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Prevalence of Fetal Alcohol Spectrum Disorders: A Pilot Study in Western Sweden

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Keywords: fetal alcohol spectrum disorders | prevalence | screening

ABSTRACT

Aim: To develop and trial a method for estimating the prevalence of fetal alcohol spectrum disorders (FASD) in Sweden.

Methods: A school-based study with a full physical examination, including a dysmorphology assessment, neuropsychological testing, behavioural ratings, academic evaluation and maternal nutritional interview conducted as an add-on to the regular health check-up in 4th grade.

Results: Out of 348 eligible children, 223 participated. In the 206 children with a dysmorphological evaluation, 9.2% ($n = 19$) met criteria for a fetal alcohol spectrum disorder, with alcohol-related neurodevelopmental disorder accounting for 4.9% ($n = 10$), fetal alcohol syndrome for 2.4% ($n = 5$) and partial fetal alcohol syndrome for 1.9% ($n = 4$). According to the conservative method using all eligible children as the denominator, the prevalence of FASD was 5.5% (95% confidence interval [CI] 3.3–8.4) and fetal alcohol syndrome 1.4% (95% CI 0.5–3.3).

Conclusion: The lowest prevalence estimate of FASD in Sweden is similar to that found in other European countries, and four orders of magnitude more common than the prevalence of the diagnosis in official hospital records. A screening procedure for large-scale studies may utilise both behavioural and anthropometric measures, including head circumference, depending on the objective.

1 | Introduction

Although fetal alcohol spectrum disorders (FASD) are considered the leading preventable cause of disability around the globe [1, 2], no population-based studies have been conducted in the Nordic countries despite being called for by health authorities and stakeholders [3, 4]. With the exception of certain high-risk populations, Swedish health authorities have considered FASD to be a rare condition, reflecting the fact that the diagnosis (Q86 according to the international classification of diseases, version

Abbreviations: ARBD, alcohol-related birth defects; ARND, alcohol-related neurodevelopmental disorder; DCD, developmental coordination disorder; ESSENCE-Q, early symptomatic syndromes eliciting neurodevelopmental clinical examinations—questionnaire; FAS, fetal alcohol syndrome; FASD, fetal alcohol spectrum disorders; HC, head circumference; NDD, neurodevelopmental disorders; NDP, neurodevelopmental problems; pFAS, partial fetal alcohol syndrome; PFL, palpebral fissure length; SDQ, strengths and difficulties questionnaire.

Summary

- This pilot study used a school-based methodology, adding dysmorphological assessments and neuropsychological testing to the regular health check-ups that proved feasible for future large-scale studies.
- A conservatively estimated prevalence of fetal alcohol spectrum disorders (FASD) among all eligible children was 5.5%, suggesting a significant underreporting in official records.
- The lower limit of the prevalence estimate in Sweden aligns with that found in other European countries, suggesting that FASD is similarly underdiagnosed across the region.

10, ICD-10) is assigned in around 60 individuals annually in Sweden [5–7]. However, several prevalence studies of FASD have found that FASD is common in North America, Africa and Europe, repeatedly reporting estimates over 1% [1, 8].

The study methodologies for prevalence studies of FASD have commonly been 'in-school' active case ascertainment with anthropometric screening, followed by diagnostic work-up by a multidisciplinary team. According to this method, apart from maternal nutritional interviews, enrolment and study examinations take place in school.

1.1 | Aim

We aimed to pilot a pragmatic method for screening for FASD that would be scalable for use in a Swedish setting. We also aimed to report a preliminary prevalence estimate based on the findings.

2 | Methods

2.1 | Setting and Participants

The study was mainly managed in regular (public) schools in western Sweden between 2018 and 2020 as part of a broad research initiative covering students' basic academic skills, general health, neurodevelopment and their possible associations with important background factors [9–11]. School principals at schools in proximity to the participating physicians in the study were approached both in person and by written correspondence. Approximately half of the schools had principals willing to engage in child health studies. Caregivers of all pupils attending 4th grade at six public and two private ('free') schools were invited to participate after an oral and written presentation of the study. Statistics from the Swedish National Agency for Education indicate that the participating schools exhibited a socioeconomic status around one standard deviation below the national average (based on parental education level, income and reliance on social benefits). At each site, one or two academic years of children were recruited, and participation constituted an add-on to the existing regular health check-up conducted in 4th grade. Data collection relied on multiple sources, including medical examinations, maternal interviews, psychological assessments, behavioural ratings for teachers and guardians, review of medical records and national academic test results. The participating schools had no pupils attending special education. All caregivers and children signed informed consent. The study was approved by the ethical review board at Gothenburg university (no. 852-17). Using the same cohort, we have previously reported on the validity of the early symptomatic syndromes eliciting neurodevelopmental clinical examinations—questionnaire (ESSENCE-Q) for detecting clinically relevant neurodevelopmental problems (NDPs) as rated by parents or by physicians when retrospectively screening medical records for detecting NDPs, as well as the prevalence of clinically relevant NDPs in the cohort [9–11]. ESSENCE is an umbrella term used to describe conditions characterised by early onset of unspecific symptoms (e.g., problems with language, motor skills, social interactions, attention, mood, sleep and general development) that with age eventually align with neurodevelopmental disorders [12]. The concept emphasises the connection of ESSENCE with etiological syndromes, such as fragile X, valproic acid syndrome and FASD [13].

TABLE 1 | Overview of diagnostic criteria for each category of fetal alcohol spectrum disorders.

FAS	A. Facial dysmorphology—2 of 3 cardinal facial features (Smooth philtrum[a], thin vermilion border[a], palpebral fissure length < 10 centile)
	B. Body growth deficiency (weight/height/BMI < 10th centile)
	C. Brain growth deficiency (head circumference < 10th centile or structural abnormalities)
	D. Neurobehavioral impairment (cognitive or behavioural impairments deviating > 1.5 standard deviation below the mean)
pFAS	With documented alcohol exposure[b]:
	A. Facial dysmorphology
	D. Neurobehavioral impairment
	Without documented alcohol exposure:
	A. Facial dysmorphology
	B or C. Body or brain growth deficiency
	D. Neurobehavioral impairment
ARND	Documented alcohol exposure
	D. Neurobehavioral impairment
ARBD	Documented alcohol exposure
	One or more severe malformations associated with alcohol exposure

Note: This table presents a summary of criteria described in the Hoyme 2016 guidelines [14].
Abbreviations: ARBD, alcohol-related birth defects; ARND, alcohol-related neurodevelopmental disorder; FAS, fetal alcohol syndrome; pFAS, partial fetal alcohol syndrome.
[a]Likert rating of 4 or 5 (range 1–5).
[b]According to the diagnostic criteria, ≥ 3 drinks on two occasions or ≥ 6 drinks/week for 2 weeks or other reliable or documented evidence of alcohol intake during pregnancy constitutes documented alcohol exposure during pregnancy.

2.2 | Measures and Procedure

We gathered the clinical information needed to assess children according to the Institute of Medicine diagnostic criteria of FASD updated in 2016, which have been the basis for prevalence studies encompassing over 10,000 children worldwide [14]. The guidelines instruct a multidisciplinary work-up led by a paediatrician, with a dysmorphological evaluation as the basis. The diagnostic criteria cover four domains: prenatal alcohol exposure, dysmorphology, growth and neurodevelopment, and are summarised in Table 1.

2.3 | Prenatal Alcohol Exposure

Prenatal alcohol exposure was assessed in an extensive maternal nutritional interview covering four domains (general, nutrition, psychosocial and heredity) comprising 125 questions, including visual descriptions of food and beverages (including standard drinks), conducted by nurses specifically trained for this task. The nutritional interview is building on a structured questionnaire adapted by the last author from the one created at the University of North Carolina by May et al. This interview has been utilised in prevalence studies of FASD in the United States and other countries [15]. Questions are designed to be answered without ambiguity, for instance, by allowing only yes or no answers, quantitative responses or similar formats. Relevant questions for this study covered areas, such as alcohol, drugs, medications, educational level, work situation and heredity.

After information about current drinking habits, queries regarding alcohol were asked in a timeline follow-back manner, including age of alcohol debut, drinking patterns 3 months before pregnancy, week of pregnancy awareness, drinking pattern during pregnancy, specifically instances of binge drinking. Questions about drinking patterns were structured to be answered in terms of the number of occasions per week and the number of alcohol units per occasion, providing visual examples of alcohol units. One alcohol unit in Sweden contains 12 g of alcohol and is equivalent to 50 cL of beer with 3.5% alcohol content, 33 cL of beer with 5.2% alcohol content, 12–15 cL of wine or 4 cL of spirits. According to the diagnostic criteria, ≥ 3 drinks on two occasions or ≥ 6 drinks/week for 2 weeks or other reliable or documented evidence of alcohol intake during pregnancy constitutes documented alcohol exposure during pregnancy.

2.4 | Dysmorphology

The cornerstone of the work-up for FASD comprises a paediatric examination, including the measurement of head circumference (HC), a dysmorphological evaluation, including the three cardinal facial features associated with prenatal alcohol exposure: thin vermilion border, smooth philtrum and short palpebral fissures [14, 16, 17]. The facial features are assessed according to Likert scales and reference values accompanying the guidelines [14]. We also assessed for the presence of short inner and outer canthal distance and short interpupillary distance, flat nasal bridge, anteverted nose, prognathism, 'railroad track' ears, hirsutism, hypoplastic nails, camptodactyly, strabismus, ptosis and epicanthic folds. They comprise a dysmorphology score of minor physical anomalies that are non-diagnostic findings occurring frequently in FAS [14, 18]. The examination also included a set of neuromotor tests, as developmental coordination disorder-like deficits (DCD) have been linked to FASD [19]. Out of four physicians, three (ML, VL and MJ) had been trained in dysmorphological evaluations and diagnostic work-up with an American–South African team led by professor Hoyme, the first author of the diagnostic criteria [14]. The fourth physician (TL) had been trained by the last author (ML) in performing the dysmorphological examination. At the time of the dysmorphology assessment (physical examination), physicians were blinded to any other clinical information regarding the participant.

2.5 | Growth

The regular medical check-up by the school nurse provided current measurements of height, weight and body mass index (BMI), and historical measurements from birth through childhood were retrieved from the child healthcare and school medical records.

2.6 | Neurodevelopment

Neurodevelopmental performance was assessed on the basis of the neuropsychological evaluation (Leiter-III non-verbal IQ test and performance ratings), structured physical examination, medical records review, teacher and parent rating scales (ESSENCE-questionnaire, strengths and difficulties questionnaire, SDQ) and academic achievement according to national academic tests [10, 20, 21]. We assessed the presence and severity of NDPs in a process validated against three clinicians with extensive experience of such work-ups. This process and the results have been reported extensively previously [11].

2.7 | Diagnostic Evaluation

All participants were thoroughly reviewed in a case conference attended by a child neurologist (ML) and neuropsychologist (LS), both with more than 25 years of clinical experience working with families of children with neurodevelopmental disorders and behavioural phenotype syndromes, including FASD and a psychiatrist (RK or VL). For the purpose of this study, all possible cases of FASD were reassessed in a case conference attended by ML, LS and DK, scrutinising the available clinical information against the diagnostic criteria for FASD (Table 1).

2.8 | Statistics

For descriptive statistics, non-parametric or parametric methods were used on the basis of the data's dispersion and distribution. When applicable, individual quantitative data were transformed to z-scores or percentiles that denote the distance of a raw score to that of the reference mean value. In the computation of the dysmorphology score, missing items were classified as normal/absent. We employed no other imputation in

instances of missing data. We presented prevalence estimates according to a conservative and an observed method. The conservative method used the number of participants with FASD as the numerator and the number of eligible children as the denominator. This method assumes that there were no children with FASD among those eligible but not enrolled in the study. The observed method used the number of participants with FASD as the numerator and the number of children with at least a dysmorphological assessment as the denominator. To calculate prevalence with confidence intervals based on the findings and sample size, the Clopper–Pearson exact method was employed. Analyses were conducted using R 4.2.2 (R Core Team) with the Binomial package.

3 | Results

A participant flow diagram is depicted in Figure 1. Out of 348 eligible children, 223 children (mean age 11.0 years, standard deviation [SD] 0.3 years) and their parents consented to participate; 206 (117 boys, 89 girls) underwent a dysmorphology evaluation and were included in the study. For these 206 participants, child health care records were missing for 106 (51%), parental behaviour ratings for 40 (19%), teacher behaviour ratings for 1 (<1%), neuropsychological testing for 37 (17%) and interview data regarding alcohol exposure for 64 (31%). Due to the COVID pandemic, scheduling of in-person interviews with mothers became unfeasible and had to be halted. Of the interviewed mothers, 73% were born in Sweden and 89% were employed, rates similar to the general population (Statistics Sweden 2020).

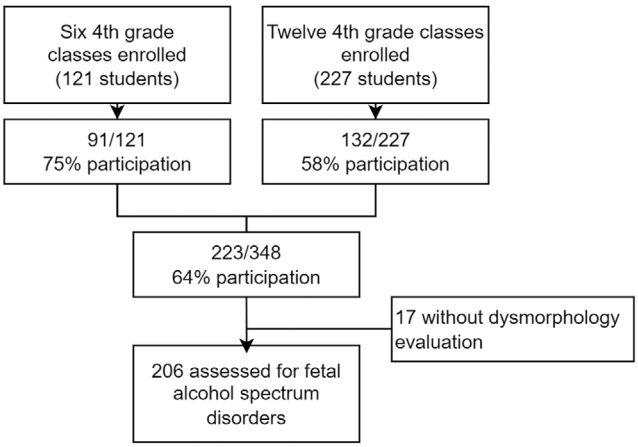

FIGURE 1 | Participant flow diagram.

3.1 | Prevalence

Out of 206 participants, 19 (9.2%) met criteria for FASD (9 boys, 10 girls), 5 of whom met criteria for fetal alcohol syndrome (2.4%), 4 for partial fetal alcohol syndrome (1.9%) and 10 (4.9%) alcohol-related neurodevelopmental disorder. Prevalence estimates with 95% confidence intervals according to the conservative and observed methods are reported in Table 2. One participant met criteria for an alcohol-related birth defect (vascular malformation), had FAS facial features and an aberrant EEG, but did not exhibit neurobehavioral impairment to the degree warranting a further FASD diagnosis according to the diagnostic criteria.

Clinical characteristics of the cohort are described in Table 3.

3.2 | Proposed Screening Procedure

In order to determine the prevalence of FASD, it is crucial to have a screening procedure balancing sensitivity and specificity. To achieve this, we assessed many options, which are presented in Table 4. We aligned the screening level for anthropometric measurements with the diagnostic criteria of growth deficiency in FASD (10th centile equivalent to −1.3 SD) and a less strict cut-off for behavioural measures (+ 1 SD in the cohort). Consistent with prior studies on screening for neurodevelopmental disorders, it is recommended that relying on a single informant alone is not enough due to inadequate sensitivity [22]. Behavioural measures may fail to identify those at risk due to observer bias or the fact that the impairment has not yet displayed. Prior prevalence studies of FASD have primarily relied on anthropometric screening measures, on the presumption that significant alcohol exposure may cause growth restriction. Although these measurements are objective, they may fail to identify individuals with marked impairment and those without accessible birth or school records. Because FAS is characterised by growth restriction, specific attention should be given to a conscious review of growth parameters, from birth onwards. Head circumference, an indicator of brain growth, needs to be reassessed, something that is rarely done in health check-ups or clinical appointments beyond the age of 2 years in Sweden.

As seen in Table 4, a screening approach that solely relies on anthropometric measurements (including HC at age 11 years) would have a high likelihood of detecting all cases of fetal alcohol syndrome (FAS) (100%) and partial fetal alcohol syndrome (pFAS) (75%), while also identifying a significant number of individuals who do not have FASD (27%). Additionally, it would

TABLE 2 | Prevalence estimates across the continuum of fetal alcohol spectrum disorders.

No. of eligible children	Statistical method	Diagnostic group, % (95% CI)			
		Fetal alcohol syndrome ($n=5$)	Partial fetal alcohol syndrome ($n=4$)	Alcohol-related neurodevelopmental disorder ($n=10$)	Total fetal alcohol spectrum disorders ($n=19$)
348	Conservative	1.4 (0.5–3.3)	1.1 (0.3–2.9)	2.9 (1.4–5.2)	5.5 (3.3–8.4)
206	Observed	2.4 (0.8–5.6)	1.9 (0.5–4.9)	4.9 (2.4–8.7)	9.2 (5.6–14.0)

Note: Conservative statistical method uses the number of eligible children as denominator, and the observed method uses the observed number of children who underwent a dysmorphological assessment as the denominator.

TABLE 3 | Clinical characteristics of participants with and without fetal alcohol spectrum disorders.

	No fetal alcohol spectrum disorder ($n=187$)	Fetal alcohol syndrome ($n=5$)	Partial fetal alcohol syndrome ($n=4$)	Alcohol-related neurodevelopmental disorder ($n=10$)
Prenatal alcohol exposure				
Confirmed prenatal alcohol exposure, *n* (%)	18 (14)	2 (40)	2 (50)	10 (100)
Dysmorphology				
Palpebral fissure length, right eye, mm (IQR)	27.0 (26.0–28.0)	26.0 (25.0–27.0)	26.5 (25.5–27.3)	27.0 (26.0–27.8)
Palpebral fissure length, left eye	27.0 (26.0–29.0)	26.0 (24.0–27.0)	27.0 (26.0–28.3)	27.0 (27.0–28.0)
Philtrum score 4–5, *n* (%)	54 (28.9)	5 (100.0)	4 (100.0)	2 (20.0)
Vermilion score 4–5	50 (26.7)	4 (80.0)	4 (100.0)	2 (20.0)
Dysmorphology score, mean (IQR)	6.0 (4.0–10.0)	13.0 (12.0–14.0)	13.0 (13.0–13.0)	4.5 (4.0–9.8)
Growth				
Birth				
Weight, mean *z*-score (SD)	0.0 (−1.0–1.0)	0.0 (−0.9–0.8)	−2.5 (−2.8–1.8)	0.1 (−0.2–0.9)
Height	0.0 (−0.5–0.9)	−1.0 (−1.5–0.5)	−2.0 (−2.5–1.0)	−0.8 (−1.1–0.6)
Head circumference	−0.5 (−1.3–0.7)	−2.8 (−2.9–1.9)	−1.0 (−1.3–0.8)	0.0 (−0.6–0.5)
Examination (11 years)				
Weight	0.7 (−0.3–1.8)	0.1 (−0.9–0.8)	0.4 (−0.9–2.5)	0.9 (−0.5–2.2)
Height	0.4 (−0.3–1.1)	−0.3 (−1.9–0.2)	0.1 (−0.2–0.7)	0.3 (0.4–1.2)
Head circumference	0.4 (−0.4–1.2)	−1.7 (−1.9–1.3)	0.1 (−0.2–0.3)	0.8 (0.2–1.5)
Body mass index	0.7 (−0.2–1.8)	0.1 (−0.2–1.1)	0.8 (−0.8–2.8)	0.9 (0.2–1.6)
Systolic blood pressure, mean centile (IQR)	57 (27–80)	56 (35–77)	99 (99–99)	12 (6–59)
Diastolic blood pressure	66 (47–88)	73 (65–82)	97 (97–97)	55 (45–58)
Neurodevelopment				
Teacher-rated strength and difficulties questionnaire, median (IQR)	5.0 (1.0–11.0)	3.0 (2.0–8.0)	11.5 (8.3–15.0)	10.5 (6.5–14.0)
Parent-rated strength and difficulties questionnaire	7.0 (3.0–12.0)	17.0 (11.0–18.5)	10.0 (6.0–14.3)	14.0 (8.5–16.5)
Parent-rated ESSENCE-*Q* score	1.0 (0.0–4.0)	5.0 (2.5–7.0)	1.0 (0.5–5.0)	10.0 (2.3–15.8)

(Continues)

TABLE 3 | (Continued)

	No fetal alcohol spectrum disorder ($n=187$)	Fetal alcohol syndrome ($n=5$)	Partial fetal alcohol syndrome ($n=4$)	Alcohol-related neurodevelopmental disorder ($n=10$)
Clinician-rated ESSENCE-*Q* score of medical records	2.7 (1.3–5.0)	4.7 (4.7–10.3)	6.3 (4.0–7.5)	4.3 (3.7–9.3)
Non-verbal IQ	110 (101–115)	98 (97–111)	107 (106–109)	108 (102–110)
Symptomatic problem areas				
Externalising, *n* (%)	35 (19)	1 (20)	2 (50)	7 (70)
Speech-language-learning	9 (5)	0 (0)	0 (0)	1 (10)
Autism spectrum	9 (5)	1 (20)	0 (0)	2 (20)
Developmental coordination	19 (5)	1 (20)	0 (0)	1 (10)
Borderline intellectual functioning	4 (3)	1 (20)	0 (0)	0 (0)
Clinical global impression—severity, median (IQR)	3.0 (1.0–4.0)	4.0 (3.0–4.0)	4.0 (3.8–4.3)	4.5 (4.0–5.0)
Any failed national scholastic test, *n* (%)	82/170 (48)	3/4 (75)	2/3 (67)	8/9 (89)

Abbreviations: ESSENCE-Q, Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations—questionnaire; IQ, intellectual quotient; IQR, interquartile range; SD, standard deviation.

fail to identify a significant proportion of cases involving alcohol-related neurodevelopmental disorder (ARND), with just 40% being detected. Using solely behavioural measures would provide similar results and would identify children at risk of other neurodevelopmental disorders, not FASD only. Allowing detection through either anthropometric or behavioural screening, a high percentage of cases might be detected. However, this approach would also result in a significant number of children without FASD being included (51%). Applying both anthropometric and behavioural screening in combination would identify as positive most cases with FAS (80%), roughly half of cases with pFAS, and ARND the least proportion of children with no FASD (9%). Some settings, such as children in special education, out-of-home placement and involved with the criminal justice system, warrant assessment without any screening procedure, since the prevalence of FASD in such settings is estimated to be 10–40 times higher than that in the general population [16, 23, 24].

4 | Discussion

4.1 | Key Results

In this cross-sectional pilot study of the prevalence of FASD in Sweden, we found the prevalence estimate to be 5.5% (95% CI 3.3–8.4) for the entire FASD continuum and 2.4% (95% CI 0.8–5.6) for the full FAS. An extended assessment of the regular health check-up in 4th grade proved feasible to assess these children and suggested that a screening procedure utilising growth parameters, including HC and behavioural measures could identify children at high risk of FASD.

4.2 | Interpretation

4.2.1 | Prevalence

The prevalence rate found is considerably higher than those obtained in the only previous study conducted in Sweden, almost 50 years ago when Olegård et al. estimated the prevalence of the full fetal alcohol syndrome (FAS) in Gothenburg to be 0.15%, based on natal service surveillance and case ascertainment [25]. Although the prototypical FAS was delineated in the 70s and has been rather stable across subsequent formalised diagnostic criteria [14, 26, 27], most studies have not been conducted in newborns. The prominence of facial characteristics is thought to be most noticeable from 6 years of age until preadolescence, and difficulties with detailed facial assessment of newborns are a contributing factor [16, 28].

A meta-analytic study by Lange et al. reports FASD prevalence in children to exceed 1% in more than 76 countries, constituting the leading preventable cause of disability worldwide [1]. Included studies reported varying rates, also within countries, such as the United States, host of the largest prevalence study of FASD to date [1, 8]. This may be statistical artefacts due to

TABLE 4 | Screening parameters for prevalence studies of fetal alcohol spectrum disorders.

	No fetal alcohol spectrum disorder ($n=187$)	Fetal alcohol spectrum disorder ($n=19$)	Fetal alcohol syndrome ($n=5$)	Partial fetal alcohol syndrome ($n=4$)	Alcohol-related neurodevelopmental disorder ($n=10$)
Antrophometric screening < −1.3 SD					
Birth					
Weight, *n* (%)	12/86 (14)	4 (29)	1/3 (33)	2/3 (67)	1/8 (13)
Height	6/86 (7)	5 (36)	1/3 (33)	2/3 (67)	2/8 (25)
Head circumference	23/86 (27)	4 (29)	2/3 (67)	1/3 (33)	1 (8) (13)
Age 11 years					
Height	17/187 (9)	3/19 (16)	2/5 (40)	0/4 (0)	1/10 (10)
Weight	11/187 (6)	4/19 (22)	1/5 (20)	1/4 (25)	2/10 (20)
Head circumference	16/187 (9)	4/19 (21)	4/5 (80)	0/4 (0)	0/10 (0)
Body mass index	6/187 (3)	1/19 (5)	0/5 (0)	1/4 (25)	0/10 (0)
Behavioural screening > +1 SD at age 11					
ESSENCE-Q parental ratings	24/144 (17)	7/16 (44)	1/3 (33)	1/3 (33)	5/10 (50)
ESSENCE-Q clinician-rated medical records	21/140 (15)	6/17 (35)	2/5 (40)	1/3 (33)	3/9 (33)
SDQ, teacher-rated total score	32/187 (17)	6/19 (32)	1/5 (20)	2/4 (50)	3/10 (30)
SDQ, parent-rated total score	28/147 (19)	8/17 (47)	2/3 (67)	1/4 (25)	5/10 (50)
Summary screening					
Any anthropometric screen positive	51/188 (27)	12/19 (63)	5/5 (100)	3/4 (75)	4/10 (40)
Any behavioural screen positive	62/188 (33)	13/19 (68)	4/5 (80)	3/4 (75)	6/10 (60)

(Continues)

TABLE 4 | (Continued)

	No fetal alcohol spectrum disorder ($n = 187$)	Fetal alcohol spectrum disorder ($n = 19$)	Fetal alcohol syndrome ($n = 5$)	Partial fetal alcohol syndrome ($n = 4$)	Alcohol-related neurodevelopmental disorder ($n = 10$)
Anthropometric or behavioural screen positive	96/188 (51)	16/19 (84)	5/5 (100)	4/4 (100)	7/10 (70)
Anthropometric and behavioural screen positive	17/188 (9)	9/19 (47)	4/5 (80)	2/4 (50)	3/10 (30)

Note: The summary screening reports the proportion screened as positive in one or more of the listed groups of screening measures (anthropometric/behavioural). Missing data for the anthropometric screen ranged from 102 to 104 for birth records and 1 to 4 at age 11 years, and for the behavioural screen from 1 to 48.
Abbreviations: ESSENCE-Q, Early symptomatic syndromes eliciting neurodevelopmental clinical examinations—questionnaire; SDQ, strengths and difficulties questionnaire.

sample sizes but also reflect the varying alcohol consumption patterns across populations. Alcohol use during pregnancy is considered to be lower in Sweden than in other European countries [29]. There are no prevalence studies of FASD in the Nordic countries for comparison, but the rates found herein accord with those of other studies conducted in Europe, such as Ireland (4.8%), Italy (4.5%), Croatia (5.3%) and the UK (3.6% and 6%), countries where alcohol use during pregnancy was estimated to be higher, with the exception of Croatia [1, 2, 30–33]. Studies on the drinking habits of Swedish mothers indicate that increased age, urban residency and higher educational attainment correlate with greater alcohol consumption [34]. The lower socioeconomic status and the rate of rural living among mothers in our study indicate that the cohort's exposure may be less than that of the overall population in Sweden. The incidence of alcohol consumption during pregnancy reported in our study exceeded that of a Swedish sample in a European study (7%) [35]. This difference is potentially attributable to the timeline follow-back method embedded in a nutritional interview employed in our study, which is deemed to elicit more accurate responses compared with direct inquiries on alcohol usage during pregnancy [14].

4.2.2 | Diagnostic Characteristics

The palpebral fissure length showed limited variation between cases and non-cases, and measuring the palpebral fissure length reliably can be a challenge in clinical practice. Because strabismus, refraction error, retinal abnormalities s and visual perception problems have been found to be common in FASD, we think a work-up should include an ophthalmological assessment [32, 33]. Such an assessment would be able to corroborate the presence of small palpebral fissures and assess the integrity of the eyes. The proportion of children with a rating of 4–5 in the philtrum and vermilion was substantial in non-cases, which is similar, albeit slightly higher than that reported in previous studies [36–38].

4.2.3 | Limitations and Generalisability

The prevalence of NDPs and socioeconomic status of the participating schools (1 SD below the national average) suggests that estimates of NDPs based on this sample may be higher than in the general population [11]. There may have been a bias favouring participation among parents concerned about NDPs in their children, given the study provided a pathway for identifying unmet needs. On the contrary, the study did not cover children in special needs classes, where previous literature indicates FASD to be overrepresented [16, 23]. Absence of data from maternal interviews and birth records in participants born abroad may also have led to inadequate recognition of prenatal adversity and alcohol exposure in this group. The maternal interview was not formally validated and may not reflect the same associations as the American version. Missing data regarding alcohol exposure may skew results towards an underestimation of the prevalence of the full spectrum of FASD in this sample. Although we applied criteria as rigorously as possible using multiple information sources, the work-up of FASD for research purposes may be different to that in a clinical situation.

Because we were unable to conduct genetic studies, such as Single Nucleotide Polymorphism arrays, we cannot definitively rule out the possibility of genetic syndromes in some cases. However, the final author's experience as a paediatric neurologist with the spectrum of behavioural phenotypic syndromes and potential genetic phenocopies of FAS, as outlined in the diagnostic criteria, somewhat limits this possibility. Without the presence of key facial features seen in the complete FAS, as is the situation with ARND, it becomes impossible to effectively separate the effects of alcohol exposure from genetic and perinatal influences. Therefore, the number of cases with ARND reported herein may be inflated. We assert that enrolling students in the 4th grade instead of the 1st grade provides more comprehensive longitudinal data on growth restriction and neurodevelopmental problems, warranting a more reliable assessment in these regards. The use of established research criteria and training directly from the author of the diagnostic criteria allows for comparisons across samples.

5 | Future Research

This pilot study was conducted to provide a scalable screening procedure and approach within a Swedish context. Prevalence studies must identify methods to encourage maximum participant enrolment to mitigate selection bias [31]. Capitalising on the routine health check-up in 4th grade proved effective and is recommended for future studies. Routine health check-ups are implemented uniformly across other Nordic countries, facilitating the potential for prevalence studies across these countries employing similar methods. The screening process of future studies is contingent upon its intended objective. For the detection of FAS, the most severe manifestation of FASD, anthropometric measurements seem adequate. For the detection of the complete spectrum of FASD, including ARND, we would suggest behavioural screening measures from at least two information sources (child/school health care records, parents, teachers). Alternatively, given the prevalence of NDPs and other health concerns in children, a proficient and adequately staffed school healthcare service, including routine examinations by a physician, is warranted [11]. The prevalence documented in the literature highlights the necessity for school physicians to be familiar with the characteristics of FASD and associated background risk factors. Knowledgeable school physicians assessing all children would represent the most efficient screening procedure both for research and practice.

6 | Conclusion

The prevalence of FASD in Sweden seems to be comparable to that of other European countries. Larger epidemiological studies are warranted and feasible to conduct as in-school studies.

Author Contributions

Valdemar Landgren: investigation; funding acquisition; writing – original draft; Methodology; writing – review and editing; software; formal analysis; project administration; data curation; validation. **Rajna Knez:** writing – review and editing; investigation; validation; data curation. **David Karlsson:** validation; writing – review and editing; data curation. **Samuel Fernmo:** investigation; methodology; software; project administration; data curation. **Mats Johnson:** investigation; conceptualization; writing – review and editing. **Leif Svensson:** conceptualization; investigation; methodology; validation; writing – review and editing; project administration; data curation. **Magnus Landgren:** conceptualization; investigation; funding acquisition; methodology; validation; project administration; supervision; resources; writing – review and editing.

Conflicts of Interest

The authors declare no conflicts of interest.

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