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Review
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The Relationship Between Breastfeeding and Attention Deficit and Hyperactivity Disorder: What Do We Know? A Systematic Review

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ABSTRACT

The aim of this study is to examine the relationship between breastfeeding, which is an important factor in protecting and improving child health, and attention deficit/hyperactivity disorder (ADHD), which is an increasingly common public health problem, and to determine the current situation in the literature. Studies published in English before May 2023 using the Web of Science, PubMed, and Scopus databases were searched. Ten cross-sectional, 10 case-control, 12 cohort studies, and 2 randomized controlled trials involving a total of 420 694 participants were included in this study. A total of 34 studies conducted between 2007 and 2022 were included in the systematic review. The lack of a standardized definition of ADHD diagnoses and breastfeeding categorizations in the included studies leads to different results between studies. The findings suggest that breastfeeding may be associated with a reduced risk of ADHD in children. Breastfeeding could potentially serve as a protective factor for ADHD; however, high-quality longitudinal studies are needed to confirm or refute this causality and to understand the underlying potential mechanisms.

Keywords: ADHD, attention deficit-hyperactivity disorder, breastfeeding, human milk, systematic review

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INTRODUCTION

Breast milk, far beyond being a physiological secretion containing highly bioavailable macro and micronutrients, is a unique substance produced for each infant. It contains various bioactive compounds, including macrophages, T lymphocytes, pluripotent stem cells, growth factors, and extracellular miRNA (microRNA). The cells within breast milk facilitate intercellular communication through cytokines and chemokines, effectively making it a living organism. The use of this "extraordinary" food by the infant is directly related to the infant's short- and long-term health and well-being. Studies have shown that breast milk provides protection against diseases related to different systems, such as necrotizing enterocolitis, inflammatory bowel disease, childhood leukemia, and asthma. It has also

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been found to reduce the risk of sudden infant death syndrome and, indirectly, protect oral and dental health from potential issues associated with bottle feeding.[1,2]

Breast milk is also an important source of omega-3 and omega-6 fatty acids, which are essential for the development of the infant's central nervous system. Docosahexaenoic acid (DHA), an omega-3 fatty acid, is an essential long-chain polyunsaturated fatty acid for humans that is found in the structure of the brain and retina and is associated with cognitive processes. Arachidonic acid (ARA), an omega-6 fatty acid, plays a significant role in brain development.[3]

However, current research continues to explore not only the physical health effects of breastfeeding but also its relationship with the neurocognitive development of the baby, its impact on bonding with the mother, and its association with complex psychiatric disorders. In this context, one of the conditions that are examined in relation to breastfeeding and have a complex pathophysiology is attention deficit/hyperactivity disorder (ADHD), among the most frequently diagnosed neurodevelopmental disorders in childhood.[4-6]

According to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), ADHD is a neurodevelopmental disorder characterized by persistent inattention and/or hyperactivity that affects functionality and development.[7] Despite various estimates regarding the prevalence of this neurodevelopmental disorder, a global prevalence of 8.0% was reported in an umbrella review published in 2023.[8,9]

Attention deficit/hyperactivity disorder diagnosis is often made during childhood, and symptoms are estimated to persist into adulthood in about half of those diagnosed.[10,11] Attention deficit/hyperactivity disorder leads to an academic decline in childhood, job failure in later years, and social problems throughout all periods. It is also associated with addiction and suicide. Furthermore, due to its increasing medical burden on national healthcare systems, ADHD is recognized as a growing public health concern.[12-14]

Attention deficit/hyperactivity disorder, diagnosed clinically, has heterogeneous findings in the literature regarding its etiology. While genetic factors play a role in ADHD development, along with fetal and perinatal conditions, pesticide exposure, maternal smoking, social and family conditions, the true causality has not yet been resolved.[5,15-21]

Considering the effects of the bioactive compounds in breast milk on the infant's neurocognitive system, it would not be surprising for breastfeeding to serve as a potential protective mechanism against ADHD. However, due to the complex structure of the components in breast milk and the yet-to-be-determined definitive etiology of ADHD, the potential protective effect of breast milk must be examined from a multidimensional perspective. This effect is likely influenced by dose/duration dependency, genetic predisposition, socioeconomic environment, and fetal-perinatal factors. Furthermore, focusing solely on the biochemical composition of breast milk in the context of the ADHD relationship may overlook other psychosocial dynamics, such as the positive effects of breastfeeding on mother-infant bonding and parenting attitudes associated with breastfeeding.[4,22-24]

Despite all the known benefits of breast milk, less than half of infants worldwide are fed breast milk for the recommended duration and frequency. Particularly in high-income countries, where access to formula is easier, breastfeeding rates are generally reported to be lower.[5,25]

Regardless of the mechanism that may underlie the potential protective effect of breastfeeding against ADHD, if proven through well-conducted studies, it will provide an additional and persuasive rationale for promoting breastfeeding. In order to demonstrate that breast milk is a unique food for infants and that formula milk is not an alternative to breast milk, it is important to highlight the relationship between breast milk and more recent, rising diseases, in addition to its well-known health benefits. In the absence of definitive evidence regarding its protective effect, it remains crucial to continue supporting the potential benefits of breastfeeding through scientific literature. This involves thoroughly analyzing the existing literature to identify gaps and planning new studies based on these insights. In this context, the aim of the present study was to review the literature on the breastfeeding ADHD relationship holistically using objective quality scores and to guide the planning of future studies.

MATERIALS AND METHODS

Study Design

This study was conducted in accordance with the Preferred Reporting Elements for Systematic Reviews and Meta-analyses (PRISMA) and was registered in the International Prospective Systematic Review Registry (PROSPERO) under the code CRD42024497325.[26]

Search Strategy

This review involved a comprehensive search of studies concerning breastfeeding and ADHD, utilizing databases such as Web of Science, PubMed, and Scopus up to March 2023. The search criteria are outlined in Tables 1-3, focusing exclusively on English-language human studies. The searches were limited to human studies that were published in English. The keywords used were "Breast Feeding" or "Breastfeeding" or "Breast Fed" or "Breastfed" or "Breast Milk" or "Milk, Breast" or "Human Milk" or "Milk, Human" to identify articles pertaining to breastfeeding. The keywords were used "Attention Deficit Disorders with Hyperactivity" or "Attention Deficit Hyperactivity Disorder" or "Attention Deficit-Hyperactivity Disorder" or "Attention Deficit-Hyperactivity Disorders" or "Deficit-Hyperactivity Disorder, Attention" or "Deficit-Hyperactivity Disorders, Attention" or "Disorder, Attention Deficit-Hyperactivity" or "Disorders, Attention Deficit-Hyperactivity" or "Attention Deficit Hyperactivity Disorders" or "Attention Deficit Disorder" or "Attention Deficit Disorders" or "Deficit Disorder, Attention" or "Deficit Disorders, Attention" or "Disorder, Attention Deficit" or "Disorders, Attention Deficit" or "Hyperkinetic Syndrome" or "Syndromes, Hyperkinetic" or "ADHD" or "ADDH" to select the studies encompassing the target population. In another systematic review conducted by Zeng et al,[13] PubMed and Embase databases were searched. In this study, Scopus and Web of Science databases were also searched along with the PubMed database using the keywords listed in Tables 1-3.

Eligibility Criteria

We incorporated studies that met the following inclusion criteria: (1) used cross-sectional, case-control, cohort studies, or randomized controlled trial (RCT) designs; and (2) explored the relationship between maternal breastfeeding and the risk of ADHD in children. Reviews, animal research studies, guidelines, commentaries, declarations, cover letters, research letters, workshops, brief reports, case reports, ecological studies, and book/book chapters were excluded.

Table 1. Search Strategy in PubMed*

Searching Terms
1. Breastfeeding [MeSH Terms]
2. Breastfeeding OR Feeding, Breast OR Exclusive Breast Feeding OR Breast Feeding, Exclusive OR Exclusive Breastfeeding OR Breastfeeding, Exclusive [Title/Abstract]
3. 1 OR 2
4. Attention Deficit Disorder with Hyperactivity [MeSH Terms]
5. Attention Deficit Hyperactivity Disorders OR Attention Deficit Disorders with Hyperactivity OR Attention Deficit-Hyperactivity Disorders OR Attention Deficit-Hyperactivity Disorder OR Deficit-Hyperactivity Disorder, Attention OR Deficit-Hyperactivity Disorders, Attention OR Disorder, Attention Deficit-Hyperactivity OR Disorders, Attention Deficit-Hyperactivity OR Hyperkinetic Syndrome OR Syndromes, Hyperkinetic OR ADDH OR Attention Deficit Hyperactivity Disorder OR Attention Deficit Disorder OR Attention Deficit Disorders OR Deficit Disorder, Attention OR Deficit Disorders, Attention OR Disorder, Attention Deficit OR Attention deficit/hyperactivity disorder OR Disorders, Attention Deficit OR Brain Dysfunction, Minimal OR Dysfunction, Minimal Brain OR Minimal Brain Dysfunction OR ADHD
6. 4 OR 5
7. 3 AND 6

MeSH, medical subject headings.
*Last search date June 2023.

Table 2. Search Strategy in Scopus*

Searching Terms
1. TITLE-ABS-KEY (“Breastfeeding”) OR (“Breast Fed”) OR (“Breast Milk”) OR (“Human Milk”) OR (“Milk, Breast”) OR (“Breastfed*”) OR (“Milk, Human”) AND TITLE-ABS-KEY
2. (“Attention Deficit Disorders with Hyperactivity”) OR (“ADHD”) OR (“Attention Deficit Hyperactivity Disorder*”) OR (“Hyperkinetic Syndrome”) OR (“Syndromes, Hyperkinetic”) OR (“Attention Deficit-Hyperactivity Disorder*”) OR (“Deficit-Hyperactivity Disorder*, Attention”) OR (“Disorder*, Attention Deficit-Hyperactivity”) OR (“ADDH”) OR (“Attention Deficit Hyperactivity Disorders”) OR (“Attention Deficit Disorder*”) OR (“Deficit Disorder*, Attention”) OR (“Disorder*, Attention Deficit”)
3. AND EXCLUDE (DOCTYPE , “re”) OR (DOCTYPE , “ch”) OR (DOCTYPE , “bk”) OR (DOCTYPE , “cp”) OR (DOCTYPE , “no”) OR (DOCTYPE , “sh”) OR (DOCTYPE , “ed”) OR (DOCTYPE , “le”) OR (DOCTYPE , “dp”) OR (DOCTYPE , “tb”)
4. AND LIMIT-TO (LANGUAGE , “English”)

ABS, abstract; KEY, keywords.
*Last search date June 2023.

Table 3. Search Strategy in Web of Sciences*

Searching Terms
1. ((((((ALL=(Breastfeeding)) OR ALL=(Breast Fed)) OR ALL=(Breast Milk)) OR ALL=(Human Milk)) OR ALL=(Milk, Breast)) OR ALL=(Breastfed*)) OR ALL=(Milk, Human) AND
2. ((((((((((((ALL=(Attention Deficit Disorders with Hyperactivity)) OR ALL=(ADHD)) OR ALL=(Attention Deficit Hyperactivity Disorder*)) OR ALL=(Hyperkinetic Syndrome)) OR ALL=(Syndromes, Hyperkinetic)) OR ALL=(Attention Deficit-Hyperactivity Disorder*)) OR ALL=(Deficit-Hyperactivity Disorder*, Attention)) OR ALL=(Disorder*, Attention Deficit-Hyperactivity)) OR ALL=(ADDH)) OR ALL=(Attention Deficit Hyperactivity Disorders)) OR ALL=(Attention Deficit Disorder*)) OR ALL=(Deficit Disorder*, Attention)) OR ALL=(Disorder*, Attention Deficit)

*Last search date June 2023.

Data Extraction

Two researchers (FYE and BÇ) independently extracted the subsequent data: first author, publication date, country, sample sizes, research design, ADHD diagnosis, percentage of ADHD female individuals, definition of maternal breastfeeding and ADHD, and potential confounders included as outcome. Any discrepancies were resolved through discussion with the other 2 researchers (ANK, ÖÖ). Since meta-analysis was not the objective of the study, the results were recorded in their original form without any standardization during the data extraction process.

Study Quality Assessment

New Castle Ottawa Scale (NOS) was used as a quality assessment tool for cross-sectional, case-control, cohort studies, and RCTs.[27,28] Two authors (KB and ED) conducted the assessment of article quality, with any disparities resolved through discussion with a third author (ÖÖ). Quality assessment of the eligible studies were demonstrated in Table 4.

Literature Search

We identified 396 articles through PubMed, Scopus, and Web of Science. After removing 143 duplicates and excluding 218 studies

Table 4. Quality Assessment

Study	Study Type	S1	S2	S3	S4	C1	O1	O2	Total	
Romanos et al,[29] 2010	Cross-sectional	1	1	1	2	2	2	1	10	
Adesman et al,[30] 2017	Cross-sectional	1	1	1	2	2	2	1	10	
Brasfield et al,[21] 2021	Cross-sectional	1	1	1	2	2	1	1	9	
Newman et al,[31] 2014	Cross-sectional	1	1	0	1	2	1	1	7	
Zhou et al,[32] 2023	Cross-sectional	1	1	1	1	2	1	1	8	
Baker et al,[33] 2023	Cross-sectional	1	1	1	1	2	1	1	8	
Deng et al,[34] 2022	Cross-sectional	1	1	1	1	2	1	1	8	
Park et al,[35] 2014	Cross-sectional	1	1	1	1	2	1	1	8	
Al Hamed et al,[36] 2008	Cross-sectional	1	1	1	1	1	1	1	7	
Soled et al,[6] 2021	Cross-sectional	1	1	1	2	2	2	1	10	
		S1	S2	S3	S4	C1	E1	E2	E3	Total
Sepehrmanesh et al,[37] 2022	Case-control	1	0	1	1	2	0	1	1	7
Golmirzaei et al,[38] 2013	Case-control	1	1	0	1	1	0	1	1	6
Gu et al,[39] 2018	Case-control	1	1	0	0	1	1	1	1	6
Say et al,[40] 2015	Case-control	1	0	0	1	1	1	1	0	5
Van Dyk et al,[41] 2014	Case-control	1	0	0	1	2	1	1	0	6
Mimouni Bloch et al,[42] 2013	Case-control	1	0	0	1	2	1	1	0	6
Stadler et al,[43] 2016	Case-control	1	0	1	0	2	1	1	1	7
Türkoğlu et al,[44] 2015	Case-control	1	0	0	0	2	1	1	1	5
Field et al,[45] 2014	Case-control	1	1	1	0	1	1	1	1	7
Sabuncuoğlu et al,[46] 2014	Case-control	1	1	0	1	2	1	1	0	7
		S1	S2	S3	S4	C1	O1	O2	O3	Total
Rodrigues et al,[47] 2022	Cohort	1	1	1	0	2	0	1	1	7
Härtel et al,[48] 2020	Cohort	1	1	1	1	2	0	1	1	7
Julvez et al,[49] 2007	Cohort	1	1	1	1	2	0	0	1	7
Lemcke et al,[50] 2016	Cohort	1	1	1	1	2	1	1	1	9
Boucher et al,[20] 2017	Cohort	1	1	1	0	2	0	0	1	6
Schwenke et al,[51] 2018	Cohort	1	1	1	0	2	1	1	0	7
Kim et al,[52] 2021	Cohort	1	1	1	1	2	1	1	1	9
Girard et al,[53] 2019	Cohort	1	1	1	1	2	0	1	1	8
Amiel Castro et al,[9] 2021	Cohort	1	1	1	1	2	0	1	1	8
Ji et al,[54] 2018	Cohort	1	1	0	0	2	1	1	1	7
Gibson et al,[55] 2022	Cohort	1	1	1	1	2	1	1	1	9
Belfort et al,[19] 2022	Cohort	1	1	1	1	2	0	1	1	8
		S1	S2	S3	S4	C1	E1	E2	E3	Total
Timby et al,[56] 2021	RCT	0	1	1	1	1	1	1	1	7
Nieto-Ruiz et al,[57] 2020	RCT	0	1	1	1	2	1	1	0	7

C, comparability; E, exposure; O, outcome; RCT, randomized controlled trials; S, selection.

based on type, topic, language, full-text availability, or exposure, 34 studies involving 420 694 children were included. One study (San Mauro et al[58]) was excluded due to a sample entirely composed of children with ADHD, which conflicted with the study hypothesis. Authors of inaccessible full texts were contacted but did not respond. A detailed flow chart is shown in Figure 1.

RESULTS

Study Characteristics

The characteristics of the 34 studies included in the review are presented in Table 5. Ten cross-sectional, 10 case-control, 12 cohort studies, and 2 RCTs involving a total of 420 694 participants were included in this study. Of the studies included in the review, 19.4% (n = 7) were conducted in the USA, 11.1% (n = 4) in Spain, 8.3% (n = 3) in Türkiye, 8.3% (n = 3) in Germany, and another 8.3% (n = 3) in China. The earliest study that met the eligibility criteria dated back to 2007, and the publication years of the studies ranged from 2007 to 2022. These studies particularly included data on children born after 2000. Studies containing data on children from the 1990s were relatively few.[9,49-51,54]

The sample size ranged from 100 to 188 052, with a median of 753. In 2 included studies, data were collected in 2 different periods of

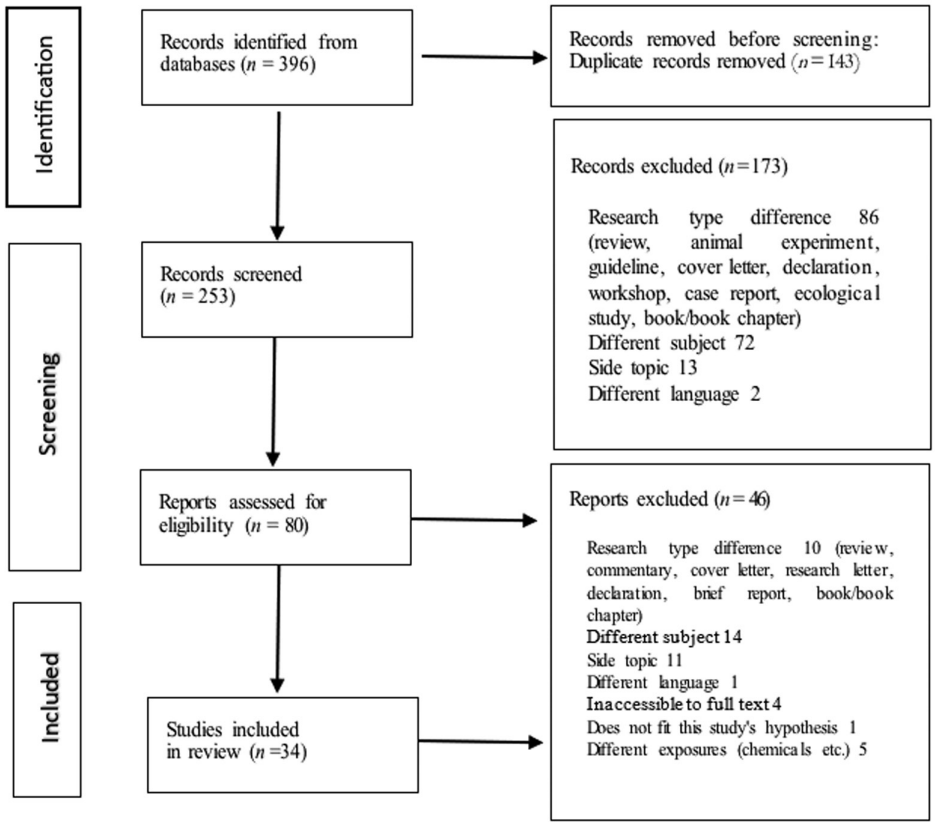

Figure 1. Article screening and selection flow chart. A total of 143 duplicate records were removed before screening. During title and abstract screening, 173 records were excluded. The full-text assessment resulted in the exclusion of 46 records. Finally, 34 studies were included in the review.

the conducted study, and the sample sizes for the periods of data collection differed.[30,57]

Various methods have been used in diagnosing ADHD. The methods used in studies included in the systematic review are as follows: Conner's Abbreviated Symptom Questionnaire (C-ASQ); The Diagnostic and Statistical Manual of Mental Disorders (DSM-III, IV, and V); Wechsler Intelligence Scale for Children-Revised (WISC-R) and Wechsler Adult Intelligence Scale-Revised (WAIS-R); Clinician diagnosis; Adult ADHD Self-Report Scale (ASRS version 1.1) Symptom Checklist; Strength and Difficulties Questionnaire (SDQ); Attention Deficit Disorders Evaluation Scale (ADDES); International Statistical Classification of Diseases (ICD 9, 10); Child Behavior Checklist (DSM-oriented scales); Diagnostic Interview Schedule for Children Version IV (DISC-IV); Conners Third Edition ADHD Index; The Conners Teacher Scale (CTRS-28), The Conners Parent Rating Scale (CPRS-48); Brown Attention Deficit Disorder Scales for Children and Adolescents (Brown-ADD); Quantified Behavior (Qb) Tests; Behavior Using the Child Behavior Checklist (CBCL) and Teacher's Report Form (TRF). Many studies have used these methods in combination. The most commonly used methods are DSM-IV, Clinician diagnosis, and Child Behavior Checklist.

Furthermore, the studies were mostly conducted in mixed-gender groups. However, in some studies (n = 6), there is no information available regarding the gender of the research group.[6,49,51,55,56,57] Only 1 study appears to have been conducted in males (Al Hamed et al[36]). It is also observed that the included studies mainly pertain to preschool and elementary school age groups.

Maternal Breastfeeding and Its Association with Attention Deficit/Hyperactivity Disorder Risk in Children

Different results have been obtained regarding the impact of breastfeeding status and duration on ADHD. In 5 studies, it was found that the breastfeeding duration was shorter in the case group compared to the control group.[6,34,37,40,44] In 4 studies, breastfeeding for less than 3 months was associated with increased ADHD risk compared to breastfeeding for more than 3 months.[32,41,42,48] In 9 studies, it was concluded that never breastfeeding increased the risk of ADHD compared to any duration of breastfeeding.[21,29,35,36,39,46,47,54,57]

In some studies, ADHD subdomains have also been considered. In a study by Boucher et al,[20] the minimally adjusted model for the "Any Breastfeeding" category showed that as the duration of breastfeeding increased, there was a significant reduction in inattention, hyperactivity, and total scores. In the study by Julvez et al,[49] inattention, hyperactivity, impulsivity symptoms, and ADHD symptoms were analyzed separately. Infants breastfed for 12-20 weeks and 20.1-28 weeks had a lower relative risk of inattention symptoms, hyperactivity symptoms, and ADHD symptoms compared to infants breastfed for 2 weeks or less, while no significant difference was found for impulsivity symptoms.

DISCUSSION

In this study, a systematic review was conducted to examine the relationship between breastfeeding and ADHD development. A total of 420 694 participants were included across twelve cohort studies, 10

case-control studies, 10 cross-sectional studies, and 2 RCTs. However, due to methodological differences among the studies and variability in breastfeeding duration, standardization was not achievable, and therefore a meta-analysis was not performed. While some studies categorized feeding methods (such as exclusive breastfeeding, bottle feeding, standard formula, experimental formula, mixed feeding) and breastfeeding duration (ever, never, <3 months, >3 months, <6 months, >6 months, 6-12 months, >12 months) for analysis, others did not apply such grouping.

Among the studies included in the systematic review, 17 indicated that breastfeeding was protective against ADHD development (Zhou et al,[32] Deng et al,[34] Soled et al,[6] Sepehrmanesh et al,[37] Golmirzaei et al,[38] Gu et al,[39] Say et al,[40] Van Dyk et al,[41] Mimouni-Bloch et al,[42] Stadler et al,[43] Türkoğlu et al,[44] Sabuncuoglu et al,[46] Härtel et al,[48] Julvez et al,[49] Lemcke et al,[50] Kim et al,[52] Belfort et al[19]), while 5 studies reported no relationship between breastfeeding and ADHD (Rodrigues et al,[47] Schwenke et al,[51] Ji et al,[54] Gibson et al,[55] Timby et al[56]). In 3 studies, breastfeeding was considered not as a primary variable but as a confounding factor and mediator in ADHD development.[31,33,45]

Some studies have found that breastfeeding has a protective effect against ADHD; however, this significance disappears when the models are adjusted for other variables.[20,21,29,30,35] Al Hamed et al[36] found no association between combined ADHD and hyperactivity/impulsivity and breastfeeding but found that breastfeeding was protective against inattention.

Four studies have linked breastfeeding beyond the first 3 months to a reduced risk of ADHD. Moreover, some research suggests that breastfeeding for 6 months or longer is associated with improved ADHD outcomes. These benefits may stem from the direct effects of breast milk, such as the provision of essential fatty acids crucial for neural development, or from its indirect effects on immune system maturation and microbiota development—both of which are closely connected to neurodevelopmental processes.

Breast milk is widely recognized for its primary benefits, notably supporting the development of the infant's immune system and fostering a healthy gut microbiota. It is rich in components that help protect against infections, including immunoglobulins—especially secretory IgA (sIgA)—as well as lactoferrin, lactadherin, mucin, and lysozyme. Among these, lactoferrin plays a notable role by exerting bacteriostatic effects and strongly binding iron, thus offering protection not only against infections but also against iron deficiency anemia, a condition that can adversely affect cognitive development.

Another crucial molecule for the immune system is secretory IgA (sIgA), the most abundant immunoglobulin in breast milk. Recent studies on sIgA have revealed that, beyond its classical antibody functions, it provides the infant with a miniature version of maternal immunity. sIgA facilitates the adhesion of beneficial microbes while preventing pathogens from attaching to the intestinal mucosa, thus contributing to the development of the infant's microbiota.

One of the significant contributions of breast milk to the microbiota is that it contains microorganisms such as Bifidobacterium, Lactobacillus, and Streptococcus. It is well-established that postnatal brain development parallels the maturation of the gut microbiota and that the microbiota acts as a crucial potential neurodevelopmental regulator. Considering that the gut microbiota is largely shaped during infancy, breast milk remains indispensable for infants from this perspective.[1,3,59]

When examining cohort studies, which rank higher on the evidence pyramid, a few studies have investigated psychological dynamics that may affect the breastfeeding experience. In a study by Amiel Castro et al,[9] pregnancy depression and postpartum depression were found to be associated with higher hyperactivity symptoms at ages 4 and 9. In a study by Girard et al,[53] it was shown that the duration of breastfeeding was influenced by the mother's employment status, but not by pregnancy depression. In a 2017 study by Boucher et al,[20] one of the sub-cohorts included a variable for the quality of family context, which was controlled in the breastfeeding duration ADHD relationship.[20] This variable did not lead to a significant change in the regression coefficients. In the same study, the presence of maternal psychopathology was found to be associated with a shorter breastfeeding duration. Additionally, maternal psychopathology and involvement in child care were included as controlled variables in the fully-adjusted model. In a study by Lemcke et al,[50] interviews conducted with mothers at 6 and 18 months asked about their experiences with child care. A significant linear relationship was identified between a mother perceiving child care as challenging and the child being diagnosed with ADHD.[50]

Moreover, there are other important variables that should be considered in the breastfeeding ADHD relationship. Beyond being a physiological process, breastfeeding is a psychological mechanism that strengthens the secure attachment between mother and infant, and contributes to the reduction of stress levels in both mother and infant through oxytocin release. Studies have shown that children with ADHD have a lower frequency of secure attachment compared to those without ADHD. Additionally, breastfeeding has been linked to parenting styles, with breastfeeding behavior supporting a parenting style characterized by infant-led and highly compassionate approaches.[4,23,24]

All of these factors represent potential contributors to the breastfeeding ADHD relationship. In future research, it is essential to collect data on these variables and incorporate them into analytical models. This approach will be crucial for identifying and elucidating potential protective mechanisms.

All of these mechanisms may play a role in the relationship between breastfeeding and ADHD; however, it is important to note that these mechanisms may differ across clinical, non-clinical, and general populations. This systematic review included studies with various methodological designs (RCTs, cohort studies, case-control studies, and cross-sectional studies) and sample populations. Some studies focused on specific clinical groups, such as very preterm infants, while others were based on general population data. This diversity suggests that the mechanisms underlying the relationship between breastfeeding and ADHD development may differ depending on the sample group. For instance, the impact of breastfeeding on neurodevelopment may be more pronounced in preterm infants, while in the general population, this effect could be more influenced by social and environmental factors. Moreover, the effects of breastfeeding on brain development, neurological function, and psychosocial interactions may vary across clinical and non-clinical populations. Clinical populations, such as children with a genetic predisposition, environmental stressors, and maternal psychopathology, may be more affected by breastfeeding, potentially intensifying its neurodevelopmental and psychological effects. This could be an area of further exploration to understand how specific variables in clinical populations contribute to the breastfeeding ADHD relationship. In

Table 5. Characteristics of the Studies Included in the Analysis of Breastfeeding and Attention Deficit/Hyperactivity Disorder

Study	Country	Conducted Year/ Follow-Up	Sample Size	Diagnosis of ADHD	Gender (%)	Outcome
Romanos et al,[29] 2011	Germany	2003-2006, Cross-sectional study/ 3-17 age	13318	ICD-10 and DSM-IV-R	50.0	Breastfeeding ever vs never ADHD ↓ (Bivariate unadjusted analysis) and Breastfeeding ever vs never ADHD NS (Multivariate adjusted analysis)
Adesman et al,[30] 2017	USA	2007, Cross-sectional study/ 3-5 age	11198	Clinician diagnosis	50.3	Formula fed (never breastfed) vs breastfed ADHD ↑
		2011/12 Cross-sectional study/ 3-5 age	12498	Clinician diagnosis	50.6	Formula fed (never breastfed) vs breastfed ADHD ↑ (unadjusted analysis), formula fed (never breastfed) vs breastfed ADHD NS (Analysis adjusted for propensity score)
Brasfield et al,[21] 2021	USA	2016-2018, Cross-sectional study/ 2-5 age	20453	Clinician diagnosis	48.2	Unadjusted Models: 6-12 months, >12 months vs No Breastfeeding (ref) ADHD ↓*, 0-6 months vs No Breastfeeding (ref): ADHD NS Adjusted model: NS
Newman et al,[31] 2014	Akwesasne	n/a, Cross-setional study/ 10-17 age	271	ADDES Home Version, ADDES School Version, Conners rating scales (CPRS-48, CTRS-28)	51.7	Main comparison: ADHD-like behavior of blood PCB levels in NS. Breastfeeding history as counfounding factor: NS
Zhou et al,[32] 2023	China	2012-2013, Cross-sectional study/ 3-12 age	35103	Conners Abbreviated Symptom Questionnaire (C-ASQ)	48.8	Breastfeeding <3 vs > 3 months ADHD ↑
Baker et al,[33] 2023	USA	2016-2018, Cross-sectional study/ 8-11 years	8514	DSM-V, Child Behavior Checklist, NIH Toolbox Flanker Attention Scores	46.8	Main comparison: maternal age and adhd relationship. Breastfeeding duration was responsible for up to 18% mediation in this relationship.
Deng et al,[34] 2022	China	2020, Cross-sectional study/ 3-7 age	7938	Conners Abbreviated Symptom Questionnaire (C-ASQ)	48.3	ADHD vs other duration of breastfeeding ↓ (Unadjusted, partial adjustment, multiple adjustment)
Park et al,[35] 2014	South Korea	n/a, Cross-sectional study/ 8-11 age	874	DISC-IV ADHD diagnostic modüle, Child Behavior Checklist	41.7	Non breastfeeding vs breastfeeding ADHD: Model 1 ↑ (adjusted age, gender, area of residence, and yearly family income) Non breastfeeding vs breastfeeding ADHD: Model 2-3 adjusted NS
Al Hamed et al,[36] 2008	Saudi Arabia	n/a, Cross-sectional study/ 6-13 age	1287	ADDES school version, and Parents' questionnaire	0	Breastfeeding vs bottle feeding: combined ADHD NS (breastfeeding vs bottle feeding Hyperactivity/impulsivity NS, breastfeeding vs bottle feeding İnattention ↓)
Soled et al,[6] 2021	USA	2011-12, Cross-sectional study/ 3-5 age	12793	Clinician diagnosis	n/a	ADHD vs other duration of breastfeeding ↓ (both) ADHD vs other Exclusive breastfeeding duration ↓ (Unadjusted) Breastfeeding <6 vs > 6 months ADHD ↑ (both)
Sepehrmanesh et al,[37] 2022	Iran	2017, Case-control study/ 6-12 age	404	Clinician diagnosis and DSM-IV	41.1	The duration of breastfeeding was significantly shorter in the ADHD group compared to the control group
Golmirzaei et al,[38] 2013	Iran	2012, Case-control study/ 4-11 age	404	DSM-IV, Clinician diagnosis, and Conners' questionnaire	37.4	Formula fed vs breast fed ADHD ↑
Gu et al,[39] 2018	China	2014-2016, Case-control study/ 6-18 age	782	DSM-IV	29.0	Breastfeeding ever vs never ADHD ↓
Say et al,[40] 2015	Türkiye	n/a, Case-control study/ 3-18 age	280	DSM-IV, WISC-R, and WAIS-R	22.0	ADHD vs control duration of breastfeeding ↓

(*Continued*)

Table 5. Characteristics of the Studies Included in the Analysis of Breastfeeding and Attention Deficit/Hyperactivity Disorder (Continued)

Study	Country	Conducted Year/ Follow-Up	Sample Size	Diagnosis of ADHD	Gender (%)	Outcome
Van Dyk et al,[41] 2014	South Africa	2013, Case-control study/ 5-13 age	100	DSM-IV	20.0	Breastfeeding <3 vs > 3 months ADHD ↑
Mimouni Bloch et al,[42] 2013	Israel	2008-2009, Case-control study/ 6-12 age	159	Clinical; Adult ADHD Self-Report Scale (ASRS version 1.1) Symptom Checklist	42.0	Breastfeeding <3 vs > 3 months ADHD ↑
Stadler et al,[43] 2016	USA	n/a, Case-control study/ 7-13 age	657	DSM-V	54.0	Shorter duration of breastfeeding ADHD ↑--Initiation of breastfeeding ADHD NS
Türkoğlu et al,[44] 2015	Türkiye	2013, Case-control study/ 7-17 age	375	DSM-III and DSM-IV; CPRS-R, WISC-R	26.0	ADHD vs control duration of breastfeeding ↓
Field et al,[45] 2014	n/a	n/a, Case-control study/ birth years 1985 through 2005	724	DSM-IV	33.0	Breastfeeding was only a risk for ADHD if the mother had psychopathology. Breastfeeding in the absence of parental psychopathology reduced ADHD risk.
Sabuncuoğlu et al,[46] 2014	Türkiye	n/a, Case-control study/ Gathered data 3 months interval, aged 7-17	200	DSM-IV, CPRS AND CTRS	25.0	Breastfeeding ever vs never ADHD ↓ ADHD vs control duration of breastfeeding ↓
Rodrigues et al,[47] 2022	Portugal	2011-2012, Cohort study / Follow-up very preterm children (VPT,<32 weeks of gestation) were 3 years of age	263	Child Behavior Checklist 1.5-5 years (CBCL/1½-5) and DSM-5 oriented scales	39.5	Breastfeeding inititating ever vs never ADHD ↑ (crude model) and ADHD NS (adjusted model), Exclusive breastfeeding <1 months vs ≥1 month, ADHD ↑ (crude model) and ADHD NS (adjusted model), Any reastfeeding <3 month vs ≥3 month ADHD NS (crude model) and ADHD NS (adjusted model)
Härtel et al,[48] 2020	Germany	2004-2009 Cohort study/ Gathered data 5-6 years old	2467	Strength and difficulties questionnaire (SDQ)	47.5	Breastfeeding <3 vs ≥ 3 months ADHD ↑ (unadjusted model, adjusted model, further adjusted model)
Julvez et al,[49] 2007	Spain	1997-1999, Cohort study/ Followed up at 1 year of age and 4 years of age - 1997-1998, Cohort study/ Followed up each year to the age of 4 years	500	DSM-IV	n/a	Breastfeeding <2 weeks vs 2-11.9, 12-20, 20.1-28, >28 weeks ADHD ↑
Lemcke et al,[50] 2016	Danimarka	1996-2002, Cohort study/ Gathered data at 6 and 18 months/ Follow-up at ADHD diagnosis or until 2012	76286	DSM-IV and ICD-10 HKD and prescription records	48.8	For exclusive breastfeeding: Never breastfeeding, <1, 2-3, 4-5 months vs ≥ 6 months ADHD ↑ For daily breastfeeding: ≤1, 2-3, 4-5 months vs ≥ 6 months ADHD ↑
Boucher et al,[20] 2017	Spain	2003-2008, Cohort study / Gathered data 6 months 14 months and 4-6.9 years old	1346	DSM-IV	49.6	Any breastfeeding (minimally adjusted model): Duration of breastfeeding ↑ ADHD ↓, Any breastfeeding (fully-adjusted model), Duration of breastfeeding ↑ ADHD NS Predominant breastfeeding (minimally adjusted model and fully-adjusted model), Duration of breastfeeding ↑ ADHD NS Exclusive breastfeeding (minimally adjusted model and fully-adjusted model), Duration of breastfeeding ↑ ADHD NS
Schwenke et al,[51] 2018	Germany	1996-1999, Cohort study/ Gathered data in 2009	573	Clinician diagnosis	n/a	None vs Several months ADHD NS; Up to 1 month vs Several months ADHD NS
Kim et al,[52] 2021	South Korea	2008 -2009, Cohort study/ Gathered data at 4- 6 and 9-12 months/ Followed up 10 years	188052	ICD-10 diagnosis and prescription records	48.9/51.4	First 4 to 6 months of age: Formula milk feeding vs exclusive breastmilk feding ADHD ↑ (matching) First 4 to 6 months of age: Formula milk feeding vs breastmilk feding ADHD ↑

(*Continued*)

Table 5. Characteristics of the Studies Included in the Analysis of Breastfeeding and Attention Deficit/Hyperactivity Disorder (Continued)

Study	Country	Conducted Year/ Follow-Up	Sample Size	Diagnosis of ADHD	Gender (%)	Outcome
Girard et al,[53] 2019	Chile	2006-2009, Cohort study/ Gathered data in 2012 (7-24 months)	3933	Child Behavior Checklist 1½–5 (CBCL)/ Attention problems are measured with 5 items.	49.4	Between 7 and 12 months breastfeeding (prematching, matching): Non-breastfed vs. breastfed Attention ↑ Up to 6 months and 13 months or more breastfeeding (prematching, matching): Non-breastfed vs. breastfed Attention NS
Amiel Castro et al,[9] 2021	UK	1991-1992, Cohort study/ 8 age	11096	The strengths and difficulties questionnaire (SDQ)	48.3	Exclusive breastfeeding ↑ hyperactivity/ attention deficit ↓, mixed feeding ↑ hyperactivity/attention deficit NS (at 4 years); Exclusive breastfeeding ↑ hyperactivity/attention deficit NS, mixed feeding ↑ hyperactivity/attention deficit ↑(at 9 years) Exclusive breastfeeding vs. mixed feeding ADHD ↓ (at 4 and 9 years) Exclusive breastfeeding vs.exclusive formula feeding ADHD ↓ (at 4 and 9 years) Mixed feeding vs.exclusive formula feeding ADHD ↓ (at 4 and 9 years) (In all of these results, 1-month nutritional characteristics were taken into account.)
Ji et al,[54] 2018	USA	1998, Cohort study/ Gathered by electronic medical records between 2003 and 2016	1180	ICD 9 and ICD 10	48.8	Bottle only vs Both or breastfed only ADHD NS
Gibson et al,[55] 2022	Australia	2004, Cohort study / Gathered data from (average age = 9 months, range = 4-19 months), assessed every 2 years (to 11 age).	5107	DSM-IV	n/a	Breastfeeding duration ADHD NS (adjusted model) (6-7 age) Breastfeeding duration ADHD NS (adjusted model) (10-11 age)
Belfort et al,[19] 2022	Australia	2001-2005, Cohort study / Gathered data at 4, 12 and 18 months/ Follow-up very preterm children (VPT,<33 weeks of gestation) were 7 years of age	586	Conners Third Edition ADHD Index	46.4	Maternal milk intake ↑ ADHD ↓ (crude model and adjusted model) Maternal milk intake ↑ ADHD ↓ (gestational age of 30 weeks or more and) Maternal milk intake ↑ ADHD NS (gestational age of less than 30 weeks)
Timby et al,[56] 2021	Sweden	2008-2012, Randomized controlled trial/ Gathered data from 6 and 6,5 years	240	WISC-IV, Brown-ADD, Quantified Behavior (Qb) tests, CBCL) and Teacher's Report Form (TRF), Child Behavior Checklist	n/a	Experimental low-energy, low-protein formula vs standard formula (breastfed reference) ADHD NS Pooled Data (Experimental low-energy, low-protein formula vs standard formula) vs Breastfeding ADHD NS
Nieto-Ruiz et al,[57] 2020	Spain	n/a, Randomized controlled trial/ Gathered data 2,5 years	103	Child Behavior Checklist	n/a	Standard Formula vs Breastfeeding ADHD (points) ↑ Experimental Formula vs Breastfeeding ADHD (points) NS (crude model) Standard Formula vs Experimental Formula vs Breastfeeding ADHD (points) NS (adjusted model) Standard Formula vs Experimental Formula vs maternal milk ADHD (categorical) NS
		n/a, Randomized controlled trial / Gathered data 18 months	132	Child Behavior Checklist	n/a	Standard Formula vs Experimental Formula vs maternal milk ADHD (points and categorical) NS (crude model and adjusted model for points)

ADDES, Attention Deficit Disorders Evaluation Scale; ADHD, attention deficit hyperactivity disorder; CPRS-28, the Conners Parent Rating Scale; CTRS-28, the Conners Teacher Scale; DSM, the Diagnostic and Statistical Manual of Mental Disorders; HKD, hyperkinetic disorder; ICD, International Statistical Classification of Diseases; n/a, not available; NIH, National Institutes of Health; NS, not significant; PCB, polychlorinated biphenyls; VPT, very preterm; WAIS-R, Wechsler Adult Intelligent Scale-Revised; WISC-R, Wechsler Intelligence Scale for Children-Revised.

future research, focusing on the role of psychological and attachment-based variables across different populations can help clarify the underlying mechanisms of the breastfeeding ADHD relationship. Investigating the neurological effects of breastfeeding in clinical populations, such as preterm infants, and the role of social environment could contribute significantly to developing a more holistic understanding of these mechanisms.

A review of the literature shows that meta-analyses have assessed the status and duration of breastfeeding. Tseng et al[60] found that children diagnosed with ADHD had shorter durations of breastfeeding compared to those without a diagnosis, while Zeng et al[13] reported that breastfed children were less likely to receive an ADHD diagnosis compared to non-breastfed children. Furthermore, according to the literature, it is believed that various factors such as genetics, prenatal factors, and environmental influences may contribute to the etiology of ADHD.[5,15-21] Considering this complexity, the presence of different results regarding the relationship between breastfeeding and ADHD necessitates further research on the subject. In studies, it has been observed that the duration of breastfeeding is questioned in various forms. Proper inquiry into breastfeeding is crucial for the reliability of results. Particularly in cross-sectional and case-control studies, when breastfeeding is queried, the risk of bias due to recall should be considered. Therefore, considering the multifactorial nature of ADHD etiology and the variability in breastfeeding assessment methods, more comprehensive and methodologically rigorous studies are needed to elucidate the association between breastfeeding and ADHD accurately.

Limitations and Strengths

This study has some limitations. Firstly, the data are predominantly derived from observational studies, particularly cross-sectional designs, which inherently limit the ability to draw causal inferences. Although the findings are largely consistent, the methodological constraints necessitate cautious interpretation. Considering all the reviewed studies, the lack of standardization between studies that involve different research designs, examine populations with varying characteristics, and use different measurement methods for breast milk dosage/duration and ADHD diagnosis/severity, along with the inherent limitation of meta-analyses in establishing causality; this further complicates the interpretation of the data. This also introduces limitations in associating the data with complex factors within the existing body of research.

Especially in studies aimed at diagnosing ADHD, the use of scales instead of clinical diagnosis also diminishes the reliability of detecting ADHD presence. In fact, it is noted that in most studies, clinical validation of identified ADHD is not conducted. However, it can be said that observations with interventions such as RCTs increase the reliability of data along with prospective observations. Furthermore, the relatively low total number of appropriate studies may carry potential risks for type 1 and type 2 errors. Upon examination, it is seen that studies meeting the eligibility criteria mainly provide data on middle and high-income countries (USA, Sweden, Australia, Denmark, UK, Germany etc). In contrast, there is only 1 study from African countries (Van Dyk et al[41]), which constitutes another limitation. Additionally, the relatively small sample sizes of case-control and RCTs deserve more careful interpretation of the findings.

The earliest study meeting the eligibility criteria dates back to 2007, indicating that this review predominantly includes data from children born after the year 2000. Although data on children from the 1990s are relatively limited, no information on adult ADHD is provided. Another notable point is that the included studies primarily focus on preschool and elementary school-aged groups. Therefore, these aspects should be considered when interpreting the review findings.

Lastly, another limitation is the inability to access the full texts of some potentially suitable studies and the lack of response from authors to the email requests. This situation may hinder the evaluation of studies that could provide relevant additional data on the topic, potentially limiting the scope of the findings.

In addition to these limitations, this research also contributes to the literature with its strengths.

This study has enabled the examination of various types of research designs, main outcomes, and quality score ratings related to the ADHD-breastfeeding relationship, including RCTs. Furthermore, all studies related to the topic found in the examined databases were included in the systematic review due to the absence of concerns regarding data standardization for meta-analysis. In addition, although there were systematic reviews on the subject in previous years by Tseng et al[60] and Zeng et al,[13] after the publication of these reviews, current studies on the subject were included in the research, and the final version of the literature was framed.[13,60]

CONCLUSIONS

The findings suggest that breastfeeding may be associated with the risk of ADHD in children. Breastfeeding could potentially serve as a protective factor for ADHD; however, high-quality longitudinal studies are needed to confirm or refute this causality and to understand the underlying potential mechanisms. Additionally, individuals' parenting styles or levels of health literacy may differ based on their breastfeeding status. Therefore, in future studies, factors such as mother-infant bonding, parenting style, and early-life stressors should be considered as variables to be investigated in clarifying the potential causal relationship between breastfeeding and ADHD.

Moreover, the lack of standardized methods for evaluating breastfeeding in conducted studies complicates the comparison of study results and meta-analysis. Therefore, it is thought that developing a scale that standardizes the representation of breastfeeding status (considering factors such as duration and the presence of complementary foods) would contribute to the literature.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

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