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Fetal alcohol syndrome in the UK

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ABSTRACT

Objective To determine the incidence of fetal alcohol syndrome (FAS) in the UK in children aged 0–16 years.

Design Active surveillance was undertaken through the British Paediatric Surveillance Unit between October 2018 and October 2019 inclusive. Data were collected from reporting clinicians using standardised questionnaires.

Patients Children aged 0–16 years in the UK and Ireland with a diagnosis of FAS seen in the previous month. This study did not include children with fetal alcohol spectrum disorder.

Main outcome measures Demographic details (including age and ethnicity), details of exposure, growth parameters, neurological and cognitive diagnoses, and service usage.

Results 148 notifications were received. After exclusions and withdrawals, there were 10 confirmed and 37 probable cases (analysed together). Just 24 of these children were newly diagnosed with FAS during the surveillance period, giving an estimated incidence rate of 3.4/100 000 live births (95% CI 2.2 to 5.0); their median age at diagnosis was just over 5 years and they were diagnosed between 3 months and 14 years 3 months of age.

Conclusions The estimated incidence rate of FAS is lower than reported by similar studies and there was a wide variation in the age that cases were diagnosed. This, combined with the fact that many cases were notified and then withdrawn or excluded, suggests that in the UK there is a lack of consistency and certainty in diagnosing FAS. The study findings strongly support the need to educate key professionals involved in the care of infants and children at risk of FAS.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Fetal alcohol syndrome (FAS) is characterised by typical facial features, growth restriction and central nervous system abnormalities.
⇒ There are internationally accepted diagnostic criteria for FAS.
⇒ The epidemiology of FAS in UK children has not previously been studied. International studies have suggested that FAS is often under-recognised and under-reported.

WHAT THIS STUDY ADDS

⇒ Only 24 confirmed/probable UK cases of FAS were identified during the surveillance period, giving an estimated incidence of 3.4/100 000 live births.
⇒ Paediatricians showed lack of consistency and certainty about the diagnosis of FAS.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Further research on the lifelong impact of FAS is indicated alongside the education of health professionals is needed to improve services for these children.

INTRODUCTION

Fetal alcohol syndrome (FAS) is a complex condition which occurs as a result of in utero alcohol exposure and is characterised by physical, behavioural and neurodevelopmental difficulties. Jones and Smith[1] described the key clinical features of FAS in 1973; characteristic facial abnormalities, impaired prenatal or postnatal growth and structural and/or functional central nervous system abnormalities. FAS can also be associated with other health conditions, including congenital cardiac defects, seizures, renal and skeletal abnormalities and vision and hearing impairment.[2–4] Children with FAS often face lifelong challenges, including poor educational attainment, drug and alcohol misuse, mental health issues and involvement in criminal activity.[5] Early, targeted interventions supporting children and their carers can mitigate some of these risks.[6–9]

The 2019 Scottish Intercollegiate Guidelines Network (SIGN) guidance highlighted issues including under-reporting of alcohol intake in pregnancy, alcohol being overshadowed by other forms of substance abuse and a reluctance by healthcare professionals to make the diagnosis (either through lack of experience or a perception that FAS is an unhelpful, stigmatising diagnosis).[10]

Both the SIGN guidelines and recently published NICE quality standards emphasise the importance of identifying 'at-risk' women and babies by documenting an early, reliable maternal alcohol history.[11] They also recommend a more standardised approach to referrals, diagnostic pathways and access to specialist support. The British Medical Association report (2016) also advocates for more robust collection of epidemiological data for both FAS and fetal alcohol spectrum disorders (FASDs).[12]

There have been several international FAS surveillance studies. An Australian Paediatric Surveillance Unit study estimated an overall prevalence of 0.58 per 100 000 children (<15 years) and birth prevalence of 6/100 000 live births between 2001 and 2004.[13] The New Zealand Paediatric Surveillance Unit was notified of 62 FAS cases between 1999 and 2001, giving an overall prevalence of 7 per 100 000.[14] A more recent Scottish study reported

Table 1 Three key clinical features required to make a diagnosis of fetal alcohol syndrome

Facial features	Poor growth	Structural or functional brain abnormality
Smooth philtrum Thin upper lip Short palpebral fissures	In utero <10th centile for gestational age Postnatal faltering growth	Head circumference <10th centile or microcephaly with increasing age Abnormal brain scan Developmental delay/learning difficulties Abnormal neurological signs

37 definite FAS cases over a 60-month period.[15] This study was limited to children under 6 years of age and therefore would not have captured those diagnosed later in childhood. The authors of the above studies consistently highlight issues of under-reporting and a lack of knowledge and awareness from paediatricians, contributing to a lower-than-expected number of reports.

The study sought to determine the incidence of FAS in the UK and Ireland in children aged 0–16 years. Additionally, the aim was to increase understanding of this patient population through reporting on demographics such as age, gender and ethnicity, comorbidities and involvement with health services. This study does not include FASD; FASD encompasses a wide variety of signs and symptoms and does not have the clear diagnostic criteria and analytic case definition used historically in FAS.

METHODS

Active surveillance was undertaken through the British Paediatric Surveillance Unit (BPSU) for a 13-month period: October 2018 to October 2019. Data were collected from reporting clinicians across the UK at notification using standardised questionnaires. The case definition used in this study matches the diagnostic criteria used by the Centers for Disease Control.[16] A confirmed history of maternal alcohol use during pregnancy was not required. Cases were also reported if alcohol use was uncertain or unknown but excluded if alcohol history was 'confirmed absent'.

Case definition

Any child <16 years old seen in the previous month with a diagnosis of FAS, based on the presence of all three of the following clinical features: typical facial features, growth impairment and structural or functional brain abnormality (table 1). A leaflet defining these characteristics was provided to clinicians at the start of the study and was available as an appendix within the questionnaire.

There was both a probable and a confirmed case definition. In probable cases, facial features were present, but centiles were either not recorded or did not specifically fit the diagnostic criteria (table 2), in confirmed cases the measurements were available.

Table 2 Definitions used to describe a confirmed or probable case of fetal alcohol syndrome

Confirmed case	Probable case
Three facial features with centiles	Three facial features without centiles
Prenatal or postnatal growth failure (weight or length <10 th percentile)	As confirmed case
Structural or functional brain abnormality (including microcephaly)	As confirmed case

Data

One hundred and forty-eight FAS case notifications were received from the UK and Ireland, of which nine were duplicates. Follow-up contact with reporting paediatricians was made for 113 (>80%) notifications. Only two cases were reported from Ireland. It was not possible to contact the referring paediatrician in either case. Forty-six cases were subsequently withdrawn by the reporting paediatrician. Reasons for withdrawal were: data for 10 cases could no longer be provided, 34 cases were thought not to fit the case definition after reconsideration, and in 2 cases the paediatrician could not be traced after initial contact. This left 67 notifications. Of these, 20 more were excluded by the study team as they did not fit the surveillance definition, leaving 37 probable cases and 10 confirmed cases.

Figure 1 summarises the case notifications received by the study group and reasons for exclusion or drop-out.

RESULTS

In view of small patient numbers, the 37 probable and 10 confirmed cases were analysed together, giving a total of 47 eligible cases.

Of these, 24 had been newly diagnosed during the surveillance period, October 2018 to October 2019 inclusive and 23 were children under 16 years of age diagnosed prior but seen during the study period.

Incidence

Twenty-four cases (14 males and 10 females) were diagnosed during the 13 months of active surveillance and were used to calculate incidence. The median age at diagnosis in this group was 5 years 2 months (range 3 months to 14 years 9 months). These 24 cases were used as a guide to the rate at which FAS cases were being recognised by paediatricians each year, taking the number of UK live births in 2019 as the denominator.[17] The estimated rate of FAS cases was 24×100 000/712 680=approximately 3.4/100 000 live births (95% CI 2.2 o 5.0).

All eligible cases

Of the total 47 cases, 20 were females and 27 were males. The median age at diagnosis was 24 months and the youngest age at diagnosis was 1 month (a probable case). Ethnicity was documented in 37 cases and, of these, 36 were documented as being white.

Only four children were living with their birth mother at the time of diagnosis, of whom three had social care involvement. Of the 43 cases not with their birth mother, 13 had been adopted, 14 were in foster care, 13 were with family members. In three cases, information about the child's placement was not provided.

A history of alcohol exposure was known in 41 cases (87%). This information was obtained through a combination of the child's biological mother, direct witness accounts and medical and/or legal records.

Ten of 47 children (21%) were known to have been exposed to opiates (heroin and/or methadone) and 21 of the 47 children (45%) were known to have been exposed to at least one substance as listed in table 3.

Ten of the 47 children (21%) were known to be exposed to two or more substances in addition to alcohol. These findings are summarised in table 3 below.

Facial features

In all but one of the probable cases, the palpebral fissure measurement was either not recorded or the measurement inconsistent with FAS (but the child had the two other facial features).

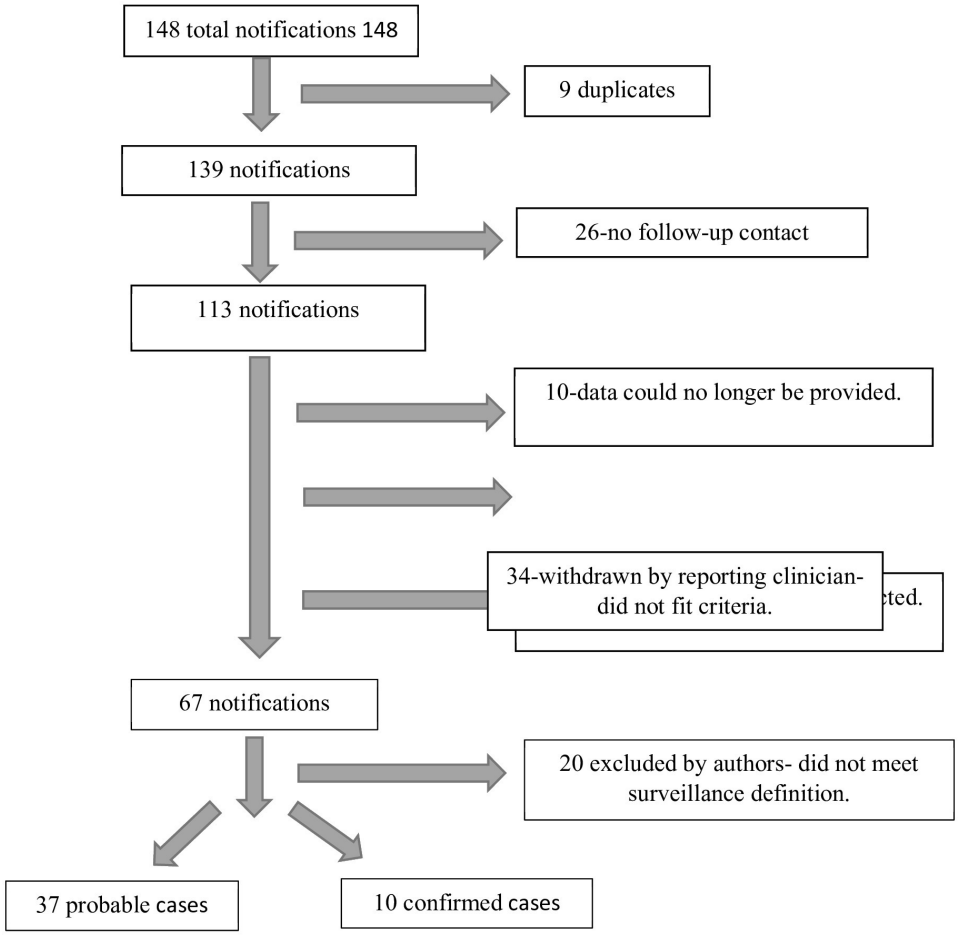

Figure 1 Case notifications received and reasons for exclusion or drop-out.

Growth

The child's birth weight or birth weight centile was available for 40 cases (85%) and 32 (80%) had a birthweight <10th percentile. At notification, 46 children (98%) had a weight measurement/weight centile available. Of these children, 25 (54%) were <10th percentile. Birth length/length centile was available in 13 cases (28%), of which 12 (92%) were <10th centile. At notification, a height measurement/height centile was available in all cases. Of these children, 26 (55%) were <10th percentile.

Nine children had confirmed congenital abnormalities, of which three had congenital cardiac conditions; two atrial septal defects and a bicuspid aortic valve.

The non-cardiac anomalies were varied:

- Oesophageal atresia and tracheo-oesophageal fistula
- Gastroschisis
- Nystagmus
- Abnormal ears and laryngomalacia
- Clinodactyly and syndactyly
- Developmental dysplasia of the hip

Table 3 In utero exposure to other substances in confirmed and probable cases of fetal alcohol syndrome

Substance	Confirmed use, n (%)	Confirmed absent, n (%)	Not documented, n (%)
Heroin	9 (19)	18 (37)	21 (44)
Methadone	6 (13)	23 (48)	19 (39)
Amphetamines	3 (6)	21 (44)	24 (50)
Cocaine	6 (13)	18 (37)	24 (50)
Cannabis	7 (15)	16 (33)	25 (52)
Cigarettes	13 (27)	14 (29)	21 (44)

Neurology

A birth head circumference measurement or centile was available for 26 cases (55%), of which 17 (65%) were <10th percentile. At notification, a head circumference measurement/centile was available in 42 cases (89%). Of these children, 35 (83%) were <10th percentile. Of the 17 children that were documented as being microcephalic (<10th percentile) at birth, 13 (76%) remained microcephalic, 2 (12%) had a head circumference >10th centile at notification and the remaining 2 children did not have a measurement at notification.

Three children were reported to have seizures. A wide range of neurodevelopmental difficulties were reported in 29 cases (table 4); reported by paediatricians or by caregivers or both. Seven children were too young to undergo a cognitive assessment.

Table 4 Neurodevelopmental difficulties reported

Speech and language delay	Low IQ
Poor executive function	Sensory processing disorder
Hyperactivity	Delayed social skills
Poor coordination	Cognitive delay
Attention deficit hyperactivity disorder	Emotional dysregulation

Service usage

All but one of the children were under the care of a community paediatrician. There was input from a general paediatrician in 20 (43%), Child and Adolescent Mental Health Services (CAMHS) in 8 (17%) and from at least one of the following therapy services: physiotherapy, speech and language, occupational therapy in 26 (55%).

Of the 47 children, 37 had genetic investigations, all of whom had an array CGH (Comparative genomic hybridisation). Nine children had testing for fragile X syndrome. Nineteen children (40%) had been seen by a geneticist. Of those tested, three were found to have variants of unknown significance. Three were awaiting results at the time of notification.

DISCUSSION

Our study found that when strict internationally agreed criteria are applied, just 47 probable/confirmed cases were identified in a year. The rate of withdrawal after the initial notification was significant; 34% of the 101 cases for which there was follow-up information were withdrawn by the reporting clinician because they did not meet the diagnostic criteria and a further 20 (19% of the 101 cases) were deemed by the study team not to meet the criteria. A comparable study by the Australian Paediatric Surveillance Unit also had significant drop-out (54% initial notifications met their criteria).[13] The particularly high numbers of exclusions and withdrawals suggest that there is a lack of experience or training about FAS among paediatricians.

This conclusion is confirmed by the striking variability in the age at diagnosis. For instance, in the 24 cases that were actually newly diagnosed during the period of active surveillance (October 2018 to October 2019 inclusive) the median age at diagnosis was just over 5 years, with a range of 13 months to 14 years 9 months. This extreme variability demonstrates that clinicians lack certainty and consistency when making the diagnosis of FAS.

In all the 47 probable/confirmed cases, the median age at diagnosis in this study was 3.25 years which is similar to the Australian Paediatric Surveillance Unit study median of 3.3 years.[13] This is somewhat lower than the median age at diagnosis for the 23 incident cases, reflecting simply a wide range in diagnostic approach and uncertainty in making the diagnosis. Early recognition and intervention in FAS and FASD are recommended to help families access support and aid the prevention of longer-term sequelae, for example, mental health issues.[18] Early diagnosis can also facilitate timely counselling and support for mothers who may have future pregnancies.[19]

FAS affects children of all ethnicities, however, the vast majority in this study were white British. This may reflect a lack of recognition of FAS features in children from black, Asian and minority ethnic (BAME) communities, inequalities in access to services and/or differences in patterns of maternal alcohol intake during pregnancy. In a recent study of FASD prevalance in UK school children, 92% children meeting the intitial screening criteria were white British, however, the overall ethnic diversity of the schools' population was not described.[20]

Although the FAS case definition in this study did not require a history of alcohol ingestion in the pregnancy, there was clear documentation of in utero alcohol exposure in 87% cases. This may suggest that FAS is more easily recognised and/or clinicians feel more confident to diagnose FAS in the context of a definite alcohol history. Over-reliance on confirmed alcohol exposure is likely to miss cases. The study by Abernethy *et al*[21] using meconium ethanol biomarkers suggested that 15% of pregnant women consumed significant quantities of alcohol in later pregnancy, despite none of the participants self-reporting heavy alcohol consumption. There was exposure to substances other than alcohol—this information can be challenging to obtain retrospectively, especially when children are looked after. Previous studies have highlighted a significant overlap between alcohol consumption and other substances in pregnancy. McGlone *et al*[22] found that almost half of infants born to mothers prescribed methadone during pregnancy had been exposed to high alcohol levels (using urine and meconium sampling). Professionals should be open-minded about the possibility of alcohol exposure and therefore FAS in infants born to mothers with known substance abuse.

Unreliable or inaccurate documentation of facial features limited the number of 'confirmed' cases to 10. This issue is not unique to this study. The New Zealand Paediatric Surveillance Unit found that 11% cases did not have consistent facial feature measurements and only 57% cases in the Australian Paediatric Surveillance Unit study had all three facial features.[13 14]

The majority of children in this study (83%) met the FAS diagnostic criteria for microcephaly at notification (<10th percentile). This suggests that microcephaly is a key diagnostic feature in this population. The New Zealand Paediatric Surveillance Unit FAS study reported that only around one-quarter of children were microcephalic, however, they used a different, more extreme definition for microcephaly (<2 SD below mean).

Rates of neurodevelopmental difficutlies, such as ADHD, were high. Some children were too young to assess formally so the proportion of children who will develop these problems is likely to be higher. Few children were in the care of their birth mother at notification, highlighting the vulnerability of the patient population and adding complexity to the diagnostic process. Looked after children are at risk of developing cognitive and behavioural problems for many reasons other than alcohol exposure.[23 24] Professionals may be more reluctant to diagnose FAS in these circumstances.

Genetic investigations are commonly performed in children with suspected FAS, aiming to exclude a contributing or alternative diagnosis. This study found that the yield from genetic investigations was low. Consistent with a retrospective case series of children with suspected FASD referred to a specialist, genetics service found that the overall diagnostic rate for a contributing genetic disorder was 3.6%.[25]

CONCLUSIONS

Only 47 confirmed/probable FAS cases were reported in a year and just 24 of these were actually newly diagnosed during the 13 months of surveillance, giving an approximate incidence rate of 3.4/100 000 live births. This is lower than reported in Australia and New Zealand and the barriers to diagnosis discussed above may have led to under-ascertainment of cases. The lack of consistency and certainty about the diagnosis of FAS demonstrated by this UK study emphasises the difficulty of performing robust epidemiological research into FAS. Population surveillance for FASD, which is thought to be more common, is even more challenging due to the lack of internationally agreed diagnostic criteria. These findings emphasise the importance of educating key professionals involved in the care of infants and children at risk of FAS.

Understanding the epidemiology of FAS is vital to guide the development of prevention strategies, referral pathways and support services. It is widely accepted that FAS and other

disorders associated with fetal alcohol exposure are under-recognised and under-reported.[10]

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