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ORIGINAL ARTICLE

Gastroenterology

Analysis of multichannel intraluminal impedance and pH monitoring values in children with cerebral palsy: A comparative multicenter study

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Abstract

Objectives: To compare the features of multichannel intraluminal impedance and pH monitoring (MII-pH) tracings in children with cerebral palsy (CP) and children without CP.

Methods: Multicenter, retrospective, analytical study. We examined tracings of children aged 1 to 15 years old, evaluated from May 2017 to January 2024. Population included two groups: Group 1 consisted of children with CP, while control group comprised children without CP who had extra-digestive symptoms suggestive of gastroesophageal reflux disease (GERD) but normal MII-pH results. Quantitative data were analyzed using analysis of variance and *t* tests. Qualitative data were analyzed using contingency tables and chi-square tests.

Results: We studied 245 children. CP group included 110 children with a mean age of 5.71 years (standard deviation [SD] ± 4.24), while control group included 135 children with a mean age of 5.73 years (SD ± 3.39). The CP group had fewer reflux episodes ($p = 0.0015$), slower mean acid clearance time ($p = 0.04$), lower mean baseline impedance and mean nocturnal baseline impedance ($p = 1.82e{-}07$ and $p = 7.50e{-}07$).

Conclusion: Children with CP have fewer reflux episodes and longer acid clearance times compared with children without CP. Prospective studies including esophagogastroduodenoscopy findings are needed to establish MII-pH reference values in children with CP.

KEYWORDS

acid reflux, gastroesophageal reflux disease (GERD), pediatrics, symptoms

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1 | INTRODUCTION

Up to 70% of patients with cerebral palsy (CP) were found to have gastroesophageal reflux disease (GERD).[1–3] Risk factors include chronic supine positioning, abnormal posture and increased intra-abdominal pressure resulting from spasticity and seizures.[1–3] The European Society for Pediatric Gastroenterology, Hepatology and Nutrition guidelines recommend the use of multichannel intraluminal impedance and pH monitoring (MII-pH) to diagnose GERD in children with CP.[1,2,4,5] Baseline impedance measurement is a useful tool for predicting esophagitis in both adults and children.[6–8] In pediatrics, a cutoff of 900 Ω has been established as a threshold correlated with esophagitis.[9] However, reference values for MII-pH in pediatrics remain controversial, as few studies have validated these standards in children, and those available were not conducted in entirely healthy individuals due to ethical concerns.[5,10,11] Moreover, research on MII-pH and baseline impedance values in populations at risk of GERD such as children with CP is even more limited, and reference values specific to this population have yet to be defined.[12–15] The aim of this study is to assess the mean baseline impedance (MBI) and mean nocturnal baseline impedance (MNBI) of children with CP.

What is Known

- Diagnosing gastroesophageal reflux disease (GERD) in children with cerebral palsy (CP) is challenging.
- Multichannel intraluminal impedance and pH monitoring (MII-pH) is the gold standard for diagnosing GERD although reference values in children remain controversial.
- Esophageal baseline impedance may help predict esophagitis, thought its role in children with CP is uncertain.

What is New

- MII-pH values differ in children with CP compared to those without neurological impairment.
- Children with CP experienced fewer reflux events, longer acidic clearance times and had lower mean nocturnal baseline impedance (MNBI); however, the baseline impedance values remain above the established cut-off points for esophagitis.

2 | METHODS

2.1 | Study population

A multicenter, retrospective, analytical study was conducted from May 2017 to January 2024. We evaluated tracings from children aged 1–15 years, performed by members of the Latin American Society of Pediatric Gastroenterology, Hepatology and Nutrition (LASPGHAN) Motility Working Group across health centers in Latin America and Spain.

The study population was divided into two groups. Group 1 included children with CP who were nonverbal or minimally verbal, whose studies were carried out before performing gastrostomy for feeding. Control group included children without CP with extradigestive symptoms of GERD, such as chronic cough, recurrent chronic laryngitis, and dysphonia, who underwent MII-pH and had normal acid exposure, no symptomatic correlation with reflux episodes and normal impedance according to Mousa et al. reference values.[10]

Children under 1 year of age, patients with esophageal atresia, abnormal esophagrams, a history of Nissen surgery, corrected or uncorrected diaphragmatic hernia, those receiving antacids or prokinetics treatment during the study, and studies lasting less than 18 h were excluded.

2.1.1 | MII-pH methodology

All patients underwent 24-h MII-pH following the same protocol. Before the study, proton pump inhibitors were discontinued at least 7 days before the study, and prokinetics and H2 antagonists were stopped 48 h prior. Age-appropriate catheters were used. The catheters were calibrated in buffer solutions at pH 4 and 7 before placement. The catheter was placed through the nares and advanced posteriorly, with the tip positioned at the second vertebral body above the diaphragm. The Strobel formula was used to determine the approximate length.[16] Position was confirmed with chest X-ray. After connecting the

catheter to the external impedance equipment, parents received instructions on its use and were provided with an event recording sheet to document any symptoms that they were unable to record directly on the device. All tracings were automatically evaluated in BioVIEW software and then analyzed manually. MBI was measured using the software's ruler tool. MNBI was calculated by averaging 3 stable 10-min measurements of the sleep period without swallowing or reflux. These measurements were taken on channels 5 and 6 and averaged.

2.1.1.1 | *Statistical analyses*

Exploratory analyses were conducted using hierarchical clustering with Euclidean distance. Data points beyond three standard deviations (SDs) from the mean were classified as outliers and excluded.[17] Quantitative variables were described by their mean ± SD and analyzed using analysis of variance and *t* tests. Qualitative variables were presented in contingency tables and assessed with the chi-square test. All analyses and visualizations were performed using the R statistical package. The *p* value was considered significant if it was less than 0.05.

2.1.1.1.1 | *Ethics statement.*

The study had the approval of the research ethics committee of Alejandro Posadas National Hospital of Argentina. The project adheres to the guidelines of the Helsinki Declaration, the CIOMS guidelines (2016), and the resolution of the Ministry of Health of the Nation number 1480/11. Registration code of this project for the CEIHP, ref 878 EMiP0S0/24. Written informed consent was obtained from all their caregivers before participation in the study.

3 | RESULTS

The study involved 11 centers from four countries and was done by members of the LASPGHAN Motility Working Group (Supporting Information S1: Table 1).

A total of 245 patients were included (119 males and 126 females), of which 110 patients had CP and 135 did not. There were no significant differences in gender ($p = 0.96$) or age ($p = 0.59$) between the CP and control groups (Table 1).

Seven participants (6.3%) in the CP group were classified under category IV, while the remaining 93.7% fell under category V of the Gross Motor Function Classification System (GMFCS).[18] All were either nonverbal or minimally verbal. Among them, 92% had spastic CP and 8% had mixed CP, with four participants diagnosed with diplegia and the rest with quadriplegia. Among them, 81 participants (73%) used a nasogastric tube for feeding during the MII-pH procedure.

TABLE 1 Summary of baseline characteristics of the study population.

	CP patients ($n = 110$)	Controls ($n = 135$)	Statistical test (p value)
Sex	56 males 54 females	63 males 72 females	$X(1) = 0.28$, $p = 0.59$
Age	Mean = 5.71 SD = 4.24	Mean = 5.73 SD = 3.39	t-welch (206) = 0.03, $p = 0.96$
Age groups (years)			$X(2) = 3.32$, $p = 0.18$
0–5	54	55	
>5–10	34	57	
>10–15	22	23	

Abbreviations: CP, cerebral palsy; SD, standard deviation.

The total number of reflux episodes in the CP group had a mean of 25.63, and this was significantly lower compared to the control group ($p = 0.0015$) (Table 2).

The number of acidic GER episodes had a mean of 13.3 in the CP group. This was significantly lower than control group ($p = 1.558e{-}05$) (Figure 1).

The number of proximal GER episodes had a mean of 9.91 in the CP group. The number of episodes that reached the upper channels was significantly higher in the control group ($p = 5.439e{-}05$) (Table 2).

he mean acid clearance time was 103.29 s (42–138) in the CP group and 78.95 s (34.5–110) in the control group. These differences were statistically significant ($p = 0.04$) (Table 2). The mean reflux index (±SD) was 1.6 ± 1.39 in the CP group and 1.53 ± 1.44 in the control group, with no statistically significant difference ($p = 0.91$).

In the CP group, the MBI and MNBI had different values and ranges. The mean values were 2052.12 (1605–2408) and 2194 (1700–2634), respectively (Table 2).

Significant differences were observed when comparing the groups in terms of MBI and MNBI, both of which were lower in the CP group ($p = 1.816e{-}07$ and $p = 7.497e{-}07$, respectively) (Figure 2).

4 | DISCUSSION

GERD is a common complication of CP.[2] However, the diagnosis is challenging, and there are few studies with MII-pH reference values in this population. Our study shows significant differences in the main variables assessed by MII-pH between the group of patients with CP and the control group. We observed a significantly lower number of GER episodes in patients with CP. Aligning with Plocek et al.,[12] who also reported fewer

TABLE 2 Distribution of reflux episodes and their associated characteristics in patients with CP and controls.

	CP group X̄ (q1–q3)	Control group X̄ (q1–q3)	Statistical test
GER total	25.63 (15–34.75)	31.9 (20–43)	$t(242) = 3.21$, $p = 0.0015$
NAGER total	12.49 (5–19)	12.57 (5–17)	$w = 7302$, $p = 0.82$
AGER total	13.3 (5–20)	19.58 (3–26.5)	$w = 9689$, $p = 4.03e{-}05$
Proximal GER	9.91 (3–12)	15.37 (6–22.5)	$w = 9939$, $p = 4.95e{-}06$
Acidic clearance time	103.29 (42–138)	78.95 (34.5–110)	$w = 6221$, $p = 0.04$
MBI	2052.12 (1605–2480)	2590.43 (2147.5–3057.5)	$t(229) = 5.38$, $p = 1.82e{-}07$
MNBI	2194 (1700–2634)	2755.3 (2192–3235.5)	$t(233) = 5.09$, $p = 7.5e{-}07$

Abbreviations: AGER, acidic gastroesophageal reflux; CP, cerebral palsy; GER, gastroesophageal reflux; MBI, mean baseline; MNBI, nocturnal mean baseline; NAGER, nonacidic gastroesophageal reflux.

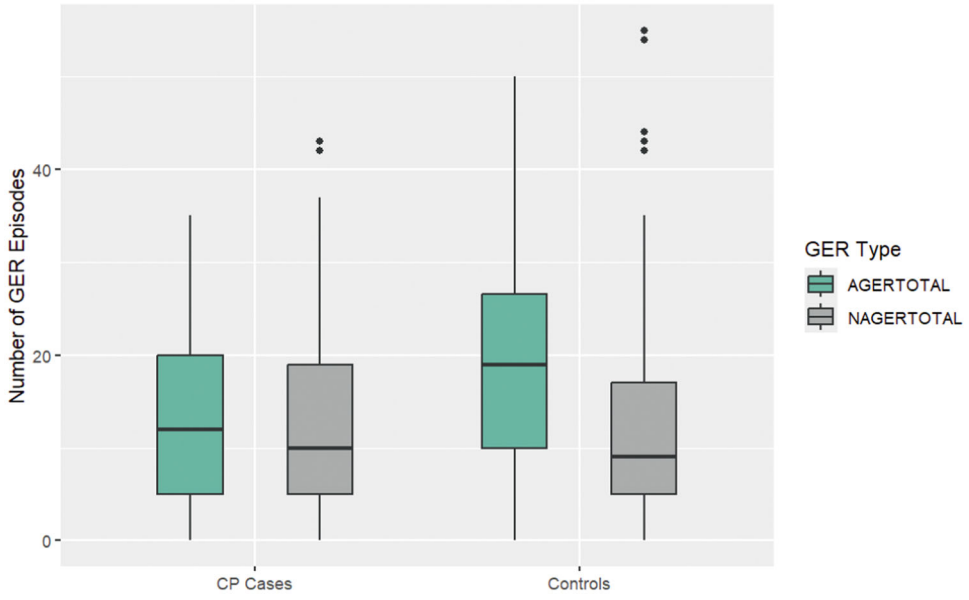

FIGURE 1 Box plot of the number of gastroesophageal reflux episodes according to acidity in patients with CP and controls. AGER, acidic gastroesophageal reflux; CP, cerebral palsy; GER, gastroesophageal reflux; NAGER nonacidic gastroesophageal reflux.

episodes compared to the general population. Interestingly, despite 73% of our CP patients being fed via nasogastric tube, we found fewer GER episodes, which contrasts with the findings of Del Buono et al.,[13] linking tube feeding to a higher number of episodes. On the other hand, our findings regarding the predominant type of reflux are consistent with those of the same study, with a predominance of nonacid reflux in children with CP.

The mean acid clearance time was prolonged and may be attributed to the esophageal dysfunction documented in CP patients. This dysfunction may result from increased transient lower esophageal sphincter relaxations or ineffective esophageal motility.[3,19,20] Simrem[21] linked severe dysmotility to slower acid clearance. In our study, we also observed statistically significantly slower acid clearance in the CP group. However, the scope of our study was limited and does not allow establishing the nature of the pathophysiological mechanisms as we did not evaluate esophageal motility. Further research is needed to correlate acid clearance time with esophageal motor disorders in children with CP.

MBI and MNBI values exhibited lower ranges and significantly lower values in the CP group. However, even the lowest values in this group did not exceed the 900-Ω thresholds associated with esophagitis in Cohen's study or the values reported by Fukahori et al.[14]

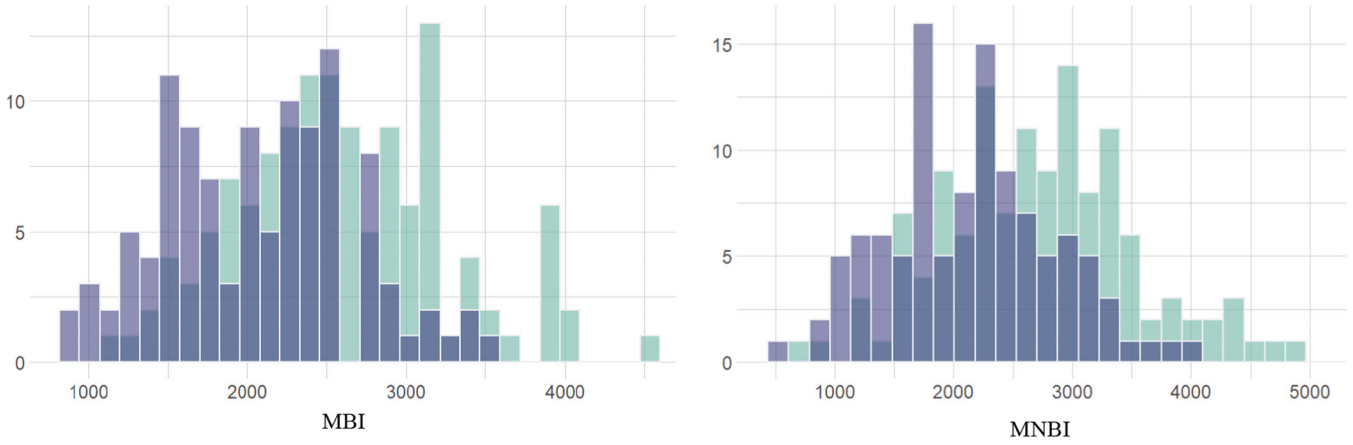

FIGURE 2 Distribution of mean baseline pH-impedance in cases and controls. The left histogram shows the mean baseline measurements for 24 h, while the right graph shows the nocturnal MBI measurements. Blue bars correspond to CP patients and light green to controls. CP, cerebral palsy; MBI, mean baseline; MNBI, nocturnal mean baseline.

Given the absence of endoscopic findings, our analysis cannot establish specific thresholds to correlate with esophagitis.[11,14,15]

This study represents the largest cohort of children with CP analyzed to date. The results of our study add valuable information to build on the data of previous smaller studies with less statistical power. The limitations of our study include its retrospective design and the sample size. Our results apply specifically to children with CP classified as GMFCS IV and V and do not allow to generalize to all children with CP. The absence of endoscopy does not allow to rule out that a subset of patients could have had eosinophilic esophagitis. Similarly, the presence of rumination was not an exclusion criterion for our study. The inclusion of patients from multiple institutions introduces variability in healthcare practices, making direct comparisons between groups more challenging. However, all the institutions used similar protocols, and those were verified for fidelity.

5 | CONCLUSION

Children with CP exhibited a longer acid clearance time, fewer reflux episodes, and lower MNBI compared to the control group. They also had significantly lower baseline pH values, though still within normal reference ranges.

Future research with a larger patient cohort, integrating symptom correlation with reflux episodes and endoscopic findings, could support the development of a symptom-based scoring system. This approach could help define baseline cutoff values, improve the identification of patients at risk for esophagitis, and guide the need for endoscopy. Moreover, establishing normal reference values in children with CP is essential, as our findings indicate significant differences from the general pediatric population.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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