Foetal Alcohol Spectrum Disorders and their Prevalence in the North West

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Foetal Alcohol Spectrum Disorders (FASDs) are a range of disorders associated with the consumption of alcohol during pregnancy and its impact on a foetus (National Organisation on Foetal Alcohol Syndrome UK, 2009). The prevalence of these disorders is difficult to measure due to the ambiguity of the disorders that are associated with FASDs. This spectrum of disorders may well affect large proportions of the population as only since 2016, UK government guidelines on drinking during pregnancy have encouraged women to abstain completely from alcohol where previously advice limited consumption to 1-2 units up to twice a week (Schölin *et al.,* 2019). The broad nature of symptoms of the disease and lack of diagnosis mechanism mean that FASDs remain a huge problem in society.

What are FASDs?

FASDs are a variety of disorders associated with the consumption of alcohol during pregnancy. It has been identified by the British Medical Association as the most common, non-genetic cause of learning disability in the UK (British Medical Association, 2007), causing significant concern over its preventability through education. Alcohol is normally processed in the body by two enzymes, alcohol dehydrogenase and cytochrome P450 2E1 (CYP2E1) (Heit *et al.,* 2013). In an adult, the enzymes would process the metabolism of alcohol, converting it to acetaldehyde for removal from the body. CYP2E1 is not present in a foetus' liver until 19, 23 and 24 weeks gestation, meaning there is a build-up of alcohol within the foetus due to a lack of action from the enzymes (Burd *et al.,* 2012). The presence of alcohol within a foetus can be detrimental, acting as an oxidative stress inducer and bringing about the destruction of cell membranes and mitochondria, whilst also interfering with cell signalling involved in development of the foetus (Gupta *et al.,* 2016). Not only this, the presence of alcohol can also alter expression of certain genes through DNA methylation and histone tail modification, and these changes to DNA can be carried for generations (Sarkar, 2016). Changes to DNA and cell death during development can be detrimental to a cell, and the random nature of DNA methylation and this cell destruction brought about by alcohol suggests why the symptoms of the disorder are so broad. Figure 1 demonstrates the changes to cellular mechanisms brought about by alcohol exposure. The effects of the aforementioned consequences of alcohol presence during development include physical defects, neural problems and behavioural issues- these include, but are not limited to, deformities of joints, intellectual disability and poor social skills respectively (Mayo Clinic, 2018).

Diagnosis and Treatment

The symptoms of FASDs are broad and lend themselves to improper diagnosis. Symptoms such as intellectual disability and poor social skills are something that cannot be assessed until the child has developed sufficiently to display such symptoms. Diagnosis of FAS at birth therefore requires three facial abnormalities, documentation of growth deficits and documentation of central nervous system abnormalities (National Organisation on Foetal Alcohol Syndrome, 2020). We are yet to discover a universal marker for FASDs, whether that be a genetic loci, or a biomarker produced only in individuals with the disorder. Despite the information we have in regards to how alcohol brings about cell death and genetic changes, we have very little understanding in regards to how to identify those with the disorder, and also how to treat them. Further study into biomarkers that are present solely in FASD individuals or understanding how alterations to physiological pathways may cause changes to similar genetic loci may bring about further investigation into treatment as a result. Investigations have been conducted into the administration of antioxidants *in vitro*, however a lack of action was seen *in vivo* due to the global and random nature of damage, meaning there was a lack of antioxidant present at the site of damage (Ehrhart *et al.,* 2018). The gaps in our understanding of how alcohol interferes with complex physiological pathways such as methylation throughout the body prevents us from finding a diagnosis method or treatment of the disease as a result.

FASD and Liverpool

The study of FASDs by region is difficult as it requires study into drinking habits and socio-economic status to provide context. Alcohol abuse remains a huge problem in Liverpool, with the city being top of the list in regards to female hospital admissions for alcohol-related abuse (BBC, 2011). We can look at a series of studies conducted by the Office for National Statistics (ONS) to provide context for the raised hospital admissions in relation to the rest of the country. A study that identified the degree of alcohol consumption in regions of the UK showed that the North West had the highest alcohol consumption in a week and heaviest drinking day, when 7100 individuals were asked a series of questions about their drinking habits (number of units of alcohol consumed) outside of the South East (John, 2017). Another study conducted into socio-economic status of participants and their drinking status found that economically inactive women (unemployed and not seeking work or enrolled as

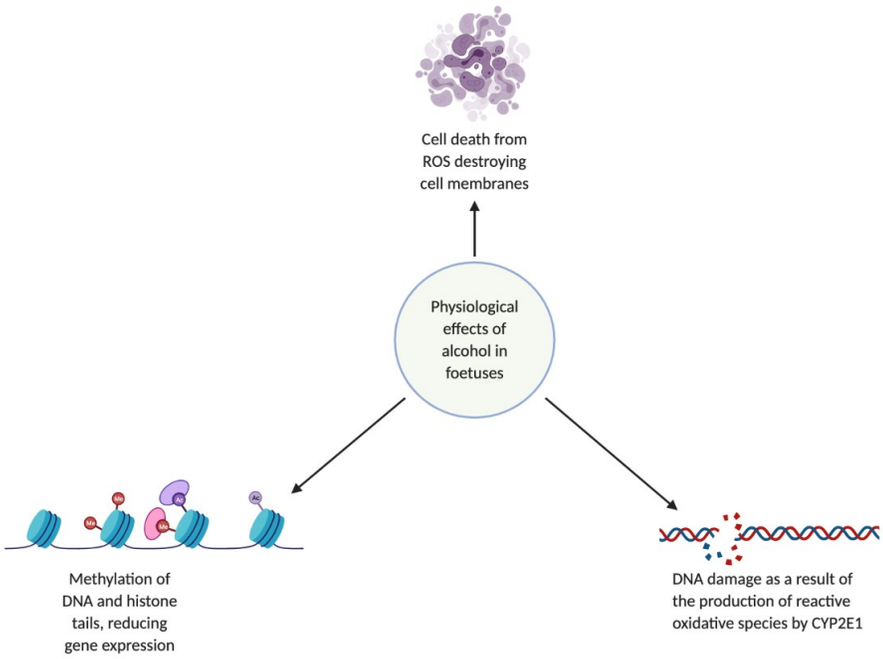

Figure 1. The effects of alcohol on cellular mechanisms in a foetus. The lack of breakdown of alcohol in the foetus allows the breakdown of DNA through the oxidative nature of the molecule. This also brings about the degradation of the cell membrane, thus resulting in apoptosis. Alcohol presence also encourages methylation, which prevents key genes from being transcribed and so bringing about the side effects commonly seen with FASDs. Created with BioRender.com

students) were the most likely to exceed 9 units of alcohol on their heaviest drinking day, and most likely to drink on 5 or more days in a week (Watson, 2018). The North West had the highest inactivity rate during the period of the study, at 23.1% (Watson, 2018). A global study into the prevalence of alcohol consumption during pregnancy places the UK second in the world, with 41% of pregnant women consuming some alcohol during their pregnancy (Popova *et al.,* 2017). These data suggest that the North West could well be one of the worst affected areas in the UK in regards to FASDs, however we cannot be sure of such a conclusion due to the lack of diagnosis methods for the disorder. Knowing why 41% of mothers in the UK consume alcohol during pregnancy despite the risk to their foetus is something we cannot for certain answer. A briefing from the National Institute for Health and Care Excellence (NICE), looking to better our treatment of FASDs in the UK, sought to better educate all women of child-bearing age, as they felt that guidance was ambiguous and misleading (NICE, 2019). Ensuring that mothers understand that any alcohol can have serious effects on their foetus is vital in ensuring that whenever we can quantitatively identify the prevalence of FASDs, Liverpool is not top of the global list.

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