Introduction

The term fetal alcohol syndrome was first used in 1973 [1,2]. Fetal Alcohol spectrum disorders are caused by drinking alcohol during pregnancy [3,4]. Prenatal exposure to alcohol can damage the developing fetus and is the leading preventable cause of birth defects and intellectual and neurodevelopmental disabilities [1,3,4]. It presented as a cluster of birth defects[1]. Fetal alcohol spectrum disorders (FASDs) encompasses a range of possible diagnoses, including fetal alcohol syndrome (FAS), partial fetal alcohol syndrome (pFAS), alcohol-related neurodevelopmental disorder (ARND), alcohol related birth defects (ARBD) and neurobehavioral disorder associated with prenatal alcohol exposure (ND-PAE).

FAS is a distinct clinical entity referring to a specific constellation of physical, behavioral, and cognitive abnormalities, resulting from prenatal alcohol exposure (PAE)-[1].

The lack of uniformly accepted diagnostic criteria for FAS and other related disorders has limited efforts to determine accurate prevalence figures. The World Health Organization (WHO) estimates the global prevalence to be 7.7 per 1000 population (95% CI: 4.9-11.7 per 1000 population). The WHO European Region had the highest prevalence (19.8 per 1000 population) and the WHO Eastern Mediterranean Region had the lowest (0.1 per 1000 population). South Africa was estimated to have the highest prevalence of FASD at 111.1 per 1000 population, followed by Croatia (53.3/1000 population)-[5].

Alcohol-related birth defects and developmental disabilities are completely preventable. When pregnant women abstain from alcohol use, neurocognitive and behavioral problems resulting from prenatal exposure are lifelong. Early recognition, diagnosis, and therapy along the FASD spectrum can result in improved outcomes. There is no amount of alcohol intake to consider safe. All forms of alcohol pose similar risk and binge drinking poses dose-related related risk to the developing fetus [6]. There is a global need to establish an universal public health message about the potential harm of prenatal alcohol exposure and a routine screening protocol, according to the WHO [5]. Globally, nearly 10 percent of women drink alcohol during pregnancy [7]. In this mini-review the various parts of the fetal alcohol spectrum disorders will be discussed. The pathogenesis, pathophysiology and treatment are beyond the scope of this mini-review.

Fetal Alcohol Syndrome (FAS)

For the diagnosis FAS, patients must have at least one growth abnormality, e.g., short stature, as well as all three characteristic facial abnormalities: short palpebral fissure length, a thin upper lip and a smooth philtrum. They must also have at least one diagnosed structural or functional abnormality of the central nervous system, e.g., microcephaly or impaired executive function. Confirmation of intrauterine exposure to alcohol is not obligatory for the diagnosis [8].

Growth abnormalities in FAS: The percentiles for weight are significantly lower in children with FAS at birth and in following outpatient consultations, compared with children without FAS in a retrospective study of 322 FAS children. Moreover 22% had a body mass index below the third percentile compared with 3% of those without FAS[9]. Day et al. (cohort study, n=580) found, that 14 year old children, whose mothers had drunk alcohol in the first and second trimester of pregnancy showed reduced body weight, and maternal alcohol consumption in the first trimester led to smaller body length [10]. Explanation of the growth disturbance by other causes as e.g. prenatal deficiency states, hormonal disorders, malabsorption, malnutrition, neglect, and genetic syndromes should be excluded [11].
Facial anomalies in FAS: Several studies described the characteristic facial abnormalities in children with FAS [12-16]. Regardless of ethnicity and sex, the most powerful discriminating features for FAS proved to be smoothing of the philtrum, a thin upper lip and short palpebral length. These facial screening criteria for FAS showed a sensitivity of 100% and a specificity of 89.4% To add quantitative assessment of upper lip thickness and philtrum smoothness Astley and Clarke developed a lip-philtrum guide with five photographs comparable to a five-point Likert scale. Upper lip and philtrum scores of 4 or 5 are considered pathological in the context of suspected FAS [17,18].

Central nervous system (CNS) abnormalities in FAS: Early injury of the brain due to alcohol toxicity may be manifested by microcephaly. Affected children and adolescents show behavioral phenotypes of toxic damage to brain structures. As most studies are exploratory case-control studies no specific neuropsychological profile of children with FAS can currently be defined. Most of these children show below-average performance [19-27]. Functional abnormalities of the CNS should be evaluated by means of standardized neuropsychological tests together with behavioral assessment by a psychologist or physician [27]. Bell et al. found in a cohort from 2 FAS centers, that 5.9% of children with FASD showed epilepsy. ThIs is much higher than the 0.6% prevalence found in the normal population [28,29]. ThIs is no agreement in the literature regarding a recorded cut-off value for the presence of microcephaly in children with FAS.

Studies about the head circumference in children with FAS yielded conflicting results. Therefore, a head circumference ≤ 3rd percentile and a head circumference ≥ 10th percentile fulfill the criteria for the diagnostic category CNS abnormalities [13,30]. Owing to the limited evidence on structural abnormalities of the CNS such as volume reduction of the cerebellum and thickening of the cortex, it is agreed that structural CNS abnormalities other than microcephaly, cannot currently be used as criteria for the diagnosis of FAS [31-36].

Importance of confirmation of maternal alcohol consumption in FAS: Burd et al. [37] investigated the importance of confirmation of alcohol consumption of the mother for the certainty of the diagnosis of FAS. In cases where maternal alcohol consumption could not be confirmed sensitivity for the diagnosis FAS was higher (unconfirmed 89%, confirmed 85%), while specificity was lower (71.1% versus 82.4%). In other words, more children with FAS actually have FAS diagnosed, when alcohol consumption by their mother is not confirmed. Documentation of maternal alcohol intake is difficult. Many mothers are not questioned about their alcohol consumption during pregnancy, because carers are worried about loss of trust in the caregiving relationship. Otherwise mothers frequently deny alcohol use during pregnancy for reasons of social acceptability. The diagnosis of FAS remains difficult, because the characteristic abnormalities in children with FAS change with age. Facial abnormalities and growth deficiencies are obvious in childhood, but less distinct in adolescence and adulthood [38].

ARND

Unfortunately children with FAS represent only the tip of the iceberg of affected children, as numerous children exposed to alcohol in utero have significant physical or neurodevelopmental abnormalities, without all the features of FAS [39]. Alcohol related neurobehavior disorder (ARND) refers to a constellation of neurobehavioral and central nervous system effects, occurring in the absence of the characteristic facial and growth abnormalities associated with FAS. These abnormalities include; head circumference < or equal to the 10th percentile, learning disabilities, poor impulse control, seizures, deficits in higher level receptive and expressive language, and problems with mathematical skills, memory, attention and judgement [40].

ARBD

Individuals that exhibit the typical FAS facies along with specific structural anomalies, that are known to be associated with alcohol exposure, such as low set ears, micrognathia, epicanthal folds, low nasal bridge, short upturned nose, strabismus, clinodactyly, “hockey stick” palmar crease, radioulnar synostosis, renal anomalies and cardiac defects, but have normal growth and development, are classified as having alcohol-related birth defects (ARBD) [41]. The prevalence of ARND and ARBD is estimated to be at least 4 times more common than FAS [42,43]. Combining prevalence rates for FAS, ARND And ARBD indicates that 1% to 3% of all children born in the United States are affected by alcohol. ThIs is probably an underestimation because primary care providers and others, who care for children, do not routinely screen for FASD [44].

Conclusion

FASDs are still the leading cause of birth defects, intellectual and neurodevelopmental disabilities. There is a global need to establish an universal public health message about the potential harm of prenatal alcohol exposure and a routine screening protocol, according to the WHO [8,10]. Ten percent of pregnant women use alcohol and 1% to 3% of all children born in the United States are affected by alcohol.

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