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REVIEW

Impact of Spina Bifida on Sleep Quality: Current Insights

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Abstract: Spina bifida (SB) is one of the most common birth defects in children. The care for patients with SB continues to evolve, and there has been notable improvement in survival outcomes, degree of disability and quality of life for these children. However, patients with SB continue to remain at higher risk for sleep-related breathing disorders (SRBD), unexplained sudden death, and potential alterations in their sleep chronotype. Previous studies report on abnormalities in the spinal cord, brainstem function, and dysfunction of upper airway maintenance as the likely mechanisms behind SRBD that is commonly seen in SB. Most studies looking at prevalence of SRBD in SB have been retrospective studies. A recent prospective study identified a prevalence as high as 42% when a polysomnography (PSG) was completed on all patients regardless of symptomatology. Treatment options vary depending on the type and severity of SRBD and can range widely. Despite advances in care for patients with SB and SRBD, a subset of these patients with myelomeningocele (MMC) continue to experience sudden unexplained death. Studies continue to evaluate ways to stratify which of these patients may be at higher risk of this devastating outcome. Given that SRBD is potentially treatable, early assessment and intervention could become an integral part of a multidisciplinary treatment strategy to optimize long-term medical and neurodevelopmental outcomes for this patient population. By understanding the impact that SB may have on a patient's sleep quality, their biological chronotype and their potential of developing SRBD, a provider may help to optimize the care a patient with SB receives from birth into adulthood.

Keywords: sleep apnea, sleep-disordered breathing, myelomeningocele, central sleep apnea, hydrocephalus, Chiari 2 malformation

Sleep-Disordered Breathing in the Child with Spina Bifida

Introduction

Spina bifida (SB) is the third most common disability of childhood in the United States, with an estimate of over 166,000 people affected nationwide.[1–3] It is a birth defect caused by abnormalities of caudal neurogenesis early in pregnancy resulting in a split ("bifid") spinal column. As a result, the posterior bony elements of the vertebrae do not close completely around the contents of the spinal canal. The term "spina bifida" ranges from milder forms of caudal neuropore failure such as spina bifida occulta and meningocele, to the most severe form of myelomeningocele (MMC) or open spina bifida. In MMC, the embryonic posterior neuropore fails to close early in gestation, leaving the spinal cord as an open placode on the back without covering of dura, bone, muscle, or skin. Children born with MMC have neurologic deficits at the level of the spinal cord defect and below, resulting in varying degrees of paralysis, numbness, bladder and bowel dysfunction.[3–7] Due to cerebral spinal fluid (CSF) escaping the open spinal defect, MMC is almost always accompanied by a Type II Chiari Malformation (CM-II), which is a developmental brain abnormality consisting of herniation of the hindbrain (brainstem and cerebellum) through the foramen magnum (Figure 1).[8] This herniation can obstruct the proper circulation of CSF and cause hydrocephalus (HC), which is widening of the ventricles as a consequence of increased CSF accumulation.[9]

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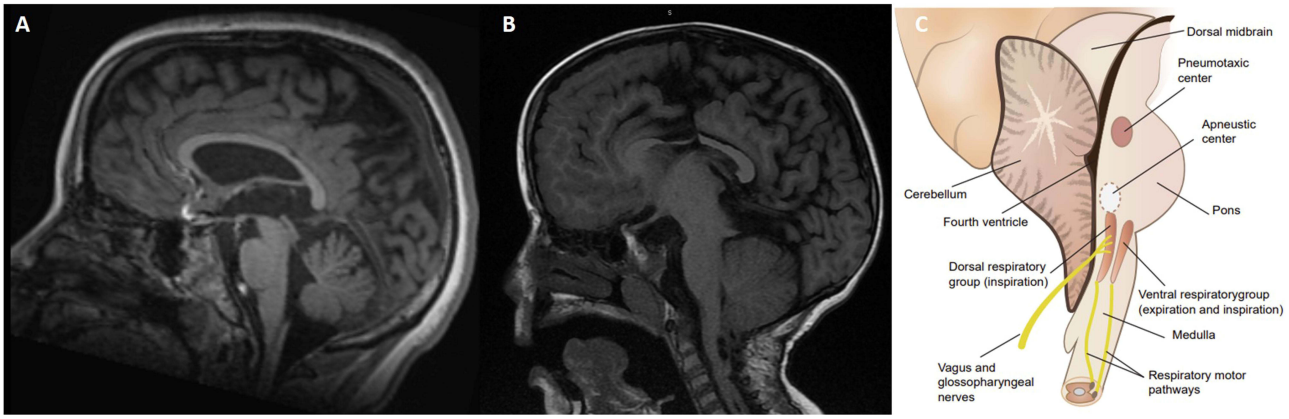

Figure 1 (**A**) Normal Brain MRI of a pediatric patient; (**B**) Brain MRI findings of a pediatric patient with Chiari Malformation Type II (CM-II); (**C**) Illustration showing elongation and compression of anatomical structures of the brainstem and spinal cord. Note that both central respiratory centers and the nuclei of the vagus and glossopharyngeal nerves are involved. This leads to increased risk of central apnea and/or upper airway obstruction.

The neurologic and medical consequence secondary to the co-morbidities of a patient with MMC have shown to affect breathing response while sleeping. This review discusses what is currently known about sleep-related breathing disorders in the SB population. As mentioned, the term SB encompasses several types of congenital abnormalities in the spinal cords, therefore we attempt to simplify the information provided by presenting evidence that pertains almost entirely to the patient population with MMC. Though patients with MMC typically will have an associated CM-II, several research articles in this review did not stratify patients with a diagnosis of MMC by the degree of Chiari malformation present. Therefore, we attempt to clarify this by noting whether a study evaluated patients with a diagnosis of MMC or with a more specific diagnosis of CM-II.

The Normal Control of Breathing

Respiration is controlled by "respiratory centers" of the brain that stimulate the contraction of the respiratory muscles.[10] Areas within the medulla oblongata and pons respond to stimuli from sensory neurons within the brain to generate rhythmic nerve impulses for muscle contraction that results in inspiration and expiration. Central chemoreceptors within the medulla oblongata help to monitor the chemistry of cerebrospinal fluid, whereas peripheral chemoreceptors within the aortic and carotid bodies help to monitor the chemistry of the blood. Changes in carbon dioxide levels, pH, or oxygen levels result in these centers modifying the inspiratory rate and force of respiratory muscles to help restore physiologic baseline. A negative feedback system helps to control the stimulation of these centers that result in the normal human respiration patterns.[10–13] During sleep, there are several normal changes in respiratory physiology. During the rapid eye movement (REM) stage of sleep, breathing becomes irregular, paralysis of accessory muscles of respiration develops, and breathing becomes dependent on the activity of the diaphragm. The upper respiratory dilator muscles become more hypotonic. Lastly, the respiratory center becomes less responsive to changes in arterial oxygen and carbon dioxide changes. These changes of respiration during sleep leave a person vulnerable to sleep dysfunction if there is any condition that may induce alterations in respiratory patterns or rate.

Impact of Sleep-Disordered Breathing in the Pediatric Population

Sleep-related breathing disorders (SRBD), also referred to as sleep-disordered breathing (SDB), represent a spectrum of disorders that lead to sleep disruption, including primary snoring, obstructive sleep apnea, central sleep apnea, and sleep-related hypoventilation. SDB is characterized by respiratory symptoms, such as snoring, gasping, and pauses in breathing.[14,15] Regardless of its severity, untreated pediatric SDB is associated with significant adverse outcomes in multiple functional domains.[11–13,16] Chronic SDB has been associated with cardiovascular changes,[17,18] poor asthma control,[15] metabolic disorders, growth failure,[19] cognitive and neurobehavioral deficits including impairments in attention,[12,15,17,20–23] behavioral regulation,[12,24] and broad executive functioning skills.[24,25] Studies have noted that

untreated SDB is costly for patients and the healthcare system, as SDB can result in an elevation in healthcare usage and increased morbidity.[13,23,26–30]

SDB is common in the general pediatric population with a prevalence reported of up to 5% in children and 11% in adolescents.[11,12] In comparison, prevalence of SDB among individuals with MMC has been noted to range from 42% (when a sleep study was performed as a screening examination in all patients)[31] to 81% in patients with MMC who presented with symptoms suggestive of SDB.[32] Kirk et al identified 996 sleep studies (including overnight in-lab polysomnography (PSG), nocturnal oximetry readings, and cardiorespiratory polygraphy) using a survey of 86 SB clinics within the United States and Canada, eliciting a 42% prevalence of SDB in this population.[33] Studies with smaller cohorts have reported similar results.[28–30] When looking at severe forms of SDB (apnea/hypopnea index [AHI] > 5 events/hour), around 20% in patients with MMC have been reported.[31,34,35] The prevalence of SDB in infants and newborns is higher and ranges from 72% in infants to as high as 100% in newborns.[36,37] These studies will be reviewed in more detail but clearly indicate that SDB is a common comorbidity in patients with MMC.

Factors Causing Abnormal Breathing Patterns in MMC

The increased risk of SDB in patients with MMC is a consequence of the abnormalities in the spinal cord, brainstem function, pulmonary function, and upper airway maintenance that are commonly appreciated in this patient population.[33,34,36,38,39] In fact, commonly associated neurological conditions like CM-II and hydrocephalus are known to affect respiratory pattern and reflex response while sleeping, leading to SDB.[32,40] Abnormalities of the brainstem and respiratory centers may serve as the mechanism involved in producing central apnea, whereas compression of the nuclei of cranial nerves IX and X may result in upper airway obstruction due to decreased ability to maintain upper airway patency[41] MMC with CM-II results in abnormal brainstem control resulting in absent arousal responses to hypoxia and hypercapnia, and absent ventilatory responses to hypoxia and hypercapnia in these patients (Figure 1).[38] Given that children with MMC are at increased risk for obesity,[4] and that obesity is an independent risk factor for SDB in all children,[12] the combination of higher obesity rates and brainstem dysfunction present in patients with MMC may place this population at increased risk for SDB and life-threatening complications, such as cardiorespiratory arrest and sudden death.[42–46] Further studies on the prevalence and severity of SDB in a patient with MMC and obesity could help in determining if frequent screenings or earlier interventions are recommended for this subset of patients.

Despite the known increased prevalence of SDB in patients with MMC, more specifically CM-II, there remains no clear signs or symptoms of SDB that may indicate which patient remains at highest risk of developing it. While some studies observed clinical symptoms or MRI findings that may have been associated with SDB in that specific cohort of patients,[31,34,38] others did not observe any correlations between clinical symptoms or MRI findings and likelihood of developing SDB or SDB severity.[47]

Current Knowledge of the Prevalence of SDB in Patients with MMC

The types of SDB described in patients with MMC include central sleep apnea (CSA), periodic breathing, obstructive sleep apnea (OSA), and central hypoventilation (Table 1).[34,36,39,48–50] SDB of central origin has been the most common type of SDB associated to patients with MMC, particularly those with brainstem involvement secondary to CM-II (Table 2). Filho and Pratesi evaluated 24 patients with CM-II and revealed a SDB prevalence of 50%, with all patients having CSA.[23] Shellhaas et al compared 19 newborns with MMC against 19 healthy control infants with polysomnography. They found that infants with MMC had significantly higher AHI compared to control patients (34 events/hour vs 19 events/hour, respectively), with majority demonstrating a more predominant CSA index (10 events/hour vs 4 events/hour) and hypopnea index (21 events/hour vs 12 events/hour), versus OSA index (3 events/hour vs 2.5 events/hour).[51]

The reported prevalence of obstructive sleep apnea is more variable. Published studies on the prevalence of OSA in this patient population report a wide range of ages. Commonly, patients have associated comorbidities for OSA such as adenoid or tonsillar hypertrophy. The degree of obstruction may also be dependent on pharyngeal dilator muscles dysfunction secondary to CM-II involvement of cranial nerves. Some studies have reported a high prevalence of mild OSA in up to 40% and moderate-to-severe OSA in up to 31% of this patient population.[11,32,34,53–55] Other studies did not report any OSA in their cohort.[23,29] Several studies did not find elevated body mass index (BMI), a known risk factor for

Table 1 Definition of Respiratory Events as per the AASM

Hypopnea	Reduction of airflow of ≥30% lasting for at least two baseline respiratory cycles and is associated with an arousal and/or a ≥3% reduction in oxygen saturation (SpO2).
Apnea	Reduction of airflow ≥90% lasting for the duration as per obstructive or central sleep apnea.
Obstructive Sleep Apnea (OSA)	An apnea for the duration of at least two baseline respiratory cycles with respiratory effort throughout the event of absent airflow.
Central Sleep Apnea (CSA)	An apnea with absence of inspiratory respiratory effort throughout the event, with at least one of the following criteria met: 1. event lasting ≥20 seconds, 2. event lasting for at least two baseline respiratory cycles and associated with an arousal and/or ≥3% reduction in oxygen saturation (SpO2), 3. event lasting two baseline respiratory cycles and is associated with an arousal and/or an episode of bradycardia in infants (Berry, 2012).
Periodic Breathing	A series of 3 or more central respiratory pauses lasting ≥3 seconds separated by ≤20 seconds of normal breathing
Hypoventilation	PaCO2 levels for >25% of total sleep time >50 mmHg*
Apnea-Hypopnea Index (AHI)	Average frequency of apnea and hypopnea events per hour of sleep

Notes: *Central hypoventilation refers to bradypnea or persistently low tidal-volume breathing that results in hypercarbia and hypoxemia. Data from these studies.[12,52]

OSA, to predict SDB in patients with CM-II, suggesting that SDB in patients with CM-II may more likely be a consequence of ventilatory control instability.

Clinical Symptoms of SDB in MMC

Reported symptoms of SDB in this population are typically similar to that of the general pediatric population and are frequently reported as snoring, apnea, blue spells, shortness of breath, irritability, choking or gasping with sleep, or fragmented sleep.[32,56] Excessive daytime sleepiness is less common in children than in adults.[57] In infants up to a year of age with MMC, the most common presentations include stridor, apnea, and feeding difficulties.[4] Waters et al evaluated for symptoms predictive of SDB and found that snoring, witnessed apnea, dysphagia, and enlarged tonsils were symptoms associated with OSA, whereas witnessed cyanosis and vocal cord dysfunction were symptoms correlated with CSA.[34] For children under the age of 2 years with MMC, the presence of SDB can result in rapid progression of neurological deterioration and can result in cardiorespiratory arrest and sudden unexplained death during sleep.[33,43,56–59]

Several studies have reported a higher prevalence of SDB in patients with MMC and CM-II by evaluating patients with the signs or symptoms suggestive of respiratory abnormalities,[36,39,53] or after retrospectively evaluating patients with MMC based on having any previously completed polysomnography.[32] Despite these findings, no clear predictors of SDB have been identified in patients with MMC and CM-II. Additionally, patients are at risk of SDB despite the absence of clinical symptoms, as was demonstrated by Rocque et al when a prevalence of SDB of 42% (diagnosed by AHI >2.5 events/h) was identified in a cohort of patients with CM-II that underwent screening with PSG regardless of the presence of symptoms suggestive of SDB.[31] Given that SDB is potentially treatable, early assessment and intervention could become an integral part of a multidisciplinary treatment strategy to optimize long-term medical and neurodevelopmental outcomes.

Screening for SDB in the MMC Population

In children, clinical evaluation along with routine exam and existing sleep questionnaires are often not accurate or sensitive enough to establish a diagnosis of SDB in patients with MMC.[33,50,56,60–62] The AAP currently recommends that each child be questioned regarding snoring and other signs and symptoms of SDB.[3] Several questionnaires designed to screen for SDB are available, such as the Children's Sleep Habits Questionnaire or the Pediatric Sleep Questionnaire (PSQ) are available. However, these instruments are not specific to patients with MMC. Beltran et al evaluated the

Table 2 Summary of Publications Reporting SDB Prevalence in Patients with SB

Publication	SB Type Included	Inclusion Criteria	Test Used**	Sample Size	Age Range	SDB Prevalence	Central Sleep Apnea (CSA)	Obstructive Sleep Apnea (OSA)	Mixed Sleep Apnea*	Hypoventilation*
Rocque 2021	MMC	All MMC patients regardless of symptoms, prospective study	PSG	n=117	1m-21y	42% (AHI ≥ 2.5)	16%	55%	28.6%	NA
Shellhaas 2018	MMC	MMC patients in newborn period regardless of symptoms, prospective study	PSG	n=19	3–9 days	Average AHI compared to healthy newborns.				
Patel 2015	MMC	Only symptomatic patients that had PSG, retrospective study	PSG	n=52	2m-24.5y	81% (AHI >5)	29%	71%	NA	NA
Alsaadi 2012	MMC	Patients with MMC and CM-II (based on MRI) referred for PSG	PSG	n=16	0.8–10y	68% (AHI>1)	68%	NA	NA	NA
Kirk 2000	MMC	Multicenter study, retrospective review subset of MMC patients with moderate to severe SDB on PSGs	PSG	n=73	<1y ->18 y	NA (AHI>5)	25%	30%	NA	16%
Water 1998	MMC and closed skin SB	Prospective study completed PSG in 83 out of 105 patients during study period	PSG	n=83	Not reported	63%	92%	35%	NA	NA
Gozal 1995	MMC and CM-II	Random sample of patients with MMC and CM-II	PSG	n=10	8y-20y	50%	100%	100%	NA	80%
Kirk 1999	MMC and closed skin SB	Survey to multiple centers asking for retrospective PSG data	PSG	n=996	Not reported	42%	36.1%	28%	NA	7.2%

Notes: *Studies vary in the way they report OSA/CSA and mixed apnea. NA ("not available") likely means there was no specific report of how many patients had a mixed phenotype. Hypoventilation is rarely reported independently in most studies. **PSG includes PSG performed at home.

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efficacy of the PSQ in predicting OSA in patients with MMC and any CM, and they found the questionnaire to be a poor tool for screening, with a sensitivity of 73.58%, specificity of 20.83%, PPV of 33.91%, and NPV of 58.82%.[37] Clinical evaluation is also not a reliable marker in determining which patients with MMC are at increased risk of SDB.[17,31,34,38,42,61] For an infant with MMC with a history of stridor, dysphagia, apnea, cyanosis or a higher spinal lesion, the accuracy and sensitivity in predicting SDB based on clinical evaluation alone is estimated to be only 83% and 65%, respectively.[38] Due to the low sensitivity of clinical evaluation alone and the notable morbidity and mortality risk associated with SDB in patients with MMC, it is recommended that all patients diagnosed with MMC undergo overnight observed polysomnography (PSG) evaluation regardless of symptom burden present.[12,32,56]

Overnight PSG is currently the "gold standard" in identifying SDB. A full pediatric PSG in an American Academy of Sleep Medicine-accredited laboratory includes monitoring of several physiologic parameters throughout the course of a night that help characterize a patient's sleep architecture and respiratory patterns. The combination of electroencephalogram (EEG), electro-oculogram (EOG) for eye movements, and sub-mental electromyogram (EMG) for muscle tone allow for monitoring wake state, various sleep stages and arousals. Respiratory function is assessed using an airflow cannula at the nose and mouth, belts at the chest and abdomen monitoring movements, oximetry, and either end-tidal or transcutaneous CO2 monitoring. Heart rate is monitored with an electrocardiogram (ECG) and limb movements are monitored using limb EMG sensors. Video recordings with audio are generally present to detect sounds and movements during sleep. The data is scored by a trained sleep technologist and then interpreted by a sleep physician, who provides a summary report that outlines a patient's overall quality and architecture of sleep and their respiratory patterns as observed in that overnight timeframe. Respiratory apneas are reported as an apnea–hypopnea index (AHI), which provides a general reflection on all obstructive events, central apneas, and hypopneas that were present overnight as an average number of events per hour. Given that a developing child is very sensitive to untreated sleep apnea, the AHI value required to classify sleep apnea severity is lower than that of adults (Table 3).[52]

Screening with PSG may help identify SDB in patients with MMC earlier. Given the known prevalence of SDB in the MMC population and the potential therapeutic options available from infancy, there is a need for improved standardization of protocols evaluating for SDB in individuals with MMC at institutions with specialized MMC programs. Given that patients with MMC remain at increased risk of SDB throughout their lifetime,[63] even after neurosurgical interventions, this is a patient population that likely warrants regular screening with PSG starting in infancy or at time of initial diagnosis into adulthood.[33,62,64] Several large centers are shifting towards providing coordinated clinical care pathways that help to optimize routine screening in the ion with MMC.[4] Screening methods remain an area for potential improvement in management and care for this patient population.

Treatment for SDB in MMC

Individuals with MMC are likely to undergo multiple surgical procedures over the course of their lives.[36,39,50] Many of these patients undergo fetal surgical closure of the open MMC prior to birth. Otherwise, the remainder of children undergo this closure within 48 hours of birth.[31,32] Overall, about 80% of children with MMC also develop hydrocephalus that requires surgical treatment.[9] While the anatomic findings associated with CM-II are present in nearly all individuals

Table 3 Classification of Sleep Apnea by AHI

Diagnosis	Pediatric AHI* (Events/Hour)	Adult AHI (Events/Hour)
No sleep apnea	<1	<5
Mild sleep apnea	1–5	5–10
Moderate sleep apnea	5–10	15–30
Severe sleep apnea	>10	>30

Notes: *Important to note that AHI thresholds have not been formally defined for infants <12 months of age. Data from these studies.[12–15,52]

with MMC, fewer than 10% of children undergo CM-II decompression surgery in the modern era.[9,36,39,50,61] Prenatal surgery has been shown to decrease the need for hydrocephalus surgery to as low as 40%, and decrease the anatomic severity of CM-II in children treated with prenatal closure compared to standard post-natal repair.[65] However, little is known about the effect of neurosurgical intervention on SDB in patients with MMC. In infants who have not had treatment for hydrocephalus, the presence of stridor is considered to be an indication for hydrocephalus treatment, and treatment often leads to reduction or elimination of stridor.[51] However, no studies have consistently demonstrated an improvement in SDB after neurosurgical treatment in any children older than infancy.[4,51]

As previously mentioned, SDB encompasses OSA, CSA, periodic breathing, and central hypoventilation. Treatment options for SDB in patients with SB vary by age, co-morbidities and complications associated with the individual patient, as well as the type and severity of the SDB present. Respiratory support recommended for patients with CSA vary depending on the age and concomitant hypoventilation. Even if a neurosurgical intervention is warranted for a patient, respiratory support will often be initiated for interval management given that CSA resolution will unlikely be immediate. Oxygen supplementation is the most common recommendation for infants.[32,38,51] Older children who can tolerate positive pressure are started on non-invasive bi-level positive pressure instead.[38] In cases with severe CSA, regardless of age and concomitant hypoventilation, bi-level positive pressure may be indicated. Invasive ventilation (via tracheostomy) may be the safest way to provide this in young children and infants or severe cases.[10,32,38]

Treatment options for OSA will also vary based on age and co-morbidities and will depend on the presence of surgically reversible airway obstruction. As with CSA, there is little data on the effectiveness of neurosurgical interventions on resolving OSA. These interventions, often discussed as improvement in pharyngeal and/or laryngeal tone, could in theory improve OSA severity and subsequently the degree of support required. Surgically reversible airway obstruction includes laryngomalacia, palatine tonsils hypertrophy, adenoid enlargement, and other less common upper airway pathologies.

While tonsillectomy/adenoidectomy remains a common treatment choice for OSA in the general pediatric patient population, it has not shown to resolve the upper airway obstruction of patients with MMC and CM-II.[34,38] The decision to perform any of these interventions often warrants a multidisciplinary discussion to determine if the benefits of surgery outweigh the outcomes that may be exhibited in these patients given their complex underlying neurological pathology and multifactorial or multilevel airway obstruction. Evaluation for interventions start with an airway evaluation that can be completed with rigid and/or flexible airway endoscopy and in some centers with specialized airway imaging like airway MRIs. These evaluations are more dependable when they are done while mimicking physiologic sleep. No studies have been conducted looking into more reliable tests in patients with MMC.

As with respiratory support for CSA, respiratory support options for OSA start with oxygen supplementation. This is commonly used in infants and young children with OSA and associated hypoxia. There is controversy in the sleep medicine community about the benefits of supplemental oxygen in patients with OSA without significant hypoxia. However, this discussion is beyond the focus of this review. In older children, noninvasive use of CPAP is the first option for OSA. In severe cases, non-invasive bi-level positive pressure is trialed in older children. Infants and young children, on the other hand, may not tolerate non-invasive positive pressure nor are they safe with this management and so may require tracheostomy placement as a bypass for the areas of airway obstruction. Older children may also require tracheostomy placement if non-invasive bi-level positive pressure fails to manage severe OSA. The need for concomitant positive pressure would depend on the presence of CSA or hypoventilation in these cases. There is not widespread use of alternative options like lingual nerve stimulation for glossoptosis, and/or high flow nasal cannula support in the pediatric population.

Studies have reported that more than half of infants with MMC will continue to demonstrate SDB often with CSA, periodic breathing, and hypoventilation despite relief of upper airway obstruction through CM decompression, shunt placement, and/or tracheostomy tube placement.[4,14,21,22,32,36,39,40,46,50] In fact, most studies reporting a high prevalence of SDB in CM-II patients were performed on patients after they had undergone neurosurgery, suggesting that SDB may develop regardless of neurosurgical intervention. Patel et al included repeat overnight polysomnography on nine children that underwent neurosurgical intervention (6 CM-II decompression, 4 HC shunt placement, 1 with both procedures), with repeat polysomnography indices indicating interval improvement in the severity of their SDB, though none of these

improvements met statistical significance. Future studies should look more closely at the role hydrocephalus may be playing in the development or exacerbation of SDB in this patient population.

Finally, behavioral interventions and treatment of concomitant obesity likely play a role in ameliorating SRDB severity or its effects in the MMC population. To our knowledge, there are no published studies that have looked specifically into these interventions in MMC.

Adult Care and Sudden Death

The Spina Bifida Association has encouraged the development of organized multidisciplinary teams with expertise to be more readily available for adults.[34,56,66] Coordinated, patient-centered programs that incorporate the patient, family, school and workplace personnel, social work services, and healthcare providers for several years prior to transition of care from childhood to adulthood have shown promising support of the adult population with MMC.[13,26,27]

Symptoms of SDB in adults with MMC are typically similar to the general population and includes snoring, witnessed cessation of breathing, gasping or choking at night, excessive daytime sleepiness, impaired cognition, and mood changes.[13,17,64] For adults, validated questionnaires to predict the presence of sleep apnea include the STOP-BANG (Snoring, Tiredness, Observed apnea, High blood Pressure-Body Mass Index (BMI), Age, Neck Circumference, Gender), Berlin, Epworth Sleepiness Scale (ESS), and OSA 50 (Obesity-Snoring-Apnea-Age > 50).[20,43] As with children, the "gold standard" evaluation for SDB in an adult with MMC remains overnight observed PSG. Considering that the risk of SDB remains with a patient with MMC throughout their lifetime, the recent US Preventive Services Task Force (USPSTF) recommends that patients with MMC be considered an exception to the recommendation of not routinely screening for SDB in asymptomatic adults.[17] More importantly, clinicians who maintain healthy vigilance of sleep problems in this patient population will likely identify opportunities to improve the overall function and health of the patient as well as decrease stress for caregivers.

Despite preventive, medical, and surgical successes in the last several decades resulting in most patients with MMC reaching into adulthood,[32,67] these individuals remain at risk for sudden unexplained death. Jernigan et al evaluated 106 patients with MMC with ages between 19 and 30 years, with 5.6% (6/106) of them experiencing sudden death. Case studies have reported on the potential correlation between sudden death in adults with MMC in the presence of chronic tonsillar herniation and hydrocephalus. While these co-morbidities have known associations with SDB, studies have not yet evaluated the impact of these specific conditions on the prevalence or severity of SDB in patients with MMC. Further research is needed to determine which characteristics may place a patient with MMC at increased risk of SDB and sudden death.[4,33]

Other Etiologies Impacting Sleep Quality in the Child with Spina Bifida

Sleep Quality in the Child with Spina Bifida

Only few studies have been able to evaluate sleep quality in the patient population with any severity of SB. To better understand sleep effects in individuals with SB, Murray et al assessed the sleep of 37 adolescents with SB against 37 adolescents without SB using sleep questionnaires, actigraphy, and sleep diaries.[63] They found that adolescents with SB experienced poorer sleep quality, reduced sleep, increased insomnia, and increased daytime fatigue compared to otherwise typically developing adolescents. This is similar to evidence that exists showing that patients with chronic illnesses have poor sleep quality.[8,24,66] Pathological and nighttime sleep deprivations have substantial adverse effects on cognition, which further worsens the burden of chronic illness.[8,23,28,29] Therefore, prompt identification and treatment of co-existing sleep problems among patients with chronic illness, such as SB, is an important step in improving the overall outcomes for these individuals.

Chronotype

Chronotype is an individual's preferred timing of sleep, activity, and cognitive performance and is often referred to as a later chronotype (evening-type) or an earlier chronotype (morning-type). Across the lifespan, chronotype is associated with psychological wellbeing, environmental and endogenous factors.[68,69] Studies have previously validated that

chronotype changes during life.[69–71] Infants and children experience earlier chronotypes. In adolescence, chronotype progresses towards later hours resulting in an evening-type chronotype for adolescents and young adults. Typically, this evening-type chronotype peaks around 20 years of age, after which chronotype typically will begin to shift back towards an earlier chronotype. Therefore, elderly have a morning-type chronotype.

Several studies have suggested that evening chronotype is associated with adverse health effects including increased risk of cardiovascular and metabolic disorders.[35,68–71] Moreover, any disruption to the normal circadian rhythm can lead to circadian misalignment producing immediate consequences of the sleep-wake cycle and results in sleep disturbances.[69] Edelstein et al explored the potential of sleep disorders due to anomalies in brain regions of MMC individuals that may influence circadian rhythmicity.[8] They measured chronotype and the presence of sleep problems in 202 individuals with MMC and 62 typically developing, healthy age peers. They found that while individuals with MMC showed the characteristic progression towards a later chronotype in adolescent and young adulthood, they peaked at an older age in comparison to controls (29.2 years versus 23.4 years). This means that at the age when later chronotype peaks for individuals with MMC, the controls were already returning to earlier sleep-wake times. Additionally, children and adults with MMC endorsed sleep problems more often than controls. Interestingly, the problems endorsed by adults appear to involve sleep timing and quality. In fact, they found that in adults with MMC endorsed problems involving sleep timing and quality, there was a correlation between chronotype and the different sleep problems.[8] The impact of this shift in circadian timing, contributing to sleep difficulties in an individual with MMC, still remains unclear but does present an important consideration in the chronic management of other sleep-related disorders in this patient population.

Conclusions

It is understood that SDB conditions such as obstructive sleep apnea or central sleep apnea are associated with developmental concerns, cognitive consequences, and risk of sudden death in the patient population with MMC.[72] Current evidence indicates a high prevalence of SDB in patients with MMC and CM-II, even when asymptomatic. Therefore, screening with PSG should occur promptly at regular intervals to avoid potentially serious complications such as sudden death. Early identification of SDB may lead to earlier assessment and treatment interventions that could help optimize long-term medical and neurodevelopmental outcomes for this vulnerable patient population. Nonetheless, there remains a paucity of data to help understand the extent to which SB and its associated co-morbidities effect sleep continuity or exacerbate other sleeping conditions. Further prospective studies that include a large number of participants will be necessary to further evaluate the potential impact of early PSG screening, surgical interventions, and/or other treatment interventions on managing SDB in patients with MMC. Future research will also hopefully provide insight on which interventions for SDB may help alleviate the risk of sudden death for this patient population.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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