Experience with full-thickness rectal biopsy in the evaluation of patients with suspected Hirschsprung's disease

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Background and purpose **Rectal biopsy is the main modality for the diagnosis of Hirschsprung's disease (HD). In Africa, transanal full-thickness rectal biopsy is commonly performed. We aimed to audit our practice of rectal biopsy in the evaluation of HD.**

Materials and methods **A retrospective review was carried out of the records of children (≤ 15 years) who were evaluated for HD between 2007 and 2011. Clinical presentation, details of the operation, and histologic result were analyzed using SPSS version 15.0.**

Results **Fifty-seven children were evaluated for suspected HD during the period. Thirty-six children underwent a rectal biopsy. There were 29 (80.6%) males and nine (19.4%) females, of which two were preterm. Neonates and infants accounted for 72.2% ($n=26$). The median age at biopsy was 90 days (range, 5 days to 9 years). Delayed passage of meconium was present in 64.7%, constipation in 85.7%, abdominal distension in 88.6%, and bilious vomiting in 55.9%. Thirty biopsies (83.3%) yielded a histologic diagnosis. Twenty-six (72.2%) confirmed HD, whereas four (11.1%) yielded normal rectal histology. In six (16.7%), the sample taken was deemed inadequate for opinion. None of the symptoms assessed was associated significantly with a diagnosis of HD, stalling further analysis. Where a single biopsy was taken, 20% ($n=5$) were inadequate for analysis; where more than one sample was taken, a histologic diagnosis was possible in 100% ($n=11$). Consultant surgeons and trainees returned inadequate samples in 15.8% ($n=3$) and 12.5% ($n=2$), respectively. An inadequate sample was obtained in four infants (15.4%) and one child older than 1 year of age (10%). Distance of biopsy from the dentate was not indicated in 63.9% ($n=23$).**

Conclusion **No clinical parameter can accurately predict a diagnosis of HD. More than one sample at a sitting may improve the diagnostic yield. Larger prospective studies are needed to confirm these findings. *Ann Pediatr Surg* 10:42–45 © 2014 Annals of Pediatric Surgery.**

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Introduction

Hirschsprung's disease (HD) is an important cause of intestinal obstruction in children. It is characterized by the absence of parasympathetic ganglia in the enteric nervous system, leading to functional obstruction from a narrow aperistaltic colon [1,2]. It is estimated to occur in one in 5000 live births, with more than 90% presenting as neonates in developed countries. In Nigeria, however, only 30–40% of cases present as neonates [3–5].

Different investigation modalities are used in the diagnosis of HD including contrast enema, anorectal manometry, rectal suction biopsy, and full-thickness rectal biopsy [1,6,7]. These vary in their diagnostic accuracy, with the mean sensitivity and specificity rates of contrast enema being 70 and 83%, respectively, those of anorectal manometry being 91 and 94%, respectively, and those of rectal suction biopsy being 93 and 98%, respectively [6]. Histological examination of rectal wall biopsy remains the gold standard for the diagnosis of HD. It shows the absence of ganglion cells, hypertrophied nerve fibers, and increased acetyl cholinesterase activity with calretinin immunohistochemistry [1,2]. Suction devices are now used more commonly to obtain tissue for examination; however, these devices as well as expertise in reporting the specimen thus obtained are not readily available in Africa. Hence, a full-thickness rectal wall biopsy is commonly performed. Both these methods are not without complications; thus, attempts to determine which patients require rectal biopsy have been made using clinical features, with mixed results [7–10].

This study was carried out to audit our practice of rectal biopsy in the investigation of children with suspected HD.

Materials and methods

We retrospectively reviewed the records of children who were evaluated for suspected HD between January 2007 and December 2011. We obtained data under the following categories:

(1) Clinical presentation (delayed passage of meconium, i.e., after 48 h, bilious vomiting, abdominal distension, and constipation).
(2) Details of the procedure (mode of initial decompression, number of biopsies, distance of the biopsy site from the dentate line, operator).
(3) Histology report and complications.

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We excluded 12 patients for whom complete records were missing.

We considered the report sent from the Histopathology Department as the pathologic diagnosis in three categories: HD, normal rectal histology, and inadequate tissue for opinion. The final diagnosis of HD was confirmed if the resected bowel at pullthrough confirmed the pathology. We contacted by phone the caregivers of those who did not have pullthrough to determine the state of the child at the time of data collection.

We obtained the rectal biopsy by placing the child supine with the hips and knees flexed and the feet strapped together under general anesthesia. We digitally dilated and retracted the anus to identify the dentate line. We placed a 3/0 absorbable suture at 3 cm above the dentate and a second suture at 2 cm. We obtained the tissue attached to this second suture with sharp scissors or blade and closed with a running stitch. Histological examination was performed as for routine pathology specimens in our center with hematoxylin and eosin staining of fixed rectal tissue, and a diagnosis of HD was made if there was absence of ganglion cells and presence of hypertrophied nerve fibers.

Analysis was carried out using SPSS, version 15 (SPSS Inc., Chicago, Illinois, USA). Data were expressed as percentages and median, whereas comparison was carried out using Fischer's exact test.

Results

Fifty-seven patients were evaluated for suspected HD during the period. Records were available for 45 of these patients. Thirty-six children were subjected to rectal biopsy as part of their evaluation, whereas nine declined, yielding a biopsy rate of 80%. The median age at presentation of the children who had a rectal biopsy was 45 days (range, 2 days to 9 years). The median age at the biopsy procedure was 90 days (range, 5 days to 9 years). Twenty-nine (80.6%) were males and seven were females (19.4%). Twenty-six patients were 1 year old or younger (72.2%) while 10 (27.8%) where older than 1 year. Only two (6.1%) were born preterm.

Delayed passage of meconium was present in 64.7% ($n = 22$), abdominal distension in 88.6% ($n = 31$), bilious vomiting in 55.9% ($n = 19$), and constipation in 85.7% ($n = 30$). Twenty-six patients (72.2%) underwent decompression with colonic washouts, whereas 10 (27.8%) required a stoma.

Nineteen biopsies (52.8%) were taken by a consultant, whereas 17 (47.2%) were taken by a trainee. Twenty-five biopsies (69.4%) were single, whereas in 11 (30.6%), more than one specimen was taken in the same sitting. In 23 (63.9%) biopsy procedures, the distance from the dentate line was not indicated, whereas in 13 (36.1%) of the biopsy procedures, the most distal specimen was taken 1 cm ($n = 4$, 11.1%), 2 cm ($n = 7$, 19.4%), and 3 cm ($n = 2$, 5.6%) from the dentate line.

Thirty biopsies (83.3%) yielded a histologic diagnosis. Twenty-six (72.2%) yielded a diagnosis of HD, whereas four (11.1%) yielded normal rectal histology. In six (16.7%), the sample taken was deemed inadequate for opinion. Of these, one (2.8%) had a repeat biopsy, which yielded a diagnosis of HD; three patients (8.3%) were managed as HD on the basis of persistence of their symptoms and a typical contrast enema, and aganglionosis was confirmed in the resected bowel in these cases. Two (5.6%) were lost to follow-up. Of the four diagnosed with normal histology, in one of the patients (a 4 year old who presented with acute on chronic intestinal obstruction requiring a colostomy), HD was confirmed through a review of colonic biopsies taken at colostomy and subsequently underwent pullthrough. One of the children with rectal biopsy diagnosing HD declined surgery and defaulted follow-up. The parents claim that the child has been symptom free for over a year after the biopsy. The diagnostic accuracy was 97%, with one false-negative result, yielding a sensitivity of 96% and a specificity of 100%.

There was no statistical relationship between presenting symptoms (delayed passage of meconium, abdominal distension, bilious vomiting, and constipation) and diagnosis (Table 1). Where a single biopsy was taken, five (20%) returned inadequate samples. Where more than one sample was taken, a diagnosis was reached in 100% ($n = 11$) ($P = 0.157$). An inadequate sample was obtained in four infants (15.4%) and one child older than 1 year of age (10%). Where the biopsy was performed by a trainee, two (12.5%) were inadequate, whereas consultants obtained nonrepresentative samples 15.8% ($n = 3$) of the time. Neither the age grouping ($P = 1.000$) nor the level of the operator ($P = 1.000$) showed a statistically relevant association with the diagnostic yield. Complications were documented in three patients (8.3%): scarring in one (2.8%) and prolonged bleeding in two patients (5.6%).

Discussion

Different investigation modalities are used in diagnosing HD. Contrast enema in HD classically shows a caliber change from a narrow or normal-looking distal aganglionic segment through a funnel-shaped transition zone to a dilated proximal ganglionic bowel. An abnormal rectosigmoid index also aids diagnosis. False negatives may, however, occur where the child has total colonic HD, a very short segment, or has undergone washouts or a digital rectal examination [2,11]. The exposure to radiation is also a disadvantage. The absence of rectoanal inhibitory reflex is considered a positive result in anorectal manometry; however, this test remains controversial in neonates and young infants [1,6,11]. It is also widely unavailable in Africa [2,4].

Table 1 Comparison between clinical features and the final diagnosis of Hirschsprung's disease

	Clinical feature [*n* (%)]			
Final diagnosis	Delayed meconium	Bilious vomiting	Constipation	Abdominal distension
Hirschsprung's disease	16 (66.7)	12 (50)	21 (84)	23 (92)
Not Hirschsprung's disease	2 (50)	4 (100)	4 (100)	3 (75)
P value	0.601	0.113	1.000	0.371

In our practice, we rely on the clinical picture and rectal biopsy in our evaluation of suspected HD. We also include contrast enema in older children. Full-thickness rectal biopsy remains the gold standard against which all other tests are measured since it was described by Swenson in 1955. It requires general anesthesia and may be complicated by bleeding, perforation, and scarring [12]. Both myenteric and submucosal plexuses are available for staining and histologic examination. Rectal biopsies are now obtained more commonly using suction devices initially made popular by Noblett [12,13]. Suction biopsies can be performed as clinic procedures. Mucosa and submucosa are obtained and stained. The diagnosis is enhanced by calretinin immunohistochemistry, but there is a high incidence of inadequate samples [6,8,13,14]. Suction biopsy may also be complicated by significant bleeding [15]. Grasp biopsy using different types of biopsy forceps is also an option [14]. We perform full-thickness rectal biopsy as suction devices are expensive and unavailable in our center. We encountered complications in three patients (8.3%), which is higher than that reported for rectal suction biopsy [10,13], but low enough to be considered a safe procedure.

The diagnostic yield in this study was 83.3%, which is comparable with the study that examined full-thickness biopsy [8]. This, however, takes on a peculiar significance when we consider that four out of six inadequate samples were from patients with a final diagnosis of HD. The ensuing delay in their management while awaiting a repeat biopsy represents extra time during which enterocolitis can occur. HD should be confirmed histologically before a pullthrough is performed. In three of the six patients with inadequate samples, a decision to proceed without a repeat biopsy was taken on the basis of the clinical picture and a typical contrast enema. This was considered against the time delay in obtaining histologic reports following a repeat biopsy in our setting and also the cost of a repeat biopsy in these financially challenged patients, and the possibility of default from clinic as a result of these reasons. Two of the patients defaulted from follow-up probably because of these reasons. Suction rectal biopsies return inadequate samples in 2–35% of procedures, more so in patients older than 3 years of age, but have the distinct advantage of being easier to repeat [9–14]. A study suggests that grasp and cut techniques have a better yield than suction across all age groups [14]. The yield appeared to be better where more than one sample was obtained and in children older than one year, but without statistical significance. The level of the surgeon performing the biopsy did not impact the yield. This was unexpected.

The need to standardize the biopsy technique and reporting is immediately obvious and may improve the yield. In most (63.9%) of the procedures, the operator did not indicate at what distance the biopsy was taken. Where it was indicated, four were documented as having been obtained 1 cm from the dentate line, which is usually considered too close. Whether patients stopped washouts was also not recorded; these factors have effects on adequacy of specimen [8].

The diagnostic accuracy was 97%, with one false-negative result, yielding a sensitivity of 96% and a specificity of 100%. The patient who had a false-negative test also underwent a colonic biopsy, which indicated aganglionosis, suggesting a misinterpretation of specimen as a cause of the false-negative result. This study, however, did not consider the level and experience of the pathologist interpreting the specimen as data for such analysis were unavailable to the authors. That the level of the surgeon performing the biopsy did not impact the yield was surprising and suggests that factors other than technical knowhow led to the inadequate specimen. Proper documentation of the important technical details of the biopsy procedure would have helped in identifying the source of the problem.

Attempts have been made to reduce unnecessary biopsy by identifying clinical features that can predict the likelihood of a positive biopsy, with mixed results. One study found that with a history of delayed passage of meconium, abdominal distension or vomiting, and a positive contrast enema, all children with HD would have been diagnosed and a third of the negative biopsies could have been avoided [7]. Ghosh concluded that onset of constipation in the newborn period should be the criterion for a rectal biopsy, but other studies suggest that selecting patients for rectal biopsy on the basis of clinical criteria would lead to many patients with HD (in one study up to 10%) being missed or a delay in diagnosis [8–10]. In this study, the incidence of delayed passage of meconium and abdominal distension among children with a diagnosis of HD was consistent with the literature, whereas bilious vomiting was more common [1,7]. These features did not, however, show a significant relationship with the final diagnosis, and hence could not be used to predict the likelihood of HD.

The limitations encountered in carrying out this study including poor documentation of the technical details of the biopsy procedure, histology reports from different pathologists, and the lack of standardization of certain terms (e.g. constipation) are because of its retrospective design. A more detailed, properly designed audit is necessary.

Conclusion

No clinical parameter can adequately predict which patients do not require a rectal biopsy; hence, rectal biopsy should still be performed in all patients who are suspected to have HD. It is relatively safe. Multiple sampling may improve the diagnostic yield. We must standardize our technique of rectal biopsy and reporting and then carry out a more detailed prospective audit with a pathologist involved.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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