Significant use of the Recto-sigmoid Index in Prediction of Hirschsprung Disease in the Newborn Period

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Objective: *There has been a debate regarding the accuracy of contrast enema (CE) in the diagnosis of Hirschsprung disease (HD) in the newborn period when a transitional zone (TZ) was not well demonstrated. The aim of this study is to determine the optimal cut-point that will improve the accuracy of the recto-sigmoid index (RSI) and other positive CE signs in predicting aganglionosis in the newborn period.*
Material and Method: *A retrospective review of newborn patients who underwent CE for suspected HD during a 3-year period (2005 through 2008) was conducted. The RSI and other positive contrast enema signs were evaluated and compared with pathological reports. Data were analyzed by Chi-square.*
Results: *Thirty-five neonates (20 M: 15 F, mean age: 19.5 days) underwent 37 preoperative CE. Aganglionosis was histologically confirmed in 20 patients (54%). The most common site of proximal extent of aganglionosis was recto-sigmoid colon (9 patients, 45%). The results of pathology and CE were concordant in 91% of the patients for transitional zone (TZ) and 68% for other CE findings. From the ROC curve, the most accurate diagnostic cut-point was RSI of the lateral view of ≤0.7 (sensitivity of 60% and specificity of 88.2%), whereas radiographic TZ had 50% sensitivity and 94% specificity. The combination of radiographic TZ and/or RSI increased the sensitivity up to 70% and specificity to 82.4%. The inter-rater reliability was 0.83 and 0.7 for 2 observers, while the intra-observer variation was 0.1.*
Conclusion: *RSI can improve the accuracy of CE for the diagnosis of HD in the newborn period. Further studies with larger sample size are required to better confirm these findings.*

Keywords: *Hirschsprung disease, Contrast enema, Transitional zone, Recto-sigmoid index, Newborn*

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Hirschsprung disease (HD) is a form of functional obstruction caused by intestinal aganglionosis of the distal bowel[1]. The incidence of HD ranges from 1: 7,000 to 1: 4,400 live births[2-5]. The diagnosis should be considered in any child who has a history of constipation with onset in the newborn period[4]. Other presenting symptoms include constipation, abdominal distension, failure to thrive and enterocolitis[6]. The classical HD with aganglionosis of the recto-sigmoid colon is the most common type (70% of cases)[1]. The surgical treatment of classical HD has improved substantially. Recently, single-stage transanal endorectal pull-through (TEPT) has become the definitive surgical procedure, which can be performed in newborns, with reportedly good outcomes. The procedure also precludes a colostomy and complications from delayed treatment, such as gut obstruction and enterocolitis, which affects the long-term quality of life.

Although the gold standard for diagnosis of HD is rectal biopsy[1], radiological study is a useful non-invasive diagnostic modality that also provides useful information during preparation for surgery. The radiographic TZ is the most accurate diagnostic sign of HD seen in a contrast enema. Other radiographic signs, including delayed evacuation of barium, abnormal rectal contraction, and stool mixed with barium, may suggest the diagnosis of HD and improve the diagnostic accuracy of the examination when combined with radiographic TZ[7].

Despite a lot of debate regarding the accuracy of CE in the newborn period, CE is still the mainstay for the diagnostic work-up of HD because it can provide an estimation of the proximal extent of aganglionosis.

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Its accuracy for early diagnosis in the newborn period is very important for pediatric surgeons working in rural regions, where there is a paucity of pathologists and frozen sections. Pochaczevsky and Leonidas[8] introduced the recto-sigmoid index (RSI) in 1975 as an aid in the neonatal diagnosis of HD in cases where an obvious radiographic transitional zone could not be demonstrated.

The present study was designed to determine the optimal RSI cut-point to improve the accuracy of the RSI in diagnosing HD and to compare the diagnostic results with other positive signs in CE findings in newborn patients.

Material and Method

Clinical manifestations, contrast studies, and pathological results of newborn cases with suspected HD from 1 January 2005 to 1 January 2008 in Siriraj Hospital were retrospectively reviewed. Inclusion criteria included patients younger than 1 month of age with suspected HD (history of delayed passage of meconium for longer than 24 hours after birth and/or abdominal distension, constipation, feeding intolerance, and enterocolitis) who underwent CE (water-soluble or barium enema) by Siriraj pediatric radiologists. Patients who underwent redo pull-through operations after initial repair, in either Siriraj Hospital or other institutions, were excluded. Patient characteristics and clinical data were obtained from medical records including: age, sex, signs and presenting symptoms, radiographic findings from plain film and contrast enema, and pathological findings.

Standard procedure of CE

Standard procedure of CE was done in all cases using the technique described by Mahboubi and Schnaufer[9]. Examinations were carried out without prior cleansing of the colon, as the repeated enema may have resulted in dilatation of the distal aganglionic segment and may have obscured the TZ. The enema tube without balloon inflation was inserted into the anus at a depth of 1 inch. Fluoroscopy was done as the distal colon was filled with contrast media, followed by overhead anteroposterior and lateral radiographs before and after evacuation of the contrast. Unless a clear-cut diagnosis of HD had been reached on the initial study, another radiograph would have been taken 24 hours later to detect delayed evacuation of the contrast media.

The RSI were calculated using the method described by Pochaczevsky and Leonidas[8]. The widest diameter of the rectum was obtained at any level below the third sacral vertebra. This point was established arbitrarily on the basis of the usual position of transition segments. The sigmoid loop was usually measured at 3 points along its course (proximal, peak of the loop, and distal sigmoid colon). The largest measurement was selected. All measurements were obtained along a transverse axis, vertical to the longitudinal axis of the colon at that point. Measurements were made in antero-posterior and lateral projections (Fig. 1).

$$\text{Recto-sigmoid index} = \frac{\text{The widest diameter of rectum}}{\text{The widest diameter of sigmoid}}$$

All patients who were diagnosed HD underwent definitive pull-through procedures and/or full thickness intestinal biopsy as required by the attending pediatric surgeons and were confirmed by a pathological report to have aganglionic bowel. All cases that were initially not diagnosed with HD were to be clinically followed for at least 1 year or until the end of the study to detect any cases that had clinical

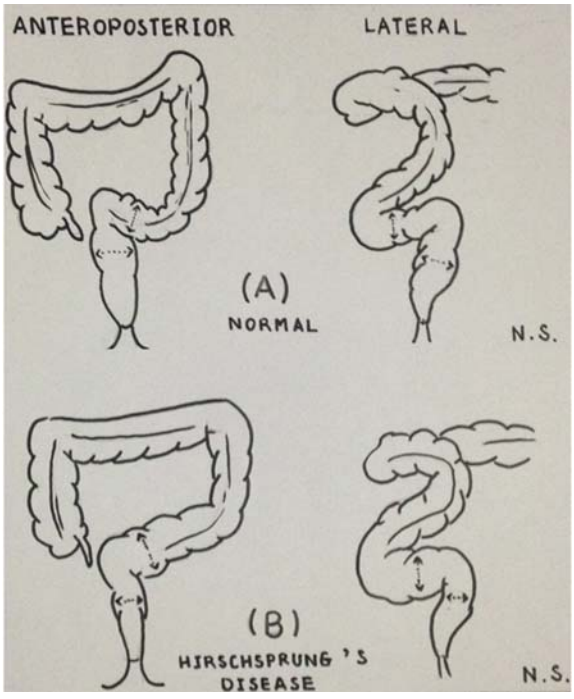

Fig. 1 Recto-sigmoid index (A) Normal: The diameter of the rectum is wider than the sigmoid colon and RSI is usually greater than 1, (B) Abnormal: In Hirschsprung's disease, the diameter of the rectum is smaller than the sigmoid colon(8) which RSI is lesser than 1.

worsening or a change of the diagnosis to HD, which would be considered false negative.

All positive CE signs were determined to be concordant if they were located in the same or adjoining bowel segment as the pathologic level of aganglionosis. They were determined to be discordant if separated from the level of aganglionosis by at least one intervening bowel segment[10].

During the review, inter-observer and intra-observer variations were determined by comparing the value of RSI measured by 2 pediatric surgical residents with the results from the researcher. All of the CE studies were reviewed by a single attending pediatric radiologist and compared with pathological reports from the surgically removed bowel.

The research proposal was approved by the Siriraj Ethical Committee.

Data analysis

In order to evaluate the accuracy of the RSI and other radiologic signs in determining Hirschsprung disease in the newborn, the data were analyzed using 2x2 tables and presented as percentages compared with the accuracy of other positive contrast enema signs. The sensitivity, specificity, accuracy, positive and negative predictive values were calculated and compared to the operative and pathological findings. The inter-observer and intra-observer variabilities were calculated.

Results

Thirty-five patients underwent 37 preoperative CE during the study period. The data showed a male predomination of 60%. The mean age of the male patients was 18.5 days, while that of female patients was 21 days. In this series, HD was more common in male patients (65%) than in female (35%) (Table 1).

Among HD patients, the most common presenting sign and symptom was abdominal distension (60%), whereas delayed passage of meconium longer than 24 hours was found in 58% of the patients, and multiple signs and symptoms were found in 57% (Table 2).

The sensitivity, specificity of the RSI (mean, AP, lateral) from various cut-points were plotted into receiver operating characteristic (ROC) curves to find the most accurate cut-point of the RSI as a diagnostic test for HD in the newborn (Fig. 2). The ROC curve for RSI lateral resulted in the largest area under the curve compared to the other RSI's. The RSI $\leq$0.7 was chosen as the optimal cut-point because of its highest sensitivity and specificity.

The accuracy of all contrast enema signs were compared. The sensitivity of radiographic TZ was 50% and the specificity was 94%. Combining TZ and the other signs, the sensitivity went up to 75% but specificity went down to 58.8%, whereas only RSI in the lateral position less than 0.7 had a sensitivity of 60% and a specificity of 88.2% with improvement of positive predictive and negative predictive values (Table 3). The inter-observer and intra-observer variations were shown in Table 4. Among all cases of HD in the present study, 2 patients received 2 contrast enemas. In the first patient, the radiographic TZ was not visualized in both studies, which the value of the RSI lateral from the first and second contrast enema were 0.62 and 0.65 respectively. This resulted in a false negative by relying only on the radiographic TZ

Table 1. Demographic data as determined by contrast study

	Male (n = 22)	Female (n = 15)
Number	22 (60%)	15 (40%)
Mean age (days)	18.5 (2 to 30)	21 (5 to 30)
Hirschsprung's disease	13 (65%)	7 (35%)
Non-Hirschsprung's disease	9 (53%)	8 (47%)

Table 2. Presenting signs and symptoms

Presenting Signs & Symptoms	Hirschsprung's disease (n = 20)	Non-Hirschsprung's disease (n = 17)
Delayed passage of meconium over 24 hours	7 (58%)	5 (42%)
Abdominal distension	15 (60%)	10 (40%)
Enterocolitis	2 (50%)	2 (50%)
Constipation	3 (37.5%)	5 (62.5%)
Poor feeding	1 (25%)	3 (75%)
Multiple signs & symptoms	8 (57%)	6 (43%)

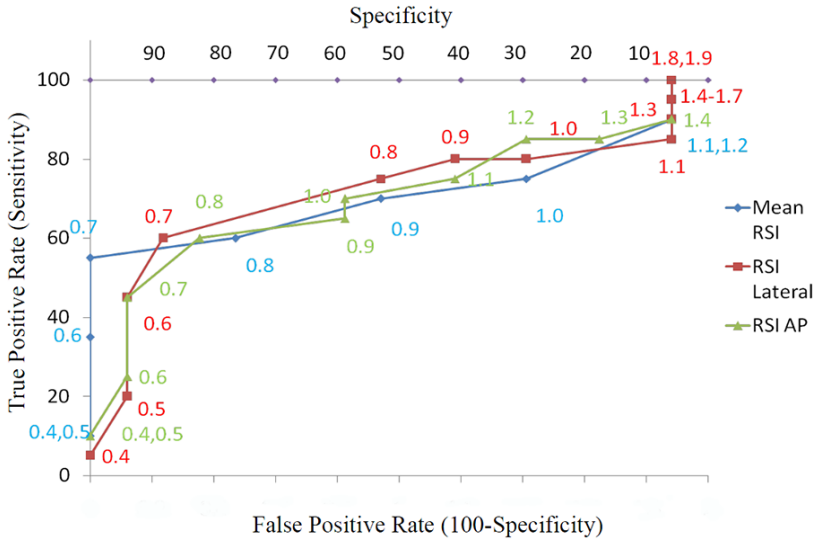

Fig. 2 A receiver operating characteristic (ROC) curve for recto-sigmoid index as a diagnostic test for Hirschsprung disease in newborns.

Table 3. The comparison of the accuracy between recto-sigmoid index lateral ≤0.7, transitional zone and the other positive contrast enema signs

Contrast enema signs	Sensitivity	Specificity	Positive predictive value	Negative predictive value
TZ*	50.0%	94%	90.99%	61.54%
TZ and others	75.0%	58.8%	68.2%	66.7%
RSI lateral** ≤1.0	80.0%	29.4%	57.1%	55.6%
RSI lateral ≤0.7	60.0%	88.2%	85.7%	65.2%
RSI lateral ≤0.7 and TZ	70.0%	82.4%	82.4%	70.0%

* TZ = transitional zone, ** RSI lateral = rectosigmoid ratio in the lateral view

Table 4. The inter-observer and intra-observer variations

	Interrator reliability	Intraobser ver variation
Observer 1	0.83	0.1
Observer 2	0.7	0.07

(Fig. 3, 4). The second patient who had long segment HD is an example of the difficulty in diagnosis by CE. The first CE was carried out at the age of 3 days, but the finding was not clear. Three weeks later, the second CE demonstrated a radiographic TZ at the splenic flexure of colon confirming the diagnosis of HD (Fig. 5, 6).

Discussion

HD accounts for approximately one-fifth of neonatal intestinal obstructions. The majority of patients show clinical symptoms within the first 6 weeks of life, affirming the importance of the early diagnosis of HD before definitive surgical intervention[6]. More recently, single stage pull-through procedures have been proven safe and effective in the newborn, at the same time eliminating the need for colostomy and reducing the number of hospitalizations[10]. The demographics of our patients confirmed the male predominance of HD (57%), and the mean age at diagnosis was 18.5 days in males and 21 days in females. The most common presenting sign and symptom was abdominal distension (67%), whereas delayed passage of meconium longer than 24 hours was found in only 35% in this series, which differed from previous reports[8].

Plain abdominal radiographs in HD commonly

Fig. 3 The first contrast enema showed no transitional zone and was reported as a negative result.

Fig. 4 The second contrast enema showed RSI <1, suspected Hirschsprung's disease.

reveal distended loops of bowel and may show a paucity of air in the rectum[6,11,12]. However, the

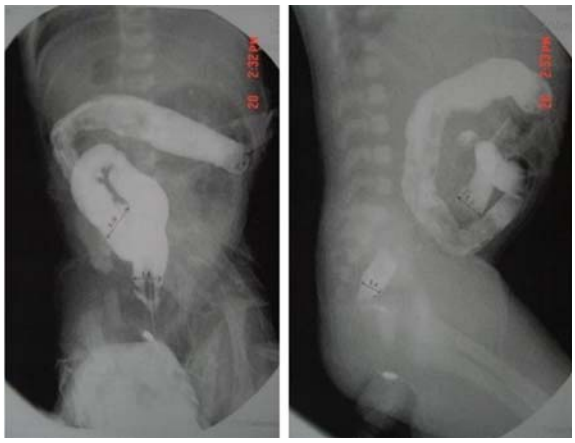

Fig. 5 The first contrast enema of the second patient showed no transitional zone with small caliber of the entire colon.

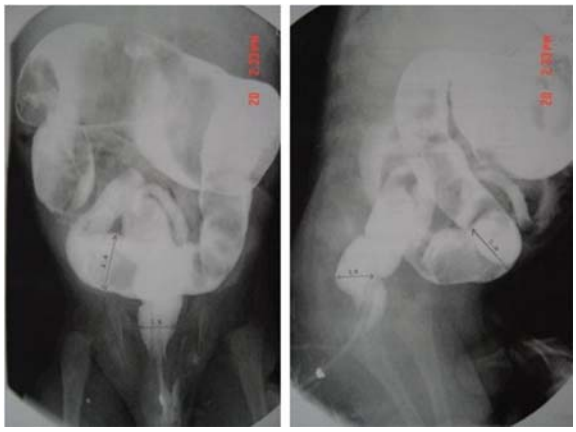

Fig. 6 The second contrast enema of the second patient showed radiographic TZ at splenic flexure of colon.

radiographic picture on the plain film is not diagnostic and should always be followed by CE or other appropriate studies[13].

CE often helps to facilitate the diagnosis of HD and determine the level of involved colon for surgical planning, as well as help in excluding other causes and treatment for meconium plug syndrome[1]. Classical CE findings are a narrow, spastic distal intestinal segment with dilated proximal segment. The most reliable radiographic finding is a transitional zone (TZ)[7,9], although the concordant between the radiographic transitional zone and the pathological extent of aganglionic bowel was only 62% diagnostic sensitivity and 100% specificity[7,9,10]. CE however has limited diagnostic efficiency in patients with poorly defined transition points such as patients with short

segment diseases or in total colonic aganglionosis and especially in the newborn[1,8].

Gupta, and Guglani reported that delayed films after 24 hours demonstrating prolonged retention of barium in the sigmoid colon is a strong indicator of HD[6]. Rosenfield et al reported that barium mixed with stool was seen infrequently but was a highly reliable sign of HD when seen. They reported that the three radiological features combined (recto-sigmoid TZ, retention of barium and stool mixed with barium) with only 2 or more positive signs had accuracies up to 87.5 to 100%, and their report showed that rectal examination prior to the contrast study did not affect visualization of a TZ[7].

Normally the caliber of the rectum is wider than that of the sigmoid colon. On the contrary, in patients with HD it is the opposite. The radiologist also uses recto-sigmoid index (RSI) to evaluate for a transitional zone in suspicious cases; more recent studies used RSI <1 in the diagnosis of HD. On the other hand, if RSI is ≥1, recto-sigmoid HD can be excluded (Fig. 2)[8,9,14]. The RSI is not useful in total colonic aganglionosis and long segment HD[8,9,14]. Garcia R, et al reported that RSI and TZ agreed with histopathological diagnosis in 79% and 87% of the cases, respectively[15].

As a result of this study, basing a diagnosis on radiographic TZ alone may not be adequate for early diagnosis, especially in the newborn. Our study shows that RSI is helpful in the diagnosis, which contradicts other reports[8,14]. Two patients were diagnosed with total colonic aganglionosis (TCA), with RSI of 1.3 and 1.12 on the lateral view, confirming that RSI is not useful in the diagnosis of TCA, which corresponds with other reports[8,14]. Four patients with ultrashort segment HD had RSI lateral >0.7, illustrating that RSI may not be useful in the diagnosis of ultrashort segment HD.

From the ROC curve, we found that if we used a cut-point of RSI less than 1, we would get a high sensitivity but the specificity was quite low. So we shifted RSI to the left and found that RSI less than or equal to 0.7 may be more suitable because of its higher specificity. We concluded that RSI lateral ≤0.7 is useful in the diagnosis of HD in the newborn, especially when radiographic TZ was not visualized. The accuracy of RSI lateral ≤0.7 had no significant difference from visualized radiographic TZ. The combination of TZ and/or RSI ≤0.7 can help in the early diagnosis of HD in the newborn.

The low inter-observer variability and relatively high inter- and intra-rater reliability in the present study reflects that the diagnostic value is easily applicable, as well-trained surgeons, even in the setting which the pediatric radiologists are not available, can interpret it.

Conclusion

The RSI can improve the accuracy of contrast enemas for the diagnosis of HD in the newborn and may help pediatric surgeons in providing early treatment.

Although the results of this study showed an improvement in the diagnostic outcome, it has some limitations due to the small sample size, which results in limited reliability. We suggest an extension of the study period in the future to increase sample size and reliability.

What is already known on this topic?

Diagnosis of Hirschsprung disease in the newborn may be difficult. Rectal biopsy, the gold standard, is invasive and cannot provide the extent of the disease. Frozen section is not available in the majority of hospitals. Therefore, contrast study is a mainstay investigation. However, transition zone is not clearly visualized in a significant portion of the patient. Using recto-sigmoid ratio (with a cut point of ≤1.0) can enhance the accuracy of the contrast study in diagnosing Hirschsprung disease (agreement with pathological diagnosis = 79%).

What this study adds?

This study confirms the ability to enhance the accuracy of contrast study in diagnosis of Hirschsprung disease. By lowering the cut point from ≤1.0 to ≤0.7, the specificity is increased from 29% to 88%, with lesser degree of decrease in sensitivity (from 80% to 60%). By combining recto-sigmoid index with transition zone, the sensitivity is improved without significant compromise of the specificity. The positive and negative predictive values are also increased compared to using recto-sigmoid index ≤1.0 as a cut point either alone or combined with transitional zone. This is useful to pediatric surgeons working in institutions where a frozen section is not available.

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Potential conflicts of interest

None.

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ประโยชน์ของ Recto-sigmoid index ในการวินิจฉัย Hirschsprung disease ในทารกแรกเกิด

นันทิกา ศิวบวรวัฒนา, มนวัฒน์ เงินฉ่ำ, เกรียงไกร เอี่ยมสวัสดิกุล, มงคล เลาหเพ็ญแสง

วัตถุประสงค์: *การวินิจฉัย Hirschsprung disease (HD) ด้วยการตรวจสวนสารทึบรังสีทางทวารหนักยังคงมีปัญหาเรื่องความแม่นยำโดยเฉพาะในเด็กทารกที่ transitional zone (TZ) อาจจะยังไม่สามารถเห็นได้ชัดเจน วัตถุประสงค์ของการศึกษานี้ คือ การหา criteria ที่เหมาะสมทางรังสีวิทยา ได้แก่ recto-sigmoid index (RSI) และการตรวจพบอื่นที่จะช่วยเพิ่มความแม่นยำในการวินิจฉัย HD ในทารกแรกเกิด*

วัสดุและวิธีการ: *การศึกษาย้อนหลังในทารกแรกเกิดที่ได้รับการตรวจสวนสารทึบรังสีทางทวารหนักเพื่อการวินิจฉัย HD ในระหว่างปี พ.ศ. 2548 ถึง 2551 โดยการประเมินความแม่นยำ RSI และการตรวจพบอื่นทางรังสีวิทยา เมื่อเปรียบเทียบกับผลตรวจทางพยาธิวิทยา*

ผลการศึกษา: *ทารกแรกเกิด 35 รายได้รับการตรวจสวนสารทึบรังสีทางทวารหนักจำนวน 37 ครั้ง ในช่วงเวลา การศึกษา อัตราส่วน ชาย: หญิง = 20:15 อายุเฉลี่ย 19.5 วัน ผลพยาธิวิทยายืนยันว่า 20 ราย (54%) เป็น HD และพบว่าตำแหน่ง proximal ที่สุดที่เริ่มไม่มีปมประสาท (aganglionosis) ส่วนใหญ่อยู่ที่ recto-sigmoid colon (9 ราย, 45%) ผลการวินิจฉัยโดยใช้ TZ จากการตรวจทางรังสีและพยาธิวิทยาสอดคล้องกันในร้อยละ 91 ของผู้ป่วย ขณะที่ผลการตรวจอื่นสอดคล้องกันร้อยละ 68 จาก ROC curve พบว่า cut-point ของ RSI ที่เหมาะสมในการวินิจฉัยคือ RSI ทางด้านข้าง ≤0.7 (ความไวร้อยละ 60 และความจำเพาะร้อยละ 88.2) ขณะที่ความไวและความจำเพาะของ TZ อยู่ที่ร้อยละ 50 และ 94 ตามลำดับเมื่อใช้ RSI กับ TZ ร่วมกันจะพบว่า ความไวเพิ่มเป็นร้อยละ 70 และความจำเพาะเป็นร้อยละ 82.4 inter-rater reliability ระหว่างผู้อ่านผล 2 คนเท่ากับ 0.83 และ 0.7 และ intra-observer variation เท่ากับ 0.1*

สรุป: *RSI สามารถเพิ่มความแม่นยำในการวินิจฉัย HD ในทารกแรกเกิด อย่างไรก็ตามควรมีการศึกษาที่มีขนาดตัวอย่างใหญ่ขึ้นเพื่อยืนยันผลการศึกษานี้*