

Outcome of Infant Regurgitation Diagnosed by Rome IV Criteria

Yosra M Awad^{1,*}, Mostafa EL-Hodhod¹, Marwa El Deeb¹, Nehal Soliman² and Yasmin AF Aly¹

¹Department of Pediatrics, Faculty of Medicine, Ain Shams University.

²Ministry of Health and Population, Egypt

*Correspondence: yosraawad@med.asu.edu.eg. Egypt. Mobile number: (+20)1001831590, ORCID: 0000-0002-5315-9774

ABSTRACT

Background: Infant regurgitation is the most prevalent functional gastrointestinal disorder in infancy. Knowing the benign outcome of such condition helps to decrease the anxiety of parents and unnecessary prescriptions by physicians.

Objectives: The aims of the current work were to detect the outcome of infant regurgitation among Egyptian infants diagnosed by Rome IV criteria and to detect its prevalence among the surveyed population.

Patients and Methods: A prospective cohort study enrolling 280 healthy infants 1-4 months diagnosed as infant regurgitation according to Rome IV criteria by fulfilling a questionnaire and undergoing examination. Parents were reassured and educated then both were repeated after 3 months. According to the outcome, infants were divided into symptomatic infants, who were either partially improved or not-improved at all and asymptomatic infants who had stopped regurgitation.

Results: The prevalence of regurgitation was 20.3% among the surveyed 1380 infants. On follow up 42.9% of infants became asymptomatic while 49.6% partially improved and only 7.5% didn't improve. Weight was properly gained for all patients except 3 who had failure to thrive, however that was not correlated with the outcome of regurgitation. Proton pump inhibitors were prescribed for 7.7% of cases, however, increasing age was the only predictor of total improvement after 3 months follow up with odds ratio=2.45 and confidence interval (1.57-3.84).

Conclusion: Infant regurgitation diagnosed according to Rome IV criteria seems to be normal behavior in early infancy which resolves by time, just requiring parental reassurance, and follow up, while no interventions are needed.

Keywords: Infants; Regurgitation, Proton pump inhibitors, Gastrointestinal diseases; Functional; Gastroesophageal reflux.

INTRODUCTION

Regurgitation is defined as the flow of refluxed gastric content into the oropharynx. In infants, it is crucial to differentiate between the physiologic and pathologic reflux. Most infants with physiologic regurgitation are healthy, happy (happy spitters), and having normal growth and development without underlying predisposing factors and no pharmacologic treatment is typically necessary⁽¹⁾.

On the other hand, the movement of gastric contents into the esophagus, either with or without regurgitation and vomiting, is known as gastroesophageal reflux (GER)⁽²⁾. Reflux is the most prevalent functional gastrointestinal disorder in the first year of life, accounting for 25% of the appointments with pediatricians and other health professionals^(3,4).

The natural progression of reflux in infants is between birth and 4 months of age⁽⁵⁾. Then usually outgrow this phenomenon by their first birthday⁽⁶⁾, however a small proportion (5-9%) of all infants with regurgitation have gastroesophageal reflux disease (GERD)^(5,7).

GERD develops when GER leads to troublesome symptoms that interfere with daily functioning and/or the occurrence of complications; as discomfort/irritability - failure to thrive - feeding refusal - dystonic neck posturing (Sandifer syndrome), hematemesia - dysphagia/odynophagia, apnea spells - brief resolved unexplained events - asthma - recurrent otitis media and recurrent pneumonia linked with aspiration⁽²⁾. Additionally, others have added choking, gagging, and coughing with feeds^(8,9).

Infant regurgitation must meet the following two requirements, according to the Rome IV diagnostic criteria, in otherwise healthy infants between the ages of three weeks and twelve months: regurgitation occurring twice daily for three weeks or longer without any feeding or swallowing issues, failure to thrive, abnormal posturing, apnea, retching, or hematemesia, and the absence of any other signs⁽¹⁰⁾.

It is crucial for healthcare professionals to understand the natural history of infant regurgitation to manage infants and offer parents evidence-based guidance⁽⁵⁾.

The primary objective of the current study was to detect the outcome of infant regurgitation among Egyptian infants diagnosed by Rome IV criteria and secondary aim was to detect the prevalence among the surveyed population.

PATIENTS AND METHODS

This prospective cohort study included a total of 280 infants with regurgitation that were diagnosed based on Rome IV criteria, visiting the General Pediatric Outpatient Clinic, Ain Shams University Hospitals. This study was conducted between December 2021 to May 2022.

Legal guardians/parents were asked to fill in a questionnaire to assess infant regurgitation according to Rome IV criteria and infants were included if they were 1-4 months old, full term, healthy and fulfilling Rome IV criteria for infant regurgitation defined as presence of regurgitation at least 2 times per day for at least 3 weeks⁽¹⁰⁾.

Infants were excluded if they had congenital anomalies, neurologic disorders, gastro-intestinal surgeries, or any red flags were present at time of enrollment as retching, hematemesis, aspiration, apnea, abnormal posturing failure to thrive, and feeding difficulties.

Sample Size: 280 infants were needed by using PASS11 program for sample size calculation, reviewing results from previous study showed that the prevalence of infant regurgitation based on Rome IV criteria was 24.1% ⁽¹¹⁾. With a margin of error=0.05 and at 95% confidence level. The study included 280 infants with regurgitation that were diagnosed based on Rome IV criteria.

Sampling Method: convenience sampling.

Study Procedures:

Each infant was subjected to thorough medical history including socio-demographic data, dietetic history, family history of similar condition. Special focus on gastrointestinal symptoms related to average number of regurgitations, which was specifically recorded into one of three categories 2-5 times/day, 5-10 times/day and > 10 times/ day. Associated symptoms such as colic and abdominal distention as well as choking, which was also documented based on average frequency per day.

Complete physical examination especially anthropometric measurements: weight, length and weight/length ratio which were plotted on Z scores and classified according to WHO growth charts ⁽¹²⁾. When an infant's weight on age- and sex-specific growth charts fell below the predicted range or crossed more than two major percentile lines downwards, they were said to have failure to thrive ⁽¹³⁾.

Legal guardians/Parents were offered reassurance and they were educated about the pathophysiology, natural history, diagnosis, and treatment of regurgitation as well as behavioral modification in the form of observation of feeding and handling of the infant during and after feeding, to help avoid overfeeding, with feeding volume and frequency appropriate for age and weight ^(14,15,16). The decision of treatment was left to the general practitioner at the clinic.

Each infant with a diagnosis of infant regurgitation according to the Rome IV criteria was then re-examined by the same pediatrician after 3 months, and the questionnaire was repeated to determine if there had been improvement or worsening of symptoms or a change in the diagnosis and to pick up any red flags or warning signs that require reassessment.

In this study cases were classified according to final outcome after 3 months follow up into 2 groups:

Group A: (Symptomatic infants), who were either partially improved or not- improved at all (having had the same number of regurgitations episodes per day).

Group B (Asymptomatic infants): Those who had stopped regurgitation totally (Total resolution)

Ethical Considerations:

An informed consent was obtained from legal guardians / parents of infants before enrollment in the study. This study follows the declaration of Helsinki, and it was approved from the local Research Ethics Committee of Ain Shams University, Faculty of Medicine, number: 750/2021.

Statistical analysis

The Statistical Package for Social Science (SPSS 25) was used to review, code, tabulate, and analyze the data that had been gathered. For parametric numerical data, the data were provided as mean, and standard deviation (SD), for non-parametric numerical data, they were presented as median and interquartile range (IQR); and for non-numerical data, they were presented as frequency and percentage. Analytical statistics was managed by Student T test, Chi-Square test and Fisher's exact test. P- value: level of significance P value < 0.05 is considered significant (S).

RESULTS

An initial survey included 1380 child, from which 280 infants had suffered from regurgitation according to Rome IV criteria and were enrolled in the study.

Table 1 shows Infants' sociodemographic and clinical data. Median age of infants was 2 months (IQR= 1-2), ranging from 1-4 months.

Table 1: Initial infants' sociodemographic and clinical data

		Mean / N	SD / %
Age (months)		1.8	±0.6
Gender	Female	144	51.4%
Residence	Urban	122	43.6%
	Rural	158	56.4%
Colic	No	149	53.2%
	Yes	131	46.8%
Regurgitation frequency	2 – 4	71	25.4%
	5 - 10	131	46.8%
	> 10	78	27.9%
Median duration of regurgitation in weeks at enrolment		7 (3 - 7)	(3 - 23)
Choking with feeding Frequency/day	No	122	43.6%
	1-2 times	96	34.3%
	3-5 times	51	18.2%
	>5 times	11	3.9%
Feeding	Breast feeding	168	60.0%
	Artificial formula	30	10.7%
	Mixed feeding	82	29.3%
Positive family History in siblings		88	31.4%
Medications	No	166	59.3%
	Yes	114	40.7%
Type of medication	Prokinetics	92	32.9%
	proton pump inhibitor	20	7.1%
	both (prokinetic & PPI)	2	0.7%

As regards to anthropometric data, 48 patients (17.1%) were overweight and 9 patients (2.5%) were obese according to weight/length z scores, and an extra 1 patient (0.4%) was obese according to z scores of weights, with a total of 20% of patients above the 90th percentiles.

Enrolled infants were followed up after 3 months, and the outcome of regurgitation was documented as shown in **table (2)**. None of the patients suffered from hematemesis, abnormal posture, aspiration, apnea, or other red flags except for failure to thrive.

Table (2): Outcome of cases and red flags occurrence after 3 months follow- up.

		N	%
Group A Symptomatic infants	No improvement	21	7.5%
	Partial improvement	139	49.6%
Group B Asymptomatic infants	Total improvement	120	42.9%
Failure to thrive	Yes	3	1.1%
Weight gain in kg after 3 months		Mean: 2.1	±0.6 (SD)
Age (in months) of resolution of symptoms in group B		Mean: 4.75 Median (IQR): 5.5 (3 - 6)	±1.83 (SD) Range: (2 - 7)

Anthropometric data after follow-up showed that 41 patients (14.6%) were overweight and 7 patients (2.5%) were obese according to weight/length z scores, and an extra 6 patients (2.1%) were obese according to z scores of weights, with a total of 19.2%, with no significant difference compared to initial assessment measures.

Weight gain was appropriate in all patients regardless the frequency of regurgitation, type of feeding was not also correlated with frequency of regurgitation (P>0.05). Comparison between patients who stopped regurgitation after 3 months follow up and those who were still symptomatic is presented in **table (3)**.

Table (3): Comparison between group A (symptomatic infants) and group B (asymptomatic infants).

Variables		Group A Symptomatic infants	Group B Asymptomatic infants	significance
		Mean ± SD N (%)	Mean ± SD N (%)	p-Value
Age (months)		1.7 ± 0.57	2.02 ± 0.69	<0.001†
Family History	Negative	106 (66.25%)	86 (71.67%)	0.334*
	Positive	54 (33.75%)	34 (28.33%)	
Gender	Male	84 (52.5%)	52 (43.33%)	0.129*
	Female	76 (47.5%)	68 (56.67%)	
Choking with feeding	No	73 (45.63%)	49 (40.83%)	0.474*
	1-2 times/day	53 (33.13%)	43 (35.83%)	
	2-5 times/day	30 (18.75%)	21 (17.5%)	
	>5 times/day	4 (2.5%)	7 (5.83%)	
Colic	No	83 (51.88%)	66 (55%)	0.604*
	Yes	77 (48.13%)	54 (45%)	
Feeding	Breast feeding only	93 (58.13%)	75 (62.5%)	0.686*
	Artificial formula only	19 (11.88%)	11 (9.17%)	
	Mixed feeding	48 (30%)	34 (28.33%)	
Failure to thrive		2 (1.25%)	1 (0.83%)	0.176‡
Medications	No	89 (55.63%)	77 (64.17%)	0.15*
	Yes	71 (44.38%)	43 (35.83%)	
Type of medication	prokinetic	55 (34.38%)	37 (30.83%)	0.305‡
	proton pump inhibitor (PPI)	14 (8.75%)	6 (5%)	
	Both (prokinetic & PPI)	2 (1.25%)	0 (0%)	

†: Student t test, *: Chi-square test, ‡: Fisher’s exact test.

Multivariate regression analysis showed that increasing age was the only predictor of total resolution after 3 months follow up, Odds ratio=2.45, confidence interval (1.57-3.84).

DISCUSSION

The current results had revealed that the prevalence of infant regurgitation diagnosed based on Rome IV criteria was nearly 20.3% among the surveyed population with no gender predilection. Choking with feeds was present in more than 56% of infants. After 3 months follow up, 42.9% of patients stopped regurgitation.

Prevalence of regurgitation among studies showed a wide variety of percentages, this is most probably related to inclusion criteria which sometimes included those with manifestations of complicated GER and sometimes limiting the observations to children with 1 regurgitation episode per day.

Most of earlier studies that didn’t follow Rome criteria had higher prevalence rate whereas *Martin et al.* included those children who spilled most feeds each day and reported a peak prevalence of 41% ⁽¹⁷⁾, while *Nelson et al.*, and *Curien-Chotard* had included children who regurgitated at least once a day and they reported a prevalence of 67% and 60% respectively ^(7,18).

On the other hand, lower prevalence rates close to the results of the current study were seen in studies using Rome criteria and this is most probably related to

the stricter definitions. Where *Campanozzi et al.* using Rome II criteria, found a prevalence of 12%, while *Van Tilberg et al.* used Rome III criteria, and showed a prevalence rate of 26%. Finally, *Robin et al.* used the Rome IV criteria and found a prevalence of 24.1% ^(19,4,11).

Regurgitation occurs equally in males and females. This has been shown in many studies ^(18,20). This study revealed that type of feeding was neither significantly correlated with frequency of regurgitation nor with the outcome. This came in accordance with *Campanozzi et al.* and *Iacono et al.* who found no significant difference between breast fed infants and artificially fed infants as regards to frequency of regurgitation, Contrarily, exclusively breastfed infants regurgitated less in another cohort. ^(19,20,21)

As physiological regurgitation should not be diagnosed in an infant with poor weight gain ^(15,22), anthropometry is of major importance ⁽¹⁶⁾. Weight gain was appropriate in all patients regardless the frequency of regurgitation, however; 3 patients crossed 2 major centiles after follow-up indicating their failure to thrive, but this was not correlated with the outcome of regurgitation. This was the only red flag which appeared

on follow up of patients, however; etiology of such a condition is diverse. *Iacono et al.* found no difference in any of the functional gastrointestinal disorders of infancy between cases with normal growth and those with failure to thrive⁽²⁰⁾.

Furthermore, contrary to earlier studies^(23,24) that did not note a poor weight gain in response to the severity and frequency of regurgitation, *Hegar et al.* findings 's revealed a transient drop in weight gain associated to the frequency of regurgitation⁽⁵⁾.

Martin et al. showed that proportion of children suffering from regurgitation decreased and reached <5% between 13-14 months of age and nearly stopped by 19 months of age⁽¹⁷⁾. However, *Curien-Chotard* showed that GER peaked at 3 months while GERD peaked at 1 month of age⁽¹⁸⁾.

Surprisingly, 40% of the enrolled infants in this study were prescribed medications by the general practitioner and 7.7% of them received proton pump inhibitor. These figures were much higher than the 5% and 9% use of medications reported by *Curien Choutard* and *Campanozzi et al.* respectively^(18,19). Obviously, these results revealed the extent of parents' anxiety with their urge to receive medications. In addition to the pediatricians' unawareness to the recent guidelines together with the availability of such medicines over the counter.

PPI prescriptions for children have increased dramatically in this era^(25,26). The authors reported that prescriptions had more than doubled in the United States in a retrospective review of PPI prescribing patterns for infants, and that it had increased among Belgians as well in another investigation^(26,27). Although PPIs were regarded as a useful treatment for erosive disease⁽²⁸⁾, a systematic review found that they had no effect on GERD symptoms in infants⁽²⁹⁾.

CONCLUSION

Infant regurgitation diagnosed according to Rome IV seems to be a normal physiological behavior in early infancy which resolves by time. Hence, parental anxiety, medical referral and overtreatment are needless.

Study Limitations

Larger sample size is required to detect exactly the prevalence of infantile regurgitations among Egyptian infants with more prolonged follow up for the outcome.

Conflict of Interest:

Authors declare no conflict of interest.

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