

## II. PEDIATRICS

# THE VALUE OF ESOPHAGEAL pH MONITORING FOR THE DIAGNOSIS OF GASTROESOPHAGEAL REFLUX

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### Abstract:

We studied the gastroesophageal reflux in a group of 31 infants using 24 hours esophageal pH monitoring. Including criteria: suspicion of gastroesophageal reflux in infants with extradigestive clinical manifestations, gastroesophageal reflux persistent after treatment, no prokinetic medication 48 hours before the examination. Excluding criteria: length of pH monitoring shorter than 18 hours, graphics with artifacts. Our results proved several significant differences for reflux parameters in symptomatic patients: subjects with chronic cough have higher reflux index (RI) and Euler score (ES) than those without cough, subjects with recurrent pneumonia have higher values for the length of the longest episode of reflux (LLER) than those with no pneumonia, subjects presenting wheezing have higher number of episodes of reflux (NER) than those with no airway obstruction symptoms, subjects with malaise have a higher ES than those without malaise, subjects showing growth failure have higher number of episodes of reflux longer than 5 minutes (NER5) than those with normal somatic development.

**Key words:** gastroesophageal reflux, pH monitoring, infant

### Background:

We aimed to evaluate the correlations between different parameters of esophageal pH monitoring and clinical manifestations. Gastroesophageal reflux (GER) is common in humans; its incidence varies with age and gender.

In infants, GER may be the first noticed “pathological” sign<sup>1</sup>, over 67% of the healthy children having more than one regurgitation during the day. Perceptible (visible) regurgitation occurs only in 20% of the episodes of GER detected by pH monitoring or gastric scintiscan<sup>7</sup>. The highest incidence of symptomatic GER, either physiological or pathological, is around the age of 4 months<sup>1</sup>. Gastroesophageal reflux affects 1 of 300 cases according to American authors<sup>3</sup>, or 1 of 500 cases according to French literature<sup>4</sup>.

Quantitative esophageal pH monitoring allows the assessment of pH variations according to certain parameters. Physiologically, the esophageal pH ranges from 4.0 to 7.0. GER is defined by the decreasing of esophageal pH below 4.0. An episode of reflux is defined as beginning

at the first decreasing of pH below 4.0 and ending at the first increasing of pH above 4.0<sup>5</sup>. The assessed parameters are:

1. **Reflux index (quotient) (RI/RQ)** – indicates the percentage of time when the pH is below 4.0; it demonstrates the exposure of the distal esophageal epithelium to gastric acid contents, but cannot specify the mechanism of reflux.
2. **Number of episodes of reflux (NER)** – is significant in assessing the function of the lower esophageal sphincter (LES).
3. **Number of episodes of reflux longer than 5 minutes (NER5)** – offers details on the esophageal clearance.
4. **Length of the longest episode of reflux (LLER)** - offers details on the esophageal clearance.

The most frequent used is **Euler score (ES)** =  $NER + 4 * NER5$ , with a normal value below 50.

The most valuable parameter for assessing the GER in children is RI<sup>6</sup>, while the other ones are useful for a more accurate interpretation<sup>7</sup>.

### Material and methods:

We have studied retrospectively a group of 31 infants (18 boys and 13 girls), most of them being of 5 to 11 weeks old, followed-up in our hospital from November 1999 through June 2002. All these patients have been investigated by 24 hours esophageal pH monitoring.

The equipment used to perform the pH monitoring consisted of:

- simple pH probe (with external reference electrode) made of stibium
- solutions for the standardization of the probes, prepared by the Institute of Chemistry “Raluca Ripan” of Cluj-Napoca
- pH meter (type D x C – 91 multi ion meter pH), provided by Datronix Computer in 1999.
- software for analyzing the information and generating the graphic of pH evolution, which is then printed on a paper.

During the continuous 24 hours esophageal pH monitoring should be recorded on a piece of paper all the sleep and the wake whiles (periods), meal whiles and any clinical manifestation.

The diagnosis of pathological acid GER has been established considering the RI for pH=4.0, its upper limit being 5%, just like in the study of Vanderplas<sup>8,9</sup>. Euler score has also been used. Data provided by the pH graphics have been processed using descriptive and analytic statistics<sup>10</sup>. Data have been expressed as mean value ± standard deviation (SD). Reflux parameters (RI, NER, NER5, LLER, ES) have been analyzed with Student test.

The differences have been considered statistical significant if  $p < 0.05$ , respectively having a very good statistical significance if  $p < 0.01$ .

**Results:**

Comparison of reflux parameters between subjects with pathological acid GER and those with physiological acid GER:

	Pathological acid GER M ± SD	Physiological acid GER M ± SD	p value
<b>RI</b>	11.58 ± 4.76	3.30 ± 0.82	2,93 E-07
<b>NER</b>	66.6 ± 19.13	19.27 ± 4.15	3,59 E-09
<b>NER5</b>	6.55 ± 5.08	2.45 ± 2.16	<b>0,0084</b>
<b>LLER</b>	25.04 ± 12.24	8.04 ± 5.52	<b>0,0422</b>
<b>ES</b>	90.95 ± 27.14	28.90 ± 9.40	2,46 E-08

Correlations among reflux parameters in subjects with pathological acid GER:

	IR	NER	NER5	LLER	ES
<b>RI</b>	0	0,5372	0.6936	0.4650	0.8271
<b>NER</b>	0.5372	0	<b>0.0159</b>	0.1411	0.6936
<b>NER5</b>	0.6936	<b>0.0159</b>	0	0.3686	0.7366
<b>LLER</b>	0.4650	0.1411	0.3686	0	0.2013
<b>ES</b>	0.8271	0.6936	0.7366	0.2013	0

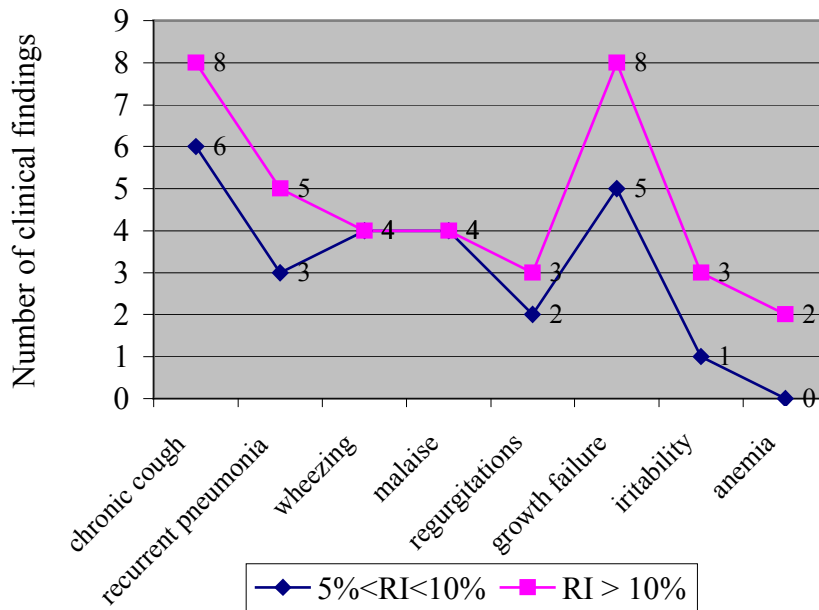
Correlations among reflux parameters in subjects with pathological acid GER:

	RI	NER	NER5	LLER	ES
<b>RI</b>	0	0.4096	0.6517	0.7474	0.6138
<b>NER</b>	0.4096	0	0.0962	0.2241	0.5463
<b>NER5</b>	0.6517	0.0962	0	0.6428	0.8775
<b>LLER</b>	0.7474	0.2241	0.6428	0	0.4897
<b>ES</b>	0.6138	0.5463	0.8775	0.4897	0

Comparison of reflux parameters in subjects with pathological acid GER, according to RI value:

	5% < IR < 10% M ± SD	RI > 10% M ± SD	p value
<b>RI</b>	7.96 ± 1.42	15.48 ± 3.48	<b>0.0082</b>
<b>NER</b>	57.9 ± 17.29	75.3 ± 17.47	<b>0,0191</b>
<b>NER5</b>	4.2 ± 4.77	8.9 ± 4.4	<b>0,0173</b>
<b>LLER</b>	10.49 ± 6.39	19.59 ± 15.15	<b>0,0486</b>
<b>ES</b>	7.51 ± 11.43	106.8 ± 29.44	<b>0.0026</b>

Comparison of clinical findings in subjects with pathological acid GER, according to RI value:



Prevalence of clinical findings:

<b>Clinical findings</b>		<b>Pathological acid GER</b>	
		YES	NO
Chronic cough	<b>YES</b>	<b>14</b>	<b>5</b>
	NO	6	6
Recurrent pneumonia	<b>YES</b>	<b>8</b>	<b>6</b>
	NO	12	5
Wheezing	<b>YES</b>	<b>8</b>	<b>4</b>
	NO	12	7
Malaise	<b>YES</b>	<b>8</b>	<b>1</b>
	NO	12	10
Regurgitations	<b>YES</b>	<b>5</b>	<b>6</b>
	NO	15	5
Growth failure	<b>YES</b>	<b>13</b>	<b>10</b>
	NO	7	1
Irritability	<b>YES</b>	<b>4</b>	<b>0</b>
	NO	16	11
Anemia	<b>YES</b>	<b>2</b>	<b>3</b>
	NO	18	8

Comparison of reflux parameters in subjects with pathological acid GER considering the presence or the absence of *chronic cough*:

	<b>YES</b> M ± SD	<b>NO</b> M ± SD	<b>p value</b>
<b>RI</b>	13 ± 4.95	8.28 ± 1.93	<b>0.0192</b>
<b>NER</b>	70.7 ± 18.92	57 ± 17.36	0.0731
<b>NER5</b>	7.64 ± 5.38	4 ± 3.75	0.0731
<b>LLER</b>	16.37 ± 13.89	11.91 ± 7.15	0.2350
<b>ES</b>	98.35 ± 29.17	73.66 ± 8.68	<b>0.0300</b>

Comparison of reflux parameters in subjects with pathological acid GER considering the presence or the absence of recurrent pneumonia:

	<b>YES</b> M ± SD	<b>NO</b> M ± SD	<b>p value</b>
<b>RI</b>	12.02 ± 3.46	11.34 ± 5.45	0.3844
<b>NER</b>	67.28 ± 15.55	66.23 ± 21.4	0.4550
<b>NER5</b>	6.42 ± 3.64	6.615 ± 5.85	0.4700
<b>LLER</b>	22.28 ± 16.69	11.13 ± 7.14	<b>0.0245</b>
<b>ES</b>	88.85 ± 20.37	92.07 ± 30.91	0.4039

Comparison of reflux parameters in subjects with pathological acid GER considering the presence or the absence of wheezing:

	<b>YES</b> M ± SD	<b>NO</b> M ± SD	<b>p value</b>
<b>RI</b>	13.81 ± 5.96	10.38 ± 3.96	0.0637
<b>NER</b>	86 ± 18.86	61.53 ± 7.95	<b>0.0412</b>
<b>NER5</b>	8.14 ± 6.46	5.69 ± 4.21	0.1583
<b>LLER</b>	17.85 ± 8.56	13.52 ± 13.91	0.2326
<b>ES</b>	109.14 ± 26.58	91.15 ± 14.17	0.0616

Comparison of reflux parameters in subjects with pathological acid GER considering the presence or the absence of malaise:

	<b>YES</b> M ± SD	<b>NO</b> M ± SD	<b>p value</b>
<b>RI</b>	13.27 ± 5.95	10.45 ± 3.62	0.1015
<b>NER</b>	73.12 ± 23.47	62.25 ± 15.16	0.1110
<b>NER5</b>	8.5 ± 6.45	5.25 ± 3.67	0.0835
<b>LLER</b>	11.66 ± 6.67	17.29 ± 14.72	0.1635
<b>ES</b>	105.6 ± 31.6	81.16 ± 19.40	<b>0.0224</b>

Comparison of reflux parameters in subjects with pathological acid GER considering the presence or the absence of regurgitations:

	<b>YES</b> M ± SD	<b>NO</b> M ± SD	<b>p value</b>
<b>RI</b>	11.4 ± 2.96	11.73 ± 5.30	0.1422
<b>NER</b>	51.6 ± 22.81	71.6 ± 15.52	0.0527
<b>NER5</b>	9 ± 4	5.73 ± 5.25	0.1285
<b>LLER</b>	21.9 ± 20.18	12.74 ± 8.03	0.0558
<b>ES</b>	81.8 ± 12.35	94 ± 30.27	0.1034

Comparison of reflux parameters in subjects with pathological acid GER considering the presence or the absence of *growth failure*:

	<b>YES</b> M ± SD	<b>NO</b> M ± SD	<b>p value</b>
<b>RI</b>	12.41 ± 5.17	10.56 ± 4.27	0.2008
<b>NER</b>	64 ± 23.52	69.77 ± 12.52	0.2582
<b>NER5</b>	8.09 ± 3.35	4.66 ± 2.91	<b>0.0185</b>
<b>LLER</b>	18.55 ± 15.12	10.74 ± 5.70	0.0806
<b>ES</b>	97.36 ± 31.43	83.11 ± 19.73	0.1266

Comparison of reflux parameters in subjects with pathological acid GER considering the presence or the absence of *irritability*:

	<b>YES</b> M ± SD	<b>NO</b> M ± SD	<b>p value</b>
<b>RI</b>	11.6 ± 3.21	11.58 ± 5.61	0.4973
<b>NER</b>	56 ± 23.7	69.25 ± 17.69	0.1122
<b>NER5</b>	9.5 ± 4.43	5.81 ± 5.08	0.1011
<b>LLER</b>	31.4 ± 9.27	13.45 ± 8.25	0.0611
<b>ES</b>	86.75 ± 6.34	92 ± 30.32	0.3697

Comparison of reflux parameters in subjects with pathological acid GER considering the presence or the absence of *esophagitis*:

	<b>YES</b> M ± SD	<b>NO</b> M ± SD	<b>p value</b>
<b>IR</b>	16.02 ± 3.49	10.10 ± 4.23	<b>0.0158</b>
<b>NER</b>	74.6 ± 11.63	63.93 ± 20.67	0.1461
<b>NER5</b>	9.6 ± 4.15	5.53 ± 5.06	0.0620
<b>LLER</b>	28.02 ± 18.07	10.71 ± 5.47	<b>0.0315</b>
<b>ES</b>	107.2 ± 17.97	85.53 ± 27.96	0.0625

**Discussions:**

We encountered the following clinical manifestations in our study group: irritability (24%), growth failure (18%), chronic cough (15%), recurrent pneumonia

(11%), wheezing (9%), regurgitations (9%), malaise (7%), anemia (4%).

We found several significant differences for reflux parameters in symptomatic patients:

- subjects with chronic cough have higher RI ( $13 \pm 4.95$ ) and ES ( $98.35 \pm 29.17$ ) than those without cough (RI =  $8.28 \pm 1.93$ ,  $p < 0.05$ ; ES =  $73.66 \pm 8.68$ ,  $p < 0.05$ )
- subjects with recurrent pneumonia have higher LLER ( $22.28 \pm 16.69$ ) than those with no pneumonia ( $11.13 \pm 7.14$ ),  $p < 0.05$
- subjects presenting wheezing have higher NER ( $86 \pm 18.86$ ) than those with no airway obstruction symptoms ( $61.53 \pm 7.95$ ),  $p < 0.05$
- subjects with malaise have a higher ES ( $105.6 \pm 31.6$ ) than those without malaise ( $81.16 \pm 19.4$ ),  $p < 0.05$
- subjects showing growth failure have higher NER5 ( $8.09 \pm 3.35$ ) than those with normal somatic development ( $4.66 \pm 2.91$ ),  $p < 0.05$

There are evidences of the involvement of GER in exacerbating the airway reactivity<sup>11</sup>. The other parameters may be considered of poor outcome, imposing a more accurate treatment: increasing the lower esophageal sphincter tone, administering antacids, H<sub>2</sub>-receptor blockers or hydrogen pump inhibitors in infants with higher NER5 and LLER, or stimulating gastric emptying in those with higher NER.

In patients with esophagitis due to reflux, RI ( $16.02 \pm 3.49$ ) is higher and so is LLER ( $107.2 \pm 17.97$ ). These results are contradictory to some published articles, which sustain that esophageal pH monitoring does not correlate to the endoscopic image of esophagitis due to reflux<sup>12</sup>.

#### Conclusions:

1. Esophageal pH monitoring is useful to assess gastroesophageal reflux in infants. RI is the most valuable parameter. NER, NER5 and LLER allow to distinguish between physiological and pathological acid GER.
2. Euler score is useful to evaluate gastroesophageal reflux in infants and allows to distinguish between physiological and pathological acid GER.
3. In infants with pathological acid GER, there is a very significant correlation between RI and NER, NER5 and ES respectively. There is also a correlation, but not so significant, between RI and LLER. No correlation could be established between NER5 and LLER.
4. In infants with physiological acid GER, there is a very significant correlation between RI and NER5 and ES respectively. There is also a correlation, but not so significant, first between RI and LLER, and then between NER5 and LLER. No correlation could be established between RI and NER.
5. Infants with pathological acid GER having RI above 10% show more clinical manifestations than those having RI between 5 and 10%.
6. Infants with pathological acid GER presenting esophagitis have higher RI and LLER compared to those without esophagitis.

#### References:

1. Snel A, Barnett C.P, Trevor L et al: Behavior and gastroesophageal reflux in the premature neonate. *J Pediatr Gastroenterol Nutr.* 2001; 30: 18-21
2. Del Rosario F, Orenstein S.R: Gastroesophageal reflux, Recent advances in Paediatrics, Ed. S.T.J. David Churchill Livingstone, 1999: 162-171
3. Nelson M, Behrman R: Textbook of Pediatrics, 14<sup>th</sup> edition, Ed. W.B. Saunders Company Philadelphia, 1992: 943-947
4. Navarro J, Schmitz J: Pediatric Gastroenterology, Ed. Oxford University Press, New-York, 1992: 105-120
5. Vanderplas Y et al: The relation between gastroesophageal reflux sleeping position and S.I.D.S and its impact on positional therapy. *Eur J Pediatr* 1991; 156: 104-106
6. Working Group of the European Pediatric Gastroenterology and Nutrition, 1992: A standardized protocol for the methodology of esophageal pH monitoring and interpretation of the date for the diagnosis of gastroesophageal reflux. *J pediatr Gastroenterol Nutr* 1992; 14: 467-471
7. Beenhamou RH, Dupont Ch: Examens complementaires du reflux gastro-oesophagien de l'infant. *M T Pediatrie*, vol 3, hors-serie, mai-juin 2000: 888
8. Vanderplas Y, Goyvaerts RN, Helven R, Sacre L: Gastroesophageal reflux as measured by 24-pH monitoring in 509 healthy infants screened for risk of sudden infant death syndrome. *Pediatrics* 1991; 88 (4): 834-840
9. Arana A, Bagucka B, Hauser B, Hegar B, Urbain D, Kaufman L, Vanderplas Y: PH monitoring in distal and proximal esophagus in symptomatic infants. *J Pediatr Gastroenterol Nutr* 2001; 32 (3): 259-264
10. Tigan S, Achimas A, Dragan T: Biostatistica medicala, Ed. Srima, Cluj-Napoca, 1999
11. Cargill G: PH-metrie oesophagienne, Ed. Masson, Paris, 1991
12. Heine GR, Cameron J, Chow W et al : Esophagitis in distressed infants. Poor diagnostic agreement between esophageal pH monitoring and histopatologic findings. *J Pediatrics* 2001; 140 (1): 14-19