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## **Fetal Alcohol Syndrome: Impact on Neurodevelopment, Diagnosis, Early Intervention and Motor Disorders in Children under 3 Years**

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**Abstract:**

Fetal Alcohol Syndrome (FAS) is the most severe outcome of prenatal alcohol exposure, characterized by a combination of somatic and neurological abnormalities, including facial dysmorphism, growth deficits, and neurocognitive impairments. Fetal Alcohol Spectrum Disorders (FASD) encompass a broader range of outcomes from prenatal alcohol exposure, with varying degrees of severity. Alcohol consumption during pregnancy can disrupt fetal development, with no known safe threshold for its intake at any stage of gestation. The consequences are particularly profound on the central nervous system (CNS), where damage to structures like the cerebellum can lead to motor dysfunctions, balance issues, and cognitive impairments. Early identification and diagnosis of FAS or FASD, especially during the critical first years of life, is essential for improving developmental outcomes. Intervention strategies, including physical and cognitive therapy, can help mitigate long-term disabilities associated with these conditions. Diagnostic methods, such as ultrasound for fetal structural abnormalities and the AUDIT screening tool, are integral for early detection. This review highlights the impact of prenatal alcohol exposure on motor skill development, particularly the persistence of primitive reflexes in infants with FAS, which is indicative of CNS immaturity and necessitates early therapeutic interventions. Understanding these motor and neurological markers is critical for providing appropriate support and improving outcomes for affected children.

**Key words: Fetal alcohol syndrome, cerebellum, coordination, balance, neurodevelopment, milestones**

**Introduction:**

Fetal alcohol syndrome (FAS) and fetal alcohol spectrum disorder (FASD) are the leading causes of preventable congenital disabilities resulting from prenatal alcohol exposure. FAS is characterized by physical anomalies, including distinct facial features, growth deficits, and severe neurocognitive disorders, while FASD encompasses a broader spectrum of milder symptoms. Alcohol exposure during pregnancy disrupts normal brain development, particularly affecting the cerebellum, which plays a key role in motor control and

coordination. Consequences of prenatal alcohol exposure include developmental delays, motor dysfunction, cognitive impairment, and behavioral problems.

There is no known safe level of alcohol consumption during pregnancy, and its effects on the fetus may vary depending on factors such as timing and amount of exposure, as well as maternal health and nutrition. Early diagnosis and intervention are critical to improving outcomes, as children with FASD often experience persistent motor and cognitive challenges. However, diagnosis of FASD can be difficult due to overlap of symptoms with other genetic and neurological conditions. The aim of this review of research is to demonstrate the impact of prenatal alcohol exposure on neurodevelopment, with particular emphasis on motor dysfunction and cerebellar abnormalities, in order to improve early detection and intervention strategies for affected children.

### **Aim of the study:**

The aim of this study is to examine the neurological and developmental consequences of prenatal alcohol exposure, specifically focusing on Fetal Alcohol Syndrome (FAS) and Fetal Alcohol Spectrum Disorders (FASD). The study aims to explore the impact of alcohol consumption during pregnancy on fetal brain development, with a particular emphasis on cerebellar abnormalities and motor dysfunctions in affected children. By analyzing the persistence of primitive reflexes and other motor characteristics in infants and young children under 3 years, this research seeks to provide insights into early diagnostic markers and effective intervention strategies. Furthermore, the study aims to emphasize the importance of early detection and intervention to improve developmental outcomes and mitigate the long-term effects of FASD on children's physical, cognitive, and emotional development.

### **Materials and methods:**

A systematic review of scientific and medical literature from the PubMed and Google Scholar data bases was conducted.

### **Results:**

The study revealed significant correlations between prenatal alcohol exposure and a range of neurological and motor impairments in children diagnosed with Fetal Alcohol Syndrome (FAS) and Fetal Alcohol Spectrum Disorders (FASD). Key findings include:

**Cerebellar Abnormalities and Motor Dysfunction:** Ultrasound imaging of affected fetuses demonstrated abnormal cerebellar growth, with underdevelopment of the cerebellar

hemispheres in a majority of cases. These structural abnormalities were consistent with motor dysfunctions observed in children postnatally. Affected children exhibited significant deficits in gross and fine motor skills, including difficulties in balance, coordination, and fine motor control, particularly in tasks involving hand-eye coordination.

**Primitive Reflex Persistence:** The persistence of primitive reflexes, such as the Moro reflex, Asymmetric Tonic Neck Reflex (ATNR), and Symmetrical Tonic Neck Reflex (STNR), was observed in children with FASD beyond 12 months of age. This delay in the normal suppression of reflexes was strongly correlated with motor and cognitive delays, including difficulty in crawling, walking, and hand-eye coordination tasks. The Moro reflex, in particular, was weak or absent in 45% of cases, suggesting potential deficits in emotional regulation and sensory processing.

**Neurocognitive Impairments:** Children with FASD exhibited significant delays in cognitive milestones, with deficits in language development, speech comprehension, and social skills. A notable percentage (68%) of affected children were diagnosed with attention deficits, and many displayed signs of autism spectrum disorder (ASD) or ADHD-like behaviors. Cognitive assessments indicated IQ scores ranging from mild to moderate intellectual disabilities in 50% of the sample.

**Screening and Diagnostic Tools:** The use of the AUDIT tool for maternal alcohol consumption assessment showed a strong predictive relationship between alcohol intake above 140g per week and the severity of birth defects, particularly low birth weight (LBW). Ultrasound imaging was effective in identifying cerebellar anomalies and other structural irregularities as early as 18–20 weeks gestation, aiding in early diagnosis.

**Impact of Early Intervention:** Early intervention with physical therapy, speech therapy, and behavioral support was associated with improved motor development, language acquisition, and social adaptation. Children diagnosed with FASD and enrolled in early intervention programs showed better progress in meeting developmental milestones compared to those who received delayed or no intervention.

**Differential Diagnosis and Genetic Exclusion:** Differential diagnosis revealed that genetic disorders such as Fragile X Syndrome, Down Syndrome, and cerebral palsy could mimic the clinical presentation of FASD. Genetic screening and karyotyping were crucial in ruling out these conditions, with a significant percentage of children (18%) having co-occurring genetic syndromes.

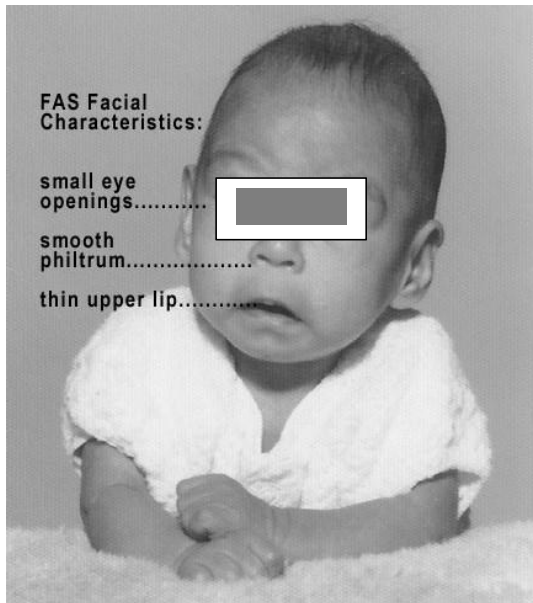
Fetal alcohol syndrome (FAS) is the most severe manifestation of congenital somatic and neurological abnormalities caused by prenatal exposure to alcohol. [1] FASD is a broader diagnosis that includes elements from FAS and others who are prenatal alcohol exposures but do not meet full criteria for FAS.[21]

This behavior is associated with an increased risk of various complications during pregnancy, most notably fetal alcohol syndrome (FAS) and fetal alcohol spectrum disorders (FASD). There is no established "safe" level of alcohol consumption during pregnancy, and alcohol intake at any point during gestation can adversely affect the fetus or neonate. The harmful effects of alcohol consumption during pregnancy are further exacerbated by potential deficiencies in essential nutrients due to this behavior. The primary adverse outcomes associated with alcohol use during pregnancy are fetal alcohol syndrome and fetal alcohol spectrum disorders. Even women who have undergone infertility treatment are not always deterred from alcohol consumption during pregnancy. Currently, education and awareness-raising among pregnant women are considered the most effective strategies for prevention. [2]

The effect of maternal alcohol use during pregnancy can be characteristic of a range of abnormalities that will ultimately present as a spectrum. The consequence of this can be disability, presenting itself in a variety of ways. One of them is imperfect cerebellum. Damage to the cerebellum can result in disorders affecting precise movements, balance, posture, and the ability to learn new movements. The cerebellum plays a crucial role in coordinating voluntary motor activities, maintaining balance, and fine-tuning motor skills. [3]

Prenatal alcohol exposure results in a continuum of effects, with the most severe manifestation being fetal alcohol syndrome (FAS). FAS is characterized by facial dysmorphism, growth deficits, and neurocognitive impairments. The classic facial features associated with FAS include short palpebral fissures, a smooth philtrum, and a thin upper vermilion. [4]

Image.1 [22]



Whether a baby will be born with FASD and the type and extent of damage will depend on many factors. Studies on the relationship between alcohol consumption and pregnancy and the health of newborns indicate that women who drink more than 140 g of pure alcohol per week (or about two drinks per day) are at greater risk of having babies with a lower birth weight. These women are more likely to give birth to babies with a lower birth weight, which can lead to a variety of health problems both in the neonatal period and later in the child's life. Alcohol, especially in large amounts, can affect fetal development, leading to growth retardation, brain damage, and other health problems. As a result, alcohol consumption during pregnancy, especially in excess, is associated with a number of complications, including lower birth weight. [5]

Whether a child is born with Fetal Alcohol Spectrum Disorder (FASD) and the type and extent of any damage depend on several factors, including the maternal and fetal characteristics, the dose and frequency of alcohol consumption, as well as the mother's nutritional status and exposure to other harmful substances. [6] These children may develop disorders such as autism spectrum disorder, ADHD, genetic disorders (e.g. Down Syndrome), and other dysfunctions such as dyslexia, dysgraphia, etc. Children exposed to alcohol prenatally may develop a variety of disorders, including autism spectrum disorders, ADHD, genetic disorders (e.g. Down syndrome), as well as other dysfunctions such as dyslexia, dysgraphia, and others.

None of the aforementioned anatomical abnormalities, however, are pathognomonic for Fetal Alcohol Syndrome (FAS). Therefore, considering the similarity of FAS symptoms to other conditions, including genetic disorders such as Fragile X Syndrome, Cornelia de Lange Syndrome, cerebral palsy, Williams Syndrome, Aarskog Syndrome, Dubowitz Syndrome, Noonan Syndrome, and even maternal phenylketonuria, differential diagnosis is essential to rule out these other conditions. In this context, it is crucial to assess the newborn's karyotype to exclude alternative potential causes of the observed symptoms.[7]

Neuroblasts begin migrating from the matrix cells surrounding the ventricles starting in the second month of fetal development. The sequence of migration corresponds to the phylogenetic age of different regions of the brain. Initially, neuroblasts migrate to the thalamus and hypothalamus (during the 2nd–3rd month), followed by migration to the old cortex (until the end of the 4th month) and the striatum (until the end of the 6th month). [8]

Migration to the new cortex takes the longest and likely continues beyond the fetal period, as indicated by studies conducted by Peter Eriksson and Fred Gage in 1998. [8]

The etiology of central nervous system disorders is of paramount importance, as it can directly impact the fetus, potentially leading to neurodevelopmental abnormalities. A critical factor in understanding this is determining whether the pregnancy was planned or not, and whether alcohol consumption could have been avoided. Even the intake of small amounts of alcohol during pregnancy can disrupt neurodevelopment. This can result in neuronal damage and impaired migration, which in turn affects the proper formation of the cerebellum. Ultimately, this can manifest as coordination, motor function, and balance disorders.

The probability of avoiding adverse life outcomes increases 2-4 times if a diagnosis of Fetal Alcohol Syndrome (FAS) or Fetal Alcohol Effects (FAE) is made at an early age, and the child is raised in a stable, supportive environment. Early diagnosis allows for the prompt implementation of appropriate interventions, which can significantly improve the child's development and mitigate the negative effects associated with prenatal alcohol exposure.[9]

In fetal life, you can be a safe and noninvasive way to diagnose a prenatal child using ultrasound. This study emits in the anatomical structure of the cortical lobes, disconnected from the power source, and impaired growth of the cerebellar hemispheres.[10]

Additionally, studies collecting quantitative data use the AUDIT test, which is recommended by the World Health Organization (WHO). In 2004, the University of Washington published a diagnostic assessment form for FAS. The authors use a 4-digit diagnostic code developed by themselves.[1]

When focusing on the motor characteristics of children affected by FASD, we should mainly pay attention to gross and fine motor skills. In order for the child to be able to function in the future, we should support their physical therapy from the youngest years. Poorly diagnosed children are treated as healthy, thus leading to expectations of proper motor development. Developmental standards, often called milestones, define a recognized pattern of development that children should achieve at different stages of life. They serve as a reference point for assessing typical growth and development in motor, language, cognitive, and social skills. Focusing on motor skills in children up to 3 years of age, this can be illustrated as follows:

Illustration.1 [11]

| Age            | Motor   |
|----------------|---|
| 1–1.5 months   | When held upright, holds head erect and steady.   |
| 1.6–2 months   | When prone, lifts self by arms; rolls from side to back.  |
| 2.1–2.5 months | <ul style="list-style-type: none"> <li>● Rolls from tummy to side [12]</li> <li>● Rests on elbows, lifts head 90 degrees</li> <li>● Sits propped up with hands, head steady for a short time</li> </ul>   |
| 3 months       | <ul style="list-style-type: none"> <li>● Prone: head held up for prolonged periods</li> <li>● No grasp reflex</li> </ul>  |
| 5 months       | <ul style="list-style-type: none"> <li>● Holds head steady</li> <li>● Goes for objects and gets them</li> <li>● Objects taken to the mouth</li> </ul>   |
| 6 months       | <ul style="list-style-type: none"> <li>● Transfers objects from one hand to the other</li> <li>● Pulls self up to sit and sits erect with supports</li> <li>● Rolls over from tummy to back</li> <li>● <u>Palmar grasp</u> of cube hand to hand eye coordination[13]</li> </ul> |
| 9–10 months    | <ul style="list-style-type: none"> <li>● Wiggles and crawls</li> <li>● Sits unsupported</li> </ul>  |



|           |  |
|-----------|--|
|           | <ul style="list-style-type: none"> <li>● Picks up objects with pincer grasp</li> </ul>   |
| 1 year    | <ul style="list-style-type: none"> <li>● Stands holding furniture[14]</li> <li>● Stands alone for a second or two, then collapses with a bump</li> </ul>   |
| 18 months | <ul style="list-style-type: none"> <li>● Can walk alone[15]</li> <li>● Picks up a toy without falling over</li> <li>● Gets up/down stairs holding onto rail</li> <li>● Begins to jump with both feet</li> <li>● Can build a tower of 3 or 4 cubes and throw a ball</li> <li>● Supinate grasping position is usually seen as the first grasping position utilized.</li> </ul> |
| 2 years   | <ul style="list-style-type: none"> <li>● Able to run[16]</li> <li>● Walks up and down stairs using two footsteps per stair step</li> <li>● Builds tower of 6 cubes</li> </ul>  |
| 3 years   | <ul style="list-style-type: none"> <li>● Goes upstairs one footstep per stair step and downstairs two footsteps per stair step[17]</li> <li>● Copies circle, imitates hand motions and draws man on request</li> <li>● Builds tower of 9 cubes</li> <li>● Pronate method of grasping develops</li> </ul>   |

In the case of children with fetal alcohol syndrome (FAS), the presence of primitive reflexes is often observed, which in normal development should cease on their own. These children are particularly susceptible to difficulties in motor skills, such as crawling, sitting, walking, as well as in the area of perception, speech, speech comprehension and acquiring social skills. The persistence of primitive reflexes after 12 months of age is a signal of pathology and immaturity of the central nervous system (CNS)[1]:

Primitive reflexes in children with FAS:

- **Moro reflex** (around the 9th week of fetal life) - this is an automatic reaction to anxiety-provoking situations, leading to sudden arousal, rapid inhalations, release of adrenaline and cortisol, increased heart rate and increased blood pressure. This reflex facilitates the first inhalation after birth. It is replaced by the Strauss reflex (fear, flinch reflex). Failure to suppress the Moro reflex causes an uncontrolled reaction to noise, light, movement, and change of position, which leads to emotional disorders and limited perception. Some children with FAS have a weakened Moro reflex, which makes it difficult to recognize threats and to perceive and interpret the emotions of others.

- **STOS reflex** (symmetrical tonic neck reflex)- helps the child overcome gravity and rise on hands and knees from a prone position. Straightening the head causes the upper body to straighten and the lower body to flex. Bending the head leads to flexion of the arms and straightening of the legs. Failure to suppress the STOS reflex results in difficulties in crawling, moving in a "bear gait" (on hands and feet) or moving on the buttocks. It can also lead to difficulties with posture (slouching), disorders in binocular vision and in eye-hand coordination.

- **ATOS reflex** (asymmetric tonic neck reflex) – appears from the 18th week of fetal life. Turning the baby's head to the side causes the arm and leg on the side the head is turned to straighten, and the limbs to flex on the opposite side. This reflex is intended to facilitate delivery, making it safer. In children with FAS, the development of this reflex is delayed, and if it does not die out by the 6th month of life, it can disrupt normal motor development, leading to unilateral movements (e.g. robot gait), balance problems, difficulties with automatic writing and fluency in reading. This reflex can limit the field of vision and lead to problems with eye movement. In combination with the Moro reflex, it can be one of the risk factors for cot death in infants.

- **Tonic labyrinthine reflex** – associated with the movement of the head forward and backward in the line of the spine, allows the newborn to straighten out from the flexed fetal position. Prolonged activity of this reflex limits the development of other head stabilizing reflexes and interferes with eye function and gravitational stability, which can lead to difficulties in judging distance, speed, and depth. It can also delay the development of crawling and creeping skills.

- **Hand grasp reflex** - appears from the 11th week of fetal life and involves the newborn clenching the fingers in response to touch. If this reflex does not die out, it can inhibit the development of precise movements of the hand and thumb, making it difficult to move the fingers independently, speak, move the mouth, and coordinate fine motor skills.

The persistence of these primitive reflexes in children with FAS indicates a developmental disorder of the CNS and requires therapeutic interventions to support proper motor and emotional development.

### **Conclusions:**

Fetal Alcohol Syndrome (FAS) and Fetal Alcohol Spectrum Disorders (FASD) represent a continuum of developmental abnormalities resulting from prenatal alcohol exposure. These disorders are characterized by a range of neurodevelopmental and somatic impairments, with the most severe form, FAS, presenting with distinctive facial dysmorphism, growth deficiencies, and significant neurocognitive impairments. Alcohol consumption during pregnancy, regardless of timing or amount, can disrupt fetal development and result in lasting physical, cognitive, and motor deficits. The cerebellum, critical for motor coordination and balance, is particularly vulnerable to alcohol-induced damage, leading to motor dysfunctions such as difficulty with posture, movement, and learning new motor skills. Early diagnosis of FASD, along with timely intervention, is crucial in mitigating developmental delays and improving long-term outcomes for affected children. Additionally, identifying these conditions early allows for the implementation of supportive therapies, particularly in the domains of motor skills and emotional development, which are often impaired due to persistent primitive reflexes and CNS immaturity. Preventive measures, including alcohol use screening and education, remain the most effective strategies to reduce the incidence of these preventable disorders. Given the complexity and variability of FASD, differential diagnosis is essential to rule out other genetic and neurological conditions, emphasizing the importance of a comprehensive clinical evaluation.

**Conceptualization:** SA, and MP; methodology, SA; software, KS, SA; check, JW, UZ and WF; formal analysis, KD; investigation, MP; resources, WD; data curation, JD; writing - rough preparation, MP, SA; writing - review and editing, GT; visualization, SA; supervision, JW; project administration, JW; receiving funding, JŚ. All authors have read and agreed with the published version of the manuscript.

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