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Prenatal Alcohol Exposure and Foetal Alcohol Spectrum Disorder- A Brief Overview

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Abstract

Maternal alcohol consumption during pregnancy results in fetal alcohol spectrum disorder (FASD) in offspring. FASD presents with distinct facial characteristics, growth delays, cognitive impairments, and various behavioural issues because of neurotoxicity of alcohol to the brain of developing foetus. Behavioural issues in children with FASD manifest early and persist throughout adulthood. While physical characteristics are crucial for diagnosing Fetal Alcohol Syndrome (FAS), it is noteworthy that neurocognitive and behavioural abnormalities may occur even in the absence of these physical traits. (alcohol related neurodevelopmental disorder or ARND). Due to the absence of a recognized safe level of alcohol consumption throughout pregnancy, it is imperative to strongly recommend abstinence from drinking for women who have conceived or expecting pregnancy.

Keywords: Neurocognitive, Liquor, Craniofacial joint, Binge drinking, Intra Uterine Growth Retarded

Introduction

There is an increasing trend worldwide of consumption of liquor by pregnant women. This causes a serious complication in new born called Foetal Alcohol Syndrome (FAS), as alcohol is regarded as a prevalent teratogenic agent. FAS is found to affect those new born whose mother used to consume liquor during the pregnancy period. It is defined by several irreversible clinical manifestations like craniofacial deformities, mental and physical retardation, cardiac septal anomalies and minor joint abnormalities. However, in few cases symptoms may get unnoticed if the manifestation is of a lesser degree. In that case, the medical condition is named Foetal Alcohol Effect (FAE), which is mainly characterized by varying degrees of mental retardation [1].

History of FAS/FAE discovery

It appears that the adverse effects of alcohol consumption during pregnancy have been recognised since ancient times. In 1834, a select committee that was investigating drunkenness submitted a report to the House of Commons in the United Kingdom. The report indicated that neonates born to alcoholic mothers occasionally exhibited a starved, shrivelled, and imperfect appearance.

Additional research was conducted on expectant women who were chronically alcoholic in 1900. It became apparent that the frequency of epilepsy in the surviving progeny was correlated with an increasing rate of abortion and stillbirth.
Nevertheless, it was Lemoine et al [2] who was credited for the first formal reported of FAS. But the French language of the article could not elicit much response until the report of Jones and Smith [3]. The study postulated several characteristic patterns of - prenatal and post-natal growth deficiency in infants of alcoholic mothers, like developmental delay, craniofacial joint abnormalities, transformed cardiac anomalies, palmar crease pattern, capillary haemangiomata, irregular external genitalia, and reduction of fine motor functions.
Finally in 1980, the definite diagnostic norms of FAS were indicated by the Foetal Alcohol Spectrum Disorders Study Group of the Research Society on Alcohol.

Effect of Alcohol on the Developing Embryo
Fetal Alcohol Syndrome (FAS)

In simple terms, there appear to be three classes of prenatal ethanol exposure that are associated with the quantity of alcohol consumed- i) heavy drinking (over 48–60 g of ethanol per day) that may lead to foetal alcohol syndrome; ii) moderately high drinking (24–48 g of ethanol per day) that might lead to "alcohol effects" (the distinctions between these categories are not pronounced); and iii) binge drinking events that involve the consumption of 4–5 drinks of ethanol (a total in excess of 90 g of ethanol per drink). The impact of ethanol consumption on the growing foetus are influenced by the quantity of alcohol consumed, the period of alcohol consumption, and the gestational age of the embryo and foetus at the time of exposure. Alcohol use of alcohol, even in moderate quantities, particularly during the initial trimester of gestation, can lead to an increased risk of spontaneous abortions [4]. Moreover, alcohol drinking is also related to infertility in both the sexes. It is important to recognize that a meta-analysis of studies concerning the frequency of neonatal deformities in women who moderately consume liquor during pregnancy did not reveal an increase in the occurrence of congenital anomalies. A statistical study by Danish National Birth Cohort revealed a hazard ratio was 1.55 amongst women who undertake binge drinking thrice or more during pregnancy [5]. Additionally, a cohort of 3,508 singleton pregnancies in Missouri reported an odds ratio of 1.4 for stillbirth. This ratio surged to 1.7 in ladies who consumed more than 5 drinks per week. The embryo's development can be significantly impacted by excessive alcohol consumption during pregnancy, as has been repeatedly observed. The extent of the deformities varies, due to FAS, which is detected in 4–6% of babies born to heavy drinkers, to little manifestations like Intra Uterine Growth Retardation (IUGR), low birth weight, a modest decrease in infant IQ, and a higher incidence of congenital deformities. It is evident that children born to mothers who intake ethanol suffer from intrauterine growth retardation and postnatal long-term height and weight deficits. In addition, Covington et al [6] revealed that the weight of children at age 7 was determined by the maternal age. Specifically, children born to 30 plus women, at the time of birth had substantially lower weights than those born to younger women [1].

Deformities of the Organ Systems

Alcohol has been observed to influence not only the central nervous system (CNS) but also organ systems that are developmentally associated to CNS derivatives, viz. the cranio-facial complex and the heart, which are dependent on neural crest cells [4].

Oro-Facial Clefts

A series of studies have examined the possible relationship between alcohol consumption and the occurrence of oral clefts. Meyer et al [7] prepared a case control surveillance report involving a cohort of 5,956 live-born infants diagnosed with Cleft Palate (CP), Cleft Lip (CL), or a combination of both CP and CL [4]. The authors were unable to establish a correlation between oral clefts and modest levels of alcohol use, as indicated by the maternal report of alcohol consumption during the first four months of pregnancy. Even the most elevated levels of alcohol consumption did not result in a greater incidence of neonates born with a cleft compared to those consuming less than one drink per week or less than one drink on any given day. Furthermore, the association between oral clefts and ethanol consumption was not altered by the folic-acid supplemented multivitamins that were utilised by the majority of the women. In contrast, Romitti et al [8] discovered a faint correlation between average pre-conceptional liquor consumption and all oro-facial clefts (combined and isolated clefts) using data from the National Birth Defects Prevention Study. Despite the limited number of

cases, a moderate correlation was found between Pierre-Robin syndrome and multiple clefts. Furthermore, babies born to mothers who binge-drank (more than 5 per occasion) throughout the first trimester of pregnancy were found to possess a high probability of oro-facial clefts. Maternal binge drinking may be particularly detrimental due to the increased peak of blood ethanol concentration. In a particular study, it was observed that the mutated ADH1C allele gene, which is implicated in ethanol metabolic pathways, conferred a protective effect against the possibility of oral clefts in carrier children, indicating that the maternal genotype holds comparatively less significance than that of the children [4].

Cardiac Deformities

It is recognised that approximately one-third of infants diagnosed with alcohol embryopathy have a high chance of congenital cardiac issues. Maternal alcohol consumption was associated with an increased risk of conotruncal heart defect, hypoplastic aortic arch, coarctation, and VSD, as well as ASD D-transposition. Krasemann and Klingebiel [9] conducted a retrospective review of the electrocardiogram (ECG) and echocardiogram (EchoCG) data in all patients who exhibited clinical indications of alcoholic embryopathy during 1976–2003. The ECG and EchoCG assessments consistently indicated a shorter QT interval in about fifty percent of patients with alcoholic embryopathy and a reduced left ventricular diameter in roughly twenty-five percent of patients. This indicates that alcohol consumption during gestation, as a principal toxin, may lead to mild cardiac anomalies, despite the absence of substantial congenital heart problems.

Neural Tube Defects

Research indicates a correlation between maternal alcohol consumption in the early stages of pregnancy and the incidence of neural tube defects. Chen [10] identified nine instances of NTD in the literature linked to prenatal exposure to ethanol. Nevertheless, he proposed that this phenomenon could stem due to folate deficiency mediated by excessive alcohol consumption. Women consuming ethanol in the preconceptual period at frequencies of less than or more than once per week exhibited hazard ratios of 1.6 and 2.1 for defects in the neural tube, respectively. Contrary to these conclusions, a population-based case-control study conducted in California from 1989 to 1991 did not demonstrate an elevated risk of neural tube defects associated with periconceptual maternal alcohol consumption.

Renal Anomalies

Kidney is sensitive to the exposure of alcohol and the damage to the renal tissue is not only caused by the alcohol itself but also by the metabolism and the metabolites so generated due to consumption of alcohol. In several observations direct effects of alcohol were assessed in comparison to acetaldehyde toxicity along synergic effects of nicotine and caffeine (26). In clear terms, mechanisms for FAS with transformed protein synthesis and hypoxemia have been dealt with (26). Two enzymes viz., Class I and Class II alcohol dehydrogenases are mainly responsible for initial degradation of alcohol and acetaldehyde in humans. It has also been observed that acetaldehyde can undergo trans placental transmission from the maternal to the foetal segments. Toxic aldehydes so liberated in the primary degradation step are re-oxidized by aldehyde dehydrogenases. It is assumed that genetic variation in alcohol metabolism may cause differential effect regarding propensity of individuals in inducing alcohol induced organ damage.

Atopic Dermatitis

The risk of atopic dermatitis in early infancy that resolved during childhood was increased by alcohol consumption during pregnancy. This effect was primarily aggravated when both parents were diagnosed with allergic disease. The peak incidence was observed in high-risk neonates whose mothers consumed more than 4 drinks/week at 30 weeks gestational age [4].

Behavioural and Developmental Changes

Alcohol is acknowledged as a risk factor for attention deficit hyperactivity disorder (ADHD), irrespective of prenatal exposure to nicotine or any other familial risk factors. In 26 infants who were prenatally exposed to alcohol, a positive correlation between ADHD and alcohol was observed. A total of 10 children were diagnosed with ADHD, 2 with Asperger syndrome (a comparatively mild variant of autistic spectrum disorder), and 1

with minor mental retardation of the 24 children who were followed up. The severity of the disorder was linearly correlated with the mother's alcohol consumption during pregnancy. Nevertheless, the withdrawal of alcohol consumption by the 12th week of pregnancy resulted in children that were normally developed, indicating that the cerebral cortex is more susceptible to the adverse effects of ethanol from the 2nd trimester of pregnancy, following the organogenesis period. Additionally, the intake of less than 1 alcoholic drink per day during the final 3 months of pregnancy, despite having consumed more alcohol earlier, did not lead to ADHD, learning disabilities, or cognitive impairment by the age of 14.

As a marker of cell membrane stabilization and myelinization, MRS (MR spectroscopy) revealed that the frontal lobes of children with FAS were smaller and had reduced choline concentrations. In children with neuropsychological impairments, the caudate nucleus was discovered to be disproportionately smaller [4]. The neurological impairment of controls was directly proportional to the prevalence of having one or more brain regions that were 2 or more standard deviations below the mean size. The fetal ultrasound conducted at 18 weeks of gestation also revealed a decrease in cerebellar development and a decrease in cranial-to-body growth in the foetuses of mothers who abuse alcohol. Cerebellar growth was consistent with the norm when mothers discontinued alcohol consumption at the commencement of pregnancy.

Psychiatric Disorders

Adults who were exposed to excessive drinking during pregnancy were found to have a higher incidence of somatoform disorders, substance dependence, paranoia, passive aggression, antisociality, and other personality disorders [4].

In early childhood, children are frequently exposed to a variety of unfavourable circumstances, including abuse, neglect, and parental alcohol and/or substance problems. These circumstances may also be associated with an increased possibility that a child was exposed to alcohol in utero [11]. Research indicates that young individuals with FASD face a 19-fold increase in the likelihood of incarceration compared to their peers without FASD on any given day within a particular year [12]. Finally, those affected by FASD often experience developmental delays, learning difficulties, and mental health issues [13]. Consequently, it is not unexpected to find a high prevalence within special education settings, such as schools for children with intellectual disabilities, as well as in specialized clinical groups, including psychiatric care facilities [14].

Worldwide prevalence of FASD

A multitude of factors underlie the prevalence of FASD within Aboriginal populations. For instance, the incidence of alcohol consumption during pregnancy among Aboriginal populations in the United States and Canada has been observed to be roughly 3-4 times greater, respectively, than that of the overall population [15]. It is particularly concerning that around 20% of females in Aboriginal populations who consume alcohol in the pregnancy period partake in binge drinking, in stark contrast to the 3% observed in the general population across both nations [15]. The significant occurrence of alcohol consumption and FASD among certain Aboriginal populations necessitates an understanding rooted in the historical and social context of colonization, as well as the socio-demographic realities at play [14].

The estimates of FASD prevalence were obtained over a span of roughly four decades, indicating that the prevalence observed in an American Indian community during the 1980s may bear little relevance to the current figures in that same community [14]. Furthermore, it may not be appropriate to compare these figures with those from an Aboriginal community in Australia recorded three decades later. A recent study indicated that the prevalence of FASD within Aboriginal populations in Australia exceeds 19% [16].

There is an urgent necessity for prevalence studies to be carried out among populations in nearly every country across the globe. Assessing and tracking the prevalence of FASD and the intake of alcohol throughout pregnancy in the overall population and specific subgroups is essential for comprehending and identifying at-risk populations, directing establishing baselines to assess the cost-effectiveness and efficacy of prevention and treatment approaches [14]. A thorough monitoring system could enhance the understanding of linked mortality and morbidity rates, quality-of-life markers, and service use rates of affected persons. This would mitigate the chance of developing other prevalent bad outcomes frequently encountered by people who have FASD later in life, including poor academic performance and dropout, psychological issues, improper sexual conduct, and substance abuse problems [17].

Conclusion

FASD is one of the primary causes of behavioural issues and intellectual disability. The prevalence of alcohol use among women is on the rise [18]. Due to the stigma attached to women and alcohol, the majority of women who visit the paediatric, obstetrics and gynaecology, or medical departments will not voluntarily disclose their history of alcohol use [19]. The American Academy of Paediatrics advises women who are already pregnant or who intend to become pregnant in near future to abstain from alcohol because there is no known safe level of drinking liquor during pregnancy.

Conflict of Interest

The author declares that there is no conflict of interest.

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