

Dear Doctor,  
Greetings from Micro Labs Limited. We are happy to bring you "PEDIA COMPANION NEWSLETTER" which contain latest and interesting news in the field of Paediatrics.

This issue contains:

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Best Regards,  
Medical Team, Micro Labs Limited

## **Combined association of sleep quality and outdoor activity with the risk of asthma and allergic rhinitis in children**

### **Introduction**

Allergic rhinitis (AR) and asthma are two common allergic diseases in children that share respiratory tract mucosal alterations and immunological pathways. The prevalence of AR in Asia is notably high, ranging from 27% to 32%, while the prevalence of childhood asthma has significantly increased in most areas over the past 20 years.<sup>1</sup> These conditions often emerge after the age of two and continue to rise throughout childhood and adolescence. So, identifying risk factors and developing targeted intervention strategies is crucial for controlling asthma/AR. Both genetic and environmental factors play a role in the development of asthma and AR. Individual behaviour and lifestyle may impact asthma/AR symptoms in addition to genetic and demographic factors. Almost half of the children worldwide suffer from sleep disorders and poor sleep quality, including decreased duration, poor quality, and sleep-related disorders, have been associated with an increased risk of AR and asthma. Although Regular physical activity is generally beneficial for maintaining overall health, its relationship with asthma and AR has yielded mixed results. While most studies found a negative correlation between physical activity and the risk of asthma and AR, some studies found a link between moderate to severe physical activity and an increased risk of asthma and AR.<sup>2,3</sup> The importance of this study resides in its possible implications for holistic health strategies that address children's sleep and activity patterns, which may eventually aid in the management and prevention of allergic diseases. This study examined the potential combined effects of outdoor activities and sleep quality on childhood asthma and AR in a large population study.



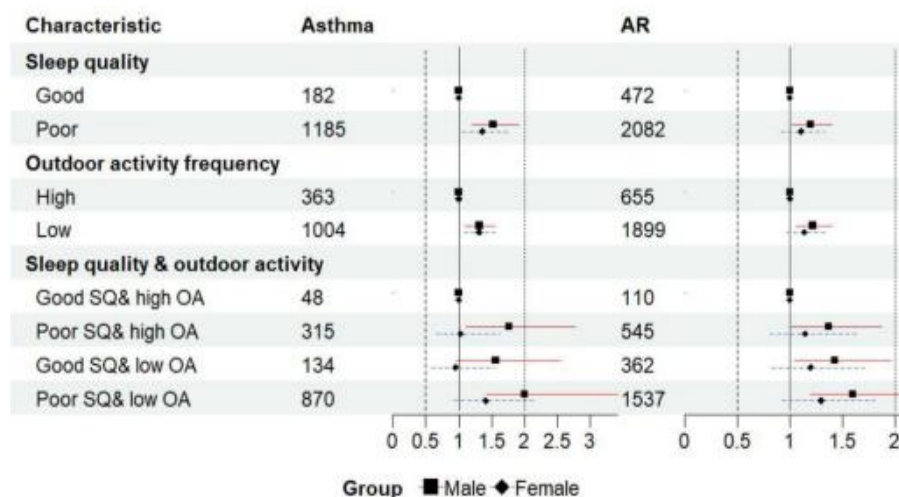
### **Methods**

This cross-sectional study included 16,936 children from kindergartens and primary schools across 13 administrative districts in Shanghai, China. The final analysis included children aged 3 to 12 years old, with 1367 cases of asthma (11.4%), 2554 cases of allergic rhinitis (9.2%), and 11,982 cases with none of them and excluded children with other allergic diseases, particularly atopic dermatitis and eczema. The International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire and the Children's Sleep Habit Questionnaire (CSHQ) were used to assess asthma, allergic rhinitis, and sleep quality, respectively. The association between outdoor activities, sleep quality, and children's asthma and allergic rhinitis was examined using

multivariable logistic regression models. SPSS software version 26.0 and R-4.1.2 were used for the analyses.

## Results

In this analysis, the prevalence rates of the allergies were 21.3% for AR and 11.4% for asthma. Asthma and AR were more prevalent in boys, high-income families, families with a history of allergies, parents with higher education levels, and parents with a history of sleep disorders. Low outdoor activity (asthma: aOR, 1.30; 95% CI: 1.14 to 1.49, allergic rhinitis: aOR, 1.18; 95% CI: 1.07 to 1.32) and poor sleep quality (asthma: aOR, 1.45; 95% CI: 1.23 to 1.73; allergic rhinitis: aOR, 1.16; 95% CI: 1.03 to 1.31) were independently linked to increased risk for both conditions. When both poor sleep quality and low outdoor activity were combined, an additive effect was observed, with the highest risk of asthma and AR (asthma: aOR, 1.76; 95% CI: 1.30 to 2.39; allergic rhinitis: aOR, 1.46; 95% CI: 1.17 to 1.82). These correlations were stronger in the sleep sufficiency group but were independent of duration of sleep. The study also looked into whether gender, premature birth, and a family history of allergy influenced the relationship. The relationships were most pronounced in males (Figure 1) and children with premature birth, but only demonstrated significance in participants without a family history of allergies.



**Figure 1. Sleep quality, outdoor activity and their combination with asthma and AR, stratified by gender**

## Discussion

This is the first large-scale study to investigate the joint effects of sleep quality and outdoor activity on asthma and AR in children. The study found that both poor sleep quality and low outdoor activity independently increase the risk of childhood asthma and AR, but their

combined effect is significantly stronger. Additionally, the study found that these associations were stronger in males and prematurely born children, as well as those with a family history of allergy. Consistent with these study findings, a study of Australian teenagers aged 14-21 found that poor sleep quality was associated with asthma.<sup>4</sup> Another study found that poor sleep quality predicts worse asthma symptoms the next day, indicating that poor sleep quality leads to increased symptom severity.<sup>5</sup>

## **Conclusion**

Sleep quality and physical activity have a significant synergistic effect that outperforms their individual effects, regardless of sleep duration. Targeted public health interventions to improve sleep quality and promote physical activity in children may reduce the risk of allergies. This highlights the need to consider the potential interactions and synthesis of lifestyle factors when examining their associations with health outcomes.

**Poor sleep quality and low outdoor activity are independently associated with a higher risk of Asthma and Allergic Rhinitis in children.**

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## **Identification of risk factors for late pulmonary artery hypertension in Extremely premature infants**

### **Introduction**

Bronchopulmonary dysplasia (BPD), a common condition affecting nearly 45% of surviving extremely preterm infants born before 28 weeks' gestational age (GA)<sup>1</sup>, is often linked to late

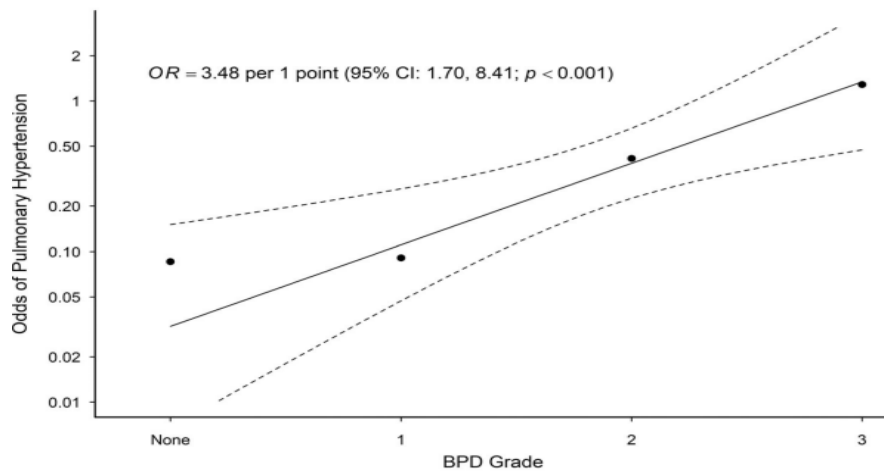
pulmonary artery hypertension (PH). Increased pulmonary artery pressure over  $\geq 36$  weeks postmenstrual age (PMA) is associated with higher morbidity and mortality.<sup>2</sup> Infants with late PH and BPD have higher readmission rates in the first year after neonatal intensive care unit discharge, as well as mortality rates of 26%-47% in the second and third years.<sup>3</sup> Despite the serious consequences of late PH, there is no standardized method for screening and diagnosing neonates. The timing and criteria for late PH screening in infants vary significantly. Echocardiography is commonly used to diagnose late PH, but the parameters used to assess pulmonary artery pressure vary between centers.<sup>4</sup> Although the pathogenesis of late PH is likely multifactorial, identifying specific risk factors remains unclear. The study aimed to address the knowledge gap by identifying risk factors and their link to the development of late PH in premature infants born before 28 weeks of gestation.

## **Methods**

This retrospective cohort study included infants born before 28 weeks' gestation who had PH screening and echocardiography at 36 weeks' post menstrual age. Patients with major congenital anomalies or undergoing extensive cardiac surgery were excluded. Data collected included infant and maternal demographics, infant outcomes, respiratory support at 1 week, 4 weeks, and 36 weeks of PMA, patent ductus arteriosus (PDA) status and treatment, and PH screening echocardiogram results. Diagnoses, clinical findings, therapies, and echocardiogram results were collected from progress notes, electronic medical records, and echo reports. PH was determined using echo parameters such as pulmonary artery acceleration time (PAAT), ventricular septal position, and estimated systemic pressures and tricuspid valve jet regurgitation velocity. Then, the infant's demographic and clinical characteristics were compared to their late PH status to determine any correlation. The data analysis was performed using R (v.4.2.1).

## **Results**

The study analysed 99 infants, of whom 20 (20%) developed late PH. There were no significant associations between maternal or neonatal characteristics and the development of late PH. Procedural closure of the patent ductus arteriosus (OR 3.72, 95% CI: 1.24–11.1,  $p = 0.02$ ), home oxygen use (80% vs. 58%,  $p = 0.04$ ), and the FiO<sub>2</sub>% requirement at 4 weeks of age were linked to late PH. Late PH was linearly correlated with the severity of bronchopulmonary dysplasia (BPD), with a 3.5-fold increase in the odds of a late PH diagnosis for every point increase in BPD severity (Figure 1). There were no significant differences in the incidence of necrotizing enterocolitis (NEC), retinopathy of prematurity (ROP), sepsis, or intraventricular hemorrhage (IVH) between infants with and without late PH.



**Figure 1. Relationship between odds of developing late pulmonary hypertension and BPD grade.**

## Discussion

This study found a strong association between BPD severity and late PH in preterm neonates born before 28 weeks' gestational age. A one-point increase in BPD grade was associated with a 3.5-fold increase in the odds of developing late PH. This suggests that impaired vascular proliferation and heterogeneous ventilation in BPD may contribute to the pathogenesis of late PH. The markers of severe respiratory disease, including FiO<sub>2</sub> requirement at 4 weeks, postnatal steroid use, home oxygen need, and procedural PDA intervention, were linked to late PH. This is consistent with the previous study that infants with late PH were more likely to be discharged home on oxygen therapy, indicating a strong link with BPD.<sup>5</sup> Additionally, infants with late PH were more likely to receive procedural PDA treatment, which may indicate that PDA shunt burden plays a part in the development of late PH, as observed by Gentle et al.<sup>6</sup>

## Conclusion

There is a strong relationship between late PH and BPD severity in extremely preterm infants, supporting the idea of a common pathophysiological mechanism. Given the increased morbidity and mortality associated with late PH, the study suggests implementing a targeted screening program for all infants with BPD at 36 weeks' PMA to assess for late PH, followed by close monitoring after discharge.

**Among infants born very prematurely, one in five experienced late PH. The onset of late PH was linked to indicators of the severity of respiratory diseases, such as the BPD grade.**

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## **Occurrence of avascular necrosis in the context of rheumatologic diseases**

### Introduction

Avascular necrosis (AVN) is a severe bone and red medulla necrosis caused by traumatic events or atraumatic risk factors, such as glucocorticoid use.<sup>1</sup> Atraumatic AVN primarily affects long-bone epiphyses, specifically the femoral head and condyles, distal end of the tibia, and humeral head.<sup>2</sup> It is influenced by several genetic and metabolic factors in addition to physical blood flow-restrictive events.<sup>3</sup> AVN has been linked to rheumatologic disorders, particularly systemic lupus erythematosus (SLE), due to inadequate bone perfusion and the reported prevalence of AVN in SLE patients ranges from 10 to 44%.<sup>4</sup> There is limited evidence on AVN in children with rheumatic diseases, with only single case reports and small series available. This study investigated the occurrence of AVN in children with underlying rheumatic disease and described the demographic and clinical characteristics of AVN patients, with a focus on treatment background.

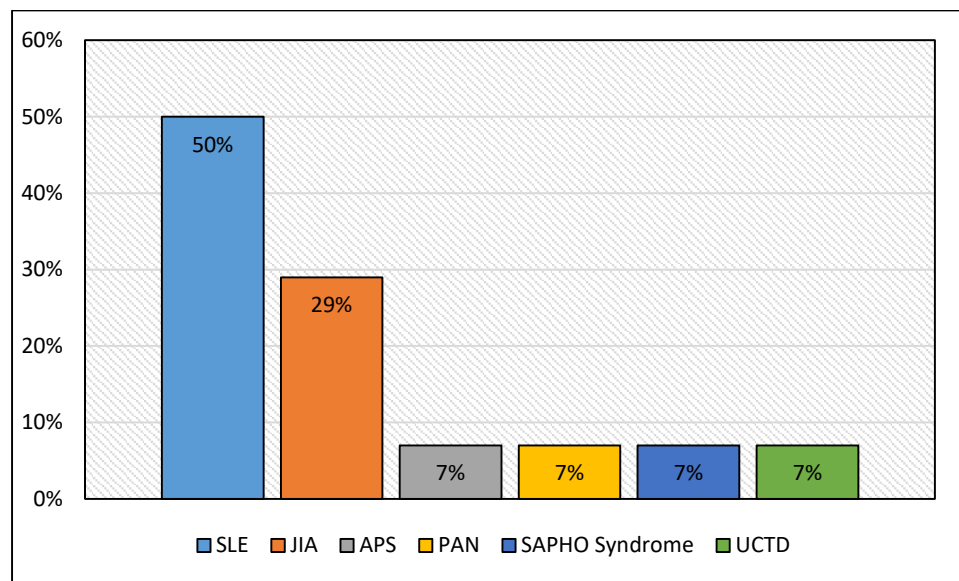
### Methods

This retrospective multicentric study included patients diagnosed with AVN confirmed by MRI before the age of 18 and affected by a rheumatic disease. Exclusion criteria consists of prior diagnoses of congenital hip dysplasia, Gaucher disease, hemoglobinopathies, cancer, and/or prior hematopoietic or solid transplantation, as well as prior orthopedic surgery performed at the site of AVN. Data collection was conducted using a standard case report form (CRF) to gather information on demographics, clinical conditions, laboratory results, imaging, and treatment history, particularly steroid exposure was documented. Further assessment of the population was conducted based on the time of AVN onset and the various underlying

rheumatologic diseases, i.e. systemic lupus erythematosus (SLE) and systemic juvenile idiopathic arthritis (sJIA).

## Results

About 14 cases were collected from seven centers (7 with SLE, 4 with JIA, and 3 others) (Figure 1). AVN affected 71% of females, with a median age of 14.3 years at diagnosis (IQR 13.2–15.4). Most of the reported multifocal involvement (93%), primarily involving the knees (28%), and femoral heads (44%). Most patients (71%) had symptoms, with pain being the most commonly reported symptom (100%), followed by joint swelling (40%) and functional limitation (70%). All patients with severe rheumatology received systemic glucocorticoids, with a median cumulative prednisone equivalent dose of 457.5 mg/kg (IQR 259.5–849). Almost all patients (93%) experienced symptoms of steroidal toxicity. Imaging revealed persistent abnormalities in all patients except one patient, despite complete symptom resolution in 6 patients. Bisphosphonate, hyperbaric oxygen, and magnetic therapy were employed in four, three, and one case, respectively. Two patients underwent orthopedic surgery. Five patients (36%) experienced a full resolution of their symptoms along with a return to normal imaging, whereas six patients (43%), experienced permanent sequelae.



**Figure 1. Rheumatologic background of collected patients with AVN**

## Discussion

The study identified AVN as a rare but severe complication of pediatric rheumatologic diseases, predominantly affecting patients with SLE. AVN is typically symmetrical, insidious, and asymptomatic in a significant number of cases, primarily involving the femoral head and

knee. Glucocorticoids are considered as the main risk factor, with almost all patients in the cohort exhibiting clinical signs of steroid toxicity.<sup>4</sup> Consistent with this study, Yang et al. found that the most significant risk factor for AVN in pediatric SLE was the maximum daily prednisone dose, even though both the cumulative and maximum daily prednisone dose were significant in determining risk for AVN.<sup>5</sup>

## **Conclusion**

Clinical characteristics and specific serum antibody response patterns varied amongst LD manifestations. Distinct serum antibody responses of the IgG isotype against six *B. burgdorferi* antigens (p100, VlsE, p58, p41, p39, and p18) were associated with Lyme arthritis, and the IgM isotype against three *B. burgdorferi* antigens (VlsE, p41, and OspC) may aid in the prediction of LNB.

**AVN, a rare but severe complication of pediatric rheumatic diseases that must be closely and actively monitored to prevent long-term damage.**

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## **A Rare Case of Presumed Pediatric Isolated Oculomotor Nerve Schwannoma**

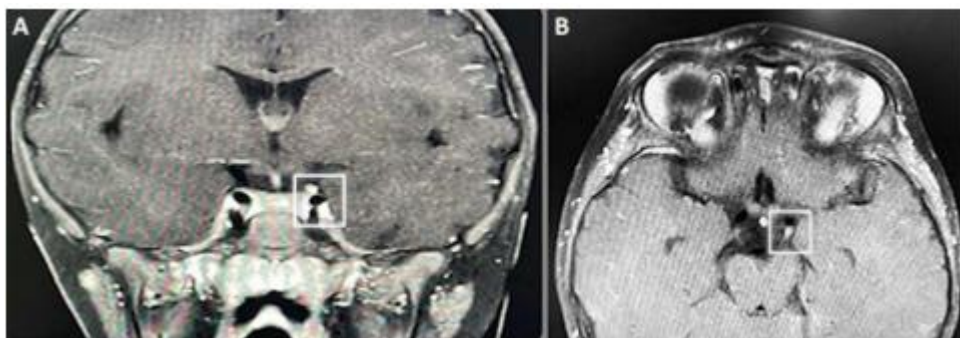
### **Introduction**

Schwannomas are slow-growing benign tumors that typically originate from the Schwann cell layer of the vestibular portion of the vestibulocochlear nerve and rarely from the lower distal cranial nerves accounting for 6% to 8% of all intracranial tumors.<sup>1</sup> Isolated pediatric oculomotor nerve schwannomas are extremely rare, especially when not associated with neurofibromatosis. When associated with neurofibromatosis type 2 (NF2), it usually happens

alongside trigeminal nerve schwannomas. Kovacs reported the first documented case of an isolated oculomotor nerve schwannoma in 1927, with a limited number of cases described in the literature.<sup>2</sup> These lesions may show signs of complete oculomotor nerve palsy, such as a non-reactive, dilated pupil, complete ptosis, and ophthalmoparesis affecting elevation and adduction. In primary gaze, the affected eye may be in abduction with slight depression and intorsion, also known as the "down and out" position.

## Case Presentation

A 2.5-year-old child presented with new onset ptosis of the left eye and headache. The child's parents denied having any history of trauma or insect bites. During the physical examination, the child showed ptosis, exotropia, and mydriasis in the left eye. An ophthalmological examination revealed an exotropically deviated and abducted left eye, with a relative afferent pupillary defect and no signs of nystagmus. Upon slit lamp examination, the anterior segment was found to be unremarkable, with no evidence of abnormal pathologic findings. Unfortunately, because of the child's lack of cooperation, visual acuity was not evaluated. The neurological examination revealed otherwise intact functional cranial nerves, with no evidence of cerebellar signs. Upon admission to the ophthalmology department, the child underwent a comprehensive evaluation, including a contrast-enhanced head CT, lumbar puncture, abdominal ultrasound, and immunological and viral panels where all results were normal. The CTA revealed no aneurysms in the anterior or posterior communicating arteries. A standard MRI was then performed, but this examination, too, revealed no lesions. During hospitalization, a high-resolution MRI was performed with 0.5 to 1 mm slice thickness which successfully identified a 5 mm diameter ovoid mass in the third cranial nerve, superior to the internal carotid artery (ICA). A 3T MRI scanner was used, resulting in higher signal strength and better visualization of lesions compared to traditional MRI. The lesion showed an isointense signal on T1-weighted images, which provided additional details. A high-resolution 3D T2-weighted MRI with a 0.5 mm slice thickness revealed a hyperintense and homogeneous lesion. An orbital MRI was also done and found no anomalies. Prednisolone was administered at 15 mg twice daily for 7 days, then tapered down to 3 mg for an additional week. On discharge, the child showed clinical improvement, including the ability to open his left eye and slightly improved ocular movements. The child underwent Botox injections to the lateral rectus muscle at another medical center due to lesions compressing the oculomotor nerve.



**Figure 1. T1-weighted MRI with gadolinium contrast and fat saturation; (A) coronal view, (B) axial view**

## **Discussion**

This case reported a very rare condition of isolated oculomotor schwannoma in pediatric population. When clinical symptoms like third nerve palsy or increased intracranial pressure are suspected, a thorough diagnostic approach is required to rule out other congenital or acquired conditions. High resolution MRI is essential for detecting small lesions, which may be missed with standard imaging. Steroid therapy improved the patient's symptoms, and botulinum toxin injections helped manage ocular misalignment, supporting a conservative approach over immediate surgical intervention.<sup>3</sup> In line with this findings, Scott AB et al. demonstrated that Botulinum toxin injection is an effective adjunct therapy, preventing the contracture of the antagonist lateral rectus muscle, facilitating improved ocular alignment, and enhancing visual function.<sup>4</sup>

## **Conclusion**

Isolated oculomotor schwannoma in children is a rare condition. To rule out congenital or acquired conditions, it's crucial to conduct a comprehensive series of tests when clinical symptoms like third nerve palsy or increased intracranial pressure are suspected. For radiological evaluation, a high-resolution MRI should be performed in three phases, both before and after Gadolinium injection. Currently, there are no specific treatment guidelines for these tumors due to their complex anatomical location and unfavorable outcomes with neurosurgical intervention.

**High resolution MRI is necessary for detecting small and complex lesions that standard imaging may fail to recognize.**

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