Assessing the relationship between infantile colic and parental migraine in infants aged 4 to 12 weeks in Urmia

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Introduction
Infantile colic affects 5% to 19% of infants. Objectives: This study aimed to investigate the relationship between infantile colic crying and migraine in parents.

Patients and Methods: In this study, the infants referred to Urmia health centers with 4 to 12 weeks old were investigated. According to the definition of infantile colic and questioning the parents, those infants were identified who cried at least three hours a day, at least three days a week, for at least 3 weeks. By filling out a questionnaire on infantile colic and migraine in parents, the relationship between migraine in parents and colic in infants was examined.

Results: In this study, 195 infants aged 4 to 12 weeks were included. Around 107 (54.9%) were male. The mean age of infants was 6.50 ± 2.10 weeks. Of the 195 infants, 65 (33.3%) had colic, 32 (49.2%) were male and 33 (50.8%) were female (P = 0.26). Around 47 (24.1%) of parents had migraine and 148 (75.9%) had no history of migraine. Of 65 infants with colic, 38 (58.5%) had migraine parents and 27 (41.5%) had no history of parental migraine. Of 130 infants without colic, 9 (6.9%) of the parents had a history of migraine and 121 (93.1%) of them had no migraine (P = 0.001). Of 65 infants with colic, 31 of the mothers had migraine, since none of the 130 infants without colic, none of their mothers complained about migraine (P = 0.001).

Conclusion: Infantile colic was significantly associated with parental migraine and it could be an early sign of disease in infants.

Key point
In a study on 195 infants aged 4 to 12 weeks, we found infantile colic was significantly associated with parental migraine and it could be an early sign of disease in infants.
leading to colic crying (18).

While the word colic may lead the reader to the problems of digestive origin, no definitive evidence has yet been found to indicate a direct cause in the gastrointestinal system that could lead to crying in the infant (19). Despite extensive researches in this area, our knowledge of the cause of these cries has not changed significantly from what we learned from the researches of Wessel in 1954 (8). Some studies have suggested that childhood periodic syndromes, such as benign attack vertigo syndrome or benign attack torticollis syndrome, may be the primary manifestations of the genes that later cause migraine (20).

In this regard, there is also information that suggests that infantile colic cries can be also an early manifestation of migraine disease (21,22). How migraine in genetics causes colic is unclear, but it has been suggested that an increased sensitivity to the stimuli such as sound, light, cold air and the movement that occurs during migraine attacks, may be the cause of these cries (23,24). In another study, parents improved their infantile colic crying by controlling and reducing environmental stimuli (14).

**Objectives**
Given the high prevalence of migraine in women, especially Caucasian women, the bad impact of colic crying on family and infant health, and the probable relationship between parental migraine and colic crying in their offspring, this study was conducted to investigate the relationship between colic crying in infants and migraine in parents.

**Patients and Methods**

**Study design**
The current study was a descriptive cross-sectional conducted on the infants aged 4 to 12 weeks old who were referred to Urmia health centers. Regarding the definition of colic and questioning the parents, those infants were identified who were crying at least three hours a day, at least three days a week for at least three weeks; then filling out a questionnaire about infantile colic and migraine in parents, the relationship between migraine in parents and colic in infants was investigated. Exclusion criteria were the existence of any disease or disorder, such as infection or urinary tract stones and gastro-esophageal reflux, which lead to crying and restlessness of the child. According to the corresponding formula for estimating the two proportions with 95% confidence and 90% power and using the results of the study of Gelfand et al (\(P_2 = 0.10, P_1 = 0.22\)) (25), the total sample size was 195 individuals. They were selected at convenience from among the parents with children aged 4 to 12 weeks, who referred to the selected urban health centers of Urmia.

**Ethical issues**
Human rights were respected in accordance with the Helsinki Declaration 1975, as revised in 1983. The informed consent was taken from the patients. The study was approved by ethics committee of Urmia University of Medical Science (Ethical cod# IR.UMSU.REC.1398.056). This study was taken from the medical thesis done by Mahsa Soleimani (#3285).

**Statistical analysis**
To describe the quantitative data, the central and dispersion indices (mean and standard deviation) were calculated and the qualitative variables were reported in frequency and percentage; appropriate tables and diagrams were used as needed. Appropriate statistical tests were used for comparison in terms of data distribution and normality like chi-square. All analyzes were performed using SPSS, version 21, software and the level of significance was lower than 0.05 in all statistical tests (\(P < 0.05\)).

**Results**
In this study, 195 infants aged 4 to 12 weeks were included in the study. Around 107 infants (54.9%) were male and 88 (45.1%) were female. The mean age of infants was 6.50 ± 2.10 weeks. The mean age of the female infants was 6.621.99 ± weeks and in the male infants was 6.40 ± 2.20 weeks. According to the t-test, there was no significant difference between the age of infants (\(P = 0.46\)). Of 195 infants, 65 (33.3%) had colic. About 47 (24.1%) of parents had migraine and 148 (75.9%) had no history of migraine (Table 1). Of 65 infants with colic, 38 parents (58.5%) had migraine and 27 (41.5%) of them had no migraine. Of 130 infants without colic, 9 parents (6.9%) had a history of migraine and 121 (93.1%) were without the history of migraine. According to chi-square test, a significant difference between the history of parental migraine and infantile colic was detected (\(P = 0.001\)). Of 65 infants with colic, 32 (49.2%) were male and 33 (50.8%) were female. Of 130 infants who did not have colic, 75 (57.7%) were male and 55 (42.3%) were female. According to chi-square test, no significant relationship between colic and infantile gender was seen (\(P = 0.26\); Table 2).

Of the 65 infants with colic, 37 (56.9%) were in the age group of 4-6 weeks, 15 (23.1%) in the age group of 6-8 weeks, 10 (15.4%) in the age group of 8-10 weeks and three infants (4.6%) were in the age group of 10-12 weeks. Of the 130 infants who did not have colic, 46 (35.4%) were in

<table>
<thead>
<tr>
<th>Variable</th>
<th>Absolute frequency</th>
<th>Relative frequency</th>
</tr>
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<tbody>
<tr>
<td>Male</td>
<td>107</td>
<td>54.9</td>
</tr>
<tr>
<td>Female</td>
<td>88</td>
<td>45.1</td>
</tr>
<tr>
<td>Total mean age (week)</td>
<td>6.50 ± 10.2</td>
<td></td>
</tr>
<tr>
<td>Male mean age</td>
<td>6.62 ± 1.99</td>
<td>P=0.46</td>
</tr>
<tr>
<td>Female mean age</td>
<td>6.40 ± 2.20</td>
<td></td>
</tr>
<tr>
<td>With colic</td>
<td>65</td>
<td>33.3</td>
</tr>
<tr>
<td>Without colic</td>
<td>130</td>
<td>66.7</td>
</tr>
<tr>
<td>History of migraine in parent, Yes/No</td>
<td>47</td>
<td>24.1</td>
</tr>
<tr>
<td>148</td>
<td>75.9</td>
<td></td>
</tr>
</tbody>
</table>
the age group of 4-6 weeks, 41 (31.5%) in the age group of 6-8 weeks, 30 (23.1%) in the age group of 8-10 weeks and three infants (10%) were in the age group of 10-12 weeks. Chi-square test showed a significant relationship between infantile colic and infant age group ($P = 0.03$; Table 3).

Of 65 infants with colic, 31 mothers of these infants had migraine, and of 130 infants without colic, none of their mothers complained of migraine. According to chi-square test, there was a significant relationship between maternal migraine and infantile colic ($P = 0.001$; Table 4).

Of 65 infants with colic, seven of their fathers had migraine, and six of the fathers of 130 infants (4.6%) had migraine. Chi-square test showed no significant relationships between father’s migraine and infantile colic ($P = 0.10$; Table 5).

**Discussion**

Studies have provided a variety of definitions of infantile colic, all of which have a common characteristic of prolonged cry. The crying of infants naturally increases in the first weeks of life, reaches its peak around the fifth and sixth weeks of life, and then gradually ceases until three months of life (6,7). The most accepted definition of infantile colic in the scientific community is “Rule 3”: crying for at least three hours a day, at least three days a week, and for at least three consecutive weeks. The first two components of this definition have been derived from the studies of Wessel et al (8). Several studies have suggested migraine headaches as the cause of these cries. Thus, the aim of this study was to investigate the relationship between infantile colic and migraine in parents of infants aged 4 to 12 weeks with 195 infants, of whom 107 (54.9%) were male and 88 (45.1%) were female. In our study, 65 (33.3%) of the infants had colic while 32 (49.2%) were male and 33 (50.8%) were female. Although in this study no significant difference between the gender of infants and colic was detected, female infants had the highest percentage of colic ($P = 0.26$). In a study conducted by Gelfand et al, 22 infants (14%) had colic and there were no significant differences in gender between colic patients. Nevertheless, 55% of female infants had colic; these results were consistent with the findings of our study in terms of infant gender, but contradicted it in terms of the percentage of infants with colic. In terms of percentage of infants with colic, 18% of mothers had migraine. The likelihood of colic in infants who had a positive history of migraine in their mothers was 2.6 times compared to the mothers who did not have migraine (29% versus 11%; prevalence ratio 2.6; CI: -1.5 - 5.5, $P = 0.02$).

In a study conducted by Tabrizi et al, a case-control study on the 5-15 year-old children, the relationship between infantile colic and childhood migraine had been examined. Ninety cases (54.88%) were female (26). This was in line with the results of the current study in infants with colic in terms of gender. In this study, 17 (41.46%) children with migraine headaches had a positive history for infant colic compared to the control group (44 , 35.7%) . The history of migraine was higher in the parents of children with colic than in children who did not have colic ($P = 0.001$), which was consistent with the results of the current study. In a study carried out by Ali et al, the incidence rate of infantile colic was 37%, which was relatively consistent with the results of the current study. In their study, 47 parents (24.1%) had migraine, and a significant relationship between infantile colic and migraine in parents was seen ($P < 0.05$). In their study, the infantile colic was evaluated based on the migraine in parents and the results showed a significant relationship between colic and maternal

<table>
<thead>
<tr>
<th>Infantile colic</th>
<th>History of migraine in parent</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>38 (58.5%)</td>
<td>65 (100%)</td>
</tr>
<tr>
<td>No</td>
<td>9 (6.9%)</td>
<td>130 (100%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Infantile colic</th>
<th>History of migraine in mother</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>31 (47.7%)</td>
<td>65 (100%)</td>
</tr>
<tr>
<td>No</td>
<td>37 (52.3%)</td>
<td>72 (100%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Infantile colic</th>
<th>History of migraine in father</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>58 (89.2%)</td>
<td>65 (100%)</td>
</tr>
<tr>
<td>No</td>
<td>124 (95.4%)</td>
<td>130 (100%)</td>
</tr>
</tbody>
</table>

Table 3. Determination of infantile colic frequency by the infant age

<table>
<thead>
<tr>
<th>Infantile colic</th>
<th>Age group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4-6</td>
</tr>
<tr>
<td>Yes</td>
<td>37 (56.9%)</td>
</tr>
<tr>
<td>No</td>
<td>46 (55.4%)</td>
</tr>
<tr>
<td>Total</td>
<td>83 (52.6%)</td>
</tr>
</tbody>
</table>
migraine. However regarding the relationship between the migraine in father and infantile colic, the results of our study showed no significant correlation. In a study by Jean and Al-Buhairi in 2001, a family history of migraine was seen in infants who had migraine (19.29 versus 9.29, P = 0.01). Infants who had a history of colic crying were more likely to have a family history of migraine than those without a history of colic (18.21 versus 10.37, P = 0.0001). These results were consistent with the findings of our study (28). Early childhood periodic syndromes, such as benign attack vertigo syndrome or benign attack torticollic syndrome, can be the primary manifestations of the genes that later cause migraine (20). As new stimuli are present at birth and given their rapid neurodevelopment, the infants’ ability to understand these stimuli rapidly increases in the first weeks of life. For example, between birth and two months of life the visual acuity of the infant is more than twice (28). This remarkable increase in ability can explain the increase in colic in the 6–8 weeks of infancy. Further studies are recommended to determine the relationship between the inherited effects of parental genes on the incidence of infantile colic, to confirm this theory.

Conclusion
The findings of the current study also confirmed that infantile colic was significantly associated with parental diseases therefore parental treatment could also improve infants’ condition; infantile colic can be also an early sign of infant disease.

Limitations of the study
Cross-sectional studies are not assessing the causality, therefore to find precise correlation between infantile colic and migraine, it is suggested to run cohort studies.

Authors’ contribution
EA and AG designed the study, observed accuracy and validity of the study. KD participated in the data collection. MS and KD supervised the project. MS and EA wrote the paper. All authors edited and revised the final manuscript and accepted its publication.

Conflicts of interest
The authors report no conflicts of interest.

Ethical considerations
Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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References
20. Giffin N, Benton S, Goadsby P. Benign paroxysmal torticollis and migraine; However regarding the relationship between the migraine in father and infantile colic, the results of our study showed no significant correlation. In a study by Jean and Al-Buhairi in 2001, a family history of migraine was seen in infants who had migraine (19.29 versus 9.29, P = 0.01). Infants who had a history of colic crying were more likely to have a family history of migraine than those without a history of colic (18.21 versus 10.37, P = 0.0001). These results were consistent with the findings of our study (28). Early childhood periodic syndromes, such as benign attack vertigo syndrome or benign attack torticollic syndrome, can be the primary manifestations of the genes that later cause migraine (20). As new stimuli are present at birth and given their rapid neurodevelopment, the infants’ ability to understand these stimuli rapidly increases in the first weeks of life. For example, between birth and two months of life the visual acuity of the infant is more than twice (28). This remarkable increase in ability can explain the increase in colic in the 6–8 weeks of infancy. Further studies are recommended to determine the relationship between the inherited effects of parental genes on the incidence of infantile colic, to confirm this theory.

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