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Original Article

Does Prebiotic Food Consumption Reduce Sleep Disorder Symptoms in Children With and Without Asthma? A Case-control Study

Prebiyotik Besin Tüketimi Astımlı ve Astımlı Olmayan Çocuklarda Uyku Bozukluğu Semptomlarını Azaltır mı? Olgu Kontrol Çalışması

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ABSTRACT

Objective: This study aims to evaluate the impact of prebiotic food consumption on sleep disturbance symptoms in children with and without asthma.

Method: This is a case-control study. Data were collected from 55 children with asthma and 70 children without asthma, aged 6 to 12 years. Data collection included the Sleep Disturbance Scale for Children (SDSC), Prebiotic Food Consumption Frequency Form, and Childhood Asthma Control Test. The asthma control level of children was determined by a pediatrician following the Global Initiative for Asthma's guidelines.

Results: The average age of children with asthma was 9.16±3.11, while for children without asthma, it was 9.39±3.24. No significant differences were found between children with and without asthma in daytime napping, nighttime awakening, SDSC score, and daily prebiotic food consumption ($p>0.05$). It was observed that children with asthma used more prebiotic-enriched products than children without asthma ($p<0.012$). There was no significant difference in asthma control level, SDSC score, and prebiotic food consumption between children with and without asthma ($p>0.05$). Furthermore, no significant relationship was found between the SDSC score and prebiotic food consumption in children with and without asthma ($p>0.05$).

Conclusion: Prebiotic food consumption's role in determining sleep disturbances and asthma control levels in children with asthma remains uncertain. Further research is needed on the use of prebiotics in children with asthma.

Keywords: Asthma, sleep disorders, prebiotic food consumption, children, case-control studies

ÖZ

Amaç: Astımlı ve astımı olmayan çocuklarda prebiyotik besin tüketim durumunun uyku bozuklukları semptomları üzerine etkilerinin değerlendirilmesi amaçlandı.

Yöntem: Bu çalışma bir olgu kontrol çalışmasıdır. Çalışmada 6-12 yaş arasında olan, astım grubunda 55, kontrol grubunda ise 70 çocuğa ait veriler elde edildi. Verilerin elde edilmesinde Çocuklar için Uyku Bozuklukları Ölçeği (ÇUBÖ), Prebiyotik Besin Tüketim Sıklığı Formu ve Çocukluk Çağı Astım Kontrol Testinden yararlanıldı. Uzman bir pediatri doktoru tarafından Küresel Astım Girişimi kılavuzu doğrultusunda çocukların astım kontrol düzeyi belirlendi.

Bulgular: Astım grubunda yer alan çocukların yaş ortalamasının 9,16±3,11, kontrol grubunda ise 9,39±3,24 olduğu saptandı. Astım ve kontrol grupları arasında gündüz uyuma ve gece uyanma durumu, ÇUBÖ puanı ve günlük prebiyotik besin tüketimi açısından farklılığın olmadığı belirlendi ($p>0,05$). Astım grubunda yer alan çocukların kontrol grubuna göre daha fazla prebiyotikle zenginleştirilmiş ürün kullandığı saptandı ($p<0,012$). Astım kontrol düzeyi ile ÇUBÖ puanı ve prebiyotik besin tüketimi açısından farklılığın olmadığı belirlendi ($p>0,05$). Hem astım hem de kontrol grubunda ÇUBÖ puanı ve prebiyotik besin tüketimi arasında anlamlı bir ilişkinin olmadığı tespit edildi ($p>0,05$).

Sonuç: Astımlı çocuklarda hem uyku bozuklukları hem de astım kontrol düzeyi üzerindeki etkisini belirlemede prebiyotik besin tüketiminin rolü belirsizdir. Astımlı çocuklarda prebiyotiklerin kullanımı ile ilgili daha fazla araştırmaya ihtiyaç duyulmaktadır.

Anahtar kelimeler: Astım, uyku bozuklukları, prebiyotik besin tüketimi, çocuk, olgu-kontrol çalışması

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INTRODUCTION

Asthma, one of the most common chronic respiratory diseases in childhood[1], is characterized by airway obstruction and chronic inflammation of the bronchial mucosa. Asthma symptoms include wheezing, difficulty breathing, and nocturnal cough attacks[2]. Asthma can lead to psychiatric issues in children[3] and adverse effects on cognitive functions and school performance[4]. Additionally, children with asthma often experience sleep disturbances, primarily worsening at night[5,6]. It has been observed that children who experience asthma symptoms more frequently tend to feel significantly more tired and sleepy during the day[6]. Furthermore, children with asthma and/or allergic rhinitis are more likely to suffer from sleep disturbances than healthy children[7,8], especially when asthma is not well controlled[8,9]. Inadequate sleep can exacerbate daytime asthma symptoms and decrease the overall quality of life for children with asthma[10].

Asthma control is paramount in improving the sleep quality of children with asthma, thereby enhancing their quality of life[8,9]. As an environmental factor, nutrition is reported to impact sleep quality. Specifically, prebiotic foods, known as indigestible carbohydrates that enhance the colonization of beneficial microorganisms in the gut, are believed to positively affect asthma symptoms and sleep quality through gut composition modulation[11]. Prebiotics offer several known health benefits and are thought to have a therapeutic effect on asthma parameters by reducing inflammation, particularly concerning asthma. Due to their beneficial effects on gut microbiota, prebiotics are considered to have a potential therapeutic role in asthma. A literature review revealed that prebiotics effectively suppress allergic and autoimmune responses, reduce allergic symptoms, and inhibit allergic airway responses in acute airway inflammation models[11-13].

Upon reviewing the relevant literature, it is evident that prebiotic food consumption could have an impact on sleep quality. The sleep quality of children with asthma is known to be influenced by asthma symptoms. In this context, the effect of prebiotic food consumption on the occurrence of sleep disturbance symptoms in children with asthma is contemplated. This study aims to assess the impact of prebiotic food consumption on sleep disturbance symptoms in children with and without asthma.

Research questions:

1. Is there a difference in sleep disturbance scale scores between children with and without asthma?

2. Is there a difference in prebiotic food consumption between children with and without asthma?

3. Is there a relationship between prebiotic food consumption and sleep disturbance symptoms in children without asthma?

4. Is there a relationship between prebiotic food consumption and sleep disturbance symptoms in children with asthma?

5. Is there a difference in asthma control levels and sleep disturbance scale scores in children with asthma?

6. Is there a difference in asthma control levels and prebiotic food consumption in children with asthma?

MATERIALS and METHODS

Design, Setting, Population, and Sample Size

The research, designed as a case-control study, was conducted at the Karabük Education and Research Hospital Children's Clinic with children aged 6-12 and their mothers. The study population consisted of children aged 6-12 diagnosed with asthma or who came for well-child follow-up at the Karabük Education and Research Hospital Children's Clinic during the study period, along with their mothers.

In the case group, the inclusion criteria for mothers were as follows: Being literate and providing written and verbal consent to participate in the research. For children, the criteria were as follows: being aged 6-12, having a diagnosis of asthma, and providing verbal consent to participate in the research.

In the control group, the inclusion criteria for mothers were as follows: being literate and providing written and verbal consent to participate in the research. For children, the criteria were as follows: being aged 6-12, not having a chronic illness, and providing verbal consent to participate in the research. The G*Power power analysis method determined that a minimum of 102 children, 51 in the asthma group and 51 in the control group, were required to achieve 80% power, a medium effect size (d=0.50), and a significance level of α=0.05. Considering potential data loss, the study was completed with 125 children, including 55 asthma patients and 70 controls.

Measures and Tools

The participant information form (PIF) consists of 21 questions generated by researchers in accordance with the literature, contains sociodemographic characteristics of parents and their children, height, and weight values, information about the children's asthma diagnosis, and sleep habits[1,4-10,14].

Sleep Disturbance Scale for Children (SDSC) developed by Bruni et al.[15] in 1996, the SDSC is a 5-point Likert-type scale (1: Never - 5: Always) that investigates sleep disorders in children aged 6-16 that have occurred within the last six months. The Turkish validity and reliability of the scale were established by Ağadayı et al.[16]. As a result, it was determined that the validity and reliability tests of the SDSC were at an acceptable level. The scale yields a minimum of 26 and a maximum of 130 points. Higher scores are interpreted in favor of sleep disorders[16].

The frequency form of prebiotic food consumption was developed by a dietitian who is also one of the researchers, and it aligns with the existing literature[11-13]. This form includes 25 foods exhibiting prebiotic properties, such as leeks, artichokes, Jerusalem, onions, and garlic. The form assesses how often and in what amounts children consume these foods with eight options: "every day", "5-6 days a week", "3-4 days a week", "1-2 days a week", "once every two weeks", "once a month", and "never". Responses regarding food consumption frequency were calculated through frequency calculations (daily food consumption frequency = quantity/day). The amounts of food and beverage consumed were multiplied by "1" for "every day," "0.7855" for "5-6 times a week," "0.498" for "3-4 times a week," "0.2145" for "1-2 times a week," "0.067" for "once every two weeks," and "0.033" for "once a month" to obtain daily average amounts.

The researchers, including a specialist pediatrician, assessed the asthma control status according to Levels of Asthma Control by Global Initiative for Asthma (GINA) criteria, which encompassed daily symptom frequency, nocturnal symptoms, bronchodilator use, degree of limitation in daily activities, and lung functions. Following evaluation, individuals were classified as having controlled, partly controlled, or uncontrolled asthma[17].

Childhood Asthma Control Test (C-ACT) was developed in 2007 by Liu et al.[18]. This scale aims to measure the levels of asthma control in children aged 4-11. The Turkish validity and reliability study of the scale was conducted by Sekerel et al.[19]. The scale consists of two parts. The first part includes four questions in a visual analog scale format with four pictorial options. These questions are posed to the child and are scored from 0 to 3. The remaining three questions are in a 6-point Likert-type format. The parent should complete this part. Scores on the scale can range from 0 to 27. A cutoff point of 19 is used for the scale, where a score of 19 or lower indicates that the child's asthma is not under control[18,19].

Procedures

Prior to the implementation of data collection forms, mothers were provided with verbal and written informed consent forms explaining the objective of the research, data confidentiality, and their right to withdraw from the study at any time. Mothers who provided consent were included in the research. In addition, the children who participated in the study provided verbal consent.

Mothers of healthy children included in the control group completed the PIF, SDSC, and the "Prebiotic Food Consumption Frequency Form".

Mothers of children with asthma in the case group completed the PIF, SDSC, "Prebiotic Food Consumption Frequency Form", and the second part of the C-ACT, the parental section. The first part of the C-ACT, the child section, was completed by children with asthma under parental and researcher supervision. Subsequently, the pediatrician within the research team determined the level of asthma control according to Levels of Asthma Control by GINA based on the child's examination findings. The assessments of asthma control levels made by parents and children were compared. The comparison revealed that assessments of asthma control levels by parents and children were consistent (Supplementary Table 1). The children's weight and height information, as well as body mass index (BMI9) [(kg)/height(m^2)] and z-scores, were calculated[20,21].

Ethical Considerations

The research was conducted following ethical principles outlined in the Helsinki Declaration. Prior to the study, necessary approvals were obtained from the Karabük University Non-Interventional Clinical Research Ethics Committee (decision no: 2022/816, date: 20.01.2022). Subsequently, institutional approval was obtained from the hospital where the study was conducted (protocol no: E-34771223-774.99). Participants were provided with written informed consent explaining

the purpose of the research, data confidentiality, the voluntary nature of participation, and the right to withdraw from the survey at any time, which was presented on the first page of the questionnaire.

Statistical Analysis

Data analysis was performed using IBM SPSS 27.0 software. Descriptive variables were presented as number (n), percentage (%), mean (X), and standard deviation. Non-normally distributed data were described using median (M) and minimum-maximum values. Data normality was assessed through visual (histograms) and analytical (Kolmogorov-Smirnov) analysis. The chi-square test was employed to evaluate differences between categorical variables among groups.

Similarly, the independent t-test was used to assess differences between normally distributed continuous variables between the two groups. The Mann-Whitney U test was applied for non-normally distributed data. The One-Way ANOVA test was utilized to examine differences in continuous variables among more than two groups. All hypothesis tests were two-tailed, and p-values <0.05 were considered statistically significant.

RESULTS

The study determined that the average age of children in the asthma group was 9.16±3.11 years, while in the control group, it was 9.39±3.24 years. No significant differences were found when comparing the groups based on age, weight, height, and maternal age (p>0.05). While there was no significant difference in BMI values between the groups (p>0.05), the BMI z-scores in the asthma group were statistically significantly higher than those in the control group (p=0.029). Examination of maternal education levels revealed that 41.8% (n=23) of the asthma group and 42.9% (n=39) of the control group had attained a university-level education or higher. There were no statistically significant differences between the asthma and control groups in terms of maternal education level, socioeconomic status, daytime napping, and nighttime awakening (p>0.05) (Table 1).

When comparing the SDSC scores and daily prebiotic food consumption (total prebiotic food intake) between the asthma and control groups, no statistically significant differences were observed (p>0.05). However, it was found that the consumption of prebiotic-fortified products in the asthma group was statistically significantly higher than that in the control group (p=0.012) (Table 2).

Examination of the relationship between SDSC scores and daily prebiotic food consumption in both groups revealed no statistically significant differences (p>0.05) (Table 3).

When comparing asthma control levels with SDSC scores and daily prebiotic food consumption, no statistically significant differences were identified (p>0.05) (Table 4).

DISCUSSION

The initial findings of our study indicated that the SDSC scores of children with asthma were higher than those of children without asthma, albeit not significantly so. Similarly, there was no significant difference between the asthma and control groups regarding daytime napping and nighttime awakening frequency. In contrast to our findings, van Maanen et al.[6] reported that children with frequent asthma symptoms were more likely to experience daytime sleepiness/fatigue than children with seldom or no asthma symptoms. Urrutia-Pereira et al.[8] also found that children with asthma and/or allergic rhinitis exhibited more frequent sleep disturbances when compared to controls. Furthermore, no difference in asthma control levels and SDSC scores was observed in the current study. In the literature, several studies have shown that as the rate of asthma symptoms increases and asthma control worsens, sleep disturbances become more common. Suleyman et al.[14] reported decreased sleep duration and increased nocturnal awakenings in uncontrolled asthma.

Similarly, when children with well-controlled asthma or no asthma were compared to those with poorly controlled asthma, it was found that children with poorly controlled asthma had poorer sleep patterns, had more problems falling asleep, and had more sleep disruptions[22]. Despite the absence of differences in sleep disturbances between our groups, the asthma group had a higher SDSC score with a borderline p-value of 0.50. This inconsistency with the literature is thought to be due to the smaller sample size of our study. Further, the literature suggests the presence of numerous factors in children, such as urban factors, that can affect sleep outcomes alongside asthma symptoms[23]. It is assumed that unaccounted factors may have influenced the study's outcomes.

Our study showed no difference in prebiotic food consumption between the asthma and control groups. Moreover, no difference was observed between asthma control levels and prebiotic food consumption. Wawryk-

Table 1. Demographic and anthropometric characteristics of the children (n=125)			
	Asthma (n=55)	**Controls (n=70)**	
	Mean ± SD/Median (min-max)[a]	**Mean ± SD/Median (min-max)[a]**	**p-value**
Age (years)[c]	9.16±3.11	9.39±3.24	0.699
Body weight (kg)[d]	30.00 (17.0-100.0)	29.50 (19.0-95.0)	0.253
Body height (cm)[d]	132.00 (104.0-182.0)	129.50 (105.0-177.0)	0.560
BMI (kg/m²)[c]	19.91±4.83	18.57±4.12	0.098
BMI (z score)[d]	0.85 (-2.18-4.26)	0.30 (-5.57-3.41)	0.029[b]
Mother's age (years)[c]	37.11±5.18	37.89±5.12	0.405
	n (%)	**n (%)**	
Mother's Educational Status[e]			
Primary school	9 (16.4)	6 (8.6)	0.599
Middle school	8 (14.5)	12 (17.1)	
High school	15 (27.3)	122 (31.4)	
University or higher	23 (41.8)	30 (42.9)	
Socioeconomic status[e]			
Income less than expense	9 (16.4)	14 (20.0)	0.522
Income equals expense	39 (70.9)	43 (61.4)	
Income more than expenses	7 (12.7)	13 (18.6)	
Daytime sleep status[e]			
Yes	7 (12.7)	6 (8.6)	0.450
No	48 (87.3)	64 (91.4)	
Night waking condition[e]			
Yes	24 (43.6)	26 (37.1)	0.462
No	31 (56.4)	44 (62.9)	

[a]Mean ± standard deviation (SD) was used in parametric tests and median [minimum-maximum (min-max] was used in non-parametric tests. [b]p<0.05. [c]Student t-test used. [d]Mann-Whitney U test used. [e]The chi-square test used, min-max: Minimum-Maximum, BMI: Body mass index

Table 2. Comparison of asthma and control groups' total prebiotic food intake and SDSC score (n=125)			
	Asthma (n=55)	**Controls (n=70)**	
	Mean ± SD	**Mean ± SD**	**p-value[a]**
The SDSC total score	43.09±10.33	39.72±8.63	0.050
Total prebiotic food intake (g/day)	529.40±281.12	519.43±288.23	0.721
Prebiotic fortified products (g)[c]	4.61±7.44	2.83±6.75	0.012[b]

[a]The Independent t-test used. [b]p<0.05. [c]The use of prebiotic fortified products was also included in the total prebiotic consumption, SDSC: Sleep Disturbance Scale for Children, SD: Standard deviation

Gawda et al.[24] found that prebiotics and synbiotics effectively reduced asthma incidence in children in the first months after birth. Stokholm et al.[25] found that infants born via cesarean section had a greater risk of asthma in their sixth year of life, indicating that cesarean delivery impacted gut composition in the first year of life. Therefore, they emphasized the importance of the appropriate composition of gut bacteria in asthma prevention. Despite the absence of differences in prebiotic food consumption between groups in our study, it was determined that using prebiotic-enriched products was higher in children with asthma.

Furthermore, in our study, asthma and control groups exhibited homogeneity regarding socioeconomic status, maternal age, and education level. Thus, it is thought that this difference in the consumption of prebiotic-enriched products may be attributed to a higher inclination of mothers of children with asthma to resort to alternative methods due to the information they acquire during

frequent doctor visits and the presence of asthma symptoms, compared to the control group. In the literature, some studies support the reduction of asthma or recurrent wheezing risk with early prebiotic use[26] and suggest that it has no effect on upper respiratory tract infections[27]. The World Allergy Organisation's guidelines on prebiotics in allergy prevention recommend prebiotic supplementation only for infants not receiving breast milk and no prebiotic supplementation for breastfed infants. However, both recommendations are based on very low-certainty evidence[28]. Moreover, the relationship between prebiotic consumption and respiratory symptoms varies depending on the strain used and the duration of consumption[29]. In conclusion, there is limited evidence to recommend prebiotic use for preventing and managing asthma in children, and better-designed studies are needed[30].

Our study did not reveal a relationship between prebiotic food consumption frequency and SDSC scores in the asthma and control groups. It is assumed that this is due to the influence of various variables affecting gut microbiota, such as sleep patterns, the immune system, the endocrine system, stress/anxiety, and environmental factors. A literature review did not yield any studies investigating the relationship between prebiotic consumption and sleep disorders in children with asthma. In line with the present study, a meta-analysis study reported that probiotic or prebiotic interventions did not significantly improve sleep quality, indicating a need for more evidence[31]. In contrast to our study, recent years have seen increasing recognition of the critical role of bidirectional communication in the gut-brain axis in the etiology and pathogenesis of sleep disorders[32]. In a randomized controlled study involving healthy infants, infants fed with prebiotic-enriched formula had shorter episodes of crying/restlessness and longer sleep onset durations than the control group[33].

Further, the literature has also examined the effects of prebiotics on sleep through various animal experiments. A study conducted by Bozorgmehr et al.[34] in mice reported that supplementation of human milk oligosaccharides, a prebiotic, had the potential to protect against the development of asthma in later life. Other animal experiments have also shown positive effects of prebiotics on sleep quality[35,36]. However, well-structured randomized controlled trials are needed to understand better the relationship between prebiotic consumption and sleep disorders in children with asthma.

Practice Implications

Prebiotic food consumption's role in determining sleep disorders and asthma control levels in children with asthma remains unclear. The findings indicate the need for further research on the use of prebiotics in children with asthma. Positive interventions to improve sleep quality in children with asthma have been reported in the literature[1]. In this context, multidisciplinary teams should plan comprehensive interventions for children and parents to improve sleep quality and prevent sleep disorders in children with asthma.

Study Limitation

One of our study's strengths is that it is one of the first to investigate the relationship between sleep disorders

Table 3. The relationship between asthma and control groups' total prebiotic food intake and SDSC score (n=125)

		Asthma (n=55)		Controls (n=70)	
		SDSC	Total prebiotic food intake (g/day)	SDSC	Total prebiotic food intake (g/day)
SDSC	r	1		1	
	p				
Total prebiotic food intake (g/day)	r	-0.114	1	-0.162	1
	p	0.416		0.181	

r: Pearson's correlation coefficient, SDSC: Sleep Disturbance Scale for Children

Table 4. The association between total prebiotic food intake and SDSC score with the asthma control level (n=55)

	Levels of asthma control by GINA			
	Controlled	Partly controlled	Uncontrolled	p-value
The SDSC total score[a]	41.00±9.89	42.75±13.62	43.29±10.33	0.948
Total prebiotic food intake (g/day)[a]	545.72±144.73	596.75±354.59	507.84±281.12	0.639

[a]One-Way ANOVA, SDSC: Sleep Disturbance Scale for Children, GINA: Global Initiative for Asthma

and prebiotic food consumption in children with asthma. Furthermore, the assessment of asthma control levels by both the pediatrician and the mother and child enhances the reliability of our study.

Study Limitation

Our study has several limitations. Firstly, other factors that can influence sleep patterns (such as stress/anxiety, light, the endocrine system, etc.) could not be controlled due to the nature of the study. Additionally, the study was conducted only in children aged 6-12 years and at a single center. The generalisability of the relationship between prebiotic food consumption and sleep disorders in children with asthma and other age groups is limited.

CONCLUSION

Sleep disorder symptoms are frequently observed in children with asthma. In recent years, the effectiveness of prebiotic consumption in improving sleep quality in children has been acknowledged. The results of this study contribute to the understanding of the relationship between sleep disorder symptoms and prebiotic food consumption in children with and without asthma. Our study discovered no differences between the asthma and control groups regarding sleep disorder scale scores and prebiotic food consumption. However, the use of prebiotic-enriched products was found to be higher in the asthma group. It was also determined that sleep disorder scale scores and prebiotic food consumption did not differ with asthma control levels.

Ethics

Ethics Committee Approval: Prior to the study, necessary approvals were obtained from the Karabük University Non-Interventional Clinical Research Ethics Committee (decision no: 2022/816, date: 20.01.2022).

Informed Consent: Written consent was obtained from all patients.

Author Contributions

Concept: E.D., A.T., B.D., Design: Ö.Ö.Ş., B.D., Y.T., Data Collection or Processing: E.D., A.T., Y.T., Analysis or Interpretation: Ö.Ö.Ş., B.D., Y.T., Literature Search: Ö.Ö.Ş., E.D., A.T., B.D., Y.T., Writing: Ö.Ö.Ş., E.D., A.T., B.D., Y.T.

Conflict of Interest: The authors have no conflict of interest to declare.

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Supplementary Table 1. Parent-child and doctor ratings of the asthma control levels in children (n=55)

		Levels of asthma control by GINA			
		Controlled	Partly controlled	Uncontrolled	p-value[a]
		C-ACT	C-ACT	C-ACT	
C-ACT	Controlled	1 (6.7)	2 (13.3)	12 (80.0)	0.526
	Uncontrolled	1 (2.5)	10 (25.0)	29 (72.5)	

[a]The chi-square test used, C-ACT: Childhood Asthma Control Test, GINA: Global Initiative for Asthma