The spectrum of diseases associated with fetal alcoholism

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Abstract

Fetal alcohol spectrum disorders (FASD) are preventable conditions secondary to the mother's consume of alcohol during pregnancy, and include fetal alcohol syndrome, partial fetal alcohol syndrome, alcohol-related birth defects and alcohol-related neurodevelopmental disorder. Their prevalence is not exactly known, due to a lack of knowledge regarding the correct diagnosis and due to the pregnant women's alcohol consumption concealment, but the estimation is that one in ten pregnant women continue to drink during pregnancy. The importance of this group of disorders is represented by the involvement of the development and functioning of the central nervous system and due to predisposition of the product of conception to alcohol dependence in adulthood. FASD management involves prevention and treatment which are important to be initiated as early as possible. Prevention recommendations include cessation of alcohol consumption, nutritional supplementation and complications' treatment, such as "secondary disabilities", that include inappropriate sexual behavior, disrupted school experience, trouble with the law and incarceration, homelessness, unemployment, and chronic mental health problems. By offering an early diagnosis, a stable and nurturing living environment, along with the absence of exposure to physical, sexual or other types of violence, the eligibility for social and educational services is essential. Thus, prevention is the main key in the FASD management, alongside the screening to identify the high-risk pregnant females and their referral to appropriate programs.

Keywords: *fetal alcohol spectrum disorders, prevention, neurodevelopment, alcohol, pregnancy*

Rezumat

Tulburările din spectrul alcoolismului fetal sunt afecțiuni secundare consumului de alcool al mamei în timpul sarcinii, care pot fi prevenite și care includ sindromul alcoolismului fetal, sindromul alcoolismului fetal parțial, malformațiile congenitale legate de alcool și tulburarea de neurodezvoltare legată de consumul de alcool. Prevalența acestora nu este cunoscută cu exactitate, din cauza lipsei de cunoștințe privind diagnosticul corect și din cauza tendinței gravidelor de a ascunde consumul de alcool; estimarea este că una din zece gravide continuă să consume alcool în timpul sarcinii. Importanța acestui grup de tulburări este reprezentată de implicarea lor în dezvoltarea și funcționarea sistemului nervos central și din cauza predispoziției produsului de concepție la dependența de alcool la vârsta adultă. Managementul acestor patologii implică prevenție și tratament, care sunt important a fi inițiate cât mai curând posibil. Recomandarea de prevenție include încetarea consumului de alcool, suplimentarea nutrițională și tratamentul complicațiilor, cum ar fi „dizabilități secundare", care includ comportament sexual inadecvat, afectarea experienței școlare, probleme cu legea și încarcerare, lipsa de adăpost, șomajul, probleme cronice de sănătate mintală, iar un diagnostic precoce, un mediu de viață stabil și primitor, absența expunerii la violență fizică, sexuală sau la alte tipuri de violență și eligibilitatea pentru servicii sociale și educaționale sunt esențiale. Așadar, prevenția este punctul principal în managementul acestor patologii, alături de screeningul pentru identificarea femeilor însărcinate care prezintă un risc crescut și îndrumarea acestora la programe adecvate de dezalcoolizare.

Cuvinte-cheie: *tulburări din spectrul alcoolismului fetal, prevenție, neurodezvoltare, alcool, sarcină*

Submission date:
12.12.2021
Acceptance date:
20.12.2021

Spectrul de afecțiuni asociate alcoolismului fetal

Suggested citation for this article: Toma AI, Bogdan RD, Salmen T, Grigoriu C, Mihai BM, Dima V, Bohîlțea RE. The spectrum of diseases associated with fetal alcoholism. Ginecologia.ro. 2021;34(4):72-75.

Introduction

Fetal alcohol spectrum disorders (FASD) include preventable conditions that may result from the mother's alcohol consumption during pregnancy, respectively fetal alcohol syndrome (FAS), partial fetal alcohol syndrome, alcohol-related birth defects (ARBD) and alcohol-related neurodevelopmental disorder (ARND)[1-3]. The spectrum of diseases associated with fetal alcoholism is the leading known cause of mental deficiency and developmental abnormalities in the Western world[4].

The prevalence of FASD in the population is not known exactly, given that the diagnosis of its different forms is not always established and because pregnant women tend to hide alcohol consumption[1,2]. However, it is estimated that half of women of childbearing age in the USA consume alcohol, and 8-11% continue to drink during pregnancy[5]. In Romania, two-thirds of the population consume alcohol regularly, while our country is on the third place in the EU in terms of the amount of alcohol consumed. The prevalence of FASD in Europe is estimated to be 2-4 cases per 100 inhabitants (Italy) and

the prevalence of FAS is 0.2-8 per 1000 births[2,6]. There are no data from Romania on the prevalence of FAS or FASD, but given the large number of women consuming alcohol, it is believed that they are at least equal if not higher than those in the European Union.

Alcohol affects the central nervous system's development and functionality through mechanisms such as placental and vascular – change in placental flow, alteration of new vessel development and vascular remodeling; nutritional effects – nutritional deficiency of the pregnant woman with altered fetal growth; specific deficiencies – retinoic acid deficiency, by hepatic antagonism of retinol, which causes the appearance of midline abnormalities such as agenesis and hypoplasia of the *corpus callosum*, folate deficiency with inhibition of absorption due to alcohol and with the appearance of neural tube defects and zinc deficiency; the cellular level – increased apoptosis, impaired cell proliferation and migration and impaired synaptogenesis; gene expression, especially in animal models; and epigenetic changes, respectively the transgenerational character, in the sense that alcohol consumption in pregnant women predisposes the product of conception to alcohol dependence in adulthood[1,8-11]. It is also important to note that different populations and individuals have different susceptibility to alcohol due to different alleles of alcohol dehydrogenase and nitric oxide synthetase[1].

The effects observed on the central nervous system in the fetuses of alcohol-consuming mothers are represented by: microcephaly with microencephaly, abnormalities of migration, midline abnormalities (agenesis of *corpus callosum*, optic-septal dysplasia), synaptogenesis abnormalities and neural tube defects; abnormalities that occur in the frontal, temporal and parietal lobes, the *corpus callosum*, the basal nuclei and the cerebellum[1]. Regarding behavior, there are cognitive, language and behavioral deficits (ADHD and opposition disorder – with an increased risk of antisocial behavior, tendency for crime or abuse of other psychotropic substances) and disorders of motor function and visual-motor

Table 1 The categories of anomalies from FAS

Growth deficit – at least one of the following abnormalities (assessed according to gestational age, gender and postnatal age): a) Birth weight or body weight <10th percentile b) Waist at birth or waist <10th percentile c) Body Mass Index <10th percentile
Facial abnormalities – all the three facial abnormalities must be present simultaneously: a) Short length of eyelid fissure (<3rd percentile) b) Filter hypoplasia (grade 4 or 5 on the rating scale) c) Thin upper lip (grade 4 or 5 on the assessment scale)
Abnormalities of the central nervous system – at least one of the criteria a or b. a) Functional abnormalities of the central nervous system – at least one of the following: i) Overall intellectual impairment of at least two standard deviations in children under 2 years of age, measured with an appropriate test. ii) Deficit of at least two standard deviations in any three of the following areas (or two if associated with epilepsy): language, fine motor skills, visual-spatial perception, learning and memory, executive functions, mathematics, attention, social and behavioral skills. b) Structural abnormalities of the central nervous system: Microcephaly <10th percentile.
Intrauterine exposure to alcohol confirmed or unconfirmed – if there are abnormalities in all other three diagnostic categories, the diagnosis of FAS should be made even in the absence of a confirmation of maternal alcohol consumption during pregnancy.

Table 2 Diagnostic criteria for partially FAS with confirmation of maternal alcohol consumption

Confirmation of maternal alcohol consumption
Characteristic pattern of facial abnormalities as the ones described in FAS – two or more different anomalies.
One of the following features: a) Proof of pre- or postnatal growth retardation. b) Evidence of growth deficit or morphogenesis abnormality – at least one of the following i) Structural brain abnormality ii) Cranial circumference <10th percentile. c. Evidence of a complex pattern of behavioral or cognitive abnormalities inappropriate to the level of development, which cannot be explained by genetic, familial or environmental predisposition – language, fine motor skills, visual-spatial perception, learning and memory, executive functions, mathematics, attention, social and behavioral skills.

Table 3 Diagnostic criteria for ARBD

Confirmation of maternal alcohol consumption
Characteristic pattern of facial abnormalities as the ones described in FAS – two or more different anomalies
Congenital malformations: at least one of the following categories of malformations or dysplasia - if only dysplasia is present – at least two malformations are necessary for diagnosis ■ cardiac malformations ■ skeletal malformations – radio-ulnar synostosis, vertebral defects, contractures of large joints such as elbow or knee, scoliosis ■ renal malformations ■ ocular malformations – strabismus, ptosis, optic nerve hypoplasia ■ auditory malformations – sensory deafness ■ minor abnormalities – hypoplastic nails, clinodactyly, palm crests "in hockey stick", in "rail" ears

Table 4 Diagnostic criteria for ARND

Confirmation of maternal alcohol consumption
At least one of the following a) Evidence of brain growth deficit or morphogenesis abnormality – at least one of the following: i) Structural brain abnormality ii) Cranial circumference <10th percentile. b) Evidence of a complex pattern of behavioral or cognitive abnormalities, inappropriate to the level of development, which cannot be explained by genetic, familial or environmental predisposition, such as language, fine motor skills, visual-spatial perception, learning and memory, executive functions, mathematics, attention, social and behavioral skills.

coordination[1]. Moreover, alcohol consumed during pregnancy causes a deficit of stature, brain and weight gain, facial characteristic abnormalities, structural and functional damage to the central nervous system, and various birth defects[1,2,3,11].

Diagnostic criteria for FASD are particular for each of the component entities. For FAS, there is minimum one anomaly from each of the categories from Table 1[2,12].

The diagnostic criteria for partially FAS with confirmation of maternal alcohol consumption includes all categories from Table 2[3].

In case of partially FAS without confirmation of maternal alcohol consumption, the criteria are the same with the partially FAS with confirmation of maternal alcohol consumption, except from the first one[3].

ARBD diagnosis requires all the criteria from Table 3[3].

The diagnostic criteria for alcohol-related neurodevelopmental disorders (ARND) require all of the elements from Table 4.

An important element in diagnosing FASD is the differentiation from genetic syndromes that may have common facial features and malformations as the ones encountered in FASD: Williams syndrome, Cornelia de Lange syndrome, di George syndrome[1,3].

The management of FASD involves prevention and treatment. Prevention starts from the pediatric primary care provider and is the most effective way of approach, because the anomalies already installed are not reversible[1-3,13]. It includes: the early identification in order to provide a better outcome; education and anticipatory guidance for the parents and caregivers in order to understand that eventually the appearance of neurobehavioral symptoms is not the result of willful misbehavior, help them to develop realistic expectations, understand the importance of a friendly home environment, provide them with guidance for behavior management techniques and to prepare them for age-related changes that will be encountered in the growth period; and family support, in order to minimize the perceived stigma and shame, acknowledgement of the challenges that they have to overcome, providing resources[14-16].

The treatment requires an early diagnosis for inclusion in a specialized rehabilitation program, nutritional supplementation with choline, experimental treatment, multidisciplinary approach to neurological and neurobehavioral involvement, with family-focused interventions, respectively educational and cognitive therapy, cognitive control, language and reading education, self-control, mathematical calculation, working memory practice and to exercise social skills[1-3,13,17,18].

Discussion and conclusions

Due to the severe consequences that develop in cases of FASD, the first recommendation is to reduce alcohol consumption to zero during pregnancy. Moreover, FASD is completely preventable by avoiding alcohol consumption in case of pregnant woman during pregnancy[1-4]. The complete avoidance of alcohol during pregnancy is preferable, but in case of giving up alcohol completely,

there are even some benefits such as preventing growth deficit. It is recommended that women with childbearing potential stop drinking alcohol when planning a pregnancy[17,18].

For pregnant women with a history of alcohol consumption, a nutritional supplement with retinol, folic acid, zinc, vitamin E and choline is required in order to avoid birth defects secondary to nutritional deficiencies that could result from alcohol consumption[1,17-20]. The "secondary disabilities" in children with FASD, especially in case of undiagnosed and untreated, include inappropriate sexual behavior, disrupted school experience, trouble with the law and incarceration, homelessness, unemployment, along with chronic mental health problems[21,22]. A higher rate of neurodevelopmental comorbidities is present in children without FASD, a risk that is increased by the adverse childhood experiences, such as parental separation or divorce, parental substance use or neglect[23].

Factors that limit the adverse outcomes are represented by diagnosis before the age of 6 years old, a stable and nurturing living environment, absence of exposure to physical, sexual or other types of violence, eligibility for social and educational services, and a diagnosis of FAS rather than one of the other FASDs[14].

In conclusion, prevention is the fundamental key in the FASD management, because it represents a leading cause of preventable birth defects and developmental disorders, and the screening to identify the pregnant females that are at high risk and their referral to appropriate program are essential[24]. ■

Conflicts of interests: The authors declare no conflict of interests.

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