

Natural course of gastroesophageal reflux disease during infancy - six-month follow-up

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Abstract

Background Very few data have been published about the natural course of gastro-esophageal reflux (GER) symptoms during infancy; further, no risk factors of GER disease (GERD) have been identified.

Objectives To determine the prevalence and natural course of regurgitation in infancy and factors of gastroesophageal reflux disease.

Methods A cohort of 223 healthy infants who attended Integrated Health Services run by local housewife (Posyandu) of Ciputat – suburb of Jakarta – between March and November 2005. Information on subjects' history of regurgitation and other reflux-related symptoms was obtained by interviewing mother and diary record. Subjects were followed up to age of 1 year irrespective of the clinical status.

Results At 6 months of age most infants (56.5%) had regurgitation 1 to 3 days per week and only 2.7% infants regurgitated daily. Regurgitation 1 to 3 episodes per day was found in 92.8% of subjects. The proportion of infants regurgitation decreased gradually with age; the proportion for the consecutive 6 to 11 month was 100%, 65.5%, 33.6%, 14.3%, 3.6% and 1.3%, respectively. At the age of 1 year no infants was found to be regurgitated. Related symptoms included hiccup (58.3%), vomiting (23.3%) and back arching (2.2%). Feeding problem occurred in 34.1% infants and occurred more likely in infants who regurgitate daily compared to 4 – 6 day per week (OR 3.5; 95%CI 2.2;5.6) and 1 – 3 day per week (OR 1.8; 95%CI 0.6;0.9).

Conclusions Regurgitation in infancy disappears spontaneously with age. Reflux-related symptoms are hiccup, vomiting and back arching. Feeding problem occurs most likely in infants who regurgitate daily. [Paediatr Indones 2007;47:211-215].

Keywords: regurgitation, gastroesophageal reflux, regurgitation

Regurgitation, defined as the effortless return of gastric contents into the mouth, is the classic symptom of gastro-esophageal reflux (GER) in infancy.¹ It occurs frequently during the first year of life with the peak incidence of 65-86.9% at 1-4 months of age and usually resolves spontaneously by 6 to 12 months of age.²⁻⁵ Regurgitation may occur in normal infants⁶ but may be accompanied by complications such as weight loss, esophagitis, anemia, or stricture; in these situations the infants are defined as having GER disease (GERD).⁷ There is a continuum between normal infants with GER and those with GERD, so there is no clear cut-off point separating physiological from pathological reflux.

It is generally accepted that infants with regurgitation have a good long-term prognosis because regurgitation disappears spontaneously by the age of 12-18 months.²⁻⁵ However, published data to support this hypothesis are limited and few available data tend to suggest the contrary to common belief that infant

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regurgitation is a physiological condition. Infants that regurgitate refuse feeding 4.2 times more frequently than those who do not regurgitate.⁸ Other study found that infants who regurgitate more than 90 days in their infancy are at higher risk of developing symptoms suggesting GERD than those who regurgitate less.⁹ Recent studies suggest that GER sometimes associated with failure to thrive, but the prevalence of this is unknown.^{3,8,10}

Very few data have been published about the natural course of GER symptoms during infancy; further, no risk factors of GERD have been identified. This study aimed to determine the natural course of regurgitation in infancy, the percentage of GERD in infantile regurgitation, and the predictive factor of GERD.

Methods

This cohort study was conducted in integrated health services (*Posyandu*), for healthy children below 5 years old supervised by Primary Health Centre, in Ciputat (suburb of Jakarta city) from March to August 2005. The main activity of Posyandu is the evaluation of children's growth by measuring body weight. Six-month old healthy infants were identified consecutively until a minimum calculated sample size of 236 subjects was achieved. We enrolled infants who regurgitated at least 1 day per week excluding infants with congenital anomalies, cerebral palsy, or previous investigation for GER-related symptoms.

We collected data from mothers by direct interview. For mothers of infants with regurgitation, we provided a diary for recording the occurrence of infants regurgitation. Data collected included sex, birth weight, gestational age, maternal education, frequency of regurgitation, other reflux-associated symptoms including vomiting, excessive crying, hiccup, back arching, feeding difficulties, failure to thrive, hematemesis, or black stools.

All infants were followed-up until they developed complication, or they did not experience regurgitation for at least 3 consecutive weeks, or reached the age of 12 months. Feeding problems identified in this study included feeding refusal, feeding time of more than 1 hour, or parent reported that they felt "upset" during mealtime. Statistical analysis was performed using Chi-

square or Fisher's exact test, as appropriate. Differences were considered significant if $P < 0.05$. Data were analyzed using SPSS 11.5 for Windows.

This study was approved by the Committee for Medical Research Ethics of Faculty of Medicine University of Indonesia. Parents were informed about the study and they signed informed consent before participating.

Results

We initially enrolled 260 infants, but during follow-up 37 infants were excluded; 9 were lost to follow-up and 28 had incomplete diaries. Analysis was performed in 223 remaining infants who completed the study based on the disappearance of regurgitation. No infants developed complications that needed treatment. The characteristics of the infants and the corresponding mothers are shown in **Table 1**.

Regurgitation of 1 to 3 episodes per day was found in 92.8% subjects. The proportion of regurgitation in these infants decreased gradually with increasing age. At 6 months of age most of the infants had regurgitation 1 to 3 days per week (56.5%) and only 2.7% infants regurgitated daily. At the age of 1 year old no infants was found to be regurgitated. Infants who regurgitated ≥ 4 episodes per day even could not be found since the age of 9 months, but

Table 1. Characteristics of infants and mothers enrolled in the study

Characteristic	Number
Sex (%)	
- Boy	118 (52.9%)
- Girl	105 (47.1%)
Gestational age (%)	
- Term	196 (87.9%)
- Preterm	27 (12.1%)
Initial body weight, g (range)	6791 (6000-8300)
Birth weight, g (%)	
- <2500 g	28 (12.5%)
- 2500-4000 g	187 (83.9%)
- >4000 g	8 (3.6%)
Nutritional status (%)	
- Obesity	3 (1.3%)
- Well-nourished	158 (70.9%)
- Undernourished	62 (27.8%)
Maternal education (%)	
- Senior high school	98 (43.9%)
- Junior high school	91 (40.8%)
- Elementary school	34 (15.2%)

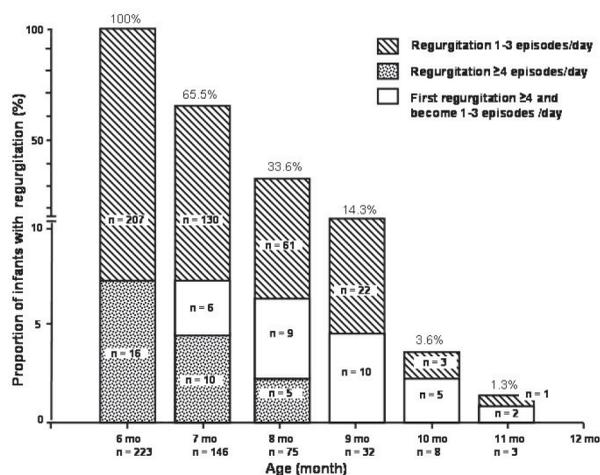


Figure 1. Proportion of infants with regurgitation during 6-month study

these infants actually regurgitated less (1 to 3 episodes per day) before outgrew regurgitation. There was no report on the re-occurrence of regurgitation after it had disappeared. Detailed profiles of this proportion are depicted in **Figure 1**.

Symptoms associated with GER reported by the mothers included hiccup (58.3%), vomiting (23.3%) and back arching (2.2%). There were no infants with daily vomiting, those who vomited had it 1-2 days per week (range of 1-3 days per week). There were 7.2% of mothers who considered regurgitation as a health problem. This parental concern was associated with the frequency of regurgitation.

Feeding problem was the only sign of GERD notified in this study; it occurred in 34.1% of the infants. No single infant had weight gain problem. **Table 2** demonstrates bivariate analysis of factors that might have association with feeding problem. The frequency of regurgitation per week was the only factors statistically significance for the occurrence of feeding problem.

Discussion

The main result of our study is the evidence that spontaneous complete resolution of regurgitation occurs with increasing age. This agrees with the findings of other studies which show that regurgitation disappear almost completely at about the age of 1 year.²⁻⁵ Regurgitation in infancy is the only symptomatic GER that is considered physiological as it believes to be benign and does not need any treatment or medical attention.^{1,11} Summary of results from those studies is shown in **Table 3**.

We noted only 7.2% infants who regurgitated more than 4 episodes per day. Compared to other studies in Asian infants²⁻⁴ our figure was quite high, but similar in the nature of early disappearance of regurgitation compared to Western infants.⁵ Nelson *et al*⁵ found 1% infants of 1 year old still regurgitated 4 or more episodes per day. Our study confirms that disappearance of frequent regurgitation does not happen all of sudden, rather this develops gradually.

Table 2. Bivariate analysis of several factors that might affect the occurrence of feeding problem as complication of GER

		Feeding problem Yes	Feeding problem No	P	OR	95% CI	
Gestational age	Preterm	12	15	0.18	1.4	0.9; 2.2	
	Term	62	134				
Nutritional status	Undernourished	18	44	0.41	0.8	0.5;1.3	
	Obese/well	56	105				
Frequency per day	≥4 episodes	8	8	0.14	1.6	0.9;2.7	
	1-3 episodes	66	141				
Frequency per week	Daily	5	1	0.00	3.5	2.2;5.6	
	4-6 day	39	52	0.00	1.8	0.6;0.9	
	1-3 day	30	96				
Age when regurgitation disappear	10-12 month	12	20	0.76	1.2	0.7;1.9	
	7-9 month	62	129				
Other symptoms	Hiccup	Yes	39	0.15	0.7	0.4;1.2	
		No	61				110
	Vomiting	Yes	13	39	0.23	0.8	0.5;1.2
		No	35	58			

Table 3. Studies on natural history of regurgitation in infancy (0-12 months)

Author	Frequency (episode/day)	Highest (month)	6 month	10-12 month
Hegar <i>et al</i> ²	1-4	1 : 55%	30%	0%
	>4	2 : 28%	0%	0%
Osatakul <i>et al</i> ³	1-3	2 : 87%	45%	7.6%
	≥4	1 : 7.5%	3.4%	0%
Miyazawa <i>et al</i> ⁴	1-2	1 : 47.1%	7 month: 6.4%	0%
	≥3	1 : 14%	7 month: 2.6%	0%
Nelson <i>et al</i> ⁵	≥1	4 : 67%	61%	5.4%
	≥4	5 : 23%	7 month: 7%	1%

Orenstein *et al*¹² developed a questionnaire to distinguish infants with GERD from GER, and it was reported that about 40% of normal infants regurgitated at least once a day whereas about 80% of the infants with GERD do so. A study of children below 2 years old in India showed that regurgitation was found in 19.6% of normal infants and 91.8% of infants suggestive GERD based on questionnaire.¹³ Thus, there is great deal of overlap between them.

Most infants with GERD have other symptoms including weight loss, feeding problem,¹⁴ irritability, abnormal posturing (back arching), esophagitis, vomiting, hematemesis¹⁰ and anemia.¹¹ Hematemesis and frequent vomiting are predictors of pathological reflux in irritable infants.¹⁰ Maternal diaries in our study recorded 3 symptoms other than regurgitation, i.e., hiccup, vomiting and back arching. Orenstein *et al* also identify these symptoms in healthy infants.¹²

Infants with GERD have significantly more feeding problems.¹⁵ Heine *et al*¹⁰ found this symptoms in half of infants (1 to 9 months old) with symptoms suggestive of GERD confirmed by pH-metry. The developing infant's nerve when exposed to acid milieu in the esophagus might cause pain hypersensitivity even in the absence of tissue damage.¹⁶ Our study found 34.1% feeding problems; this figure was high because we used the most common problem reported by parents. Indeed was feeding problem is common in this age group,^{17,18} indicating its multifactorial etiology that was not investigated in this study. Mothers of GER infants are experiencing greater difficulties in feeding their infants. Furthermore, they had greater feelings of anger and frustration and feel less enjoyable.¹⁵

This study intended to investigate the predictor of GERD in regurgitated infants. Chi-square analysis

revealed that frequency of regurgitation per week was the only factor differed significantly between infants with and without feeding problems. Infants with frequency of regurgitation 4 or more episodes per day tend to be more likely to develop feeding problem than group of 1-3 episodes per day, the percentage were 50% and 31.9% respectively. This was not statistically different.

Information on natural course of regurgitation is important to be anticipatory guidance to parents, regarding this common symptom can results in significant parental anxiety^{2,5,11}. Parents of infants in this study concerning regurgitation as problems was low compare to other studies.^{2,5} Practicing physician can also obtain information on clinical course as guidance to monitor infants appropriately with this problem for later difficulties. Majority of infants stopped regurgitating by the age of 13-14 months, However, those with frequent regurgitation (>90 days) were more likely to have GER symptoms at 9 years of age.⁹

In conclusion, majority of healthy infants have uncomplicated regurgitation and generally resolves spontaneously by 12 months of age. Our study contributes data to obtain better understanding the natural course of symptomatic GER in infancy. This study found feeding problems as symptoms that developed in infants with history of regurgitation. Infants with daily regurgitation were more likely to have feeding problem. Future research should be performed to investigate this potentially problematic morbidity to determine the association to GER in infancy.

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