British Journal of Nutrition (2020), 123, 768–779 doi:10.1017/S0007114519003271

Association of infant and young child feeding practices with cognitive development at 10–12 years: a birth cohort in rural Western China

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(Submitted 12 August 2019 – Final revision received 28 November 2019 – Accepted 9 December 2019 – First published online 13 December 2019)

Abstract

We aimed to comprehensively examine the association of breast-feeding, types and initial timing of complementary foods with adolescent cognitive development in low- and middle-income countries. We conducted a prospective cohort study of 745 adolescents aged 10–12 years who were born to women who participated in a randomised trial of prenatal micronutrient supplementation in rural Western China. An infant feeding index was constructed based on the current WHO recommendations. Full-scale intelligence quotient (FSIQ) was assessed and derived by the fourth edition of the Wechsler Intelligence Scale for Children. The duration of exclusive or any breast-feeding was not significantly associated with adolescent cognitive development. Participants who regularly consumed Fe-rich or Fe-fortified foods during 6–23 months of age had higher FSIQ than those who did not (adjusted mean differences 4·25; 95 % CI 1·99, 6·51). For cows'/goats' milk and high protein-based food, the highest FSIQ was found in participants who initially consumed at 10–12 and 7–9 months, respectively. A strong dose–response relationship of the composite infant feeding index was also identified, with participants in the highest tertile of overall feeding quality having 3·03 (95 % CI 1·37, 4·70) points higher FSIQ than those in the lowest tertile. These findings suggest that appropriate infant feeding practices (breast-feeding plus timely introduction of appropriate complementary foods) were associated with significantly improved early adolescent cognitive development scores in rural China. In addition, improvement in Fe-rich or Fe-fortified foods complementary feeding may produce better adolescent cognitive development outcomes.

Key words: Breast-feeding: Iron: Complementary foods: Feeding practices: Early adolescence: Cognitive development

Exclusive breast-feeding for 6 months with partial breast-feeding continued up to 2 years of age is recommended by the WHO due to its clear short-term benefits for decreasing morbidity and mortality from infections[1–3]. Infant feeding practices, mainly breast-feeding and complementary feeding, are also increasingly recognised as important in shaping brain development that may result in positive effects on cognitive development[4,5].

Mounting of observational studies examined the associations of duration of exclusive/any breast-feeding with later cognitive development[6–8], but only a few studies have examined the long-term consequences of breast-feeding on cognitive development in late childhood, adolescence or beyond and reported inconsistent results[9–14]. One study from Brazil reported that breast-feeding improved intelligence performance in adults, but the mean scores for breast-feeding duration ≥12 months were similar to those in the category of 6–11·9 months[15]. Similar patterns, that is, the longest duration of any breast-feeding not predicting the highest cognitive test scores later in life,

Abbreviations: FSIQ, full-scale intelligence quotient; WISC-IV, Wechsler Intelligence Scale for Children, fourth edition; WMI, Working Memory Index.

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were evident in other studies[14–18]. Only one randomised trial of breast-feeding promotion has been conducted in Belarus that has examined child development and found a positive effect on verbal function at age 6·5 years[19] but the effect size substantially decreased by adolescence[20].

The extent of the association between optimal duration of any breast-feeding and long-term cognitive development remains unclear. Exclusive breast-feeding may meet nutritional requirements of infants during the first 6 months and possibly longer, but the risk of micronutrient deficiencies among infants exclusively breast-fed for longer than 6 months has been reported in some studies[21–23]. One systematic evaluation found that significant associations between any breast-feeding and intelligence were observed in high-income countries but not in low- and middle-income countries[7], where maternal undernutrition is widely prevalent[24] and may lead to a poor quality of human milk[25].

There are also sparse data on the relationship of complementary food composition and child development outcomes. Some studies have reported that >90 % of the Fe requirements of a breast-fed infant must be met by complementary foods[26]. Recently, one review of studies mostly from developed countries concluded that complementary feeding with substantial amounts of Fe, such as meats or Fe-fortified foods, could provide an adequate amount of Fe or prevent Fe deficiency for breast-fed infants who were not receiving adequate Fe from another source[27]. However, the corresponding effects of these Fe-rich or Fe-fortified foods on child development outcomes were inconsistent[28]. Similarly, protein is associated with the global development of the brain[29], but the evidence on association between complementary high protein-based foods and child cognitive development is lacking. Furthermore, the association of timing of introducing complementary foods, one key aspect of complementary feeding which might be associated with micronutrient status among infants[27], with development outcomes also remains unclear[28].

According to the Chinese National Nutrition and Health Survey in 2013, the exclusive breast-feeding rate under 6 months was 18·6 % and the complementary feeding practice was also suboptimal with a prevalence of 25·1 % for minimum acceptable diet among children aged 6–23 months in China[30]. Here, we used a birth cohort study from rural Western China. We examined the associations between the duration of exclusive or any breast-feeding, the consumption of Fe-rich or Fe-fortified foods, and the initial timing of complementary foods, and adolescent cognitive development at age 10–12 years. We also constructed an infant feeding index grounded in WHO recommendations, which comprehensively represented the feeding components above, and further examined its association with child cognitive outcomes. These results are intended to provide evidence on the long-term benefits of appropriate infant and young child feeding practices.

Methods

Study design and participants

The present study was a prospective birth cohort study of the offspring born to women who participated in a trial of antenatal micronutrient supplementation (ISRCTN 08850194), which has been described in detail elsewhere[31].

In summary, the original trial was a cluster randomised controlled trial in rural Western China from 2002 to 2006 with three treatment arms (folic acid, Fe/folic acid and multiple micronutrients). A total of 4604 singleton live births were obtained from the trial, but only 1400 births after 2004 were registered for further follow-up. Among them, twelve infants were excluded due to death (*n* 3), congenital diseases (*n* 7), maternal hearing loss (*n* 1) and paternal amentia (*n* 1). There were 1388 infants who completed the infancy follow-up stage from birth through 1, 3, 6, 9, 12, 18, 24–30 months of age. At the adolescence follow-up stage, 643 of these children were lost to follow-up as they had moved away from the study area, and thus there were 745 adolescents aged 10–12 years who were enrolled and had been followed from birth through infancy into early adolescence. Thus, to achieve 80 % power at a significance of 0·05, the minimum mean difference of test scores between groups that could be detected using our sample size was 2·60, assuming equally sized subgroups and a mean of test score at 98·1 (SD 12·5) within our sample.

Ethical approval

All procedures performed in studies were in accordance with the ethical standards of 1964 Helsinki declaration and its later amendments or comparable ethical standards. The protocol of follow-up studies including infant and adolescent development evaluation was approved by the ethics committee of Xi'an Jiaotong University Health Science Center. Written informed and oral consent were obtained from parents/caregivers and adolescents, respectively, after the purpose of the follow-up study was explained.

Measurements

Breast-feeding, timing of initiation of complementary food and consumption of iron-rich or iron-fortified foods. Detailed information about each infant's feeding was prospectively collected by interviewer-administered questionnaires with mothers during the infant follow-up stage. At each visit from birth to 30 months of age, we asked mothers the following same questions to classify the type and duration of breast-feeding: 'For all infants: 1. Have you ever breast-fed your baby? 2. Are you now feeding your baby any breast milk? 3. Are you now feeding your baby other food, including water, micronutrient supplements, animals' milk or infant formula aside from breast milk?'; and 'For weaned infants: How old was your baby (in exact days) when you stopped breast-feeding?' Mothers who were not exclusively breast-feeding were subsequently asked detailed questions about when/which solid foods and non-breast-milk liquids were introduced using FFQ, including the following: infant formula; animals' milk, such as cow and goat; beans, eggs or meat; vitamin/mineral supplements; just water; sugar water; rice porridge; noodles; and vegetables and fruits. The FFQ was previously validated among pregnant women in the study area[32].

According to the WHO[33], any breast-feeding (duration in exact months) was defined as receiving any breast milk and exclusive breast-feeding (duration in exact months) referred to infants receiving only breast milk from his/her mother or expressed breast milk and no other liquids or solids, with the exception of drops or syrups consisting of vitamin/mineral supplements. Regular consumption of Fe-rich food or Fe-fortified foods during 6–23 months was defined by receiving infant formula or the frequency of meat/fish consumption beyond 5–6 times/week at any visit of 6, 9, 12, 18 or 24 months of age[33]. Complementary food was assessed in the following two groups: cows'/goats' milk and high protein-based foods (beans, eggs and meats). In the present study, the high protein-based food group did not include infant formula and/or cows'/goats' milk. The timing of introducing complementary food groups was calculated based on the birth and interview dates at every follow-up visit, and it was determined by the earliest age of introduction of items within the group (in exact days and converted into months).

Assessment of cognitive development. The outcome of interest was adolescent cognitive development, assessed by the Wechsler Intelligence Scale for Children, fourth edition (WISC-IV)[34]. Four composite indexes (Verbal Comprehension, Perceptual Reasoning, Working Memory (WMI) and Processing Speed) and the full-scale intelligence quotient (FSIQ), which represents general cognitive ability, were derived from the ten subtests and four complementary subtests. The Chinese norms of WISC-IV were established by using a nationally representative sample[35] and the scores on all tests were age-standardised.

Postgraduate students administered the tests according to the Chinese WISC-IV technical manual in a school meeting room free of distractions. When the interviewers performed fully accurate administrations and agreed on the scoring of items, they were certified to collect data in the field. Scoring accuracy was reviewed by the field team leader.

All the fieldworkers administering cognitive tests were unaware of the adolescent's infant breast-feeding and complementary feeding status.

Other data collected relevant to the analyses: covariates

All relevant covariates were grouped into seven domains: (1) socio-demographic characteristics, indicated by parental age, education, occupation and household wealth at enrolment; (2) maternal preconception nutrition, indicated by mid-upper arm circumference; (3) maternal reproductive history, indicated by parity; (4) randomised regimen (folic acid, Fe/folic acid and multiple micronutrients); (5) birth outcomes, indicated by small for gestational age and infant sex; (6) adolescent nutrition status, indicated by BMI-for-age z-score and (7) home environment, indicated by household wealth and type of school (village, town or county level) at adolescence. Data in domains 1–5, and 6 and 7 were collected in the original trial and the adolescent follow-up stage, respectively. Small for gestational age was defined as birth weight below the 10th percentile of weight-for-age and sex, as defined by INTERGROWTH standards[36]. Gestational age at birth was calculated by self-reported last menstrual period. BMI was estimated as body weight divided by height squared (kg/m^2). Thinness was defined as BMI-for-age z-score below 2 SD from age- and sex-specific references for WHO growth standards, and overweight was defined as BMI-for-age z-score above 1 SD[37]. Household wealth was established from an inventory of seventeen local household assets or the ownership of goats, cattle, horses and poultry by principal component analysis[38], which was then classified into tertiles as an indicator of the low-, middle- and high-income households.

Statistical analysis

The baseline characteristics were described as counts/percentages for categorical variables and mean values and standard deviations or medians with interquartile ranges for continuous variables. Generalised estimating equation models were used to examine the relationships between infant and young child feeding practices and adolescent cognitive development, with an independent correlation structure and adjusting for assessors of intelligence tests and covariates from the seven domains mentioned above. We used age-standardised FSIQ as the primary outcome and aspects of WISC-IV, that is, Verbal Comprehension Index, WMI, Perceptual Reasoning Index, and Processing Speed Index, as the secondary outcomes.

We created the infant and young child feeding index scores by summing the related variables (Table 1) grounded in the principles of WHO recommendations for breast-feeding and how to assess infant and young child feeding practices (online Supplementary Table S1)[2,3,33]. Specifically, we assumed that longer durations of any/exclusive breast-feeding with starting/timely complementary feeding just after exclusively breast-feeding for 6 months would produce the largest benefits. Taking the duration of exclusive breast-feeding as an example, the infants who were exclusively breast-fed for 6 months received the highest score of 4, and other infants received relatively lower scores by the durations, that is, score 1 for less than 1 month, 2 for 2–3 months, 3 for 4–5 months and 1 for longer than 7 months. Feeding index was then divided into three levels

Table 1. Construction of infant feeding index scores*

Infant feeding practices	Cut-off points for scoring
Exclusive breast-feeding duration (months)	≤1 = 1; 2–3 = 2; 4–5 = 3; 6 = 4; ≥7 = 1
Any breast-feeding duration (months)	≤3 = 1; 4–6 = 2; 7–12 = 3; 13–18 = 4; >18 = 5
Vitamin/mineral supplements	No supplements = 0; ever received supplements = 1
Initial time of beans and eggs (months)	0 = 0; ≤6 = 1; 7–9 = 4; 10–12 = 3; ≥13 = 2
Initial time of cows'/goats' milk (months)†	0 = 0; ≤6 = 1; 7–9 = 2; 10–12 = 3; ≥13 = 4
Regular consumption of Fe-rich food or Fe-fortified foods during 6–23 months‡	No = 0; yes = 1

* Cut-off points for scoring were grounded in the principles of WHO recommendations for breast-feeding and how to assess infant and young child feeding practices, that is, indicators for assessing infant and young child feeding practices. Specifically, we assumed that longer durations of any/exclusive breast-feeding with starting/timely complementary feeding just after exclusively breast-feeding for 6 months would produce the largest benefits.

† Regarding the timing of introducing cows'/goats' milk, the related recommendations differed by countries, such as 12 months in the USA and UK, 9 months in Denmark and 10 months in Sweden. As a result, we used the recommendation in China, that is, 12 months.

‡ Regular consumption of Fe-rich food or Fe-fortified foods during 6–23 months was defined by receiving the infant formula, or the frequency of meat/fish supplementation beyond 5–6 times per week at any visit of 6, 9, 12, 18 or 24 months of age.

by tertiles to indicate the appropriate level of infant and young child feeding practices.

In order to account for missing adolescent development outcome data and potential bias due to differential loss to follow-up, we conducted a sensitivity analyses using inverse probability weighting[39], with randomised regimen, paternal age, education and job, small for gestational age and sex as predictors of missingness in the logistic model. The missingness model produced similar distributions of weights among complete and incomplete cases, no zero fitted probabilities and a reasonable model fit, that is, a P value of 0·287 for Hosmer–Lemeshow goodness-of-fit test. Statistical significance was set at $\alpha < 0.05$ (two-tailed), and all analyses were performed using Stata 12.0 (StataCorp).

Results

Cohort characteristics

Fig. 1 shows the flow chart of participants. A total of 745 adolescents aged 10–12 years were followed. Of them, forty-three (5·8 %) were excluded in final analyses for never receiving breast milk (n 33) and for refusing intelligence tests (n 10). The characteristics of children and parents who were followed up were relatively similar to those lost to follow-up (online Supplementary Table S2).

Socio-demographic characteristics of participants

The socio-demographic characteristics of 745 mother–participant pairs are summarised in Tables 2 and 3. The mean age of mothers was 24·5 (SD 4·5) years. About 54·0 % of them had a secondary education. In addition, majority of families were farmers. Among the adolescents, the mean age was 11·3 (SD 0·6) years and 60·4 % of them were male.

Infant feeding practices of adolescents

As shown in Table 3, 18·2 % of the infants were exclusively breast-fed for 4–6 months, 33·4 % had a duration of any breast-feeding of 13–18 months, while 12·8 % had a duration of any breast-feeding of >18 months. In total, 55·3 % had frequently consumed Fe-rich or Fe fortified foods between the ages of 6 and 23 months; 63·2 % had consumed cows'/goats' milk during the first 2 years of life, and among those who did, the median age of initial consumption was 9 (interquartile range 3, 18) months. The median age of initial consumption of high protein-based food was 8 (interquartile range 6, 9) months.

Duration of any or exclusive breast-feeding and cognitive development. We found that duration of exclusive/any breast-feeding was not significantly associated with any domain of adolescent cognitive development with or without adjusting for the twelve potential covariates (Table 4).

Timing and composition of complementary food introduction and cognitive development. Participants who regularly consumed Fe-rich or Fe-fortified foods at age 6–23 months had higher FSIQ scores than those who did not (adjusted mean differences 4·25; 95 % CI 1·99, 6·51; Table 5). The similar results

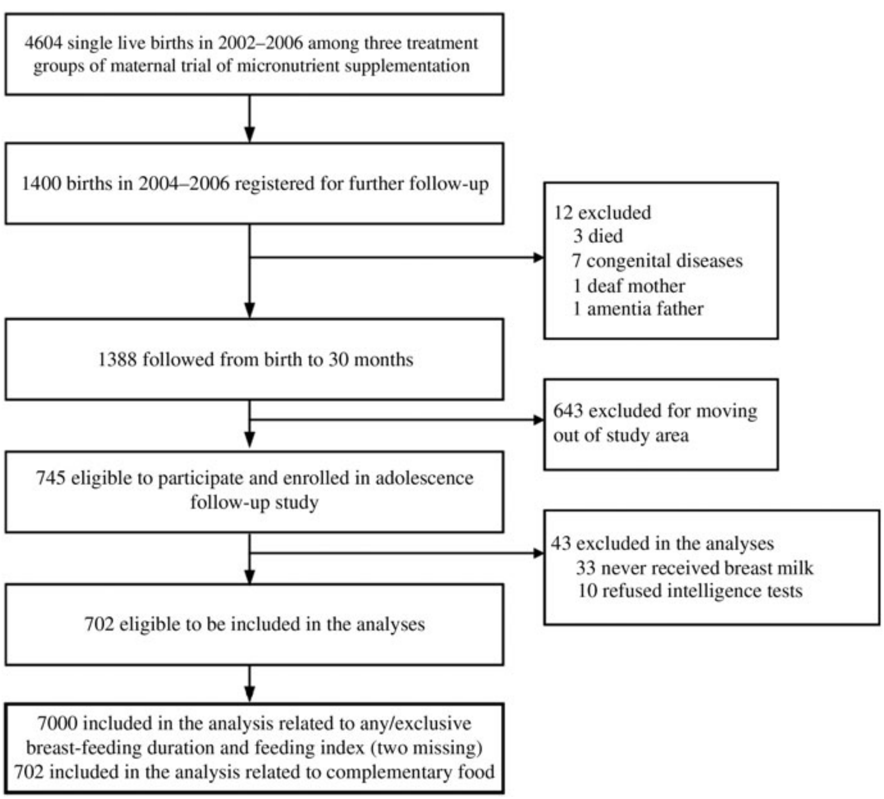

Fig. 1. Participant flow chart.

Table 2. Background characteristics of participants' parents*
(Numbers and percentages; mean values and standard deviations)

Items	n		%
Number of pregnant women	745		100·0
Maternal age (years)			
Mean		24·5	
SD		4·5	
15–19	70		9·4
20–24	365		49·0
25–29	178		23·9
30–34	116		15·6
35+	16		2·2
Maternal education			
<3 years	30		4·0
Primary	192		25·8
Secondary	404		54·4
High school+	117		15·8
Maternal occupation			
Farmer	622		83·7
Others	121		16·3
Paternal age (years)			
Mean		27·7	
SD		4·2	
15–19	0		0·0
20–24	197		26·4
25–29	307		41·2
30–34	183		24·6
35+	58		7·8
Paternal education			
<3 years	9		1·2
Primary	80		10·8
Secondary	472		63·6
High school+	181		24·4
Paternal occupation			
Farmer	555		74·7
Others	188		25·3
Parity at enrolment			
0	508		68·2
1	196		26·3
>2	41		5·5
MUAC (cm)			
Mean		23·2	
SD		1·8	
Trial treatment			
Folic acid	266		35·7
Fe/folic acid	239		32·1
Multiple micronutrients	240		32·2
Household wealth at enrolment			
Poorest	180		24·2
Medium	294		39·5
Richest	271		36·4

MUAC, mid-upper arm circumference.
* Data are missing for maternal education (*n* 2), father's education (*n* 3), mother's job (*n* 2), father's job (*n* 2) and maternal MUAC (*n* 7).

were observed for aspects of WISC-IV, that is, Verbal Comprehension Index, WMI, Perceptual Reasoning Index and Processing Speed Index. Among those who did, we found that the timing of Fe-rich or Fe-fortified foods within the period of 6–23 months was not associated with development outcomes (online Supplementary Table S2).

We also examined the relationship between the timing of transition to consumption of cows'/goats' milk with development outcomes. Among adolescents who received cows'/goats' milk, the highest scores were found in participants who initiated consumption at 10–12 months compared with those after 13 months (Table 6) with an adjusted mean difference of 2·61 (95 % CI 0·13, 5·09) FSIQ points. Besides, adolescents who received the cows'/goats' milk within 6 months had 2·90 (95 % CI 0·68, 5·12) points lower WMI scores as compared with those with an initial age of after 13 months.

In addition, adolescents who initiated high protein-based foods within 6 months had the lowest test scores as compared with those with an initial age of 7–9 months (Table 6). The adjusted mean differences were −2·42 (95 % CI −4·24, −0·61) points for the FSIQ.

Composite feeding score and cognitive development. We constructed a composite feeding score based on WHO feeding recommendations (Table 1). We identified a significant dose–response relationship of feeding index score with FSIQ, Verbal Comprehension Index, WMI and Processing Speed Index (Table 7). Adolescents in the highest tertile of feeding score (best) had higher FSIQ (adjusted mean differences 3·03; 95 % CI 1·37, 4·70) than those in the lowest tertile.

Sensitivity analyses. We conducted sensitivity analyses using inverse probability weighting to account for potential bias due to dependent censoring (loss to follow-up). There were no qualitative differences in our findings using inverse probability weighting models (online Supplementary Tables S4–S7).

Discussion

Based on a prospective birth cohort study in rural China, we found that infant and young child feeding practices following WHO recommendations were associated with significantly improved cognitive development of adolescents aged 10–12 years. Specifically, regular consumption of Fe-rich or Fe-fortified foods during infancy may contribute to better early adolescence cognitive development.

Interpretations of findings and implications for public health

Our finding that the duration of any or exclusive breast-feeding was not significantly associated with adolescent cognitive test scores after rigorously controlling for covariates from multiple domains is consistent with findings from other similar studies[12,13,40–42] and one systematic evaluation[6]. Two systematic reviews that included nine studies adjusted for maternal intelligence and two studies adjusted for socio-economic variables and stimulation at home reported the significant benefits of breast-feeding on child cognitive development[8,17], respectively, but majority of these studies were based on populations from developed countries. Further, the few studies from low- and middle-income countries had inconsistent findings[20,40,43–45]. Horta *et al.*[8] and Huang *et al.*[46] summarised the possible mechanisms on the benefits of breast-feeding for child development including rich nutrients in human milk such as long-chain PUFA and DHA, nurturing and skin contact with the mother, which should also apply to populations in low- and middle-income countries. As a result, the null findings from our study

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Table 3. Background characteristics of offspring*
(Numbers and percentages; mean values and standard deviations; medians and interquartile ranges (IQR))

	Infants				Adolescents		
	n		%		*n*		%
Number of infants	745		100·0	Number of adolescents	745		100·0
Sex				Age (years)			
Male	450		60·4	WISC-IV test scores			
Female	295		39·6	FSIQ			
				Mean		98·1	
				SD		12·5	
Birth weight (g)	3197		400	VCI			
				Mean		102·9	
				SD		15·6	
Weeks of gestation at birth				WMI			
Mean		39·9		Mean		94·5	
SD		1·5		SD		11·0	
Preterm	19		2·6	PRI			
				Mean		96·0	
				SD		12·5	
Low birth weight	25		3·4	PSI			
				Mean		100·0	
				SD		13·7	
SGA	84		11·6	FSIQ at different grades			
Duration (months) of exclusive breast-feeding				Grade 4			
Median		3		Mean		89·0	
IQR		1, 3		SD		12·8	
≤3	592		79·7	Grade 5			
4–6	135		18·2	Grade 6			
≥7	16		2·2	Grade 7			
				Mean		102·5	
				SD		9·6	
Duration (months) of any breast-feeding				School type			
Median		12		Located in village	125		16·8
IQR		6, 16		Township	308		41·3
≤3	130		17·4	County	312		41·9
4–6	72		9·7	Current household wealth			
7–12	198		26·7	Poorest	236		31·7
13–18	248		33·4	Medium	233		31·3
>18	95		12·8	Richest	276		37·1
Whether consumed Fe-rich or Fe-fortified foods at 6–23 months				Weight (kg)			
No	333		44·7	Mean		37·1	
Yes	412		55·3	SD		7·8	
				Height (cm)			
				Mean		146·5	
Age (months) of initial cows'/goats' milk intake				SD		7·2	
Median		9		BMI (kg/m^2)			
IQR		3, 18		BMI-for-age *z*-score			
≤3	127		17·1	Thinness (<–2 SD)	54		7·4
4–6	71		9·5	Normal weight	582		79·2
7–9	58		7·8	Overweight (>1 SD)	99		13·5
10–12	77		10·3				
≥13	138		18·5				
None	274		36·8				
Age (months) of initial high protein-based food intake							
Median		8					
IQR		6, 9					
≤6	313		42·0				
7–9	273		36·6				
10–12	95		12·8				
≥13 or none†	64		8·6				
Feeding index scores‡							
Median		11					
IQR		9, 13					
Q1, the lowest	272		38·1				
Q2	229		32·1				
Q3, the highest	213		29·8				

WISC-IV, Wechsler Intelligence Scale for Children, fourth edition; FSIQ, full-scale intelligence quotient; VCI, Verbal Comprehension Index; WMI, Working Memory Index; PRI, Perceptual Reasoning Index; PSI, Processing Speed Index; SGA, small for gestational age.
* Data are missing for birth weight (*n* 9), SGA (*n* 135), any/exclusive breast-feeding duration (*n* 2), feeding index scores (*n* 31), WISC-IV test scores (*n* 10), adolescent height (*n* 2) and weight (*n* 10).
† Twenty-eight did not receive complementary beans, eggs or meat in the infancy period.
‡ Feeding index scores were categorised into three-level appropriate feeding groups using their tertiles.

Table 4. Wechsler Intelligence Scale for Children, fourth edition (WISC-IV) test scores of adolescents with respect to duration (months) of any/exclusive breast-feeding
(Numbers; mean values and standard deviations; adjusted mean differences and 95 % confidence intervals)

WISC-IV	Exclusive breast-feeding duration (months)	*n*	Mean	SD	Adjusted mean differences*	95 % CI	*P*	Any breast-feeding duration (months)	*n*	Mean	SD	Adjusted mean differences*	95 % CI	*P*
FSIQ							0·75†							0·20†
	≤1	211	98·9	12·5	Ref.			≤3	96	100·6	13·2	Ref.		
	2–3	342	97·9	13·1	–0·40	–2·68, 1·89	0·73	4–6	71	101·0	14·5	0·44	–2·90, 3·79	0·79
	4–6	131	97·0	12·1	0·26	–2·36, 2·88	0·85	7–12	195	99·7	12·9	1·08	–1·49, 3·65	0·41
	≥7	16	96·0	10·3	1·45	–4·54, 7·44	0·64	13–18	244	97·1	11·5	–0·48	–3·04, 2·07	0·71
								>18	94	92·1	11·1	–3·17	–7·26, 0·93	0·13
VCI							0·89†							0·24†
	≤1	211	104·2	16·1	Ref.			≤3	96	106·9	17·1	Ref.		
	2–3	342	102·5	15·7	–0·75	–3·85, 2·35	0·64	4–6	71	105·0	16·6	–1·26	–6·18, 3·66	0·62
	4–6	131	101·9	15·2	0·14	–3·94, 4·22	0·95	7–12	195	103·8	14·9	–1·26	–4·61, 2·10	0·46
	≥7	16	101·6	11·8	1·32	–4·78, 7·42	0·67	13–18	244	101·7	14·9	–1·77	–5·12, 1·58	0·30
								>18	94	98·5	15·7	–3·58	–8·76, 1·61	0·18
WMI							0·83†							0·68†
	≤1	211	94·6	10·7	Ref.			≤3	96	95·2	9·9	Ref.		
	2–3	342	94·5	11·8	0·06	–1·60, 1·73	0·94	4–6	71	96·5	11·0	0·97	–2·00, 3·94	0·52
	4–6	131	93·7	10·2	0·50	–1·89, 2·89	0·69	7–12	195	95·7	12·7	1·75	–0·50, 4·00	0·13
	≥7	16	90·7	10·0	–0·76	–6·84, 5·33	0·81	13–18	244	93·8	10·3	0·85	–1·00, 2·70	0·37
								>18	94	90·0	9·7	–1·23	–4·21, 1·76	0·42
PRI							0·90†							0·14†
	≤1	211	96·6	13·1	Ref.			≤3	96	97·1	12·2	Ref.		
	2–3	342	95·7	12·4	–0·61	–2·78, 1·55	0·58	4–6	71	98·6	13·6	1·74	–1·21, 4·69	0·25
	4–6	131	95·1	12·5	–0·04	–2·51, 2·44	0·98	7–12	195	97·6	13·3	2·24	–0·35, 4·84	0·10
	≥7	16	95·5	10·4	1·49	–3·80, 6·77	0·58	13–18	244	95·3	11·6	–0·14	–2·64, 2·37	0·92
								>18	94	90·6	11·7	–2·51	–5·94, 0·92	0·15
PSI							0·74†							0·35†
	≤1	211	100·1	11·8	Ref.			≤3	96	100·9	12·7	Ref.		
	2–3	342	99·9	15·0	0·29	–1·97, 2·55	0·80	4–6	71	102·7	18·0	0·79	–2·66, 4·24	0·66
	4–6	131	99·1	14·2	0·18	–2·56, 2·92	0·90	7–12	195	101·0	14·7	0·85	–2·12, 3·81	0·58
	≥7	16	98·1	8·3	1·66	–4·13, 7·45	0·57	13–18	244	99·3	12·2	0·15	–2·68, 2·98	0·92
								>18	94	94·9	11·9	–2·71	–7·29, 1·86	0·25

FSIQ, full-scale intelligence quotient; VCI, Verbal Comprehension Index; WMI, Working Memory Index; PRI, Perceptual Reasoning Index; PSI, Processing Speed Index; MUAC, mid-upper arm circumference; SGA, small for gestational age.
* Adjusted for covariates including parental age, job and education at pregnancy enrolment, household wealth at pregnancy enrolment, maternal MUAC at pregnancy enrolment, maternal parity, randomised regimen, birth outcome (SGA), adolescent sex and school type in general estimating equation linear models.
† $P_{\text{for trend}}$ values are calculated in general estimating equation linear models and adjusted for covariates (parental age, job and education at pregnancy enrolment, household wealth at pregnancy enrolment, maternal MUAC at pregnancy enrolment, maternal parity, randomised regimen, birth outcome (SGA), adolescent sex and school type).

Table 5. Wechsler Intelligence Scale for Children, fourth edition (WISC-IV) test scores of adolescents with respect to frequent consumption of iron-rich or iron-fortified foods during 6–23 months*
(Numbers; mean values and standard deviations; adjusted mean differences and 95 % confidence intervals)

WISC-IV	Whether regularly consumed Fe-rich or Fe-fortified foods at 6–23 months	*n*	Mean	SD	Adjusted mean differences†	95 % CI	*P*
FSIQ	No	320	94·8	12·2	Ref.		
	Yes	382	100·7	12·5	4·25	1·99, 6·51	<0·001
VCI	No	320	99·6	15·4	Ref.		
	Yes	382	105·7	15·3	4·46	1·60, 7·31	0·002
WMI	No	320	92·5	10·5	Ref.		
	Yes	382	95·8	11·4	1·99	0·35, 3·62	0·02
PRI	No	320	93·5	12·5	Ref.		
	Yes	382	97·9	12·3	3·07	0·95, 5·20	0·01
PSI	No	320	97·3	13·1	Ref.		
	Yes	382	101·9	14·0	3·48	1·24, 5·73	0·002

FSIQ, full-scale intelligence quotient; VCI, Verbal Comprehension Index; WMI, Working Memory Index; PRI, Perceptual Reasoning Index; PSI, Processing Speed Index.
* Regular consumption of Fe-rich food or Fe-fortified foods during 6–23 months was defined by receiving the infant formula, or the frequency of meat/fish supplementation beyond 5–6 times per week at any visit of 6, 9, 12, 18 or 24 months of age.
† Adjusted for covariates (including parental age, job and education at pregnancy enrolment, household wealth at pregnancy enrolment, maternal mid-upper arm circumference at pregnancy enrolment, maternal parity, randomised regimen, birth outcome (small for gestational age), adolescent sex, and school type) in general estimating equation linear models.

and other studies in low- and middle-income countries warrant further explanations. In the present study, one possible explanation was due to the low statistical power, in which a minimum mean difference of test scores between groups that could be detected was 2·60.

Generally, timely Fe supplementation or complementary feeding with Fe-rich/Fe-fortified foods was necessary for the depletion of infant Fe stores after exclusive breast-feeding for 6 months[26]. However, the results of Fe supplementation trials during infancy on long-term cognitive development are inconsistent and appear to vary by different population[47–49]. There is also a concern of adverse effects of Fe supplementation, including hampering brain development, due to the excess intake of Fe[50]. Thus, some studies suggest that timely/starting complementary Fe-rich/Fe-fortified foods just after exclusive breast-feeding for 6 months is more practical than the use of Fe supplements[47]. In the present study, we found positive associations of the consumption of Fe-rich/Fe-fortified foods with adolescent cognitive development. Although this finding may be context-specific such as the different vitamin C-rich diets influencing the uptake of nonheme Fe as the reviewer commented, it implies that promotion or provision of Fe-rich/Fe-fortified complementary foods during the first 2 years of life can meet Fe requirements of infants and contribute to their long-term cognitive development.

Unmodified cows'/goats' milk does not contain sufficient Fe and folate to meet infant dietary requirements, and early introduction of these foods is negatively associated with Fe status[51,52]. Some studies also reported that Fe deficiency was negatively associated with the development of white matter, hippocampal–frontal and striatal–frontal areas of the brain[29]. Consequently, early introduction of animals' milk may hamper the child development; however, to our knowledge, no studies have examined the associations of initial age of cows'/goats' milk with child cognitive development. We observed that among adolescents who ever received cows'/goats' milk at infancy, those who initiated before 6 months had insignificantly lower FSIQ and significantly lower WMI scores. In addition, introducing high protein-based foods before 6 months was also significantly associated with lower FSIQ scores, which may be due to that introducing high-protein foods before 6 months was the interference of exclusive breast-feeding and digestion, resulting in protein deficiency. Protein deficiency was found to be negatively associated with the global development of the brain[29]. Taken together, these findings suggest that introducing complementary feeding before 6 months may not only comprise the exclusive breast-feeding but also hamper the long-term development of children. Regarding the optimal initial age, the highest FSIQ scores for cows'/goats' milk were found in participants who initiated between 10 and 12 months compared with an initial age of beyond 13 months, which was conflicted in the ongoing Chinese guideline of waiting until 12 months. The possible explanation may be due to the prevalent undernutrition and poor resource in study area where animals' milk was used as the primary food of providing protein requirements for infant and young child. In our study area, the proportions of initiating cows'/goats' milk before 10 and 12 months were 34·4 and 44·7 %, respectively. In terms of high protein-based food, participants who initiated between 7 and 9 months had higher test scores, which was in line with the Chinese guideline on complementary feeding.

We examined the relationship between a composite feeding practice score and development outcomes. This analysis may be the most informative as crudely dividing feeding practices by breast-feeding duration and complementary food introduction may not adequately capture the nuances of infant and young child feeding experience. We found that adolescents in the highest tertile of feeding scores had 3·03 higher points on general cognitive ability as compared with those in the lowest tertile. In our sample, from grade 4 to grade 7, FSIQ scores increased on average by 4·51 points per school year (Table 3). Consequently, the effect sizes of improving appropriate feeding during the early years of life are relatively large and are approximately equivalent to an additional 8-month schooling. As discussed above, some studies explained the

Table 6. Wechsler Intelligence Scale for Children, fourth edition (WISC-IV) test scores of adolescents with respect to the initial age (months) of introduction of cows'/goats' milk and high protein-based food in infancy
(Numbers; mean values and standard deviations; adjusted mean differences and 95 % confidence intervals)

		Cows'/goats' milk							High protein-based food					
WISC-IV	Age of initiation (months)	*n*	Mean	SD	Adjusted mean differences*	95 % CI	*P*	Age of initiation (months)	*n*	Mean	SD	Adjusted mean differences*	95 % CI	*P*
FSIQ	≤6	173	97·9	12·8	−1·83	−4·48, 0·81	0·18	≤6	292	97·7	12·5	−2·42	−4·24, −0·61	0·01
	7–9	55	99·0	14·0	−0·96	−5·21, 3·29	0·66	7–9	258	98·8	13·0	Ref.		
	10–12	73	102·0	10·3	2·61	0·13, 5·09	0·04	10–12	90	96·8	12·9	−1·88	−5·48, 1·72	0·31
	≥13	135	98·4	13·1	Ref.			≥13 or none†	62	98·3	11·9	−0·47	−3·41, 2·48	0·76
	None	266	96·7	12·6	−1·84	−4·08, 0·40	0·11							
VCI	≤6	173	103·2	16·2	−1·48	−4·70, 1·75	0·37	≤6	292	102·7	16·0	−2·27	−5·00, 0·46	0·10
	7–9	55	104·3	18·2	−0·03	−5·44, 5·39	0·99	7–9	258	103·6	15·2	Ref.		
	10–12	73	105·8	14·0	1·79	−2·03, 5·61	0·36	10–12	90	102·1	16·5	−1·64	−5·85, 2·58	0·45
	≥13	135	102·8	15·6	Ref.			≥13 or none†	62	102·7	14·7	−0·75	−5·10, 3·61	0·74
	None	266	101·8	15·2	−1·10	−4·02, 1·83	0·46							
WMI	≤6	173	93·6	10·1	−2·90	−5·12, −0·68	0·01	≤6	292	93·9	11·1	−1·71	−3·62, 0·19	0·08
	7–9	55	94·1	12·0	−2·84	−7·22, 1·55	0·21	7–9	258	94·8	10·8	Ref.		
	10–12	73	95·7	10·2	−0·48	−3·14, 2·17	0·72	10–12	90	94·4	12·6	−0·20	−2·84, 2·44	0·88
	≥13	135	95·4	12·3	Ref.			≥13 or none†	62	93·8	10·5	−1·08	−3·64, 1·47	0·41
	None	266	93·8	11·2	−1·90	−4·20, 0·40	0·11							
PRI	≤6	173	96·2	13·4	−0·03	−3·41, 3·34	0·99	≤6	292	96·2	12·7	−0·81	−2·67, 1·05	0·40
	7–9	55	97·2	13·2	0·95	−3·20, 5·09	0·66	7–9	258	95·9	13·3	Ref.		
	10–12	73	99·9	12·1	3·20	0·08, 6·33	0·05	10–12	90	94·3	11·1	−1·64	−5·28, 2·01	0·38
	≥13	135	96·1	13·8	Ref.			≥13 or none†	62	96·8	10·9	0·69	−1·95, 3·33	0·61
	None	266	94·2	11·1	−2·15	−4·40, 0·11	0·06							
PSI	≤6	173	99·2	13·9	−1·58	−3·97, 0·81	0·20	≤6	292	98·9	12·7	−3·19	−4·95, −1·43	<0·001
	7–9	55	99·5	12·4	−2·11	−5·55, 1·33	0·23	7–9	258	101·1	14·6	Ref.		
	10–12	73	104·3	14·2	3·88	0·97, 6·80	0·01	10–12	90	98·3	13·7	−2·78	−6·56, 0·99	0·15
	≥13	135	99·6	13·3	Ref.			≥13 or none†	62	100·6	14·9	−0·40	−3·80, 3·00	0·82
	None	266	99·2	14·0	−0·54	−2·69, 1·61	0·62							

FSIQ, full-scale intelligence quotient; VCI, Verbal Comprehension Index; WMI, Working Memory Index; PRI, Perceptual Reasoning Index; PSI, Processing Speed Index.
* Adjusted for covariates (including parental age, job and education at pregnancy enrolment, household wealth at pregnancy enrolment, maternal mid-upper arm circumference at pregnancy enrolment, maternal parity, randomised regimen, birth outcome (small for gestational age), adolescent sex and school type) in general estimating equation linear models. For high protein-based food, the potential covariates also included durations of exclusive breast-feeding.
† Number of participants who did not consume high protein-based food in infancy was 28.

Table 7. Wechsler Intelligence Scale for Children, fourth edition (WISC-IV) test scores of adolescents with respect to tertiles of infant feeding index scores (Numbers; mean values and standard deviations; adjusted mean differences and 95 % confidence intervals)

WISC-IV	Feeding index scores	*n*	Mean	SD	Adjusted mean differences*	95 % CI	*P*	$P_{for\ trend}$†
FSIQ	Q1, lowest	239	97·6	12·6	Ref.			<0·001
	Q2	224	98·5	13·0	2·63	0·59, 4·67	0·01	
	Q3, highest	209	98·2	12·5	3·03	1·37, 4·70	<0·001	
VCI	Q1, lowest	239	102·8	15·9	Ref.			0·03
	Q2	224	103·4	15·8	2·53	–0·34, 5·40	0·08	
	Q3, highest	209	102·6	15·3	2·27	0·08, 4·45	0·04	
WMI	Q1, lowest	239	94·2	10·6	Ref.			0·03
	Q2	224	94·2	12·0	0·93	–0·83, 2·69	0·30	
	Q3, highest	209	94·8	11·0	2·35	0·25, 4·46	0·03	
PRI	Q1, lowest	239	95·5	12·2	Ref.			0·08
	Q2	224	96·7	12·8	2·53	0·14, 4·91	0·04	
	Q3, highest	209	95·5	13·0	1·74	–0·25, 3·74	0·09	
PSI	Q1, lowest	239	98·9	13·3	Ref.			0·009
	Q2	224	99·9	14·1	2·10	0·02, 4·17	0·05	
	Q3, highest	209	100·8	13·7	3·43	1·56, 5·30	<0·001	

FSIQ, full-scale intelligence quotient; VCI, Verbal Comprehension Index; WMI, Working Memory Index; PRI, Perceptual Reasoning Index; PSI, Processing Speed Index.
* Adjusted for covariates (including parental age, job and education at pregnancy enrolment, household wealth at pregnancy enrolment, maternal mid-upper arm circumference at pregnancy enrolment, maternal parity, randomised regimen, birth outcome (small for gestational age), adolescent sex and school type) in general estimating equation linear models.
† $P_{for\ trend}$ values are calculated in general estimating equation linear models with the original feeding index scores as a continuous exposure variable, and adjusted for the same covariates as above.

mechanisms for the individual component of the composite score such as breast-feeding, Fe and protein[8,29,46,47], but our study could not provide evidence for the mechanisms behind the observed association of the feeding index with development outcome. Generally, the brain still develops rapidly during the first 2 years of life including the visual/auditory cortex, angular gyrus/Broca's area and the prefrontal cortex, which may thus be vulnerable to early undernutrition, Fe deficiency and other environmental factors that lay the foundation for brain architecture and functional capacity, and that extend the effects to adolescence or beyond[53].

Although great efforts to increase breast-feeding duration have been made, our findings indicate that programmes should also equally focus on high-quality complementary foods to harness the potential long-term development benefits of optimal infant and young child feeding practices.

Strengths and limitations

The strengths of our study include the prospective birth cohort design with regular visits at infancy, the length of follow-up to early adolescence and the standardised, culturally appropriate intelligence evaluation scales (WISC-IV) for Chinese children. To our knowledge, this is the first study in which associations between infant and young child feeding practices, comprehensively emphasising on the durations of exclusive/any breast-feeding and initial ages and types of complementary foods, and adolescent cognitive development have been examined.

Our study was limited by a few facts. Firstly, participants in our study were born to women who had participated in a micronutrient supplementation trial. Although we adjusted for randomised regimen in the analysis, the generalisability to mothers who would not participate in a clinical trial should be considered. Secondly, 643 (46·3 %) out of 1388 moved away from the study areas and were not able to be followed up. Nevertheless, the majority of the background characteristics between followed and lost to follow-up were balanced (online Supplementary Table S2), and the sensitivity analyses of using inverse probability weighting to account for missing observed similar result patterns. Thirdly, although the infant feeding index was constructed by principles of appropriate feeding practices, it was not validated and needs replication in future studies. Besides, we did not consider the weights or the relative importance of different feeding practices and specify the type of supplements (Table 1) the participants received in the data collection form. In addition, the effect sizes of categorising the index into tertiles should cautiously be generalised to other populations as they may have different distributions of infant feeding factors that contributed to our score. Finally, we did not have information on maternal intelligence which may be associated with feeding practices and cognitive development and can allow for residual confounding[6,17]. Randomised trials of breast-feeding and complementary feeding promotion are needed to determine causal effects.

Conclusion

Appropriate infant feeding practices (breast-feeding plus appropriate timing of the introduction of high-quality complementary foods), based on the current WHO recommendations, were associated with significantly improved early adolescence cognitive development in rural China. Specifically, consumption of Fe-rich or Fe-fortified foods during infancy may contribute to better cognitive development.

Acknowledgements

The authors thank all the field workers for helping to collect data. The authors are also grateful for all the women, adolescents and their families who participated in the study.

This work was supported by the National Natural Science Foundation of China (L. Z., grant no. 81872633); the National Key Research and Development Program of China (H. Y., grant no. 2017YFC0907200, 2017YFC0907201) and the China Scholarship Council (Z. Z., grant no. 201806280188). All the founders had no role in the design, analysis or writing of this article.

Z. Z., Y. C., H. Y., M. J. D. and L. Z. planned and designed the study; Z. Z., Y. C., Y. L., S. M., M. E. and S. T. conducted the study; Z. Z., Q. Q., S. L., H. L., W. W. F. and C. R. S. analysed data and interpreted results; Z. Z. wrote the paper; L. Z. had primary responsibility for final content and all authors reviewed, revised and approved the final paper.

There are no conflicts of interest.

Supplementary material

For supplementary material referred to in this article, please visit https://doi.org/10.1017/S0007114519003271

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