Infant Colic

Empirical Evidence of the Absence of an Association With Source of Early Infant Nutrition

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**Background:** The etiology of infant colic remains unknown, despite an abundance of research on the topic.

**Objective:** To determine whether breastfeeding has a protective effect in colic’s development.

**Design:** A prospective cohort study of 856 mother-infant dyads. Eligible participants included English-speaking adult residents of a region in Ontario, who gave birth, at term, to a live singleton whose birth weight was appropriate for gestational age. Self-administered questionnaires, mailed to mothers at 1 and 6 weeks post partum, requested information on several infant and maternal factors, including source of infant nutrition (exclusively breastfed, complementary fed, and exclusively formula fed). Cases of colic were identified by applying modified Wessel criteria to data recorded in the Barr Baby Day Diary or by interpreting responses to the Ames Cry Score.

**Main Outcome Measures:** Prevalence of colic among breastfed, formula-fed, and complementary-fed infants; and adjusted odds ratios (AORs) reflecting the prevalence of colic among formula- and complementary-fed infants relative to those who were breastfed.

**Results:** Of 856 mothers, 733 (86%) completed the first questionnaire and 617 (72%) completed the second questionnaire. Overall, the prevalence of colic at 6 weeks was 24%. No association was seen between the source of infant nutrition and colic’s development. In multivariate analyses, higher levels of maternal trait anxiety (AOR, 1.22; 95% confidence interval [CI], 0.96-1.54), maternal alcohol consumption at 6 weeks (AOR, 1.57; 95% CI, 1.03-2.40), and shift work during pregnancy (AOR, 1.27; 95% CI, 0.73-2.21) were associated with an increased likelihood of colic, after controlling for feeding method, maternal age, and parity. In these same analyses, being married or having a common-law partner (AOR, 0.30; 95% CI, 0.10-0.87) and being employed full-time during pregnancy (AOR, 0.60; 95% CI, 0.32-1.14) were associated with a reduced likelihood of colic.

**Conclusions:** Breastfeeding did not have a protective effect on the development of colic. Although colic was statistically associated with several variables, including preexisting maternal anxiety, much of colic’s etiology remains unexplained.

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Infant colic remains enigmatic, despite its long history and its relatively frequent occurrence. While apparently innocuous, an infant’s colic can prompt lasting parental distress.1-6 The potential severity of an episode of colic is highlighted by the fact that, for certain individuals, the stress of caring for an inconsolable infant may trigger physical abuse, such as that seen in shaken baby syndrome.7,8

Colic is characterized by excessive and inconsolable crying, hypertonicity, and wakefulness that cluster in the evening. Its onset usually occurs between the second and sixth weeks of life, and its disappearance, around 3 months, is typically sudden and unexplained. Consensus has not been reached regarding a definition for colic, but most research efforts have relied on modified Wessel criteria.9 Estimates of colic’s prevalence range from 5% to 40%, depending on the definition and methods used.10

Psychological,11,12 gastrointestinal,13-16 and hormonal17,18 explanations for colic’s development have been suggested, but methodological shortcomings have restricted the confidence that can be placed in the findings of many works. These methodological issues include inconsistent definitions for colic, the failure to control for covariates, and potentially biased assessments of exposure and/or outcome variables because of nonprospective study designs. Consequently, there is contradictory evidence regarding colic’s etiology. This uncertainty, along with colic’s frequent occurrence, colic’s potential impact on the family, and the absence of an...
effective cure, underlines the importance of continued research.

Although previous studies have considered dietary causes of colic, methodological issues, including those previously outlined, have limited the comparability of studies and, therefore, precluded definitive conclusions regarding colic’s etiology. Our study was based on the hypothesis that the prevalence of colic among breastfed infants would be lower than among those who were formula fed. The rationale for this hypothesis was derived from the nutritional and immunological superiority of breast milk, relative to formula, and knowledge that the act of breastfeeding provides a unique opportunity for mother-child interaction. By addressing some of the methodological issues noted in earlier works, we believed that this study’s methodological rigor would provide a degree of confidence in its findings that has not been previously conveyed.

METHODS

Approval for this study was received from The University of Western Ontario’s Review Board for Health Sciences Research Involving Human Subjects. An a priori sample-size calculation indicated that 660 participants would need to be enrolled to detect a 10% difference in the proportion of colic among breastfed and formula-fed infants, at a power of 80% and an alpha error of 5%. This estimate was then inflated by 30% to allow for nonparticipation and missing values, resulting in a final sample size of 856.

Data were collected from a cohort of 856 mother-infant dyads; the mothers were delivered of an infant in either of the 2 London hospitals providing obstetrical services. London, located in southwestern Ontario, has a population of 330,000 and approximately 4600 births annually. Both hospitals are affiliated with The University of Western Ontario and provide a full range of obstetrical services that are available 24 hours a day. Eligible participants included English-speaking adult residents of the region who gave birth, at term, to a live singleton whose birth weight was appropriate for gestational age. Mothers were approached in person, before their discharge from the hospital. Those who wanted to participate were provided written consent and an address to which surveys could be mailed.

Self-administered questionnaires, mailed to mothers at 1 and 6 weeks post partum, solicited information on maternal health behaviors, demographic variables, biological factors, and the current source of infant nutrition (exclusively breastfed, complementary fed, and exclusively formula fed). Infants were considered exclusively breastfed if their only milk source was breast milk (including expressed milk). Infants who received any quantity of nonhuman milk along with breast milk were categorized as complementary fed. Standardized instruments that assessed maternal anxiety, postnatal depression, and social support were incorporated into the first questionnaire because these constructs have been suspected of playing a role in colic’s development and/or in mothers’ decisions to breastfeed. These instruments are described further.

The State-Trait Anxiety Inventory is composed of 2 self-report scales that measure 2 distinct anxiety concepts: state anxiety and trait anxiety. The Trait scale asks participants how they generally feel and is indicative of anxiety proneness. The State scale asks participants how they currently feel and sensitively indicates participants’ levels of transitory anxiety. Possible scores range from 20 to 80 on each scale. The psychometric properties of the State-Trait Anxiety Inventory are well established.

The Edinburgh Postnatal Depression Scale is a 10-item self-report scale that was developed specifically for use in the postpartum population. Each item has 4 possible response categories that are scored from 0 to 3; thus, the total score can range from 0 to 30. The Edinburgh Postnatal Depression Scale has optimal sensitivity and specificity when compared with diagnoses of depression made through psychiatric interviews.

Because adequate social support can attenuate the effects of stressful events, a shortened version of the Support Behaviors Inventory was incorporated into the first questionnaire. A total score is calculated by summing the items on which an affirmative response was indicated; thus, this construct is measured on a continuous scale, with scores ranging from 0 to 11.

At 6 weeks post partum, mothers were asked to complete 2 instruments that detailed their infant’s current cry/fuss behaviors: the Barr Baby Day Diary and the Ames Cry Score. The psychometric properties of the Barr Baby Day Diary are well documented. It consists of a series of time rulers that are shaded by parents during the course of a day, for 7 consecutive days. Four horizontal rulers represent each day; each ruler reflects several 6-hour periods, with the smallest division on each ruler being 5 minutes. Within each ruler, parents were asked to shade the appropriate time frame according to which behavior their infant was displaying at that time. Parents were provided with a key that described the manner in which they were to shade the time ruler according to 6 mutually exclusive infant behaviors: sleeping, awake and feeding, awake and content, awake and fussing, awake and crying, and awake and sucking. Cases of colic were then identified as those infants whose cry/fuss behaviors, as recorded in the diary, fulfilled modified Wessel criteria. For this study, a colicky infant was defined as one who was “otherwise healthy and well fed, but who had paroxysms of irritability, fussing, or crying lasting for 3 or more hours in any 1 day and occurring on 3 or more days in any 1 week.”

Because we anticipated that some mothers would find the demands of diary keeping to be onerous, particularly in low socioeconomic status subgroups, mothers were also asked to complete a short questionnaire-based instrument, the Ames Cry Score. The Ames Cry Score is composed of 3 questions, each with 4 response categories that are scored from 0 to 3. It asks about the frequency and average and maximum duration of an infant’s crying during the past week. Overall scores, calculated by summing the scores of individual items, range from 0 to 9, with a score of 3 or greater indicating colic.

Reminder postcards were sent to all participants, and follow-up mailings were used if necessary. The postcards requested that mothers simply return the questionnaire and the Ames Cry Score if they had been unable to complete the diary.

Data were analyzed by the Statistical Product and Service Solutions 9.0 for Windows statistical program (SPSS Inc, Chicago, Ill). The overall prevalence of colic at 6 weeks of age was calculated; similar calculations provided the prevalence of colic among exclusively breastfed, exclusively formula-fed, and complementary-fed infants. For all analyses, the exposure variable was the source of infant nutrition at 1 week post partum, while the outcome, colic, was defined at 6 weeks post partum. This approach addressed one of the shortcomings of earlier works because it permitted an examination of the potential temporal relationship between the source of infant nutrition and colic’s development. All variables were categorical, with the exceptions of labor and social support, maternal anxiety, and postnatal depression, which were measured on continuous scales.

The 2-sample t test, the Mantel-Haenszel χ² test, and the Fisher exact test were used, where appropriate, to analyze group differences. The multivariate analysis was based on binomial logistic regression, using a backward stepwise procedure. For the regression analysis, trait and state anxiety scores were transformed from continuous to scaled variables. Each unit increment on the scale represented a change of 10 points on the origi-
Results

Eligible mothers were approached between January 15 and September 16, 1999. Consent was received from 84% (856/1019) of eligible mothers who were approached. Response rates were above 80% at each stage of data collection (Figure 1), with 72% of those who consented to participate returning a completed study package at 6 weeks post partum. Of those who participated at 6 weeks post partum, 70% completed the Barr Baby Day Diary (Figure 1).

Of the 733 participants who completed the first questionnaire, 680 (93%) were married or had a common-law partner, 611 (83%) were delivered of an infant vaginally, and 611 (83%) were aged 20 to 34 years. Participants tended to be older (mean age, 29.4 years; SD, 4.9 years) and were more likely to be married than those who gave consent but did not complete questionnaires (ie, dropouts) (Table 1). Multiparous mothers were underrepresented in the study sample, relative to the general population (45% vs 58.7%) (Ontario Livebirth Database, 1997). In addition, this sample was well educated, with 75% of mothers indicating that they had completed at least some postsecondary education. Almost 70% of the participants were breastfeeding their infant at 1 week post partum, and a similar proportion of our study sample responded that their annual household income was in excess of Can $40000.

Overall, the prevalence of colic was 24%. When examined separately, the prevalence of colic based on interpretation of the Barr Baby Day Diary was 23%, while that derived from the Ames Cry Score was 29%. The distribution of cry/fuss behaviors (Figure 2) was derived from detailed examination of the 431 diaries that were returned. The mean amount of crying/fussing recorded during an infant’s sixth week of life was more than 13 hours (SD, 7.7 hours). While this is, on average, less than 2 hours per day, the cry/fuss behavior of some infants was truly excessive, with one mother recording that her infant cried/fussed for 45 hours during that week.

The prevalence of colic among exclusively breastfed, exclusively formula-fed, and complementary-fed infants was 23%, 21%, and 29%, respectively (Table 2). In univariate analyses (Table 2), there was no statistically significant relationship between the source of early infant nutrition, measured at 1 week post partum, and the development of colic at 6 weeks post partum (P = .50). Only those additional variables with P < .10 are listed in Table 2. For the multivariate analysis (Table 3), we controlled for several variables: source of early infant nutrition as the risk factor of interest; maternal age and parity, because the experiences of these populations were expected to differ qualitatively; and maternal trait anxiety and shift work, because these variables had been identified as classic confounders (ie, statistically significantly associated with the risk factor and the outcome). Maternal state anxiety was also identified as a classic confounder, but, owing to its high correlation with trait anxiety (r = 0.80), it was permitted to enter the multivariate

Table 1. Characteristics of the Sample

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Participants (n = 733)</th>
<th>Those Who Dropped Out (n = 123)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>53 (65)</td>
<td>28 (35)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Partner†</td>
<td>680 (88)</td>
<td>95 (12)</td>
<td></td>
</tr>
<tr>
<td>Mode of delivery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaginal</td>
<td>611 (85)</td>
<td>108 (15)</td>
<td>.22</td>
</tr>
<tr>
<td>Cesarean section</td>
<td>118 (89)</td>
<td>14 (11)</td>
<td></td>
</tr>
<tr>
<td>Maternal age, y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>14 (54)</td>
<td>12 (46)</td>
<td></td>
</tr>
<tr>
<td>20-34</td>
<td>611 (86)</td>
<td>100 (14)</td>
<td>.001</td>
</tr>
<tr>
<td>≥35</td>
<td>108 (92)</td>
<td>9 (8)</td>
<td></td>
</tr>
<tr>
<td>Parity</td>
<td></td>
<td></td>
<td>.92</td>
</tr>
<tr>
<td>Primiparous</td>
<td>403 (86)</td>
<td>66 (14)</td>
<td></td>
</tr>
<tr>
<td>Multiparous</td>
<td>330 (85)</td>
<td>56 (15)</td>
<td></td>
</tr>
</tbody>
</table>

*Data are given as number (percentage) of mothers. Percentage are based on row totals.
†Being married or having a common-law partner.
model only if it satisfied the variable selection criteria. With the exception of maternal trait anxiety ($P = .007$), none of these factors significantly predicted colic's development.

On the other hand, several other variables did prove predictive (Table 3). If a mother was employed or attended school full-time before being delivered of an infant, her infant was significantly less likely to exhibit colic. Infants born to mothers who were married or had a common-law partner were 70% less likely to exhibit colic, relative to infants born to single mothers. Elevated levels of postnatal depression also seemed protective against colic's development, but this association failed to reach statistical significance ($P = .08$). Abstaining from alcohol was also statistically associated with a reduced likelihood of colic; however, because these 2 variables were measured at the same time point (ie, at 6 weeks), we cannot infer whether mothers did not begin drinking if their infants were not colicky or whether the reverse is true.

Finally, because pacifier use was expected to affect breastfeeding and infant cry/fuss behavior, we considered it a potential confounder. In the end, our results did not change, regardless of whether pacifier use was included in the multivariate model. This observation, taken along with recent evidence that pacifier use is not causally related to early weaning and does not markedly affect the daily duration of cry/fuss behavior,29 prompted our decision to present only those findings derived from the multivariate model that did not include pacifier use.

Despite using prospectively defined, a population-based sample, and multivariate techniques, our results failed to document any relationship between the source of early infant nutrition and colic's development. The absence of a protective effect of breastfeeding on colic's development is robust across time, geography, and study design.1,7,11,27,30-35 These observations lend support to the belief that organic causes (eg, protein intolerance) are responsible for only a small subgroup of cases of colic.36 This, along with the absence of a marked effect of the practice of on-demand nursing on the cry/fuss behaviors of colicky infants,37,38 implies that infants with colic are intrinsically different from infants without colic. Thus, recommendations for the early weaning of colicky infants39 are unfounded.

Our results suggest that almost 1 in 4 infants experienced colic at 6 weeks of age. 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.40,42 The noted discrepancy in the prevalence of colic assessed prospectively (by the Barr Baby Day Diary), compared with an instrument that relied on 1-week recall (the Ames Cry Score), supports the notion that retrospective estimates exceed those derived prospectively.9,11,30-32,41-49 Nevertheless, the Ames Cry Score is reasonably valid for identifying cases of colic when directly compared with the Barr Baby Day Diary (T.J.C., M.K.C., K.N.S., and F.G., unpublished data, 2000).

Given the similarity in the crying patterns of infants with and without colic,31 one limitation of this study...
is its reliance on modified Wessel criteria. At its peak, the median amount of crying is 2.75 h/d, but there exists substantial intraindividual and interindividual variability.\textsuperscript{38,40,41} The distribution of cry/fuss behaviors derived from this cohort (Figure 2) confirms that there is substantial variability in this behavior. Thus, it is still unknown whether the modified Wessel criteria describe a clinically meaningful subgroup of crying infants.\textsuperscript{37,41}

Elevated levels of maternal anxiety have received considerable attention as a contributing factor in colic’s development.\textsuperscript{3,5,11,24,50} In our multivariate model, elevated levels of maternal trait anxiety, measured at 1 week post partum, predicted colicky behavior at 6 weeks; however, this finding failed to reach statistical significance. In addition, the clinical importance of this association is limited given that the multivariate model predicted only 9% of cases of colic. Moreover, the levels of trait anxiety reported in our sample (Table 2) were not remarkable and correspond well with levels seen in another sample\textsuperscript{51} of mothers of healthy children.

There has also been debate about the connection between maternal health behaviors and colic’s development. In contradiction to previous works,\textsuperscript{32,52-54} data collected in this study failed to implicate an infant’s exposure to tobacco smoke in the etiology of colic. In addition, no parturial relationship cannot be inferred. Nevertheless, this may hint at the potential sequelae of an episode of colic, by suggesting that an infant’s excessive crying may prompt the mother to adopt unhealthy behaviors, such as drinking, as a means to cope.

In a novel finding, our study suggests that infants born to mothers who were married or had a common-law partner were 70% less likely to develop colic, relative to infants born to single mothers. The persistence of this variable in the multivariate model suggests that the positive influence of a supportive partner is independent of other factors. Coping skills can be enhanced by social support that is provided by a partner, family members, or friends.\textsuperscript{54} As such, one might speculate that provision of additional support to single mothers during the early postpartum period might have tangible benefits to mother and child. Future research may want to examine this issue in detail.

Admittedly, because the participants in our study were, on average, well educated and relatively affluent, our findings may not generalize to populations that differ in their socioeconomic background and/or access to health care. Nevertheless, the internal validity of our study is high because of the inclusive nature of the study population and high response rates. This internal validity lends support to our conclusion that, in most cases, recommendations to alter an infant’s diet in the hope of ameliorating his or her colic are unfounded.

Although continued uncertainty about colic’s etiology may be viewed in a negative light, our findings should provide comfort to parents: we provide further evidence that parents are not responsible for their infants’ colic. Of course, much work remains to be done to improve our understanding of the underlying processes responsible for colic and to minimize their potential effects on families, particularly those who are already at elevated risk of distress from less-than-ideal financial, social, and/or medical circumstances. If, as some suggest,\textsuperscript{55,56} the origins of colic can be found in disjuncted rhythms, future research needs to determine an optimal manner for identifying infants who are at an elevated risk of state regulatory disorders and to determine methods for entraining their rhythms. Colic’s relatively frequent occurrence and potential sequelae command our continued attention.

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REFERENCES


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