Original Article

Spectrum of esophagitis in children with cerebral palsy - A clinical, endoscopic, and histopathological correlation

Manjari Tiwari[1], Shrish Bhatnagar[1], Savitri Thakur[1], Nishi Tandon[2]

From [1]Department of Paediatrics, [2]Pathology, Eras Lucknow Medical College and Hospital, Lucknow, Uttar Pradesh, India

Correspondence to: Dr. Shrish Bhatnagar, Department of Paediatrics, Eras Lucknow Medical College and Hospital, Lucknow, Uttar Pradesh, India. Phone: +91-9918208555. E-mail: drshrishbhatnagar@gmail.com

Received - 24 January 2018 Initial Review - 26 February 2018 Published Online - 11 May 2018

ABSTRACT

Background: Gastrointestinal disease is frequent in children with severe neurological impairment and developmental disability. Dysphagia may worsen due to concurrent gastroesophageal reflux disease (GERD) and non-GERD esophagitis in children. **Objective:** The aim of our study was to study the spectrum of causes of esophagitis in cerebral palsy (CP) children with feeding difficulty. **Methods:** Children of CP with feeding difficulties in the age group of 1–18 years were included after written consent. Dysphagia in these children was categorized according to the dysphagia disorder survey (DDS) score. Children who were unfit for endoscopy or having profound dysphagia were excluded from the study. UGI endoscopy and histopathological evaluation of esophagus was done in all the children. **Results:** Children of CP had a mean DDS score of 4.02±2.50. Endoscopic evidence of esophagitis was seen in 22 children (24.4%). Histological evidence was seen in 15 children; out of them, 11 had GERD-related esophagitis and 2 each had eosinophilic and fungal esophagitis. The mean DDS score and weight significantly improved in children with GERD after they were given specific treatment. **Conclusion:** Esophagitis whether GERD or non-GERD is an important and treatable cause of dysphagia in children with CP. Effort should be made to recognize and treat these causes for effective nutritional rehabilitation of this subset of children.

Key words: *Cerebral palsy, Dysphagia, Esophagitis*

Cerebral palsy (CP) describes a group of permanent disorders of the development of movement and posture causing activity limitation that are attributed to non-progressive disturbances that occurred in the developing infant or fetal brain. The motor disorders of CP are often accompanied by disturbances of sensation, perception, cognition, communication, and behavior by epilepsy and by secondary musculoskeletal problems. Gastrointestinal disease is frequent in children with severe neurological impairment and developmental disability [1,2].

Dysphagia in children with CP is characterized by deficiencies in oral, oropharyngeal, and esophageal phases of swallowing; dysphagia can be assessed by many scores; out of them, dysphagia disorder survey (DDS) score is one [3]. It can be caused by oromotor dysfunction, anatomical anomalies (e.g., cleft palate), abnormal neurological maturation, oral sensory impairment, or esophageal motility disorders and may worsen due to concurrent gastroesophageal reflux disease (GERD) and non-GERD esophagitis [4-7]. So as to ascertain the spectrum of esophagitis in children with CP, a clinical, endoscopic, and histopathological correlation was done in these patients.

METHODS

The present study was carried out at the department of pediatrics and neonatology at a referral hospital in Lucknow between January 2016 and July 2017 for a period of 18 months. Estimating an 80% power of study and 10% loss to follow the sample size was calculated to be 90. Ethical clearance was taken from the institutional ethical committee and written consent was taken from the parents before recruitment. Children diagnosed with CP having feeding difficulties in the age group of 1–18 years were included in the study. Most of the children are in follow-up in pediatric neurology clinic at our hospital.

Dysphagia in these children was categorized according to the DDS score into no, mild, moderate-to-severe, and profound category by the principal investigator of the study as shown in Table 1 [3].

Children who were unfit for endoscopy or having profound dysphagia were excluded from the study. Upper gastrointestinal (UGI) endoscopy was done by a trained pediatric gastroenterologist using OLYMPUS GIF 150 series endoscope to look for the signs of the esophagitis in all the patients. The Los Angeles (LA) classification was used for grading the esophagitis on UGI endoscopy which uses a four-grade system (Table 2) [8]:

Histopathological evaluation for GERD and non-GERD causes of esophagitis was done in all cases. The biopsy specimen obtained after endoscopy were sectioned. The sectioned tissues were stained with hematoxylin for 15 min followed by differentiation 1.1% HCl and NH_3 solution for 2 min. They were then washed with water. Sections were then dehydrated in ascending series

of alcohol reaching up to 90% alcohol (2–3 min in each grade). Sections were then stained with eosin for 1 min and differentiated in 90% alcohol. Subsequently, they were dehydrated in absolute alcohol for 2–3 min. They were then viewed under microscope.

Tissue changes reflective of esophagitis were looked for the presence of fungal hyphae, and cellular pattern was studied. On the basis of histopathological evaluation, the outcome was graded as:

1. No esophagitis
2. Esophagitis: Characterized by increased basal layer thickening, elongated papillae, and mild inflammation with occasional eosinophils
3. Eosinophilic esophagitis: It has basal cell hyperplasia and elongated papillae but contains a marked increase in intraepithelial eosinophils
4. Fungal esophagitis: Characterized by the presence of Candida hyphae within squamous mucosa.

The treatment for esophagitis, if present, was given to these patients as per the standard protocol apart from the routine nutritional and neuromuscular rehabilitation. For GERD, lansoprazole (1.4 mg/kg/day) single dose was given for 12 weeks and then it was tapered over 2–3 months as rebound hyperacidity is known after sudden stoppage of proton-pump inhibitors. For fungal esophagitis, fluconazole at 6 mk/kg for 2 weeks was given while eosinophilic esophagitis was treated with fluticasone 440–880 µg per day for 6–8 weeks as mental developmental index along with lansoprazole (1.4 mg/kg/day) single daily dose. After 3 months, these patients were reviewed clinically and evaluated for the improvement in dysphagia symptoms and DDS score.

The statistical analysis was done using the Statistical Package for the Social Sciences version 21.0 Software. The values were represented in number (%) and mean±SD.

Table 1: Classification of dysphagia

Severity levels	Criteria
No dysphagia	Score of 0 on DDS Part 2
Mild dysphagia[a]	Score of>0 on DDS Part 2 Score of 0 on DDS Part 2 items "oral-pharyngeal swallow" and "post-swallow signs"
Moderate-to-severe dysphagia[b]	Score of>0 on DDS Part 2 Score of>0 on DDS Part 2 items "oral-pharyngeal swallow" and "post-swallow signs"
Profound dysphagia[c]	Nil by mouth

[a]Signs of dysphagia are present; however, pharyngeal phase problems are not suspected. [b]Pharyngeal phase problems are highly suspected. [c]Children in this category were not observed during mealtime; however, due to their exclusively non-oral diet, the presence of severe dysphagia with high risk of aspiration is presumed. DDS: Dysphagia disorder survey

Table 2: The Los Angeles classification for grading the esophagitis on UGI endoscopy

Type	Description
A	One (or more) mucosal break 5 mm or less that does not extend between the tops of two mucosal folds
B	One (or more) mucosal break more than 5 mm long that does not extend between the tops of two mucosal folds
C	One (or more) mucosal break that is continuous between the tops of two or more mucosal folds but that involves<75% of the circumference
D	One (or more) mucosal break that involves at least 75% of the esophageal circumference

The subjective interpretation of the scale was done as follows: Normal - no esophagitis, Grade A and B - mild esophagitis, and Grade C and D - severe esophagitis. UGI: Upper gastrointestinal

RESULTS

A total of 115 patients of CP with feeding difficulty were enrolled. 25 participants were excluded either due to lack of consent or being unfit (*n*=15) for endoscopy or had profound dysphagia (*n*=5) on DDS score. Therefore, total 90 patients were included in the study. The mean age was 3.5±1.83 years. Total 52 (57.8%) children were male. 80% of the children had severe stunting and 90% had severe wasting according to the WHO classification. 75% of the children had mild dysphagia and 15% had moderate-to-severe dysphagia. Mean DDS score was 4.02±2.50 (2–10).

On UGI endoscopy, changes suggestive of esophagitis according to the LA classification were seen in 22 patients (24.4%) and rest 68 (75.6%) were normal. Out of these 22 children, 10 (11.1%) had Grade A esophagitis, 10 (11.1%) had Grade B/C esophagitis, and 2 (2.2%) had Grade D esophagitis (Figs. 1-4). The histopathological assessment of 90 patients is given in Table 3. Seven patients who had evidence of Grade A esophagitis did not show any histological evidence of esophagitis (Figs. 5-7).

These 22 children were given treatment as per protocol for GERD; fungal and eosinophilic esophagitis defined earlier and was reviewed after 3 months. On follow-up of 3 months, the mean DDS score showed a significant improvement in children given specific therapy (Table 4).

Further evaluation of mean DDS score in children in respect to histopathological diagnosis was done. It was seen that in GERD-related esophagitis and eosinophilic esophagitis, there

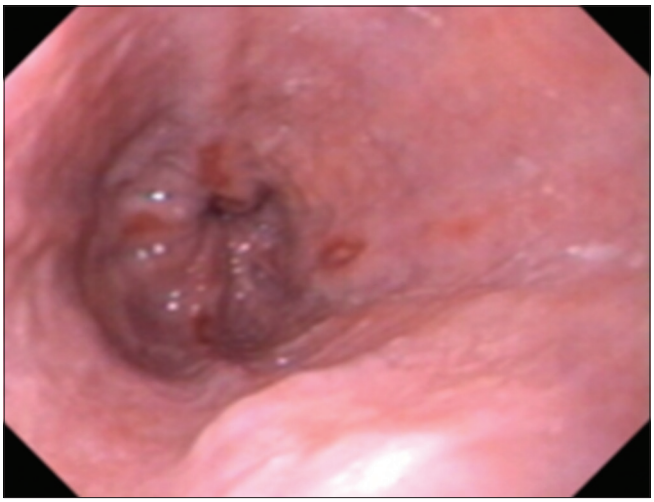

Figure 1: Los Angeles Grade A showing several erosions limited to the mucosal folds and no larger than 5 mm in extent

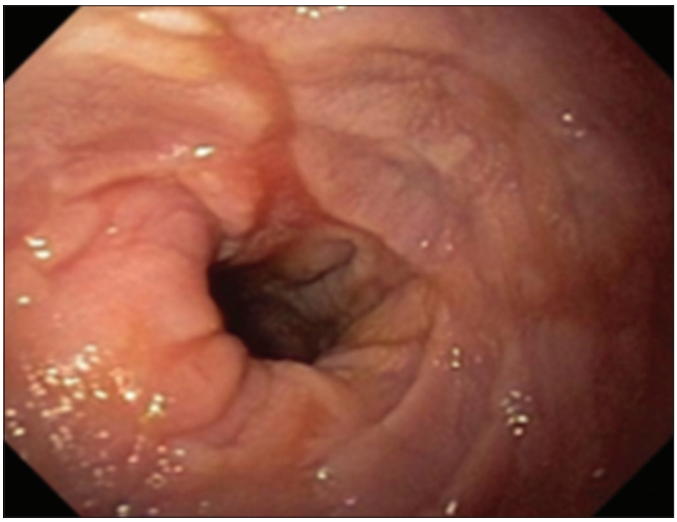

Figure 2: Los Angeles Grade B showing several erosions limited to the mucosal fold(s) and larger than 5 mm in extent

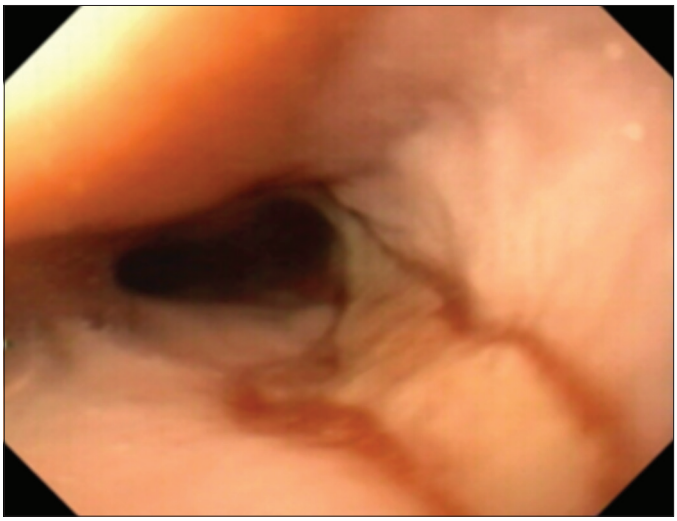

Figure 3: Los Angeles Grade C showing erosions extending over mucosal folds but over less than three-quarters of the circumference

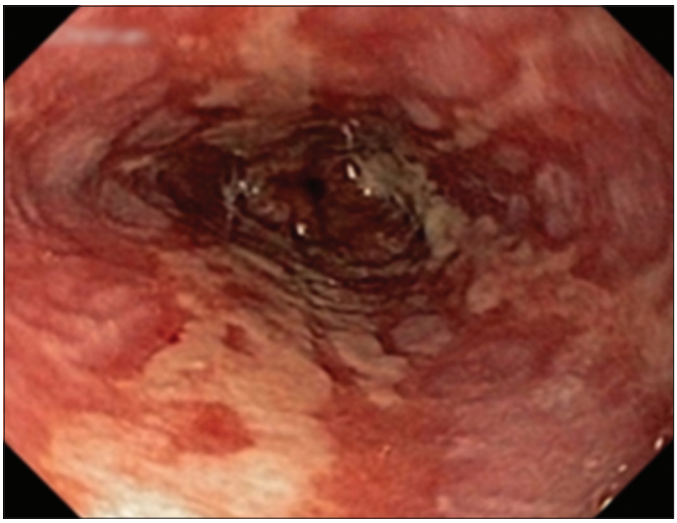

Figure 4: Los Angeles Grade D showing confluent erosions extending over more than three-quarters of the circumference

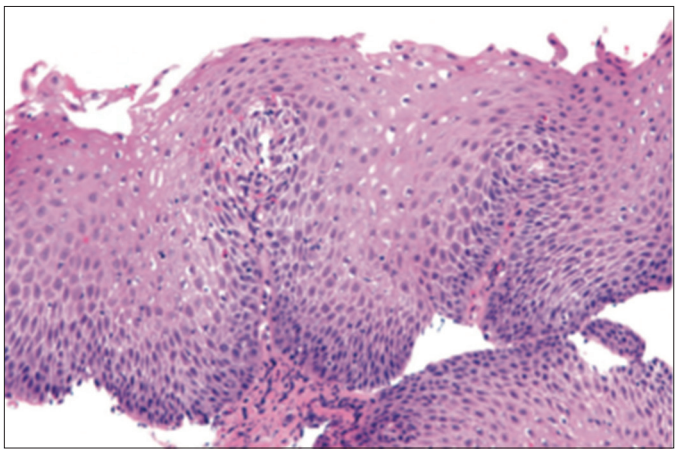

Figure 5: Gastroesophageal reflux disease esophagitis characterized by increased basal layer thickening, elongated papillae, and mild inflammation with occasional eosinophils

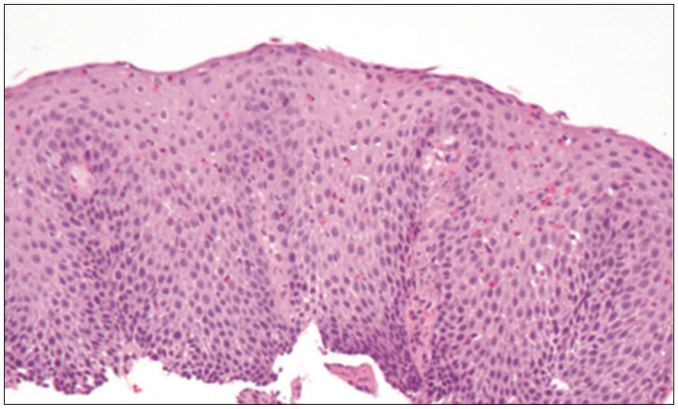

Figure 6: Eosinophilic esophagitisalso has basal cell hyperplasia and elongated papillae but contains a marked increase in intraepithelial eosinophils

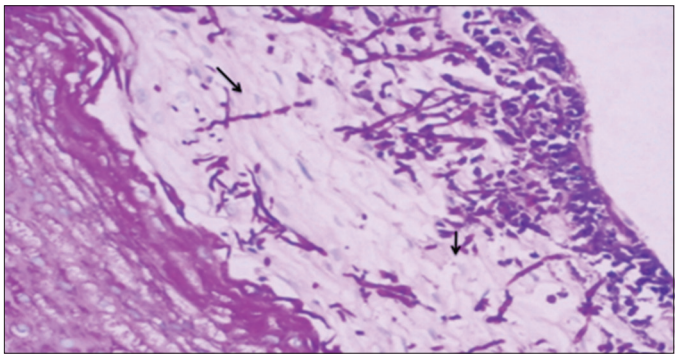

Figure 7: Candida esophagitis - candida hyphae (arrow) are present within squamous mucosa

was a significant improvement in DDS score on follow-up but not in cases of fungal esophagitis (Table 5).

On follow-up of 3 months, there was a significant weight gain in children with GERD-related esophagitis (Table 6).

DISCUSSION

Different gastrointestinal problems are present in a child with CP. Delay in growth and malnutrition is common and the sequels

of malnutrition are important to recognize. As a result of that, endurance or ability of a child can be affected. Children with CP commonly have feeding disorders and swallowing problems (dysphagia) that in many instances place them at risk for aspiration with oral feeding, with potential pulmonary consequences [1]. They also commonly have reduced nutrition/hydration status and prolonged stressful meal times. Dysphagia can be classified into four categories, based on the location of the swallowing impairment: oropharyngeal, esophageal, esophagogastric, and paraesophageal [2].

Calis *et al.* assessed the clinical indicators and severity of dysphagia in a representative sample of children with severe generalized CP and intellectual disability [9]. A total of 166 children (85 males, 81 females) with Gross Motor Function Classification System Level IV or V and IQ <55 were recruited from 54 day-care centers. Mean age was 9 years 4 months (range: 2 years 1 month-19 years 1 month). Clinically apparent presence and severity of dysphagia were assessed with a standardized mealtime observation, DDS, and dysphagia severity scale. Additional measures were a parental report on feeding problems and mealtime duration. Of all 166 participating children, 1% had no dysphagia, 8% mild dysphagia, 76% moderate-to-severe dysphagia, and 15% profound dysphagia (receiving nil by mouth), resulting in a prevalence of dysphagia of 99%.

Benfer *et al.* conducted a study on 130 children with CP having a mean age of 27.4 months [10]. 84.6% of CP children had pharyngeal dysphagia using the DDS schedule. In our study, the mean age of children was 3.5±1.83 years. 75% of children had mild dysphagia and 15% had moderate-to-severe dysphagia with a mean DDS score of 4.02±2.50 (2–10). The reason for this variation in age and grade of dysphagia could be that ours and Benfer *et al.* were hospital-based studies where children come at an earlier age for evaluation and treatment as compared to day-care center where children of all age group and advanced disease are living.

Gastroesophageal reflux in children with CP is a very well-known entity. Many studies have implicated it with feeding difficulties in these children [4-6]. Our study is the first study which has demonstrated the histopathological evidence of GERD. 11/22 (50%) patients who had esophagitis on endoscopic evaluation had histopathological evidence of GERD. On follow-up after treatment for GERD, there was a significant improvement in DDS score and weight of children.

Esophageal eosinophilia in children with CP has been a rarely diagnosed entity. A study by Napolis *et al.* showed that 7/131 patients had eosinophilic esophagitis [7]. These children mainly presented with vomiting and dysphagia. In our study, 2/90 children had evidence of eosinophilic esophagitis. On treatment, there was a significant reduction in mean DDS score from 5±1.41 to 1±1.41 in our children.

Our study is perhaps the first study of its kind which has evaluated all children of CP with feeding difficulty both by UGI endoscopy and histopathological examination for the presence of esophagitis. Our study has shown that these children suffer from esophagitis, and by giving treatment for the specific causes of esophagitis, there is an improvement in both dysphagia and nutritional status of children. However, there are certain limitations in our study. First is that we have only evaluated the esophagitis aspect of dysphagia in detail and not the neuromuscular dysfunction these children suffer. During management phase, we gave specific treatment

Table 3: The histopathological assessment of enrolled children with CP

Finding	Number of cases (%)
Normal	75 (83.3)
Eosinophilic	2 (2.2)
Fungal	2 (2.2)
GERD-related esophagitis	11 (12.2)

CP: Cerebral palsy, GERD: Gastroesophageal reflux disease

Table 4: Change in dysphagia disability scores after 3 months (*n*=22)

Variable	At enrolment	At follow-up
Range	2–10	0–8
Mean±SD	6.43±2.09	1.83±1.99
Mean change (±SD)	4.61±1.64	

t=13.44; *P*<0.001 Paired t-test. SD: Standard deviation

Table 5: Change in DDS scores on follow-up in different etiologies

Diagnosis	Mean±SD			Significance of change (Paired t-test)	
	DDS at enrolment	DDS at follow-up	Change	t	p
GERD related (n=11)	7.09±2.26	1.82±1.66	−5.27±1.01	17.33	<0.001
EE (n=2)	5.00±1.41	1.00±1.41	−5.00±1.41	5.00	<0.001
FE* (n=2)	6.00±0.00	1.00±1.41	−4.00	-	-

*Test of significance could not be employed owing to the same SDs on both occasions. DDS: Dysphagia disorder survey, GERD: Gastroesophageal reflux disease

Table 6: Change in mean weight in different etiologies

Diagnosis	Mean±SD			Significance of change (Paired t-test)	
	Weight at enrolment (kg)	Weight at follow-up (kg)	Change	t	p
GERD related (n=11)	10.62±6.66	10.90±6.63	0.28±0.08	12.45	<0.001
EE (n=2)	8.50±1.41	8.75±1.34	0.25±0.07	5.00	0.126
FE* (n=2)	9.60±2.26	9.85±2.33	0.25±0.07	5.00	0.126

GERD: Gastroesophageal reflux disease, SD: Standard deviation. *P*=0.126,NS

to children with esophagitis and only standard nutritional and feeding advice children with feeding difficulties without evidence of esophagitis. Our management lacked robust nutritional and neuromuscular rehabilitation due to the lack of infrastructure. We also did not have long-term follow-up of these children with feeding difficulties regarding the persistence of improvement in condition of the children. Hence, we recommend that long-term multicentric study with a large sample size is conducted which covers all the limitation in our study.

CONCLUSION

Feeding difficulty in children with CP is an important cause of malnutrition in these children. Esophagitis whether GERD or non-GERD is an important and treatable cause of dysphagia. Effort should be made to recognize and treat these causes for effective nutritional rehabilitation of this subset of children.

REFERENCES

1. Arvedson JC. Feeding children with cerebral palsy and swallowing difficulties. Eur J Clin Nutr 2013;67:S9-12.
2. Wolf DC. Dysphagia. In: Walker HK, Hall WD, Hurst JW, editors. Clinical Methods: The History, Physical, and Laboratory Examinations. 3rd ed. Ch. 82. Boston: Butterworths; 1990.
3. Sheppard JJ. In: Veugelers R, Penning C, editors. Dysphagia Disorders Survey and Dysphagia Management Staging Scale, Users Manual and Test Forms revised. Netherlands edition Lake Hopatcong, NJ: Nutritional Management Associates; 2002.
4. Reyes AL, Cash AJ, Green SH, Booth IW. Gastroesophgeal reflux disease in children with cerebral palsy. Child Care Health Dev 1993;19:109-18.
5. Bozkurt M, Tutuncuoglu S, Serdaroglu G, Tekgul H, Aydogdu S. Gastroesophageal reflux disease in children with cerebral palsy: Efficacy of cisapride. J Child Neurol 2004;19:973-6.
6. Gangil A, Patwari AK, Aneja S, Ahuja B, Anand VK. Feeding problems in children with cerebral palsy. Indian Pediatr 2001;38:839-46.
7. Napolis A, Alves F, Rezende E, Segundo G. Esophageal eosinophilia in pediatric patients with cerebral palsy Einstein(Sao Paulo) 2015;13:232-7.
8. Lundell LR, Dent J, Bennett JR, Blum AL, Armstrong D, Galmiche JP, *et al.* Endoscopic assessment of esophagitis: clinical and functional correlates and further validation of Los Angeles Classification. Gut 1999;45:172-80.
9. Calis EA, Veugelers R, Sheppard JJ, Tibboel D, Evenhuis HM, Penning C. Dysphagia in children with severe generalized cerebral palsy and intellectual disability. Dev Med Child Neurol 2008;50:625-30.
10. Benfer KA, Weir KA, Bell KL, Ware RS, Davies PS, Boyd RN. Validity and reproducibility of measures of or pharyngeal dysphagia in preschool children with cerebral palsy. Dev Med Child Neurol 2015;57:358-65.

Funding: None; Conflict of Interest: None Stated.

How to cite this article: Tiwari M, Bhatnagar S, Thakur S, Tandon N. Spectrum of esophagitis in children with cerebral palsy - A clinical, endoscopic, and histopathological correlation. Indian J Child Health. 2018; 5(4):244-248.