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Fetal alcohol spectrum disorders:
Prevention, identification, and intervention

Abstract: Fetal alcohol spectrum disorders (FASD) remain a common cause of intellectual disability in infants and children, with an estimated incidence of 9.1 out of every 1,000 U.S. live births. This article discusses methods for identifying and assisting women who consume alcohol prenatally and referring infants and children with FASD for intervention.

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Fetal alcohol spectrum disorders (FASD) describe a group of conditions seen in individuals who experienced prenatal alcohol exposure (PAE). FASD remain one of the most common causes of intellectual disability, with an estimated incidence of 9.1 out of every 1,000 live births in the United States.[1] FASD, along with the most severe form, fetal alcohol syndrome (FAS), has serious and long-term consequences for infants, families, and communities. No known safe limits currently exist for maternal alcohol consumption during pregnancy.[1-3]

Although the public has been warned about the risks of birth defects related to PAE since mandatory labeling of alcoholic products began in 1988, alcohol use during pregnancy continues; therefore, identifying pregnant women who consume alcohol remains an important clinical and public health issue.[4,5]

Alcohol consumption during pregnancy

The National Institute on Drug Abuse indicates that alcohol consumption during pregnancy ranges from 17% (ages 15 to 17) to 10% (ages 26 to 44).[6] The National Survey on Drug Abuse and Health reported one in eight pregnant women ages 15 to 44 admitted to drinking alcohol during their pregnancies.[7] The CDC reports that alcohol consumption among women of reproductive age (18 to 44) ranges from 25.2% in Utah to 69.6% in Washington, D.C.[8]

The effects of PAE in the infant and child can be difficult to detect because the signs and symptoms can vary significantly. Identifying those with FASD is challenging in part due to insufficient information on maternal drinking risks.[9,10] Individuals at greatest risk for having a child with FASD are sexually active, reproductive-age women who consume alcohol.[11]

Etiology/pathophysiology

The exact etiology of the characteristics seen in children with PAE remains under investigation and is confounded by covariables of tobacco use, poor maternal nutrition, poverty, and poor prenatal care. It is known that alcohol is a teratogen that freely crosses the placenta and may interfere with fetal

Keywords: alcohol use, child health, fetal alcohol spectrum disorders, fetal alcohol syndrome, infant health, pregnancy, prenatal alcohol exposure, substance use, women's health

development, which causes FASD. The pattern of alcohol consumption—higher amount, faster rate, and/or greater frequency—is the key teratogenic factor.[12]

Once alcohol crosses the placenta, it enters the fetal circulation. Research has shown that fetal blood alcohol levels vary significantly, from one-third to twice that of the mother's blood alcohol level.[13] Fetal blood alcohol exposure is compounded by the immaturity of the fetal liver, compromising the ability of the fetus to metabolize alcohol. In addition, nonmetabolized alcohol is excreted into the amniotic fluid via fetal lungs and urine and is available for reingestion as the fetus swallows amniotic fluid.[13] This extends the anticipated exposure period significantly.

Because neural cell growth takes place on a continuum throughout gestation, the presence of alcohol at any time during pregnancy creates the risk of permanent changes in neural development. Studies reveal significant differences in brain volume between individuals with FASD and those without. Most of these changes occur in the deep gray matter and subcortical regions of the brain and could be correlated with the degree of alteration in the facial features and neurobehavioral deficits noted in FASD.[14]

Children with FASD are characterized by wide-ranging deficits and anomalies in growth, anatomy, behavior, and cognition.[15] Characteristics of FAS include prenatal and/or postnatal growth restriction, central nervous system (CNS) dysfunction (with or without obvious brain malformation), and a characteristic pattern of craniofacial malformation.[9] FASD dysfunctions include learning disabilities, intellectual disability, poor executive function, attention problems, and several specific behavioral problems, such as poor communication skills (talking too fast and interrupting others), emotional lability, and difficulty reading facial expressions (putting the individual at risk for social isolation).[9,15,16]

Current healthcare recommendations from the U.S. federal government and the American Congress of Obstetricians and Gynecologists (ACOG) urge women to completely avoid drinking alcohol during pregnancy.[2,17-19] The important clinical tasks for advanced practice registered nurses (APRNs) include counseling women on the importance of abstinence from alcohol while pregnant; identifying women with heavy prenatal drinking patterns, which put the fetus at greater risk for FASD; and identifying and referring infants and children with FASD.

Clinical presentation in women

Accurately detecting alcohol consumption in women of reproductive age can be difficult. Clinicians have reported multiple barriers to screening their patients for alcohol use, such as gaps regarding best practices for alcohol use screening during pregnancy and a lack of financial and system support for screening and brief interventions.[20]

In addition, women often underreport their alcohol consumption, especially during pregnancy. However, to potentially prevent PAE, the primary care APRN must employ alcohol screening in order to provide an opportunity for early identification of alcohol use in pregnant women; education to raise awareness of the dangers of alcohol use, including PAE and FASD; and additional alcohol-focused interventions and referrals when needed (see *Alcohol screening questionnaires*). Women identified with an alcohol use disorder may need referral for detoxification or treatment.

The most frequently recommended tools for identifying heavy drinking in pregnant women include the Tolerance, Annoyance, Cut-down, Eye-opener (T-ACE), Tolerance, Worried, Eye-opener, Amnesia, K/cut-down (TWEAK), and the Alcohol Use Disorders Identification Test-Consumption (AUDIT-C).[21,22] The T-ACE and TWEAK are validated for use with pregnant women.[23,24] The Car, Relax, Alone, Forget, Friends, and Trouble (CRAFFT) Screening Interview has been validated among adolescents ages 14 to 18 and used successfully to identify levels of alcohol and other substance use in pregnant adolescents.[25,26] The Timeline Followback (TLFB) Procedure, a more extensive interview technique, has been validated for use in various settings with good sensitivity but is not practical for use in many clinic settings due to time limitations.[27]

The ACOG Toolkit incorporates the standard T-ACE and, while widely available for use by healthcare providers, it is underused due to the previously discussed barriers.[2,28,29] The T-ACER3, a brief, easy-to-use screen, is feasible for nursing practice in clinical and private settings and expands the usefulness of the T-ACE.[30] The T-ACER3 identifies risk drinkers with increased specificity compared to the T-ACE and little reduction in sensitivity.[30]

The questions on the T-ACE and the T-ACER3 are identical; the only change is the total score cut-point (in other words, the score above which further investigation is recommended), which was increased from 2 to 3, respectively. The T-ACER3 cut-point identifies fetal risk level drinking with improved selectivity and improves identification of nondrinking mothers and their infants who are at lower risk of FASD.[30,31] The higher T-ACER3 cut-point also improves prediction of child neurobehavioral outcomes. Effective screens for risk drinking during pregnancy afford greater opportunities for interventions, which could decrease the risk of PAE and assist with earlier identification of infants at risk for FASD.

A long history of research focuses on identifying and examining biomarkers for either chronic alcohol use by perinatal women or infant PAE.[32,33] Gamma-glutamyltransferase, mean corpuscular volume, and carbohydrate deficient transferrin were among the earliest identified maternal serum biomarkers of alcohol-induced pathology.[32,33] These indirect biomarkers identify chronic maternal alcohol use.

Alcohol screening questionnaires[20,23-25,30]

Tool and date developed	Populations	Structure	Advantages/disadvantages
AUDIT-C 1998	Adults, pregnant women	• 3 items, derived from the AUDIT-C questionnaire (score range 0 to 12) • Cut-point >3 (a score of 3 or more requires further assessment)	• Can be completed in less than 2 minutes
CRAFFT 1999	Adolescents ages 14 to 18 including pregnant adolescents	• 6 items (CRAFFT score range 0 to 6) • Cut-point <2 (a score of 2 or more requires further assessment)	• Highly correlated with the Personal Involvement with Chemicals Scale
T-ACE 1989	Adults, pregnant women	• 4 items derived from MAST and CAGE questionnaires (T-ACE score range 0 to 5) • Cut-point >2 (a score of 2 or more requires further assessment)	• Can be completed in about 1 minute • Specifically developed for determining if pregnant women are using alcohol to excess
T-ACER3 2014	Adults, pregnant women	• 4 items derived from T-ACE questionnaire (T-ACER score range 0 to 5) • Cut-point >3 (a score of 3 or more requires further assessment)	• Can be completed in about 1 minute • Specifically developed for determining if pregnant women are using alcohol to excess
TWEAK 1979	Adults, pregnant women	• 5 items derived from CAGE and MAST questionnaires • Scores range from 0 to 7 • Cut-point >2 (a score of 2 or more requires further assessment)	• Can be completed in about 1 minute • Specifically developed to determine if pregnant women are using alcohol to excess

Maternal biomarkers for identification of heavy alcohol use are less plentiful, however, and their usefulness is limited. More sensitive and reliable biomarkers capable of detecting alcohol use or exposure for longer periods of time than those currently available need to be developed.[32,33]

Alcohol use: Treatment of pregnant and lactating women

Interventions aimed at preventing alcohol use among pregnant women and women of reproductive age who may become pregnant are among the top recommendations for preventing FAS and other FASD.[33,34] Referral or collaboration with the patient's nurse midwife or obstetrician is recommended. However, women who are identified with an alcohol use disorder, a history of daily alcohol use, or positive blood alcohol results may require additional assistance to safely eliminate alcohol from their bodies.

The risk of alcohol withdrawal syndrome must be included in the discussion when counseling on the dangers of alcohol and encouraging abstinence. Withdrawal protocols include monitoring vital signs, respiratory status, mental status, temperature, and urine output. The Clinical Institute Withdrawal Assessment for Alcohol, revised (CIWA-Ar) is a validated and commonly used tool to evaluate the patient's withdrawal status and assist with determining medication needs.[35] Guidelines from the World Health Organization (WHO) for managing substance use and substance use disorders during pregnancy recommend inpatient detoxification for pregnant women (when possible) to monitor the woman and fetus.[36]

Medications are often needed to prevent or decrease the severity of withdrawal symptoms for safe alcohol detoxification. A careful evaluation, including a risk benefit analysis, is necessary when considering the use of medications to treat alcohol use disorders in pregnant women. Medications used to treat alcohol use and symptoms of alcohol withdrawal are classified as pregnancy category C. Potential benefits may warrant medication use in pregnant women despite potential risks.[37,38]

In compliance with new FDA drug label guidelines, information on drug labels related to pregnant and nursing women will change.[39] The lettering system A, B, C, D, and X will be eliminated. The new label guidelines provide clearer information on how each drug affects women and nursing infants.[39]

Benzodiazepines are the preferred drug class to avoid alcohol withdrawal seizures.[36,40-43] Tapered dosing of a benzodiazepine is the most frequently reported practice for medication-assisted alcohol detoxification in pregnant women.[43] No widely accepted standards are currently available to guide the choice of benzodiazepine, dose, or administration frequency. For pregnant women, the WHO recommends use of a long-acting benzodiazepine.[36] The selected benzodiazepine is frequently given on a predetermined schedule with the dose gradually tapered or based on the presence of withdrawal symptoms.[36]

The CIWA-Ar score is helpful to monitor withdrawal status and determine the benzodiazepine dose.[35,36] Clinical assessment findings must also be considered. Depending on the dose in the prenatal vitamins, thiamine, a multivitamin, and folic acid supplements may be given to counteract damage related to chronic vitamin deficits associated with alcohol use.[38]

Medications given to the mother postpartum must also be evaluated for the potential effect on a breastfed infant. The relative infant dose (RID) is a key consideration when selecting the appropriate medication. Medications with less than 10% RID are safest.[44]

Clinical diagnosis: Infants and children

One of the most promising techniques for identifying PAE in the newborn is analysis of meconium for the presence of fatty acid ethyl esters.[33,45] Although meconium only provides information about exposure during the second and third trimesters, this tool has been shown to correlate well with the quantity of known alcohol intake and thus can be important in early identification of infants exposed to alcohol during those trimesters.

Individuals with FASD may present with characteristics (short, flat philtrum; thin upper lip; narrow palpebral fissures; growth retardation; mental, behavioral, and/or learning disabilities) of varying degrees that may be missed early in life.[46] FAS identification criteria are well established, and children with FAS are usually identified early. If identification is delayed, early interventions to assist those with FASD may be limited. Clinical diagnosis requires the presence of three distinct identifiers: the three facial features listed above, growth retardation (either prenatal or postnatal), and CNS problems of wide variation.[21]

The prominence of the facial dysmorphology associated with FASD varies over time and from individual to individual; however, the classic triad of flat philtrum, thin upper lip, and small palpebral fissures serves as the primary facial markers for suspected PAE.[44] The developmental deficits resulting from PAE also vary in severity, and characteristics change throughout development. Newborn growth deficits are most often seen as smaller head circumference (associated with decreased brain growth) as well as deficits in birth weight and length (5th to 25th percentile compared to nonexposed cohorts).

These deficits generally do not improve with age, and symptoms often change over time. Infants may present with feeding difficulties and irritability, which later change to intrusive talkativeness, inattention, poor understanding of abstract concepts, and lower levels of independent activities of daily living.[47] A constellation of all three category findings (facial dysmorphia, growth retardation, and CNS damage) must be present to confer the diagnosis of FAS. Other variations in presentation are categorized as FASD.

The FASD 4-Digit Diagnostic Code is a tool for identification and grading the three categories required to diagnose FAS versus FASD (facial dysmorphia, growth retardation, and CNS damage).[48] The tool, along with a narrated presentation, is available online for free at http://depts.washington.edu/fasdpn/htmls/order-forms.htm.

Older children can be evaluated with neuropsychological tests with good success. Mattson and colleagues reported 77% accuracy in appropriately classifying FAS and 70% accuracy in appropriately classifying FASD; they also reported discriminating between FASD and attention deficit/hyperactivity disorder in nonexposed children ages 8 to 17.[49] The tests included in their study are the Cambridge Neuropsychological Test Automated Battery and the Delis-Kaplan Executive Function System, which screen for various components of executive functioning commonly displayed in individuals with FASD.

Because many clinical features of FASD are not apparent until the child fails to achieve developmental milestones (typically between ages 2 and 16), the clinician is obligated to consider FASD whenever a child presents with deficits that may be attributable to PAE.[50] The clinician must also be aware that siblings of children diagnosed with FASD are at risk for FASD as well.

Interventions and treatment management for infants

Infants should be screened as soon as possible for characteristic features of FASD to facilitate the earliest possible interventions when primary intervention is not achieved and PAE is known or suspected. Current therapeutic interventions include pharmacologic treatments and behavioral-oriented and educational programs geared toward reducing long-term developmental deficit severity. To date, the success of any treatment has shown limited results.

Following the enactment of the Children's Health Act of 2000, the CDC issued five research awards to develop specific and systematic interventions focused on improving neurodevelopmental outcomes for children with FASD. These studies looked at methods to improve social skills through development of friendships with other children; learning skills to improve mathematical skills; fostering of self-regulation skills; parental behavioral training focused on decreasing child externalizing behavior problems; and improvement of caregiver self-care skills.[51] Each intervention was associated with improvements in neurobehavioral development to some extent. However, the success of these interventions was highly dependent upon successful parental training and explicit instruction methods for the children.[51]

In another systematic review of interventions, Peadon and colleagues reported that interventions geared toward language, literacy, and mathematics may improve cognitive skill development.[52] Furthermore, behavioral programs designed to improve attention and reasoning skills along with cognitive

control training may improve social-emotional skills in individuals with FASD.[52]

APRN implications

Based on provisions in the Affordable Care Act, screening and brief intervention services are now billable services through commercial insurance, Medicare, and Medicaid. The use of a structured assessment tool is required.[53,54] Many policies and laws related to alcohol use during pregnancy vary by state.[55]

Child protective services may be required to investigate for child endangerment and neglect. APRNs must be aware of state-level reporting requirements and laws/policies related to how results of diagnostic blood tests may be used to enforce child endangerment laws. Excellent resources are available online to assist with implementing screening, brief intervention, and referral to treatment in a variety of settings, including resources from the Substance Abuse and Mental Health Services Administration, the Centers for Medicare and Medicaid Services, and Medicare Learning Network 2012.[56,57]

Carson and colleagues published guidelines for counseling and communicating with women about alcohol use.[58] Key areas covered include assessments for the presence or risks for substance use disorders; sharing and discussing information about the dangers of alcohol use during pregnancy; healthy options appropriate to the woman's reproductive stage; and assisting women with getting the help they need. Important factors necessary for achieving successful outcomes when counseling pregnant women include a nonjudgmental caring relationship, clear messages and information presented in a format appropriate to the population served, and respect for individual differences.

APRNs have the necessary skills and expertise to lead efforts that increase substance use screening, interventions, and referrals in settings serving pregnant women, other women of reproductive age, and children. Although not every infant exposed to alcohol during pregnancy develops FASD or FAS, PAE prevention would eliminate the risks of these conditions. NP

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