



Sleep-Disordered Breathing as a Mediator Between Premature Birth and Behavior Problems in School-Aged Children: A Cross-Sectional Study of 6–10 Year Olds in Shanghai, China

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Background: Premature birth poses a major challenge in global obstetric clinical practice. The relationship between preterm infants and behavioral problems in school-aged children remains debatable, and the mediating role of sleep-disordered breathing (SDB) in this connection has not been investigated. This study aimed to address these gaps through a large-scale cross-sectional survey.

Methods: We recruited 18,138 children aged 6–10 from schools. Data on demographics, prematurity, SDB, and childhood behavioral problems were collected. The Paediatric Sleep Questionnaire (PSQ), a validated screening tool, assessed SDB symptoms, and the Conners' Parent Rating Scale (CPRS) evaluated behavioral problems. Path analysis with bootstrap methods was used for statistical analysis.

Results: Among 18,138 participants, 8% ($n = 1,450$) were premature. After adjusting for age, gender, BMI z -score, maternal age, and maternal education level, prematurity showed a positive association with total PSQ score ($B = 0.411$, $p < 0.01$). Higher total PSQ scores were significantly associated with all six CPRS dimensions (all $p < 0.05$). While prematurity was not directly associated with Conduct, Psychosomatic, Impulsive-hyperactive, or Hyperactivity scores in CPRS (all $p > 0.05$), it demonstrated significant associations with Learning problems ($\beta = 0.063$, $p = 0.005$) and Anxiety scores ($\beta = 0.076$, $p = 0.003$). Mediation analysis showed PSQ accounted for a large proportion of associations between prematurity and Conduct, Psychosomatic, Impulsive – hyperactive, and Hyperactivity problems (95% Bootstrap CI excluded 0).

Conclusion: Premature infants may exhibit behavioral problems significantly associated with SDB, though our cross-sectional design precludes causal inference and parent-reported SDB severity may bias true associations. Future studies should utilize longitudinal cohorts to explore whether SDB is involved in the relationship between prematurity and behavioral problems (eg, anxiety). Additionally, they should conduct pilot randomized controlled trials of SDB interventions in preterm infants to assess neurodevelopmental benefits. Final conclusions require subsequent causal validation.

Keywords: premature birth, behavioral problems, sleep-disordered breathing

Introduction

Preterm birth ($<37 + 0$ weeks of gestation) disrupts the normal process of organogenesis in fetuses, resulting in a wide range of multisystem disorders and long-term consequences.¹ In 2010, an estimated 14.9 million babies (with an uncertainty range of 12.3 to 18.1 million) were born preterm, accounting for 11.1% of all live births globally, with rates ranging from about 5% in several European countries to 18% in some African countries.^{2,3} Complications in premature infants include lung function impairments, such as altered airway mechanics and significant reductions in

pulmonary function, growth disturbances including growth retardation, neurodevelopmental impairments characterized by cognitive dysfunction, behavioural issues, mental health problems, and motor disorders such as cerebral palsy and related conditions.^{4–7}

Sleep-disordered breathing (SDB) affects approximately 4–11% of term-born infants.⁸ Premature infants, however, are 3–5 times more likely to develop SDB compared to term-born infants.⁹ SDB, marked by upper airway collapse during sleep, mainly manifests as primary snoring (PS, a mild condition with loud snoring and minimal self-health impact) and obstructive sleep apnoea syndrome (OSAS, a severe one with recurrent apnea/hypopnea and multiple complications, diagnosed via polysomnography).^{10,11} Risk factors for SDB include adenoid and tonsil hypertrophy, allergic rhinitis, obesity, among others.^{12–14} Attaching importance to these factors is conducive to early screening, early treatment, and early recovery.

In recent years, internalizing and externalizing problems have garnered significant attention. Studies have indicated that children with SDB often exhibit behavioural challenges, including hyperactivity, inattention^{15,16} externalizing behaviours such as aggression and rule-breaking^{17,18} and internalizing issues such as anxiety, depression, somatic complaints, and social difficulties.^{19,20} These symptoms significantly impact children's current and future social functioning. Regarding behavioral problems, premature infants are more likely to experience behavioral challenges and related issues during childhood.^{21,22} However, there were also studies that put forward different viewpoints. One study exploring the impact of different perinatal morbidity rates on the school performance of 12-year-old premature infants found that all premature infant groups performed comparably to the full-term infant group in terms of social skills and problematic behaviors, with no significant differences observed.²³ Another study on the cognitive and behavioral outcomes of school-aged extremely preterm (EP) children revealed that, except for lower social maturity, there were no significant differences in behavioral problems between EP children and their full-term peers.²⁴ These inconsistent findings emphasize the necessity of further exploring the relationship between premature infants and the behavior of school-aged children in large community samples, while utilizing standardized tools to assess behavior problems and taking into account necessary covariates. Therefore, this study hypothesized that SDB may act as a mediator in the relationship between prematurity and behavioral problems in school-aged children.

Exploring the relationships among prematurity, sleep-disordered breathing, and behavioral problems in school-age children was conducive to a deeper understanding of their connections, and this understanding could provide a foundation for targeted and diversified intervention strategies.

At the same time, it helped clinical personnel and families of affected children to recognize the need for attention when premature infants exhibited sleep-disordered breathing.

Methods

Study Design and Setting

This was a cross-sectional investigation conducted in Xuhui District, Shanghai, China.

Participants

Invitation letters were sent to the administrative offices of all 47 primary schools in the district. Of these, 13 schools declined to participate. As a result, the initial sample included 26,827 registered primary school students from 34 schools. Between September and December 2019, class teachers distributed informed consent forms and an online questionnaire with a QR code to the guardians of each student. A total of 19,033 guardians agreed to participate and completed the online survey, yielding a consent rate of 71.0%. For the purposes of this analysis, 18,138 children in grades one to five, aged 6–10 years, were selected as study participants. Missing data, such as incomplete body mass index (BMI) z-scores, maternal age, and maternal education level, were excluded from the analysis.

Class teachers distributed informed consent forms and online questionnaires, which included login codes, to the guardians of each student. The guardians provided demographic information, medical history, and responses to the PSQ and CPRS through the online survey. Anthropometric data, including height and weight, measured within the previous 3

months, were obtained from the physical examination database of the Shanghai Municipal Education Commission. Informed consent was obtained from all parents of the children through the online platform.

Ethics Approval

The study protocol was performed in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Sixth People's Hospital Affiliated to Shanghai Jiao Tong University (Approval No: 2018–008). Class teachers distributed informed consent forms and online questionnaires, which included login codes, to the guardians of each student. Informed consent was obtained from all parents of the children through the online platform.

Measurement Tools and Research Variables

Demographic Characteristics

The questionnaire included items designed to assess demographic characteristics, such as age, sex, and maternal education level. WHO Anthro Plus software was used to calculate age- and sex-adjusted BMI z-scores (SD scores).²⁵ The covariates included in this study are age, sex, BMI z-score, mother's age, and education level. During data collection, we lacked procedures to capture potential unmeasured confounders like socioeconomic status and perinatal complications, but will consider including them in future research. Additionally, some parental health condition data were missing and unusable, so we did not incorporate them into the analysis.

Prematurity

In accordance with Chinese guidelines, preterm birth was defined as delivery occurring after 28 weeks, but before 37 completed weeks of gestation.²⁶ Information regarding prematurity was collected via the online questionnaire. Guardians were asked, “Has your child been diagnosed with prematurity by a doctor?” If the response was affirmative, further details were gathered by asking, “Was the gestational age more than 28 weeks, but less than 37 weeks²⁶?” If the guardian responded affirmatively, additional relevant information was collected.

Sleep Problems and High Risk of SDB Symptoms

The PSQ includes a sleep-related breathing disturbance (SRBD) scale and is widely used to screen for SDB in children aged 2–18 years.²⁷ In this study, the presence or absence of each symptom was indicated by different scores, with “Yes” scored as 1, “No” scored as 0, and “Don't Know” recorded as a missing value. The final score was derived by calculating the average score of non-missing items across all entries. A cut-off value of 0.33 was found to be most effective for screening and classifying children with SDB, specifically paediatric OSAS.²⁸ The Chinese version of the PSQ demonstrated good sensitivity (77.6%) and specificity (86.7%).²⁹ SDB screening was conducted using the PSQ, where a score of >7/22 symptoms indicated a higher risk of SDB diagnosis. In this study, a PSQ score of ≥ 8 was considered abnormal.²⁹ We have obtained permission to use the Chinese version of the PSQ questionnaire. A systematic review³⁰ shows that the PSQ exhibits higher sensitivity (0.76) compared to the OSA-18 (0.56) in identifying children with obstructive sleep apnea (OSA). This higher sensitivity reduces the likelihood of missed diagnoses during initial screening, rendering the PSQ an excellent choice for large-scale studies. The PSQ questionnaire takes relatively little time to complete and was well-received by parents, making it suitable for use in home or community settings. It encompasses respiratory symptoms, daytime sleepiness, and behavioral issues associated with SDB. We chose the PSQ questionnaire to evaluate OSA mainly because of its superior accuracy.

Behavioral Outcomes

The Conners' Parent Rating Scale (CPRS) was used to assess common behavioral problems. The CPRS consists of 48 items encompassing six factors: conduct problems, learning problems, psychosocial problems, impulsive—hyperactive, hyperactivity, and anxiety.³¹ Each item is rated on a 4-point scale ranging from 0 to 3, with higher scores indicating more pronounced behavioral problems. The CPRS scale was used only for non-commercial academic research. For transparency and accountability, the original paper of the CPRS³¹ and the Chinese version used in the study were properly cited. To ensure homogeneity in the scale scores, the scores for each dimension of the scale were standardized, and these

standardized scores were used as the dependent variable values for the analysis in this study. To standardize the CPRS scores, the mean (M) and standard deviation (SD) values for different sexes and age groups on the Chinese version of the CPRS were used to convert the actual scores (X) of each child across various dimensions into z-scores using the formula $Z = (X - M)/SD$. In this study, a z-score >2 was considered indicative of abnormal behavioral.³²

Before data collection, informed consent was obtained from the families of all participating paediatric patients. The researcher provided a detailed oral explanation of the questionnaire completion process to the families. Families were instructed to scan a QR code on the paper form to access and complete the online questionnaire. For answers to any questions or clarifications, the families were encouraged to contact the researcher directly. Prior to finalizing the data collection process, the researcher thoroughly reviewed the data for completeness. In cases of uncertainty or ambiguity, the researcher contacted the families to verify the information provided.

Data Analysis

Data analysis utilized SPSS 24.0 and PROCESS 4.1.³³ Categorical variables were presented as frequencies (%); continuous variables as M ± SD or median (P25–P75) based on distribution.

Mann–Whitney *U*-test assessed differences in CPRS dimensions. Spearman correlation analyzed relationships among variables. Multiple linear regression models examined the link between preterm birth and behavioral problems, stratified by PSQ scores. PROCESS Model 4 evaluated the mediation effect of PSQ score on prematurity-behavioral problems, controlling for age, sex, BMI z-score, mother’s age, and education. The association between preterm birth and behavioral problems in both the normal PSQ group and the abnormal PSQ group (two subgroups) was analyzed using multiple linear regression models. Bias-corrected bootstrap CI (5,000 samples) determined statistical significance for indirect effects. Partial mediation was indicated by significant direct and indirect effects; full mediation by significant indirect effect only. Missing values were excluded. The sensitivity analysis of the mediating effects was conducted using R version 4.0.5 software. Significance level was $\alpha = 0.05$.

Results

Demographics and Clinical Characteristics

The mean age of primary school students was 7.86 years (SD = 1.388). The average age of their mothers was 37.54 years (SD = 3.73). The number of boys was 9,625, accounting for 53.1% (See Table 1). In our sample, the prematurity rate was 8% (1450/18,138). PSQ total scores and all six CPRS dimensions were non-normally distributed, so Mann–Whitney *U*-tests were used (Tables 2). When grouped by prematurity, all PSQ and CPRS dimension scores (conduct, learning, psychosomatic, impulsive-hyperactive, anxiety, hyperactivity) differed significantly ($P < 0.05$; see Table 2).

Table 1 Characteristics of Study Participants

Characteristics	Mean ± SD/M (P25, P75)
Age, year	7.86±1.388
BMI z-score	0.55±1.34
Boy, n (%)	9625(53.1)
Mother’s Age	37.54±3.73
Mother’s education	
Below High School, n (%)	2892(16.0)
Junior College/Diploma, n (%)	4832(26.7)
Bachelor’s Degree, n (%)	9474(52.4)
Graduate Degree /Postgraduate, n (%)	866(4.8)
Premature Infants (yes), n (%)	1450(8.0)
Total score of the PSQ Abnormal, n (%)	1593(8.8)
Conduct problems score abnormal, n (%)	958(5.3)
Learning problems score abnormal, n (%)	1252(6.9)

(Continued)

Table 1 (Continued).

Characteristics	Mean ± SD/M (P25, P75)
Psychosomatic problems score abnormal, n (%)	769(4.2)
Impulsive—hyperactive score abnormal, n (%)	1476(8.1)
Anxiety score abnormal, n (%)	1179 (6.5)
Hyperactivity score abnormal, n (%)	1373(7.6)
Total score of the PSQ	2(1,5)
Conduct problems score	−0.310 (−0.920, 0.542)
Learning problems score	−0.022 (−0.774, 0.796)
Psychosomatic problems score	−0.652 (−0.654, 0.115)
Impulsive—hyperactive score	−0.170 (−0.911, 0.878)
Anxiety score	−0.219(−0.895, 0.563)
Hyperactivity score	−0.265(−0.882, 0.737)

Notes: CPRS questionnaire: Conners' Parent Rating Scale questionnaire, a z-score > 2 was considered indicative of abnormal behavior score, PSQ abnormal: PSQ score of ≥ 8 was considered abnormal.

Abbreviation: PSQ:Pediatric Sleep Questionnaire.

Table 2 Inter-Group Comparison Based on Dichotomous Variable Groupings of Prematurity Status, PSQ and the Six Dimensions of CPRS

	Non-Premature Group, M (P25, P75)	Premature Group, M (P25, P75)	Z	P
Total score of PSQ	2.0(1.0,5.0)	3.0(1.0,5.0)	−5.434	<0.001
Conduct problems score	−0.310(−0.920, 0.542)	−0.240(−0.885, 0.694)	−3.55	<0.001
Learning problems score,	−0.022(−0.774, 0.796)	0.170(−0.735, 1.065)	−4.513	<0.001
Psychosomatic problems score	−0.652(−0.654, 0.115)	−0.652(−0.654, 0.217)	−2.806	0.005
Impulsive—hyperactive score	−0.170(−0.911, 0.878)	−0.170(−0.911, 0.894)	−3.647	<0.001
Anxiety score	−0.219(−0.895, 0.563)	−0.219(−0.895, 0.625)	−3.845	<0.001
Hyperactivity score	−0.265(−0.882,0.618)	−0.053(−0.842,0.882)	−4.147	<0.001

Abbreviations: PSQ, Pediatric Sleep Questionnaire; CPRS questionnaires, Conners' Parent Rating Scale.

Bivariate Correlation Descriptive Analyses

Table 3 shows bivariate correlation results. Mother's age was negatively linked to the total PSQ score and all six CPRS dimensions (all rho < 0, P < 0.05). The total PSQ score was positively associated with conduct, psychosomatic,

Table 3 Bivariate Correlation Coefficients of the Study Variables (N = 18,318)

Variables	1	2	3	4	5	6	7	8	9	10	11
1. Age	–										
2. BMI z-score	0.111**										
3. Mother's Age	0.274**	0.006									
4. Mother's education	0.024**	0.013	−0.061**								
5. Total score of PSQ	0.014	0.100**	−0.061**	0.030**							
6. Conduct problems score	−0.015*	(0.001)	−0.026**	(0.009)	0.533**						
7. Learning problems score	(0.001)	(0.008)	−0.060**	0.026**	0.575**	0.695**					
8. Psychosomatic problems score	−0.283**	−0.109**	−0.081**	(0.004)	0.270**	0.354**	0.332**				
9. Impulsive—hyperactive	−0.036**	(0.007)	−0.065**	0.009	0.567**	0.732**	0.661**	0.310**			
10. Anxiety score	−0.032**	−0.067**	−0.043**	0.010	0.328**	0.498**	0.485**	0.290**	0.398**		
11. Hyperactivity score	0.002	(0.009)	−0.050**	0.013	0.619**	0.817**	0.891**	0.347**	0.868**	0.507**	–

Notes: Spearman's Rho, **p < 0.01, *p < 0.05.

impulsive-hyperactive, anxiety, and hyperactivity problem scores (all rho > 0, P < 0.01). The six CPRS dimensions are also positively correlated with each other (all rho > 0, P < 0.01).

Mediation Models

Definitions of Direct, Indirect, and Total Effects

In the context of this study, the direct effect refers to the direct influence of the independent variable (prematurity) on the dependent variable (scores on the six dimensions of the CPRS questionnaire) without going through the mediator (the total PSQ score). The indirect effect represents the influence of prematurity on the CPRS scores that is transmitted via the total PSQ score. The total effect is the combined influence of prematurity on the CPRS scores, encompassing both the direct and indirect effects. When performing mediation analysis, the system automatically excludes missing values (Table 4).

The Relationship Between Prematurity, the Total PSQ Score, and Behavior Problems

After controlling for the effects of age, gender, BMI z-score, maternal age, and maternal education level, prematurity was found to be positively correlated with the total PSQ score (B = 0.411, P < 0.01). Furthermore, the total PSQ score had a significant direct impact on all six dimensions of the CPRS questionnaire (all P-values <0.05). See Table 4.

Direct Effects

Prematurity had no direct link to Conduct, Psychosomatic, Impulsive – hyperactive, or hyperactivity scores (all P > 0.05). But it was directly correlated with Learning problems (β = 0.063, p = 0.005) and Anxiety scores (β = 0.076, p = 0.003) (Table 5 and Figure 1).

Table 4 Analysis of Preterm Birth’s Influence on PSQ Total Score and the Combined Effects on CPRS Dimensions

N = 17765	PSQ Total Score	Conduct Problems Score	Learning Problems Score	Psychosomatic Problems Score	Impulsive—Hyperactive Score	Anxiety Score	Hyperactivity Score
Path	B(SE)	B(SE)	B(SE)	B(SE)	B(SE)	B(SE)	B(SE)
Constant	5.066(0.251)**	-0.794(0.085)**	-0.606 (0.083)**	-0.801(0.079)**	-0.44(0.089)**	-0.366(0.089)**	-0.730(0.082)**
X = premature birth	0.411(0.080)**	0.021(0.027)0.44	0.073(0.262)**	0.024(0.025)0.35	0.043(0.028)0.12	0.083(0.028)**	0.045(0.026)0.84
M = PSQ		0.214(0.003)**	0.236(0.003)**	0.115(0.002)**	0.256(0.003)**	0.136(0.003)**	0.261(0.002)**
R	0.166	0.543	0.589	0.352	0.595	0.371	0.630
R ²	0.028	0.294	0.347	0.124	0.354	0.138	0.398
F	83.693**	1057.727**	1348.315**	359.410**	1387.288**	405.547**	1673.288**

Notes: M: mediator variable, X: independent variable, Control variable: age, Gender, BMI z-score age of mother, education of mother, cases with missing values were automatically excluded from the statistical analysis; ** p < 0.01.

Abbreviation: PSQ:Pediatric Sleep Questionnaire.

Table 5 Mediating Role of PSQ Total Score in the Scores of Six CPRS Dimensions Among Premature Infants

CPRS Dimensions	Effect Type	B(SE)	β	95% CI	p
Conduct problems score	Total effect	0.109(0.032)	0.095	(0.047,0.171)	<0.001
	Direct effect	0.021(0.027)	0.018	(-0.032,0.073)	0.438
	Indirect effect	0.088(0.017*)	0.077	(0.055,0.122*)	–
Learning problems score	Total effect	0.170(0.032)	0.146	(0.107,0.234)	<0.001
	Direct effect	0.073(0.026)	0.063	(0.022,0.124)	0.005
	Indirect effect	0.097(0.019*)	0.083	(0.060,0.136*)	–
Psychosomatic problems score	Total effect	0.071(0.027)	0.074	(0.019,0.123)	0.008
	Direct effect	0.024(0.025)	0.025	(-0.025,0.073)	0.345
	Indirect effect	0.047(0.0095*)	0.049	(0.029,0.067 *)	–

(Continued)

Table 5 (Continued).

CPRS Dimensions	Effect Type	B(SE)	β	95% CI	p
Impulsive-hyperactive score	Total effect	0.149(0.035)	0.119	(0.081,0.217)	<0.001
	Direct effect	0.043(0.028)	0.035	(-0.012,0.098)	0.121
	Indirect effect	0.105(90.0207*)	0.084	(0.065,0.147*)	-
Anxiety score	Total effect	0.139(0.030)	0.128	(0.080,0.198)	<0.001
	Direct effect	0.083(0.028)	0.076	(0.028,0.139)	0.003
	Indirect effect	0.056(0.011*)	0.052	(0.034,0.079*)	-
Hyperactivity score	Total effect	0.152(0.033)	0.127	(0.087,0.218)	<0.001
	Direct effect	0.045(0.026)	0.037	(-0.006,0.096)	0.836
	Indirect effect	0.107(0.021*)	0.090	(0.068,0.151*)	-

Note: *Bootstrap, B(SE): Coefficient (Standard Error), 95% CI:95% Confidence Interval.

Mediated Effects

The correlations between prematurity and the Z-scores of Conduct, Psychosomatic, Impulsive – Hyperactive, and Hyperactivity problems scores across six CPRS dimensions, mediated by total PSQ score, were significant (95% Bootstrap CI excluded 0) (Table 5 and Figure 1). Prematurity correlated with all six CPRS dimensions, with significant total effects ($p < 0.001$), and all mediated correlations via PSQ were significant.

Partial Mediation

In an exploratory analysis, there was a pattern suggesting that prematurity had a direct association with Learning problems ($\beta = 0.063$, $p = 0.005$) and Anxiety scores ($\beta = 0.076$, $p = 0.003$) in CPRS, and the total PSQ score seemed to play a partial role in the relationship pattern (Table 5 and Figure 1).

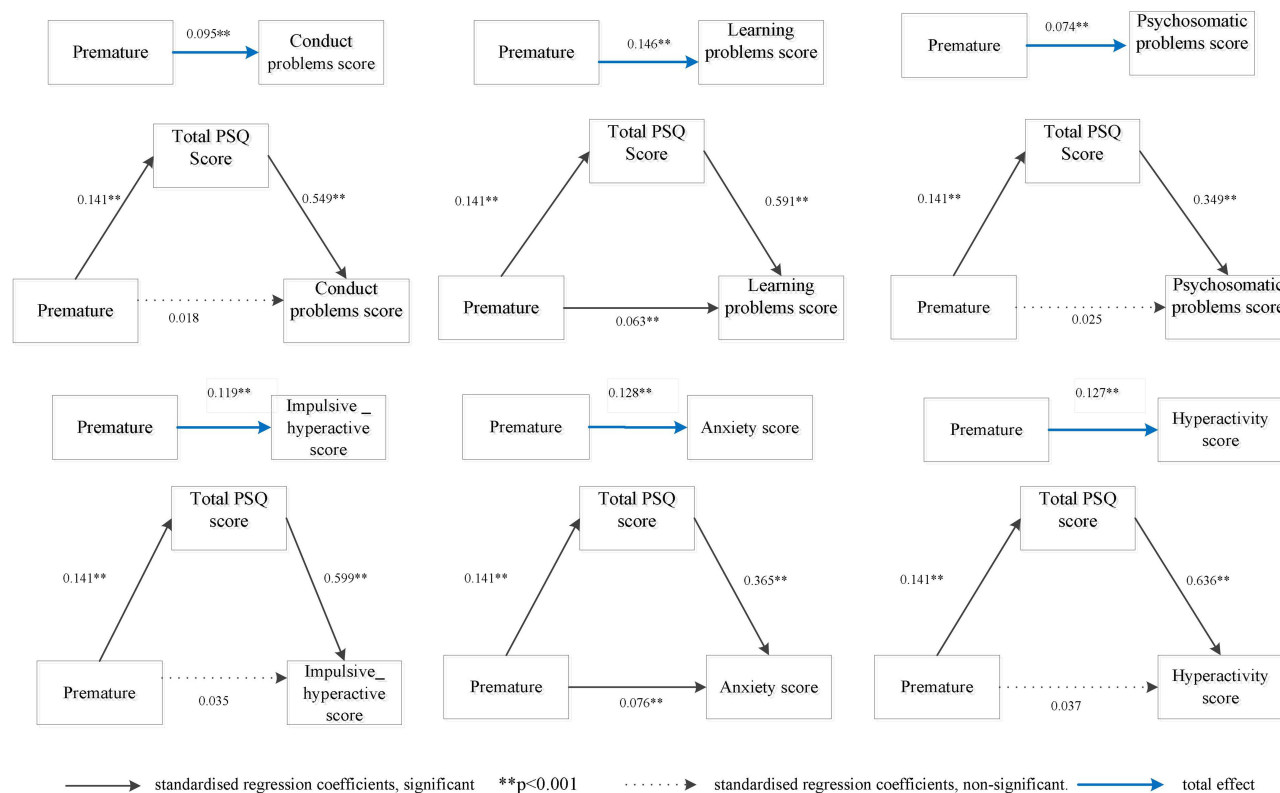


Figure 1 Mediating effect of total PSQ score on the association between the six dimensions of CPRS and premature infant development.

Table 6 Sensitivity Analysis Results of Mediating Effect of Preterm Birth & PSQ Total Score on CPRS 6 Dimensions

CPRS Dimension	Mediating Effect (ACME)	Direct Effect (ADE)	Total Effect	Mediation Proportion	Sensitivity Index (ρ Critical Value)	Robustness Evaluation	Sensitivity Index R ² _MR ² _Y Critical Value	Robustness Evaluation
Conduct problems score	0.0881***	0.0208	0.1089***	80.93%	0.55	High	0.303	High
Learning problems score	0.0972***	0.0727**	0.1699***	57.19%	0.6	Extremely High	0.36	High
Psychosomatic problems score	0.0473***	0.0236	0.0709*	66.73%	0.35	Medium	0.123	Relatively Robust
Impulsive-hyperactive score	0.1053***	0.0433	0.1486***	70.89%	0.6	Extremely High	0.36	High
Anxiety score	0.0558***	0.0829***	0.1388***	40.24%	0.35	Medium	0.123	Relatively Robust
Hyperactivity score	0.1074***	0.0448	0.1522***	70.58%	0.65	Extremely High	0.422	High

Notes: ***p < 0.001, **p < 0.01, *p < 0.05, Extremely high - ρ critical value >0.6, High - ρ critical value 0.4–0.6, Medium - ρ critical value <0.2–0.4.

Full Mediation

In an exploratory analysis, no significant direct association was observed between prematurity and the following CPRS dimensions: Conduct problems: direct effect ($\beta = 0.018$, $p = 0.438$), Psychosomatic problems: direct effect ($\beta = 0.025$, $p = 0.345$), Impulsive-hyperactive problems: direct effect ($\beta = 0.035$, $p = 0.121$), Hyperactivity: direct effect ($\beta = 0.037$, $p = 0.836$). These findings suggest that the total PSQ score fully mediated the relationships between prematurity and these CPRS dimensions (Table 5 and Figure 1).

Overall Significance

The mediated correlation between prematurity and six CPRS dimensions by total PSQ score was significant (95% Bootstrap CI excluded 0) (Table 5 and Figure 1). Prematurity showed significant overall correlations with Z-scores of all six CPRS dimensions (all $P < 0.05$).

Sensitivity Analyses

Based on Table 6, the sensitivity analysis of mediating effects revealed that the mediating effect of the total PSQ score on the Z-scores of Conduct, Learning problems, Impulsive-hyperactive, and Hyperactivity problems scores in preterm infants had been quite robust (ρ critical value >0.4). The mediating effect of the total PSQ score on the Z-scores of Psychosomatic and Anxiety scores in preterm infants had been relatively robust (ρ critical value <0.4). It was advisable to incorporate additional confounding variables (such as family history) in future research focusing on these two variables.

Discussion

The results of this cross-sectional study reveal the relationship between premature birth, sleep-disordered breathing (total score of PSQ), and behavioral problems (CPRS questionnaire) in children. After controlling for confounding factors such as age, gender, BMI z-score, mother’s age, and mother’s education, our main research findings indicate that sleep-disordered breathing (total score of PSQ) in premature infants partially or fully mediates children’s behavioral problems. It is important to highlight that the mediation effect observed in this cross-sectional study merely suggests a statistical association and does not imply any causal relationships among the variables.

The mechanism of sleep is closely related to the sleep centre and the activity status of the cerebral cortex.³⁴ Premature infants, due to insufficient neurophysiological development, may experience various sleep abnormalities, including a high incidence of SDB.³⁵ Potential biological pathways may involve prematurity-related neurodevelopmental vulnerabilities and SDB-induced intermittent hypoxia/inflammation collectively impacting neural circuits and neurotransmitter systems regulating behavior. The indications of externalizing,^{17,18,36} and internalizing symptoms³⁷⁻³⁹ are manifested often through parental behavior ratings in SDB cases. Those studies suggest an association between sleep disorders in premature infants and various behavioral problems in children, indicating that sleep - disordered breathing may be related to the relationship between premature infants and childhood behavior in an exploratory sense.³⁷⁻⁴⁰ Those were consistent with our research hypothesis. Our study offered an in-depth analysis and explanation of the correlations, showing how

SDB in premature infants had been associated with the emergence of internalizing and externalizing behavioral problems in children, suggesting its mediating role in this relationship.

Studies have shown that group cognitive-behavioral therapy can be successfully applied in urban schools to reduce the increasing risk for externalizing and internalizing disorders.⁴¹ The literature on the effectiveness of mental health interventions in low-income urban schools has mostly reported disappointing results,⁴¹ which suggests that interventions for children's behavioral issues require schools with adequate resources and high-quality intervention measures. This highlights the need for health management departments to pay close attention to behavioral problems among children in remote areas and intervene promptly.

Regarding the relationship between SDB and behavioral problems in children, our results indicated that the total PSQ score correlated positively with the six dimensions of the CPRS questionnaire (Table 3). Previous studies had also reported findings consistent with ours, indicating that behavioral issues were more common in children with SDB among primary school students.⁴² Sleep quality played an important role in children's academic performance and healthy development. Studies had shown that SDB was associated with poor academic performance, particularly in language, art, math, science, and learning problems.⁴³ A recent high-quality meta-analysis had reported that children with SDB exhibited deficiencies in multiple cognitive domains, particularly in full-scale intelligence quotient as well as subdomains, such as problem-solving, working memory, processing speed, and language.⁴⁴ This indicated that prioritizing screening for SDB and actively treating it could reduce undesirable behavioral in children. The aforementioned studies had indicated that prioritizing screening and treatment for SDB was extremely important. OSAS was a common clinical manifestation of SDB. Adenotonsillectomy was widely considered the primary treatment for OSAS in children.⁴⁵ A systematic review had demonstrated enhanced quality of life following adenotonsillectomy, with no significant postoperative complications.⁴⁶ Future cohort or intervention studies are necessary to figure out the causal relationships among prematurity, SDB, and how children behave. Specifically, longitudinal studies should track SDB development trajectories in premature infants using polysomnography, combined with neuroimaging biomarkers to explore neural mechanisms. Multi-center trials could also validate whether early adenotonsillectomy for SDB intervention alters behavioral outcomes in former preterm children.

Limitations

Assessment Bias: The evaluation of children's SDB and behavioral issues relied on parent-completed questionnaires using parent-reported instruments, which may introduce subjective bias. The absence of objective diagnostic methods like polysomnography impeded the verification of clinical severity, potentially masking true associations. To reduce this bias, relevant explanations, materials were given to guardians before questionnaire completion, and contact information for consultation was provided. The robustness of findings was partly shown by consistent strong associations in subgroup analysis.

Sample Limitation: The sample was restricted to Xuhui District, Shanghai, limiting the generalizability of results. Future research should gather data from different cities or regions for a more diverse sample.

Causality Establishment Issue: As a cross-sectional study with data collected at a single time point, it is impossible to determine the temporal sequence of variables, making it hard to distinguish causes from effects. For instance, although an association between SDB and children's behavioral problems was found, it is unclear whether SDB caused the problems, behavioral issues triggered sleep disturbances, or both were influenced by unmeasured factors such as the family environment.

Unmeasured Confounders: Potential unmeasured confounders like socioeconomic status, perinatal complications, or parental health conditions may affect the observed associations.

Despite these limitations, the study has a large sample size. There are relatively few studies on the mediation analysis of prematurity, SDB, and child behavior. The findings offer early warning knowledge for future research and inform clinical staff and parents of premature infants to pay attention to SDB and conduct screening.

Conclusion

This cross-sectional study reveals an association between prematurity and children's behavioral problems, suggesting SDB may act as a partial or full mediator. However, the findings are limited by parental-reported data bias and the cross-sectional design's inability to infer causality. Future cohort or intervention studies are needed to explore causal relationships among prematurity, SDB, and behavioral problems.

The Clinical Implications

While preliminary data hinted at possible links between sleep - disordered breathing (SDB) and behavioral problems in premature infants, these observations did not establish causality and required validation through longitudinal or interventional studies. Current practice may have included monitoring SDB symptoms and tracking behavioral outcomes over time, but any interventions for behavioral issues should not attribute causation to SDB alone without comprehensive multidisciplinary assessment. Future research needs to clarify whether these associations reflect direct pathways, shared vulnerabilities, or confounding factors to guide evidence - based care.

Data Sharing Statement

As per IRB application and permission, research data will not be made available in the public. However, the relevant data can be obtained from the corresponding authors upon qualified request and with the consent of Shanghai Sixth People's Hospital Affiliated to Shanghai Jiao Tong University School of Medicine.

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Author Contributions

Yuli Hu: Writing – original draft, Writing – review & editing, Methodology, Formal analysis, Data curation, Validation, Visualization, Funding acquisition. Siqiong Jiang: Writing – review & editing, Methodology, Resources, Supervision. Shiyin Yang: Writing – review & editing, Investigation, Data curation. Chunsheng Wang: Software, Validation, Visualization, Formal analysis, Data curation, Writing – review and editing. Jianyin Zou: Methodology, Writing – review and editing, Jian Guan: Conceptualization, Writing – review & editing, Project administration and Supervision. Yupu Liu: Writing – review & editing, Project administration, Data curation and Supervision. Qunfeng Lu: Writing – review & editing, Methodology, Resources, Funding acquisition, Conceptualization and Supervision.

All authors have made substantial contributions to the research presented in this work, spanning key stages such as conceptual framing, research methodology formulation, practical implementation, data collection, in-depth analysis, and result interpretation, with some contributing across multiple or all of these domains. They have actively participated in the writing process, either by drafting initial versions, refining content through revisions, or providing critical feedback to enhance the article's quality. Furthermore, all authors have collectively endorsed the final paper for publication, reached a consensus on the target journal for submission, and committed to taking full responsibility for the integrity and accuracy of every aspect of the research.

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Disclosure

The authors declare no conflicts of interest.

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