fariborz Mansour-Ghanaei, MD
Professor of Gastroenterology and Hepatology, Gastrointestinal and Liver Diseases Research Center (GLDRC), Gilan University of Medical Sciences, Sardar-Jangle Ave, Razi Hospital, Rasht 41448-95655, Iran.
Tel: +98 131 5535116
Fax: +98 131 5534951
E-mail: ghanaei@gums.ac.ir
Received: 21 December 2008
Accepted: 1 April 2009

ABSTRACT

BACKGROUND

Hirschsprung's disease (HD) is a congenital disease in which intestinal ganglionic cells are absent, leading to intestinal obstruction. The disease has various clinical manifestations and different lengths of bowel may be involved. Our aim was to study Hirschsprung's clinical presentations and its rate of intestinal involvement in hospitalized patients in a six year course study in Gilan, a northern province of Iran.

METHODS

We studied patients diagnosed with HD who were referred to the Gilan Surgery Referral Center in Poursina Hospital from 1995 until 2001. In this cross sectional descriptive-analytical study, all data were collected from patients' files and questionnaires. Data included demographics, clinical presentations, diagnostic methods, involved intestinal segments, type of surgical procedure, and surgical complications.

RESULTS

There were 58 cases of HD during this six year period that underwent surgery. Of these, 19 patients were female and 39 were male whose ages ranged from one day to 18 years old. A variety of clinical findings such as: constipation, abdominal distension, failure to pass meconium, diarrhea, and other less common manifestations were present. We found three different pathological types: rectosigmoid, ultra short segment and total colonic involved segment. No differences between disease presentations were discovered among these three types. The following surgical procedures were performed: Swenson, Soave–Boley, and Lynn. Early complications, which occurred during the first month following surgery, were anastomotic leakage, wound infection, hemorrhage and anastomosis stenosis. Late complications, occurring at least one month after surgery, comprised the following: long-term constipation, enterocolitis, incontinence, and obstruction due to adhesion. No significant difference between the complications of these surgical procedures and any accompanying anomalies were found.

CONCLUSION

Most patients had chronic constipation and abdominal distension regardless of the types of involvement, age or clinical presentations. There were few associated anomalies amongst the patients. In some cases, surgical complications were less than those seen in other studies; therefore, it seemed that the performed procedures had fewer complications or may have been performed at the appropriate time.

KEYWORDS

Hirschsprung's disease; Abdominal distension; Anomalies; Iran

INTRODUCTION

Hirschsprung's Disease (HD) or aganglionic megacolon is a congenital disorder characterized by the absence of enteric ganglia along a variable length of the intestine, resulting in functional obstruction.[1] Most HD cases are diagnosed in infancy, although some may not be diagnosed until adolescence or early adulthood.

There is a more familial background in mothers.[2] The incidence of HD ranges from 1:4400 to 1:7000 live births,[3] with a male predominance of approximately 4:1.[4] The disease has no race predilection and is a relatively common problem in gastroenterology and pediatric surgery departments. The main symptom of HD is constipation, which cannot be treated using laxatives or softeners.

Clinical features of the disease, its diagnostic approaches and treatment vary. Some cases of the disease have been seen with associated anomalies[5] that account for 25% of familial cases and 10% of non-familial cases.[2] HD can be either a life-threatening or chronic disorder. Only with early diagnosis, will patients be referred to specialized surgery units to undergo proper treatment. Because of the different anatomic forms and manifestations of HD, a large number of patients are misdiagnosed and mistakenly treated over a number of years, with a delay in proper treatment.

HD can involve different lengths of the intestine, from a few centimeters of the distal rectum to the entire colon and even a part of the terminal ileum. Clinical manifestations can vary from mild to severe constipation seen at various ages, to the failure to pass meconium stool at 24-48 hours at birth with a prominent distension. Perforation of the proximal colon and peritonitis during the first few days after birth was seen. Iranian researchers, however, have not placed much emphasis on this disease.

In an Iranian study, a high percentage of patients with HD presented with constipation and abdominal distension whereas incontinence and peritonitis were the least common symptoms. Among these patients, different anomalies such as G6PD deficiency, congenital heart disease, microcephaly, and hypostasis were observed.[5] In a study by Bonomo et al., it has been stated that HD is usually diagnosed during the neonatal period. In this study, the prevalence of HD in patients was diagnosed with natural barium enema as one of the diagnostic procedures for this disease, in addition to manometry and rectal biopsy.[6] In a study by Larini et al., the major postoperative complications were known to be related to the different extents of dysganglionosis and neuronal bowel dysplasia.[7] In another study, the other effective treatment for this disease has been attributed to the histology of the proximal segment.[8] Also, in a study in 2001, a comparison of the two surgical treatments was studied.[9] We have conducted this study to discover zhe various aspects of HD as well as the relationship between the length of involved bowel and the different types of clinical manifestations in patients with HD who presented to Poursina Hospital, one of the important surgical treatment referral centers in northern Iran during a six year period.

MATERIALS AND METHODS

Patients who presented to the Specialized Referral Medical Center at Poursina Hospital in Gilan, northern Iran, between 1995 and 2001 with a diagnosis of HD were studied. In this cross-sectional descriptive-analytical study, the data were extracted from the patients' medical records and classified in tables. The data consisted of age, sex, disease manifestation, diagnostic procedures leading to the definitive diagnosis, affected segment, type of surgery performed, surgical complications, and treatment outcomes. Ultimately, data were analyzed with statistical SPSS software (version 10, Chicago, IL, USA).

For statistical analysis of qualitative data, the Chi-Square and Fisher's Exact tests were used. A *p*-value less than 0.05 was considered significant. Information was obtained from patients' hospital records and medical records in addition to physicians' offices and private centers. In order to study postoperative complications, there was a limitation for patients who, due to more recent surgeries, were not yet in the long follow up period. Therefore, in these patients, late postoperative complications were not possible to be assessed.

Thus, it was likely that surgical complications were underreported in this study.

RESULTS

In this study, 58 hospitalized patients with HD were enrolled. Of these, 19 patients (33%) were females and 39 males (67%). The ratio of females to males was 1:2. The majority of patients (N=40) were classified in the age group of 1-6 years (Table 1) with an age range of 1 day to 18 years.

Table 1: **Distribution of age and sex in studied patients.**

	Sex	Male	Female		Total
Age	Frequency	%	Frequency	%	
<48 hr after birth	5	8.62	0	0	5
>48 hr and <1month	6	3.44	2	3.44	8
> 1 month and	26	44.82	14	24.13	40
<6 yrs	5	5.17	3	3.44	2
>6 yrs	2	3.44	3	5.17	5
Total	39	67.22	19	32.78	58

Table 2: **Distribution of clinical signs and symptoms in studied patients.**

Signs and Symptoms	Frequency	%
Delay of meconium defecation	10	17.24
Diarrhea and enterocolitis	3	5.17
Chronic constipation	46	79.31
Abdominal distension	39	67.24
Perforation of diverticulitis	1	1.72
Soiling	2	2.44
Over-flow incontinence	1	1.72
Prolapse	1	1.72
Imperforated anus	1	1.72
Vomiting	5	8.62

Table 3: **Distribution of different types of involved segment.**

Type of involved segment	Frequency	%
Rectosigmoid	49	84.48
Ultra-short segment	3	5.17
Total-colonic	5	1.72
Uncertain	1	8.62
Total	58	100

With respect to symptoms and clinical manifestations, the most prominent symptoms were chronic constipation and abdominal distension. In terms of the various clinical signs and symptoms, no statistically significant difference was found among the different age groups as well as between the two sexes (p>0.41 and p>0.24, respectively). Other disease symptoms included failure to pass meconium stool, constipation, diarrhea, vomiting, overflow incontinence and other less prevalent symptoms (Table 2).

Diagnosis for all patients (N=51) was based on rectal biopsy, however 38 individuals had prior barium enemas and one person underwent manometry of the rectum and colon.

The length of the involved segment was divided to three types: recto-sigmoid segment, very short segment and total colon.

One person was placed in the uncertain segment group due to a sporadic involvement site (Table 3).

Clinical manifestations of the patients showed no difference with respect to both type and time of presentation. Surgeries were performed using the Swenson abdominal perineal pull-through,[10] Soave-Boley [endorectal pull-through],[10] and Lynn [posterior anorectal myectomy to correct short-segment agangliosis][10] procedures. Surgical procedures were performed on 44, 9 and 5 patients, respectively, amongst all types. All Lynn surgical operations were performed on patients who had involvement of the ultra short segment. Early complications (within one month after surgery) and late complications (more than one month postoperatively) are documented in Tables 4 and 5.

There was no statistically significant difference seen in the incidence of post-operative complications (p>0.05). No associated anomalies were observed in these patients; for instance, Down syndrome, major cardio-vascular diseases and urogenital abnormalities.

The anomalies associated with HD in the present study were as follows: in the gastro-intestinal (GI) tract there was one case of imperforate anus which improved with surgery. There were two cases of premature neonates whose gestational ages were less than 38 weeks. One neonate had polydactyly in his hands and feet and another one was born with a cleft palate. Both newborns were treated with the appropriate surgeries during this period.

Regarding post-operative complications, one patient died due to undetected enterocolitis as a post-operative complication, one year following surgery. This patient presented with diarrhea and severe dehydration due to a delay in referral to the medical center.

Table 4: Distribution of early surgical complications.

Complication	Frequency	%
Leakage of anastomotic fistula	5	10.2
Wound infection	1	2.04
Cuff Abscess	1	2.04
Anastomotic stenosis	2	4.08
Bleeding of anastomosis	1	2.04

Table 5: Distribution of late surgical complications.

Complication	Frequency	%
Incontinence	3	6.12
Constipation	5	10.2
Enterocolitis	4	8.16
Soiling	1	2.04
Adhesion Band	1	2.04

DISCUSSION

As inferred from our results in addition to other studies, the frequency of girls diagnosed with HD is less than boys (ratio 1:2). However, according to Lee et al. in a study on long-segment disease, the incidence in females increases. HD is uncommon in premature infants,[4] which is similar to our study. HD is manifested mostly within the first weeks of life, and is diagnosed in those aged five years or younger. Occasionally, HD is diagnosed during adulthood.[10,11] As seen in Tables 1 and 2, the frequency of patients one to six years of age is relatively high, which could be attributed to the presence of minor symptoms, thus causing HD to be neglected.

Therefore, chronic constipation and abdominal distension should be considered as the most prominent symptoms of HD during these ages. Severe signs of HD such as the failure to pass meconium stool within 24-48 hours after birth, along with other acute symptoms such as vomiting and peritonitis due to severe distension of the proximal colon and its perforation, or diarrhea and enterocolitis are not considered in this age group, as well. Thus it is not unexpected that cases with more extensive involvement are more likely to be familial.[1]

Although we know that the problems a child will experience with HD depend on the extent which the intestine has normal innervation, but in our study, no statistical correlation between the type of the involved segment and the type of clinical manifestations among patients was seen.

It can not be seen in other studies, though here this issue should be noted that this study's sample size was too small to reach the conclusion that "severe symptoms should not be attributed to the more prolonged involved segment".

On the other hand, post-operative complications that were seen amongst patients undergoing one of the three surgical procedures of Swenson, Soave-Boley and Lynn were the same. The Lynn procedure, however, was only performed in cases with an ultra short segment, which could be due to low sample size. The same result, as mentioned by Harjai, who stated that there were no important differences with regard to outcome and long-term function in patients treated with these surgical procedures.[12]

In a study by Sarioglu, it was determined that stenosis of the anastomosis in Swenson procedure was considerably higher than for those patients who had the Duhammel procedure; unfortunately, in our study no patients underwent the Duhammel procedure.

The authors of that article have suggested that the Duhammel procedure is a safe and easy technique for HD treatment.[9] A literature review of 229 cases of adult HD has suggested that the Duhamel procedure is the procedure of choice due to a lower rate of morbidity and better functional outcome.[10]

Duhamel's operation, as modified by Ikeda-Sopor, very effective in treatment of congenital megacolon, being associated with complications, and is the prerequisite for achieving excellent functional results.[13]

Although the Swenson operation is the most physiological, however it is a difficult operation and the extensive pelvic dissection leads to trauma to the pelvic nerves. The Duhamel operation requires less pelvic dissection and is safe in infants as well as in adults but the residual spur is problematic.

Soave's procedure is easy to perform with no pelvic dissection required, however a disadvantage is that repeated dilatations are necessary.[12]

According to other studies, common complications include H.D-associated enterocolitis (HAEC) after the Swenson operation, diarrhea and incontinence after the Soave endorectal pull-through procedure and constipation after the Duhamel procedure.[11]

Associated anomalies were seen in only three cases (5.1%). Some studies estimated the associated anomalies of HD to range between 10%-30%,[14] however this ratio was not apparent in our study patients. Furthermore, it is different from the associated anomalies in other studies in which H.D is a frequent finding in cases of Down syndrome.[1]

Among 179 children, one or more associated abnormalities were seen in 22% of these children which involved the neurological, cardiovascular, urogenital, and gastrointestinal systems.[15]

There were four cases with diarrhea and enterocolitis, of which one case expired. Studies states that diarrhea is seen in one-third of the children in whom the diagnosis was made prior to three months of age[16] and in 12-58% cases with HD, if untreated, enterocolitis will occur.[17-21]

Enterocolitis is the most severe complication of HD that could occur either pre- or postoperatively[22] and, in our study, cases were seen postoperatively. The Primary Laparoscopic Pull-through Procedure (PLPP) as performed in infants with HD is a minimally invasive surgery that is an effective, problem-free approach for treating neonatal HD. It has replaced the standard two stage open procedure in babies with uncomplicated presentation.[23]

Unfortunately, there were no cases of PLPP in our study. We conclude that a substantial number of patients with HD present with the chronic symptoms of abdominal distension and constipation. Among these, the extent of the affected segment does not exert much effect on the onset and type of symptoms. Common anomalies that have been observed in other studies were not seen in our patients. Thus, the association of this disease with anomalies, in our study, appears less important. Post-operative complications in our patients are less than those of other studies. This probably was due to the surgical techniques that were performed with lower complications or perhaps due to the suitable timing of the surgeries performed on our patients. Therefore, further studies with larger sample sizes are needed to assess the relations which have been discussed in this study.

CONFLICT OF INTEREST

None declared.

REFERENCES

1. McKusick VA. Hirschsprung Disease. Johns Hopkins University. September 10, 1993; http://www3.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=142623. *Updated* September 19,2005.
2. Holschneider A, Ure BM. Hirschsprung's Disease. In: Ashcraft KW, Murphy JP, Sharp RJ, eds. Pediatric Surgery. 3rd ed. *WB Saunders* 2000;453-72.
3. Teitelbaum DH, Coran AG, Weitzman JJ, Ziegler M, Kane T. Hirschsprung's disease and related neuromuscular disorders of the intestine. In: O'Neill JA, Rowe MI, Grosfeld JL, eds. 5th ed. Mosby-Year Book, *Inc* 1998;1381- 424.
4. Lee SL, Dubois. JJ. Hirschsprung Disease. http://www.emedicine.com/med/topic1016. htm. Updated August 5, 2005.
5. Ahmadi J, Delshad S, Kalantar M, Mosavi M, Ameli S. Kinds of surgery in Hirschsprung's disease. *Iranian Pediatr J* 1993;**11(3)**:307-26.
6. Reid JR, Buonomo C, Moreira C, Kozakevich H, Nurko SJ. The barium enema in constipation: comparison with rectal manometry and biopsy to exclude Hirschsprung's disease after the neonatal period. *Pediatr Radiol* 2000; **30(10)**:681-4.
7. Meyrat BJ, Lesbros Y, Laurini RN. Assessment of the colon innervation with serial biopsies above the aganglionic zone before the pull-through procedure in Hirschsprung's disease. *Pediatr Surg Int* 2001;**17(2-3)**:129-35.
8. Schulten D, Holschneider AM, Meier-Ruge W. Proximal segment histology of resected bowel in Hirschsprung's disease predicts postoperative bowel function. *Eur J Pediatr* Surg 2000;**10(6)**:378-81.
9. Sarioglu A, Tanyel FC, Senocak ME, Buyuk-pamukcu N, Hicsonmez A. Complications of the two major operations of Hirschsprung's disease: a single center experience. *Turk J Pediatr* 2001;**43(3)**:219-22.
10. Miyamoto M, Egami K, Maeda S, Ohkawa K, Tanaka N, Uchida E, et al. Hirschsprung's diseasein adults: report of a case and review of the literature. *J Nippon Med Sch* 2005; **72(2)**:113-20.

11. Yoshida C, Faintuch S. Hirschsprung's disease. http://www.emedicine.com/radio/topic343.*htm*. Updated March 31, 2004.

12. Harjai MM. Hirschsprung's disease: revisited. *J Postgrad Med* 2000;**46(1)**:52-4.

13. Vidiscak M, Kirnak J, Smerk M. Results of surgery in children with congenital megacolon. *Rozhl Chir* 2001; **80(4)**:197-200.

14. Kaiser G, Bettex M. Clinical generalities. In: Holschneider A, ed. Hirschsprung's Disease. Stuttgart/ New York: *Thieme Stratton* 1982:43-53.

15. Ryan ET, Ecker JL, Christakis NA, Folkman J. Hirschsprung's disease: associated abnormalities and demography. *J Pediatr Surg* 1992; **27(1)**:76-81.

16. Puri P, Wester T. Enterocolitis complicating Hirschsprung's disease. In: Holschneider A, Puri P, eds. Hirschsprung's Disease and Allied Disorders. London: *Harwood Academic Publishers* 2002;522-65.

17. Elhalaby EA, Coran AG, Blane CE, Hirschl RB, Teitelbaum DH. Enterocolitis associated with Hirschsprung's disease: a clinical-raiological characterization based on 168 patients. *J Pediatr Surg* 1995;**30(1)**:76-83.

18. Carneiro PMR, Brereton RJ, Drake DP. Enterocolitis in Hirschsprung's disease. *Pediatr Surg* 1992;**7**:356-60.

19. Ikeda K, Goto S. Diagnosis and treatment of Hirschspr ung's disease in Japan: An analysis of 1628 patients. *Ann Surg* 1984;**199(4)**:400-5.

20. Shanbhogue LK, Bianchi A. Experience with primary Swenson resection and pull through for neonatal Hirschsprung's disease. *Pediatr Surg Int* 1990;**5**:446-54.

21. Surana R, Quinn FMJ, Puri P. Evaluation of risk factors in the development of enterocolitis complicating Hirschsprung's disease. *Pediatr Surg Int* 1994;**9(4)**:234-41.

22. Cass D, Manglick P, Singh S. Final report of completed studies on Hirschsprung disease. Department of Surgery, Children's Hospital at Westmead. http://apsu. inopsu.com/hs2000.pdf. Accessed January 30,2006.

23. Jona Juda Z. Laparoscopic pull through for Hirschsprung's disease in infants. *J Indian Assoc Pediatr Surg* 2005;**10(1)**: 28-30.