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Histomorphological Findings and Clinico Radiological Correlation of Intestinal Atresia at a Tertiary Care Centre

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Abstract

Background: An atresia is a congenital defect of a hollow viscus that results in complete obstruction of the lumen. Intestinal atresia is one of the most frequent causes of bowel obstruction in the newborn and can occur at any point in the gastrointestinal tract. This study was undertaken to study the histomorphological findings of intestinal atresia and to correlate it with different subtypes and clinico-radiological feature.

Material and Methods: This was a prospective observational study conducted in 24 months on the resected gastrointestinal tract of 40 neonatal intestinal obstruction cases admitted in pediatric surgery ward received in the Department of Pathology, Indira Gandhi Institute of Medical Sciences, Patna. Control Group A total of 5 cases of vitello-intestinal duct patency were taken as control and compared with the study group.

Results: With respect to total 40 cases, there were six, i.e. 15.0% female babies and 34, i.e. 85.0% male babies studied. Out of that, 15 i.e. 37.50% were full term and 25, i.e. 62.5% were premature. Mucosa showed edema, ulceration and flattening in 9 cases. Apart from flattening and edema, mucosa was denuded at some places and also showed congestion and extravasated blood in 6 cases each. Abnormal villus configuration, calcium deposition in 4 cases each and hypertrophied mucosa were found in 3 cases. Luminal narrowing, loss of mucosa, duplication of mucosa and gangrene were found in one case each. Sub mucosal changes showed congestion in 33 cases, edema in 15, Fibrosis in 4, thickened submucosa in 2 cases and dilated irregular branching blood vessels, extravasated blood, calcification in 1 case each. Muscularis propria having changes i.e. thinning in 16 cases, congestion, hypertrophy in 4 cases each, focal loss in 3 cases, calcification in 2 cases and thinning in 2 cases. Similarly, histopathological changes in serosa show serositis in 16 cases, congestion in 11 cases and thinning in 3 cases. Edema and congestion were present in 2 cases, hypertrophy and calcification in 1 case each.

Conclusion: In this study spectrum of histomorphological changes in the atretic segment has been described. Histomorphological changes at atretic segment can be valuable to surgeons in deciding the type of surgery and minimizing the postoperative intestinal dysmotility, which remains the most common complication of intestinal atresia.

Keywords: Intestinal atresia; Congenital; Gastrointestinal tract; Mucosa; Edema

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Introduction

An atresia is a congenital defect of a hollow viscus that results in complete obstruction of the lumen. Intestinal atresia is one of the most frequent causes of bowel obstruction in the newborn and can occur at any point in the gastrointestinal tract [1]. The reported incidence of intestinal atresia ranges from 1.3 to 3.5 per 10,000 live births of which approximately 20 percent have associated anomalies vary by anatomical site. Duodenal atresia occurs in approximately 50 percent of small intestinal atresia [1]. It is characterized by obliteration of bowel lumen and its replacement by fibrous cord that connects the proximal and distal segment. It can involve any portion of small bowel and distal segment. It can involve any portion of small bowel [2]. The morphological classification into four types according to Grosfeld Modification of Louw's classification 1979 has both prognostic and therapeutic implications.

Type I atresia (23%) is a transluminal septum with proximal dilated bowel in continuity with collapsed distal bowel. The bowel is usually of normal length. Type II atresia (10%) involves two blind-ending atretic ends separated by a fibrous cord along the edge of the mesentery with mesentery intact. Type IIIa atresia (15%) is similar to type II, but there is a mesenteric defect and the bowel

length may be foreshortened. Type IIIb atresia (19%) ("Apple peel" or "Christmas tree" deformity) consists of a proximal jejunal atresia, often with malrotation with absence of most of the mesentery and a varying length of ileum surviving on perfusion from retrograde flow along a single artery of supply. Type IV atresia is a multiple atresia of types II, III, and I like a string of sausages. Bowel length is always reduced. The terminal ileum, as in type III, is usually spared [3].

It most commonly presents within first week of life with complaints of bilious vomiting, not passing meconium since birth and absence peristalsis. Complication included gangrene, perforation and meconium peritonitis and at times fungal infection (Mucormycosis) [4]. The management of intestinal atresia has greatly improved in recent decades due to refinements in neonatal intensive care, operative technique, use of total parenteral nutrition and neonatal anesthesia [5]. Outcome of the intestinal atresia following surgical repair is very good. In general, morbidity and mortality depend upon associated medical conditions such as prematurity or cystic fibrosis, other congenital anomalies, the complexity of the lesion, and surgical complications [6]. This study was undertaken to study the histomorphological findings of intestinal atresia and to correlate it with different subtypes and clinico-radiological feature.

Objectives

To evaluate clinical characteristic and radiological signs of intestinal atresia, to study the gross morphological features of different sub types of intestinal atresia and to study the histopathological findings of different atresia.

Material and Methods

This was a prospective observational study conducted on the resected gastrointestinal tract specimen fixed in buffered 10% formalin of 40 neonatal intestinal obstruction cases admitted in pediatric surgery ward of either sex received in the Department of Pathology, Indira Gandhi Institute of Medical Sciences, Patna, Bihar. Ethical committee approval was obtained from ethics committee for Post Graduate Studies of Government Medical College & Tertiary Care Centre. The confidentiality of the study participants was ensured.

Examination was done as following

Gross morphology: Clinical examination of the resected intestinal specimen was done meticulously to classify and subtype the intestinal atresia. After noting the relevant findings, proper sectioning of the intestine was performed, with special care to take sections from the resected margins and the fibrotic or atretic segment.

Gross morphology

- The biopsy specimen was processed using Thermo Fischer Scientific processor.
- The section was embedded in paraffin wax, labeled and blocks were made.
- The section was cut using "Leica rotatory microtome at a setting of 4 µm".
- The section was floated on water bath at 60°C.
- The section was mounted on a slide which was precoated with glycerol egg albumin.
- Four serial section of biopsy was prepared. One of them was stained with hematoxylin-eosin and three others subjected to special stains.

Special stain: Masson trichrome, Von Kossa and Perl's staining had been done to demonstrate fibrosis, calcification and hemorrhage.

Radiological evaluation was done in the radiology department with the help of radiologist.

Duration of the study: 24 months.

Inclusion criteria: Cases of neonatal intestinal obstruction.

Exclusion criteria: Cases where intestinal obstruction was due to intussusception, volvulus, meconium ileus, malrotation and Hirschsprung's disease and inability to give consent. Control Group- A total of 5 cases of vitello-intestinal duct patency were taken as control and compared with the study group.

Data entry and analysis

All the data was tabulated and analyzed with appropriate statistical tools "SPSS 25th version". Data was presented as a mean with standard deviation or proportions as appropriate. Mean, standard deviation and variance was calculated and following statistical significance tests was applied. "Chi square Test" and "Fisher's exact test" was used for statistical significance test. Student's T-test was used as the statistical tool to test for significance of observed mean differences. The calculated value finally was compared with the tabulated value at particular degree of freedom and finds the level of significance. A "p-value" was considered to be non-significant if >0.05 and significant if <0.05. The probability of error at 0.05 was considered significant, while at 0.01 and 0.001 are highly significant (Figure 1, 2).

Results

A prospective observational study conducted on the resected gastrointestinal tract specimen fixed in buffered 10% formalin of 40 neonatal intestinal obstruction cases admitted in Pediatric surgery ward of either sex received in a tertiary care centre. Among 40 patients of bowel atresia were operated and analyzed which resulted in 40 patients, 2 had Jejunoileal atresia, 17 had Ileal atresia and 14 had jejunal atresia and 7 had large bowel atresia (Tables 1-3 and Figure 3).

With respect to Table 3, there were six, i.e. 15.0% female babies and 34, i.e. 85.0% male babies studied. Out of that, 15 i.e. 37.50% were full term and 25, i.e. 62.5% were premature. Result is statistically not significant as p value >0.05.

Table 4 shows that with respect to feeding habits, there were 3 cases noted having normal feeding, 19 children presented with refusal of feeding and rest 18 were found to have vomiting after feeding. On examination, all 40 cases were found to have abdominal distension.

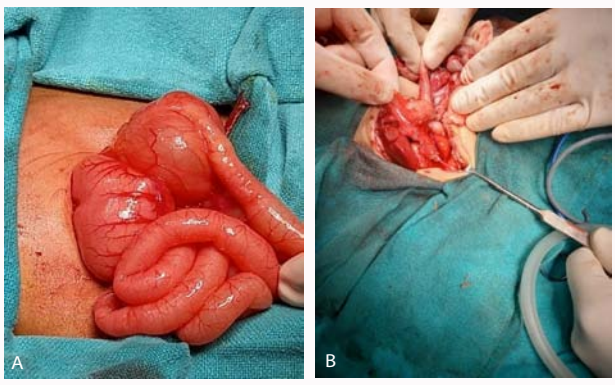

Figure 1: A) Nature of surgery - Laparotomy and B) Resections of proximal and distal atretic segment and ends to back anastomosis.

Figure 2: Image of part of gut (10 cm in length), one end of the gut is 1.6 cm diameter and the end is blind.

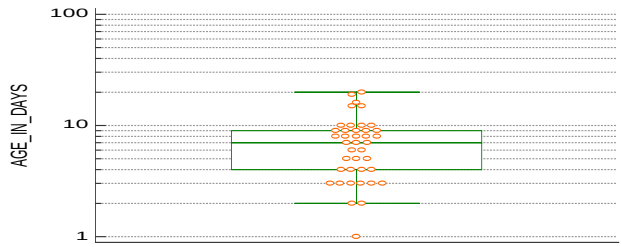

Figure 3: Box-and-Whisker plot for age of studied cases.

Table 1: Age analysis of studied cases.

Variable	Age (Days) n=40
Sample size	40
Lowest value	1
Highest value	20
Geometric mean	6.125
95% CI for the Geometric mean	4.9586 to 7.5658
95% CI for the median	5.0000 to 8.6478
Coefficient of Skewness	-0.4668 (P=0.2002)
Coefficient of Kurtosis	0.1679 (P=0.6445)
95% CI of Trimmed mean	5.0249 to 7.7261

On enquiry, it was found that 19 cases had not passed meconium since birth. Bilious vomiting noted in 35 cases and jaundice were present in 25 children.

With reference to Table 5 and Table 6, it shows types of atresia based on gross findings and found that 16 cases (40.0%) had type 1 atresia, 2 cases (05.0%) type 2 atresia, 8 cases (20.0%) type 3a, 3 cases (07.50%) type 3b and 11 cases (27.50%) had type 4 atresia. On gross examination, specimen of 31 cases (77.50%) had congestion, 12 cases (30.00%) had perforation and 3 cases (07.50%) had gangrene. Other associated findings include 1 case (02.50%) each with meconium pseudo-cyst, pouching of gut, duplication cyst and meconium ileus.

With reference to the Table 7 representing histological features found, on microscopic examination: Mucosa showed edema, ulceration and flattening in 9 cases. Apart from flattening and edema, mucosa was denuded at some places and also showed congestion and extravasated blood in 6 cases each. Abnormal villus configuration, calcium deposition in 4 cases each and hypertrophied mucosa were found in 3 cases. Luminal narrowing, loss of mucosa, duplication of mucosa and gangrene were found in one case each. Submucosal changes showed congestion in 33 cases, edema in 15, Fibrosis in 4,

Table 2: Correlational between age, weight and maturity of studied patients.

	Age (days)		Weight (Kg)	
Maturity	**Full term**	**Premature**	**Full term**	**Premature**
N	15	25	15	25
Minimum	2	1	2	1.7
Maximum	20	10	3.5	2.7
Mean	10.6	5.52	2.927	2.16
95% CI	6.337 to 12.921	3.844 to 6.111	2.659 to 3.153	2.041 to 2.268
Median	10	5	3	2.1
Variance	28.9714	6.6767	0.1821	0.075
SD	5.3825	2.5839	0.4267	0.275
25 - 75 P	7.250 to 15.0	3.000 to 8.0	2.550 to 3.150	2.000 to 2.425
Normal Distr.	0.0709	0.0902	0.0255	0.0623

Table 3: Correlational between maturity and gender of studied patients.

Maturity	Sex				Total	
	F		M			
	Number	%	Number	%	Number	%
Full term	2	5	13	32.5	15	37.5
Premature	4	10	21	52.5	25	62.5
Total	6	15	34	85	40	100
Chi-squared	0.051					
Significance level	P=0.8214					

Table 4: Distribution of studied cases based on clinical findings.

Clinical findings*		Number of patients	Percentage
Feeding pattern	Feeding	3	7.50%
	Not feeding	19	47.50%
	Feeding + vomiting	18	45.00%
Abdominal distension		40	100.00%
Bilious vomiting		35	87.50%
Not passing meconium		19	47.50%
Jaundice		25	62.50%

*clinical findings were overlapping

Table 5: Representing types of atresia based on gross findings.

Type of atresia		Number pf patients	Percentage
I		16	40.00%
II		2	5.00%
III	III A	8	20.00%
	III B	3	7.50%
IV		11	27.50%

thickened submucosa in 2 cases and dilated irregular branching blood vessels, extravasated blood, and calcification in 1 case each. Muscularis propria having changes i.e. thinning in 16 cases, congestion, hypertrophy in 4 cases each, focal loss in 3 cases, calcification in 2 cases and thinning in 2 cases. Similarly, histopathological changes in serosa shows serositisin 16 cases, congestion in 11 cases and thinning in 3 cases. Edema and congestion were present in 2 cases; hypertrophy and calcification in 1 case each (Figure 4).

Discussion

Intestinal atresias are one of the most common causes of intestinal

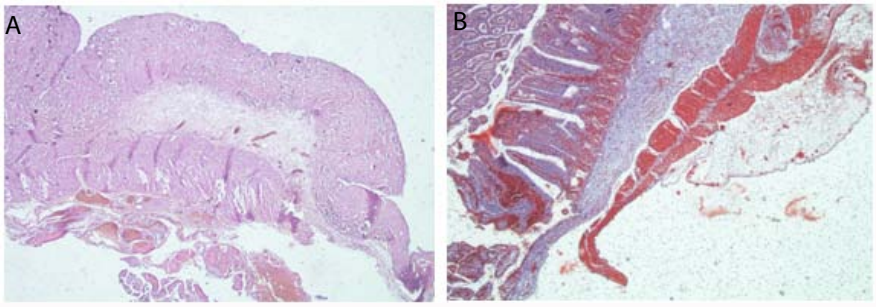

Figure 4: A) LS showing atrophy of muscular lining and replacement by fibrosis at the level of atresia and hypertrophy of muscle layers proximally. B) LS showing mucosal atrophy and loss of submucosa in the segment of gut just proximal to the atresia.

Table 6: Other associated findings on gross examination.

Gross findings*	Number pf patients	Percentage
Congestions	31	77.50%
Perforation	12	30.00%
Gangrene	3	7.50%
Meconium pseudocyst	1	2.50%
Pouching gut	1	2.50%
Duplication cyst	1	2.50%
Meconium cyst	1	2.50%

*findings were overlapping

obstruction in the neonate with an incidence of 1 in 5,000 new born [7]. In the present study of 40 neonatal intestinal obstructions, all were due to atresia. Duodenal atresia occurs in approximately 1 infant per 10,000 births, and represents up to 60 percent of small intestinal atresia [8]. In present study out of 40 cases of intestinal atresia, no case belongs to duodenal atresia. Small intestinal atresia accounts for majority of the cases while colonic atresia is quite rare according to Etensel et al [9]. In this study, also we found colonic atresia in 6 cases out of 40. Four types of intestinal atresia were recognized, type 1 (Septal atresia), type 2 (Fibrous cord joining atretic ends), type 3A (Atretic end separated by v shaped mesenteric defect), type 3B (Multiple atresia), type 4 (Apple-peel atresia). The most common type of atresia in this study is type I, which accounts for 59%.

The incidence of multiple atresias is said to be 15% by Davis et al. [10]. Similar study by Thomas V Santulli [11] on 76 cases and found multiple atresia in single case and said that incidence of multiple atresia given by Davis et al. [10], was probably higher. In our study also we found multiple atresias in 6 cases (15%). Various pathogenetic mechanisms have been proposed to explain the development of both duplication cysts and intestinal atresia. Favara et al. [12], and Sinha et al. [13], attributed the occurrence of atresia secondary to mesenteric volvulus as being initiated by the duplication cyst leading to vascular compromise of the involved intestinal segment. In our study also we found 2 cases of intestinal atresia where according to above mechanism that supports pathogenesis of atresia. One case was found to be associated with duplication cyst and the other 1 was with meconium pseudocyst.

Santulli and Blanc [11], study observed that there was presence of lanugo, squames and meconium distal to an atretic segment. Similar study done by Schultz and Lawrence [14] reviewed the perinatal deaths of 56 cases that showed gut ischemia of varying degrees of severity, and in 19 out of 56 cases concluded stenosis and atresia were sequela of previous gut ischemia. Thus we found out the presence of meconium distal to the atretic segment of intestine and thus explained ischemia as an etiological factor rather than failure of recanalization (Figure 3, 4). In the present study out of 40 cases, 36 cases have presence of meconium distal to atretic segment of intestine that suggested ischemia was causative factor.

Further, a phase of obliterative epithelial proliferation is not seen in the small bowel below the duodenum but Johnson [15] found that it was an explanation of stenosis/atresia of the small or large bowel were compromised leading to segmental absence of muscle in atresia cases. Thus, the histological changes observed in the Jejunoileal atresia is the most common cause of congenital intestinal atresia, and the most frequent cause of neonatal intestinal obstruction. In affected

Table 7: Histological features.

Mucosa (no. of cases)	Submucosa (no. of cases)	Muscularis propria (no. of cases)	Serosa (no. of cases)
Oedema, congestion & denudation (6)	Edema(15)	Congestion (4)	Edema & Congestion (2)
Ulceration + flattening of mucosa (9)	Congestion (33)	Thickening (2)	Congestion (11)
Flattening of mucosa (6)			
Abnormal villus configuration (4)	Dilated irregular branching vascular channels (1)	Thinning (16)	Serositis (16)
Gangrene (1)	Extravasated blood (1)	Focal loss (3)	
Hypertrophied mucosa (3)		Hypertrophied (4)	Thinning (3)
Luminal narrowing (1)	Fibrosis (4)		Hypertrophied (1)
Duplication of mucosa (1)			
Calcium deposition (4)	Calcification (1)	Calcification (2)	Focal calcification (1)
Loss of mucosa (1)	Thickened (2)		
Extravasated blood 6			

patients, there was no known gender skewing in the incidence, but when compared with Dizygotic twins and singletons, monozygotic twins are reportedly at a higher risk. In our study we also found that jejunal and ileal atresia are the commonest type, but dominance of male neonates occurred. This study revealed that in neonates with small bowel atresia, the musculature of the bowel wall up to 2 cm away from atretic segment were found to show some histology consistent with atretic changes and ganglions were present. Therefore, adequate resection seems to be mandatory for the prevention of post-operative dysmotility.

Hamdy et al. [16] reported that in the dilated bowel at 2 cm proximal to the atresia, the inter muscular ganglion was smaller and less in number and muscle layers were thinner on the antimesenteric side when compared to those on the mesenteric side in control specimens. In our study, the ganglion cells were normal both on the mesenteric and antimesenteric sides at 2 cm away from the atresia. Muscle layers were irregular with segmental muscular hypertrophy.

Conclusion

In this study spectrum of histomorphological changes in the atretic segment has been described. Histological changes seen the mucosa were flattening of villi, abnormal villous configuration, ulceration, denudation, gangrene, hypertrophy, luminal narrowing, calcium deposition and extravasated blood. Submucosal changes were edema, congestion, dilated irregular branching vascular channel, extravasated blood and fibrosis in the atretic segment. Muscularis propria congestion, thickening, thinning, focal loss, hypertrophy and calcification were seen. Muscle fibrosis was present in few sections. Ganglion cells were present in all sections. All layers were normal in the control specimens.

Histomorphological changes at atretic segment can be valuable to surgeons in deciding the type of surgery and minimizing the postoperative intestinal dysmotility which remains the most common complication of intestinal atresia. This study has limitation due to small sample size and could not contribute in establishing predetermined limit of resected bowel for histomorphological analysis. A large and adequate sample size is required for this.

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