

Maternal breastfeeding and autism spectrum disorder in children: A systematic review and meta-analysis

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Objectives: Autism spectrum disorder (ASD) refers to a group of conditions variably affecting communicative and social interactive abilities presenting alongside behaviors with various restricted and repetitive patterns. In addition to genetic factors that influence the onset of the symptoms, there is growing interest in the potential involvement of non-genetic environmental factors. Some aspects of breastfeeding practices, including rates, timing, or optimality, have been put forward as environmental risk factors for autism. However, previous studies showed a controversial relationship between ASD and breastfeeding.

Methods: A meta-analysis on the association between maternal breastfeeding and ASD in children was conducted. We also explored potential moderating factors which might influence this association. Articles reporting the association between breastfeeding and a diagnosis of ASD were included.

Results: Seven articles were included in the meta-analysis. Cumulatively, children with ASD ($n = 1463$), either in the form of clinical diagnosis or self-report, were significantly less likely to have been breastfed than children without ASD ($n = 1180$) (OR = 0.61, 95% CI = 0.45–0.83, $P = 0.002$). Subgroup analyses revealed that results remained significant for children who were breastfed with additional supplementation.

Discussion: This meta-analysis provides evidence that breastfeeding (exclusively or including additional supplements) may protect against ASD. Prospective longitudinal research is required to disentangle the complex relationships and to explore potential pathophysiological mechanisms.

Keywords: Autism, Breastfeeding, Protective effect, Systemic review

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Introduction

Autism spectrum disorder(s) (ASDs) are not uncommon, with an estimated prevalence ranging between 20.0 and 116.1 per 10 000 people.^{1,2} Children and adults diagnosed with an ASD typically have problems with communication and social interaction, and the presence of repetitive and restricted patterns of behaviors. ASD is associated with substantial lifetime healthcare cost,³ alongside multiple social, academic, and occupational adversities.

The neurobiological etiology of ASD was suggested to include, at least partially, by an imbalance of dopamine, glutamate, and acetylcholine.⁴ Recent studies have suggested early-life environmental factors also play an important role in the risk of ASDs.⁵ These factors include maternal metabolic syndromes during pregnancy, exposures to viral and bacterial infections (cytomegalovirus, congenital rubella), air pollution, nutritional deficiency, and exposure to various medications such as anticonvulsants during critical period of pregnancy.⁶ Only few protective factors were thought to reduce the risk of ASD to date, including young maternal age at offspring conception/birth, and suitable folate intake during early preconception and the first trimester.⁵ Understanding potentially modifiable factors for ASD may aid in the development of potential preventive strategies.

Breastfeeding (i.e. direct sucking of breastmilk from the breast in an infant) has emerged as a putative protective factor for ASD. A number of mechanisms have been proposed to mediate the potential effects of breastfeeding on the pathophysiology of ASD, including nutrition theory,⁷ oxytocin stimulation,⁸ and the capability of breastmilk to secrete specific neurotrophic factors.⁹ The results of previous studies have however been inconsistent and controversial. Some studies have demonstrated a significant protective effect of breastfeeding on the development of ASD,^{7,10} whereas other investigations failed to replicate these findings.¹¹ To date and to the best of our knowledge, no previous meta-analysis has synthesized the available evidence examining the association between breastfeeding and ASD.

The aim of the current study was to provide a systematic review and meta-analysis (MA) investigating the relationship between breastfeeding practices and the diagnosis of ASD in children. Furthermore, we set out to explore potential moderators, which might account for this association including but not limited to breastfeeding methods (exclusive breastfeeding versus non-exclusive breastfeeding) and duration of breastfeeding.

Methods

The current meta-analysis was conducted in accordance to the *Meta-Analysis Of Observational Studies*

in *Epidemiology* (MOOSE) guidelines (see [Supplemental material 1](#)). An *a priori* defined yet unpublished protocol was followed.

Eligibility criteria

Inclusion criteria comprised: (1) quantitative observational studies including cohort or cross-sectional studies; (2) studies had to provide prevalence rate of children that did/did not receive breastfeeding or other effect sizes (ESs) related to group difference of breastfeeding among children with ASD or without ASD; and (3) original peer-reviewed studies published in English. The exclusion criteria included: (1) non-human studies; (2) case reports or case series; and (3) studies which were written in other (i.e. non-English) languages.

Search strategy, study selection and data extraction

Two independent authors searched databases from inception until 29 April 2017 using the key words: '(Breastfeeding) AND (autism* OR Asperger*)'. The following databases were searched: (1) PubMed/Medline; (2) ScienceDirect; (3) Cochrane CENTRAL, and (4) ClinicalTrials.gov database. This search strategy was augmented through hand searching reference lists of included articles and reviews to identify potentially eligible studies.

Upon completion of the searches, duplicates were electronically removed. Two independent authors then screened the titles and abstracts of all results for the eligibility. Two authors then developed a list of articles to be considered in a full-text screening through consensus. At the full-text screening, both authors independently applied the eligibility criteria and a list of articles meeting the inclusion criteria was established. Disagreements were resolved through consensus. When a consensus could not be reached, a third investigator made a final decision regarding inclusion.

From the eligible articles, two independent authors extracted data using a predetermined database. The variables of interest included the prevalence/incidence rate of ASD, prevalence rate of breastfeeding, age, gender distribution, mean duration of breastfeeding, and parental age at offspring birth. We also included information on parental cognitive function, children cognitive function, maternal and paternal educational and occupational levels, parental tobacco and alcohol consumption, frequency of preterm birth, frequency of low birth body weight, different ethnicity (including African, Caucasian, Asian, and Hispanic), first-born child, prevalence of parental diagnosis of ASD, and study follow-up duration (in units of month).

Primary outcomes

The primary outcomes were the frequency, in the form of odds ratio (OR), of receiving breastfeeding among children with/without ASD. We hypothesized that the duration of breastfeeding could significantly vary among included studies. We followed recommendations from the World Health Organization (WHO), which suggest that breastfeeding duration be at least 6 months (http://www.who.int/nutrition/topics/infantfeeding_recommendation/en). Among this part of meta-analysis, the primary outcomes were the prevalence rate of breastfeeding 'more than 6 months' in children with ASD and those without ASD.

If the outcome data were not available in potentially eligible studies, we contacted the authors to request the original data. If we did not receive a response after 1 week, an email request was sent again. When there was no direct prevalence/incidence rate available, we used other statistical parameters, such as samples size and related *P* values for the comparison of prevalence rate between ASD group and control group, to estimate ESs wherever possible according to the user manuscript of Comprehensive Meta-Analysis ver. 3.

Meta-analysis

Owing to the anticipated heterogeneity, a random-effects model was employed for this meta-analysis. In brief, random-effects modeling is more stringent than fixed-effects modeling and incorporates a between-study variance in the calculations. The ESs were calculated as the OR to indicate the difference of the prevalence rate of breastfeeding in children with/without ASD. Two-tailed *P* values were considered statistically significant. All analyses were conducted with Comprehensive Meta-Analysis software, version 3 (Biostat, Englewood, NJ, USA).

Sensitivity test

In order to find any potential outliers in recruited studies, we arranged a sensitivity test using one study removal test.

Heterogeneity evaluation

We investigated the heterogeneity among included studies through the Cochrane *Q* test¹² and the *I*², which stands for the proportion of heterogeneity.¹³ Potential sources of heterogeneity were explored through subgroup and meta-regression analyses. Subgroup analyses were conducted to compare results according to exclusive breastfeeding and non-exclusive breastfeeding (*defined as including predominant breastfeeding, partial breastfeeding, no breastfeeding, or breastfeeding plus supplementing formula*).¹⁴ In addition, we conducted subgroup analyses to investigate whether results differed according to the duration of breastfeeding. Specifically, across

breastfeeding duration periods of 'over 1 month', 'over 3 months', 'over 6 months', and 'over 12 months' compared to those children who were not breastfed. We also conducted a priori planned subgroup analyses to explore the prevalence rate of breastfeeding in children with a dual diagnosis of ASD and Attention deficit hyperactivity disorder (ADHD). Subgroup analyses were considered whenever there were at least three datasets for a subgroup.¹⁵

Meta-regression

We investigated the influence of several pre-determined potential moderators through unrestricted maximum likelihood random-effects meta-regression analyses on ES estimates whenever data on a potential moderator were available for at least four datasets. Specifically, we considered age; gender distribution; duration of breastfeeding; parental age at delivery; severity of ASD (rated through rating scales); parental and children's cognitive function; parental education and occupational levels; parental tobacco smoking (%) and prevalence of alcohol consumption rate; preterm birth and low birth body weight rates; ethnicity; first-born child rate (%); prevalence of parental diagnosis of ASD; and study follow-up duration.

Publication bias

In order to test for publication bias, we conducted a visual inspection of funnel plots¹⁶ and the Egger's regression test.¹⁷ If evidence of publication bias was detected, we used the Duval and Tweedie's trim and fill test to adjust the ESs for publication bias.¹⁸

Results

Studies included in the meta-analysis

Figure 1 shows details of the search results and reasons for exclusion at full-text review (a full list is presented in supplemental material 2 and 3). Briefly, 20 studies were deemed potentially eligible, of which seven were included in the current study of meta-analysis considering the odds of children receiving breastfeeding between children with or without a diagnosis of ASD.^{7,8,10,11,19–21} The reasons for study exclusion included irrelevance to comparisons of breastfeeding in children with/without ASD, review and commentary articles and the lack of data on children without ASD used (see Supplemental material 2). Among these seven studies, the total numbers of ASD children were 1463, and 1180 for control children^{7,8,10,11,19–21} (Table 1). No prospective cohort study was identified.

Main results of the meta-analysis of primary outcome of the prevalence rate of breastfeeding in children with/without ASD: Is breastfeeding less common in children with ASD?

The pooled meta-analysis found that children with ASD (*n* = 1463, mean age = 7.1, mean female

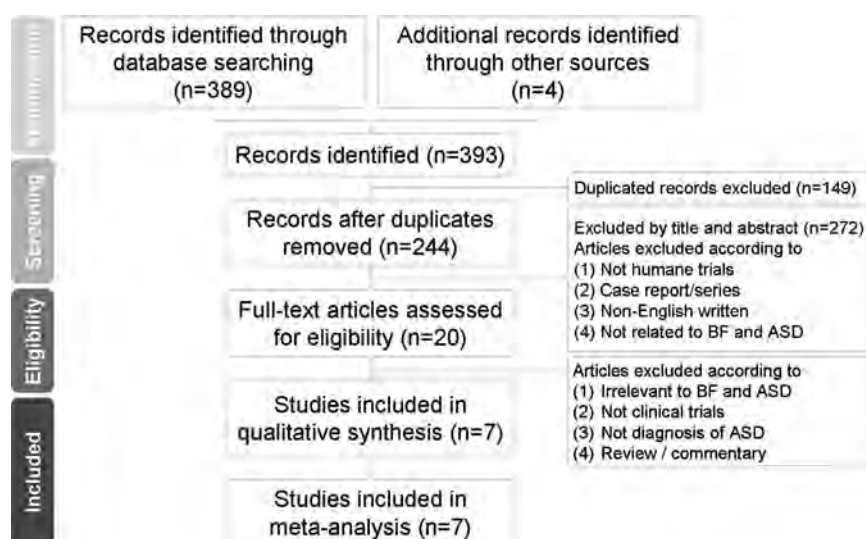


Figure 1 Flowchart of the selection strategy and inclusion/exclusion criteria for the current meta-analysis.

Table 1 Summary of included studies in current meta-analysis

Author (year)	Diagnosis of ASD	Groups	Numbers	Comparison	Primary outcome	Mean age	Female (%)	Country
Say, G.N. (2016)	DSM-IV	ASD	100	Breastfeeding duration (month)	12.2 ± 10.5	8.6 ± 4.2	22.6	Turkey
Field, S.S. (2014) male	DSM-IV	Control	80		13.0 ± 8.7			
Field, S.S. (2014) female	DSM-IV	ASD	26	Breastfeeding > 4 months	12 (46.2%)	n/a	0.0	USA
George, B. (2014)	DSM-IV	Control	320		144 (45.0%)			
	CARS*	ASD	5	Breastfeeding > 4 months	4 (80.0%)	n/a	100.0	USA
		Control	152		72 (47.4%)			
		ASD	143	Breastfeeding Occasionally/frequently	114 (79.7%)	3.5	31.6	India
		Control	200		184 (92.0%)			
Shafai, T. (2014)	n/a [#]	ASD	26	Breastfeeding (>6 months)	12 (46.2%)	n/a	n/a	USA
		Siblings control	21		16 (76.2%)			
Al-Farsi, Y.M. (2012)	DSM-IV	ASD	102	Exclusive Breastfeeding < 6 months	1 (1.0%)	6.6 ± 3.1	24.6	USA
		Control	102		4 (3.9%)			
Schultz, S.T. (2006) age 2–18	Self-report	ASD	861	Breastfeeding	(25.0%)	7.8 ± 4.0	n/a	USA
		Control (>6 months)	123		(36.0%)			
Schultz, S.T. (2006) age 2–4	Self-report	ASD	150	Exclusive Breastfeeding	(8.0%)	3.2 ± 0.5	n/a	USA
		Control	38		(16.0%)			
Burd, L. (1988)	DSM-III	PDD	50	Rate of breastfeeding	13 (26.0%)	8.9 ± 4.7	34.0	USA
		Controls (other patients)	50		11 (22.0%)			
		Older Siblings of PDD	64		29 (45.3%)			
		Younger Siblings of PDD	30		12 (40.0%)			

*Diagnosed with Childhood Autism Rating Scale (CARS) cut off score of more than 30.

[#]Not reported.

Abbreviations: n/a: not available; DSM-III: diagnostic and statistical manual of mental disorders, third edition; DSM-IV: diagnostic and statistical manual of mental disorders, fourth edition; DSM-5: diagnostic and statistical manual of mental disorders, fifth edition; ICD-10: international statistical classification of diseases and related health problems 10th revision; ASD: autistic spectrum disorder; AP: attention problems scale; OA: over-activities problems scale; DISC-IV: diagnostic interview schedule for children, fourth edition.

proportion = 24.0%) were significantly less likely than those not diagnosed with ASD ($n = 1180$, mean age = 6.5, mean female proportion = 32.1%) to receive breastfeeding (OR = 0.61, 95% CI = 0.45–0.83, $P =$

0.002) (Fig. 2A). No significant heterogeneity (Q value = 15.24, $df = 10$, $I^2 = 34.38\%$, $P = 0.124$) or publication bias via Egger's regression ($t = 0.04$, $df = 9$, $P = 0.970$) or funnel plot (Fig. 2B) was evident.

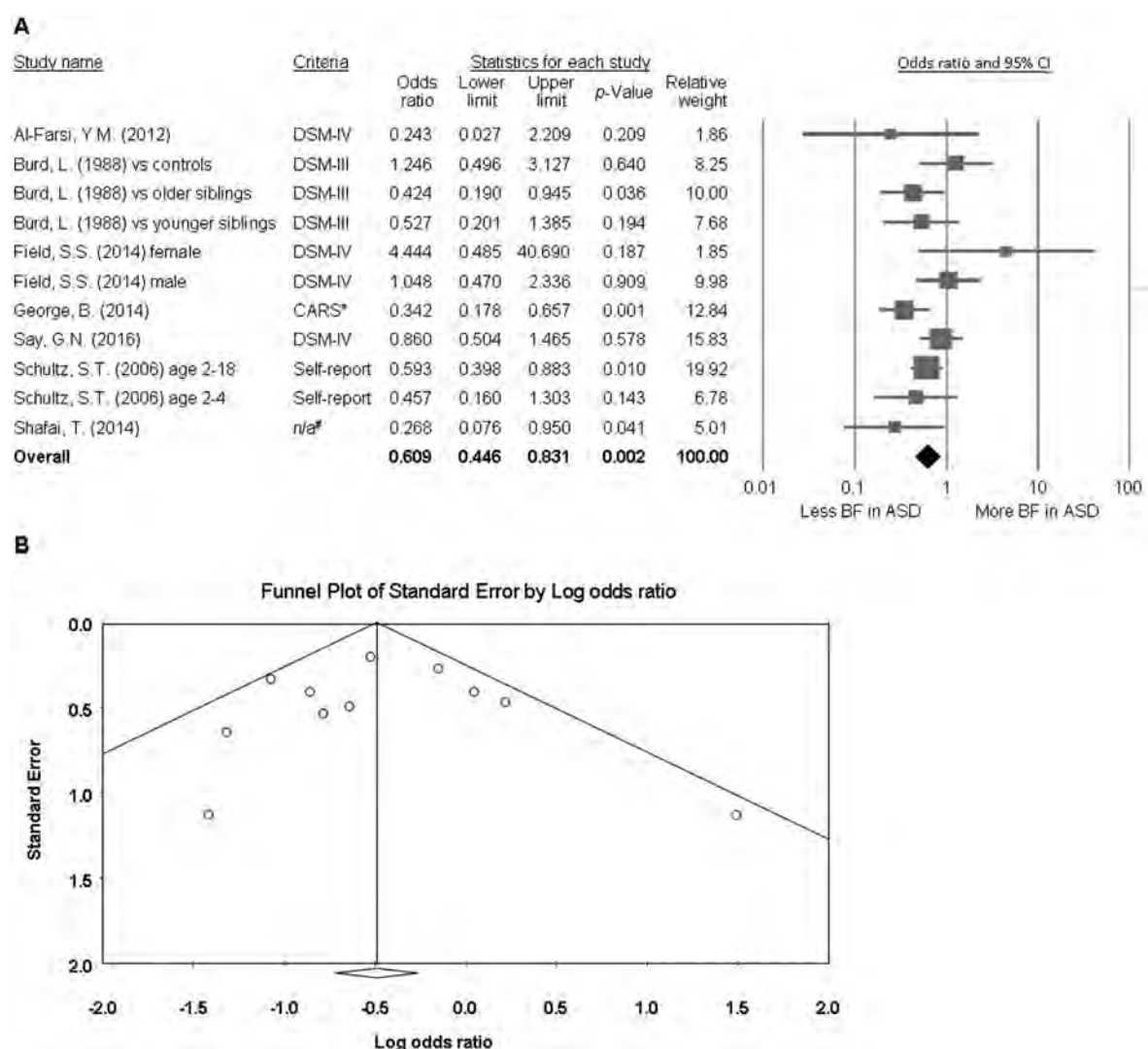


Figure 2 (A) Forest plot showing ESs (odds ratio) and 95% confidence intervals (CIs) from individual studies and pooled results of all included studies comparing the prevalence rate of breastfeeding in children diagnosed with ASD and not diagnosed with ASD, and (B) a funnel plot that examined the publication bias in the meta-analysis of studies comparing the prevalence rate of breastfeeding in children with and without ASD. *: Diagnosed ASD with Childhood Autism Rating Scale (CARS) cut off score of more than 30. #: not reported diagnostic method. Abbreviations: ASD: Autism spectrum disorder; BF: breastfeeding; CARS: Childhood Autism Rating Scale; CI: confidence interval; DSM: The Diagnostic and Statistical Manual of Mental Disorders; MA: meta-analysis; OR: odds ratio.

If we focused on studies with a diagnosis of ASD based on The Diagnostic and Statistical Manual of Mental Disorders (DSM) system,^{7,10,11,21} either DSM-III or DSM-IV, the sample sizes dropped to 283 ASD children and 798 controls only and the result of meta-analysis would change to insignificance (OR = 0.78, 95% CI = 0.52–1.18, $P = 0.239$) without significant heterogeneity (Q value = 7.94, $df = 6$, $I^2 = 24.44\%$, $P = 0.242$) or publication bias ($t = 0.10$, $df = 5$, $P = 0.921$) (supplemental material 4).

Sensitivity test

The sensitivity test via the one study removal test showed that the significant result of meta-analysis would not change after removal of any one of the recruited studies. This indicated the significant result

of the current meta-analysis was not influenced by any outlier within the recruited studies.

Meta regression analyses

Meta-regression demonstrated that there was no significant association with the prevalence rate of breastfeeding and mean child age, proportion of females, and percentage of preterm birth (supplemental material 5). Data from at least four datasets were not provided for the other potential moderators (i.e. parental age at delivery; severity of ASD; parental and children's cognitive function; parental education and occupational levels; parental tobacco smoking (%) and prevalence of alcohol consumption rate; low birth body weight rates; ethnicity; first-born child rate (%); prevalence of parental diagnosis of ASD; and study follow-up duration).

Subgroup analyses

We divided the included studies into two subgroups (i.e. those evaluating 'exclusive breastfeeding used' or not). The prevalence rate of children receiving breastfeeding in those diagnosed with ASD was significantly less than those not diagnosed ASD in both the exclusive breastfeeding subgroup (study numbers = 5, numbers of ASD = 1287, numbers of controls = 1481)(OR = 0.46, 95% CI = 0.33–0.63, $P < 0.001$)^{7,8,11,19,21} and non-exclusive breastfeeding subgroup (study numbers = 3, numbers of ASD = 2776, numbers of controls = 713)(OR = 0.56, 95% CI = 0.45–0.68, $P < 0.001$).^{10,19,20}

The prevalence rate of children receiving breastfeeding were significantly less in children diagnosed with ASD than those without a diagnosis of ASD in the subgroups of breastfeeding duration of 'more than 1 month' (number of studies = 5, number of children with ASD = 1230, number of children without ASD = 525, OR = 0.48, 95% CI = 0.35–0.66, $P < 0.001$)^{7,8,19–21} and 'more than 6 months' (number of studies = 3, number of children with ASD = 1011, number of children without ASD = 244, OR = 0.55, 95% CI = 0.40–0.76, $P < 0.001$)^{8,19,21} and with a trend to statistical significance in the 'more than 3 months' group (number of studies = 4, number of children with ASD = 461, numbers of children without ASD = 878, OR = 0.54, 95% CI = 0.26–1.12, $P = 0.098$)^{7,8,11,21} (Fig. 3). The subgroup analysis of those with breastfeeding 'more than 12 months' could not be performed because there are only two studies included in this subgroup.^{8,21}

Breastfeeding and co-occurring ASD/ADHD

Finally, we investigated the association between breastfeeding and a dual diagnosis of ASD and ADHD. However, among the included studies, none provided information on this dual diagnosis. Two studies included both children with ASD and ADHD.^{11,21} However, both used the diagnostic criteria of Diagnostic and Statistical Manual of Mental Disorders fourth edition (DSM-IV), which contains reference to the criteria of ADHD with exclusion to ASD.²² Although this 'rule-out' criteria have been removed in Diagnostic and Statistical Manual of Mental Disorders fifth edition (DSM-5),²³ there have not been any studies using the DSM-5 criteria in this area. Therefore, a subgroup analysis was not possible.

Discussion

To the best of our knowledge, the current meta-analysis represents the first published account to consider the relationship between breastfeeding and ASD in children. Our collected results suggest that children diagnosed with ASD were less likely to have been in receipt of breastfeeding compared with children not diagnosed with ASD. The results held even when we considered both exclusive breastfeeding as well as non-exclusive breastfeeding. Cumulatively, our results suggest that breastfeeding may confer a potentially protective association related to offspring risk of ASD. While our data are novel, one should note the observational nature of these preliminary findings, whereby causation can clearly not be determined.

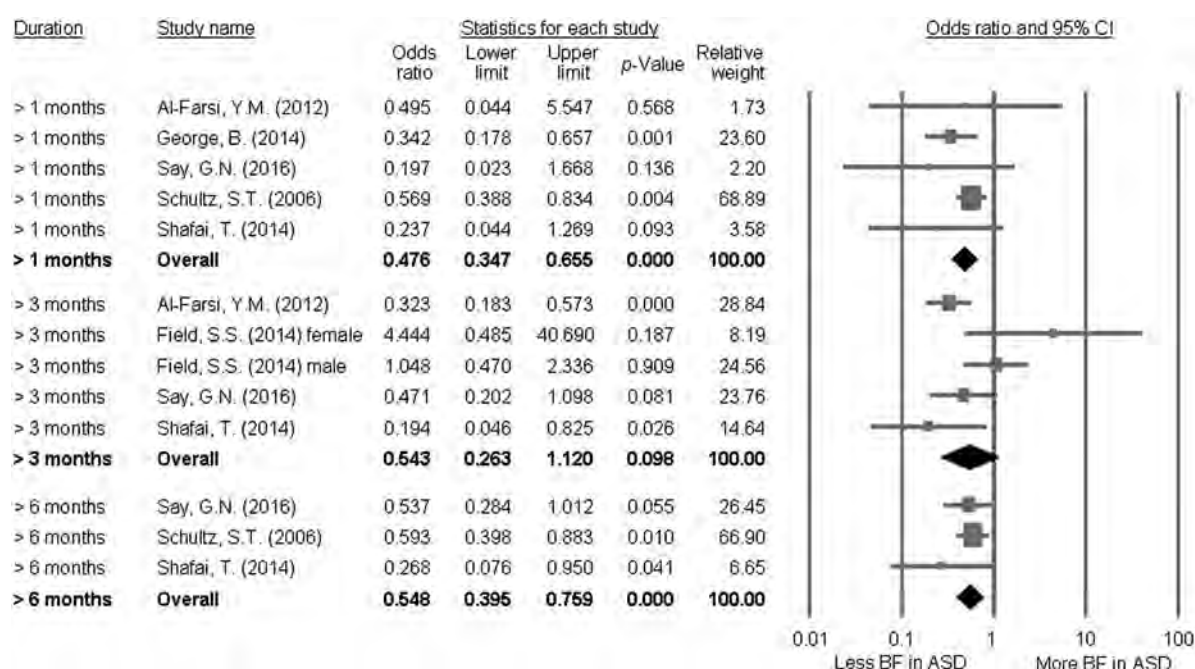


Figure 3 Forest plot showing ESs (odds ratio) and 95% confidence intervals (CIs) comparing the prevalence rate of breastfeeding in children with ASD and controls without ASD with different breastfeeding durations, more than one month, more than 3 months, and more than 6 months. Abbreviations: ASD: Autism spectrum disorder; BF: breastfeeding; CI: confidence interval; OR: odds ratio.

Previous review articles have demonstrated that the etiology of ASD is predominantly genetic with reported dominantly genetic heritability.^{24–26} Our findings could also be interpreted by the notion that infants who later meet criteria for ASD may have already had some of the hallmarks of the condition (e.g. reduced social interaction and un-cooperation) which may have made breastfeeding more challenging for their mothers.²⁷ More and more evidence, however, is indicating that the onset of ASD might not be attributed solely due to genetic and heritable reasons but also due to non-genetic environmental and nutritional factors, too.^{5,6} For instance, a sibling controlled study by Shafai et al. (2014) provides some evidence regarding the protective effect of breastfeeding in the ASD children. Specifically, Shafai et al. (2014) found a significantly reduced rate of breastfeeding in children with ASD compared with unaffected sibling controls.⁸ Such sibling controls were also ‘presumed genetically susceptible individuals’ in light of the available heritability data. Further, the authors found that those formula feeding and breastfeeding via a milk-bottle also had significantly higher risk of ASD compared with those with exclusive breastfeeding but not via a milk-bottle; results which were partially consistent with our pooled analyses.⁸ The finding of lower breastfeeding rates in children with ASD than in sibling controls was also supported by another report by Burd *et al.*¹⁰

The potential pathophysiological mechanisms through which breast milk may influence the risk of ASD are unclear and warrant further investigation. Various findings have linked ASD to a multitude of biological factors. The increasing oxytocin levels experienced during external stimulation²⁸ may also be protective against the development of ASD.⁸ Compared to formula feeding or breastfeeding via a milk-bottle, direct ‘breastfeeding’ may be a more significant driver of oxytocin secretion in the infantile brain²⁹ via skin to skin contact and the mother–baby interaction process.⁷ Increasing serum insulin-like growth factor (IGF) levels in infants were more prominently observed in breast milk fed infants than those given other forms of bovine milk or formula feeding.⁹ A deficiency of IGF has previously been suggested to be pertinent to the pathophysiology of ASD via dysregulating myelination among other potentially important processes.³⁰ Breastfeeding therefore, might reduce the risk of ASD through the restoration of IGF levels. Cytokine production may also play an important role in the protective effect of breastfeeding to ASD tapping into a growing body of research literature implicating immune function in relation to ASD. In a recent clinical trial, an opposite shifting of T Helper 1 (Th1) cytokines by breastfeeding and formula-feeding was observed. Infants receiving

breastfeeding had higher percentages of blood IL-4 positive T helper cells where those receiving formula-feeding had significantly higher blood interferon-gamma levels, which is a bio-signature cytokine of Th1 cells.³¹ Interestingly too, children with ASD may have significantly lower peripheral interferon-gamma levels than healthy controls.³²

Outside of any neurotrophic or hormone theory, insufficient intake of ‘beneficial’ omega-3 and omega-6 polyunsaturated fatty acids (PUFAs) derived, either from the mother during pregnancy or from breastfeeding during the infant period, may also play an important role in ASD. Both of these PUFAs are abundant in the colostrum, which is secreted during the first 2–3 days after delivery. The higher risk of ASD in children with late initiation of breastfeeding provides evidence for a potential nutrition theory of the development of ASD.^{7,11} This hypothesis could be confirmed by two way, one is the significantly lower PUFAs levels noted in ASD compared with controls,³³ and also the improvement of ASD severity after PUFAs supplementation.³⁴ Drawing also on hypotheses linking cases of ASD to issues with casein, the primary milk protein, the idea that constitutional differences between breast milk and alternatives may play a role in the findings should also be further explored. Ideas related to casein peptide fractions (beta-casomorphin 1–7) present in supplementary milks related to non-breastfeeding contributing to delayed infantile psychomotor development have been previously discussed.³⁵ There may also be other influences potentially relevant to the positive impact of breast milk including a potential effect on the programming of the infant gut microbiome.

In addition, our subgroup analysis showed that the OR was not significantly different among studies with different duration of breastfeeding. However, these results should be interpreted with caution due to the limited number of datasets included in each subgroup. Furthermore, some children with ASD do have dysregulated patterns of breastfeeding behaviors. As affected children grow up, their behavioral problems may also have increased which in turn could have made breastfeeding more difficult. Early weaning associated with an early cessation of breastfeeding could also be associated with the risk of ASD. Such discontinuation of breastfeeding may lead to lower levels of some of the important biological parameters (PUFAs, IGF, and stimulation of oxytocin) previously mentioned.⁸

Our subgroup analyses found that both exclusive breastfeeding and breastfeeding plus complementary food were associated with reduced odds of ASD. Our data, therefore, suggest that it may be unnecessary to focus on exclusive breastfeeding alone where complementary feeding may also offer some protection. Finally, another important topic to be addressed is

the insignificant result of our other subgroup analysis, which focused on studies with diagnosis of ASD using the DSM system of the diagnostic classification. In this subgroup meta-analysis, the *P* value of result, after noticeably reducing cases from 1463 ASD and 1180 controls to 283 ASD children and 798 controls, would change from 0.002 to 0.239 with wider 95% CI (0.45–0.83 change to 0.52–1.18). Reliant on the forest plots, we found that the most studies in this subgroup meta-analysis point in a similar direction, that is the children with ASD were less likely than those not diagnosed with ASD to receive breastfeeding. Furthermore, there was no significant heterogeneity among this subgroup meta-analysis. This would indicate that insignificance may have resulted from the much smaller sample sizes.

Limitations

There are several limitations to the current study. First, the number of included studies (particularly in subgroups) is small. Second, we could not control or adjust for the potential confounding factors within recruited studies. Third, in the previous report, there are some hidden and un-quantifiable factors influencing maternal willingness to breastfeed, such as maternal tobacco smoking in the lactation period, maternal psychological status, and the introduction of a pacifier.³⁶ Some of these variables could contribute to a higher risk of ASD.³⁷ However, we could not elucidate the potential effect of these factors in the current study because of a lack of data. Fourth, the recruited studies drew on a wide range of diagnostic criteria. We tried to focus on those with a diagnosis using the DSM system but the results turned out to be insignificant. This would implicate the clinical application of our results. Fifth, among the recruited studies, there was an obvious male gender dominance, although there was no significant association between the main results of meta-analysis and gender distribution according to the meta-regression result. This might be due to sampling bias. However, based on the limitation of meta-analysis, we could not make further adjustment for this bias. Sixth, in addition, although we had tried to include other clinical variables with potential moderating effect to ASD, such as parental age at delivery and severity of ASD, we could not perform further meta-regression procedures because of a lack of suitable data. Finally, we planned to investigate the protective effect of breastfeeding in the ASD + ADHD dual diagnosis category. There were, however, no studies providing such information.

Conclusion

The results of this meta-analysis suggest that children diagnosed with ASD were less likely to have been breastfed. Our results suggest that both exclusive and

non-exclusive breastfeeding may confer a protective effect. The observational nature of the data precludes any causal explanations, but our data add further credence to the importance of breastfeeding on the health of the developing infant. The design of prospective studies is required to confirm the relationships herein observed. Finally, the elucidation of potential mechanistic pathways underpinning these associations may represent a relevant research direction.

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Supplementary material

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