

Multiple limb anomalies such as syndactyly, ectrodactyly and clubfoot have also been reported in past studies[17]. Growth retardation as found in our study and the dose response effect of alcohol intake has also been observed by other researchers[5, 9].

It has been studied that under normal embryonic development process by the time the mouse embryo has about 24 pairs of somites (late day 10 of gestation). the fore limb buds appear at the level of somites 5 to 12; and by the end of day 12 the hindlimb can be observed. The basic development of both forelimbs and hindlimbs is completed by day 16 of development. At birth, all five digits (of each limb) are formed .[17] Limb anomalies as found in the present study can be explained on this basis. The dosage days in sub group A :0-18 days & Subgroup B :6-15 days predisposed for the limb anomalies in the fetuses. Variable musculoskeletal and limb defects were found in approximately 40% of cases, ranging in severity from minor problems such as contractures of the finger joints to more severe lesions, such as congenital hip dislocations and thoracic cage abnormalities [18].

In one study in past[19] 49% of the fetuses were resorbed or dead and 46% of the survivors showed forelimb ectrodactyly. Ectrodactyly induced by ethanol was primarily of the forelimb and exclusively postaxial. In another study on mice ,out of 102 treated fetuses, 44 had limb defects affecting the distal ends of forelimbs.[11] In the present study as well 4 mice (IIIA & IIA group) showed total resorptions. The survivors showed curly tail, forelimb anomalies as ectrodactyly, syndactyly, club hands. Many of the fetuses, which were exposed to higher dose of alcohol throughout the intrauterine life, exhibited multiple anomalies, thus, suggesting that alcohol acts as general embryotoxin.

The failure of closure of the spinal neural tube, which leads to spina bifida in the mouse, has been traced back to a tissue-specific defect of cell proliferation in the tail bud of the E9.5 embryo. This cell proliferation defect results in a growth imbalance in the caudal region that generates ventral curvature of the body axis. Neurulation movements are opposed, leading to delayed neuropore closure and spina bifida, or tail defects. [21] The higher incidence of curled tail in the present study signifies the neural tube defects resulting as an adverse effect of alcohol.

It has been demonstrated repeatedly that high alcohol consumption during pregnancy may seriously affect the developing embryo. The higher the blood alcohol of the mother, the greater the damage to the developing fetus[9,11,19,21,22] . The severity of the malformations ranges from FAS, to minor effects, such as low birth weight, Intra Uterine Growth Retardation (IUGR), a slight reduction in IQ of the infants and increased rate of congenital anomalies [3,5,23-25]. Similarly the anomalies were found higher in high dose group in the present study.

The results found in the mouse model in this study can be correlated with the adverse effects of alcohol as observed in humans. In humans by the end of the 36th day, often long before the woman even realises that she is pregnant, the

neural tube is clearly present and open, and most of the rudimentary organs have already been formed, such as limbs, heart, brain, eyes, mouth, digestive tract. It is therefore obvious that if a teratogenic substance such as alcohol is consumed during this most critical period of rapid growth of cell development and organ formation, this can result in various forms of malformation in the newborn, such as defective heart, musculoskeletal abnormalities, mental handicap etc., without any specific outward signs of FAS.

5. Conclusion

It can be concluded that the ethanol is an embryotoxin. It may result in resorptions and intrauterine growth retardation. The dose effect relationship and time effect relationship was established conveying that the amount of alcohol ingested, the length of period consuming alcohol and the developmental stage of the foetus at exposure mediate the effects of ethanol intake on the developing foetus. Alcohol consumption can be an underlying cause of infertility and missed abortions in females. The intrauterine growth retardation, morphological limb anomalies, curled tail implying neural tube defect are the adverse effect of alcohol on the pregnancy outcome. Alcohol is a poison at all levels, and therefore no totally safe level of alcohol use during pregnancy can be established.

6. Conflict of Interest

None

7. Acknowledgement

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Legends of Figures



Figure 1: Uteri with late resorptions



Figure 2: Resorbed fetus



Figure 3: Uterus with pinpoint resorption

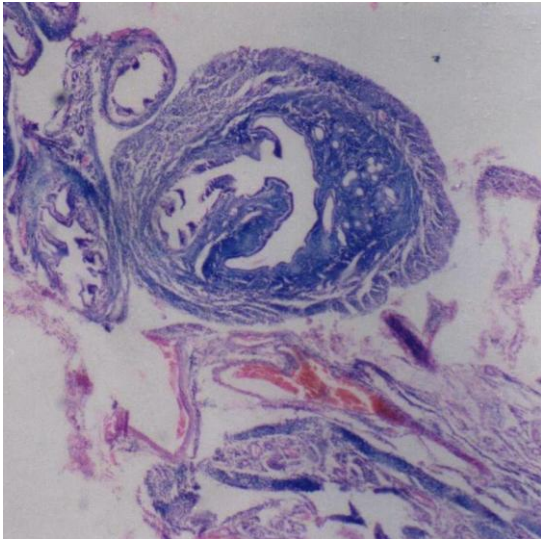


Figure 4: Histological examination of Uteri showing rupture of embryoblast & Placental Haemorrhage signifying early abortion.



Figure 7: Fetus with Ectrodactyly of middle finger, Syndactyly with 2, 3 digits & 3, 4 digits of hind limb



Figure 5: Fetus with IUGR, Dome shaped head, Arthrogyrosis of shoulder joint, elbow joint, wrist joint, knee joint and curly tail



Figure 8: Fetus with wrist drop and curly tail.



Figure 6: Fetus with Partial Ectrodactyly of middle finger, Syndactyly with 2 & 3 digits