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# Relationship between moderate to late preterm, diet types and developmental delay in less-developed rural China

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#### **ABSTRACT**

**Aim:** To measure the development of moderate to late preterm children by Ages and Stages Questionnaires (ASQ) and explore the relationship between moderate to late preterm, diet types and development delay in less-developed rural China.

**Methods:** Data were collected from a cross-sectional community-based survey, which recruited 1748 children aged 1–59 months in eight counties of China. Caregivers of these children completed the Chinese version of ASQ-3 (ASQ-C) while physical examination and questionnaires on sociodemographic characteristics were conducted. Multivariate logistic regressions were used to analyze the association between moderate to late preterm and suspected developmental delay, as well as the association between diet types and suspected developmental delay. Consumption of certain food types was compared between moderate to late preterm and full-term children.

**Results:** The prevalence of suspected overall developmental delay was 31.3% in the moderate to the late preterm group, compared with 21.6% in the full-term group. Moderate to late preterm birth was not associated with total suspected developmental delay and developmental delay in all the domains of ASQ, except for fine motor (OR = 2.43 95% C.I.: 1.04–5.56). The intake of vegetables and fruits had a protective influence on developmental delay in fine motor function, and moderate to late preterm children had lower relative consumption of fruits and vegetables than full-term children.

**Conclusion:** Moderate to late preterm children in rural China showed an increased likelihood of developmental delay in fine motor function. Future interventions to improve the intake of vegetables and fruits in moderate to late preterm children are recommended.

#### **KEYWORDS**

Moderate to late preterm; Diet types; Developmental delay; China

#### Introduction

Preterm birth is defined as giving birth before 37 weeks of gestation [1]. According to gestational age, preterm birth is categorized as three groups: extremely preterm (<28 weeks), very preterm (28~32 weeks) and moderate to late preterm (32~37 weeks). The previous studies mainly focus on infants with extremely preterm and very preterm for their high risk of mortality and morbidity. Moderate to late preterm accounts for 84.3% preterm birth globally, making this population an important public health concern [2]. The evidences have shown that compared with full-term children, moderate to late preterm infants are at higher risk of death and morbidity in infancy and childhood, such as from respiratory diseases and infections [3,4].

Whether moderate to late preterm children can catch up with neurological, psychological and behavioral milestone in comparison with full-term children have been a global health discussion. Several studies in Western countries indicated that compared with full-term children, moderate to late preterm children were at increased risk for development delay in domains of cognitive, motor, language and social-emotional competence, and were more likely to have impaired attention skills, learning problem and behavioral abnormalities [5–8]. Nevertheless, there are relatively few studies exploring early child development of preterm children in China. Most of these studies in Chinese populations used Bayley scales of infant development and the Gesell Developmental Scale to evaluate developmental

outcomes of preterm infants [9,10]. Given that these measurement tools require professional medical staff to apply, previous studies in China have mainly been conducted in hospital-based samples in urban areas with relatively small sample sizes [11,12]. Moreover, to our knowledge, developmental outcomes of moderate to late preterm infants have not been studied in China.

Diet plays an essential role in neurodevelopmental outcomes for children. Many studies focused on the influence of dietary nutrients on child neurodevelopment. Leventakou et al. found that food content high in fat, salt and sugar at preschool age were associated with poor verbal and cognitive ability [13]. Makrides et al. conducted a randomized controlled trial and indicated that docosahexaenoic acid improved neurodevelopmental outcomes among 18-month girls with preterm [14]. Steinmacher et al. also suggested that iron supplement could improve some neurodevelopmental outcomes for preterm infants [15]. It is difficult to implement interventions with dietary nutrients, especially among low-income and middle-income populations on a large-scale. Dietary diversity defined as the sum of food groups received in last 24 h has been applied as an effective indicator to assess nutrition intake among children and assess large-scale population-based intervention [16]. According to the definition of the Multiple Indicator Cluster Survey (MICS), dietary diversity includes seven food groups: (1) grains, root and tubers, (2) legumes and nuts, (3) dairy products (including milk, yogurt, and cheese), (4) flesh foods (meat, fish, poultry and liver/organ products), (5) eggs, (6) vitamin A-rich fruits and vegetables and (7) other kind fruits and vegetables. The majority of studies exploring health outcomes of food groups have focused on physical growth [17,18]. A study in rural Bangladesh reported that low dietary diversity was associated with an increased risk of stunting among 6-59 months old children [19]. However, there is little evidence on the relationship between dietary diversity and neurodevelopment amongst children in general and even less in preterm children. Therefore, understanding the relationship between preterm birth, dietary diversity and neurodevelopment is essential for further design and implementation of diet-related interventions.

The Ages and Stages Questionnaire is recommended as a developmental screening tool by the American Academy of Pediatrics [20], which has been widely applied and adapted across many different settings [21,22]. In 2010, in China, it was translated and adapted into Ages and Stages Questionnaires-Chinese (ASQ-C) with consideration of culture difference, and cutoff scores of ASQ-C were established [23,24]. ASQ-C has excellent psychometric properties, test-retest reliability of 80%, and sensitivity of 87.5% and specificity of 84.4%, providing the opportunity to conduct largescale studies related to child neurodevelopment in China [25]. Although there were several studies using ASQ-C to screen for neurodevelopmental delay in the general Chinese children population [23,26], no previous study has applied it to describe neurodevelopmental outcomes among children with preterm birth in China.

The present study aimed to (1) evaluate the development of moderate to late preterm children in central and western China using the ASQ-C, and (2) analyze the relationship between moderate to late preterm birth, dietary intake and suspected developmental delay.

#### **Methods**

## **Participants**

This study was a cross-sectional survey on early childhood development in 2016, covering 8 rural counties in four provinces of China (Xinjiang, Qinghai, Jiangxi and Ningxia), as part of the maternal and child health program funded by UNICEF. The total population in the project counties was 3,639,000 in 2016. The annual income per capita of rural population was1263 US dollars, below the national average 1736 dollars in rural areas in 2016.

A multistage sampling method was employed to select townships and villages in each county. First, 15 administrative villages per county and two nature villages per administrative village were selected at random with population proportional to size (PPS). In China, each administrative village has many naturally formed group (nature villages) with geographic boundaries. Some natural villages are far away from each other, especially in the western rural area of China. Thus, we randomly selected households within each nature village instead of an administrative village given the feasibility and representativeness of the survey. Within each selected nature village, 10 households with children under three years of age were selected according to a full registration list for each village by simple random sampling; the list of children was provided by local village doctors. Random numbers for selection criteria were generated by a random number table, and staff members of this program completed all the sampling processes. The youngest children and one of their primary caregivers (the person who knows the child best in the family) in each selected household were interviewed face-to-face. The study procedures were explained to each caregivers and informed verbal consent was obtained for all of the caregivers involved in the study. The Peking University

Health Science Center Institutional Review Board approved this study.

Because this study was designed to collect relevant baseline data for an intervention project, we expected to see a decreased prevalence of suspected development delay in the final evaluation. The following formula was used to calculate the sample size:

$$n = 2\bar{p}\,\bar{q}(Z_{\alpha} + Z_{\beta})^2/(p_1 - p_0)^2, \quad \bar{p} = (p_1 + p_0)/2,$$
  
 $\bar{q} = 1 - \bar{p}$ 

We used 0.05 as the statistical significance ( $\alpha$ ) and set the power of the test  $(1-\beta)$  as 0.8. We assumed the baseline prevalence of suspected development delay  $(p_0)$  would be 40% and expected a relative 20% decrement of prevalence  $(p_1 - p_0)/p_0$ . Finally, considering an 80% response rate, the required total sample size of children would be 1410 (705:705).

#### **Data collection**

Generally, we extracted the gestation age from birth certificates. For primary caregivers who did not have birth certificates during the interview, the recall of the primary caregivers about gestation age and whether their child was preterm birth or not. We defined the moderate to late preterm (32-37 weeks) and full term (37-42 weeks) based on gestational age, and the children with post-term birth (>42 weeks) were excluded. Since our interested population was moderate to late preterm and the prevalence of extremely and very preterm birth was relatively low in our study (4 cases), we also exclude these cases from the analysis.

The child neurodevelopment was assessed using the Chinese version of the Ages & Stages Questionnaires, Third Edition (ASQ-C) in our study. The ASQ-C is a series of 21 parent/caregiver-completed questionnaires designed to screen the developmental performance among children aged 1-66 months. There are different questionnaires for children of different ages. Corrected calendar age was only used for age calculations among preterm children younger than 24 months, and uncorrected calendar age was used for age calculations among the rest of the children, following the ASQ-C manual. The ASQ-C comprised five major developmental domains: communication, gross motor, fine motor, problem solving and personal-social domains. In each domain, there were six items on developmental milestones. The caregivers were asked to answer questions about some things their child could and could not do, such as 'Does your baby pick up a crumb or Cheerio or the fruit of Chinese wolfberry or other pea-sized items with the tips of his thumb and a finger'. The

caregivers would answer yes, sometimes or not yet to each question. This process took about 10–15 min.

A self-designed structured questionnaire for caregivers was used in our survey. Items in the questionnaire were selected from 'Multiple indicator cluster survey (MICS) manual' published by UNICEF. The questionnaire was adjusted based on a pilot survey conducted in the Yulong County in Yunnan Province, and the workflow and guideline of the field survey were prepared. Before doing the formal fieldwork, all interviewers were trained according to the investigation guideline, including using of digital survey equipment, how to administer, the way to question the questionnaire, and the standards and requirements of measurements. All data collection was accomplished through tablet computers installed with the Goodata entry system. Information on age of the child, gender of children, number of older siblings (0, 1, 2 or more), birthweight (low birthweight (<2500 kg) or not), gestational age at birth, delivery method of the children (cesarean section or vaginal delivery), education of the caregivers (illiterate, primary school, secondary school, college and above), household income level (poorest, poor, middle, richer, and richest) and breastfeeding during the past 24 h (yes or no) were collected. Moreover, the questionnaire asked caregivers whether or not a child had consumed the following 7 types of food during the past 24 h: (1) grains, root and tubers, (2) legumes and nuts, (3) dairy products (including milk, yogurt, and cheese), (4) flesh foods (meat, fish, poultry and liver/organ products), (5) eggs, (6) vitamin A-rich fruits and vegetables and (7) other kind fruits and vegetables. The proportion of food intake for each type of food among the whole study population was calculated. Since exclusive breastfeeding from birth until 6 months is recommended by WHO, we only analyze dietary status among 6-59-month-old children. According to the WHO guideline, the minimum dietary diversity was defined as receiving food from 4 and above groups 24 h before the survey was given.

#### Statistical analysis

In this study, each item on ASQ-C was scored as 10 (yes), 5 (sometimes) or 0 (not yet) according to whether the child has achieved a milestone. The item scores on each domain were summed to obtain a domain score. The ASQ-C domain scores of less than two standard deviations from the mean of the Chinese rural reference group in a certain domain was considered as suspected developmental delay in that domain. A suspected developmental delay in any of the above five domains was defined as the suspected total development delay.



Socio-economic characteristic distributions prevalence of suspected development delay were calculated and compared between moderate to late preterm and full-term children using chi-square tests or t tests. Multivariate logistic regression analyses were used to examine the relationships between moderate to late preterm and the suspected developmental delay, and between dietary types and the suspected developmental delay, leading to crude, adjusted prevalence odd ratios (ORs) and 95% confidence interval for the suspected developmental delay. Age of child, gender of child, number of older siblings, caregiver's education, household income level, method of delivery breastfeeding in the past 24 h and low birthweight were adjusted in the multivariate model exploring the influence of moderate to late preterm birth on the suspected developmental delay. Preterm birth was added to adjustment in the model exploring effects of diet types on the suspected developmental delay. Additionally, the proportion of different types of food intake and prevalence of minimum dietary diversity were also calculated and compared between 6 and 59 months children with moderate to late preterm birth and with full-term birth. All analyses were conducted using STATA version 15.0, with a statistical significance level set at p < 0.05.

#### Results

As shown in Table 1, a total of 1748 children aged 1-59 months were included in the present study (Table 1). Among them, 83 children reported moderate to late preterm birth. Full-term groups and moderate to late preterm groups did not show disparity based on age, gender, number of older siblings, caregivers' education, breastfeeding during the past 24 h and household income level. However, the moderate to the late preterm group had more cesarean section as compared with the full-term group (moderate to late preterm: 37.5%, fullterm: 22.5%, p < 0.001). The proportion of low birth weight (<2500 kg) in the moderate to the late preterm group was much higher than that in the full-term group (moderate to late preterm: 41.0%, full-term: 5.7%, *p* < 0.001).

As shown in Figure 1, the prevalence of suspected developmental delay in moderate to late preterm and full-term groups was compared (Figure 1). The prevalence of suspected overall developmental delay was 31.3% in the moderate to the late preterm group, compared with 21.6% in the full-term group. There was a significant difference between two groups (p < 0.05). Further analysis showed that the moderate to the late preterm group had a higher prevalence of suspected developmental delay in the fine motor domains than

Table 1. Characteristics of children aged 1-59 months with fullterm and moderate to late preterm birth.

	10 10 1010 p. 1			
			Moderate to	_
N (%)	Total	Full-term	late preterm	Ρ
Gestational age	1748(100.0)	1665(95.25)	83(4.75)	
weeks, mean	39 <sup>+3</sup> (32 <sup>+6</sup> -	39 <sup>+4</sup> (37 <sup>+1</sup> -	35 <sup>+3</sup> (32 <sup>+6</sup> -	
(range)	41 <sup>+6</sup> )	41 <sup>+6</sup> )	36 <sup>+6</sup> )	<0.001
Age of child,				0.79
months, n(%)				
1–11	353(20.2)	334(20.1)	19(22.9)	
12–23	455(26.0)	433(26.0)	22(26.5)	
24-59	940(53.8)	898(53.9)	42(50.6)	
Gender of child, n				0.72
(%)				
Boys	939(53.7)	896(53.8)	43(51.8)	
Girls	809(46.3)	769(46.2)	40(48.2)	
Number of older				0.99
siblings, n(%)				
0	691(39.5)	658(39.5)	33(39.8)	
1	752(43.0)	716(43.0)	36(43.4)	
>=2	305(17.5)	291(17.5)	14(16.9)	
Caregiver's				0.916
education, n(%)				
Illiteracy	226(12.9)	217(13.0)	9(10.8)	
Primary	391(22.4)	373(22.4)	18(21.7)	
Secondary	995(56.9)	945(56.8)	50(60.2)	
College and	136(7.8)	130(7.8)	6(7.2)	
above				
Method of delivery,				< 0.001
n(%)				
Cesarean section	402(23.2)	372(22.5)	30(37.5)	
Vaginal delivery	1332(76.8)	1282(77.5)	50(62.5)	
Breastfeeding in last	328(20.3)	309(20.0)	19(27.9)	0.111
24 h, n(%)				
Low Birth weight, n	123(7.3)	91(5.7)	32(41.0)	< 0.001
(%)				
Income, n(%)				0.494
Poorest	378(22.4)	358(22.2)	20(24.7)	
Poor	294(17.4)	285(17.7)	9(11.1)	
Middle	362(21.4)	341(21.2)	21(25.9)	
Richer	218(12.9)	206(12.8)	12(14.8)	
Richest	439(26.0)	420(26.1)	19(23.5)	

the full-term group with significant statistical differences (p < 0.05). Although the differences between two groups were not statistically significant, the proportions of suspected developmental delay in the gross motor, problem solving and personal-social domains in moderate to the late preterm group were higher than that in the fullterm group.

The association between moderate to late preterm birth and suspected developmental delay is shown in Table 2. In the crude model, moderate to late preterm children had higher odds of total suspected developmental delay (OR = 1.65 95% C.I.: 1.02-2.67) and development delay in fine motor (OR = 2.04 95% C.I.: 1.02-4.06) compared to full-term children. But after taking other confounders into the regression model, there was no statistically significant association between moderate to late preterm and total suspected developmental delay. The odds ratio of suspected developmental delay in the fine motor domain comparing moderate to late preterm children with full-term children is 2.43 (95% C.I.: 1.04-5.56). No significant association was found

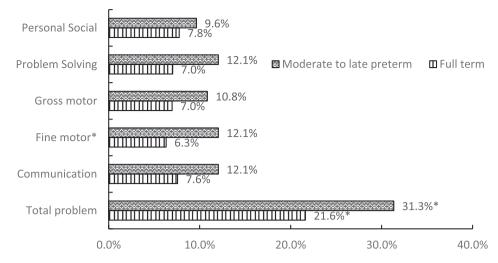


Figure 1. Comparison of prevalence of suspected developmental delay in moderate to late preterm and full-term groups.

**Table 2.** Association between abnormal ASO scores and moderate to late preterm birth.

	Crude model			Adjusted model		
		Moderate-to-late preterm			Moderate-to-late preterm	
Developmental outcomes	Full term	OR for developmental outcomes	95% C.I.	Full term	OR for developmental outcomes	95% C.I.
Total problems	Reference	1.65	(1.02-2.67)	Reference	1.70	(0.84–2.89)
Communication	Reference	1.67	(0.84 - 3.32)	Reference	2.27	(0.95 - 5.35)
Fine motor	Reference	2.04	(1.02-4.06)	Reference	2.43	(1.04-5.56)
Gross motor	Reference	1.62	(0.79 - 3.33)	Reference	1.61	(0.69 - 3.76)
Problem solving	Reference	1.81	(0.91 - 3.60)	Reference	1.49	(0.63 - 3.56)
Personal social	Reference	1.27	(0.60-2.69)	Reference	1.02	(0.35-2.95)

Crude Model: unadjusted; Adjusted Model: adjusted for age of child, gender of child, number of older siblings, caregiver's education, income, method of delivery, breastfeeding in the last 24 h and low birth weight.

between preterm birth and developmental delay in gross motor, communication, problem solving and personal social in neither the crude model nor the adjusted model.

Table 3 indicates the relationship between dietary intake and suspected developmental delay among 6-59 months children (Table 3). Although the minimum dietary diversity is not associated with total suspected developmental delay nor suspected developmental delay in fine motor, the intake of some specific kinds of food affects the prevalence of suspected developmental delay. Children being fed with grains, roots and tubers (OR = 0.47 95% C.I.: 0.28-0.80), legumes and nuts (OR = 0.56 95% C.I.: 0.41-0.76), and other fruits and vegetables (OR = 0.55 95% C.I.: 0.42-0.72) were less likely to be suspected of total developmental delay. Intake of fruits and vegetables significantly decreased the prevalence odd ratio of suspected developmental delay in fine motor function (vitamin A-rich fruits and vegetables: OR = 0.60 95% C.I.: 0.38-0.96; other fruits and vegetables: OR = 0.54 95% C.I.: 0.35-0.83).

Table 4 compares the proportion of different diet types between 6 and 59 months children with moderate to late preterm birth and full-term birth (Table 4). The proportion of intake of all the above types of food was

similar between moderate to late preterm and full-term children except for fruits and vegetables. The proportion of vitamin A-rich fruits and vegetables consumed in the past 24 h was 9.2% higher among full-term 242 children compared to moderate to late preterm children (83.9%

Table 3. Relationship between food types and suspected developmental delay among 6-59 month children.

Total suspected developmental delay		Suspected developmental delay in fine motor	
OR	95%CI	OR	95%CI
0.47	028-0.80	0.51	0.26-1.00
0.56	0.41-0.76	0.67	0.40-1.11
1.07	0.79-1.44	1.64	0.96-2.81
0.93	0.67-1.29	1.16	0.69-1.96
1.02	0.78-1.33	1.19	0.78-1.82
0.98	0.70-1.37	0.60	0.38-0.96
0.55	0.42-0.72	0.54	0.35-0.83
0.74	0.53-1.03	1.05	0.61–1.80
	OR 0.47 0.56 1.07 0.93 1.02 0.98 0.55	developmental delay  OR 95%CI  0.47 028-0.80 0.56 0.41-0.76 1.07 0.79-1.44 0.93 0.67-1.29 1.02 0.78-1.33 0.98 0.70-1.37 0.55 0.42-0.72	Total suspected developmental delay         developmental delay           OR         95%CI         OR           0.47         028-0.80         0.51           0.56         0.41-0.76         0.67           1.07         0.79-1.44         1.64           0.93         0.67-1.29         1.16           1.02         0.78-1.33         1.19           0.98         0.70-1.37         0.60           0.55         0.42-0.72         0.54

Note: adjusted for age of child, gender of child, number of older siblings, caregiver's education, income, method of delivery, breastfeeding in the last 24 h, low birth weight, moderate to late preterm birth.

<sup>\*</sup>Measured by whether or not a child consumed the certain type of food in last 24 h. ORs the odds for developmental delay comparing children who consumed certain type of food versus children who did not consume as reference group.



**Table 4.** Comparison of food types among 6–59 month children with full-term and moderate to late preterm birth, n(%).

	Full-term	Moderate to Late Preterm	Р
Grains, roots and tubers*	1476(94.7)	73(92.4)	0.370
Legumes and nuts*	484(31.1)	23(29.1)	0.714
Dairy products*	1127(72.3)	59(74.7)	0.649
Flesh foods*	1215(78.0)	64(81.0)	0.525
Eggs*	682(43.8)	32(40.5)	0.568
Vitamin A-rich fruits and vegetables*	1307(83.9)	59(74.7)	0.032
Other Fruits and vegetables*	1069(68.6)	41(51.9)	0.002
Minimum dietary diversity*	1264(81.1)	60(76.0)	0.253

<sup>\*</sup>Measured by whether or not a child consumed the certain type of food in last

versus 74.7%, p = 0.032), and the difference for other fruits and vegetables was 16.7% (68.6% versus 51.9%, p = 0.002). Moreover, the prevalence of minimum dietary diversity did not differ significantly between the two groups.

#### **Discussion**

In this study conducted in rural areas of China, the prevalence of developmental delay among moderate to late preterm children was 31.3% compared with 21.6% in the full-term group. Those with moderate to late preterm birth were more likely to have developmental delay in the fine motor domain. The intake of vegetables and fruits during the past 24 h was shown to have a protective effect on developmental delay in fine motor function, and we also found that moderate to late preterm birth children had a lower reported intake of vegetables and fruits than full-term birth children. This suggests the relationship between moderate to late preterm birth and suspected developmental delay might be partly explained by the intake of vegetables and fruits.

Neurodevelopment of moderate to late preterm children in rural areas of China faces a serious challenge, as in the present study nearly a third of children with moderate to late preterm birth were showing signs of neurodevelopmental delay. Our findings suggest that developmental delay in moderate to late preterm children is more severe in rural areas of China than studies from developed countries. A study from the Netherland indicates that among moderate to late preterm children, the prevalence of overall developmental delay evaluated by ASQ was 12.5%, 7.8% and 5.6% in low, intermediate and high social economic status groups, respectively [27]. Another study in Australia using Bayley scales reported that 5.6%, 13.7% and 6.7% of moderate and late preterm children had cognitive, language and motor delay (less than -2SD) [6].

In China, with the constraint of limited measurement tools, the number of studies which focuses on early child

development is limited. A study with 100 preterm infants estimated that the rate of development delay in mental and psychomotor domains was 31% and 29% using Bayley Scales [9]. Another hospital-based study with Gesell Scales reported that more than 40% of preterm infants have abnormal developmental quotient (DQ) scores [10]. Although there are variations in measurement tools, thresholds, gestational age of participants, time of screening and whether the study was conducted in high-risk population, the present literature indicates that the neurodevelopmental problem of preterm children and the role of dietary diversity still remain unresolved and require more attention. In the present study, we employed the ASQ to measure child neurodevelopment. Although it is a feasible screening tool, ASQ cannot provide valid diagnostic results. Therefore, our finding should be interpreted carefully.

In the present study, we found fine motor was more consistently associated with moderate to late preterm birth than other domains. This is in line with Kerstjens's study, which reported that children with moderately preterm birth had a great prevalence of problems with fine motor rather than gross motor functions, compared with full-term children [28]. In term of pathogenesis, pre-oligodendrocytes are one of the major targets in cerebral white matter injury which is the most common brain injury among preterm infants, and its impairment would lead to defects in motor function in preterm children [29]. A study from Australia also reported that compared with full-term controls, moderate to late preterm children had widespread white matter microstructural alteration at term-equivalent age, which resulted in delayed white matter development [30]. As fine motor requires a highly integrated and efficient brain network, even less severe white matter injury could easily influence fine motor skills. In conclusion, given that having lower fine motor skills is unfavorable for child development in reading and writing [31-33], more intervention on fine motor skills should be implemented among moderate to late preterm infants.

The findings from the present study also provide evidence that diet types might mediate the association between moderate to late preterm birth and developmental delay, especially for the fine motor domain. According to Baron and Kenny's strategy, mediation is demonstrated when: (1) the response variable (i.e. developmental delay in fine motor domain in our study) is significantly associated with the independent variable (moderate to late preterm birth); (2) the independent variable is significantly associated with a protentional mediator (whether or not certain types of food are consumed) and (3) the response variable is significantly associated with the potential mediator [34]. In

conclusion, our findings provide statistical evidence for the mediating effect of diet to some extent. Although the evidence has shown that multi dietary diversity during the prenatal period is beneficial for child neurodevelopment [35-36], the role of diet during the postnatal period on child neurodevelopment is limited, and likely more significant in the neurodevelopment of preterm birth children. However, most studies have focused on diet and cognitive development in adulthood. A review concluded that higher intake of fruits, vegetables, legumes and nuts might be associated with reduced risk of cognitive deficits and Alzheimer's disease in adults [37]. Findings from the Helsinki Study of Very Low Birth Weight Adults also indicated that higher energy and human milk intake during the first nine weeks were associated with better neurocognitive abilities in adulthood among preterm birth and very low birthweight children [38]. Compared to the study, our study has provided more evidence on daily diet and various types of food intake during early childhood and examined the role of diet by comparing moderate to late preterm children and full-term children, which to some extent confirmed the speculation proposed by that study that postnatal nutrition should be a mediator between neonatal conditions and neurodevelopment. But it is also important to point out that the validity of 24-hour recall applied in the our study is not as strong as other measurements, and we merely collected the information on whether the child had been fed specific types of food and not the amount of food in the previous 24 h. However, 24-hour recall is more feasible for a large population-based study and has been applied in the UNICEF Multiple indicator cluster survey (MICS) which was conducted in many low-income and middle-income countries.

We also noticed that the prevalence of moderate to late preterm in our study was lower than the prevalence of preterm birth in previous studies in China. Even if we did not exclude the cases of extremely and very preterm from the analysis, the total prevalence of preterm birth in our study population was still relatively low. Firstly, although the majority of interviewed families provided birth certificates for us to abstract valid gestation age, some primary caregivers did not provide birth certificates on the date of interview. So, for those families, the information on gestation age was collected by asking primary caregivers directly. Admittedly, there is potential recall bias for gestational age and classification of preterm birth, so we might miss some cases of preterm birth. Secondly, given the low level of health care in poor and lagging area, the mortality for preterm newborns is relatively high. Our study only evaluated preterm birth among live children, so the children with

preterm birth who died early would not be included in our study, which might decrease the prevalence of preterm birth in our study.

The first strength of the present study was the use of data from a community-based sample in poor central and western areas of China. To the best of our knowledge, this is the first study to compare neurodevelopmental outcomes of preterm children and full-term children in rural China by ASQ. Previous studies conducted among children in rural western areas of China mainly focus on indicators of physical growth, like height or weight [39]. Thus, the number of studies focusing on early child development is limited, and the present literature is based on hospital-based samples in urban areas, which limits the generalizability and reliability of results [9,40]. Secondly, although several studies in other countries indicated preschool and school age children born moderate to late preterm were at higher risk of developmental delay, few studies took nutritional factors into consideration when analyzing the relationship. Therefore, our study provides important evidence to understand the influence of diet types on early children development in moderate to late preterm population.

In addition to the limitations outlined in the above discussion, the study suffered from unmeasured confounding caused by maternal complications during pregnancy. Considering the high proportion of cesarean section in our study population, we could speculate that the majority of preterm births were medically indicated; and evidence has shown that maternal complications are associated with the child's developmental delay. Therefore, maternal complications during pregnancy are likely to confound our estimated association between preterm birth, dietary diversity and child's developmental outcomes.

### **Conclusion**

Our study indicated that moderate to late preterm children with 1-59 months had a higher burden of suspected developmental delay compared with full-term peers, especially developmental delay in the fine motor domain. The intake of vegetables and fruits could partially explain the above association. Public health professionals should consider dietary interventions to improve the neurodevelopmental outcome of preterm children. A future study including detailed measurement of diet is necessary to understand thoroughly the role of diet and nutrition on neurodevelopment among preterm birth children.

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#### References

- [1] World Health Organization. WHO: recommended definitions, terminology and format for statistical tables related to the perinatal period and use of a new certificate for cause of perinatal deaths. Modifications recommended by FIGO as amended October 14, 1976. Acta Obstet Gynecol Scand. 1977;56(3):247-53.
- [2] Blencowe H, Cousens S, Oestergaard MZ, Chou D, Moller AB, Narwal R, et al. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. Lancet. 2012;379(9832):2162-72.
- [3] Gouyon JB, Iacobelli S, Ferdynus C, Bonsante F. Neonatal problems of late and moderate preterm infants. Semin Fetal Neonatal Med. 2012;17(3):146-52.
- [4] Kramer MS, Demissie K, Yang H, Platt RW, Sauve R, Liston R. The contribution of mild and moderate preterm birth to infant mortality. Fetal and infant health study group of the Canadian perinatal surveillance system. JAMA. 2000;284(7):843-9.
- [5] Dotinga BM, Eshuis MS, Bocca-Tjeertes IF, Kerstjens JM, Van Braeckel KN, Reijneveld SA, et al. Longitudinal growth and neuropsychological functioning at age 7 in moderate and late preterms. Pediatrics. 2016;138(4):e20153638.
- [6] Cheong JL, Doyle LW, Burnett AC, Lee KJ, Walsh JM, Potter CR, et al. Association between moderate and late preterm birth and neurodevelopment and socialemotional development at age 2 years. JAMA Pediatr. 2017;171(4):e164805.
- [7] Putnick DL, Bornstein MH, Eryigit-Madzwamuse S, Wolke D. Long-term stability of language performance in very preterm, moderate-late preterm, and term children. J Pediatr. 2017;181:74-79. e3.



- [8] de Jong M, Verhoeven M, van Baar AL. School outcome, cognitive functioning, and behaviour problems in moderate and late preterm children and adults: a review. Semin Fetal Neonatal Med. 2012;17(3):163-9.
- [9] Zhang M, Qian HY, Kuang XN, Yu Z, Tan L, Xia C. Neurodevelopmental features of preterm infants at the corrected age of 1 year. Zhongguo Dang Dai Er Ke Za Zhi. 2017;19(2):147-51.
- [10] Li J, Bo T, Chen TQ, Kuang XN, Yu Z, Zhang L, et al. Neurobehavioral development in preterm infants: a retrospective study of 181 cases. Zhongguo Dang Dai Er Ke Za Zhi. 2014;16(7):696-700.
- [11] Zhang Z, Lu H, Zhu Y, Xiang J, Huang X. Correlation of serum KL-6 and CC16 levels with neurodevelopmental outcome in premature infants at 12 months corrected age. Sci Rep. 2015;5, article no. 8121.
- [12] Chen GF, Zhang YF, Chen MQ, Wang XL, Long Q, Kong O, et al. Early multi-disciplinary intervention reduces neurological disability in premature infants. Zhongguo Dang Dai Er Ke Za Zhi. 2014;16(1):35-9.
- [13] Leventakou V, Roumeliotaki T, Sarri K, Koutra K, Kampouri M, Kyriklaki A, et al. Dietary patterns in early childhood and child cognitive and psychomotor development: the Rhea mother-child cohort study in Crete. Br J Nutr. 2016;115(8):1431-7.
- [14] Makrides M, Gibson RA, McPhee AJ, Collins CT, Davis PG, Doyle LW, et al. Neurodevelopmental outcomes of preterm infants fed high-dose docosahexaenoic acid: a randomized controlled trial. JAMA. 2009;301(2):175-82.
- [15] Steinmacher J, Pohlandt F, Bode H, Sander S, Kron M, Franz AR. Randomized trial of early versus late enteral iron supplementation in infants with a birth weight of less than 1301 grams: neurocognitive development at 5.3 years' corrected age. Pediatrics. 2007;120(3):538-46.
- [16] Kennedy GL, Pedro MR, Seghieri C, Nantel G, Brouwer I. Dietary diversity score is a useful indicator of micronutrient intake in non-breast-feeding Filipino children. J Nutr. 2007;137(2):472-7.
- [17] Amugsi DA, Dimbuene ZT, Kimani-Murage EW, Mberu B, Ezeh AC. Differential effects of dietary diversity and maternal characteristics on linear growth of children aged 6-59 months in sub-Saharan Africa: a multi-country analysis. Public Health Nutr. 2017;20(6):1029-45.
- [18] Wang A, Scherpbier RW, Huang X, Guo S, Yang Y, Josephs-Spaulding J, et al. The dietary diversity and stunting prevalence in minority children under 3 years old: a cross-sectional study in forty-two counties of western China. Br J Nutr. 2017;118(10):840-8.
- [19] Rah JH, Akhter N, Semba RD, de Pee S, Bloem MW, Campbell AA, et al. Low dietary diversity is a predictor of child stunting in rural Bangladesh. Eur J Clin Nutr. 2010;64(12):1393-8.
- [20] Disabilities COCW, Committee SODB, Committee BFS, Committee. MHIF. Identifying infants and young children with developmental disorders in the medical home: an algorithm for developmental surveillance and screening. Pediatrics. 2006;118(1):405-20.
- [21] Simard MN, Luu TM, Gosselin J. Concurrent validity of ages and stages questionnaires in preterm infants. Pediatrics. 2012;130(1):e108-14.
- [22] Kwun Y, Park HW, Kim MJ, Lee BS, Kim EA. Validity of the ages and stages questionnaires in Korean compared

- to Bayley scales of infant development-II for screening preterm infants at corrected age of 18-24 months for neurodevelopmental delay. J Korean Med Sci. 2015;30 (4):450-5.
- [23] Bian X, Yao G, Squires J, Hoselton R, Chen C, Murphy K, et al. Translation and use of parent-completed developmental screening test in Shanghai. J Early Child Res. 2012;No.2:162-75.
- [24] Yao G, Bian X, Squires J, Wei M, Song W. Cutoff scores of the ages and stages questionnaire-Chinese for screening infants and toddlers. Chinese J Pediatr. 2010; No.11:824-8.
- [25] Bian XY, Yao GY, Squires J, Wei M, Chen CI, Fang BH. Studies of the norm and psychometric properties of Ages and Stages questionnaires in Shanghai children. Zhonghua Er Ke Za Zhi. 2010;48(7):492-6.
- [26] Wei OW, Zhang IX, Scherpbier RW, Zhao CX, Luo SS, Wang XL, et al. High prevalence of developmental delay among children under three years of age in poverty-stricken areas of China. Public Health. 2015;129 (12):1610-7.
- [27] Potijk MR, Kerstjens JM, Bos AF, Reijneveld SA, de Winter AF. Developmental delay in moderately preterm-born children with low socioeconomic status: risks multiply. J Pediatr. 2013;163(5):1289-95.
- [28] Kerstjens JM, de Winter AF, Bocca-Tjeertes IF, Ten VE, Reijneveld SA, Bos AF. Developmental delay in moderately preterm-born children at school entry. J Pediatr. 2011;159(1):92-8.
- [29] Bos AF, Van Braeckel KN, Hitzert MM, Tanis JC, Roze E. Development of fine motor skills in preterm infants. Dev Med Child Neurol. 2013;55(Suppl 4):1-4.
- [30] Kelly CE, Cheong JL, Gabra FL, Leemans A, Seal ML, Doyle LW, et al. Moderate and late preterm infants exhibit widespread brain white matter microstructure alterations at term-equivalent age relative to term-born controls. Brain Imaging Behav. 2016;10(1):41-9.
- [31] Suggate S, Pufke E, Stoeger H. The effect of fine and grapho-motor skill demands on preschoolers' decoding skill. J Exp Child Psychol. 2016;141:34-48.
- [32] Volman MJ, van Schendel BM, Jongmans MJ. Handwriting difficulties in primary school children: a search for underlying mechanisms. Am J Occup Ther. 2006;60(4):451-60.
- [33] Berninger VW. Highlights of programmatic, interdisciplinary research on writing. Learn Disabil Res Pract. 2009;24(2):69-80.
- [34] Baron RM, Kenny DA. The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. J Pers Soc Psychol. 1986;51(6):1173-82.
- [35] Starling P, Charlton K, McMahon AT, Lucas C. Fish intake during pregnancy and foetal neurodevelopmenta systematic review of the evidence. Nutrients. 2015;7 (3):2001-14.
- [36] Monk C, Georgieff MK, Osterholm EA. Research review: maternal prenatal distress and poor nutrition - mutually influencing risk factors affecting infant neurocognitive development. J Child Psychol Psychiatry. 2013;54 (2):115-30.
- [37] Gu Y, Scarmeas N. Dietary patterns in Alzheimer's disease and cognitive aging. Curr Alzheimer Res. 2011;8(5):510–9.



- [38] Sammallahti S, Kajantie E, Matinolli HM, Pyhala R, Lahti J, Heinonen K, et al. Nutrition after preterm birth and adult neurocognitive outcomes. PLoS One. 2017;12(9):e0185632.
- [39] Dang S, Yan H, Wang D. Implication of World Health Organization growth standards on estimation of malnutrition in young Chinese children: two examples from
- rural western China and the Tibet region. J Child Health Care. 2014;18(4):358-68.
- [40] Luo F, Chen Z, Ma XL, Lin HJ, Bao Y, Wang CH, et al. Infant Neurological International Battery predicts neurological outcomes of preterm infants discharged from the neonatal intensive care unit. Zhongguo Dang Dai Er Ke Za Zhi. 2013;15(1):5-8.