Prenatal Alcohol Exposure and Sleep Alterations in Children: A Systematic Review

Exposición prenatal al alcohol y alteraciones del sueño en niños: Una revisión sistemática

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El presente trabajo ha sido desarrollado íntegramente por la autora en lengua inglesa sin usar ningún tipo de traductor externo o programa informático.

A mis padres y abuela Ángeles, por siempre darme libertad y apoyo para cumplir mis sueños.

A mis primas Ana y Cecilia, por creer en mí ciegamente.

A todas las personas que he conocido durante estos años: gracias, os llevo conmigo.

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Abstract

This systematic review had the purpose of summarize the current knowledge on sleep alterations in children with prenatal alcohol exposure (PAE). A literature search was performed using Scopus and Web Of Science (WOS), using the following equations: (1) Sleep AND Prenatal alcohol exposure children and (2) Sleep AND Fetal alcohol exposure. Of the 216 articles, 14 were retrieved for inclusion in this review. The studies were gathered by the main technique used: actigraphy (n= 5), electroencephalography (n= 2), video (n= 2), polysomnography (n= 3) and other methods (n= 2). Children and infants that were prenatally exposed to alcohol were reported to have disturbed sleep through the manifestation of low sleep efficiency, sleep fragmentation, shorter sleep duration, altered respiratory indices, hypermotor events (mini foot movements, foot rubbing, limb movements and scratching) and affected melatonin production. Most studies (n= 13) identified this difference among controls and PAE/Fetal Alcohol Spectrum Disorder (FASD) sample, but just one (Hanft et al., 2006) reported different results, highlighting that there was no difference between groups (PAE vs. control) in quiet sleep (QS%) and active sleep (AS%) at any age across the first year of life. Results showed that children that has been prenatally exposed to alcohol struggle with sleep alterations, and that these alterations can even appear when the mother's alcohol consumption is low but continuous: the volume is not important per se but rather the absence or presence of alcohol.

Keywords: Fetal Alcohol Spectrum Disorder, Prenatal Alcohol Exposure, Neurobehavioural Disorder Associated with Prenatal Alcohol Exposure, Neurodevelopmental Disorders, Sleep, Children, Sleep Disorder

Resumen

Esta revisión sistemática tiene el propósito de resumir el conocimiento actual que se tiene sobre las alteraciones del sueño en niños expuestos prenatalmente al alcohol (PAE). Se hizo una búsqueda de literatura usando Scopus y Web Of Science (WOS) con las siguientes ecuaciones: (1) Sleep AND Prenatal alcohol exposure children and (2) Sleep AND Fetal alcohol exposure. De 216 artículos, 14 se escogieron para esta revisión. Los estudios se agruparon según su principal técnica usada: actigrafía (n= 5), electroencefalografía (n= 2), video (n= 2), polisomnografía (n= 3) y otros métodos (n= 2). Niños y bebés con PAE reportaron tener un sueño alterado, manifestado a través de una baja eficacia, fragmentación del sueño y duración reducida del sueño, índices respiratorios alterados, eventos hipermotores (movimientos y roce de pies, movimiento de extremidades y rascado) y una producción de melatonina afectada. La mayoría de los estudios (n= 13) señalaron esta diferencia entre grupos controles y la muestra expuesta prenatalmente al alcohol o con trastorno del espectro, pero solo uno (Hanft et al., 2006) presentó resultados diferentes, resaltando la nula diferencia entre los grupos (PAE vs. control) en sueño tranquilo (QS%) y sueño activo (AS%) durante el primer año de vida. Esta revisión sistemática muestra cómo los niños expuestos prenatalmente al alcohol tienen alteraciones en el sueño, y que estas aparecen incluso cuando la madre tiene un bajo pero continuo consumo: el volumen no es importante per se, si no la ausencia o presencia del alcohol.

Palabras clave: Trastorno del Espectro Alcohólico Fetal, Exposición Prenatal al Alcohol, Trastorno Neuroconductual Asociado con la Exposición Prenatal al Alcohol, Trastornos del Neurodesarrollo, Sueño, Niños, Trastorno del Sueño.

Introduction

Fetal alcohol spectrum disorders (FASD) describes a spectrum of conditions that develops due to prenatal alcohol exposure (PAE) (Benson et al., 2023), making the individuals to manifest some abnormalities across three or more domains of brain function (≤2 standard deviations) (Mughal, Hill, et al., 2020). This spectrum includes fetal alcohol syndrome (FAS), partial fetal alcohol syndrome (pFAS), alcohol related neurodevelopmental disorder (ARND) (Dylag et al., 2021), alcohol related birth defect (ARBD) (Chudley, 2005; Dylag et al., 2021; Hoyme et al., 2016) and neurobehavioural disorder (American Academy of Pediatrics, 2000). However, due to the nature of a spectrum, a wider range of symptoms and, disorders that have just not been discovered, could be expressed by PAE (Riley et al., 2011), even sudden infant death (Burd & Hofer, 2008).

It is known that PAE is one of the first causes of neurodevelopmental disorders (American Academy of Pediatrics, 2000), even though alcohol has been established for years as a teratogen that could affect the developing fetus (American Psychiatric Association, 2022; Popova et al., 2021). For example, in Canada, a four level model of FASD prevention (Poole, 2008) was developed with the intention of reducing the amount of alcohol consumed during pregnancy or gestation, focusing in 4 different levels that had different approaches on how to do it such as raising awareness to the problem, discussing alcohol use with people in childbearing age, assisting those people in risk and giving postpartum support to those with alcohol problems.

In 76 countries the prevalence is < 1%, while in United States it sits between in 1.13% and 5% of the population (May et al., 2018). Europe is the region where it is estimated to be at its highest at 1.98 % of the population being affected by it (Lange, Probst, et al.,

2017; Popova et al., 2017). Additionally, it is also Europe is reported to be the continent with the highest prevalence of alcohol use during pregnancy at 25.2% (Popova et al., 2017).

Initially, FAS diagnosed children shared some characteristics: prenatal-onset growth deficiency, craniofacial dysmorphology, and central nervous system dysfunction (Jones & Smith, 1975; Riley et al., 2011). However, most individuals that have been prenatally exposed to alcohol do not have the facial abnormalities required for this diagnosis, making it clear that not all the children with PAE express the same range of symptoms (Riley et al., 2011). Due to that topic, the term pFAS was coined for those children who displayed just some typical characteristics of the disorder but not all of them (Carpita et al., 2022).

In 2000, the FASD term included children without the craniofacial dysmorphology and growth retardation, but with the presence of neurobehavioral difficulties, hyperactivity, attention-deficit, reduced impulse control and arrested social development, even with average intelligence (Rasmussen et al., 2011). This modification highlighted that each FASD infant could face different barriers and also could represent diverse clinical pictures. Some of them, not only do they experience the neurobehavioral aspects, but also report problems regarding excretion (Roozen et al., 2017, 2020), nutrition (Werts et al., 2014) and sleep (Dylag et al., 2021).

Guidelines have been published to diagnose FASD (Cook et al., 2016). The guide shows step by step directions on how to perform an assessment for FASD, which includes the following: (1) medical assessment including the family history, maternal

alcohol history, physical examination for the characteristic features and differential diagnosis and (2) neurodevelopmental assessment, regarding qualities in the child like inattention, social abilities, executive function deficits and learning disabilities despite the fact that there is no neuropsychological measures specific to FASD. This document claims that a correct FASD diagnosis needs from the participation of a multidisciplinary team compound by doctors, psychologists, physicians, occupational therapists and speech-language pathologists among other child development specialists, showing the diversity of symptoms these patients could display.

In the American Psychiatric Association's (APA) Diagnostic and Statistical Manual (DSM; American Psychiatric Association, 2022) defines FASD as "neurobehavioural disorder associated with prenatal alcohol exposure (ND-PAE)", being found then in the neurodevelopmental disorders category. The proposed criteria to diagnose it are summed up as follows: (A) More than minimal exposure to alcohol during gestation, (B) impaired neurocognitive functioning manifested by one or more of the following: global intellectual performance, executive functioning, learning, memory and/or visual-spatial reasoning, (C) impaired self-regulation manifested by one or more of the following: mood regulation, attention deficit and/or impulse control, (D) impairment in adaptative functioning manifested by two or more of the following: communication deficit, social communication and interaction, daily living skills and/or motor skills, (E) all symptoms named above must happen during childhood, (F) it must cause significant disturbance in important areas of functioning and (G) symptoms are not better explained by other disorders.

Sleep is an essential brain process (Hirshkowitz, 2004) and so its alteration could have important impacts in those who suffer them (Gemke et al., 2024). It is composed by 3 stages: Light NREM sleep, deep NREM sleep and REM sleep (Walker, 2018). NREM sleep, at the same time, is divided in three stages: N1, N2 and N3 or slow-wave sleep (Gemke et al., 2024). Even though not any stage is more important than the others, losing any type of sleep could cause disturbances in the brain (Walker, 2018). Additionally, a good sleep efficiency (defined as actual sleep time divided by the time in bed; Pesonen et al., 2009), is considered to be over 85% (Jiang, 2019).

Sleep architecture during the first years of life differs substantially from sleep in older children, teenagers and adults. Neonatal sleep includes Active Sleep (AS) or Paradoxical Sleep, Quiet Sleep (QS) and Indeterminate Sleep (IS), that is considered as such when elements from AS and QS are both present. These sleep cycles last around 60 minutes each, going from AS to QS and vice versa during a mean of 15 hours a day. Rapid eye movements, body and limb movements and irregular breathing are often found in AS, a process that also helps in the maturation of the central nervous system (CNS). QS plays a role in energy maintenance and the release of growth hormones. Since birth, AS takes up a great percentage of the sleep cycle and as the children matures, the time in AS decreases and QS increases up to 35-50% in the first year of life (Lenehan et al., 2023).

From 2 to 4 months old, sleep cycle changes from an ultradian rhythm to a process that progressively reaches adult levels of NREM sleep and REM sleep, a circadian rhythm. This last process lasts for about 90 minutes each cycle. In newborns (36 to 44 weeks

postmenstrual age), REM sleeps take up to 50% of the total sleep time (TST), and it reduces to 30% at 12 months old with 12 hours of TST (Lenehan et al., 2023).

Factors such as natural or caesarean birth, method of feeding, co-sleeping or season when the infant is born are crucial for understanding sleep in children. Infants that were born vaginally and those born by an emergency caesarean-section after some time in labour spend more time in QS. This response is a temporary phenomenon due to the stress of labour. Breastfed babies have more night-awakenings when compared with formula-fed children. Co-sleeping makes children have more night-awakenings and a shorter sleep duration. Also, children born in summer had a shorter TST (Lenehan et al., 2023).

During these years, brain restructures and reorganises itself by brain growth and neuroplasticity. Learning, memory and emotional regulation are some aspects that has been associated with sleep (Lenehan et al., 2023). Sleep deprivation or poor sleep quality have been proved to affect: (1) learning and memory, (2) emotional regulation and (3) general cognitive and language development (Jiang, 2019). Those sleep deprived present weight gain and obesity, more chances of developing obstructive sleep apnoea (OSA), poor cognitive function, worse emotional regulation and a poor developmental outcome in general (Lenehan et al., 2023).

It has been demonstrated that sleep in childhood, specially in the first five years of life (Dahl, 1996), contributes to a healthy neurodevelopment (Mughal, Joyce, et al., 2020), playing an important role in neuroplasticity, brain maturation (Hirshkowitz, 2004; Walker, 2018), cognition and optimal daytime functioning (Mughal, Hill, et al., 2020), and also it is known as an essential process, particularly in children with

neurodevelopmental disorders (NDD) (defined as a group of conditions with onset in the developmental period; Bruni et al., 2025). It has also been reported that children with more night-time sleep have a more developed executive function and social learning (Lenehan et al., 2023).

The prevalence of sleep disorders in the general pediatric population is estimated to be between 28% and 36% (Meltzer et al., 2014), but it increases to 86% in children with NDD (Bruni et al., 2025) such ASD (autism spectrum disorder), Down syndrome and ADHD (Robinson-Shelton & Malow, 2016).

Knowing this, regrettably, in children with FASD sleep disorders often go undiagnosed and untreated (Ipsiroglu et al., 2013), affecting their cognitive and behavioural outcomes in the following ways: adaptive dysfunction, academic difficulties and psychopathology (Donald et al., 2015). Untreated sleep alterations can lead to mental health problems. Some of these alterations according to literature are: (1) obstructive sleep apnoea (OSA), a disorder characterized by the upper airway obstruction during the sleep due to hypertrophy of the tonsils and adenoids, craniofacial abnormalities, neuromuscular disorders and/or obesity, (2) Restless legs syndrome (RLS), a neurological disorder that makes the patients have an urge to move their legs, specially while in resting or during inactivity periods, (3) delayed sleep phase syndrome (DSPS) which is an alteration of the circadian rhythm causing delay in the sleep–wake cycle, (4) hypersomnia, characterized by an excessive daytime sleeping behaviour or long sleep time, (5) insomnia, a disorder that affects the sleep onset and/or a difficulty in sleep maintenance, (6) parasomnias, commonly known as non-desirable physical events occurring during NREM or REM sleep, having experiences such as sleep-walking,

sleep-talking, night terrors, muscle paralysis, nightmares and confusional arousals (Gemke et al., 2024), (7) central sleep apnoea (CSA), a phenomena where there is a pause in breathing but no evidence of respiratory effort, (8) catathrenia, a variant of apnoea where the person presents expiratory moaning and (9) sleep-related epilepsy, an appearance of nocturnal seizures accompanied by spams that frequently occurs during sleep-wake transitions (Carter & Wrede, 2017).

It has been proposed that prenatal alcohol exposure could be related to an inhibited growth or function of prefrontal and parietal areas, leading to a certain behavioural and cognitive profile (Khoury et al., 2015). This outcomes were also complemented by animal studies (Earnest et al., 2001; Hilakivi, 1986; Sakata-Haga et al., 2006; Wengel et al., 2011) were sleep-wake behaviour disruption, circadian rhythmicity and protein alteration appeared when alcohol-exposed (Pandey et al., 2020). Some of these abnormalities in proteins that appear due to sleep difficulties had been associated in children with FASD with a display of a wide range of behavioural and cognitive difficulties, such as working memory and organisational issues, challenging daytime behaviour, impulsivity, hyperactivity, inattentiveness (Coriale et al., 2013; Green et al., 2009), behavioural and psychological executive function (Mazurek & Sohl, 2016; Mughal, Hill, et al., 2020), affecting their cognition, behaviour, and health due to the sleep alterations having such an important role in brain structures such as the prefrontal cortex (Bruni et al., 2025).

Moreover, not just cognitive functions are altered, but organs like the liver, kidney, and heart are affected, as well as the endocrine and gastrointestinal systems. Their brains are also affected by this condition, leading them to have a reduced grey and white matter in both the cerebrum and the cerebellum, specifically in the amygdala, hippocampus,

putamen, caudate, thalamus and pallidum. However, the rate of their brain volume growth is similar to children of the same age as them, having so an opportunity for intervention if early diagnosed (Popova et al., 2021).

It is known that these disturbances that had been mentioned would follow them through their lifespan, having major consequences in their life, their caregivers' and society (Inkelis et al., 2024). For example, regarding to their own lives, these children have higher chances to experiment academic failure, substance abuse, mental health problems, frequent contact with law enforcement, and inability to live independently. In addition, suicide is a high-risk behaviour commonly shown among people with FASD due to their impaired affect regulation, already mentioned in the criteria of the disorder (American Psychiatric Association, 2022). It also affects the society in terms of the patients of this disorder needing a constant demand from the health care system, educational system, mental health professionals and child protection services (if needed) (Popova et al., 2021). Lastly, their caregivers, a critical role in these children's lives, who report having more stress than caregiver of children without developmental disabilities (Gault et al., 2023).

Children affected with FASD display attentional problems around vigilance, reaction time, the speed or inhibition of information processing (Lange, Rovet, et al., 2017), patterns of inattentiveness, hyperactivity, and impulsivity (Coriale et al., 2013), just like children with ADHD. Indeed, investigation with humans (Coriale et al., 2013) and animals (Wang et al., 2021), proves that FASD have a high comorbidity (around 60 %) with ADHD (attention-deficit hyperactivity disorder), making it one of the most common comorbidities in the spectrum (Fryer et al., 2007), although research showed

that they could have different neuropsychological characteristics, consequently getting diverse reactions to pharmacological treatments (American Psychiatric Association, 2022). Comorbidity with symptoms of bipolar and depressive disorder, substance use disorders, oppositional defiant disorder and conduct disorder have also been reported (American Psychiatric Association, 2022).

ASD is also a neurodevelopmental disorder whose sleep patterns are affected by an inefficient REM sleep (Devnani & Hegde, 2015) and, even though there is still not enough studies about this association, Lyall et al. (2014) reports that ASD is present in 2.6% of the FASD population. ASD happen to be characterized by deficits in social skills, narrow interests and repetitive behaviours (Carpita et al., 2022), symptoms that are similar in some children with FASD such as social impairment, reduced attentional capacity (Senju et al., 2009), as noted above and deficits in hand dexterity, of which the last two are also characteristics shared with children with ADHD (Carpita et al., 2022).

Despite the progress made through the years, some investigation is still needed as a result of some studies (Chen et al., 2012; Dylag et al., 2021) emphasizing the fact that sleep problems in FASD infants are not well characterized, as well as circadian rhythm disruptions (Das et al., 2024). It is documented that the effects of prenatal alcohol exposure on sleep quality have been understudied, despite having reports made by caregivers of children with fetal alcohol spectrum disorders that display elevated levels of sleep alterations (Inkelis et al., 2024).

Therefore, trying to contribute to the study of this condition, this systematic review has the objectives of summarizing the current knowledge on sleep alterations in children with PAE.

Method

Study Design

This systematic review was not preregistered but was conducted under the quality standards recommended in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement protocol (Page et al., 2021).

Study eligibility was defined according to the PICO criteria (Stern et al., 2014) (population, intervention, comparison and outcomes): Population (children aged <12 years old); Intervention (prenatal exposition to alcohol); Comparison (not applicable); Outcomes (the main outcome was to assess the presence of "sleep alterations" in original studies).

Search Strategy and Selection Criteria

A literature search was performed using Scopus and Web Of Science (WOS) (covering PubMed, alongside with all databases indexed in it). The main search equations were as follows: (1) Sleep AND Prenatal alcohol exposure children and (2) Sleep AND Fetal alcohol exposure. Not only were both equations composed of the term 'sleep' but also had interchangeable terms with 'prenatal' and 'fetal', trying to get all articles mentioning these topics (children and sleep) retrieved. Furthermore, these publications were filtered by year (2000-2025) and by language (English and Spanish).

Exclusion criteria: studies in animals or adults, in languages other than English or Spanish, not indexed publications, publications only using self-inform measures,

systematic reviews, capsule commentaries, patents, book chapters or letters to the editor were also not included.

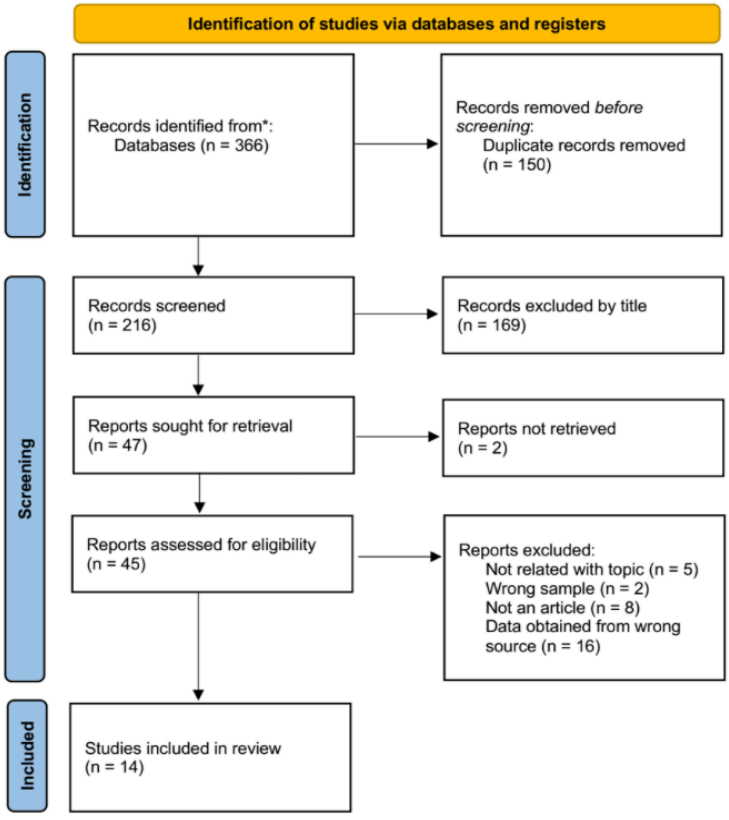
Data Extraction and Analysis

A data extraction spreadsheet was created, and all the searches were exported in 'Comma Separated Values' (CSV) or XLS and included into this document. Authors name, article title, abstract, digital object identifier (DOI), type of publication and publication date were incorporated in the spreadsheet.

First, those articles duplicated were eliminated to avoid data duplication. Each article included was screened by both authors independently and, if any doubt arose, a discussion was held to solve it. Figure 1 shows the flow chart used.

Figure 1

Flow Chart of the Article Search and Selection Strategy



Results

A final total of 14 articles met the inclusion criteria (Fig.1). Trying to ease the results presentation, articles have been gathered by the main type of technique that is used to obtain the data, making the aggrupation as follows: the majority used actigraphy (n= 5), the rest employed electroencephalography (n= 2), video (n= 2), polysomnography (n= 3) or other methods (n= 2) to gather evidence.

Table 1 presents the authors names, the patients, method(s) used and main results.

Actigraphy

Five studies (Benson et al., 2023; Inkelis et al., 2024; Mughal, Hill, et al., 2020; Pesonen et al., 2009; Wengel et al., 2011) assessed sleep in alcohol-exposed children using actigraphy.

Within five studies, three (Benson et al., 2023; Mughal, Hill, et al., 2020; Pesonen et al., 2009) of them highlighted that sleep efficiency was affected in the alcohol exposed (AE) groups.

One of them (Pesonen et al., 2009) reported that children exposed to higher amounts of alcohol (M = 0.5, SD = 0.8, p = 0.01) during gestation had low sleep efficiency and had shorter sleep duration (M = 7.7, SD = 0.5, p <0.001), results that coincide with Mughal et al., (2020) and Benson et al. (2023), where sleep efficiency was seen significantly affected.

In another two studies (Pesonen et al., 2009; Wengel et al., 2011), sleep duration alterations were also reported and infants showed a shorter sleep duration (p < .001; M

= 7.6, *SD* = 0.5, *p* <0.001 respectively). Regarding sleep fragmentation, two studies (Inkelis et al., 2024; Mughal, Hill, et al., 2020) showed that it was present (*p* = 0.05; *M* = 8.5, *SD* = 3.19, *p* = 0.05 respectively) in the results retrieved from the actigraphy data when related to the FASD or AE groups.

Three of the studies (Benson et al., 2023; Inkelis et al., 2024; Mughal, Hill, et al., 2020) also notified that, alongside with the reduced sleep duration, PAE children displayed more variability than control groups (*p* <0.001; *M* = 7:27 hours; *M* = 54, *SD* = 24.22, *p* = 0.002 respectively).

Other variables were informed to be disturbed in the sleep of AE infants, namely sleep onset latency (*p* = .002) in Wengel et al. (2011) and wake after sleep onset (WASO; *M* = 24.1, *SD* = 13.05, *p* = 0.002) in Inkelis et al. (2024).

Three articles (Benson et al., 2023; Inkelis et al., 2024; Wengel et al., 2011) used questionnaires like the Children's Sleep Habits Questionnaire (CSHQ; Owens et al., 2015) or the Pediatric Sleep Questionnaire (PSQ; Chervin et al., 2000) as a complementary assessment to actigraphy, and their results replicate and complement the outcomes from actigraphy data.

Electroencephalography

Two articles (Gerstner et al., 2023; Troese et al., 2008) used electroencephalography (EEG) to investigate sleep in alcohol-exposed children.

Troese et al., (2008) reported that infants with high maternal alcohol use exhibited atypical sleep state and movement parameters: they were associated with

proportionately more wake (t (10) = 2.2, $p < 0.056$) and wake epoch duration and also, higher spontaneous movement bout duration (t (9) = −2.5, $p < 0.037$; r = −0.611, $p <$ 0.046). Despite that, sleep duration between groups (AE vs. non AE) showed no difference (p = 0.10).

Gerstner et al., (2023) found that 13 out of 53 (24.5%) children showed an altered EEG and they were distributed in the following way: 9 of them showed epileptiform activity, 2 showed generalized slowing and 2 of them showed focal slowing.

Two articles also used the Michigan Alcohol Screening Test (MAST; Selzer, 1971) and Sleep Disturbance Scale for Children (SDSC; Bruni et al., 1996) were used and they confirmed the results that the EEGs retrieved: disturbed sleeping among children with FASD.

Video

Two articles (Hanft et al., 2006; Ipsiroglu et al., 2019) used video recording or videosomnography, respectively, as their main technique to obtain results related to sleep in AE infants.

While LSP appeared to be lower in those with FASD at 6 months (t = −2.66, $p < .05$), the same effect was observed with total sleep time (TST) at 3 (t = −2.92, $p < .05$.), 6 (t = −2.41, $p < .05$) and 12 months (t = −2.88, $p < .05$) when compared to the control group. In spite of all these results, no difference between groups was found in quiet sleep (QS%) and active sleep (AS%) at any age across the first year of life, showing the

expected increase of QS% and decline of AS% from 1 to 12 months old (Hanft et al., 2006).

Ipsiroglu et al., (2019) informed that: behaviours such as restless sleep, tossing, turning and kicking movements and periodic limb movements were seen in 95% of the participants (n = 38). This confirms the results from the video-recording task, where all recorded infants presented hypermotor events, leading to: (a) mini foot movements and foot rubbing, (b) bigger limb movements and (c) 'tossing', 'kicking,' and 'scratching'.

Polysomnography

Three articles (Chen et al., 2012; Dylag et al., 2021; Goril et al., 2016) used polysomnography (PSG) outcomes to assess sleep in FASD patients.

First, in relation to sleep architecture, Chen et al. (2012) conducted PSG in 5 children and no group differences were found in terms of sleep stage distribution, but fragmented sleep was seen among them with an index of 11.1 events/h (IQR: 10, 16). These results complement the data reported by Goril et al. (2016), where FASD children had lower sleep efficiency (SE) than normative data published in Scholle et al. (2011), being the SE percentages distributed as follows across the different age groups: 81.3% in age 6-9 and 84.0% in age 10-12.

Then, in addition, Dylag et al., (2021) and Chen et al. (2012) reported that respiratory indices were disturbed. Goril et al. (2016) observed that the FASD group had higher AHI (*M* = 2.8 events/h) and End-tidal CO2 levels (*M* = 45.2 mm Hg, *SD* = 3.5 mm Hg) when compared to the control group (*M* = 0.7, *SD* = 0.8; *M* = 40.7 mm Hg, *SD* = 4.5

mm Hg respectively). Moreover, Goril et al. (2016) reported an abnormal melatonin secretion curve in 19 out of 24 (79%) AE individuals when performing a dim light melatonin onset test.

This studies used the CSHQ (Owens et al., 2015) and results reveal a high sleep complaint, complementing the conclusions retrieved from the PSGs: AE infants' sleep have significant differences when compared to controls.

Other methods

Two articles (Das et al., 2024; Sania et al., 2023) used a different technical approach to study sleep in AE infants.

Das et al. (2024) tried analysing saliva looking for the expression patterns of clock genes and clock regulatory genes, Sania et al. (2023) used electrocardiogram, blood pressure and respiration rate.

Das et al. (2024) analysed saliva, leading to the following results: Core Clock Genes (BMAL1, CLOCK, PER1, PER2, PER3, CRY1 and CRY2) fluctuated throughout the day in control subjects ($p = 0.00874$; $p = 0.0001$; $p = 0.00048$; $p = 0.0000$; $p = 0.00014$; $p = 0.00001$; $p = 0.00001$ respectively). However, in the AE group, the expression of these genes were altered ($p = 0.31104$; $p = 0.0906$; $p = 0.09267$; $p = 0.09403$; $p = 0.2263$; $p = 0.49685$; $p = 0.41161$ respectively), showing a rhythmicity alteration. Also ARRB1 and epigenetic modifiers that interact with CLOCK:BMAL1 complex (MLL1, P300, SIRT1, EZH2, HDAC3, JAR1D1) happened to fluctuate during the day in control subjects ($p < 0.00001$; $p < 0.0482$; $p = 0.0003$; $p = 0.0001$; $p = 0.0002$; $p =$

0.0001; $p = 0.0001$ respectively), but not in AE subjects ($p = 0.52837$; $p = 0.3623$; $p = 0.5244$; $p = 0.8999$; $p = 0.2649$; $p = 0.2769$; $p = 0.6653$ respectively).

On the other hand, clock regulatory genes like NPAS2, showed a circadian rhythm in both the control ($p < 0.00218$) and AE groups ($p = 0.00609$), like DEC1 and DBP, but their acyclic expression was seen in some cases in the second group ($p = 0.00127$; $p = 0.03293$ respectively). Meanwhile, NFL3, NR1D1, and DEC2 did not show rhythmicity in either the control ($p = 0.1733$; $p = 0.1463$; $p = 0.82459$ respectively) or AE groups ($p = 0.86879$; $p = 0.16733$; $p = 0.45444$ respectively).

Sania et al. (2023) reported the following: The results retrieved from this electrocardiogram illustrated that children from the low-continuous drinking group had a lower heart rate and diastolic blood pressure during quiet sleep ($p = 0.006$; $p = 0.05$ respectively) and a reduced ratio of low frequency/high frequency during active sleep ($p = 0.008$). Also, the moderate-to-high-continuous drinking group ($p = 0.03$) had a lower systolic blood pressure.

Furthermore, they detected that the low-continuous drinking group had a less pronounced decrease in breathing rate in active sleep ($p = 0.02$) when compared to the non-drinking group.

Table 1 presents key aspects of included articles: authors name, patients characteristics, method(s) used and main results.

Table 1

Published Articles Reporting Sleep in Prenatal Alcohol Exposed Children

Authors	Patients	Method(s)	Results
	Sample (N), age mean ± standard deviation (when reported)		
Hanft et al. (2006)	Alcohol exposed (17) and non-exposed (17)	Videosomnography	AE group had higher LSP at 6 months ($t = -2.66$, $p < .05$) and TST at 3 ($t = -2.92$, $p < .05$.), 6 ($t = -2.41$, $p < .05$) and 12 months ($t = -2.88$, $p < .05$) vs. Non AE group.
Troese et al. (2008)	Mother-infant dyads (13)	Questionnaires, electroencephalography (EEG), electro-oculogram (EOG), actigraphy and infrared time-synchronized videography.	Higher MAST score mothers' made children had less AS (t (10) = −2.2, $p < 0.05$) vs. Low exposure group. Higher alcohol use rised the AS group's W epoch (t (10) = 2.2, $p < 0.056$) and spontaneous movements (t (9) = −2.5, $p < 0.037$; $r = -0.611$, $p < 0.046$).
Pesonen et al. (2009)	Urban cohort (912)	Questionnaires and actigraphy	Low sleep efficiency children were exposed to higher amounts of alcohol ($M = 0.5$, $SD = 0.8$, $p = 0.01$) and it decreased over all nights ($M = 74.1$, $SD = 3.4$, $p < 0.001$) and on weekdays (M = 74.0, $SD = 4.5$, $p < 0.001$). Also, they had shorter sleep duration ($M = 7.7$, $SD = 0.5$, $p < 0.001$), even on weekdays ($M = 7.6$, $SD = 0.5$, $p < 0.001$).

Wengel et al. (2011)	FASD children (19), 4y11m and CON children (12), 4y4m	Questionnaires and actigraphy	FASD group reported longer sleep onset latency (p = .002), more bed resistance (p = .013), shorter sleep duration (p < .001), higher sleep anxiety (p = .008), more night awakenings (p = .044) and parasomnias (p = .008) due to their higher rates of sleep disturbance (p = .008) vs. control group.
Chen et al. (2012)	FASD group (33), 7.5 ± 2.2 and CON group (418)	Questionnaires and polysomnography	FASD group reported a high level of sleep complaint (M = 51.7, SD = 11.0), AHI (M = 2.8 events/h) and end-tidal CO2 levels (M = 45.2 mm Hg, SD = 3.5 mm Hg) vs. community sample (M = 38.8, SD = 5.6; M= 0.7, SD = 0.8; M = 40.7 mm Hg, SD = 4.5 mm Hg, respectively).
Goril et al. (2016)	Individuals (36), 10.0 ± 3.2	Polysomnography and DLMO	AE children had lower SE in age 6-9 (81.3%) and in age 10-12 (84.0%) vs. normative data. Also, 19 out of 24 (79%) had an abnormal melatonin secretion curve, confirming the sleep disorders that 58% of participants had, like parasomnias (19.5% NREM parasomnia, 5.6% REM parasomnia, and 2.8% NREM and REM parasomnia) and insomnia (16.7%), alongside sleep apnoea (5.6%), nocturnal enuresis (2.8%) and sleep fragmentation and sleep complaints (19.5%).
Ipsiroglu et al. (2019)	FASD patients (40), 9.1	Video recording	FASD patients presented restless sleep, tossing, turning and kicking movements (hypermotor events) (85%; n = 34). Also, periodic limb movements (95%; n = 38), problems falling asleep (98%) and sleep maintenance problems (93%), disordered breathing (95%), upper airway narrowing (68%) and parasomnias (73%).

Mughal et al. (2020)	FASD group (29), 9.60, autism group (21), 8.42 and typical development group (45), 8.12	Actigraphy	There were some differences between groups in actual sleep time (p <0.001), sleep efficiency (p <0.001), mean sleep bouts (p = 0.02), night waking duration (p = 0.01,), and fragmentation index (p = 0.05). Meanwhile, in the TD group, boys (M = 27.98, SD = 9.97) moved significantly more and had higher mean activity epochs (t (39) = 2.04, p = 0.04) than girls (M = 21.32, SD = 10.87).
Dylag et al. (2021)	FASD group (40), 8 and CON group (40)	Questionnaires and polysomnography	There were some differences between groups in FASD group sleep onset delay (M = 1, p = 0.02), night wakings (M = 4, p = 0.01), parasomnias (M = 9, p = 0.0003), sleep disordered breathing (M = 3, p = 0.02) and daytime sleepiness (M = 9, p = 0.0009) in the CSHQ questionnaire vs. control. Furthermore, the FASD group spent less time in N3 and REM (M = 42.5, p = 0.03) while having higher respiratory indices vs. control group.

Sania et al. (2023)	Details published in Dukes et al., 2014	Electrocardiogram, blood pressure and respiration rate	Infants from the low-continuous drinking group had lower heart rate in quiet sleep ($p = 0.006$) vs. infants from the non-drinker group. Also, infants from the low-continuous drinking group ($p = 0.05$) and quit-early group ($p = 0.06$) had lower diastolic blood pressure during quiet sleep vs. non-drinkers mothers' group. Breathing rate decreased in active sleep in the low-continuous drinking group ($p = 0.02$) vs. non-drinking and systolic blood pressure decreased in the moderate-to-high-continuous drinking group ($p = 0.03$) vs. non-drinking group.
Gerstner et al. (2023)	Total sample (53), 10.1 ± 3.8, FAS/pFAS group (24%), status encephalopathy group (35%) and neurobehavioral disorder (41%)	Questionnaires and EEG	Disturbed sleeping is common among FASD patients (79%; n = 42), accompanied with sleeping problems like DISM (74%), STWD (70%) and DA (59%). Also, pathological EEGs were found in 13 children (24.5%).
Benson et al. (2023)	FASD group (29), ASD (21) and TD (45)	Questionnaires and actigraphy	Group differences were reported in sleep onset delay (F (2,85) = 11.30, $p < 0.001$, ηp2 = 0.21), night waking (F (2,83) = 12.44, $p < 0.001$, ηp2 = 0.23) and daytime sleepiness (F (2,81) = 10.07, $p < 0.001$, $\eta p2 = 0.20$), making FASD group have higher scores ($M = 2.640$, $SD = 1.29$; $M = 5.92$, $SD = 1.44$; $M = 11.17$, $SD = 3.17$ respectively) in these subscales vs. ASD and TD group. Also, TST was significantly different between FASD (M = 7:27 hours), ASD (M = 7:46 hours, t (38.03) = 3.007, $p = 0.013$) and TD group (M = 8:34 hours; t (56.77) = –4.50, $p = 0.001$)

Inkelis et al. (2024)	AE (35), 8.8 and CON (39), 8.0	Questionnaires, diaries and actigraphy	AE group showed more variability in WASO (M = 24.1, SD = 13.05, p = 0.002), number of wake bouts (M = 6.8, SD = 2.37, p = 0.012;), sleep time (M = 54, SD = 24.22, p = 0.002), percent sleep (M = 3.7, SD = 2.04, p = 0.008), and fragmentation index (M = 8.5, SD = 3.19, p = 0.05) vs. control group. Also, there was a significant main effect of group on night wakings (F [1,66] = 6.678, p = 0.012), parasomnias (F [1,66] = 10.473, p = 0.002), snoring (F [1,66] = 7.224, p = 0.009), sleepiness (F [1,66] = 5.233, p = 0.025) and behaviour (F [1,66] = 25.52, p < 0.001) in the questionnaires.
Das et al. (2024)	AE (23), 8.6 ± 1.61 and CON (26)	Saliva analysis (expression patterns of clock genes and clock regulatory genes)	AE group showed altered expression of genes: BMAL1, CLOCK (p = 0.31104; p = 0.0906 respectively), PER1, PER2, PER3, CRY1, CRY2 (p = 0.09267; p = 0.09403; p = 0.2263; p = 0.49685; p = 0.41161 respectively), ARRB1 (p = 0.52837) vs. control group, whose expression levels fluctuated during the day. Also, epigenetic modifiers (MLL1, P300, SIRT1, EZH2, HDAC3, and JAR1D1) showed arrhythmicity in AE subjects.

Abbreviations: AE = Alcohol exposed, LSP= Longest Sleep Period, EEG = Electroencephalography, TST = Total Sleep Time, MAST = Michigan Alcohol Screening Test, FASD = Fetal Alcohol Spectrum Disorder, CON = Control, AHI = Apnoea hypopnea index, SE = Sleep efficiency, DLMO = Dim Light Melatonin Onset Test, NREM = Non-rapid eye movement, REM = Rapid eye movement, CRSD = Circadian rhythm sleep disorder, CSHQ = Children's Sleep Habits Questionnaire, TD = Typical Development, FAS = Fetal Alcohol Syndrome, pFAS = Partial Fetal Alcohol Syndrome, DISM = Initiating and maintaining sleep, STWD = Sleep-wake transition, DA = Disorders of arousal, ASD = Autism Spectrum Disorder and WASO = Wake after sleep onset.

Discussion

The main objective of this systematic review was to study sleep alterations in prenatally alcohol exposed children. The results show how children that have been prenatal exposed to alcohol struggle with sleep alterations. The articles in this review reported that they suffer from low sleep efficiency, shorter sleep duration, sleep fragmentation, more infant wakefulness periods, high spontaneous movements (tossing, turning and kicking) and hypermotor events (mini foot movements, foot rubbing, limb movements and scratching) as seen in the research. Moreover, other factors such as disturbed respiratory indices, higher End-tidal CO2 levels and an abnormal melatonin secretion curve were also reported.

These alterations can even appear when the mother's alcohol consumption happens to be low but continuous, making it clear that is not volume of the substance that is important per sé, but rather the presence or absence of alcohol. That is why a safe dose of alcohol use during pregnancy has not been stablished yet (Popova et al., 2021).

Furthermore, it is also relevant to mention that the majority of articles in this review suggest that PAE could lead to sleep alterations but there is just one original research (Hanft et al., 2006) whose results seem to support a different theory: there is no difference between groups (PAE vs. control) in quiet sleep (QS%) and active sleep (AS%) at any age across the first year of life. This study is the only article that investigate these alterations during this period of time, showing that some investigation in that field is needed in order to compliment these results.

Different reasons are proposed to explain sleep alterations in children exposed to alcohol. First, structural and anatomical anomalies, where they explain that physical anomalies such as an anormal cerebellar vermis, narrow upper airways (Chen et al., 2012), micrognathia or high-arched palate or an anormal corpus callosum (Dylag et al., 2021) could cause these conditions. The neurobiological systems dysfunction point out the influence of neurotransmitters, genetic alterations (Dylag et al., 2021), thalamic, hypothalamic and endocrine changes (Gerstner et al., 2023) and alterations in the autonomic nervous system (Sania et al., 2023) and hypothalamic-pituitary-adrenocortical axis (Pesonen et al., 2009). Circadian rhythm and sleep homeostasis have also been proposed as an explanation to these disturbances, where they add some factors that could be affecting them like melatonin production (Goril et al., 2016), genes alteration (Inkelis et al., 2024) or an inadaptative stress response (Wengel et al., 2011). Finally, environmental and behavioural factors were proposed highlighting the important role of ambient factors and stress responses (Inkelis et al., 2024), in relation with cortical and subcortical brain maturation playing a role in these sleep disturbances.

Suggested by these results, some practical applications could be named. Mainly, the risk of drinking alcohol while pregnant is again being emphasized, and a rise of social awareness for this phenomenon is needed. Also, knowing the possible factors that could be maintaining the issues, as explained above, addressing the primary causes and seeking for the development of treatments for these children could enhance these children and their caretakers' quality of life, alongside with practicing sleep hygiene, stress response management and taking care of their respiratory difficulties.

Some questions happen to remain unanswered or poorly stated. A series of prospects for future research are displayed as follows: (1) To delineate accurately the role that specific factors could be playing in these conditions, such as biomarkers or clock genes, (2) To understand these factors and be able to develop personalized treatments to improve the quality of life of these patients, (3) To elaborate a better normative data cohort for comparison studies, (4) To investigate how interaction between alcohol and other drugs affects sleep, (5) To research the effects of PAE through these patients' lifespan in their sleep with longitudinal studies, (6) To study and understand the comorbidities of FAS with other neurodevelopmental disorders and find their common mechanisms, (7) To further investigate the subject suggested by Hanft et al. (2006), (8) To investigate if exposition to different alcohol quantities correlate with different extremes of the spectrum, (9) To determine, based on the last question, which could be the extremes of the spectrum, to the most stereotypical patient to the least, (10) To investigate the influence of alcohol in different stages of development of the fetus, (11) To investigate the mother's factors that could be influencing to the symptoms displayed later in life and (12) To study the influence of alcohol in identical and fraternal twins and look for protective factors that could be influencing in the process.

Limitations

Limitations regarding this review and those related to the articles described are presented. First, some limitations related to the articles included in this review can be named: (1) Studies conducting PSG found it difficult to implement it in large samples, leading to small samples, (2) small sample sizes in general, (3) presence of comorbidities such as ADHD or depression in the control groups, (4) use of pharmaceutical treatments that could bias the results, (5) decrease of quality in measure

accuracy in videosomnography, (6) selection bias where families already preoccupied for their children's sleep decide to participate in these studies and (7) most of the articles were conducted in western countries, making it difficult to generalize results to other cultures, countries or races.

Second, regarding the limitations concerning this review, these could be summed up in the following way: (1) just articles in Spanish or English were selected, building up for the possibility of some original research in this field not being included because of this criterion, (2) not performing a metanalysis and just it being a descriptive systematic review, (3) just gathering articles from 2000 to 2025 that could lead to some type of lack of data and (4) children were considered as such if they were less than 12 years old, not taking into consideration the difference of development between infants, toddlers and preadolescents.

Conclusions

In this systematic review, studies that reported sleep alterations in prenatally alcohol exposed children with objective measures of sleep alterations such as actigraphy, electroencephalography, video, polysomnography and other methods were included. 13 out of 14 studies reported that PAE children and infants experience difficulties in their sleep in form of: low sleep efficiency, shorter sleep duration, sleep fragmentation, more infant wakefulness periods, high spontaneous movements (tossing, turning and kicking), hypermotor events, disturbed respiratory indices, higher End-tidal CO2 levels and an abnormal melatonin secretion curve.

One article, Hanft et al. (2006), need their results to be highlighted due to the divergence of those according to the general consensus. This study expressed that no difference was found between control and PAE children in their active or quiet sleep and so needing some more research.

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