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Italian Guidelines for the diagnosis and treatment of Fetal Alcohol Spectrum Disorders: clinical hallmarks

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Summary. Fetal Alcohol Spectrum Disorders (FASD) are a condition that arises when a person is exposed to alcohol during pregnancy. The main clinical manifestations include craniofacial anomalies, growth retardation, birth defects and change in brain structure and function. These alterations can result in deficits across various domains such as cognition, executive function, memory, vision, hearing, motor skills, behavior, and social adaptation. The effects of alcohol extend beyond the brain, affecting other systems including sensory organs, heart, and kidneys. Given that diagnosing FASD involves excluding other conditions, it is crucial for physicians to be familiar with its main characteristics to facilitate early identification and implement appropriate health strategies for the patient. Moreover, there is a pressing need for primary prevention strategies centered around raising awareness about the risks associated with alcohol consumption during pregnancy. The articles for this report aimed to analyze and evaluate studies focusing on the clinical features observed in FASD children were sourced from online databases such as Medline, Medline Complete and PubMed, covering literature published between 1981 and 2024, written in English, using search terms such as fetal alcohol spectrum disorders, fetal alcohol syndrome, prenatal alcohol exposure, and alcohol-related birth defects. The evidence gathered underscores that prenatal alcohol exposure primarily affects the brain and its functions, resulting in severe impacts. Furthermore, abnormalities in other vital organs such as the sensory, cardiovascular, and renal systems are frequently observed.

Key words. Alcohol-related birth defects, fetal alcohol spectrum disorders, fetal alcohol syndrome, prenatal alcohol exposure.

Linee guida italiane per la diagnosi e il trattamento dei disturbi dello spettro feto-alcolico: caratteristiche cliniche.

Riassunto. Il disturbo dello spettro feto-alcolico (FASD) è una condizione che si verifica quando una persona è esposta all'alcol durante la gravidanza. Le principali manifestazioni cliniche includono anomalie craniofacciali, ritardo della crescita, difetti alla nascita e cambiamenti nella struttura e nella funzione del cervello. Queste alterazioni possono causare deficit nelle capacità cognitive, nella funzione esecutiva, nella memoria, nella vista, nell'udito, nelle capacità motorie, nel comportamento e nell'adattamento sociale. Gli effetti dell'alcol si estendono oltre il cervello, influenzando altri sistemi tra cui organi sensoriali, cuore e reni. Dato che la diagnosi di FASD implica l'esclusione di altre condizioni, i medici devono avere familiarità con le sue caratteristiche principali per facilitare l'identificazione precoce e implementare strategie sanitarie appropriate per la paziente. Inoltre, c'è un'urgente necessità di strategie di prevenzione primaria incentrate sulla sensibilizzazione sui rischi associati al consumo di alcol durante la gravidanza. Gli articoli estratti in questa rassegna mirano ad analizzare e valutare studi incentrati sulle caratteristiche cliniche osservate nei bambini con la FASD; sono stati reperiti da database online come Medline, Medline Complete e PubMed, che coprono la letteratura pubblicata in lingua inglese tra il 1981 e il 2024, utilizzando termini di ricerca come disturbi dello spettro feto-alcolico, sindrome feto-alcolica, esposizione prenatale all'alcol e difetti alla nascita correlati all'alcol. I dati sottolineano che l'esposizione prenatale all'alcol colpisce principalmente il cervello e le sue funzioni, con conseguenti gravi impatti. Inoltre, si osservano frequentemente anomalie in altri organi vitali come i sistemi sensoriale, cardiovascolare e renale.

Parole chiave. Difetti congeniti legati all'alcol, disturbi dello spettro feto-alcolico, esposizione prenatale all'alcol, sindrome feto-alcolica.

Introduction

Prenatal alcohol exposure (PAE) can cause birth defects and developmental disabilities, collectively referred to as fetal alcohol spectrum disorders (FASD). Maternal alcohol consumption results in fetal exposure through placental diffusion and distribution fetal tissues via amniotic fluid accumulation, disrupting the normal development of the baby's organs and tissues[1,2]. Additionally, low concentrations of fetal metabolic enzymes prolong alcohol elimination. Coupled with amniotic reuptake, this leads to

extended exposure and potential adverse effects[3]. FASD encompasses a wide range of symptoms and signs, such as birth defects, craniofacial anomalies, growth retardation, neurological abnormalities, and cognitive and behavioral impairments[4-7].

The term FASD includes different conditions resulting from PAE, including[8]:

- *Fetal Alcohol Syndrome* (FAS): This represents the most severe form of FASD, characterized by specific physical, cognitive, and behavioral alteration. FAS should be strictly used to describe individuals exhibiting the triad of facial dysmorphology, growth retardation and neurocognitive deficits, regardless of whether there is confirmed maternal alcohol consumption during pregnancy[9];
- *Partial Fetal Alcohol Syndrome* (pFAS): this term applies to patients who display some, but not all, of the characteristic features of FAS[10];
- *Alcohol-Related Neurodevelopmental Disorder* (ARND): this category includes individuals with confirmed maternal prenatal alcohol use and evidence of neurobehavioral impairment, but without the FAS-associated physical features[11];
- *Alcohol-Related Birth Defects* (ARBD): individuals diagnosed with ARBD have documented PAE and present with one or more physical abnormalities, such as those affecting the heart (e.g., atrial septal defects, ventricular septal defects), kidneys (e.g., hypoplastic kidneys, hydronephrosis), eyes (e.g., strabismus, retinal vascular abnormalities), bones (e.g., scoliosis, hemivertebrae, clinodactyly) and ears (e.g., conductive or sensory hearing loss)[10].

Even though variations in physiologic parameters (height, weight, and cranial circumference), and anomalies in facial structure are the prominent signs of the syndrome, the central nervous system damages are more dramatic and invalidating since they compromise a regular neuro-behavioral development[12]. Unfortunately, no treatment has been discovered to reverse the alcohol-induced damage to the CNS. Early intervention during pregnancy in alcohol-abusing mothers holds the key to mitigating the severity of FASD[13]. Despite the well-known risks of alcohol consumption during pregnancy and its potential to cause FASD, some pregnant women continue to drink alcohol.

The prevalence of alcohol consumption during pregnancy varies among countries, being on average the lowest (0.2%) in countries in the Eastern-Mediterranean region, and on average the highest in countries in the European region (25%)[14]. Determining the exact number of children affected by FASD is challenging. Estimates suggest that FASD affects between 2% and 5% of individuals in the United States and Western Europe, with variations depending on the country and epidemiological methodology employed[15].

The clinical assessment of the presence or absence of clinical features should be integrated into the dysmorphology evaluation of children suspected of having FASD. The dysmorphology score, an updated system based on objective observations of growth and minor anomalies in 370 children with FASD, quantifies the overall dysmorphic variation in each child (table 1)[10].

This score facilitates objective comparisons among groups of children with FASD and serves as a valuable research tool. Furthermore, it aids in the differential diagnostic process when evaluating characteristics of genetic or other teratogenic disorders that may resemble FASD (table 2)[16-18]. The score has been found to significantly correlate with prenatal maternal alcohol intake and with the cognitive and neurobehavioral characteristics of children with FASD[1].

Table 1. Dysmorphology Scoring System (a weighted score based on the analysis of the frequency of growth restriction and minor anomalies in 370 children with FAS)[10].

Feature	Score	No. Affected
OFC ≤10%	3	354
Growth deficiency		
Height ≤10%	2	327
Weight ≤10%	1	322
Short PFL (≤10%)	3	313
Smooth philtrum	3	307
Thin vermilion	3	293
Hypoplastic midface	2	216
Epicanthal folds	2	204
Decreased IPD or ICD (≤25%)	2	202/204
Flat nasal bridge	2	179
Altered palmar crease	2	173
Fifth-finger clinodactyly	2	149
Long philtrum (≥90%)	2	122
Anteverted nares	2	118
Camptodactyly	2	114
Ptosis	1	64
"Railroad track" ears	1	57
Heart murmur or confirmed CHD	1	50/6
Strabismus	1	35
Limited elbow supination	1	31
Hypoplastic nails	1	23
Prognathism	1	21
Hypertrichosis	1	19
Total possible score	**41**	

Legend: OFC= occipitofrontal circumference; PFL= palpebral fissure length; IPD= inter pupillary distance; ICD=- inner canthal distance; CHD= congenital heart defects.

Table 2. Genetic and teratogenic conditions to be considered in the differential diagnosis of FASD.

Malformation syndrome	Etiology	Clinical features
Cornelia de Lange syndrome	Autosomal dominant (Mutations in NIPBL, 60%)	Mild to severe phenotypic spectrum characterized by poor growth, developmental delay, hypertrichosis, and characteristic facial dysmorphisms. These include the synophrys, short depressed nasal bridge with anteverted nostrils, microcephaly, micrognathia, long philtrum, and thin lips[20].
Noonan syndrome	Autosomal dominant (Mutations in RAS-MAPK signal transduction pathway genes, PTPN11, SOS1, KRAS, NRAS, and others)	Congenital heart defects, short stature, varying degrees of developmental delay, and characteristic facies including a broad forehead, hypertelorism, down-slanted palpebral fissures, and posteriorly rotated ears. The phenotype is very variable and epicanthus and depressed nasal bridge may also be present among the dysmorphisms[21].
Dubowitz syndrome	Autosomal recessive	Mental and growth retardation (including prenatal), multiple congenital anomalies and immunological defects, as well as peculiar facial features such as broad forehead, narrow palpebral fissures, ptosis, wide and flat nasal root, hypertelorism and epicanthus[22].
Williams-Beuren syndrome	Chromosome microdeletion (del 7q11.23, a contiguous gene syndrome incorporating the elastin gene)	Cardiovascular problems (especially supravalvular stenosis of the aorta), the peculiar appearance of the face (small head, broad forehead, narrow palpebral fissures, long philtrum, epicanthus), developmental delay of varying degrees and growth retardation[23].
22q11.2 microdeletion syndrome	Chromosome microdeletion (del 22q11.2)	High phenotypic variability characterized by congenital heart abnormalities, hypocalcemia, typical facies with small mouth, narrow palpebral fissures, small pinnae, prominent nose, hypertelorism and micrognathia, low birth weight, neurodevelopmental deficit and disorders of the immune system[24].
Blepharophimosis, ptosis, and epicanthus inversus (BPES)	Heterozygous mutations (FOXL2 gene); cases of homozygosity have rarely been reported.	Eyelid abnormalities: narrow palpebral fissures (blepharophimosis), inverse epicanthus, drooping eyelids (ptosis) and increased distance between the inner corners of the eyes (telecanthus)[25].
3-M syndrome	Autosomal recessive (CUL7 gene); rarely the OBSL1 and CCDC8 genes.	Pre- and postnatal growth retardation, low birth weight, normal psychomotor development and distinctive dysmorphisms including triangular face, prominent forehead, midfacial hypoplasia, long philtrum, depressed nasal bridge and full lips[26].

Materials and methods

Articles for this narrative eview were sourced online from databases such as Medline, Medline Complete, PubMed, and Health Source: Nursing/Academic Edition. The search within these databases was limited to the human population, publications dated between 1981 and 2024, and articles written in English. Keywords included but were not limited to: "fetal alcohol spectrum disorders," OR "fetal alcohol syndrome," OR "prenatal alcohol exposure," OR "alcohol-related birth defects".

As far as study selection and inclusion criteria are concerned, only the most relevant full-text articles published in English and analyzing the clinical characteristics of FASD were considered eligible. To highlight the state of actual clinical evidence, animal models were excluded in the analysis of the main results related to the comprised pathologies. Investigators independently screened and assessed titles and abstracts before retrieval of the full manuscripts.

The selected full papers were reviewed for eligibility according to the inclusion criteria and clinical relevance. References in the selected papers were scrutinized for additional articles in a further effort to ensure that relevant publications were not missed. All controversies concerning study selection or data extraction were resolved by consensus with a third group of reviewers. Evidence from available literature is presented in this review in a narrative way to offer a clear overview of the many findings.

Clinical presentation

Craniofacial dysmorphology

The most frequent features of craniofacial dysmorphology include short palpebral fissures, a smooth

philtrum, and a thin upper lip vermilion (figure 1)[28]. Identifying craniofacial dysmorphology is pivotal for diagnosis when developmental brain abnormalities, neurobehavioral deficits, or a history suggestive of PAE are present. The dysmorphic features, however, are not commonly recognized[10]. In addition, PAE is associated with minor physical anomalies, such as railroad-track ears, ptosis, epicanthal folds, anteverted nares, midface hypoplasia, joint contractures, camptodactyly, and altered palmar creases[29]. Even though none of these features are diagnostic of FASD, the number of minor physical anomalies correlates with the extent of PAE[10].

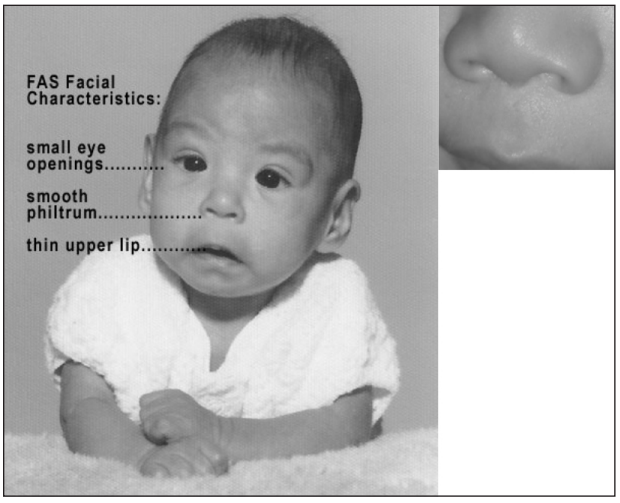

Figure 1. FAS baby showing some of the characteristic facial features. In the right upper panel is shown the smooth philtrum seen on a six-month-old FAS baby. Images free of use under CC BY-SA 3.0 and CC BY-SA 4.0 licenses. See also for further info Teresa Kellerman - http://www.come-over.to/FAS/fasbabyface.jpg.

Growth retardation

Growth retardation is defined as falling at or below the 10th percentile on standard growth curves for height and weight measurements[8]. PAE detrimentally impacts fetal growth, especially when exposure occurs during the periconceptional period or the second trimester[30]. Cho et al. investigated the association between maternal alcohol consumption and fetal growth restriction in 95,761 pregnant Japanese women. They discovered that maternal alcohol consumption in the second/third trimester exceeding 5, 20, and 100 g/week might affect fetal growth in terms of body weight, body length, and head circumference, respectively[15]. Growth retardation in FASD is likely not attributed to a deficiency of growth-promoting hormones, but rather to peripheral unresponsiveness[31].

Neuropathological abnormalities

The brain is the most severely impacted organ in FASD. The variety of neuropathological alterations observed in FASD stems from various interacting factors, including the variability of alcohol timing and dosage, nutrition, genetics, and comorbid substance abuse. For instance, alleles of the alcohol dehydrogenase gene *ADH1B* accelerate alcohol metabolism and mitigate alcohol teratogenicity[7]. The large variability in neuropathological findings among individuals with PAE poses a challenge in defining diagnostic criteria and necessitates categorizing fetal alcohol disorders as a spectrum, rather than a single diagnostic entity[32]. Several researches have investigated brain structure, development, and abnormalities, using magnetic resonance imaging (MRI) techniques[33]. The aim of these MRI studies was to examine brain structures and regions and elucidate the nature of brain abnormalities associated with PAE[34]. One of the most common observations in individuals exposed to alcohol in utero is reduced brain volumes, including diminished volumes of white and gray matter within the brain[35].

Another typical finding is malformations of the corpus callosum[36]. MRI imaging has revealed complete and partial agenesis, indicating the organ's failure to fully develop, as well as callosal thinning. The splenium, which facilitates communication between the parietal and temporal lobes, fundamental for linking visual areas, has also been reported to be severely affected by being displaced inferiorly and anteriorly[37]. Additionally, the more severe the anterior displacement, the more detrimental the impact on verbal learning ability[38]. The frontal lobes are also affected, determining alterations in attention and working memory. The left hemisphere of the ventral frontal lobe demonstrates decreased volume, while the right ventral frontal lobe shows increased cortical thickness[39]. The temporal lobes, involved in memory formation, auditory processing, and language comprehension, are impacted similarly to the parietal lobes. Studies have indicated significantly reduced activation in the left medial and posterior temporal regions in individuals with FASD[40].

The parietal lobes, associated with visuospatial functions and attention, are impacted similarly to the temporal lobes. Sowell et al. observed a reduction in white matter alongside bilateral increased thickness of parietal lobes[41], suggesting an excessive amount of gray matter, possibly due to lessened myelination of white matter or incomplete neuronal pruning. The subcortical region just below the cerebral cortex, known as the "subcortical region", is also heavily affected. Structures such as the basal nuclei, particularly the caudate nucleus within the basal nuclei, exhibit smaller size, resulting in compromised motor control, learning abilities, and behavioral inhibition[42]. A study involving 72 children affected by FASD detected alteration in the cerebellum, vascular anomalies, gliosis, perivascular space dilation, pituitary hypoplasia, ventriculomegaly, cavum septum

pellucidum, and a simplified gyral pattern[43]. Remarkably, the hippocampus appeared to be the only subcortical structure that was unaffected[40].

Neurological deficits

Possible neurological system defects are non-specific, but children affected by FASD can show alterations such as hypotonia, cranial nerve abnormalities, reflex changes, limb and gait ataxia, coordination issues, balance problems, and dysarthria, identifiable through neurological examination[44,45]. Infants exposed to alcohol may also display delays in walking and problems with balance and coordination[46]. Lucas et al. conducted a systematic review and meta-analysis of 11 studies, demonstrating that children (mean age 3 days to 13 years) diagnosed with FASD or exposed to moderate (2 to ≥14 drinks per week) to heavy (>10 to 28 drinks per week) or binge (≥5 drinks per occasion) PAE exhibited deficits in gross motor functioning more frequently compared to children without PAE[47].

Moreover, PAE was linked to larger foot angles, increased step width, and greater gait variability compared to non-exposed children. In addition, a review of 24 studies indicated that fine motor deficits (e.g., visual-motor integration problems) were more frequent in children with FASD. These deficits were associated with lower fine motor composite scores and manual coordination scores, as well as poorer graphomotor skills (e.g., handwriting and grasping), compared to healthy controls[48]. Fine and gross motor deficits are frequently detected in children with FASD using standardized tests (e.g., Bruininks-Oseretsky Test of Motor Proficiency)[49].

Neuropsychological disorders

Individuals with FASD might manifest developmental delay during infancy, but a single assessment is insufficient. Indeed, neurobehavioral alterations manifest differently at various ages. Cognitive impairments range from profound intellectual disability to specific deficits in attention, executive function, memory, visual-spatial and visual-motor abilities, and academic performance (e.g., reading and mathematics)[50,51]. Emotional and behavioral disorders may present as inappropriately excessive or deficient behavior[52,53]. It is recognized that conditions such as hyperactivity, impulsivity, aggression, and poor social skills can affect school and workplace performance and might lead to criminal justice connections[54]. Naturally, attributing adverse social outcomes solely to FASD is challenging, as they may also be influenced by individuals' disruptive social circumstances, such as living in foster homes, exposure to violence, physical and sexual abuse, and poverty[53].

Skeleton system

The impact of PAE on skeletal growth remains relatively unexplored in clinical populations. Young et al. found that children with FASD were shorter and exhibited lower areal bone mineral density and lean tissue mass compared to typically developing peers[55]. Other observed findings in children included congenital scoliosis and fusion of upper limbs, such as radio-ulnar synostoses[56].

Sensory system

Individuals with FASD often display deficits in processing across all sensory modalities[57,58]. Alcohol can affect brain regions and sensory neurons involved in odor and taste perception, leading to impaired odor identification in children with FASD[59]. Ocular function and morphology can also be affected by the effects of alcohol on fetal development, resulting from two possible mechanisms: direct cellular toxicity and indirect alterations to the normal inductive effect of adjacent brain tissue. Complete ophthalmologic examinations in children with FASD commonly reveal alterations such as strabismus. epicanthus, blepharoptosis, telecanthus, nystagmus, and cataract[60]. Ocular fundus abnormalities found in FASD include anomalies of the retinal fundus and minor changes in the outer region of the eyes[61], with ocular abnormalities often presenting asymmetrically[62].

Furthermore, conductive, sensorineural, and central hearing loss have been reported[63], leading to impaired speech and language communication due to auditory processing disorders[64]. In individuals with FASD, language development alterations compound neurocognitive deficits, contributing to attention and memory problems. In fact, cognitive deficits range from profound intellectual impairment to specific disorders in attention, executive functioning, memory, visual-spatial and visual-motor abilities, and academic performance (e.g., reading and mathematics)[65].

Cardiac abnormalities

Although extensive research has been conducted on the impact of maternal alcohol consumption on congenital heart defects (CHDs), the conclusions remain inconsistent. A recent meta-analysis of 20 studies investigated the association between PAE and the risks of CHDs and CHDs subtypes, concluding that PAE was significantly associated only with the conotruncal defects (CTDs) subtypes[66,67], which represent congenital malformations of the outflow tract of the heart. In addition, alcohol consumption during pregnancy was significantly associated with transposition of the great arteries (d-TGA), a subtype of CTDs in which the aorta is connected to the right ventricle

and the pulmonary arteries are connected to the left ventricle, resulting in oxygenated blood flowing into the lungs and deoxygenated blood flowing into the body. Mothers who consumed alcohol during pregnancy were found to be 1.64 times more likely to have a newborn with d-TGA. The evidence also indicates that both prenatal heavy drinking and binge drinking were strongly associated with the overall risk of CHDs[13].

Renal abnormalities

The association between FASD and kidney birth defects remains inconclusive. A systematic review found nonspecific abnormalities linked to FASD across three organ systems (kidney, liver, and gastrointestinal tract)[68]. Kidney anomalies include hypoplasia (underdevelopment of the organ), agenesis (absence of the kidney), and hydronephrosis (kidney swelling due to abnormal drainage)[68].

Nutrition implications

The consumption of alcohol during pregnancy can also altered the maternal nutritional status that is crucial for proper fetal development, although the specific interactions are not well understood[69]. Poor maternal nutrition is a significant problem in FASD, as the nutrients essential to support fetal development and preserve maternal health are often deficient with heavy alcohol use[70]. For this reason, recently, much attention has been paid to the role of nutrition as a protective factor against alcohol teratogenicity. There are a great number of papers related to nutritional treatment of nutritional deficits due to several factors associated with maternal consumption of alcohol.

Although research showed the clinical benefits of nutritional interventions, most of work was in animal models, in a preclinical phase, or in the prenatal period. However, a minimum number of studies refer to postnatal nutrition treatment of neurodevelopmental deficits. In particularly, Young et al. focus on different nutrients (vitamin A, docosahexaenoic acid, folic acid, zinc, choline, vitamin E, and selenium) that may prevent or alleviate the development of FASD. Unfortunately, since FASD is the consequence of multiple metabolic impairments, supplementation with 1 nutrient may not be effective to fully reverse the damage induced by alcohol consumption[13]. Another research showed that, compared to National Health and Nutrition Examination Survey (NHANES) sample, children with FASD had lower intakes of saturated fat, vitamin D, and calcium. The majority (> 50%) of children with FASD did not meet the Recommended Dietary Allowance (RDA) or Adequate Intake (AI) for fiber, n – 3 fatty acids, vitamin D, vitamin E, vitamin K, choline, and calcium[71]. These findings indicate that these children are vulnerable to nutritional inadequacies. Furthermore, data recommend a specific profile of dietary intake in this population. As several nutrients are important for cognitive development, targeted interventions in clinical populations might be effective in boosting outcomes[72]. Since nutrient deficiencies may exacerbate FASD, nutrient supplementation may reduce risk by ameliorating inadequate nutritional state or by acting via pathways that positively influence development. Consequently, managements of nutritional status both during or after pregnancy may help as potential interventions for FASD. In addition, considering the role of nutrients on brain and behavioral development, nutritional supplements may successfully reduce the severity of symptoms in children with FASD, whether compensating for nutritional deficiencies or by acting on pathways that enhance behavioral and cognitive functioning[69]. In conclusion, nutritional supplementation in children with FASD could have a dual objective: to overcome nutritional deficiencies and to reverse or improve the cognitive deleterious effects of prenatal alcohol exposure. During the care of children with FASD, a continuous evaluation of nutritional status, height, and weight is necessary. When nutritional problems are identified, it is important to consider also nutritional support, to improve the care of the child with FASD, since some children will require high-calorie foods and supplements. Further research is necessary to determine optimal amounts of nutrients needed in supplementation, and to investigate the collective effects of simultaneous multiple-nutrient supplementation.

Conclusions

FASD arises from alcohol exposure during pregnancy and is associated with craniofacial abnormalities (e.g., small palpebral fissures, flattened philtrum, and thin upper lip)[10], as well as various neuropathological anomalies and related cognitive, behavioral, and social impairments[73]. Given that FASD represents a significant global public health concern, often underrecognized and underdiagnosed despite its high prevalence[74,75], it is imperative for pregnant mothers to understand that the only way to prevent this untreatable condition is to abstain from drinking during pregnancy[76,77]. Early recognition of potentially affected children is crucial for providing appropriate medical care and initiating interventional behavioral strategies. However, diagnosing FASD remains primarily clinical, and the lack of a single diagnostic guideline contributes to diagnostic challenges[78]. A comprehensive assessment, including prenatal, medical, and family history along with a thorough

physical examination, is essential to ensure accuracy in diagnosis.

Furthermore, genetic and malformation syndromes must be considered in the differential diagnosis, and FASD should remain a diagnosis of exclusion[79,80]. To provide the most comprehensive approach to the management and treatment, evaluation by a multidisciplinary team consisting of a dysmorphologist/clinical geneticist, pediatric, neuropsychologist or psychologist and education specialist is recommended. Increased awareness of the clinical presentations of FASD can empower physicians to provide patients with education, comorbidity assessment, and appropriate referrals. Enhanced recognition of FASD and greater awareness of the risks of PAE could spur public health initiatives aimed at reducing alcohol-exposed pregnancies, improving diagnostic tools, and developing treatments addressing the effects of PAE across multiple levels of functioning.

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