

RAPID COMMUNICATION

## Incidence and risk factors for infantile colic in Iranian infants

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Author contributions: Talachian E and Bidari A designed research; Talachian E and Rezaie MH performed research; Talachian E, Bidari A, and Rezaie MH analyzed data; and Bidari A and Talachian E wrote the paper.

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Received: December 17, 2007 Revised: February 19, 2008

Accepted: February 26, 2008

Published online: August 7, 2008

lation of Iranian infants. Except for birth order status, no other variable was significantly associated with infantile colic.

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**Key words:** Infantile colic; Incidence; Iran; Risk factors

**Peer reviewer:** Yvette Taché, PhD, Digestive Diseases Research Center and Center for Neurovisceral Sciences and Women's Health, Division of Digestive Diseases, Department of Medicine, David Geffen School of Medicine at UCLA, University of California, Los Angeles and VA Greater Los Angeles Healthcare System; 11301 Wilshire Boulevard, CURE Building 115, Room 117, Los Angeles, CA, 90073, United States

Talachian E, Bidari A, Rezaie MH. Incidence and risk factors for infantile colic in Iranian infants. *World J Gastroenterol* 2008; 14(29): 4662-4666 Available from: URL: <http://www.wjgnet.com/1007-9327/14/4662.asp> DOI: <http://dx.doi.org/10.3748/wjg.14.4662>

### Abstract

**AIM:** To assess the incidence of infantile colic and its association with variable predictors in infants born in a community maternity hospital, Tehran, Iran.

**METHODS:** In this prospective cohort study, mothers who gave birth to live newborns between February 21 and March 20, 2003 at the hospital were invited to join to the study. For every infant-mother dyad data were collected on infant gender, type of delivery, gestational age at birth, birth weight, birth order, and mother's reproductive history. Then mothers were given a diary to document the duration of crying/fussiness behaviors of their infants for the next 12 wk. We scheduled home visits at the time the infants were 3 mo of age to collect the completed diaries and obtain additional information on infants' nutritional sources and identify if medications were used for colic relief. Cases of colic were identified by applying Wessel criteria to recorded data. Chi-square and Mann-whitney *U* tests were used to compare proportions for non-parametric and parametric variables, respectively.

**RESULTS:** From 413 infants, follow-up was completed for 321 infants. In total, 65 infants (20.24%) satisfied the Wessel criteria for infantile colic. No statistical significance was found between colicky and non-colicky infants according to gender, gestational age at birth, birth weight, type of delivery, and, infant's feeding pattern. However, firstborn infants had higher rate for developing colic ( $P = 0.03$ ).

**CONCLUSION:** Colic incidence was 20% in this popu-

### INTRODUCTION

Infantile colic refers to a behavioral syndrome occurring during the first 3 mo of life. Crying is the core symptom, but clinicians differ on what other behaviors constitute the syndrome. By far the most widely used quantitative definition of colic is the one proposed by Wessel & his colleagues known as the "rule of threes"<sup>[1]</sup>.

Infants are considered to have colic if they cry for more than 3 h a day, for more than 3 d a week, and for more than 3 wk. It is usually self-limiting, without long term adverse consequences, but caring for an infant with colic can be distressing and frustrating for parents<sup>[2]</sup>. Estimates of cumulative incidence have varied from 10% to 40%<sup>[3-7]</sup>. This wide range may reflect differences in definitions, methods of data gathering, and study design<sup>[3,8]</sup> but also it may be related to a true difference in the occurrence rate of infantile colic among different communities. Notably, most studies are from western societies and many reviews only use data from selected populations<sup>[9-13]</sup>. While, due to the possible contribution of psychosocial factors to colic incidence<sup>[14-17]</sup>, it is unclear whether the data from developed countries can be applied to others, there are scarce reports on colic incidence from developing countries. On December 1, 2007 we performed a Medline search (1966-2007) using "colic"

as a text free word. The search was limited to “humans” and “infants (age up to 23 mo)”. No other limitation was made in order to contain the search sensitivity. The Medline search revealed 795 citations. No study was found to evaluate the occurrence rate of infantile colic in the Middle East countries. We conducted this study in an effort to contribute new data from Iran as well as to identify risk factors for developing infantile colic.

## MATERIALS AND METHODS

### **Study setting and subjects**

This prospective cohort study was performed in Shahid Akbar Abadi maternity hospital, a high volume maternity hospital that serves as a major facility for a non-selected population of pregnant women in the southern part of Tehran, Iran; the majority of them having no medical problem. Anticipating the prevalence of colic in infants less than 3 mo to be 25% and absolute precision to be 5% ( $d = 0.05$ ), the chance of which should be at least 95%; a sample size of 289 was required. Considering the average hospital census of about 500 live births per month, and predicting a drop-out rate of up to 40% for nonparticipation or follow-up losses, we chose to consecutively include all live births at the hospital throughout a month period. Accordingly, between February 21 and March 20, 2003, all mothers of newborn babies at the hospital were invited to join the study.

### **Data collection**

Upon agreement to enter to the study, for every infant-mother dyad data were extracted from hospital files on infant gender, type of delivery, gestational age at birth, birth weight, birth order, and mother's reproductive history. Whenever the data were obscure or insufficient in charts, clarification was made by direct interviews with mothers. Within 3 d of delivery and before leaving the hospital, participating mothers received a 12 sheet diary leaflet, for the coming 12 wk. The diary format was based on a design introduced by Canivet *et al* elsewhere<sup>[18]</sup>. Briefly, it included a detailed form with squares for every 5 min period of 24 h for one predetermined day (Wednesday) of each week. Parents noted “crying” and “fussiness” separately and recorded them at their earliest convenience with letter symbols in relevant blocks on Wednesdays. The selection of 1 d out of a week, was a compromise to improve parents compliance in filling the forms and, therefore, to improve the diagnostic quality of estimating crying duration. As to the other 6 d of the week, parents made an estimation of crying and fussing time. Mothers were told not to register episodes of crying that were without any doubt related to hunger, fatigue or diaper changing. The crying thus had to cease instantly when the baby was fed, had fallen asleep, or when the diaper change was completed, and in no case continue for more than 5 min.

### **Follow-up**

When the children assessed in the perinatal study were 3 mo old, a home visit was made in order to obtain ad-

ditional information on whether medication had been required to manage crying/fussing lasted 1 wk or more, whether feeding formula had been added to or substituted for breast milk by the age of 2 mo and finally to collect the diaries. Arrangement was made to set the date of home visit not to exceed a time frame of  $\pm 3$  d from the exact age of 3 mo for any individual infant. Cases of colic were identified by applying Wessel criteria to recorded data. Crying and fussiness both were accounted for colic identification. We also accepted colic when crying/fussing continued for 3 h per day on 3 d for at least 1 wk and needed drug intervention to be controlled. This has been known as Wessel medication subcriterion<sup>[18]</sup>. We excluded cases if the diary questionnaire was returned incomplete or could not be reached, or if the infant was not alive by the age of 3 mo.

### **Statistical analysis**

The statistical analysis was performed using SPSS 11 for Windows. Chi-square was used for comparison of proportions. For reporting of results only variables with a *P* value less than or equal to 0.05 was considered significant.

## RESULTS

### **Baseline and follow-up data**

During the enrollment period a total of 442 infants were born from 437 mothers; 29 infants were not included in the study as their mothers chose not to be enrolled ( $n = 18$ ) or could not reliably fill in the diaries as they were illiterate ( $n = 11$ ). As a result 413 infants were initially entered to this study. At the follow-up visit 90 infants were excluded from the study-as parents could not be reached at home either due to nonattendance or moving to another address ( $n = 49$ ) or their diaries returned incomplete ( $n = 41$ ). We also excluded 2 premature infants who died early in their neonatal period. The rate of overall drop-out after enrolling to the study was 22%. Of 316 successful home visits, we gathered complete data for 321 infants (312 were singletons, 3 twins, and 1 triplet). Subsequent analyses were performed on these 321 infants who completed the study protocol. Of them, 168 cases (52.3%) were male and 153 (47.7%) were female. The range of birth orders was from 1 to 8; with the most frequent one was the first order which comprised 169 infants (52.6%). According to gestational age at birth, 229 infants (71.3%) were born full-term, 85 (26.5%) pre-term and 7 (2.2%) post-term. Type of delivery was vaginal delivery in 198 cases (61.7%) and cesarean section in 123 cases (38.3%). The mean  $\pm$  SD of birth weights was  $3072 \pm 580$  g (range: 1200-5000 g). In total, 57 infants (17.7%) had a low birth weight ( $< 2500$  g). By 2 mo of age, the frequencies of exclusive breast-fed, exclusive formula-fed, and complementary-fed infants were 273 (85%), 17 (5.3%), and 31 (9.7%), respectively.

### **Colic incidence and risk factors**

In total, 65 infants fulfilled the Wessel criteria for infantile colic; all had cry/fuss behaviors of at least 3 h a day on

**Table 1** Comparison of potential predictors of infantile colic in colicky and non-colicky subgroups

Factor	Colicky group (n = 65)	Non-colicky group (n = 256)	P
Gender			
Male	31	137	
Female	34	119	
Ratio	0.91	1.15	0.40
Mode of delivery			
Vaginal	42	156	
Cesarean	23	100	
Ratio	1.82	1.56	0.58
Gestational age at birth			
≥ 37 wk	45	191	
< 37 wk	20	65	
Ratio	2.25	2.93	0.38
Birth weight			
≥ 2500 g	50	214	
< 2500 g	15	42	
Ratio	3.33	5.09	0.21
Birth order			
First born	42	127	
Later born	23	129	
Ratio	1.82	92	0.03
Mode of feeding			
Exclusive breastfed	54	219	
Non-exclusive breastfed	11	37	
Ratio	4.90	4.76	0.24

3 d per week, lasting for 3 wk or more. No infant met the Wessel medication subcriterion i.e. their symptoms resolved after 1 wk by taking medication. Overall, the cumulative incidence rate of colic was found to be 20% in this study.

The frequency of selected potential risk factors for infantile colic in colicky and non-colicky subgroups has been demonstrated in Table 1.

Being the firstborn infant was more probable in colicky population ( $P = 0.03$ ), but no significant difference for other variables including gender, mode of delivery, gestational age at birth, birth weight, and mode of feeding was found between the two subgroups.

## DISCUSSION

The cumulative incidence rate of colic in the first 3 mo of infancy was 20% in this study. This rate is in concert with most reports from developed countries<sup>[3]</sup>. We enrolled all the infants whose mothers consented to participate in the study if they were literate enough to reliably fill in the diary. We did not exclude the infants born prematurely and/or needed special care at neonatal care unit. The only two infants who died over the study period (both within 2 wk after enrollment) were excluded from the study, as there was no chance to detect colic.

It has been claimed that surveys recruiting cases from well baby clinics reported lower occurrence rates compared to recruitment from birth-registered hospitals<sup>[3]</sup>. Hence, according to the non-selective design of our inclusion criteria and the site of the study which was a maternity hospital, the rate of 20% for infantile colic may be considered an overestimate if the figure

is to be extrapolated to the reference community. Nonetheless, in urban areas in Iran, the vast majority of all births occur in hospitals. In such settings, the results of prevalence studies on newborns in hospital settings could be considered representative of general population.

It has been suggested that the vast majority of infants with colic are presented by the age of 6 wk. Collection of cry/fuss data at this time point was expected to capture most cases of colic because the sixth week of life represents the peak of infant crying<sup>[19]</sup>. Colic is widely believed to remit by 3 mo of age<sup>[1,2]</sup>. Therefore it would be improbable that we missed significant number of colics by following the infants for 90 d.

We defined the occurrence of colic using the criteria proposed by Wessel, which are the criteria for diagnosis of colic in infants, which has gained most acceptance<sup>[19]</sup>. Although we also adopted Wessel medication subcriterion for colic definition, not even a single case required to be enrolled only by this definition. The popularity of colic definition in this study would make our results more comparable with the counterpart studies from western societies.

The reported occurrence rates of infantile colic vary within a wide range up to 40%. There is a tendency to attribute the different results to inconsistencies in case definitions and study protocols<sup>[3]</sup>. Little attention has been paid to the possibility of true epidemiological differences, probably due to paucity of qualified data from non-Western societies. Different diet and care taking activities, both of potential relevance to colic incidence<sup>[3]</sup> between developed and developing countries make comparative studies more plausible. Two retrospective studies published from India and Brazil revealed colic prevalence of 16% and 16.3%, respectively<sup>[12,20]</sup>. In a prospective study of 160 Korean infants, no case of infantile colic was found<sup>[21]</sup>. Interestingly, the latter survey was adequate according to the quality criteria in this study as the researchers use a 24 h diary and a definition of infantile colic that included a time criteria<sup>[3]</sup>.

The only variable showed to be predictive of colic development in this study was the birth order. Other factors including gender, weight at birth, type of delivery, mode of feeding and prematurity were not associated with the development of colic. The literature is very controversial in defining the risk factors for colic. Some methodological issues have been blamed to be responsible. Those include inconsistent definitions for colic, the failure to control covariates, and potentially biased assessments of exposure and/or outcome variables because of non-prospective study designs<sup>[19]</sup>.

Our study showing no difference regarding gender for colic presentation is in accordance with most other reports<sup>[5,22-25]</sup>. In a systematic review only one study reported a significantly higher proportion of boys crying more than 3 h per day<sup>[3,22]</sup>. Mode of delivery was not associated with colic in our study, which is in agreement with a report by Hogdall *et al*<sup>[24]</sup>. Like our study, no association between colic and low birth weight was

found in Lucassen's review<sup>[3]</sup>. That is contradicting with Crowcroft's study<sup>[2]</sup>.

We were unable to demonstrate a protective role of exclusive breastfeeding on the development of colic. Among surveys compared breast fed and formula fed infants: four found no difference<sup>[17,18,26,27]</sup>, in three studies the occurrence rates among breast fed infants were slightly higher<sup>[2,28,29]</sup>, and in one it was slightly lower<sup>[22]</sup>. When analyzing the presence of association between breastfeeding and the development of colic, reverse causality is an important distorting factor, since the mother of crying children may stop breastfeeding because they relate the condition to feeding or believe that their milk is insufficient or weak. In order to prevent this deviation we used the same definition used by Saavedra *et al* in their cohort study, i.e. children were considered exclusively breastfed if they were receiving only their mother's milk at the onset of colic<sup>[28]</sup>.

Despite observing some trend toward less colic in breast fed subgroup we were not able to reproduce the results of the latter study. Our smaller sample size might have caused the inability to detect meaningful differences in subgroups, but methodological differences could be the reason. Data were collected retrospectively in that study applying a questionnaire by the time the infants were 3 mo of age. In our study data gathering was performed prospectively by using diaries. It seems further prospective studies are needed to resolve this issue.

Being first borne was the single predicting factor for colic in our study. Surprisingly, this association has been evaluated in very few studies. Crowcroft *et al* published similar result but Lucassen *et al* and Saavedra *et al* reported contradicting finding<sup>[2,3,28]</sup>, the latter although benefited from a large sample size, was a retrospective study.

To evaluate the incidence and risk factors of infantile colic, we took the primary advantage of cohort studies for being not susceptible to reverse causality distortions<sup>[28]</sup>. Furthermore, we used diaries to collect data on cry/fuss behaviors. The prospective design of the study yields more reliable estimates of occurrence rates than retrospective studies, as the latter are prone to recall bias<sup>[3]</sup>.

Our study had two main limitations. Firstly, this was a single-center study and accordingly prone to selection bias distorting the application of the results to the reference community. Admittedly, because of differences in referral pattern in community and private hospitals, we can not exclude this potential source for selection bias. Nevertheless, the site in which our study was performed is located in the southern part of Tehran, where a minority of births occurs in private hospitals. Secondly, we lost 22% of cases initially enrolled to the study. This may raise the possibility of selection bias in the results. Higher rates for drop-out, however, are usual in other prospective studies. Moreover, the part of case loss which might be more important to selection bias was the subgroup who excluded for having incomplete

diaries. This subgroup consisted of 41 infants (10%) out of 331 infants initially recruited, a figure which was reasonably low.

In summary, this was a rare prospective cohort study conducted in a developing country to detect the occurrence rate of colic. The cumulative incidence rate for colic was defined 20% in the study group. The only significant predictor for developing colic was being the first live-born infant. According to this study, similar to Western societies, infantile colic is a common condition in Iranian infants.

## COMMENTS

### Background

Published data from developing countries on the incidence and/or risk factors of infantile colic are scarce. The possible contribution of cultural, nutritional, and socioeconomic factors to colic development make it prudent to conduct more studies in developing countries.

### Research frontiers

There is consensus in the literature on the complexity of the nature and heterogeneity of the risk factors associated with infantile colic. Most data on this issue has been obtained from the studies conducted in Western societies, especially in North America and Scandinavian countries. Those populations differ in the frequency of many infantile colic risk factors from developing countries.

### Innovations and breakthroughs

Our study is one of the rare prospective studies which have ever performed in developing countries to define the infantile colic incidence and its associated risk factors. During 3 mo follow-up of a population of Iranian infants, around 20% met the Wessel criteria for infantile colic which is in concert with most reports from developed countries. We also found firstborn infants were at higher risk to develop colic.

### Applications

Despite difference in many demographical, social and cultural factors between developed and developing countries, we demonstrated a comparable incidence of infantile colic in our study population. Although further studies are needed to define colic incidence in developing countries, our results may suggest colic occurrence is not tightly related to social or cultural variables.

### Peer review

It's a well-written paper. The study showed that colic incidence was 20% in this population of Iranian infants. Except for birth order status, no other variable was significantly associated with infantile colic.

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S- Editor Zhong XY L- Editor Alpini GD E- Editor Ma WH