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RESEARCH ARTICLE

Correlation of Breastfeeding with Disease Development and Progression in Patients with Multiple Sclerosis

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Abstract

Objective: Breastfeeding during infancy has been shown to be protective against autoimmune diseases. This study aimed to determine the correlation between breastfeeding during infancy and disease development and progression in patients with multiple sclerosis (MS).

Materials and Methods: This study included 180 participants, comprising 90 patients with MS and a control group of 90 healthy individuals. Demographic characteristics, duration of disease, age of onset, number of attacks, annual relapse rate, expanded disability status scale (EDSS) scores, and duration of breastfeeding of patients with MS were recorded.

Results: No significant difference was found between the two groups; the duration of breastfeeding was 13.67±9 months in the MS group and 14.3±9.4 months in the control group. Furthermore, there was no statistically significant difference in age of onset, annual relapse rate, number of attacks, or EDSS values between groups with ≤4 months and >4 months of breastfeeding and between ≤6 months and >6 months of breastfeeding.

Conclusion: According to the results of this study, breastfeeding duration was not significantly correlated with disease development, age of onset, or disease progression in patients with MS. However, further studies with a larger sample group are required to validate the findings.

Keywords: Breastfeeding, multiple sclerosis, disease progression, attack

Introduction

Multiple sclerosis (MS) is a chronic central nervous system disease marked by demyelination and axonal degeneration. The disease exhibits heterogeneity in symptoms, disease course, and outcomes (1). MS is a global problem, and non-traumatic neurological disability is a major cause of disability among young adults. The prevalence of the disease is increasing, and 2.8 million people worldwide are estimated to be living with MS (approximately 900,000 in the United States of America) (2-4). In relapsing MS, women are affected almost three times more frequently than men, and the average age of onset is approximately 30 years (4-6). MS phenotypes are defined as relapsing-remitting MS (RRMS), primary progressive MS (PPMS), active secondary progressive MS (SPMS), and non-relapsing SPMS (7). RRMS is the most common phenotype, affecting approximately 85% of patients with MS. This condition is characterized by alternating episodes of neurological dysfunction, known as relapses, and episodes of relative clinical stability without new neurological symptoms, known as remissions (8).

Diverse environmental and genetic factors are involved in the etiology of MS. Environmental factors such as age, sex, smoking, sunlight exposure, vitamin D levels, race, and climate are known to play a significant role in the development of MS (9). Diet is a crucial environmental exposure during early development (10). Breast milk contains various immunological, biochemical, and cellular components that can considerably alter infection susceptibility and neonatal immunity (11). The correlation between breastfeeding and MS has been examined in several studies so far, but the results are conflicting (12,13). In recent studies, breastfeeding for at least 4 months has been reported to be a protective factor against the risk of MS development, but the role of breastfeeding in determining the risk of MS is yet to be established (14). No previous studies have shown a

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correlation between the duration of breastfeeding and disease progression and the age of onset in patients with MS. Therefore, this study aims to investigate the correlation between breastfeeding during infancy and disease development and progression in patients with MS.

Materials and Methods

A total of 90 patients with MS who were followed up in the MS outpatient clinic of the Neurology Department of Ataturk University Faculty of Medicine between April 1st, 2020, and April 1st, 2021, whose breastfeeding periods were determined, and who met the 2010 McDonald MS diagnostic criteria were included in the study. As a control group, 90 individuals who applied to the outpatient clinic of the Department of Neurology of Ataturk University Faculty of Medicine with the complaint of headache, whose cranial magnetic resonance imaging was normal, and whose age and sex were matched were included in the study. The duration of breastfeeding was learned by contacting the patients' mothers. Individuals who were under the age of 18, whose mothers were not alive, and who had autoimmune diseases and other systemic diseases were excluded from the study. The demographic characteristics and expanded disability status scale (EDSS) scores of the patients with MS were determined.

The approval of the Clinical Research Ethics Committee of the Ataturk University Faculty of Medicine was obtained before commencing the study (decision no: 02, date: 26.03.2020). Informed consent was obtained from the participants.

Statistical Analysis

Means and standard deviations for normally distributed data and medians with minimum and maximum values for non-normally distributed data were used to calculate the summary statistics for all participants. The D'Agostino-Pearson test was used to assess normality. The χ^2 test was used to evaluate categorical variables that were nominal. To compare continuous variables with a normal distribution between the two groups, the Student's t-test was used. The Mann-Whitney U test was used to compare non-normally distributed data, whereas the Spearman rank correlation was used to determine the correlation between non-parametric variables. The Spearman rank correlation was used to ascertain the correlation between non-parametric variables. Two-sided p-values of <0.05 were used to indicate statistical significance. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS 20.0) for the Windows version.

Results

Of the people with MS, 71.1% were women and 28.9% were men. The mean disease duration in the MS group was 8.05±5.5 years. The mean EDSS score was 2.13±1.76. Table 1 presents the demographic and clinical characteristics of both the MS and control groups. The duration of breastfeeding was recorded as 13.67±9 months in the MS group and 14.3±9.4 months in the control group, with no statistically significant difference between the two groups (p>0.05). Furthermore, no significant difference was observed in the duration of breastfeeding between men and women with MS (p>0.05). In addition, there was no statistically significant difference in breastfeeding duration between patients with RRMS and those with progressive MS (SPMS and PPMS) (p>0.05) (Table 2). Moreover, our analysis showed no significant correlation between the duration of breastfeeding and EDSS scores, age of onset, number of relapses, or annual relapse rate (Table 3). The patients with MS and the control group were classified based on the duration of breastfeeding: ≤4 months, >4 months but ≤6 months, and >6 months. The patients with MS did not differ significantly from the controls. In addition, there were no statistically significant differences in EDSS score, age at onset, annual relapse rate, or number of attacks between patients with MS breastfed for ≤4 months and >4 months and between those breastfed for ≤6 months and >6 months (p>0.05) (Table 4).

Discussion

In our study, although the duration of breastfeeding was lower in the MS group than in the control group, the difference was not significant. The duration of breastfeeding was not correlated with the patients' EDSS scores, age of disease onset, number of attacks, or annual relapse rate. Patients with MS and the control group were categorized into groups based on their breastfeeding duration as ≤4 months and >4 months and ≤6 months and >6 months. No statistically significant difference was observed between the MS and control groups in terms of these durations and age of disease onset, annual attack rate, number of attacks, or EDSS values.

Numerous studies have been conducted on environmental risk factors in MS, indicating the significance of environmental effects during infancy and youth. Diet, especially breast milk, is a crucial environmental exposure during early development (14,15). Breast milk, which is a rich source of immunoglobulin, lactoferrin, lysozyme, cytokine, and several other immunologic factors, provides the infant with active and passive immunity. Leukocytes account for 2% of healthy breast milk (16). Leukocytes primarily provide active immunity and support the development of immunity in infants (17). Furthermore, miRNAs, which are present at high levels in breast milk, play a role in promoting the survival of leukocytes in the infant's gastrointestinal tract and might possess immune-protective functions (18). Better Th1 responses have been noted in children breastfed earlier than those breastfed with baby formulas exhibiting immunomodulatory effects (19). Different gut microbiota and stronger memory T-cells and Th17 cell

populations have been reported to develop in breastfed infants compared with those who were bottle-fed (20). Therefore, the World Health Organization recommends that infants be exclusively breastfed for the first 6 months after birth and that partial breastfeeding be continued until at least 2 years of age (21).

Previous studies have identified breastfeeding as a protective factor against bronchial asthma, atopic dermatitis, type 1 diabetes mellitus, and Crohn's disease (22-24). Breastfeeding duration has been shown to exert a gradual effect on certain diseases, such as celiac disease. Breastfeeding for >6 months has been documented to have a protective effect (25,26).

Table 1. Clinical and demographic characteristics of patients with MS and the control group

	MS n=90 mean ± SD; median (min-max)/n(%)	Control n=90 mean ± SD; median (min-max)/n(%)	p-value
Age (year)			
Women	35.76±9; 36 (20-56)	35.78±9; 36 (20-56)	0.76*
Men	35.15±8.2; 35 (21-53)	35.15±8.2; 35 (22-53)	0.76*
Total	35.58±8.7; 36 (20-56)	35.60±8.7; 36 (20-56)	0.99*
Sex			
Female	64 (71.1%)	64 (71.1%)	
Male	26 (28.9%)	26 (28.9%)	
Duration of breastfeeding (month)	13.67±9; 12 (0-48)	14.3±9.4; (0-36)	0.57**
Age of onset (year)	27.51±8.5; (10-50)	–	–
Duration of the disease (year)	8.05±5.5; 7 (1-24)	–	–
Total number of attacks	3.62±2.3; 3 (1-10)	–	
Annual relapse rate	0.57±0.35; 0.5 (0.1-2)	–	–
EDSS	2.13±1.76; 1.75 (0-7)		
Type of disease			
RRMS	77 (85.6%)		
SPMS	11 (12.2%)		
PPMS	2 (2.2%)		
Immunomodulatory medications			
Interferon beta 1a	26 (28.9%)		
Interferon beta 1b	7 (7.8%)		
Glatiramer acetate	7 (7.8%)		
Fingolimod	24 (26.7%)		
Teriflunamide	10 (11.1%)		
Dimethyl fumarate	6 (6.7%)		
Natalizumab	2 (2.2%)		
Ocrelizumab	8 (8.9%)		

*Student's t-test, **Mann-Whitney U test, EDSS: Expanded disability status scale, SD: Standard deviation, MS: Multiple sclerosis, RRMS: Relapsing-remitting MS, PPMS: Primary progressive MS, SPMS: Secondary progressive MS

Table 2. Correlation between sex and type of disease and breastfeeding in patients with MS

	Duration of breastfeeding (months) Mean ± SD; median (min-max)	p-value
Gender		
Male	14.46±8.9; 12 (0-36)	0.52**
Female	13.35±9.2; 12 (0-48)	
Type of disease		
RRMS	13.46±8.86; 12 (0-48)	0.59**
PMS (SPMS + PPMS)	14.92±10.6; 12 (0-30)	

**Mann-Whitney U test, SD: Standard deviation, MS: Multiple sclerosis, RRMS: Relapsing-remitting MS, PPMS: Primary progressive MS, SPMS: Secondary progressive MS

Table 3. Correlation of the duration of breastfeeding with EDSS, age of onset of MS, number of attacks, and annual attack rate in patients with MS

		EDSS	Age of onset of MS, year	Duration of MS, year	Number of attacks	Annual relapse rate
Duration of breastfeeding	r	0.082	-0.081	0.083	0.182	0.037
	p	0.442	0.443	0.436	0.085	0.727

EDSS: Expanded disability status scale, MS: Multiple sclerosis

Table 4. Clinical findings in patients with MS according to breastfeeding durations of ≤4 months and >4 months and ≤6 months and >6 months

	Breastfeeding					
	≤4 months	>4 months	p-value	≤6 months	>6 months	p-value
Healthy control n(%)	29 (24.4%)	61 (75.6%)	0.515*	22 (46.3%)	68 (53.7%)	0.19*
MS n(%)	25 (16.7%)	65 (83.3%)		15 (51.6%)	75 (48.4%)	
Age of onset	25.46±7.3; 23 (16-46)	27.9±9.1; 27 (10-50)	0.939**	25.46±7.3; 23 (16-46)	27.9±9.1; 27 (10-50)	0.28**
EDSS	2.1±2.09; 1 (0-7)	2.14±1.7; 2 (0-7)	0.913**	2.1±2.09; 1 (0-7)	2.14±1.7; 2 (0-7)	0.62**
Annual relapse rate (3)	0.54±0.3; 0.45 (0.1-1.2)	0.58±0.3; 0.5 (0.1-2)	0.967**	0.54±0.3; 0.45 (0.1-1.2)	0.58±0.3; 0.5 (0.1-2)	0.73**
Number of attacks	3.8±2.7; 3 (1-10)	3.57±2.2; 3 (1-10)	0.807**	3.8±2.7; 3 (1-10)	3.57±2.2; 3 (1-10)	0.83**

*Chi-square, **Mann-Whitney U test, EDSS: Expanded disability status scale, MS: Multiple sclerosis

Research has established a positive correlation between the duration of breastfeeding and the development of white matter pathways from 10 months to 4 years of age (27). In a separate study, breastfed children were found to experience a prolonged period of white matter development between 16 months and 2 years of age, resulting in an overall increase in detectable myelin by the age of 2 years, which continues throughout childhood (28). Consistent with the research indicating that breastfeeding impacts myelination timing, children with a longer breastfeeding experience showed increased encephalon volume, cortical thickness, and white matter volume (27,29). Several studies have explored the association between breastfeeding and MS, but the findings have been conflicting. In their study, Spencely and Dick (12) failed to observe a correlation between breastfeeding and the risk of developing MS. In another study, the researchers compared patients with MS who were breastfed for 8.4 months with the control group who were breastfed for 12.5 months. The study revealed a correlation between extended breastfeeding and a reduced risk of MS (13). Breastfeeding for at least 4 months was determined to be related to a reduced risk of developing MS by Conradi et al. (14). Human milk is believed to play a protective role in the pathogenesis of MS owing to its ability to protect against toxins and pathogens as well as modulate the immune response (30,31). Furthermore, breastfeeding may be linked to the ability to promote the development of immunity, including the production of interleukin-10 and immunomodulatory effects with antiinflammatory transforming growth factor-β (27,32). The present study compared the duration of breastfeeding between patients with MS and a healthy control group, and no significant difference was observed. The association between breastfeeding duration and the risk of MS is currently a debatable topic (33). In a case-control study, Ragnedda et al. (34) reported that men who were breastfed for <4 months had an increased risk of MS. Brenton et al. (35) conducted a study that demonstrated a significant correlation between not breastfeeding and the likelihood of developing pediatric-onset MS. Nevertheless, the researchers did not observe a correlation with the duration of breastfeeding. Our study compared patients with MS and a healthy control group with breastfeeding durations of ≤4 months and >4 months and ≤6 months and >6 months but found no significant difference between them. No studies have so far examined the correlation between breastfeeding duration and MS disease progression or number of attacks. Our study found that the duration of breastfeeding was not correlated with EDSS scores, age of onset, number of attacks, or annual relapse rate of patients with MS. To the best of our knowledge, this is the first study on this topic.

Study Limitations

The limitations of our study include the relatively small sample size and the fact that the duration of breastfeeding was obtained from subjective data based on self-reporting.

Conclusion

In conclusion, we report for the first time the absence of a significant association between the duration of breastfeeding in infancy and disease development, age of disease onset, annual attack rate, and disease progression in patients with MS. We recommend conducting the study with a larger sample group.

Ethics

Ethics Committee Approval: The approval of the Clinical Research Ethics Committee of the Ataturk University Faculty of Medicine was obtained before commencing the study (decision no: 02, date: 26.03.2020).

Informed Consent: Informed consent was obtained from the participants.

Footnotes

Authorship Contributions

Surgical and Medical Practices: N.B., Y.D., F.D., F.Ş., Concept: N.B., Y.D., F.D., F.Ş., Design: N.B., Y.D., F.D., F.Ş., Data Collection or Processing: N.B., Y.D., F.D., F.Ş., Analysis or Interpretation: N.B., Y.D., F.D., F.Ş., Literature Search: N.B., Y.D., F.D., F.Ş., Writing: N.B., Y.D., F.D., F.Ş.

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