"What can be done to lessen morbidity associated with Fetal Alcohol Spectrum Disorders?"

Raja Mukherjee 1,2 * : Consultant Psychiatrist

Penny A. Cook 2

Kate M. Fleming3

Sarah H. Norgate 2

*=corresponding author and address

***Raja.mukherjee@sabp.nhs.uk**

1:FASD Specialist behaviour clinic, Surrey and Borders partnership NHS Foundation trust, Gatton Place, St Matthew's Road, Redhill, Surrey, RH1 1TA, Tel: 01883383787 Fax: 01883385504 *

2: University of Salford, School of Health Sciences, Allerton Building, Salford M6 6PU

3: Public Health Institute, Liverpool John Moores University, Henry Cotton Building, Liverpool L3 2ET

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Abstract

Fetal alcohol Syndrome (FAS) and its wider spectrum of presentation Fetal Alcohol Spectrum Disorders (FASD) represent a range of disorders that are sometimes difficult to recognise as they may present in a way that overlaps with other conditions. This makes identification and recognition challenging, which increases the burden associated with the disorder. When considering the reduction in morbidity, both prevention of exposure to alcohol by the fetus but also early identification of cases is required. This selective review seeks to highlight some of the complexities involved as well as highlighting the challenges. By considering populations particularly at risk to exploring the reality of alcohol risk it will seek to offer some solutions to begin the process of change.

Introduction

Prenatal alcohol exposure on the developing fetus has been demonstrated now for over 40 years to have both direct and indirect developmental impacts across the human lifespan[1].Yet because such developmental outcomes and pathways have not yet been systematically attributed to the effects of prenatal alcohol on the fetus, such risks of morbidity largely tend to remain unrecognised and therefore neglected in intervention design and development, public health education, multiprofessional practice and service provision.

Fetal Alcohol Syndrome (FAS) is the most easily recognised part of the spectrum of presentation. This however only represents a small proportion of the range of difficulties seen. Far more common are the neurological deficits, but due to timing of alcohol exposure the facial and physical characteristics are less evident. According to DSM V framework (APA, 2013), the term Neurodevelopmental Disorder associated with Prenatal Alcohol Exposure (ND-PAE)[2] has been proposed. This is a term that has yet to have wider utilisation, but increasing research is being conducted in order to identify and establish the utility of this diagnosis, with the term Fetal Alcohol Spectrum Disorders (FASD) more widely used at present. Further, the relationship with prenatal alcohol exposure and wider neurodevelopmental outcomes such as Autism and ADHD, whilst conceptualised, continues to be debated in terms of the nature of the relationship[3 4]. This lack of easy recognition, a lack of consistent diagnotic guidance and uncertain impact of prenatal alcohol between individuals all combine to lead to a high level of public health risk. Actions to reduce the morbidity associated with FAS include prevention/reduction of alcohol exposure during pregnancy to prevent damage in the first place, while lessening the morbidity for those with FASD also requires timely identification of cases and appropriate long term support for affected individuals.

When considering the relationship of FASD to morbidity, which will include prevention of the condition alongside the individual and societal impact of the disorder, wider factors also have to be considered. Evidence from a 30-year cohort follow-up of diagnosed individuals identified significant levels of mental health problems, criminalisation, sexual exploitation as well as addictions in affected individuals[1]. A recent systematic review also identified 438 different ICD10 conditions linked to prenatal alcohol exposure[5]. This highlights the significant range of conditions that have been attributable to the effects of alcohol on the fetus. This morbidity often goes unattributed to prenatal alcohol therefore recognition of the impact of alcohol consumption during pregnancy is not made[5].

In order to begin addressing some of these issues it is important to understand what level of knowledge and information exists within both professionals and the public of FASD but also more detailed understanding as far as possible as to the types and range of disorders that are attributable. Studies from around the world, including studies in the UK, have identified that the level of knowledge about FASD is limited. Increasingly people have heard of the condition but, unlike conditions of arguably similar prevalence (e.g. autism), know little else about it. Professionals, public and carers of individuals with FASD all highlighted that there is a lack of knowledge and understanding broadly about FASD including appropriate care and support pathways for individuals

who are affected[6-8]. Further, for many, labels are perceived to be stigmatising leading to an unwillingness to consider the diagnosis[7]. This in itself has an impact on accurate identification.

Ascertaining prevalence

May and Gossage [9] summarise the common methods to assess prevalence. Passive systems, which are efficient for well recognised conditions that are easy to diagnose, are less useful for capturing the prevalence of FASD than they are for other more recognisable conditions, because the diagnosis is not obvious[9]. Diagnosis is dogged by difficulties, including the fact that many healthcare professionals know little about FASD and specialist training is needed to make a diagnosis. A diagnosis is generally made by a team of different professionals following a thorough assessment of the child that involves a physical examination, intelligence tests, occupational and physical therapy, and psychological, speech and neurological evaluations, as well as genetic tests to rule out genetic causes of problems[10]. Another difficulty with obtaining a diagnosis is that the behavioural and developmental problems typical of FASD may not emerge until a child is at primary school, and in some cases even later in life, by which time evidence about whether the birth mother drank during pregnancy, especially in the adopted or looked after childrens group, may be missing. This information is crucial to make a diagnosis if the distinctive facial features seen in full-blown FAS are not present. Another difficulty is that people with FASD often have other disorders (such as ADHD or autism spectrum disorder), making it difficult to isolate FASD. Moreover the condition rarely leads to a child being hospitalised, thus utilisation of hospital data sources is not reliable[11 12]. Clinic-based studies tend to follow up women during and after pregnancy, and are prospective, but a serious drawback with these is that FASD is diagnosed later in the child's life[9 12]. Prevalence estimates using active case ascertainment are considered the 'gold standard' and, at their best, involve screening a cross section of the general population of children[13]. The substantial drawback to this method is the significant cost involved in conducting a rigorous study using active case ascertainment.

A recent systematic review[13] found 48 articles with data on 166 samples, most of which (81%) were from suspected high prevalence sub-populations, such as looked after children. Most studies were carried out in USA, Australia, Canada and South Africa. There were no UK studies. Among the samples based on the general population, the global prevalence of FAS was found to be 0.2% and FASD was estimated to be 2.3%, but the estimates for individual countries varied widely. Prevalence was highest in South Africa (FAS 5.5%; FASD 11.3%) and lowest in New Zealand (FAS 0.01%; no data for FASD). In the only two European countries for which there there were data, the prevlance of FASD was estimated to be 4.7% in Italy (with FAS 0.8%), while in Croatia there were no estimates for FASD but FAS was estimated to be 1.1%. Of particular note, the study in Italy used active case ascertainment for the whole range of FASD and revealed a substantially higher prevalence than has previously been suspected[14]. Given that drinking levels in women of childbearing age are substantially higher in the UK compared to Italy (7 litres of pure alcohol in 2010 compared to under 4 litres in Italy[15]), rates of prenatal exposure in the UK may be at least comparable to those elsewhere in Europe, if not higher.

Hospital episode statistics from the UK and results of screening through a passive surveillance approach in Scotland have identified far lower levels of reported diagnosis than would be expected based on broader prevalence[11 16]. To date no specific prevalence study has been undertaken in the UK.

Studies within specific subgroups show substantially higher prevalence include the following:

Criminal Justice Settings

Because the consequences of unsupported FASD include addiction, mental health problems, disengagement with education and inappropriate behaviour, many individuals with FASD find themselves in trouble with the law[17]. Thus, the criminal justice setting is likely to have a higher prevalence of individuals with FASD. A systematic review of studies carried out in the criminal justice system (e.g. prisons) in 2011[18] found that all the studies had been carried out in either Canada (five studies) or USA (one). Studies using active case ascertainment (two Canadian studies) found prevalences of FASD substantially higher than the general population at 10.8% to 23.3%. A more recent systematic review to inform an analysis of the costs of FASD to the criminal justice system[19] did not reveal any further more recent estimates for this vulnerable population.

Looked after children

Most of the emergent trends with 'looked after' children relate to data from international /transnational adoptions. For instance, children adopted from Central and Eastern Europe have often been reported to be prenatally exposed to alcohol[19]. A meta-analysis of studies published in 2013[20] came up with a pooled estimate of 17% for FASD in child care settings (for studies using the gold standard method, active case ascertainment), ranging from 52% in children from Eastern Europe adopted by Swedish families to 0% in two studies (USA children adopted from China and Eastern European children adopted from Romania Ukraine and Moldovia). The pooled prevalence for FAS was 6%. Not included in the review was a study on mixed race looked after children in England, which showed a prevalence of 30%[21]. More recent studies confirm the very high prevalence rate in this group: 29% of looked after children referred for behavioural problems in Chicago, USA[22]; 27% of looked after children referred for behavioural problems in Peterborough, UK[23]; 31% of children from Poland adopted to Dutch families[24]; and 17% children in a Brazilian orphanage[25] had FASD.

Alcohol use in pregnancy and its associated harms

That heavy drinking during pregnancy can cause damage to the fetus, sometimes manifesting as FAS, is no longer controversial, but attempts to identify whether there is a safe threshold of drinking during pregnancy have not reported consistent findings. A series of systematic reviews and meta-analyses have examined the association between different drinking patterns, particularly light to moderate drinking and episodic or binge drinking, and a range of pregnancy and childhood outcomes[26-31].Variously, individual studies have shown no association between moderate drinking during pregnancy and congenital anomaly[31], no association between moderate drinking during pregnancy and a variety of pregnancy outcomes including miscarriage, stillbirth, prematurity or birth defects[28], a small positive association between mild-to-moderate prenatal consumption and childhood cognition[27], significant detrimental association between binge drinking prenatally and childhood cognition,[27]and no evidence of association between low-moderate consumption during pregnancy and speech and language outcomes[29]. Overall, these studies have not been able to show a relationship between low levels of alcohol consumption during pregnancy and adverse outcomes for the child[30].

Methodological limitations in the majority of the individual studies included in these reviews mean that they are not optimal to examine the association between low levels of drinking during pregnancy and FASD. These include imprecise measures of exposure with most studies relying on self-report and not taking into account the triad of dose, pattern and timing of consumption[32], alongside insufficiently discriminative assessment of outcome. Many studies rely on educational achievement measures to represent neurodevelopmental deficit, many examine children at an age when these deficits may yet present, and few studies have fully assessed the full range of physical developmental characteristics which can be ascribed to FASD. Perhaps most importantly, these studies are unable to account for all potential confounding factors: both before birth, e.g. concurrent substance misuse and exposure to other teratogens, and parental education and social class / networks; and after birth, particularly more psychosocial factors such as attachment styles.

The limitations of traditional observational studies can be particularly highlighted when considering the findings from the well characterised Avon Longitudinal Study of Parents and Children (ALSPAC) study. An observational analysis of children's IQ at age 8 and educational achievement at age 11 showed modest improvements in the children born to mothers who had consumed a moderate amount of alcohol during early pregnancy compared to mothers who had abstained, yet the quasi-experimental method utilising Mendelian randomization on the same cohort showed that even small levels of alcohol consumption were associated with reduced educational attainment[33]. The authors argue that the positive association seen in the observational study reflected residual confounding with factors associated with maternal social position and education.

This lack of knowledge of a "drinking harm threshold" in pregnancy has led to confusion in previous guildelines from both governments and professional bodies and only in 2016 has the chief medical officer of the UK revised guidelines on drinking in pregnancy to recommend that "women who are pregnant or planning a pregnancy should be advised that the safest approach is not to drink alcohol at all". This puts the UK in line with other countries including Canada, the USA, Australia, New Zealand, Denmark, France, Spain, the Netherlands and Ireland recommending abstinence in both pregnancy and the pre-conception period.

A recent multi-national study, Screening for Pregnancy Endpoints (SCOPE), reports a substantial variation in the prevalence of reported alcohol consumption in pregnancy ranging from 40% of women in Australia, to 82% in Ireland[34]. In the UK, there is no standardised recording of alcohol exposure during pregnancy or the pre-conception period, despite it being stipulated in national antenatal care guidelines that this should be collected[35]. Estimated alcohol consumption in the UK from SCOPE is 75% of women drinking at any time during pregnancy, with 33% of these women reporting at least one episode of binge drinking. Arguably the best estimate of the consumption of alcohol during pregnancy in the UK comes from the infant feeding survey, last conducted in 2010[36] This survey reports that 49% of mothers who drank before pregnancy gave up completely during their pregnancy, with a further 46% reducing their consumption. This does however mask age-related differences in drinking, with drinking more common in older mothers, and older mothers more likely to reduce their consumption rather than give up completely[36] with similar demographic differentials displayed in more localised UK studies[37].

With an estimated half of all pregnancies being unplanned[38] it is clear that even if guidelines recommending abstinence are heard and followed there is still a window of early pregnancy during

which damage to the unborn fetus, unbeknownst to the mother, could occur. Given that the harmful effects of alcohol are mediated both in early pregnancy during the development of the neural crest and organogenesis and throughout the remainder of pregnancy when neural pathways are being expanded, laid down and strengthened, women should be encouraged to reduce their consumption of alcohol at all stages of pregnancy regardless of when consumption is identified, in keeping with current UK guidance.

Prevention strategies

On the basis of available published evidence, the country with the best developed approach to prevention of FASD is Canada[10 39]. The Canadian model divides prevention services into four levels, with level 1 comprising universal prevention initiatives, for example general education of pregnant women and the public about effects, including awareness campaigns and labelling on alcoholic products. Such interventions, that predominantly rely on education, are thought to be among the least effective alcohol interventions[40]; for example, a recent review suggests that labelling of alcoholic products may not be very effective[41]. Addressing the social and cultural determinants of alcohol consumption during pregnancy is imperative in order to prevent FASD, although relatively few interventions that take this approach have been subject to rigorous evaluation[42].

Selective prevention with non-pregnant women with risk factors such as substance misuse use issues, and mental ill-health and poverty form the second level of the Canadian model. In level 3, prevention is further focused using one-to-one contacts with pregnant women. Interventions to support this include: training of midwives; screening pregnant women for alcohol use and providing brief interventions if necessary; and treatment of alcohol addiction problems[10]. The final tier of the Canadian model includes interventions that provide further support for those who have given birth but not changed their alcohol consumption, and this includes follow up and support for children.

In the UK, policy around FASD is less well developed, though recent revised Department of Health guideline on alcohol now states that there is no safe alcohol limit for pregnant women (as above). This message now needs to be delivered consistently in a clinical setting[10]. Barriers to this may include midwives' confidence to tackle alcohol consumption in pregnancy: recent UK research found that less than 2% of professionals who took part were 'very prepared to deal with the subject'[43]. The All Party Parliamentary Group on FASD, set up in 2015, calls for FASD to be at the forefront of the adoption process and the strengthening of healthcare professionals' training and care pathways around FASD, and a focus on looked after children and the criminal justice systems[44].

Any serious attempt to prevent FASD would involve moving prevention efforts further upstream and should consider the wider context of pro-alcohol social norms in countries like the UK, and the need to reduce population-level alcohol consumption. The most effective ways of doing this is through action on price and availability of alcohol[40 45]. This is a step further than the Canadian model which stops short at 'broad awareness building' and 'health promotion efforts'[10]. Another upstream prevention strategy would focus on the prevention of unintended pregnancies[46], due to the high proportion of pregnancies that are unplanned[38] and the high prevalence of alcohol consumption prior to knowledge of pregnancy[47] (see above).

Training and whole system change

Complexities exist with both recognising and identification of alcohol consumption risks as well as diagnosis of FASD. To modify this requires an almost whole system change in order to effect significant reductions in morbidity. For example, if at the antenatal stage alcohol consumption is not recognised and information adequately recorded, later in life it cannot be used in order to help facilitate a diagnosis. Going back even further into a more education and social setting outside the healthcare sector, if wider society does not recognise the impact of alcohol on the developing fetus and consumption rates remain at a high level harm may inadvertently occur. Because of the wide health impact of prenatal alcohol, a single approach is insufficient to address the problem.

For many practitioners in multiple health and social care fields, the difficulties of recognition highlighted above are impacting on morbidity. For many, the lack of ability to first recognise and then manage the conditions, combined with the relatively limited evidence base in research for interventions, impacts on those affected. For example there is a clinical supposition that a FASD diagnosis in itself does not affect the management of the children, therefore making the diagnosis is not warranted. Yet, as shown, where recognition is made, even where other conditions such as ADHD are recognised as part of the wider profile, the FASD becomes an effect modifier to management[3]. Consenus guidance for the management of people with ADHD and FASD compared to those without FASD have recently been accepted for publication and will highlight the importance of recognising the differences further (ref).The need to understand that the cause of an outcome modifies the treatment approach seems to not be widely recognised[7].

The specific management should to be tailored to the individual, taking into account other factors including comorbid conditions, the indiviudal's current and previous environment (e.g. whether adopted at birth from biological parent with history of alcohol abuse, remaining with birth parents or fostered/adopted later in childhood) and the timing of the diagnosis (e.g. as an infant, child or adult). The involvement of multiple disciplines to provide adequate, personalised services is essential. Promising interventions are available, although as yet these are not systematically applied in the UK to the same extent as they are, for example, in Canada. For example there are effective interventions that improve self-regulation and attentional control, social communication and behaviour[48].

Finally, it is not sufficient to take an exclusively child focused approach without taking a wider, holistic approach, with consideration for the family. Hearing the parent voice is vital for psychosocial provision and optimising social support for child care [49] and there is evidence that parent support programmes are effective in improving outcomes for parents (in terms of confidence, decreasing stress) and children (e.g. educational attainment, improvement in behaviour)[48]

The only way for this knowledge to improve is for curriculae in many professional backgrounds to be developed, from university level upwards, to recognise and train people. Better integration into healthcare systems including supports between national, regional and local services, suggested by groups such as the BMA, when implemented into practice, make a difference to the support available both to professionals but also those affected. Based on the consensus meeting of 70 professionals held in 2013 the BMA Board of Science recently updated their guidance highlighting

pathways developed at the consensus meeting to identify, record information accurately, as well as follow-up individuals through to diagnosis[10]. In keeping with this approach to reduce morbidity both prevention and management are important. The burden of alcohol exposure has increased but exposure does not equate to necessary harm and stopping drinking early will generally always have a better outcome than continuing. There will yet be some people who despite stopping drinking during pregnancy, will give birth to affected children and understanding the needs of this group is also vital.

Conclusions

Reducing the morbidity associated with prenatal alcohol exposure is not a simple task, yet when considering both prevention and management of this condition, steps are being made. The UK Parliamentary APPG on FASD published its report in 2015 identifying those stages and steps would be required in order to facilitate this system wide change[44] and with increasing recognition, through education and involvement in curriculum both for schoolchildren, undergraduates and postgraduates of all associated specialties including non-healthcare specialties such as social work education, these long-term changes may well take place. Progress can already be seen for example, based simply on the number of reports, conferences and meetings taking place related to FASD in the UK compared to 10 years ago. The journey has begun but a long road is still yet to be trod if this preventable condition is to be adequately managed and the morbidity of this condition lessened.

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