Am J Transl Res 2025;17(8):5928-5938
www.ajtr.org /ISSN:1943-8141/AJTR0166327

Original Article

Clinical significance of serum interleukin-4, interleukin-12, interleukin-13, and transforming growth factor-β levels in children with sleep-disordered breathing

Yijie Du[1,2], Xiaoli Dai[1], Yuzhu Jiang[2], Jinmei Ren[3], Yang Wang[3], Yulong Jiang[4]

[1]Qingpu District Traditional Chinese Medicine Hospital, Shanghai 201799, China; [2]Shanghai Qingpu Mental Health Center, Shanghai 201799, China; [3]Qingpu Branch of Zhongshan Hospital Affiliated to Fudan University, Shanghai 201799, China; [4]Shanghai Qingpu District Zhujiajiao People's Hospital, Shanghai 201799, China

Received May 25, 2025; Accepted July 22, 2025; Epub August 15, 2025; Published August 30, 2025

Abstract: Objective: To investigate the clinical significance of serum interleukin-4 (IL-4), IL-12, IL-13, and transforming growth factor-β (TGF-β) levels in children with sleep-disordered breathing (SDB). Methods: A total of 107 children with SDB (research group) and 75 healthy children (control group) were enrolled. Serum cytokine levels were measured in all participants. Receiver operating characteristic curve analyses were used to evaluate diagnostic efficacy. Spearman correlation analysis was applied to assess the relationship between cytokine levels and disease severity, while Pearson correlation examined associations with sleep-related parameters, including microarousal index (ArI), apnea-hypopnea index (AHI), lowest arterial oxygen saturation ($LSaO_2$), and mean oxygen saturation ($MSaO_2$). Changes in cytokine levels before and after surgery were also analyzed. Results: Compared with the control group, children in the SDB group exhibited significantly higher levels of IL-4, IL-13, TGF-β, ArI, and AHI, and lower levels of IL-12, $LSaO_2$, and $MSaO_2$ (all $P<0.05$). Serum cytokine levels were significantly correlated with sleep-related parameters (all $P<0.05$). The combined diagnostic model (IL-4+IL-12+IL-13+TGF-β) yielded an area under the curve (AUC) of 0.880, outperforming individual markers (AUC range: 0.714-0.741). Disease severity was negatively correlated with IL-12 ($r=-0.381$) and positively correlated with IL-4, IL-13, and TGF-β ($r=0.338$-0.434; all $P<0.001$). After surgery, IL-4, IL-13, and TGF-β levels decreased, while IL-12 levels increased significantly (all $P<0.05$). Conclusion: Serum levels of IL-4, IL-12, IL-13, and TGF-β may serve as potential biomarkers for the diagnosis, severity assessment, and therapeutic monitoring of SDB in children.

Keywords: Sleep-disordered breathing, interleukin-4, interleukin-12, interleukin-13, transforming growth factor-β

Introduction

Sleep-disordered breathing (SDB) is a clinical condition characterized by abnormal respiratory patterns during sleep and is commonly associated with cardiopulmonary comorbidities such as pulmonary embolism, pulmonary hypertension, and chronic heart failure [1]. Clinically, SDB encompasses a spectrum of disorders, ranging from chronic snoring and upper airway resistance syndrome to obstructive sleep apnea syndrome (OSAS), with OSAS being the most prevalent subtype [2]. Epidemiological studies estimate that SDB affects approximately 33% of adults aged 30-70 years in Europe and 10-17% of children, significantly impairing sleep quality and overall health [3-6]. Emerging evidence indicates that untreated pediatric SDB may be linked to neurobehavioral and cognitive dysfunction, as well as long-term metabolic, endocrine, and cardiovascular complications [7]. Given these potential adverse outcomes, early and accurate diagnosis of SDB in children is critical for optimizing clinical management and developing individualized treatment strategies [8].

Polysomnography (PSG) remains the gold standard for diagnosing SDB due to its high accuracy; however, its clinical utility is often limited by time-consuming procedures and substantial financial cost [9]. Given these limitations, there is an urgent need to explore effective and accessible alternative diagnostic biomarkers. OSAS, the most common form of SDB, has been closely linked to multiple pathophysiological

https://doi.org/10.62347/YMVG7620

mechanisms, including upper airway inflammation, systemic inflammatory responses, oxidative stress, endothelial dysfunction, and metabolic dysregulation [10-12]. Among immune mediators, interleukin-4 (IL-4) and IL-12, representing T helper 2 (Th2) and Th1 cytokines, respectively, are thought to contribute to OSAS pathogenesis through imbalances in Th1/Th2 immune responses [13]. IL-13 has also been implicated in inflammatory and asthmatic pathways in children with OSAS-asthma comorbidity, and elevated serum IL-13 levels have been observed in pediatric patients with uncontrolled asthma, suggesting a potential link to poorly controlled OSAS [14]. Moreover, previous research has demonstrated that monocytes in OSAS patients can inhibit natural killer cell activity via TGF-β, further highlighting the relevance of this cytokine in the pathophysiology of SDB [15].

This study aims to evaluate the clinical significance of IL-4, IL-12, IL-13, and TGF-β in pediatric SDB. The findings may underscore the diagnostic and prognostic relevance of these inflammatory markers, potentially offering a less invasive and more accessible alternative to traditional diagnostic methods. Such an approach could support earlier detection and more individualized management of pediatric SDB.

Materials and methods

Study population and design

This retrospective study included 107 pediatric patients diagnosed with SDB who were admitted to Qingpu District Traditional Chinese Medicine Hospital between September 2022 and February 2025. A control group of 75 age-matched healthy children undergoing routine physical examinations during the same period was included for comparison. No significant differences in baseline demographic characteristics were observed between the two groups ($P>0.05$), confirming their comparability. The study protocol was approved by the Institutional Ethics Committee of Qingpu District Traditional Chinese Medicine Hospital.

The sample size was calculated based on methods proposed by Obuchowski and Hanley [16, 17], assuming an anticipated area under the curve (AUC) of 0.7 (indicating moderate diagnostic utility), a two-sided significance level (α) of 0.05, and a statistical power (1-β) of 80%. Given a case-to-control ratio of 1.5:1, the required sample size was estimated to be 105 cases and 70 controls. The final enrollment of 107 SDB patients and 75 controls met these criteria.

Eligibility criteria

Inclusion criteria: Diagnosis of SDB based on established clinical guidelines [18]; Age between 2 and 12 years; Presence of clinical symptoms, including habitual snoring (≥3 nights per week), observed apnea, excessive daytime sleepiness, or attention deficits; Tonsillar hypertrophy graded I to III; Completion of standard PSG and lateral nasopharyngeal X-ray imaging; Presence of sleep-related symptoms such as snoring (with or without mouth breathing), breath-holding, restless sleep, labored breathing, or recurrent respiratory infections.

Exclusion criteria: Presence of craniofacial syndromes (e.g., Pierre-Robin syndrome, Down syndrome, Crouzon syndrome) or neuromuscular disorders; Acute upper respiratory tract infection within the past two weeks; Coexistence of other severe primary diseases; Diagnosed upper airway obstruction or advanced heart failure; History of chronic insomnia, hypothyroidism, or neuropsychiatric disorders; Use of glucocorticoids, immunosuppressants, or antibiotics within one month prior to enrollment; Diagnosis of non-respiratory sleep disorders, such as narcolepsy or periodic limb movement disorder.

Polysomnographic assessment

After a three-day hospitalization, all pediatric SDB patients underwent overnight PSG. On the day of monitoring, participants were advised to avoid strong tea, coffee, alcohol, and sedative-hypnotic medications. PSG recordings lasted at least seven hours, and only data with a total sleep time exceeding four hours were included in the analysis. PSG data were analyzed using dedicated software and manually scored by trained technicians. Parameters recorded included electroencephalogram, electrooculogram, oronasal airflow, thoracoabdominal movement, and arterial oxygen saturation (SaO_2). Key indices derived from the recordings included the arousal index (ArI), apnea-hypopnea index (AHI), lowest arterial oxygen saturation ($LSaO_2$), and mean oxygen saturation ($MSaO_2$).

Table 1. Comparison of baseline characteristics

Data	Control group (n=75)	Research group (n=107)	χ^2/t	P
Sex distribution (male/female)	39/36	65/42	1.378	0.241
Age (years)	7.39±2.49	7.67±2.85	0.687	0.493
Body mass index (kg/m^2)	17.52±2.69	17.20±2.77	0.776	0.439
Disease duration (months)	25.83±7.13	24.02±6.86	1.724	0.087
Parental education level (< high school/≥ high school)	45/30	59/48	0.425	0.514
Family history of snoring (no/yes)	6/69	11/96	0.271	0.603
Disease severity (mild/moderate/severe)	-	30/43/34	-	-

Adenotonsillectomy procedure

Adenotonsillectomy was performed as the primary treatment for pediatric patients diagnosed with SDB. With the patient in the supine position, a mouth gag was inserted to facilitate adequate oropharyngeal exposure. Bilateral tonsillectomy was conducted using the cold dissection technique under direct visualization. To access the nasopharynx, a catheter was inserted transnasally on both sides and retrieved through the oral cavity. The soft palate was retracted by securing the catheter ends externally, thereby ensuring sufficient visualization for adenoid removal. Adenoidectomy was then performed under direct endoscopic guidance using a 70° nasal endoscope, employing a combination of curettage and powered instrumentation. Hemostasis was achieved through compression or electrocautery, depending on intraoperative bleeding status.

Severity classification criteria

The severity of SDB was classified according to the AHI as follows: mild SDB (AHI: 1-5 events/hour), moderate SDB (AHI: 5-10 events/hour), and severe SDB (AHI: >10 events/hour) [19].

Biochemical measurements

Fasting venous blood samples (5 mL) were collected from all participants between 8:00 and 9:00 AM the morning prior to PSG examination. Samples were promptly centrifuged and stored at -80°C until analysis. Serum levels of IL-4, IL-12, IL-13, and TGF-β were measured using enzyme-linked immunosorbent assay kits (IL-4: K0331214; IL-12: K0331124; IL-13: K0331235; all from Beijing Asnail Biotechnology Co., Ltd.; TGF-β: JLC-R13550, Jiangxi Institute of Biological Products Co., Ltd.). All procedures were conducted by an experienced technician in following the manufacturer's protocols. Additionally, paired analyses were conducted to assess changes in serum cytokine levels in children with SDB before and after adenotonsillectomy.

Statistical analysis

Data analyses were performed using SPSS version 23.0 (IBM Corp., Armonk, NY, USA), and graphical visualizations were generated with GraphPad Prism version 7.0 (GraphPad Software, San Diego, CA, USA). Continuous variables were expressed as mean ± standard error of the mean (SEM). Between-group comparisons were conducted using independent two-sample t-tests, while one-way analysis of variance followed by least significant difference post-hoc tests was employed for comparisons among multiple groups. Categorical variables were presented as percentage and compared using the chi-square test. The diagnostic performance of serum biomarkers (IL-4, IL-12, IL-13, and TGF-β) for SDB was evaluated using receiver operating characteristic (ROC) curve analysis. Pearson's correlation coefficients were used to evaluate associations between serum cytokine levels and sleep-related parameters. Spearman's rank correlation coefficients were applied to examine relationships between cytokine levels and SDB severity. A two-tailed *P*-value <0.05 was considered statistically significant.

Results

Comparison of baseline characteristics

No significant differences were observed between the two groups regarding sex distribution, age, body mass index, disease duration, parental education level, or family history of snoring (all P>0.05, **Table 1**), indicating compa-

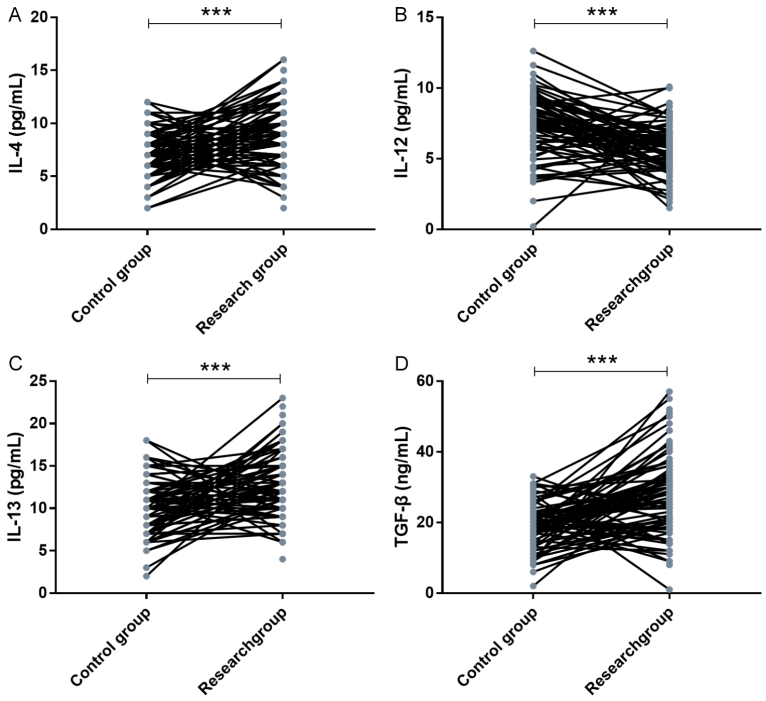

Figure 1. Comparison of serum cytokine levels. A. IL-4 comparison. B. IL-12 comparison. C. IL-13 comparison. D. TGF-βcomparison. Note: IL, interleukin; TGF-β, transforming growth factor β. Statistical significance is indicated as ***P<0.001.

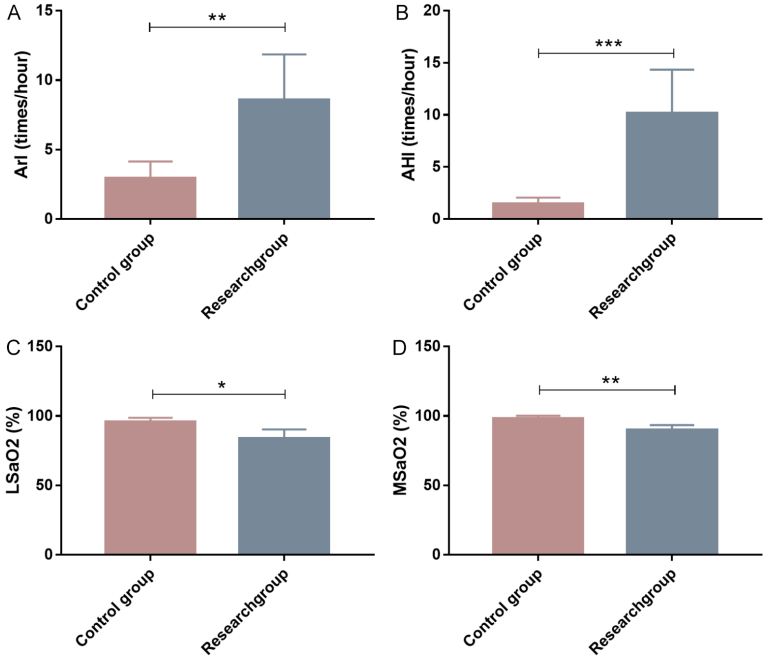

Figure 2. Comparison of sleep monitoring parameters. A. ArI comparison. B. AHI comparison. C. $LSaO_2$ comparison. D. $MSaO_2$ comparison. Note: ArI, arousal index; AHI, apnea-hypopnea index; $LSaO_2$, lowest oxygen saturation; $MSaO_2$, mean oxygen saturation. Statistical significance is indicated as *P<0.05, **P<0.01, ***P<0.001.

rability between the two cohorts at baseline.

Comparison of serum cytokine levels

As illustrated in **Figure 1**, the research group exhibited significantly higher serum levels of IL-4, IL-13, and TGF-β compared to the control group (all P<0.001). In contrast, IL-12 levels were markedly lower in the research group (P<0.001).

Comparison of sleep monitoring parameters

The research group exhibited significantly higher ArI and AHI values compared to the control group, while $LSaO_2$ and $MSaO_2$ were markedly lower (all P<0.05, **Figure 2**).

Correlation between serum cytokine levels and sleep monitoring parameters

Pearson correlation analysis demonstrated significant associations between serum cytokine levels and sleep parameters in the SDB group. IL-4 was moderately positively correlated with ArI (r=0.321, P<0.001) and AHI (r=0.294, P=0.002), and negatively correlated with $LSaO_2$ (r=-0.256, P=0.008) and $MSaO_2$ (r=-0.307, P=0.001). IL-12 was negatively correlated with AHI (r=-0.290, P=0.003) and positively correlated with $LSaO_2$ (r=0.196, P=0.043) and $MSaO_2$ (r=0.250, P=0.010). IL-13 exhibited positive correlations with ArI (r=0.307, P=0.001) and AHI (r=0.316, P<0.001), and negative correlations with $LSaO_2$ (r=-0.385, P<0.001) and $MSaO_2$ (r=-0.338, P<0.001). TGF-β was positively correlated with ArI

Table 2. Correlation between serum cytokine levels and sleep monitoring parameters

Indicators	ArI (times/hour)		AHI (times/hour)		$LSaO_2$ (%)		$MSaO_2$ (%)	
	r	P	r	P	r	P	r	P
IL-4 (pg/mL)	0.321	<0.001	0.294	0.002	-0.256	0.008	-0.307	0.001
IL-12 (pg/mL)	-0.171	0.078	-0.290	0.003	0.196	0.043	0.250	0.010
IL-13 (pg/mL)	0.307	0.001	0.316	<0.001	-0.385	<0.001	-0.338	<0.001
TGF-β (ng/mL)	0.321	<0.001	0.129	0.186	-0.227	0.019	-0.153	0.117

Note: ArI, arousal index; AHI, apnea-hypopnea index; $LSaO_2$, lowest oxygen saturation; $MSaO_2$, mean oxygen saturation; IL, interleukin; TGF-β, transforming growth factor β.

(r=0.321, P<0.001) and negatively associated with $LSaO_2$ (r=-0.227, P=0.019), while no significant correlations were observed with AHI or $MSaO_2$. Correlation coefficients and significance levels are provided in **Table 2**.

Diagnostic performance of serum cytokines in identifying SDB

Figure 3 displays the ROC curves for serum IL-4, IL-12, IL-13, and TGF-β in diagnosing SDB, and the corresponding diagnostic metrics are summarized in **Table 3**. The AUC values for IL-4, IL-12, IL-13, and TGF-β were 0.714, 0.741, 0.729, and 0.730, respectively. Importantly, the combined analysis of all four cytokines significantly improved diagnostic performance, achieving an AUC of 0.880, with a sensitivity of 84.11% and a specificity of 78.67%.

Comparison of serum cytokine levels across SDB severity groups

Figure 4 compares serum cytokine levels of IL-4, IL-12, IL-13, and TGF-β across various SDB severity groups. Significant differences were observed among the groups. IL-4 levels were markedly higher in severe cases compared to moderate (P<0.05) and mild cases (P<0.001). IL-12 levels were highest in the mild group and significantly decreased in moderate and severe patients (both P<0.05). IL-13 levels were lower in mild cases than in moderate and severe cases (both P<0.01). Similarly, TGF-β levels were significantly lower in mild cases compared to severe cases (P<0.01).

Correlation between serum cytokine levels and SDB severity

Figure 5 presents the results of Spearman's correlation analysis between serum cytokine levels of IL-4, IL-12, IL-13, TGF-β and the severity of SDB. Disease severity was scored numerically as 1 (mild), 2 (moderate), and 3 (severe). Significant positive correlations were observed between SDB severity and serum levels of IL-4, IL-13, and TGF-β (all P<0.001). In contrast, IL-12 levels exhibited a significant negative correlation with disease severity (P<0.001).

Diagnostic performance of serum cytokines in assessing SDB severity

Figure 6 displays the ROC curve analysis evaluating the diagnostic utility of serum IL-4, IL-12, IL-13, and TGF-β levels in stratifying SDB severity. The AUC values were 0.720 for IL-4, 0.678 for IL-12, 0.692 for IL-13, and 0.696 for TGF-β, indicating moderate discriminatory power. Notably, the combined use of all four cytokines significantly enhanced diagnostic accuracy, achieving an AUC of 0.835. Detailed diagnostic metrics are provided in **Table 4**.

Treatment-associated changes in serum cytokine levels in SDB patients

After treatment, significant changes were observed in serum cytokines among SDB patients. IL-4, IL-13, and TGF-β levels decreased significantly, while IL-12 levels increased notably (all P<0.05). These findings are illustrated in **Figure 7**.

Discussion

SDB in children encompasses a spectrum of conditions, ranging from primary snoring, the mildest form without major clinical consequences, to OSAS, the most severe phenotype characterized by recurrent upper airway obstruction during sleep [20, 21]. Notably, prior studies have reported a high prevalence of inattention, hyperactivity, and increased risk of behavioral and emotional disturbances in pedi-

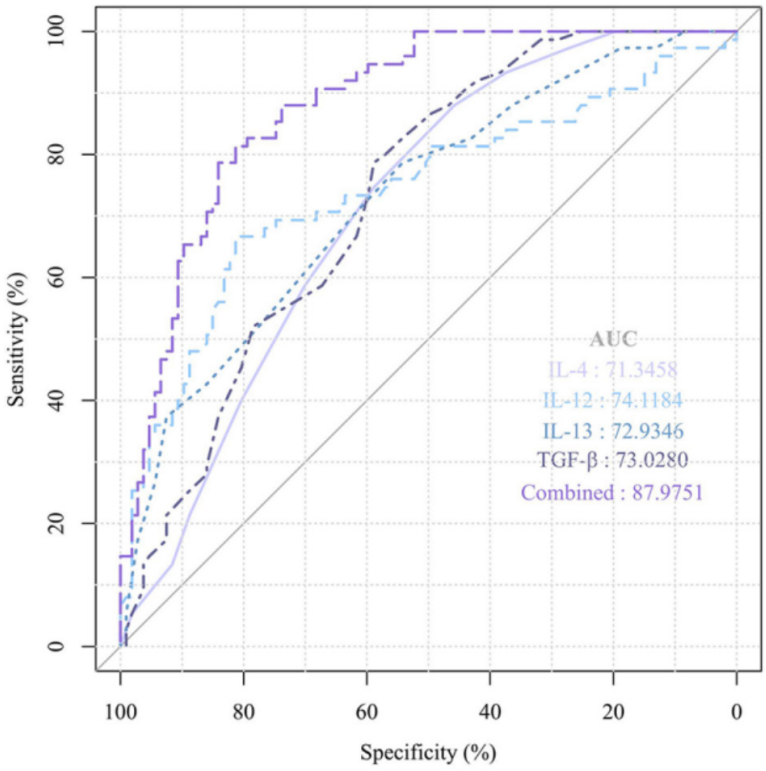

Figure 3. ROC curve analysis of serum cytokines and their combination. Note: ROC, receiver operating characteristic; AUC, the area under the curve; IL, interleukin; TGF-β, transforming growth factor β; SDB, sleep-disordered breathing.

Table 3. Diagnostic performance of serum cytokines in identifying SDB

Serum index	AUC	95% CI	Specificity	Sensitivity	*P* value
IL-4	0.714	0.640-0.787	88.00%	45.79%	<0.001
IL-12	0.741	0.664-0.818	66.67%	81.31%	<0.001
IL-13	0.729	0.656-0.803	78.67%	54.21%	<0.001
TGF-β	0.730	0.659-0.802	78.67%	58.88%	<0.001
Combined	0.880	0.832-0.928	78.67%	84.11%	<0.001

Note: IL, interleukin; TGF-β, transforming growth factor β; SDB, sleep-disordered breathing; AUC, the area under the curve; CI, confidence interval.

atric SDB patients, regardless of disease severity [22]. To enhance diagnostic accuracy and guide therapeutic strategies for pediatric SDB, the present study investigated serum levels of key cytokines, including IL-4, IL-12, IL-13, and TGF-β, and evaluated their clinical significance in relation to disease presence and severity.

Our findings revealed significant alterations in inflammatory cytokines among children with SDB, characterized by markedly elevated serum levels of IL-4, IL-13, and TGF-β, alongside a substantial reduction in IL-12. These results are consistent with those of Li et al. [23], who reported elevated inflammatory mediators in patients with OSAS and found a positive correlation between these markers and obesity severity, further supporting our observations. SDB has been associated with pulmonary fibrosis, a condition driven by excessive and persistent extracellular matrix deposition in the lung parenchyma, ultimately impairing respiratory function [24]. IL-4 and IL-13, as Th2 cytokines, are commonly elevated in airway inflammatory diseases and contribute to pulmonary fibrosis by promoting fibroblast differentiation and collagen production [25]. Elevated IL-4 levels have also been independently associated with cognitive dysfunction in obese patients with OSAS [26]. Moreover, the pathogenesis of SDB involves increased oxidative stress, which can upregulate TGF-β expression and perpetuate chronic inflammation, explaining its elevated levels in affected children [27]. In contrast, the downregulation of IL-12 may be result from suppression of monocyte-driven inflammatory responses, potentially mediated via the T lymphocyte immunoglobulin and mucin domain-containing molecule-3 signaling pathway [28].

Additionally, children with SDB exhibited significantly elevated ArI and AHI, along with marked reductions in $LSaO_2$ and $MSaO_2$, indicating pronounced sleep fragmentation, frequent respiratory events, and intermittent hypoxemia. Notably, the combination of elevated AHI and decreased $LSaO_2$ underscores the urgency of timely and targeted interventions to prevent long-term hypoxia-related complications, in-

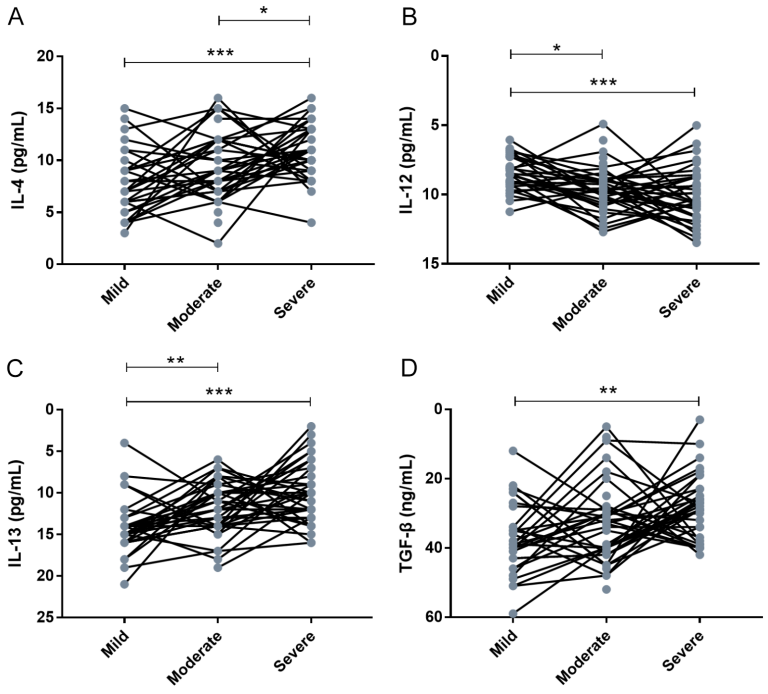

Figure 4. Comparison of serum cytokine levels across SDB severity groups. A. Serum IL-4 levels across severity subgroups. B. Serum IL-12 levels across severity subgroups. C. Serum IL-13 levels across severity subgroups. D. Serum TGF-β levels across severity subgroups. Note: IL, interleukin; TGF-β, transforming growth factor β; SDB, sleep-disordered breathing. Statistical significance is indicated as *P<0.05, **P<0.01, and ***P<0.001.

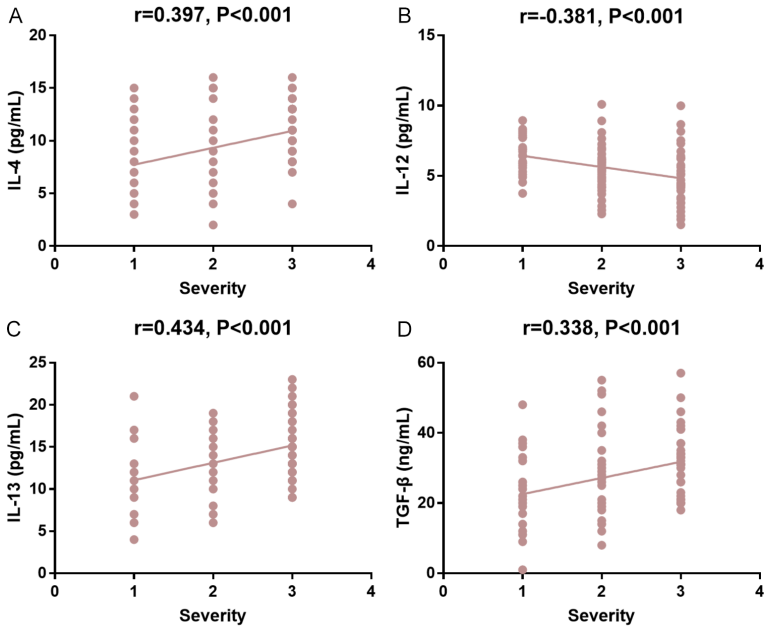

Figure 5. Correlation between serum cytokine levels and SDB severity. A. Correlation between IL-4 levels and SDB severity. B. Correlation between IL-12 levels and SDB severity. C. Correlation between IL-13 levels and SDB severity. D. Correlation between TGF-β levels and SDB severity. Note: SDB, sleep-disordered breathing; IL, interleukin; TGF-β, transforming growth factor β.

cluding cognitive deficits and cardiovascular diseases [29, 30]. Correlation analyses revealed that IL-4 and IL-13 were positively associated with ArI and AHI but negatively correlated with $LSaO_2$ and $MSaO_2$ in pediatric SDB cases. In contrast, IL-12 showed an inverse relationship with AHI and a positive correlation with $LSaO_2$ and $MSaO_2$. TGF-β exhibited a positive correlation with ArI but a negative link to $LSaO_2$. These observations suggest that IL-4, IL-13, and TGF-β may contribute to SDB progression, whereas IL-12 appears to exert a protective effect. This pattern may reflect a self-reinforcing cycle involving inflammation, hypoxia, and tissue remodeling in SDB, wherein dysregulated immune responses contribute to adenoidal hypertrophy and fibrosis, thereby exacerbating airway obstruction and increasing AHI. The resulting hypoxemia, as evidenced by reduced $LSaO_2$, may further intensify inflammatory and fibrotic processes. IL-12 may mitigate this pathological cascade by modulating the Th2-mediated immune responses [25, 31].

Subsequent analyses revealed that the individual AUC values of IL-4, IL-12, IL-13, and TGF-β for diagnosing SDB ranged from 0.714 to 0.741, indicating moderate diagnostic utility. When these four biomarkers were combined, the AUC significantly increased to 0.880, indicating substantially improved diagnostic accuracy. Among the individual markers, IL-4 demonstrated the highest specificity (88.00%), while IL-12 exhibited the highest sensitivity (81.31%). The combined panel achieved a balanced diagnos-

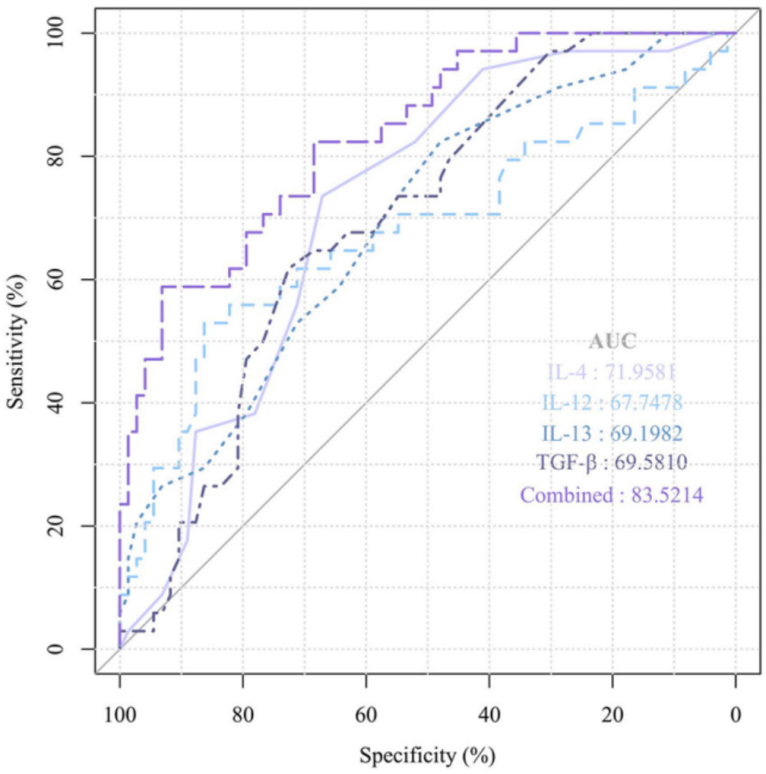

Figure 6. ROC curve analysis of the diagnostic efficacy of serum IL-4, IL-12, IL-13, and TGF-β levels in evaluating SDB severity. Note: ROC, receiver operating characteristic; IL, interleukin; TGF-β, transforming growth factor β; SDB, sleep-disordered breathing.

Table 4. Diagnostic performance of serum cytokines in assessing SDB severity

Serum index	AUC	95% CI	Specificity	Sensitivity	*P* value
IL-4	0.720	0.622-0.818	67.12%	73.53%	<0.001
IL-12	0.678	0.558-0.797	86.30%	52.94%	<0.001
IL-13	0.692	0.587-0.797	47.95%	82.35%	<0.001
TGF-β	0.696	0.596-0.796	72.60%	61.76%	<0.001
Combined	0.835	0.756-0.914	93.15%	58.82%	<0.001

Note: IL, interleukin; TGF-β, transforming growth factor β; SDB, sleep-disordered breathing; AUC, the area under the curve; CI, confidence interval.

tic performance, with 78.67% specificity and 84.11% sensitivity. These results align with those of Fiedorczuk et al. [32], who reported AUCs of 0.724, 0.677, and 0.745 for IL-6, tumor necrosis factor-alpha, and C-reactive protein, respectively, in differentiating OSAS from non-OSAS individuals.

Furthermore, stratification by disease severity revealed that serum levels of IL-4, IL-13, and TGF-β increased progressively with worsening SDB severity, whereas IL-12 exhibited an inverse trend, decreasing as the disease advanced. Correlation analyses confirmed these associations, with IL-4, IL-13, and TGF-β positively correlated with disease severity, and IL-12 negatively correlated. These findings are supported by a study conducted by Chuang et al. [33], which reported positive correlations between OSAS severity and levels of IL-6, IL-9, basic fibroblast growth factor, platelet-derived growth factor-BB, as well as regulated upon activation, normal T cell expressed and secreted, further reinforcing the role of inflammatory mediators in disease progression.

ROC curve analysis demonstrated that serum levels of IL-4, IL-12, IL-13, and TGF-β had moderate diagnostic performance for assessing SDB severity, with AUC values ranging from 0.678 to 0.720. Notably, the combined use of these biomarkers significantly improved the diagnostic accuracy, achieving an AUC of 0.835. Among the individual biomarkers, IL-12 displayed the highest specificity (86.30%), while IL-13 showed the greatest sensitivity (82.35%). Importantly, the combined diagnostic method further enhanced the specificity to 93.15%, substantially improving the accuracy of SDB severity assessment. Finally, we observed significant post-treatment changes in serum IL-4, IL-12, IL-13, and TGF-β concentrations in children with SDB, highlighting their potential as biomarkers for therapeutic response. Prior studies have reported elevated TGF-β levels in the exhaled condensates of OSAS patients, which normalized after continuous positive airway pressure intervention [34], supporting its role as an indicator of treatment efficacy. However, evidence regarding the responsiveness of other biomark-

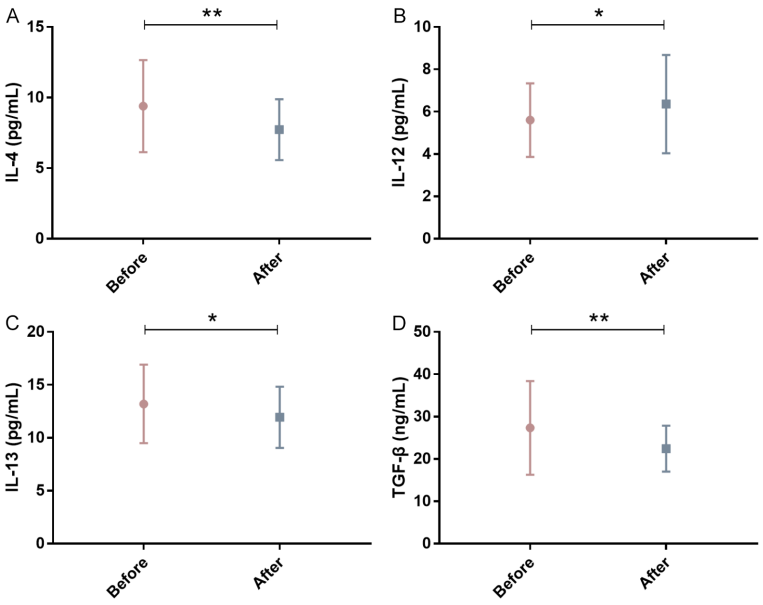

Figure 7. Treatment-associated changes in serum cytokine levels in SDB patients. A. IL-4 levels pre- and post-treatment. B. IL-12 levels pre- and post-treatment. C. IL-13 levels pre- and post-treatment. D. TGF-β levels pre- and post-treatment. Note: SDB, sleep-disordered breathing; IL, interleukin; TGF-β, transforming growth factor β. Statistical significance is indicated as *P<0.05, **P<0.01.

ers to SDB treatment remains limited and warrants further investigation.

The association between serum biomarkers and the severity of pediatric SDB has been investigated in several studies. Locci et al. [35] demonstrated an inverse correlation between 25-hydroxyvitamin D levels and OSAS severity in children. Similarly, Ji et al. [36] reported markedly elevated serum periostin and tumor necrosis factor-alpha levels in pediatric OSAS patients with hypoventilation syndrome, with both biomarkers showing strong positive correlations with disease severity. Furthermore, Zou et al. [37] found substantially decreased serum titin levels in OSAS patients, which exhibited a significant negative association with disease severity.

This study has several limitations. Notably, its retrospective design precluded the evaluation of changes in sleep parameters (ArI, AHI, $LSaO_2$, and $MSaO_2$) before and after treatment. Future longitudinal studies are warranted to clarify the temporal relationship between improvements in respiratory events and cytokine profiles (IL-4, IL-12, IL-13, TGF-β). Such investigations may help identify the objective physiological markers for treatment response and facilitate the development of a combined predictive model incorporating both sleep indices and inflammatory biomarkers.

In summary, children with SDB demonstrate significant dysregulation of serum IL-4, IL-12, IL-13, and TGF-β concentrations. These cytokines individually demonstrate potential as diagnostic and severity-assessing biomarkers. Notably, their combined use significantly enhances diagnostic accuracy and clinical evaluation. Furthermore, their strong correlations with disease severity underscore their utility in both tracking disease progression and monitoring therapeutic response in pediatric SDB.

Acknowledgements

This work was supported by the National Key R&D Program 2021YFC2501405.

Disclosure of conflict of interest

None.

Address correspondence to: Yulong Jiang, Shanghai Qingpu District Zhujiajiao People's Hospital, No. 99 Shijiabang Road, Shanghai 201799, China. Tel: +86-18116016537; E-mail: jyl19730607@163.com

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