

New sonographic feature (C-sign) to improve the prenatal accuracy of jejunal atresia

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Abstract

Objectives: To describe a new sonographic feature of the C-sign for prenatal diagnosis of jejunal atresia and evaluate its role in prenatal jejunal atresia, particularly preceding bowel dilatation and polyhydramnios.

Methods: This was a retrospective study from a tertiary maternal hospital. Patients with prenatal sonographic examination and confirmed small bowel atresia postdelivery were included. All sonographic images were reviewed by two senior sonographers. Comparison of sonographic images between prenatal jejunal and ileal atresia using the C-sign resembles the shape of the entire duodenum and other traditional sonographic features. The control group without bowel atresia was assessed for the presence of the C-sign.

Results: The C-sign and combined bowel dilatation with polyhydramnios were more frequent in jejunal atresia than ileal atresia, but the C-sign can be used to detect jejunal atresia earlier. The C-sign can be more likely to diagnose jejunal atresia in persisting bowel dilatation and polyhydramnios. The C-sign was not reported in any of the control fetuses.

Conclusion: The C-sign is a new sonographic feature that can be used to improve the prenatal accuracy and early detection of jejunal atresia. However, further prospective validation is needed.

Key words: ileal atresia, jejunal atresia, nonduodenal small bowel atresia, prenatal diagnosis, prenatal ultrasound.

Introduction

Small bowel atresia (SBA), one of the common causes of congenital bowel obstruction, can occur in the duodenum, jejunum, or ileum. The prevalence varies from 1.3 to 2.8 per 10 000 livebirths,¹ and the pathophysiology is still debated. The most accredited hypothesis relates to the failure of recanalization of the duodenum during embryonic development, and atresia or stenosis of the jejunum and ileum is caused by vascular accidents in utero.^{1–3} Although congenital SBA has excellent outcomes after initial surgical correction, the

morbidity in neonates with nonduodenal SBA (ND-SBA) has increased in recent decades, and some patients are affected by short bowel syndrome, sepsis, and long-term parenteral nutrition.^{3,4}

Duodenal atresia is commonly predicted by the presence of the “double-bubble” sign, while the antenatal detection rate of ND-SBA remains a challenge; the rate varies widely from 10% to 100%, with an overall prediction of 50.6%.⁴ Bowel dilatation and polyhydramnios are the best-reported markers of ND-SBA, but are not specific because they can be found in other congenital gastrointestinal anomalies,

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such as meconium ileus, colonic atresia, and imperforate anus.^{5,6} Previous studies have revealed the sonographic features of ND-SBA, and fewer studies have mentioned jejunal atresia independently. However, accurate prenatal diagnosis can provide a suitable prenatal consultation on management, including prompt surgical intervention⁷ and reduced parental anxiety.⁶

Herein, we describe the C-sign (Figure 1), a new sonographic feature based on sharpness and location rather than measurement for prenatal diagnosis of jejunal atresia, and we evaluate its role in prenatal diagnosis of jejunal atresia, particularly preceding bowel dilatation and polyhydramnios.

Methods

Study participants

This was an 8-year retrospective observational study conducted at a tertiary maternal and children hospital

in Guangzhou, China. Data were collected from the hospital medical system, Picture Archiving and Communication Systems (PACS), from 1st January 2013 to 31st December 2020. The inclusion criteria were as follows: (a) all neonates were confirmed to have SBA by operation or autopsy, and (b) prenatal sonographic examinations were performed in our ultrasound department with available images. The exclusion criteria were: (1) duodenal atresia, (2) associated chromosomal abnormalities or structural abnormalities, and (3) missing details in the surgical record.

Gestational age (GA) was calculated from the last menstrual period or crown-rump length at 11⁺⁰ to 13⁺⁶ weeks if there was a discrepancy of more than 5 days between days. All sonographic images were reviewed by two senior sonographers specializing, with professional qualification of prenatal ultrasound diagnosis in China, in prenatal gastrointestinal obstruction, performed on Voluson E10, E8, or E6 (GE Healthcare, Zipf, Austria) with 1.0–8.0 MHz

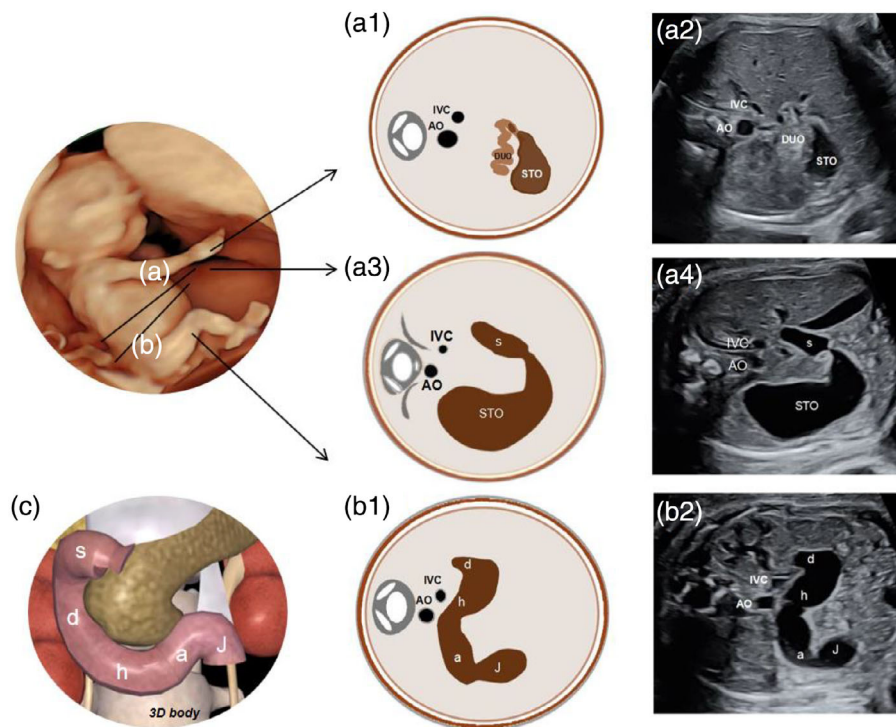


FIGURE 1 Schematic diagrams showing the fetal stomach (line a) and duodenum (line b) in transverse fetal abdominal view while fetal in right sacrum transverse position. Figures a1 and a2 revealed normal fetuses in which the stomach was located on the left side without a distended duodenum. In jejunal atresia, particularly in the proximal segment, the duodenum becomes distended (a3, a4), and the shape of the entire duodenum can be clearly observed as the letter “c” due to dilatation (b1, b2) in ultrasound compared with the anatomy diagram (c). a, Ascending part of duodenum; AO, aorta; d, descending part of duodenum; DUO, duodenum; h, horizontal part of duodenum; IVC, inferior vena cava; J, jejunum; STO, stomach; s, superior part of duodenum

curved transabdominal transducers (RM6C, RAB4-8, 4C-D, and C1-5-D) in two-dimensional grayscale and color Doppler mode.

C-sign

The duodenum is divided into four segments: the superior (duodenal bulb), descending, horizontal, and ascending parts. Although it is difficult to distinguish different segments prenatally, as it is normally nondistended,⁸ it appears clearly during bowel dilatation in ND-SBA, particularly proximal jejunal atresia. The C-sign resembles the shape of the entire duodenum according to anatomy. Furthermore, this characteristic shows the transition from the stomach to the jejunum, making it helpful in determining the location of jejunal atresia.

To assess the presence of the C-sign, the features should be obtained in the transverse view of the fetal abdomen at the level of the duodenum, which shows the superior duodenum connecting with the pylorus of the stomach, the descending part backing up to the spine next to the head of the pancreas, the horizontal portion in front of the aorta and inferior vena cava paralleling the fetal back, and the ascending part transitioning to the jejunum.

Statistical analysis

We compared jejunal and ileal atresia using obstetric and pediatric data and prenatal sonographic features. Obstetric and pediatric data included maternal age, GA at diagnosis, and delivery, male to female ratio and fetal birth weight.

C-sign and traditional sonographic features (bowel dilatation, polyhydramnios, combined bowel dilatation with polyhydramnios, echogenic bowel, abdominal mass, and ascites) were used to compare jejunal and ileal atresia. Bowel dilatation was defined as fetal small bowel lumen >6 mm.⁹ A deepest vertical pocket (DVP) > 80 mm or amniotic fluid index (AFI) > 250 mm indicates polyhydramnios.¹⁰⁻¹² Then, significant sonographic features and prenatal magnetic resonance imaging (MRI) were compared with the C-sign in the prenatal diagnosis of jejunal atresia. Finally, we described the C-sign using initial detection in GA, maximum diameter in different GA, and the relationship between the anatomical location of atresia and C-sign.

Descriptive statistics were used to analyze the collected data. Comparisons for categorical variables were made using the chi-square test or Fisher's exact test; the Mann-Whitney test was used to compare

continuous variables; $p < 0.05$ was considered statistically significant.

Control group

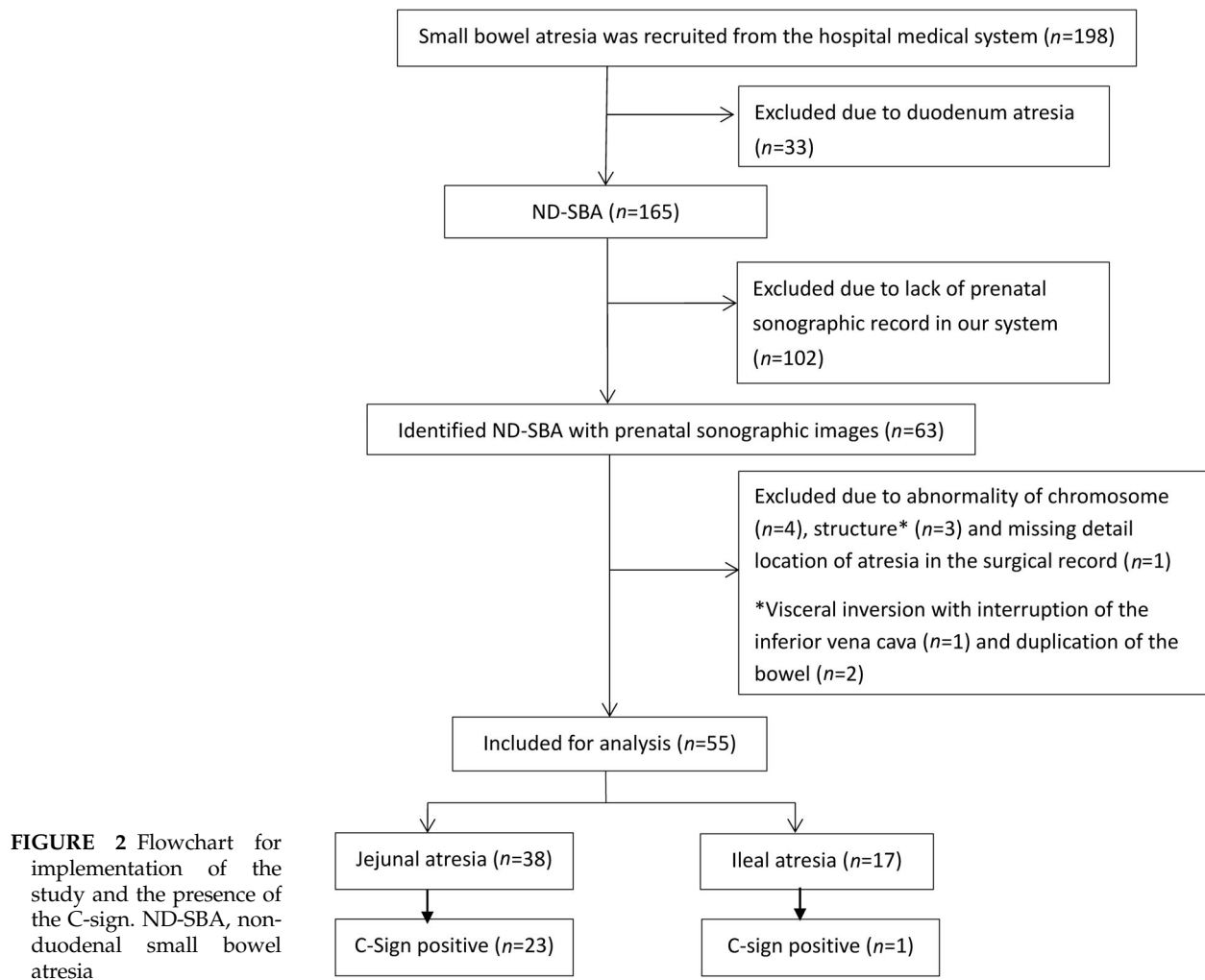
To confirm that the C-sign cannot be seen in pregnancies unaffected by ND-SBA, we created a control group from the population of all women attending our hospital for the 2nd- and 3rd-trimester prenatal ultrasound performed from January to May 2020. One author (Chen Dan) performed the prenatal ultrasound and actively searched for the C-sign. Then, we followed the selected case until delivery to confirm that the control group had not been diagnosed with bowel atresia or any other abnormality during pregnancy.

Results

In total, 165 patients had ND-SBA (Figure 2), of which 102 patients (including 49 with jejunal atresia, 21 with ileal atresia, and 32 with ND-SBA without detailed classification) who only delivered without prenatal investigation in our hospital were excluded due to a lack of prenatal sonographic records. There were 55 patients who had full data and were included in the analysis. Thirty-eight (69.1%) patients had jejunal atresia, and 17 (30.9%) had ileal atresia. There was no significant difference in maternal age ($p = 0.543$), GA at diagnosis ($p = 0.297$), or male to female ratio ($p = 0.432$) between jejunal and ileal atresia. However, earlier delivery ($p = 0.005$) and lower fetal birth weight ($p = 0.011$) were associated with jejunal atresia (Table 1).

C-sign and combined bowel dilatation with polyhydramnios were more frequent in jejunal atresia than ileal atresia ($p = 0.0001$ and 0.0437 , respectively), and echogenic bowel was more frequent in ileal atresia ($p = 0.0219$) (Table 2). Meanwhile, other sonographic features were not significantly different in jejunal and ileal atresia, including isolated bowel dilatation ($p = 0.0663$), isolated polyhydramnios ($p = 0.2447$), and abdominal ascites ($p = 0.6636$).

In the prenatal diagnosis of jejunal atresia, there was no significant difference between the C-sign and combined bowel dilatation with polyhydramnios ($p = 0.1994$); the C-sign and MRI also showed no significant differences ($p = 0.3202$). Combined with the C-sign, bowel dilatation and polyhydramnios were more likely to be associated with a diagnosis of

**TABLE 1** General characteristics of the included cases

Characteristics	Total (n = 55)	Jejunal atresia (n = 38)	Ileal atresia (n = 17)	p-value
Maternal age (year)	29.4 (±4.5)	29.1 (±4.4)	29.9 (±4.8)	0.543
Gestational age (GA) at diagnosis (week)	29.3 (±3.9)	29.7 (±3.86)	28.5 (±3.93)	0.297
GA at delivery (week)	36.0 (±3.1)	35.3 (±3.25)	37.3 (±1.89)	0.005
Male:female ratio	1:1.04	1:0.9	1:1.43	0.432
Fetal birth weight (kg)	2.8 (±0.59)	2.7 (±0.61)	3.1 (±0.40)	0.011

Note: Values are the means ± SD.

jejunal atresia than combined bowel dilatation with polyhydramnios ($p = 0.0045$).

Twenty-four cases had a C-sign, of which 11 (45.8%) had a follow-up sonographic examination, and 10 (90.9%) maintained a C-sign. The C-sign (mean GA = 30.3 ± 3.85 weeks, median GA = 31 weeks) detected jejunal atresia earlier than

combined bowel dilatation with polyhydramnios (mean GA = 34.1 ± 2.24 weeks, median GA = 34.5 weeks), and the p -value was 0.000057 (Table 3). The C-sign can also detect jejunal atresia as early as 23 weeks GA, compared with 29 weeks GA in combined bowel dilatation with polyhydramnios. Figure 3 reveals that the maximum diameter of the C-

TABLE 2 C-sign and other sonographic features in jejunal and ileal atresia

	C-sign	Isolated bowel dilatation	Isolated polyhydramnios	Bowel dilatation with polyhydramnios	Echo-genic bowel	Abdominal mass	Abdominal ascites
Jejunal atresia (n = 38)	23	36	23	23	7	3	4
Ileal atresia (n = 17)	1	13	7	5	9	3	3
p-value	0.0001	0.0663	0.2447	0.0437	0.0219	0.3549	0.6636

TABLE 3 Comparison of the first detection in gestational age (GA) between the C-sign and bowel dilatation with polyhydramnios

	1st detection in GA (weeks)	Mean ± SD (weeks)	Median (weeks)	p-value
C-sign	23–37	30.3 ± 3.85	31	0.000057
Bowel dilatation with polyhydramnios	29–38	34.1 ± 2.24	34.5	

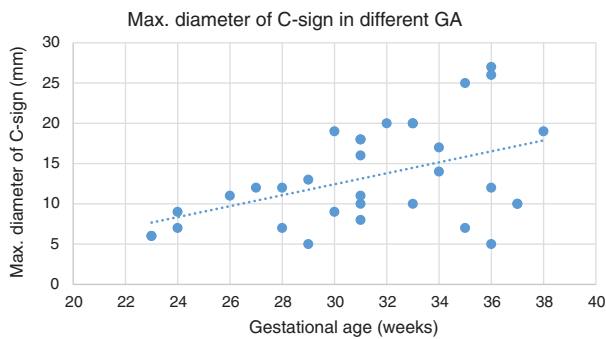


FIGURE 3 Maximum diameter of the C-sign in different gestational age (GAs)

sign increased progressively as GA increased. Anatomically, 61.5% of cases with the C-sign were found to have a distance of atresia ≤50 cm distal to the Treitz ligament: 74.2% in ≤40 cm, 88% in ≤30 cm, and 91.3% in ≤20 cm.

In the control group, 110 cases were included, and there were no reports of the C-sign in patients without bowel atresia or any other abnormality with no false positives.

Discussion

Although prenatal sonographic findings and time of diagnosis of ND-SBA did not affect the neonatal outcome,¹³ it is clear that prenatal diagnostic accuracy can influence the mode of delivery, prenatal

consultation, and overall parental anxiety during pregnancy⁷ and potentially lead to termination of the pregnancy.¹⁴ A study¹⁵ revealed many differences between ND-SBA, such as the mean birth weight and GA in delivery, mortality, and postoperative course; therefore, jejunal and ileal atresia may be considered separate diseases. Our study found that fetuses with jejunal atresia had lower birth weights and earlier deliveries than fetuses with ileal atresia, which is similar to the above study.

The most important finding in our study is that the C-sign with preceding bowel dilatation and polyhydramnios is likely to increase the accuracy of detecting jejunal atresia prenatally, as it could clearly separate the prenatal diagnosis of jejunal and ileal atresia. In previous literature, bowel dilatation and polyhydramnios have a low specificity in detecting jejunal atresia, even ND-SBA prenatally⁴; polyhydramnios and enlarged stomach are more commonly associated with jejunal atresia than ileal atresia,⁴ and the prenatal diagnosis of jejunal atresia is open to question. We found a previous study that revealed distended proximal bowel in all neonates with SBA during the routine sonographic examination,¹⁶ but it did not include details. As the apparatus is proximal to the jejunum, the duodenum generally extends along with the pressure from jejunal atresia, particularly in the proximal portion. The dilated duodenum, even the stomach, is progressive with time. C sharp duodenum was formed in accordance with the consequent change. This may be the principle of the C-sign.

To the best of our knowledge, there is no previous literature describing similar sonographic findings prenatally.

The C-sign improved the prenatal accuracy of jejunal atresia and also led to earlier detection of jejunal atresia than traditional sonographic features, such as bowel dilatation and polyhydramnios. Anatomically, this implied that it was easier to detect the C-sign closer to the Treitz ligament; over 70% of cases presented with the C-sign if the location of atresia was below 40 cm distal to the Treitz ligament. The above findings will support clinicians in tailoring suitable prenatal consultations and perinatal management. The shape of the C-sign is stable and progressive in diameter with time, and we can observe the C-sign based on the shape and location rather than measurements; therefore, it would be easy to apply. However, several factors affect the accuracy of the C-sign, such as sonographer experience in the recognition of the duodenum and follow-up of ultrasound scans. Bowel perforation could also cause reduced pressure leading to the absence of the C-sign.

Our study also found that the C-sign had similar accuracy as MRI at detecting jejunal atresia. However, MRI can provide additional information to evaluate SBA.^{17,18} In MRI, fetal meconium with high signal intensity on T1-weighted imaging in the rectum and anus is usually noticed until 22–24 weeks of gestation.¹⁹ On the other hand, jejunal atresia is suspected, while dilated small bowel displays decreased T1 and increased T2 signal intensity and increased T1 and intermediate T2 signal intensity in ileal atresia.²⁰

Although it contributes to the literature, this study has several limitations: (a) It was a retrospective study for new sonographic features, and the next step should be prospective validation by multiple blinded operators. (b) Data from a single institution may result in selection bias. (c) Approximately 60% of cases with ND-SBA were excluded due to a lack of prenatal sonographic records that made sensitivity inaccurate. This study was conducted in a tertiary hospital and most of the patients were transferred for prenatal consultation which led to fewer cases with complete information on both prenatal sonographic image and postnatal diagnosis. Therefore, this study focused on sonographic features in fetuses with ND-SBA, exclusively in prenatally suspected cases. (d) There may have been bias in the diagnostic ability of the C-sign to detect ND-SBA. All scans were performed by sonographers with different experience levels, and some sonographers did not record images of the C-sign due to a lack of awareness. (e) Interpretation of the

results must be based on preceding sonographic features, such as polyhydramnios and bowel dilatation.

In conclusion, the new sonographic feature of the C-sign can improve the prenatal accuracy and early detection of jejunal atresia based on preceding bowel dilatation and polyhydramnios. However, further prospective validation is needed.

Author Contributions

Concept of the study: Dan Chen. *Design and draft manuscript:* Dan Chen and Kwong Ho Tam. *Statistical analysis:* Kwong Ho Tam. *Sonographic image analysis:* Dan Chen and Yiwei Xiao. *MRI image analysis:* Yu Tan. *Graphic design:* Juan Geng. *Data collection:* Jiixin Chen, Xiaochun Zhu, Wuping Ge and Jialiang Zhou. *Data about operation:* Shangjie Xiao. *Critical revision of the manuscript:* All authors.

Conflict of Interest

None declared.

Data Availability Statement

Data available on request from the authors.

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