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Moderate and late preterm and internalizing or externalizing disorders of school-aged children

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Abstract

Background: There is increasing concern that preterm birth may be associated with children's behavioral problems and most of previous studies focused on very preterm (<32-week gestation) or very low birth weight (1,500 g) infants, while research on long-term outcomes for moderate preterm (32–33 weeks' gestation) and late preterm (34–36 weeks' gestation) birth is sparse. This study aims to explore the association between moderate-to-late preterm birth and internalizing or externalizing disorders of children aged 6-11 years.

Methods: Totally 2236 children at 6-11 years old from 3 primary schools in Xiamen, China were assessed and included for analysis. Behavior problems were assessed by Child Behavior Checklist (CBCL).

Results: In addition to rule-breaking behaviors, the percentages of externalizing disorders, internalizing disorders, and the corresponding subscales in moderate-to-late preterm children were higher than full-term children, and significant group differences were found in externalizing disorders($\chi2$=7.805, P=0.005), depression($\chi2$=6.481, P=0.011), withdrawn ($\chi2$=7.869, P=0.005) and aggressive behavior ($\chi2$=8.874, P=0.003). After adjusted the potential covariates, moderate-to-late preterm children who were significantly associated with the increased risk of externalizing disorder (OR=1.600, 95%CI=1.072-2.389), depression (OR=1.705, 95%CI=1.113-2.613), withdrawn (OR=1.5181, 95%CI=1.006-2.290), aggressive behavior (OR=1.574, 95%CI=1.053-2.354) compared with full-term births.

Conclusions: Moderate to late preterm infants are at risk of developing behavioral problems, especially for externalizing disorders, at school age. Long-term follow-up and policy support are required for moderate-to-late preterm children.

Introduction

With the adjustment of fertility policy and the improvement of neonatal intensive care and life support technology, preterm infants has increased significantly in China. It is estimated that preterm birth occurs in 11.1% of all worldwide deliveries, of which 85%-90% are moderate preterm (32–33 weeks' gestation) and late preterm (34–36 weeks' gestation) [1], and these populations would potentially have a large influence on public health. Over the past two decades, there is increasing concern that preterm birth may be associated with children's behavioral problems [2]. Most of those previous studies focused on very preterm (<32-week gestation) or very low birth weight (1,500 g) infants [3,4], while research on long-term outcomes for moderate-to-late preterm birth is sparse [5]. Moderate to late preterm births are considered to be at low risk for abnormal behavioral outcomes and may not show signs of abnormal brain function in early infancy, they are usually not paid Insufficient attention and lack of proper follow-up [6,7].

In this study, we evaluate whether moderate-to-late preterm is related to a higher risk of internalizing or externalizing disorders in school-aged children through a large number of data, which in turn may remind doctor to pay attention to long-term follow-up evaluation of moderate-to-late preterm infants.

Materials and Methods

Subjects

1st - 4th grade students from three primary schools in Xiamen City, Fujian Province, China was invited to take part in child behavior assessment and questionnaire survey. Subjects met the following criteria were selected for data analyses: a) completed both behavior assessment and valid questionnaires; b) children were born full-term (37-41 weeks) or moderate-to-late preterm (32–36 weeks' gestation); c) no reported psychoses or neurologic diseases since birth.

Methods

Child Behavior Checklist (CBCL) (the version for 4-18 years of age) was used to assess child potential behavior problems. The CBCL is a questionnaire composed of 113 items rated on a three-step response scale ranging from 0 (absent) to 2 (very often present). Higher scores correspond to more problems. Five specific syndromes (depression, withdrawn, somatic complaints, social, rule-breaking behavior and aggression) and two composite scales, internalizing disorders (sum of scores on the depression, withdrawn, somatic complaints scales) and externalizing disorders (sum of scores on the rule-breaking behavior and aggressive behavior scales) was analyzed in this study.

The possible risk factors of behavioral problems were collected through the General Status of Children Questionnaire which was

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self-designed. The questionnaire included such questions as: child and neonatal factors (gender, birth weight, birth age and medical history, etc), parental factors (parent education background, tobacco consumption, family income, upbringing style, etc) and prenatal factors (maternal medication use during pregnancy, delivery method, etc).

Statistical analysis

Statistical analyses were performed with SPSS version 20.0. T-scores for the five specific syndromes and two composite scales of children's behavioral problems were standardized to a mean=50 and SD=10, and dichotomized into two groups for each syndrome: abnormal (T- score ≥ 60) and normal (T- score < 60). Pearson Chi-Square test was used to assess the differences between children born in moderate-to-late preterm and full-term children in each syndrome and composite scales. Finally, logistic regression analysis model was used for multi-factors analysis so as to further explore the association between moderate-to-late preterm and children's behavioral problems. Thirteen independent variables were analyzed in the model: age (years), gender (0=female, 1=male), educational attainment of children's mother (0=≤primary school, 1=middle school, 2=high school, 3=technical school, 4=≥college/university), educational attainment of children's father (0=≤primary school, 1=middle school, 2=high school, 3=technical school, 4=≥college/university), family income(0=5000 yuan/month, 1=5000 yuan/month~, 2=10000 yuan/month~, 3=15000 yuan/month~, 4=20000 yuan/month~), parents upbringing style, delivery method (0=vaginal delivery, 1=abdominal delivery), passive smoking (0=no, 1=yes), history of poor pregnancy of mother (0=no, 1= yes), maternal medicine use during pregnancy(0=no, 1=yes), moderate-to-late preterm(0=no, 1=yes) , low birth weight (0=no, 1=yes), duration of breastfeeding(0=never breastfed or breastfed <6 months, 1=breastfed ≥6 months). As a study variable, moderate-to-late preterm was entered the model forcibly, and the other variables were screen by backward regression method with P<0.15 as variable inclusion and exclusion criteria as potential confounds. All results were considered to be statistically significant when p-value was less than 0.05.

Ethics statement

This study was reviewed and approved by the Ethics Committee of Xiamen Children's Hospital. Informed consent was obtained from the parents when they were invited to participate in this study.

Result

Characteristics of subjects

A total of 2,443 questionnaires were handed out and 2,322 were returned (the respond rate was 95.04%), of which the valid questionnaires was 2,257(the valid rate was 97.20%). Twenty-one children were excluded because of ineligible for the selected criteria. Finally, a total of 2236 children were eligible for data analyses. Among these subjects, 1204 (53.8%) were boys and 1032(46.2%) were girls; 172(7.7%) were moderate-to-late preterm and 2064(92.3%) were full-term. Characteristics of subjects were shown in Table 1.

Behavioral problems

In addition to rule-breaking behaviors, the percentages of externalizing disorders, internalizing disorders, and the corresponding subscales in moderate-to-late preterm children were higher than full-term children, and significant group differences were found in externalizing disorders (χ^2=7.805, P=0.005), depression (χ^2=6.481, P=0.011), withdrawn (χ^2=7.869, P=0.005) and aggressive behavior (χ^2=8.874, P=0.003). After adjusted the potential covariates, moderate-to-late preterm children who were significantly associated with the increased risk of externalizing disorder (OR=1.600, 95%CI=1.072-2.389), depression (OR=1.518, 95%CI=1.006-2.290), withdrawn (OR=1.5181.705, 95%CI=1.006-2.290), aggressive behavior (OR=1.574, 95%CI=1.053-2.354) compared with full-term births.

Discussion

Previous studies focused on behavioral outcomes and very preterm (<32-week gestation) or very low birth weight (1,500 g) infants, and concluded infants born very preterm are at high risk for behavioral problems. A meta-analysis of VP/VLBW and attention-deficit/hyperactivity disorder (ADHD) demonstrated that VP/VLBW subjects have a higher ADHD risk (odds ratio [OR] = 3.04 higher than controls; 95% confidence interval [CI] 2.19 to 4.21) [8]. Some studies included executive function and aca demic achievement in school-aged children who were born prematurely, showing their deficits which lags behind full term-born peers [8-10]. Meanwhile, long-term behavioral outcomes of moderate and late preterm infants are relatively unknown. Recently, Jin et al [7] reported on the single-center long-term behavioral outcomes of children born moderate to late preterm; and found Borderline or clinically relevant internalizing problems were noted in 13.5% on the Child Behavior Check List. This is the first Korean report of a wide range of neurodevelopmental outcomes including cognition, executive function, and behavioral problems of school-aged former moderate to late preterm infants. Yue CH et al compared 97 late preterm and 107 full term children, and found the total score of behavioral problems of children in late preterm delivery group (25.67±20.07) was significantly higher than that of children in normal control group (20.85±18.29) (P<0.001) [11]. In our study, after adjusting for the potential confounding factors, moderate-to-late preterm children were significantly associated with the increased risk of externalizing disorders, compared with full-term births. As to specific syndromes, children born moderate-to-late pre-

Table 1. Characteristics of the subjects.

Characteristics	Category	Participants	
		N	%
Age (years old)	6	214	9.6
	7	315	14.1
	8	540	24.2
	9	569	25.4
	10	371	16.6
	11	227	10.2
Gender	Male	1204	53.8
	Female	1032	46.2
Birth	Moderate-to-late preterm	172	7.7
	Full-term	2064	92.3
Educational attainment of mothers	≤Middle school	1083	48.4
	High school	530	23.7
	Technical school	329	14.7
	≥College/university	294	13.1
Educational attainment of fathers	≤Middle school	793	35.5
	High school	682	30.5
	Technical school	306	13.7
	≥College/university	455	20.3
Family income (Yuan/month)	<5000	243	10.9
	5000~	606	27.1
	10000~	657	29.4
	15000~	482	21.6
	≥20000	248	11.1

Table 2. Differences of behavioral problems between moderate-to-late preterm and full-term children

Behavioral problems	Moderate-to-late preterm (n=172)	Full-term (n=2064)	Pearson Chi-Square test		Logistic regression model	
			χ^2	p-value	OR (95%CI)	p-value
Internalizing disorders	26 (15.1%)	220 (10.7%)	3.222	0.072	1.406 (0.893, 2.213)	0.141
Depression	30 (17.4%)	227 (11.0%)	6.481	**0.011**	1.705 (1.113, 2.613)	**0.014**
Withdrawn	33 (18.6%)	235 (11.4%)	7.869	**0.005**	1.518 (1.006, 2.290)	**0.047**
Somatic complaints	24 (12.4%)	241 (11.7%)	0.061	0.804	0.948 (0.601, 1.495)	0.817
Externalizing disorders	33 (19.2%)	245 (11.9%)	7.805	**0.005**	1.600 (1.072, 2.389)	**0.021**
Rule-breaking behavior	16 (9.3%)	226 (10.9%)	0.446	0.504	0.957 (0.581, 1.576)	0.863
Aggressive behavior	33 (19.2%)	237 (11.5%)	8.874	**0.003**	1.574 (1.053, 2.354)	**0.027**

term showed that percentages of depression, withdrawn and aggressive behavior were significantly higher than those of full-term children. The result suggests that moderate-to-late preterm is related to an increased risk of behavior problems in children at 6-11 years old.

Similar to the cause of early preterm, there were some possible reasons for our results. Preterm infants suffer from chewing and swallowing dysfunction, which tends to develop to malnutrition and neurodevelopmental delay; at the same time, they were at higher risk of respiratory infection, due to the relatively low immunity, which would result in single or multiple defects in physical movement, sense, intelligence, language, etc., and may further affect their emotions and behaviors [12]. What's more, clinical studies have shown that preterm and low birth weight may damaged brain function, and the hippocampus and cingulate gyrus of the brain's limbic system may disrupt and induce emotional changes [13]. This also explains why preterm infants are more activeat school age, and their social adaptability is worse than normal children.

Major neurodevelopmental morbidities are usually detected during the first 2 years of life. Nevertheless, minor behavioral problems may not become apparent until school age, when more complex skills such as reading and writing are required for scholastic performance [14]. It suggests that doctors need to pay close attention to preterm infants for a long time, conduct routine behavioral problems screening, and provide timely help and supports according to the screening results. Parents of preterm infants should also have awareness and psychological preparation for their behavioral problems, and learn more about relevant knowledge in order to provide better family support and parental education for preterm infants. Schools should also provide additional support and help for preterm infants with behavioral problems.

There are several limitations in the study. Firstly, although maternal recall of preterm is relatively accurate, recall bias may be existed due to the use of retrospective data in this study. Secondly, children's behavior disorders may be affected by many factors may affect. Some potential factors may not be considered in the model. Therefore, a larger and long-term epidemiological study should be conducted for further study to explore the association between breastfeeding and internalizing or externalizing disorders of school-aged children.

Conclusions

Our findings indicated that moderate to late preterm infants are at risk of developing behavioral problems, especially for externalizing disorders, at school age, which provide strong evidence that long-term follow-up and policy support are required for moderate-to-late preterm children with regard to children's behavioral problems.

Author contributions

WSQ and HTT—Made contributions to study conception and design; HTT, ZM, YYH, CYD—Participated in data collection; WSQ, HTT—Dedicated to data analysis and interpretation; WSQ — Involved in drafting of the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate.

This study was reviewed and approved by the Ethics Committee of Xiamen Children's Hospital. Informed consent was obtained from the parents when they were invited to participate in this study.

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Conflict of interest

The authors declare no conflicts of interest statement.

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