International Journal of Advances in Engineering and Management (IJAEM)
Volume 5, Issue 4 April 2023, pp: 1136-1139 www.ijaem.net ISSN: 2395-5252

# Toxicity and teratogenicity can cause by Alcohol, Drug medication and birth defects

Tejas Prakash Sali, Simran Bapu Wadile

Date of Submission: 12-04-2023 Date of Acceptance: 22-04-2023

**ABSTRACT:-**
Heavy alcohol consumption during pregnancy can cause significant mental retardation and brain damage. some illegal drugs, and some prescription and over-the-counter medications are known to cause birth defects if taken during pregnancy.
Drugs that can cause birth defects are called 'teratogens'. A teratogen is a substance that interferes with the normal development of a fetus.
Alcohol exposure can result in growth, cognitive, and behavioral deficits owing to the toxic and teratogenic effects of alcohol.
A strong teratogen, ethanol. Its harmful neurological effects are partially mediated by foetal neurogenesis disruption.
Medical science cannot always predict how exposure to a teratogenic drug will affect a developing fetus.
KEY WORDS: TERATOGEN; DRUG SAFETY; BIRTH DEFECTS; PREGNANCY; SURVEILLANCE; TRENDS ALCOHOL RELATED NEURODEVELOPMENTAL DISORDER

## I. INTRODUCTION:-

Prenatal alcohol exposure (PAE), also known as foetal alcohol spectrum disorders (FASDs), is associated with growth and developmental impairments. Alcohol can function as both a toxic and a teratogen.(1)

Ethanol is a potent teratogen. Its adverse neural effects are partly mediated by disrupting fetal neurogenesis. The teratogenic process is poorly understood, and vulnerable neurogenic stages have not been identified(2)

Reference Recent prevalence estimates indicate that in the US, 1e5% of school-age children have a FASD (3)

Within the vulnerable population of foster/adoptive children, one study found the rates of FASDs to be 28.5% in a group of children and adoles-cents referred to clinics for behavioral issues (4)

Alcohol is an unusual drug because unlike most toxins that are biologically active in the submicromolar range, alcohol is voluntarily consumed and has its psychological effects at millimolar levels. Blood alcohol concentration (BAC) of 46 mg/dL indicates that even at the lowest levels of casual social consumption, blood alcohol content can exceed 10 mM.(5) and in persons with alcohol use disorders, blood alcohol content can reach levels higher than 100 mM (BAC: 460 mg/dL) (6)

Contrarily, the maximum dose permitted by US Environmental Protection Agency standards for other tumor-gens is substantially lower.For instance, less than the micromolar (20 mM copper) to nanomolar (72 nM lead) range (7) Other drugs with abuse potential are also generally used in the nanomolar range, including nicotine (8)and morphine equivalents(9) for medication-assisted therapy for opioid addiction(10) Moreover, research in primate models has shown the same dose of ethanol (200e300 mg/dL) may be toxic to some fetuses but teratogenic to others, suggesting that ethanol exposure can produce a range of outcomes(11)

**Ethanol as a toxicant and teratogen in the cerebral cortex**

The development of the cerebral cortex can be partic-ularly vulnerable to the toxicant and teratogenic effects of alcohol/ethanol,(12) that is cells within the cerebral cortex can undergo cell death acutely after exposure or have long-term changes in cellular function after expo-sure. A large portion of cortical development occurs during the late first and second trimesters of in utero development d a time when pregnancies may still be unrecognized, in part, owing to continued high rates of unplanned pregnancies in the US We can observe both the toxicant, or acute, effects of alcohol/ethanol consumption on foetal development during this window, as well as alcohol's teratogenic, or abnormal programming, effects. development of the cortex (13), stem cells, including neuroepithelial neural stem cells (NSCs)

International Journal of Advances in Engineering and Management (IJAEM)
Volume 5, Issue 4 April 2023, pp: 1136-1139 www.ijaem.net ISSN: 2395-5252

and radial glia, are capable of self-regeneration and differ-entiation into the transit-amplifying intermediate pro- genitors. Cell division from these intermediate progenitors can create postmitotic, lineage-committed precursor blast cells (e.g. neuroblasts) that migrate into location and form the terminally differentiated gluta- matergic neurons, astrocytes, and oligodendrocytes of the cortex (reviewed in the study by Sun and Hevner Alcohol has different impacts on different cell groups; progenitor blast cells and growing neurons are particularly susceptible to its harmful effects, whereas

The teratogenic effects of ethanol are susceptible to the stem cells.In immature and developing neurons, ethanol exposure
(120e950 mg/dL) can act as a toxicant to increase apoptosis and cell death (14 ,15)

In vivo and in vitro studies have shown that the stem cells and transit-amplifying popu-lations are resilient to ethanol-induced cell death, which instead display alterations to their self-renewal and differentiation capabilities. NSCs show a decreased number of cells and rate of proliferation, whereas the transit-amplifying population increases their prolifera- tion (46e460 mg/dL of ethanol) (16,17)

This resil-ience to ethanol-induced toxicity is not limited to
NSCs but also occurs for stem cell populations throughout the body (reviewed in the study by Mahnke et al (18)

This differentiation stateedependent vulnerability to ethanol toxicity means that regions of the developing brain have specific windows of vulnera-bility to ethanol exposure based on their developmental timeline (19)

Recent work in a mouse model of ethanol exposure (80 mg/dL) during the period of cortical neurogenesis has shown that along with disrupted migration, subse-quently formed cortical neurons also show transient decreases in dendritic architecture and changes to neuronal excitatory/inhibitory input in the pyramidal neurons of the deeper cortical layers (20)

**Neuroinflammation after PAE**

Alteration to inflammation-associated pathways after PAE can be found in early cortical development. After ethanol exposure (245 mg/dL), NSCs have elevated release of proangiogenic cytokines, including vascular endothelial growth factor A and interleukin-12 (21) Early postnatal immune function has been found to be altered by prenatal ethanol exposure, including a diminished peripheral immunological response to early-life stress.(22)

Some of these changes, such as increased cerebral cortical interleukin-1b and decreased synaptotagmin and myelin basic protein, persist into early adulthood. Alterations in early brain chemokine/cytokine pathways may be due to alcohol effects both on the developing fetus and on maternal inflammatory pathways. In humans, heavy alcohol exposure was found to alter maternal peripheral immune and inflammation markers. Networks of these altered chemokines and cytokines were found to be predictive of both PAE and neurodevelopmental delays (23) These data implicate maternal inflammation, or downstream fetal pathways, in effects of PAE on in utero neurodevelopment.

**Risk factors for birth defects-**

Medical science cannot always predict how exposure to a teratogenic drug will affect a fetus. The potential for harm depends on a range of factors including:

- the type of drug
- the size of the dose
- how often it's taken
- the stage of fetal development (gestational age) at the time of drug exposure
- the individual response of the fetus to the drug
- other factors, such as maternal diet or illness.

**Teratogenic drugs and birth defects-**

Each of the following drugs or drug groups may cause birth defects in a developing fetus:

- ACE (angiotensin converting enzyme) inhibitors
- angiotensin II antagonist
- isotretinoin (an acne drug)
- alcohol
- cocaine
- high doses of vitamin A
- lithium
- male hormones
- some antibiotics
- some anticonvulsant medications
- some cancer-fighting medications
- some drugs that treat certain rheumatic conditions
- some thyroid medications
- thalidomide
- the blood-thinning drug warfarin
- the hormone diethylstilbestrol (DES).

**General recommendations**

- Give your doctor or midwife a list of all drugs you take or have recently taken, including prescription and over-the-counter medicines, nutrition supplements and complementary therapies (such as herbal medicine). Tell your doctor or

midwife if you smoke, drink alcohol or take illegal drugs, even if you only take them occasionally or socially.

• Remember that non-prescription drugs and complementary medicines can be harmful to the unborn baby.

• Ask your doctor or midwife for advice or seek counselling if you need help to stop taking alcohol or other drugs.

• If you take medication to manage a chronic illness, don't stop or alter the dose without the knowledge and consent of your doctor.

• If you are concerned about your long-term medication, the doctor may, in some cases, be able to prescribe a similar medication that does not have any known effects on the fetus.

• Take folic acid supplements prior to conception and during the first trimester as directed by your doctor. Folic acid is known to reduce the risk of neural tube defects in the developing baby.

## II. CONCLUSION :

Alcohol functions as a teratogen, transforming stem cells and causing cell death in developing neurons and glia in the developing brain.

Changing how cells work. Alcohol concentrations as low as 46 mg/dL have been demonstrated to rewire cellular behaviour, but binge-like alcohol consumption has been shown to have neurotoxic effects on cells at levels of 120 mg/dL and higher. We are only beginning to comprehend how genetics and maternal variables affect the likelihood of long-term neurobehavioral impairments caused by PAE.

Because of this, prenatal alcohol intake may have undetectable, subtle impacts on foetal development, but when paired with other risk factors, it may have overt teratogenic effects

## REFERENCE :-

[1]. Hoyme HE, Kalberg WO, Elliott AJ, Blankenship J, Buckley D, Marais AS, Manning MA, Robinson LK, Adam MP, Abdul-Rahman O, et al.: Updated clinical guidelines for diagnosing fetal alcohol spectrum disorders. Pediatrics 2016, 138.

[2]. Tingling JD, Bake S, Holgate R, Rawlings J, Nagsuk PP, Chandrasekharan J, Schneider SL, Miranda RC: CD24 expres-sion identifies teratogen-sensitive fetal neural stem cell subpopulations: evidence from developmental ethanol exposure and orthotopic cell transfer models. PLoS One 2013, 8. e69560.

[3]. Toxicant and teratogenic effects of prenatal alcohol Amanda H. Mahnke, Amy M. Adams, Andrew Z Wang and Rajesh C. Miranda

[4]. Bakhireva LN, Sharkis J, Shrestha S, Miranda-Sohrabji TJ, Williams S, Miranda RC: Prevalence of prenatal alcohol expo-sure in the state of Texas as assessed by phosphatidyle- thanol in newborn dried blood spot specimens. Alcohol Clin Exp Res 2017, 41:1004–1011

[5]. Davies BT, Bowen CK: Estimation of peak blood alcohol concentration in research and highway safety. Annu Proc Assoc Adv Automot Med 1999, 43:251–264

[6]. Adachi J, Mizoi Y, Fukunaga T, Ogawa Y, Ueno Y, Imamichi H: Degrees of alcohol intoxication in 117 hospitalized cases. J Stud Alcohol 1991, 52:448–453.

[7]. U.S. Environmental Protection Agency. In National primary drinking water regulations. In 40 CFR 141 80; 2018.

[8]. Rose JE, Mukhin AG, Lokitz SJ, Turkington TG, Herskovic J, Behm FM, Garg S, Garg PK: Kinetics of brain nicotine accu-mulation in dependent and nondependent smokers assessed with PET and cigarettes containing 11C-nicotine. Proc Natl Acad Sci U S A 2010, 107:5190–5195.

[9]. Bodor GS: The laboratory's role in opioid pain medication monitoring. EJIFCC 2012, 23:55–62.

[10]. Bakhireva LN, Holbrook BD, Shrestha S, Leyva Y, Ashley M, Cano S, Lowe J, Stephen JM, Leeman L: Association be-tween prenatal opioid exposure, neonatal opioid withdrawal syndrome, and neurodevelopmental and behavioral out-comes at 5–8 months of age. Early Hum Dev 2019, 128:69–76

[11]. Clarren SK, Bowden DM: Fetal alcohol syndrome: a new pri-mate model for binge drinking and its relevance to human ethanol teratogenesis. J Pediatr 1982, 101:819–824.

[12]. Finer LB, Zolna MR: Declines in unintended pregnancy in the United States, 2008-2011. N Engl J Med 2016, 374:843–852

[13]. Sun T, Hevner RF: Growth and folding of the mammalian ce-rebral cortex: from molecules to malformations. Nat Rev Neurosci 2014, 15:217–232.

[14]. Ikonomidou C, Bittigau P, Ishimaru MJ,

Wozniak DF, et al.: Ethanol-induced apoptotic neurodegeneration and fetal alcohol syndrome. Science 2000, 287:1056–1060

[15]. Cheema ZF, West JR, Miranda RC: Ethanol induces Fas/Apo [apoptosis]-1 mRNA and cell suicide in the developing cere-bral cortex. Alcohol Clin Exp Res 2000, 24:535–543.

[16]. Tingling JD, Bake S, Holgate R, Rawlings J, Nagsuk PP, Chandrasekharan J, Schneider SL, Miranda RC: CD24 expres-sion identifies teratogen-sensitive fetal neural stem cell subpopulations: evidence from developmental ethanol exposure and orthotopic cell transfer models. PLoS One 2013, 8. e69560.

[17]. Vangipuram SD, Grever WE, Parker GC, Lyman WD: Ethanol increases fetal human neurosphere size and alters adhesion molecule gene expression. Alcohol Clin Exp Res 2008, 32:339–347.

[18]. Mahnke AH, Salem NA, Tseng AM, Fincher AS, Klopfer A, Miranda RC: Fetal alcohol spectrum disorders: a stem-cell-opathy? In Stem cells in birth defects research and develop- mental toxicology. Edited by Rasmussen TP, Wiley; 2018: 223–260.

[19]. Parnell SE, Holloway HE, Baker LK, Styner MA, Sulik KK: Dysmorphogenic effects of first trimester-equivalent ethanol exposure in mice: a magnetic resonance microscopy-based study. Alcohol Clin Exp Res 2014, 38:2008–2014.

[20]. Delatour LC, Yeh PW, Yeh HH: Ethanol exposure in utero disrupts radial migration and pyramidal cell development in the somatosensory cortex. Cerebr Cortex 2019, 29:2125–2139.

[21]. Camarillo C, Kumar LS, Bake S, Sohrabji F, Miranda RC: Ethanol regulates angiogenic cytokines during neural development: evidence from an in vitro model of mitogen-withdrawal-induced cerebral cortical neuroepithelial differentiation. Alcohol Clin Exp Res 2007, 31:324–335.

[22]. Raineki C, Bodnar TS, Holman PJ, Baglot SL, Lan N, Weinberg J: Effects of early-life adversity on immune function are medi-ated by prenatal environment: role of prenatal alcohol expo-sure. Brain Behav Immun 2017, 66:210–220.

[23]. Bodnar TS, Raineki C, Wertelecki W, Yevtushok L, Plotka L, Zymak-Zakutnya N, Honerkamp-Smith G, Wells A, Rolland M, Woodward TS, et al.: Altered maternal immune networks are associated with adverse child neurodevelopment: impact of alcohol consumption during pregnancy. Brain Behav Immun