Fetal alcohol syndrome: Diagnosis and management

Tanushree Sahoo, Krishna Mohan Gulla

From Research Officer, Department of Pediatrics, All India Institute of Medical Sciences, New Delhi, India

Correspondence to: Dr. Tanushree Sahoo, 477, 2nd Floor, Hardevpuri, Gautam Nagar, New Delhi - 110 049, India. E-mail: tanushree_sony206@yahoo.co.in

Received - 05 August 2019 Initial Review - 18 August 2019 Accepted - 26 September 2019

ABSTRACT

With the increase in urbanization and socioeconomic status in Indian subcontinent, the incidence of alcoholism in women is rising alarmingly, so as its consumption in pregnancy. Alcoholism in pregnancy is associated with a wide spectrum of neurological manifestations covered under the umbrella of fetal alcohol syndrome (FAS). Hence, it is the need of the hour that the physicians should be aware of the condition and its phenotypic variations. In the absence of the availability of any definite treatment, supportive treatment and abstinence during pregnancy are the only available solution for preventing further progress and recurrence in future pregnancy.

Key words: *Alcoholism, Microcephaly, Teratogenic*

Alcohol is one of the most common substances abused in pregnancy. In the US, nearly half of all women in child-bearing age have a history of alcohol intake in the past 1 month [1]. The prevalence of alcoholism in pregnancy varies from 7.6% to 30% [2]. Incidence of fetal alcohol syndrome (FAS) in the US is reported to be 1000 live births and affecting around 2–5% of pre-schoolers [3]. A recent meta-analysis report lowers the prevalence of alcohol intake in pregnancy as well as fetal alcohol spectrum disorder (FASD) in southeast region (1.8%/100 pregnancy and 2.7%/10,000 live births, respectively) as compared to rest of the world [4].

Although alcoholism in pregnancy is less common in Indian subcontinent, nevertheless with urbanization and better economy, it is gradually expanding like an epidemic which is worrisome. Exact incidence of alcohol intake in pregnancy as well as alcoholic spectrum disorder from our country is unknown. Only available WHO report ("Gender, Alcohol, and Culture: An International Study") mentions the prevalence of 5.8% among Indian women [5]. Nevertheless, it is one of the preventable causes of congenital defect and developmental morbidity. Thus, in the current review, we tried to summarize briefly the clinical features and management aspects of FAS from the prospective of Indian subcontinent.

Definition

FASD is a broad terminology that is used to describe a group of phenotypes in an individual who has a history of exposure to alcohol in prenatal period in the womb of mother [6].

FASD typically constitutes the below mentioned five groups, namely [7,8]:

1. FAS
2. Partial FAS
3. Alcohol-related neurodevelopmental disorder
4. Neurobehavioral disorder associated with prenatal alcohol exposure sometimes called neurodevelopmental disorder associated with prenatal alcohol exposure
5. Alcohol-related birth defects.

PATHOGENESIS

Alcohol is a teratogen that crosses placenta freely. Thus fetal level equalises with maternal levels within couple of hours of maternal intake. Elimination is dependent on the maternal metabolism in liver by alcohol dehydrogenase (ADH) enzyme. The expression of ADH gene allele varies from one pregnant woman to other resulting in variable degree of accumulation of alcohol in the body which subsequently crosses the placenta. It causes irreversible damage to central nervous system (CNS) and facial structures in early organogenesis phase (gastrulation and post-gastrulation stages) [9]. Alcohol (ethanol) causes apoptotic cell death of neurons as well as epithelium destined to form future facial structures by dual mechanism, i.e., activation of GABA receptors and inhibition of NMDA receptors [10,11]. This results in several pathological findings in CNS such as reduced brain volume (especially of frontal lobe, striatum, caudate nucleus, thalamus, and cerebellum); thinning of the corpus callosum; and abnormal functioning of the amygdala. Similarly, the facial defects can be explained by the irreversible damage to the epithelial lining of future nasal cavity as well as commissural plate of telencephalon [12].

However, it is noteworthy that apart from early gestation, alcohol is notorious to affect fetus potentially at all gestational age [13-15]. Selective exposure in the first trimester and early second trimester is associated with spontaneous abortion and major structural anomalies [15]. Though 3rd trimester exposure

results in universal growth restriction, neurobehavioral problems may happen with exposure to any stage. However, neurobehavioral problems may happen to an infant with a history of alcohol exposure at any stage of gestation.

It is worth mentioning that exact level of alcohol intake during pregnancy to cause FASD is unknown and varies from women to women. Some contributing factors are pattern of drinking (occasional/regular), amount of drink (heavy drinker or light drinker), genetic variation, difference in metabolism of alcohol in liver, and last but not the least variations of vulnerability of several regions of brain to alcohol toxicity.

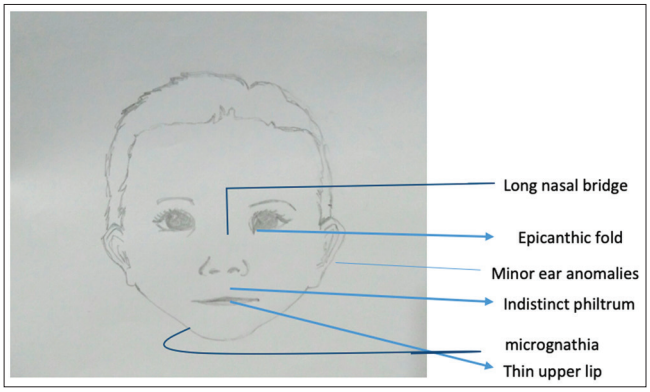

Figure 1: Classic facial features of fetal alcohol syndrome

PREVALENCE

Various studies have reported varied prevalence. In a recent meta-analysis of 24 studies, the estimated global prevalence of FASD in the general population of children aged 0–16.4 years was 7.7/1000 population (95% CI 5–12/1000 population) [4]. The prevalence was highest (20/1000 population) in the WHO European region and lowest (0.1/1000 population) in the WHO Eastern Mediterranean region. However, the reported data can be truncated due to selective reporting and restricted reporting from the regions where alcoholism is regarded as a social stigma.

Various maternal risk factors associated with antenatal alcohol consumption include positive history of alcoholism in the family, low educational level, higher maternal age, higher gravity, and poor maternal nutrition. The reported prevalence of alcoholism among Indian women as noted by the WHO is 5.8% in general population [5]. However, it is more prevalent among women from lower socioeconomic status, tribal women working in tea plantation, and commercial sex workers with recent upsurge in women from upper economic classes where it is counted as status symbol. The reported prevalence in these high-risk groups is as high as 28–48% [16].

CLINICAL FEATURES

The three classic facial features of FASD are short palpebral fissures, thin vermillion border, and smooth philtrum (Fig. 1). The presence of combinations of these facial features differentiates FAS from normal population with almost certainty. Other common facial anomalies include hypoplastic midface, epicanthal folds, flat nasal bridge, palmar abnormalities (altered paler creases, 5th finger clinodactyly, and camptodactyly), decreased intercanthal distance, ptosis, and strabismus ear anomalies [17-19].

Other less common but not so rare systemic involvement includes cardiac (atrial septal defect/ventricular septal defect and conotruncal), skeletal (joint contractures, pectus excavatum, and hemivertebrae), renal (aplasia and hypoplasia), ocular (strabismus and optic nerve hypoplasia visual problem), and auditory (conductive defect).

CNS involvement [20-22] could be structural such as microcephaly, decrease brain matter in imaging, or only neurologic abnormalities on clinical examination such as abnormal reflex and tone. More commonly, it can have only functional abnormalities such as irritability, jitteriness, autonomic instability in infancy, hyperactivity, inattention, poor cognitive performance, language delay in childhood period and poor social skills, and executive function in adulthood. Many of them have associated comorbid mental problems such as sleep disorders, anxiety, adjustment disorders, eating disorders, and impulsive behavior. They themselves are more vulnerable to fall into track of alcoholism and other substances abuse later in the life. Prenatal as well as postnatal growth retardations are one of the diagnostic features of FASD. Growth failure and short stature extend well into adulthood.

In recent case–control study from India by Nayak *et al*., it was concluded that children with FAS are more likely to have mild physical anomalies and ADHD (nearly 40%) as compared to their normal counterpart [23]. This was in contrast to the previously reported study from other parts of world, where there was not much difference in anthropometry as well as facial parameters (with exception being philtrum smoothness) among cases and controls. This could be attributed to higher prevalence of underlying malnutrition in both the groups [23].

IMAGING

The salient feature of magnetic neuroimaging of brain of affected children includes varying degree of decrease in overall size of brain, especially that of basal ganglia, hippocampus, corpus callosum, and cerebellum.

DIAGNOSIS

Diagnosis of FASD is purely clinically depending on the presence of structural defects, functional neurological deficits. The diagnosis is mentioned below in tabular format [Table 1] as below.

A detailed toolkit comprising flow diagram, checklist, and answer to frequently asked questions related to FASD is available on AAP website [25]. The toolkit has been developed with purpose of raising awareness, promotion of surveillance and screening, and for ensuring timely intervention of all affected children. The website assists in proactive developmental surveillance for the presence of signs and symptoms of FAS by

Table 1: Major diagnostic category for FASD [24]

Major category	Diagnostic criteria
FAS	1. At least two of three facial features such as short palpebral fissures, thin vermillion border, and smooth philtrum 2. Growth retardation (defined as weight or height below 10th centile as per age) 3. CNS abnormalities (structural, neurologic, or functional) If all of the three are present, then prenatal alcohol exposure need not to be documented
Partial FAS	History of documented prenatal alcohol exposure plus 1. At least two of three facial features such as short palpebral fissures, thin vermillion border, and smooth philtrum and One of the points 2 or 3 mentioned above
Alcohol-related birth defects	History of documented prenatal alcohol exposure and one specific major malformation for FASD
Alcohol-related neurodevelopmental disorder	History of documented prenatal alcohol exposure and CNS involvement which includes only neurobehavioral impairment
Neurobehavioral disorder associated with prenatal alcohol exposure	History of documented prenatal alcohol exposure and impaired neurocognitive function, self-regulation, and adaptive function

FAS: Fetal alcohol syndrome, CNS: Central nervous system

health-care professionals for early diagnosis and management by home visit or at community health facilities. It emphasizes on the presence of certain clinical features such as the presence of growth retardation (height or weight below 10th centile as per age), short palpebral fissures, thin upper lip, CNS anomalies, smooth philtrum, and presence of a history of alcohol abuse in mother during pregnancy for picking up cases in surveillance. Such suspected cases are referred to higher center for detailed neurological evaluation by experts and initiation of early rehabilitation.

MANAGEMENT AND PROGNOSIS

Management comprises detailed assessment for diagnosis and interventions. Detailed assessment includes evaluation of degree of physical deficit, IQ testing, screening of learning disability, assessment of neurocognitive functioning, neuroimaging, and functional abilities**.** Treatment of FASD is difficult and most of the time only supportive therapy is advised. Recent clinical trial has shown some preventive role of choline supplementation in cognitive deficit [26]. For children who are already affected by FASD, some of the targeted areas of intervention depending on the degree of involvement are as follows: (1) Visual rehabilitation; (2) environmental modification; (3) organization of specific tasks; (4) physiotherapy; (5) cognitive-behavioral therapy; and (6) building of support system by family as well as society. Specific medical/neurological or behavioral problems identified by detailed examination should be addressed individually as per existing guidelines for that particular problem.

In the absence of definitive treatment for FASD, primary preventive strategy remains mainstay of therapy at present. Counseling of the family for the prevention of recurrence in future pregnancy is utmost important. As there is no clearly safe limits (in terms of duration, amount and frequency of alcohol consumption) for prevention of FASD, full abstinence during pregnancy from alcohol is the only guard proof solution. As organogenesis happens in the first trimester and early second trimester, it is advisable that women should give up alcohol before planning pregnancy itself. Supplementation of deficient nutrients in pregnancy such as retinoids, folic acid choline, B-complex, and Vitamin E may have a role.

CONCLUSION

FASD is one of the preventable causes of neurodeficits and behavioral problems. As alcoholism is regarded as a social stigma/taboo in India, such history is rarely revealed by pregnant women in antenatal clinic. Hence, utmost effects should be made for eliciting these facts among pregnant ladies in antenatal clinic, especially in high-risk group. Upon finding such history, it is advisable to follow full abstinence throughout pregnancy as the safe level of alcohol intake is unknown.

REFERENCES

1. Alcohol Use and Binge Drinking Among Women of Childbearing Age—United States, 2006–2010. Available from: https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6128a4.htm?s_cid=mm6128a4_w. [Last cited on 2018 May 21].
2. Ethen MK, Ramadhani TA, Scheuerle AE, Canfield MA, Wyszynski DF, Druschel CM, *et al.* Alcohol consumption by women before and during pregnancy. Matern Child Health J 2009;13:274-85.
3. May PA, Gossage JP, Kalberg WO, Robinson LK, Buckley D, Manning M, *et al.* Prevalence and epidemiologic characteristics of FASD from various research methods with an emphasis on recent in-school studies. Dev Disabil Res Rev 2009;15:176-92.
4. Lange S, Probst C, Gmel G, Rehm J, Burd L, Popova S, *et al.* Global prevalence of fetal alcohol spectrum disorder among children and youth: A systematic review and meta-analysis. JAMA Pediatr 2017;171:948-56.
5. Obot IS, Room R, GENACIS, World Health Organization, editors. Alcohol, Gender and Drinking Problems: Perspectives from Low and Middle Income Countries. Geneva: World Health Organization, Department of Mental Health and Substance Abuse; 2005. p. 227.
6. Popova S, Lange S, Burd L, Rehm J. The economic burden of fetal alcohol spectrum disorder in Canada in 2013. Alcohol Alcohol 2016;51:367-75.
7. Common Definitions. Available from: https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/

fetal-alcohol-spectrum-disorders-toolkit/Pages/Common-Definitions.aspx. [Last cited on 2018 May 21].
8. National Organization on Fetal Alcohol Syndrome – FASD. Available from: https://www.nofas.org/about-fasd. [Last cited on 2018 May 21].
9. Riley EP, Infante MA, Warren KR. Fetal alcohol spectrum disorders: An overview. Neuropsychol Rev 2011;21:73-80.
10. Dunty WC Jr., Chen SY, Zucker RM, Dehart DB, Sulik KK. Selective vulnerability of embryonic cell populations to ethanol-induced apoptosis: Implications for alcohol-related birth defects and neurodevelopmental disorder. Alcohol Clin Exp Res 2001;25:1523-35.
11. Kotch LE, Sulik KK. Patterns of ethanol-induced cell death in the developing nervous system of mice; neural fold states through the time of anterior neural tube closure. Int J Dev Neurosci 1992;10:273-9.
12. Sulik KK. Genesis of alcohol-induced craniofacial dysmorphism. Exp Biol Med (Maywood) 2005;230:366-75.
13. Muggli E, Matthews H, Penington A, Claes P, O'Leary C, Forster D, *et al.* Association between prenatal alcohol exposure and craniofacial shape of children at 12 months of age. JAMA Pediatr 2017;171:771-80.
14. Goldschmidt L, Richardson GA, Stoffer DS, Geva D, Day NL. Prenatal alcohol exposure and academic achievement at age six: A nonlinear fit. Alcohol Clin Exp Res 1996;20:763-70.
15. Feldman HS, Jones KL, Lindsay S, Slymen D, Klonoff-Cohen H, Kao K, *et al.* Prenatal alcohol exposure patterns and alcohol-related birth defects and growth deficiencies: A prospective study. Alcohol Clin Exp Res 2012;36:670-6.
16. Bovet P. Alcohol consumption patterns and association with the CAGE questionnaire and physiological variables in the Seychelles Islands (Indian Ocean). In: Surveys of Drinking Patterns and Problems in Seven Developing Countries. Geneva: World Health Organization; 2001. p. 79-101.
17. Watkins RE, Elliott EJ, Wilkins A, Mutch RC, Fitzpatrick JP, Payne JM, *et al.* Recommendations from a consensus development workshop on the diagnosis of fetal alcohol spectrum disorders in Australia. BMC Pediatr 2013;13:156.
18. Astley SJ, Clarren SK. Diagnosing the full spectrum of fetal alcohol-exposed individuals: Introducing the 4-digit diagnostic code. Alcohol Alcohol 2000;35:400-10.
19. Hoyme HE, Kalberg WO, Elliott AJ, Blankenship J, Buckley D, Marais AS, *et al.* Updated clinical guidelines for diagnosing fetal alcohol spectrum disorders. Pediatrics 2016;138:e20154256.
20. Mattson SN, Riley EP. A review of the neurobehavioral deficits in children with fetal alcohol syndrome or prenatal exposure to alcohol. Alcohol Clin Exp Res 1998;22:279-94.
21. Olson HC, Feldman JJ, Streissguth AP, Sampson PD, Bookstein FL. Neuropsychological deficits in adolescents with fetal alcohol syndrome: Clinical findings. Alcohol Clin Exp Res 1998;22:1998-2012.
22. O'Connor MJ, Paley B. Psychiatric conditions associated with prenatal alcohol exposure. Dev Disabil Res Rev 2009;15:225-34.
23. Nayak R, Murthy P, Girimaji S, Navaneetham J. Fetal alcohol spectrum disorders – a case-control study from India. J Trop Pediatr 2012;58:19-24.
24. American academy of pediatrics. Committee on substance abuse and committee on children with disabilities. Fetal alcohol syndrome and alcohol-related neurodevelopmental disorders. Pediatrics 2000;106:358-61.
25. Algorithm for Evaluation. Available from: https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/fetal-alcohol-spectrum-disorders-toolkit/Pages/Algorithm-for-Evaluation.aspx. [Last cited on 2018 May 21].
26. Wozniak JR, Fuglestad AJ, Eckerle JK, Fink BA, Hoecker HL, Boys CJ, *et al.* Choline supplementation in children with fetal alcohol spectrum disorders: A randomized, double-blind, placebo-controlled trial. Am J Clin Nutr 2015;102:1113-25.

Funding: None; Conflict of Interest: None Stated.

How to cite this article: Sahoo T, Gulla KM. Fetal Alcohol Syndrome: Diagnosis and management. Indian J Child Health. 2019; 6(9):470-473.

Doi: 10.32677/IJCH.2019.v06.i09.002