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The Complexity of Sleep Disorders in Children with FASD

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Abstract

Introduction and Purpose:
Fetal alcohol spectrum disorders (FASD) is a group of conditions that can occur after prenatal alcohol exposure. In recent years, it is estimated that about 10% of women consume alcohol during pregnancy. The aim of this study is to draw attention to sleep quality in children with FASD and highlight the need for implementing appropriate diagnostic and therapeutic strategies that can improve their overall functioning and quality of life.

Methods and Materials:
This article is based on a review of scientific literature from PubMed and other databases, mainly from the years 2020 to 2025. The following keywords were used: *"fetal alcohol syndrome", "fetal alcohol spectrum disorder", "sleep disturbances"* and *"prenatal alcohol exposure".*

Conclusion:
The clinical manifestations of FASD are highly complex and affect all organ systems. Poor sleep hygiene in children with FASD has a significant impact on multiple areas of life, often leading to additional dysfunctions. Elevated emotional distress, difficulties with emotional regulation and cognitive impairments are closely associated with reduced sleep quality. While several validated tools are available to assist in the diagnosis of sleep disorders, the treatment of FASD symptoms remains more complex and is primarily focused on symptom management. Importantly, the most effective approach remains prevention — namely, complete abstinence from alcohol during pregnancy.

Keywords: fetal alcohol syndrome, sleep, fetal alcohol spectrum disorder, FAS, FASD, PAE, prenatal alcohol exposure.

Introduction

Fetal alcohol syndrome (FAS) is a spectrum of fetal alcohol spectrum disorder (FASD). FAS is a result of intrauterine exposure to alcohol [1]. According to data from the World Health Organization's (WHO) 2018 Global Information System on Alcohol and Health, the estimated average global alcohol consumption per adult woman of child-bearing age in 2016 was 2.3 liters. In 2016, 32.1% of women of childbearing age worldwide reported alcohol consumption. The highest percentage of current drinkers in this group was found in the European Region, where 53.9% of women consumed alcohol. Furthermore, **around 10% of women globally continue to drink alcohol during pregnancy.** The WHO European Region (EUR) is estimated to have the highest rate of alcohol consumption during pregnancy, at 25.2% [2].

Table 1. Global prevalence of any amount of alcohol use and binge drinking (4 or more drinks on a single occasion) during pregnancy, and of FAS and FASD among the general population, by WHO Region in 2012, and corresponding 95% confidence intervals.

Region	Alcohol Use (Any Amount) during Pregnancy (%) [a]	Binge Drinking during Pregnancy (%) [b]	FAS (per 10,000)	FASD (per 10,000) [c]
Globally	9.8 (8.9, 11.1)	-	9.4 (9.4, 23.3)	77.3 (49.0, 116.1)
WHO Regions $				
African	10.0 (8.5, 11.8)	0.1 (0.1,6.1)	8.9 (8.9, 21.5)	78.3 (53.6, 107.1)
America	11.2 (9.4, 12.6)	0.1 (0.1,5.6)	11.0 (11.0, 24.0)	87.9 (63.7, 132.4)
Eastern Mediterranean	0.2 (0.1, 0.9)	-	0.2 (0.2, 0.9)	1.3 (0.9, 4.5)
European	25.2 (21.6, 29.6)	0.0 (0.0, 5.3)	24.7 (24.7, 54.2)	198.2 (140.9, 280.0)
South-East Asia	1.8 (0.9, 5.1)	-	1.3 (1.3, 8.1)	14.1 (6.4, 53.1)
Western Pacific	8.6 (4.5, 11.6)	0.0 (0.0, 3.5)	7.7 (7.7, 19.4)	67.4 (45.4, 116.6)

Source: Popova et al., 2021 [2].

[a] The prevalence of any amount of alcohol use during pregnancy is inclusive of the prevalence of binge drinking during pregnancy. [b] It was not possible to estimate the prevalence of binge drinking during pregnancy for the Eastern-Mediterranean or South-East Asia Regions due to a lack of available data for countries in these regions; therefore, the global prevalence could not be estimated. [c] The prevalence of FASD includes the prevalence of FAS.

A safe dose of alcohol use during the pregnancy has not been established, the complete abstinence of alcohol is recommended [1]. Alcohol easily crosses the placenta and may disturb fetal development [3]. Symptoms include prenatal and/or postnatal growth retardation, facial dysmorphology, central nervous system dysfunction,

neurobehavioral disabilities, but also patients experience disorders of urination, defecation and sleep [4]. Regarding facial dysmorphia characteristics, the most distinctive features are short palpebral fissures, a thin upper lip, and a smooth philtrum. Neurobehavioral disabilities in FASD include impairments in overall intellectual ability and cognition, as well as difficulties with behavior, self-regulation, and adaptive skills [1]. Caregivers of children with FASD frequently mention that their child struggles with sleep, and sleep disturbances are among the most common co-occurring conditions with FASD, alongside intellectual disabilities and ADHD. Caregivers of children with FASD have reported that sleep disturbances in these children often involve trouble falling asleep, frequent nighttime awakenings, and waking up early in the morning. Additionally, children with FASD tend to experience more bedtime resistance, sleep-related anxiety, and a higher occurrence of parasomnias, such as bedwetting, sleep talking, and night terrors [5]. In comparison children with FASD typically get about an hour less sleep than other children their age [6]. A study conducted in Finland found that prenatal alcohol exposure nearly tripled the risk of short sleep duration and more than tripled the risk of reduced sleep efficiency by the age of 8 [7]. Getting enough quality sleep is critical to healthy development. Sleep disturbances are an important but under-researched symptom of FASD, which is why we aim to explore this topic further in our work.

Mechanisms

Sleep is a fundamental biological process essential for maintaining overall health and well-being. It plays a critical role in physical recovery, cognitive function, emotional regulation, and the consolidation of memories. Sleep is crucial for the brain, as it processes information and experiences from the day, supporting learning and mental performance. Fetal Alcohol Spectrum Disorders (FASD) can indeed be associated with various sleep problems. The specific causes of these disturbances in FASD patients remain unclear, however, there are several theories about the potential mechanism of sleep disorders in children with FASD.

Prenatal alcohol exposure (PAE) can lead to **structural abnormalities** in the central nervous system, particularly affecting the corpus callosum. Research indicates a relationship between defects in the corpus callosum and changes in sleep patterns, particularly a reduction in REM sleep. PAE can also lead to structural alterations in the cerebellum, which is involved in the homeostatic regulation of Non-Rapid Eye Movement (NREM) sleep [4, 8]. Furthermore R. Mughal et al. [9]. suggest that PAE can impair cortical and subcortical connectivity which can lead to dysfunction of NREM sleep.

Animal studies have demonstrated that prenatal exposure to alcohol can lead to changes in the **thalamus, hypothalamus, endocrine system**, as well as long-term disruptions in sleep-wake rhythms. Appropriate development of the thalamus and hypothalamus is crucial for the control of sleep [12].

Another potential mechanism explaining sleep disturbances in FASD sufferers is dysfunction of **neurotransmission**. A link has been identified between prenatal alcohol exposure (PAE) and changes in orexinergic and cholinergic neurons within brain regions that regulate circadian rhythms [4, 12, 18].

PAE may also affect the **epigenetic mechanism** on the neurons of the suprachiasmatic nuclei (SCN), which are responsible for natural rhythms. Using an animal model, it was suggested that PAE influences the expression of genes responsible for the circadian function of β-endorphin neurons in the hypothalamus [4, 8, 10, 14].

The studies showed the **central apneic/hypopneic** events are common in patients with FASD, even though none of the patients were obese. The probable cause of airway obstruction appears to be anatomical characteristics associated with FASD, such as micrognathia or a high-arched palate.

Moreover, research indicates that children with FASD often have an altered **melatonin profile**, which can affect their sleep cycle [4, 8, 6, 14].

The effect of PEA on **Cell adhesion molecules (CAMs)** was also postulated. CAMs are essential for the formation and development of the neural pathways that make up our nervous system. Prenatal alcohol exposure, particularly during the first trimester, can interfere with neuronal proliferation, migration, and synapse formation, processes that rely on cell adhesion molecules. CAMs function is crucial for proper developmental and behavioral growth after birth [10].

Diagnostic

There are several methods used to examine sleep in patients with FASD.

1. **Questionnaires**

There are numerous questionnaires used to assess sleep in children. Among these, researchers frequently utilize the Children's Sleep Habits Questionnaire (CSHQ), the Sleep Disturbance Scale for Children (SDSC), the Child Behavior Checklist (CBCL), and the Pediatric Sleep Questionnaire (PSQ) [12, 13, 15, 16, 17]. The most widely used is CSHQ. It is a tool consisting of 33 questions, completed by parents to evaluate their child's sleep patterns. In line with the questionnaire instructions, the caregivers have to answer the questions about the child's habits based on their observations from the most recent typical week. It uses a three-point Likert scale, with responses ranging from 'rarely' (0–1 times per week) to 'usually' (5–7 times per week). A score of 41 or higher is considered clinically significant. The questions address difficulties with bedtime routines, signs of inadequate sleep, and instances of waking during the night [4, 8].

2. Actigraphy

Due to the fact that the CSHQ is not always an objective method of measuring sleep (it is based on observations of the caregivers), other tests are used to confirm the result. One of these is Actigraphy. Actigraphs are compact, computerized devices worn by children on their non-dominant wrist or ankle. They track activity levels (limb movements) to give an overall estimate of sleep-wake patterns. To collect reliable data, children should wear the actigraphs for a minimum of 1–2 weeks. Actigraphs cannot distinguish between actual sleep and simply lying still, which may lead to an overestimation of sleep duration. However, research also indicates that actigraphy might underestimate total sleep time. As a result, actigraphy is considered more appropriate for assessing general circadian rhythms rather than providing an accurate measurement of sleep [6, 8, 9].

3. Sleep diary

A sleep diary is a caregivers report containing information about bedtimes, waking up times, naps or night wakings, and any unusual occurrences or activity. They are popular because of their ease of administration. Sleep diaries offer a general overview of a child's sleep-wake patterns and can be used on their own or in combination with actigraphy [6, 9].

4. Polysomnography (PSG)

PSG is considered the gold standard when it comes to analyzing sleep. The examination consists of an electroencephalogram (EEG), electrooculogram (EOG), and chin electromyogram (EMG) which are used to monitor brain activity and body movements while sleeping. In addition to the aforementioned examinations, an electrocardiogram, ventilatory monitoring, breathing effort, pulse oximetry, snoring and body position are also frequently performed. While polysomnography (PSG) is regarded as the gold standard, it is also time-consuming and expensive. This makes it challenging to use with large study samples. Additionally, it can be difficult to implement with children, especially those with FASD, as they may struggle with the equipment or have difficulty sleeping outside their usual environment. PSG provides information about sleep time (TST), sleep onset latency (SOL), wake after sleep onset (WASO) and sleep efficiency [4, 6].

Consequences of sleep deprivation

Sleep is more than just the absence of being awake; it is an active state in the brain that supports neural well-being. Growing evidence shows that sleep during childhood plays a crucial role in neurodevelopment by aiding in neuroplasticity and the maturation of the brain [9]. There are many complications associated with sleep deprivation. A pilot study of young children with FASD showed a link between the amount of sleep and behavior issues [6]. It has been proved that patients experience working memory impairments. It is possible that sleep disturbances may be the cause, but results are not clear. Another reason might be the structural and functional damage caused by prenatal alcohol exposure led to these deficits. It is unclear whether this connection would improve with sleep interventions, but this finding highlights the need for further research in this area [9]. Other studies have revealed that sleep deprivation can impact the speed of emotional working memory processing, benefiting reactions to positive images but negatively affecting responses to negative ones. These findings enhance our understanding of how emotional significance affects working memory in individuals who are sleep-deprived [20]. Another issue that patients experience is anxiety. It has been shown that sleeping problems were strong predictors of it [21]. Preliminary data suggest that sleep duration and language skills are also linked in children with FASD [6]. The complications of sleep deprivation in children with FASD are many, but the amount of publications on the subject is not enough. That is why it is so important to spread this problem.

The Specificity of Sleep Disorders

Understanding the specifics of sleep problems in children with FASD is crucial to developing effective support and intervention strategies. This article aims to explore the sleep challenges in this group of children, understand their causes, and present possible solutions and coping strategies that can help improve the quality of sleep and overall functioning of these children [12].

Sleep disturbances are highly common in children with FASD, with difficulty falling asleep being the most frequently reported issue, followed by difficulty staying asleep and waking early [22]. Children with FASD often struggle with maintaining regular sleep patterns, as well as frequent nighttime awakenings, difficulty falling asleep, and excessive daytime sleepiness. The high emotional distress, difficulty regulating emotions, and cognitive dysfunctions that are characteristic of FASD can further complicate their ability to achieve healthy sleep. These problems not only impact the quality of life of children, but can also impair the functioning of families and caregivers.

Cortical damage from prenatal alcohol exposure leads to significant cognitive challenges in children with FASD, including difficulties with working memory, short-term memory, and memory consolidation [9]. Clinical evidence from parents indicates that children with FASD frequently experience sleep disturbances from infancy through adolescence. While approximately 20% of parents report sleep disturbances in healthy school-aged children, the prevalence of sleep problems in children with FASD is significantly higher, ranging from 50% to 80% [12].

Scientists found an association between FASD and reduced sleep duration and higher fragmentation of sleep (characterized by repetitive short interruptions of sleep) [6, 12]. Researchers noticed that 79% of FASD children scoring above the cutoff for clinically significant sleep disturbances confirm the high prevalence of sleep disorders in this group. In a longitudinal study in Finland, prenatal alcohol exposure was linked to almost a three-fold higher risk of short sleep duration and more than a three-fold higher risk of reduced sleep efficiency by the age of 8 [6]. Scholars often compare children with FASD with other specific groups like individuals with autism and groups with typical development [12]. Mughal and colleagues reported that there were significant differences in sleep duration, sleep quality, sleep bouts, night wakings, and fragmentation among the three groups, patients with FASD, autism (ASD) and typical developing (TD). Children with FASD had the shortest sleep duration, lowest sleep efficiency, and highest fragmentation compared to children with autism and typically developing children, who showed progressively better sleep patterns. However, tests showed that bedtimes, wake times, and assumed sleep were comparable between the autism and FASD groups.Although children with autism and FASD had similar bedtimes, wake times, and sleep durations, children with FASD experienced poorer sleep quality during their actual sleep time. This suggests that children with FASD likely had more frequent night wakings compared to patients with autism. The increased fragmentation in the FASD group, compared to both the autism and TD groups, may account for the poorer sleep efficiency and shorter sleep duration observed in the FASD group, despite comparable bedtimes and wake times between the two clinical groups [9].

Children with FASD had the most frequent night wakings and the greatest daytime sleepiness. They also scored significantly higher than children with ASD and typically developing children on measures of attention problems, somatic complaints, social difficulties, delinquent and aggressive behaviors, panic, and separation anxiety. Additionally, research indicates that children with FASD sleep, on average, an hour less per night than their typically developing peers [23].

These sleep disturbances can worsen mood dysregulation and impair emotion-related executive functions, particularly in those who have experienced trauma. Symptoms often include reduced sleep duration, increased resistance to bedtime, sleep anxiety, and, especially in children, frequent night awakenings and parasomnias [18]. Children with FAS/pFAS—the most severe forms of FASD—did not experience worse sleep compared to those in other FASD subgroups. Sleep problems did not differ according to age or FASD subgroup, underlining the need for sleep assessment as an integral part of the multidisciplinary diagnostic assessment for any child with FASD [12].

There are differences among scholars regarding the connection between sleep-related difficulties, age and socioeconomic status in children. Significant differences have been identified with regard to healthy adolescence, which had increased sleep-related difficulties caused by lower socioeconomic status and less stable caregiving. However, in groups with children with FASD there was not any notable deviation [12, 24].

Sleep disturbances are a significant and common issue in children with FASD. These sleep problems can lead to a range of negative outcomes, including behavioral issues and increased anxiety, affecting both the children and their families. Effective screening, diagnosis, and tailored interventions are crucial for managing sleep disturbances in this population, highlighting the need for comprehensive and individualized treatment approaches.

Therapy

We already know that alcohol permanently damages the fetal central nervous system, so there is currently no causal treatment for FASD- a group of conditions resulting from prenatal alcohol exposure (PAE) [5, 10]. However, it is possible to alleviate the symptoms associated with FASD.
The foundation of treatment should be a safe, balanced environment created by the caregivers of a child with FAS. The surroundings of a child with FAS have a huge impact on the progression of symptoms, as well as their severity throughout the patient's life.
Before describing possible treatments, it should be said that the priority in this case is prevention - that is not consuming alcohol during pregnancy [10].
In a situation where a pregnant woman consumes alcohol, dietary supplementation seems promising, based on the theoretical evidence presented in the literature. Offspring showed fewer symptoms of FASD when women who consumed alcohol prenatally were given dietary supplements such as folic acid, selenium, omega-3 fatty acids, choline, iron and glutamine to reverse oxidative stress. It is worth emphasizing that studies conducted on humans are few so such dietary supplements cannot be considered as part of effective prevention [3, 18, 25].
Sleep is a complex physiological process that is extremely important for the proper development of a child. Until the age of 5, we spend our time mainly sleeping. Based on this evidence, we can surmise that the effects of sleep-related disorders in children with FASD can be enormous. Sleep problems are widely documented in this population and are estimated to occur in 85% of people with FASD [4, 5, 18, 19].
Based on a series of studies, it is claimed that many of the behavioral, adaptive and cognitive problems resulting from FASD can be linked to sleep problems [12, 27].
Given the wide range of possible effects resulting from insufficient sleep, therapy should be based on non-pharmacological interventions and must be individualized according to the preferences and needs of the patient with FASD [3, 10, 18].
In order to maintain the effects of treating the complications of disturbed sleep, the first thing to do is to start by introducing proper sleep hygiene for a child with FAS [5, 10, 12, 18,].
Providing a better sleep environment, calming afternoon and evening activities and planning a sleep routine are all part of good sleep hygiene.
It is recommended to reduce the amount of external stimuli in the environment of a child with FAS before bedtime, as well as during sleep. We can achieve this by limiting the amount of time the child spends in front of a screen, turning off lights in the room earlier and using earplugs [5, 19, 26].
Sound therapy techniques, including special devices that generate white noise, can also be effective in this case [5, 10, 19].
Positive effects have been reported in the treatment of sleep disorders by using self-relaxation techniques such as meditation, breathing exercises [5, 19].
It is important to emphasize the significant role of parents in therapy. Their help in teaching the child to self-regulate and follow the rules is crucial to therapeutic success. Caregivers can also support behavioral therapy by rewarding the child for adhering to a set sleep schedule and presenting sleep as positive and necessary [3, 5, 10, 19].

The second therapeutic line is the pharmacological treatment of sleep disorders and their many consequences. It is possible to use melatonin in FASD patients with present sleep deficits [5, 10, 12, 18, 19, 26].
Melatonin has the ability to decrease sleep onset latency, increase total sleep time and uncommon mild side effects [5, 19].
Exogenous melatonin is a synthetic form of endogenous melatonin, a neurohormone responsible for synchronizing sleep-wake cycle and circadian rhythm [11].
The European Medicines Agency has approved a brand of melatonin (Slenyto) for pediatric use, which is available as extended-release pills [11, 19].
There are also doubts about the efficacy and safety of long-term use of melatonin preparations. There are not enough studies on the effect of melatonin according to the type of sleep disorder, as well as the long-term effect of the preparation on the body of a child with FASD [5, 11, 19].
As for the use of other pharmaceutical preparations, our knowledge is considerably limited. Moreover, the polypragmasy often practiced by doctors can exacerbate sleep-related disorders [11, 18].
Medications used by patients with FASD and psychiatric and neurological comorbidities commonly take drugs such as stimulants, antiepileptic drugs and psychotropic drugs that interfere with correct sleep patterns [11].

The most effective treatment for insomnia in children with FAS, and its long-term consequences, is combination therapy. Cognitive-behavioral therapy sessions with controlled use of melatonin for a short period of time appear to be the most promising method for treating sleep problems caused by alcohol exposure during pregnancy [5, 19].

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