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Title: Effect of Maternal Depression and Environmental Factors on Infantile Colic

Running Title: Maternal Depression and Infantile Colic

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ABSTRACT

Objective: Infantile colic, a condition with unclear etiology that typically occurs in the evening in the first three months of life among healthy infants, occurs less frequently after three months, the intensity and continuous nature of the act of crying is utterly saddening and wearing for parents. Therefore, we aimed to investigate the effect of maternal depression and other environmental factors on infantile colic.

Material and methods: The mothers of 100 patients diagnosed with infantile colic according to the Rome 4 criteria and 50 healthy control subjects were asked to complete a questionnaire questioning environmental factors and demographic properties

Results: In the comparison of the patients' PHQ2 and PHQ9 test scores, PHQ2 test score was 1.42 ± 1.40102 (0-5) in the control group and 4.09 ± 1.61492 (0-6) in the infantile colic group ($P < 0.001$) according to the PHQ9 test, mothers in the control group attained 6.28 ± 4.915578 (1-21) points, while those in the infantile colic group had 16.47 ± 6.95070 (3-26) points. ($P < 0.001$).

Conclusion: In conclusion, in addition to the importance of using breast milk alone in the first 6 months and avoiding unnecessary antibiotherapy to eliminate risk factors for infantile colic, questioning maternal depression for solving problems of infants with frequent crying attacks is also of importance for family and public health.

Keywords: maternal depression, infantile colic, breastfeeding

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Introduction

In infantile colic, a condition of excessive crying due to unclear etiology, which mostly occurs as attacks in the evenings in healthy infants, is a stressful problem for parents. It is seen in one in every 10 infants. It usually starts in the first weeks after birth and peaks at 6-8 weeks. Although its prevalence decreases between 3 and 6 months, intensity and persistence of the act of crying is utterly saddening and wearing. When maternal depression is added to this stressful condition, infant-mother relationship may be negatively affected (1, 2). Therefore, we aimed to investigate the effect of maternal depression and other environmental factors on infantile colic.

Materials and methods

Patient selection:

This study enrolled a total of 100 patients who presented to the Pediatric Gastroenterology Division and were diagnosed with infantile colic according to the Rome 4 criteria (2) between July 2017 and September 2018, and 50 healthy infants without infantile colic or other chronic disorders who presented to Sütçü İmam University Faculty of Medicine, Department of Pediatrics. A questionnaire form questioning environmental factors and demographic properties and the Patient Health Questionnaire (PHQ) 2 test were completed by patients' mothers under the supervision of a physician. Informed consent and ethical committee approval were obtained prior to study onset (Ethics committee date:11.10.2017 Session:16, Ethics committee Decree No:09, Ethics committee protocol No:161).

Maternal depression:

In order to detect maternal depression, mother of every enrolled patient was administered the PHQ2 test that includes the first two questions (little interest or pleasure in doing things, feeling down, depressed, or hopeless) of the PHQ9 test used to detect depressive emotional status in the last 2 weeks. All mothers were asked to sign one of the answers "not at all=0, several days, more than half the days, nearly everyday". Patients having 3 points or higher were asked to complete the PHQ 9 test (3). According to their scores in the PHQ 9 test, their depression severity was classified as follows:

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Depression severity:

- No depression for point scores of 0-4,
- Mild depression for point scores of 5-9,
- Moderate depression for point scores of 10-14,
- Moderately severe depression for point scores of 15-19,
- Severe depression for point scores of 20-27.

A PHQ-9 score of ≥ 10 has a sensitivity of 88% and a specificity of 88% for major depression (4). Thus, mothers having a score of 10 or higher were considered to be depressed. When they were diagnosed to be depressed, they were referred to adult psychiatry outpatient clinic.

Environmental factors:

A questionnaire form questioning environmental factors was filled by every infantile colic patient. The questioned parameters included maternal psychological prenatal preparation, maternal prenatal nervousness and concern, age of colic onset, gestational week, birth weight, sex, first pregnancy status, newborn jaundice, history of phototherapy, use of formula in the first week of life, maternal antibiotic use in the first week, maternal educational status, maternal occupation, the number of household, maternal smoking status, and household smoking status.

Statistical analysis:

Statistical analyses were performed using Statistical Package for the Social Sciences for Windows (SPSS Inc., Chicago) 16.0 software package. The variables were expressed as mean \pm standard deviation, number (n) and percentage (%). The distribution of the continuous variables was tested using Kolmogorov Smirnov test. Normally distributed variables were compared with Student's t-test or one-sided analysis of variance (ANOVA); non-normally distributed variables were compared using Mann Whitney U-test or Kruskal Wallis test. Chi-square test, Student's t-test or Mann Whitney U-test was used to test statistical significance. Logistic regression analysis was used to show a correlation between a dependent variable and one or multiple variables. A p value of $<0,05$ was considered statistically significant.

Results

A comparison of the groups by demographic properties showed that the mean age was $86.14 \pm 39,435$ days (23-180 days) in the control group and 72.83 ± 47.114 days (23-180 days) in the

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infantile colic group ($P=0.071$). The female/male ratio was 23/27 in the control group and 31/69 in the infantile colic group ($P=0.071$).

A comparison of the patients by mode of delivery revealed that in the control group the number of caesarean sections (C/S) was 19 (38%) and the number of deliveries by normal spontaneous vaginal route (NSVR) 31 (62%) whereas the corresponding figures in the infantile colic group were 55 (55%) and 45 (45%) ($P=0.050$).

There was no significant difference between the study groups with respect to be the first child, receiving phototherapy for jaundice, maternal educational status, maternal occupation, maternal smoking, or housefild smoking ($P=>0.05$). However, prenatal maternal nervousness, maternal antibiotic use in the first week, and use of supplemental food in the first week were significantly more common in the infantile colic group than the control group ($P=0.026$, $P= 0.036$, and $P=0.002$, respectively) An assessment of of patients' mothers by the PHQ2 test revealed that a total of 94 (62.7%) mothers had a score of three or higher. However, depression was deemed non-existent as five patients in the infantile colic group and 2 from the control group, making a total of 7 patients, obtained less than 10 points from the PHQ9 test. Accordingly, only 87 (58%) patients had more than 10 points in the PHQ9 test. Of these, 78 (78%) were mothers of patients with infantile colic and nine (18%) were mother of the subjects in the control group($P=<0.001$).

A comparison of the patients by their scores of the PHQ2 and PHQ9 tests indicated that the mean PHQ2 test score was 1.42 ± 1.40102 (0-5) in the control group and 4.09 ± 1.61492 (0-6) in the colic group ($P=<0.001$) (Table 2). According to the PHQ9 test, mothers in the control group attained 6.28 ± 4.915578 (1-21) points while those in the infantile colic group attained 16.47 ± 6.95070 (3-26) points, with the difference being significant ($P=<0.001$) (Table 2).

A comparison of maternal depression grades between the groups showed that in the control group the number of non-depressed mothers was 28 (56%); the number of mildly depressed ones was 13 (26%); the number of those moderately depressed was 4(8%); the number of moderately severely depressed ones was 4 (8%); and the number of severely depressed ones was 1 (2%). The corresponding figures for mothers of infants with infantile colic were 11

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(11%), 13 (13%), 17 (17%), 26 (26%), and 32 (32%). The inter-group difference was statistically significant ($P < 0.001$) (Table 2).

A logistic regression analysis of factors potentially affecting developing infantile colic showed that gender, age, birth weight, birth week, maternal profession, and maternal educational status did not significantly affect infantile colic risk (Table 3). An evaluation made by delivery mode revealed a significantly higher rate of caesarean section in the infantile colic group ($P = 0.050$) (Table 1). However, a logistic regression analysis did not show that mode of delivery was a risk factor for developing infantile colic (Table 3).

We found that, as independent predictors of infantile colic, using supplemental food other than breast milk in the first month after birth increased the rate of developing infantile colic by 2.792 folds (OR: 2.792 95% confidence interval 1.298-6.005; $P = 0.009$), using formula in the first month by 3.019 folds (OR: 3.019 95% confidence interval (1.489-6.121). (Table 3). We also noted that antibiotic use by breastfeeding mother on the first week increased the odds of infantile colic by a factor of 2.135, a maternal score of three or greater in the PHQ2 test by a factor of 17.310, and a score of 10 or greater by a factor of 16.152. Similarly, among infants with infantile colic, the prevalence of maternal depression was 16.152 fold greater. ($P < 0.01$ for both conditions) (Table 3).

Discussion

Although the exact cause of infantile colic, a condition that deeply affects domestic life, cannot be explained, it is reported to occur more commonly in the first 3 months and show no sex predilection (5, 6). Although a domestic study reported by Akman et al. indicated that infantile colic risk was increased in female gender, our study findings showed that gender is not a risk factor for infantile colic, supporting other studies reporting similar findings (7-9).

An evaluation of maternal working status and mode of delivery by former studies has shown, in agreement with our study, that maternal working and educational status birth weight and gestational week did not affect infantile colic development (6, 9-11). However, as our study, several studies reported that delivery by caesarean section mildly increase infantile colic risk, albeit without statistical significance (11-13).

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Although there are conflicting data about smoking in the literature, it is hypothesized that nicotine increases motilin levels, resulting in phasic intestinal contractions and thus pain (15). Alagöz et al. reported that smoking in the household increased infantile colic risk by 2.4 times (12). Canivet et al. reported that maternal daily smoking increased infantile colic risk (odds ratio (OR) 1.74 (95% confidence interval 1.08-2.82); they reported that there was not any significant correlation between maternal smoking and colic among 5-week-old infants, but they added that breastfeeding reduced infantile colic risk, including those of smoking mothers (13). Although there exist studies advocating that breastfeeding has no protective role on colic development, we demonstrated that smoking in the household did not increase infantile colic risk ($P=0.131$) whereas feeding with supplemental food increased infantile colic rate by a factor of 2.792 (OR:2.792 95% confidence interval (1.298-6.005) $P=0.009$) and using formula in the first week by a factor of 3.019 (OR: 3.019, 95% confidence interval (1.489-6.121) (Table 3) (5).

As for the relationship between infantile colic and antibiotic use, Osterloo et al. reported that using antibiotics in the first week of life was an independent risk factor for developing infantile colic (OR 1.66 (95%CI 1.00-2.77) $P = 0.05$) (15). We also observed that mother's antibiotic use in the first week postpartum increased the risk of infantile colic by a factor of 2.135 (95% confidence interval (1.043-4.330) $P=0.038$). This corroborates the emphasis made by Leppälehto et al. that intrapartum antibiotic exposure paves the way for a change of intestinal microbiota content and colic development by acting on early intestinal colonization (16).

To date, plenty of studies have been done to investigate the effects of maternal depression on infants. It has been stressed that maternal depression may cause unfavorable parent-child interaction as well as a deterioration of domestic relations (17). Radesky et al (1) reported that prolonged crying attacks, particularly those that exceeded 10 minutes, were associated with postnatal depression. Vik et al. reported that, not only mothers and other family members of infants with infantile colic, but also those of prolonged crying episodes had increased prevalence of depression and various other emotional problems (18).

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In our study with PHQ test, the PHQ2 and PHQ9 test scores were about 2.5 times higher among mothers of patients with infantile colic than those of mother in the control group.

We also found that infantile colic increased maternal depression by 16 times compared to the control group, and infants of mothers who scored three or more points had an approximately 17-times increased incidence of infantile colic. This in fact defined the risk of cooccurrence of infantile colic and maternal depression.

The major limitations of our study are absence of keeping infant crying diary and lack of detailed questioning of other factors that can cause maternal depression. However, it gives an idea about whether depressed mothers and other environmental factors increase the rate of infantile colic.

In conclusion, this study showed that only breastfeeding in the first six months and avoidance of unnecessary antibiotherapy could reduce the risk of colic. In addition to this, it is important for family and community health to question the depression of mothers while evaluating the infants with frequent crying attacks.

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Table 1. Comparisons of patients with infantile colic and control groups with respect to demographic and environmental risk factors

	Control group (50)	Patients with infantile colic (100)	P
Age(days)	86.14±39.435(23-180)	72.83±47.114(23-180)	0.071
Sex			0.071
Male	27(54%)	69(69%)	
Female	23 (46%)	31(31%)	
Mode of delivery: C/S	19(38%)	55(55%)	0.050
NSVR	31(62%)	45(45%)	
First infant	18(36%)	39(39%)	0.721
Phototherapy	10(20%)	18(18%)	0.767
Formula use in the first week	23(46%)	72(72%)	0.002
Illiteracy	1(2%)	6(6%)	
Primary school graduate	19(38%)	43(43%)	0.437
High school graduate	19(38%)	27(27%)	
College graduate	11(22%)	24(24%)	
Housewife	41(82%)	75(75%)	0.334
Working mother	9(18%)	25(25%)	
Maternal antenatal nervousness	23(46%)	65(65%)	0.026
Maternal smoking history	8(16%)	15(15%)	0.873
Smoking in the household	32(64%)	51(51%)	0.131
Maternal antibiotic use in the first week	16(3%)	50(50%)	0.036
Chi square,			

C/S: Delivery by caesarean section, NSVR: Normal spontaneous vaginal route.

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Table 2. Inter-group comparison of maternal depression

	Control group (50)	IC patients (100)	P
PHQ 2 score	1.42±1.40102 (0-5)	4.09±1.61492 (0-6)	<0.001
PHQ 9 score	6.28±4.915578 (1-21)	16.47±6.95070 (3-26)	<0.001
Number of depressed mothers	9 (18%)	87 (87%)	<0.001
Number of non-depressed mothers	28 (56%)	11 (11%)	
Mild depression	13 (26%)	14 (14%)	
Moderate depression	4 (8%)	17 (17%)	<0.001
Moderately severe depression	4 (8%)	26 (26%)	
Severe depression	1 (2%)	32 (32%)	
Chi square, Independent student T test			

IC: Infantile colic, PHQ: Patient health Questionnaire

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Table 3. Logistic regression analysis of factors affecting infantile colic development

	p	ODDS	Confidence interval	Risk
Sex	0.073	0.527	0.262-1.061	No
Age	0.089	0.994	0.986-1.001	No
Mode of delivery	0.051	1.994	0.996-3.991	No
Week of delivery	0.942	1	0.999-1.001	No
Birth weight	0.532	0.504	0.059-4.306	No
Use of formula in the first week	0.002	3.019	1.489-6.121	Yes
Use of supplementary food apart from breast milk in the first month	0.009	2.792	1.298-6.005	Yes
Use antibiotics by mother in the first week	0.038	2.135	1.043-4.330	Yes
Mother's profession	0.336	1.519	0.648-3.,559	No
Mother's educational status	0.466	0.865	0.586-1.278	No
Mothers earning a score of 3 or greater from the PHQ 2 test	<0.001	17.310	7.410-40.439	Yes
Mothers earning a score of 10 or greater from the PHQ 9 test	<0.001	16.152	6.816-38.275	Yes
Maternal depression	<0.001	16.152	6.816-38.275	Yes
Logistic regression analysis				

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