Mental Health in School-Aged Children Prenatally Exposed to Alcohol and Other Substances

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ABSTRACT: Prenatal exposure to substances can possibly influence a child's neurodevelopment and may impact on subsequent mental health. We investigated the mental health status of school-aged children referred to a pediatric hospital with a history of prenatal exposure to alcohol or other substances. Mental health was assessed using the Strengths and Difficulties Questionnaire and compared with a reference group. A total of 105 of 128 (82%) eligible children prenatally exposed to substances participated in the study, with 48 children exposed to alcohol and 57 to other substances. Strengths and Difficulties Questionnaire subscale mean scores, total difficulties scores, and total impact scores were statistically significantly higher in the group of exposed children, compared with the reference group. In this hospital-based population of school-aged children prenatally exposed to alcohol or other substances, the exposed group had an increased risk of mental health problems, compared with the reference group.

KEYWORDS: Mental health, development, alcohol exposure, drug effects, child development

Introduction

Background

Alcohol, opiates, and most illicit drugs cross the placenta and can affect the fetus through direct effects on fetal development and indirectly through pharmacological effects on the pregnant mother.[1–5] Prenatal substance exposure may result in neurodevelopmental impairments through adverse effects on the fetal brain and can possible impact on subsequent mental health outcomes.[2–4,6,7] Substance exposure in pregnancy represents a public health problem.[1] Furthermore, it is difficult to estimate the prevalence due to inconsistent reporting from pregnant women and the illegal nature of illicit drug use.[1,8,9]

Prenatal exposure to alcohol

Alcohol is a well-known teratogenic substance, and alcohol exposure during pregnancy may result in fetal alcohol spectrum disorders (FASD).[1,10,11] Fetal alcohol spectrum disorder comprises a spectrum of conditions presenting with mild to severe neurodevelopmental consequences such as cognitive impairment and an increased risk of specific learning disabilities, attention-deficit/hyperactivity disorder (ADHD), and anxiety and mood disorders.[1,10–12] Other important sequelae associated with prenatal alcohol exposure include an increased risk of miscarriage, preterm birth, prenatal and postnatal growth restriction, and sudden death

infant syndrome, as well as effects on various organ systems such as the cardiovascular, musculoskeletal, renal, ocular, and auditory systems.[1,12] The impact of maternal alcohol use on fetal development depends on a variety of factors, including the timing and level of alcohol exposure and genetic background.[13] Recent research exploring the epigenetic mechanisms involved in fetal exposure to alcohol suggests a link between the genetic background, environmental factors, and neurodevelopmental outcomes.[13]

Prenatal exposure to substances other than alcohol

Prenatal substance exposure also includes exposure to opioids, amphetamine, methamphetamine, cocaine, and cannabis and the illegal use of benzodiazepines. Exposure to these substances is associated with low birthweight, preterm births, and, particularly in the case of opioids, neonatal abstinence syndrome (NAS).[1,14,15] Systematic reviews of children exposed to substances other than alcohol have reported an increased risk of cognitive and behavioral impairments later in preschool age.[3,6] Furthermore, some longitudinal studies found that cognitive difficulties in preschool-aged children persisted into school and adolescence age, and a recent study reported effects in children of exposure to substances other

than alcohol on cognition increasing over time, compared with nonexposure.[6,7,16,17] Less is known about the mental health outcomes of prenatal exposure to other substances in school-aged children.[3]

Genetics and environmental factors affecting mental health

Children prenatally exposed to substances are influenced by several risk factors, including biological, genetic, environmental, and socioeconomic factors that are associated with mental health outcomes.[6,18–21] Parental substance use increases the risk of poverty, family stress, low level of parental education, poor prenatal care, and family instability, as well as being a risk factor for placement of children into foster care.[22,23] Exposure to inadequate caregiving conditions earlier in life may affect the mental health later in life, and optimizing care conditions is likely to have a positive effect on mental health outcomes.[23,24] For youth placed in foster care in western countries, the prevalence of mental disorders has been estimated to be higher than that for the general population.[23,25]

Aim of the study

The aim of this hospital-based follow-up study was to assess mental health in school-aged children prenatally exposed to alcohol and other substances, in comparison with a reference group as control. We hypothesized that prenatal exposure to substances would result in higher mean scores on the Strength and Difficulties Questionnaire (SDQ) in exposed children, compared with controls. Furthermore, given the known teratogenic effects of alcohol, we expected higher mean SDQ scores in children mainly exposed to alcohol, compared with those mainly exposed to other substances.

Methods

Participants

The study included a hospital-based population of children referred to the pediatric department at Haukeland University Hospital in Bergen, Norway, between January 1997 and December 2012. Referral criteria included the presence of developmental impairments and a concomitant past medical history of prenatal alcohol or other substance exposure. Referrals to the pediatric department were from healthcare providers, social workers, and physicians in primary community care units and pediatric and child psychiatric units.

A follow-up study on mental health status was conducted at school age. At this point, in the study, 128 children aged between 6 and 14 years were invited to participate; of whom, 111 gave informed written consent (87%). Of the 111 children, 105 (95%) had their caregivers complete the SDQ questionnaire.

The reference group

The reference group consisted of children participating in the Bergen Child Study (BCS), which is a longitudinal population-based study. There were no exclusion criteria,[26] and all children attending grades 2 to 4 at 79 schools in a geographically delineated area in the academic years of 2002 and 2003 were invited to participate in the study (n = 9430). Parent SDQ questionnaires were completed for about two-thirds of the participating children (n = 6297).[26] Of the participating children in BCS, about 2 out of 3 lived in a family categorized as having good or very good family economy, and about 50% of the mothers and fathers had higher education.[27] More details about the reference group are presented in the papers by Heiervang et al,[26] Boe et al,[27] and Stormark et al.[28] In this study, participants from the first 2 waves were included. The first wave of the BCS, conducted in autumn 2002, comprised a target population of 9430 primary school children aged 7 to 9 years, and informed consent to participate was received from 7007 (74%) parents prior to study inclusion. The second wave was conducted 4 years later during spring 2006, comprising 5683 children aged 11 to 13 years (60% of the original target population). For every participating child in the hospital-based group of children prenatally exposed to substances, 3 children from the BCS population, who were sex and age matched (±0.9 years), were randomly selected into the reference group. Three controls were included for each case to improve the robustness of the analyses.[29] As we considered age to be an important matching factor in this study, we used a relatively narrow matching criterion of ±0.9 years, which hence allows 3 eligible controls from the BCS. We considered that a 3:1 ratio worked best with the available data, as to achieve a 4:1 ratio between the controls and cases would require the age matching criterion to be extended to about ±2 years.

Ethics

The study was approved by the Regional Committee for Medical Research Ethics in Norway. For children prenatally exposed to substances, informed written consent was obtained from all participating caregivers: biological parents for children living in their biological home and foster parents for children living in foster care. For children in foster care, the social welfare office legally responsible for the participating child also gave written consent. Children 12 years and older, gave their independent consent to participate in the study. For the reference group, children's caregivers gave informed written consent.

Care situation

The following data were collected from medical records and questionnaires completed by the caregivers: the present care situation and age at time of placement in cases where the child was placed in a foster home before and after 1 year of age.

Participant categorization according to prenatal substance exposure

Children with confirmed prenatal exposure to substances, including alcohol, illicit drugs, illegal use of prescription drugs, and opioids used in opioid management treatment (OMT) programs, were included in the study. History of exposure was confirmed by information obtained from the mothers and obstetric or pediatric records, including data from referring units and medical reports of neonatal withdrawal symptoms after birth. Data were systematically recorded based on the mother's main drug of use during pregnancy, and the children were categorized into 2 groups: (1) prenatal exposure to alcohol (FASD group) and (2) prenatal exposure to other substances. No valid information was available on doses of substance used in pregnancy, including the number of units of alcohol consumed or the exact timing of exposure during pregnancy.

If there was evidence from the data collected that a child had been exposed to both alcohol and other substances, the child was placed in the FASD group if alcohol was the main drug of use by the mother and if there were reported regular, or more often than occasional, episodes of alcohol use during pregnancy. Also, if a child met the criteria for FASD, he or she was automatically placed in the FASD group, which meant that no children in the other substances group met the FASD criteria.

Fetal alcohol spectrum disorders. The FASD group included cases of both fetal alcohol syndrome (FAS) and FASD. The diagnosis of FAS or FASD was given after evaluation of the medical history and clinical examination by a pediatrician with relevant specialized training and neuropsychological testing. Differential diagnoses were considered in all cases, and pediatricians specially trained in the field, including pediatric endocrinologists, were consulted in cases of uncertain diagnosis. Fetal alcohol syndrome was diagnosed if a child with confirmed prenatal alcohol exposure met all of the following Centers for Disease Control and Prevention (CDC) criteria:[10] (1) presence of facial dysmorphic features, (2) growth restriction, and (3) central nervous system (CNS) impairment. Children who did not fulfill all 3 FAS criteria were diagnosed with FASD.

Central nervous system impairment was defined as the presence of learning disabilities (defined as an IQ below 85) or having ADHD. Intellectual level was determined using either the Wechsler Preschool and Primary Scale of Intelligence (WPPSI) test or the Wechsler Intelligence Scale for Children-Revised (WISC-R) test. An IQ below 70 was defined as intellectual disability and an IQ of 70 to 84 as low IQ. Attention-deficit/hyperactivity disorder was diagnosed by a pediatrician and a child psychiatrist according to the International Classification of Diseases, Tenth Revision criteria.

Prenatal exposure to other substances. This group included children exposed to street drugs and polydrug use, as well as those exposed to opioids as part of the national OMT (the latter including 9 children). The most common "other substances" reported in this group were opiates and polydrug use. Children in this group either had a medical history of prenatal drug exposure to one or more drugs or were diagnosed with NAS after birth. None of the children in this group met the criteria for FASD. Although nondocumented (ie, unknown) use of alcohol could not be totally excluded, but the mother's main drug of use included substances other than alcohol. Any involvement of the mother in the national OMT during pregnancy was also recorded.

Mental health

The SDQ is a behavioral screening questionnaire for 4 to 17-year-old children.[30–32]

In this study, the SDQ questionnaire was completed by the children's caregivers. It consists of 25 items describing positive and negative attributes of the children, and it is divided into 5 subscales: (1) emotional problems, (2) hyperactivity problems, (3) conduct problems, (4) peer problems, and (5) prosocial behavior. For subscales other than the prosocial behavior subscale, a higher score represents more mental health problems. A total difficulties score (TDS) was computed by adding the first 4 subscale scores. Each item is scored on a 3-point scale, ie, "not true," "somewhat true," and "certainly true," with total subscale scores ranging from 0 to 10 and TDS from 0 to 40.[30]

The impact supplement of the SDQ is activated by a positive response to one screening item, indicating difficulties in areas of emotions, concentration, behavior, or social skills. The impact supplement of the SDQ examines overall distress and social impairment at home, with friends, at school, and with leisure activities. Each item is rated on a 4-point scale, rating difficulties as "not at all," "only a little," "quite a lot," and "a great deal." This is summed up to a total impact score with a maximum score of 10. If the child is not considered to have a problem, the impact score is scored as 0.[30]

The SDQ is widely used in groups of at-risk children such as children with chronic illness, those with intellectual disabilities, and those prenatally exposed to substances.[7,30,33–35] Its use as a screening instrument for mental health disorders in foster children has been previously validated.[36]

Statistical analyses

First, independent *t* tests were used to compare mean scores on symptom subscales, TDS, and total impact scores between the group of children prenatally exposed to alcohol or other substances and the reference group. Cohen *d* was used to quantify the differences between the groups, and standard interpretation was used (0.20 = small, 0.50 = moderate, and 0.80 = large). Second, the FASD group and the group of children exposed to substances other than alcohol were each compared with the reference group, and third, the FASD group and the group of children exposed to other substances

Table 1. Sample characteristics of a hospital-based population of school-aged children exposed to drugs during pregnancy and of a reference group.

	REFERENCE GROUP (N=313)	TOTAL SUBSTANCE-EXPOSED GROUP (N=105)	FASD[a] (N=48)	SUBSTANCES OTHER THAN ALCOHOL[b] (N=57)			
Mean age in years (SD)	10.5 (2.0)	10.6 (2.2)	10.8 (2.2)	10.3 (2.2)			
Gender (boys) (%)	188 (60)	63 (60)	27 (56)	36 (63)			
COMPARING SUBGROUPS OF CHILDREN WITH FASD AND CHILDREN EXPOSED TO SUBSTANCES OTHER THAN ALCOHOL					MD	95% CI	*P*
Mean IQ (SD)		88 (21)	80 (20)	94 (20)	13 (MD)	5.1–21	.001
In foster care (%)		90 (86)	36/48 (75)	54/57 (95)	2.0 (OR)	0.04–0.63	.004
In foster care ≤1 year (%)		29/90 (32)	9/36 (25)	20/54 (37)	1.4 (OR)	0.7–2.8	.200

Abbreviations: CI, confidence interval; FASD, fetal alcohol spectrum disorder; MD, mean difference; OR, odds ratio.
[a]Fetal alcohol spectrum disorders.
[b]Opioids, amphetamine, methamphetamine, cocaine, cannabis, and benzodiazepines.

were compared with each other. The characteristics of the 2 groups (ie, FASD group and group exposed to other substances) were analyzed using a χ^2 test for gender and care situation. Finally, a regression analysis for the substance was performed, with the TDS as the dependent variable and gender, age, IQ, drug group, and care situation as independent variables. Information about care situation and IQ was not available for the reference group. We also used the Mann-Whitney *U* test to assess if this test affected the statistical significance when comparing the groups. This test is suitable for small-sized samples and where the distribution is not normal. IBM SPSS version 22 for Windows was used for all analyses. The significance level was set at $P \leqslant .05$.

Results
Participants

The mean age of substance-exposed children was 10.6 years and comparable with the reference group (Table 1). Of the 105 children exposed to substances, 48 had FASD and 57 were exposed to substances other than alcohol.

Of the 48 children in the FASD group, 20 (42%) met all 3 CDC criteria and were given a diagnosis of FAS. The remaining 28 children in the FASD group had some of the dysmorphic facial features associated with FAS but did not fulfill all the CDC criteria for dysmorphic facial features, although they all met the other CDC criteria for growth restriction and CNS impairment.

Of the 57 children in the group exposed to substances other than alcohol, 41 (72%) had symptoms of NAS, 5 were reported as not having symptoms of NAS, whereas no valid information about the NAS status was available for the remaining 11 children.

Overall, 3 children were living with their biological families, 12 were adopted, and 90 were in foster care. In all, 11 children were placed in foster care at birth, a further 18 within the first

year, and 61 after 1 year of age. There were no significant gender or age differences between the 2 groups. Compared with the FASD group, the mean IQ was significantly higher ($P=.001$) in the group exposed to substances other than alcohol. The mean IQ of the 20 children diagnosed with FAS was 75 (SD: 17.6, 95% CI=67-83), with a median IQ of 70, whereas the mean IQ for the remaining 28 children in the FASD group was 85 (SD: 20.9, 95% CI=76-92), with a median IQ of 85. There were no statistically significant differences ($P=.13$) between the groups.

Mental health in the substance-exposed group compared with the reference group

Mean scores for the SDQ subscales, TDS, and total impact scores for the substance-exposed group, compared with the reference group, are presented in Table 2. There were statistically significant differences in all 5 SDQ subscales, TDS, and total impact scores between the group of alcohol-exposed and substance-exposed children and the reference group. A large effect size was obtained for all subscales and TDS ($d \geqslant 0.80$), with the greatest difference noted for the hyperactivity subscale between the group prenatally exposed to substances and the reference group ($d = 2.29$). After accounting for multiple testing and using the Bonferroni correction (critical $P=.05$/number of tests), we found that the group differences remained statistically significant for all tests. Use of the Mann-Whitney *U* test to compare SDQ scores between the groups did not change the statistical significance of the results.

When comparing the FASD group and the group of children exposed to other substances, no statistically significant differences were found in any of the 5 SDQ subscale scores, TDS, or total impact scores (Table 3).

Within the group exposed to other substances, 9 children were born to mothers in the national OMT. There were no differences in mean scores on any of the SDQ subscales between these children and the other 48 children in the group.

Table 2. Mental health problems based on Strengths and Difficulties Questionnaire scores in a hospital-based population of school-aged children prenatally exposed to substances, compared with a reference group.

	TOTAL SUBSTANCE-EXPOSED GROUP[a] (N = 105)	REFERENCE GROUP (N = 313)	MD	95% CI	*P*	COHEN *D*[b] (CI)
Emotional problems (SD)	4.0 (2.5)	1.3 (1.7)	−2.7	−3.1 to −2.3	<.01	1.93 (0.92–1.59)
Conduct problems (SD)	3.6 (2.3)	1.0 (1.3)	−2.6	−3.0 to −2.3	<.01	1.61 (1.18–1.76)
Hyperactivity problems (SD)	7.6 (2.3)	2.5 (2.2)	−5.0	−5.5 to −4.5	<.01	2.29 (1.85–2.54)
Peer problems (SD)	3.6 (2.5)	1.1 (1.6)	−2.5	−3.0 to 2.1	<.01	1.34 (0.86–1.52)
Prosocial behavior (SD)	6.4 (2.4)	8.5 (1.5)	2.0	−1.6 to 2.4	<.01	1.19 (1.02–1.65)
Total difficulties (SD)	18.9 (6.7)	5.9 (5.0)	−12.9	−14.2 to −11.7	<.01	2.37 (1.09–2.93)
Impact score[c] (n = 87) (SD)	4.2 (3.0)	0.4 (1.4)	−3.8	−4.3 to −3.4	<.01	1.97 (1.40–2.13)

Abbreviations: CI, confidence interval; FASD, fetal alcohol spectrum disorder; MD, mean difference.
[a]Clinical population of children exposed to alcohol and other substances.
[b]Cohen *d*: 0.20 = small, 0.50 = moderate, 0.80 = large.
[c]n for FASD = 45; n for other substances = 42.

Mental health and care situation in the substance-exposed group

Among the 90 children living in foster care, there were no statistically significant differences in the mean TDS between those taken in foster care at birth, those placed before 1 year of age, and those placed after 1 year of age (mean TDS: 17, 18, and 20, respectively; *P* = .30).

In a regression analysis with the TDS as the dependent variable and referral age, gender, IQ, substance group, and care situation as independent variables, only low IQ was a significant factor explaining a variance of 6% (adjusted R^2 = 0.06; 95% CI = 16-32; *P* = .01).

Discussion

In this hospital-based study of school-aged children prenatally exposed to alcohol and other substances, we found that the exposed children were at increased risk of mental health problems, compared with the reference group. In addition, mental health problems had a more marked impact on daily life functioning in the exposed group, in comparison with the reference group.

In this study, most of the prenatally exposed children had mental health problems affecting their daily life functioning; both the FASD group and the group of children exposed to other substances had high SDQ scores. This indicated an increased risk of mental health problems, compared with the reference group, with no statistically significant differences between the 2 study groups. The increased risk of mental health problems is in agreement with other studies of prenatally exposed children.[4,6,7,20,37]

The greatest mean difference between the exposed group and the reference group was obtained in the hyperactivity SDQ subscale, which is consistent with previous studies that reported high scores of hyperactivity symptoms both in the FASD group as well as in the group of children exposed to substances other than alcohol.[1,6,37–39] When comparing the exposed group with the reference group, the mean difference in the hyperactivity subscale could only partly explain the mean difference in the TDS between the groups, indicating that children exposed to substances present with a wider range of mental problems. Irner et al[7] who, also using the SDQ, reported a higher proportion of hyperactivity in a group of prenatally exposed children, compared with British norms.

Children may be genetically predisposed to ADHD, and a recent review highlighted that ADHD may develop as a result of a complex process involving both genetic and nongenetic factors.[40] Studies of adults having substance use disorder have found a higher rate of ADHD symptoms, with ADHD itself as an independent risk factor for substance abuse.[41] Other previous studies have also described an association between maternal mental health and behavioral problems in their children.[42,43] However, we were not able to investigate this issue in our study because most of the children were not living with their biological parents.

The increased risk of mental health problems in children prenatally exposed to alcohol and other substances may thus be due to factors other than the direct or indirect effects of alcohol and other substances on the developing brain. This is supported by findings from previous studies showing that factors such as children's socioeconomic status, caregiving environment, and learning disabilities influence mental health outcomes.[18,21,23,27] In this study, we found an association between cognitive impairments and poorer mental health status, in line with previous reports.[18] Furthermore, numerous studies have found that a high proportion of children prenatally exposed to alcohol and other substances were placed in foster homes and that changes in care environment could affect the mental

Table 3. Mental health problems based on SDQ scores in the group of children prenatally exposed to alcohol (FASD[a]) and the group of children prenatally exposed to substances other than alcohol[a], compared with the reference group and with each other.

	REFERENCE GROUP (N=313)	FASD[a] (N=48)	OTHER SUBSTANCES[b] (N=57)	FASD COMPARED WITH REFERENCE GROUP			CHILDREN EXPOSED TO OTHER SUBSTANCES[a] COMPARED WITH REFERENCE GROUP			FASD GROUP COMPARED WITH GROUP OF CHILDREN EXPOSED TO OTHER SUBSTANCES[a]		
Mean SDQ scores (SD)				d	95% CI	P	d	95% CI	P	d	95% CI	P
Emotional problems	1.3 (1.7)	4.5 (2.4)	3.6 (2.5)	1.8	1.1–2.0	<.01	1.3	0.6–1.44	<.01	0.4	−0.3 to 1.0	.07
Conduct problems	1.0 (1.3)	3.4 (2.1)	3.7 (2.4)	1.7	1.1–1.8	<.01	1.8	1.2–1.9	<.01	0.1	−0.7 to 0.5	.50
Hyperactivity problems	2.5 (2.2)	7.8 (2.1)	7.4 (2.5)	2.4	1.8–2.7	<.01	2.2	1.5–2.4	<.01	0.2	−0.4 to 0.8	.30
Peer problems	1.1 (1.7)	4.0 (2.5)	3.3 (2.6)	1.6	0.9–1.8	<.01	1.2	0.5–1.4	<.01	0.3	−0.4 to 1.0	.10
Prosocial behavior	8.5 (1.5)	6.3 (2.4)	6.5 (2.4)	1.3	1.2–2.0	<.01	1.2	1.0–1.8	<.01	0.1	−0.8 to 0.5	.70
Total difficulties	5.9 (5.0)	19.6 (5.8)	18.2 (7.4)	2.7	1.0–3.2	<.01	2.3	0.3–2.8	<.01	0.2	−1.4 to 2.1	.30
Impact score[c] (n=87)	0.4 (1.4)	4.8 (2.9)	3.8 (3.0)	2.7	1.8–2.8	<.01	2.0	1.1–2.2	<.01	0.3	−0.5 to 1.3	.07

Abbreviations: d, Cohen d; CI, confidence interval; FASD, fetal alcohol spectrum disorders; SDQ, Strengths and Difficulties Questionnaire; Cohen d: 0.20 = small, 0.50 = moderate, 0.80 = large.
[a]Fetal alcohol spectrum disorders.
[b]Opioids, amphetamine, methamphetamine, cocaine, cannabis, and benzodiazepines.
[c]n for FASD = 45; n for other substances = 42.

health status.[44–46] In our study population, an increased risk of mental health problems was found in school-aged children, with no statistically significant differences between children placed in foster care before and those placed after 1 year of age. It has been suggested that prenatally drug-exposed children are biologically vulnerable to the effects of poor caretaking and a poor caregiving environment and that optimizing care conditions may thus improve developmental outcome.[19,47–49]

In this study, there were no differences in mental health outcomes between children prenatally exposed to alcohol and those exposed to substances other than alcohol. This suggests that exposure to other substances may also affect neurodevelopment and mental health, as also suggested by earlier studies.[1,3,4,7,50] In addition, mental health problems impaired the children's daily life functioning, irrespective of the main type of substance exposure and environmental factors, to such an extent that it calls for special focus for this group of children. These findings indicate a need for mental health assessment of children prenatally exposed to alcohol and other substances to provide early intervention if necessary.

Our study results should be interpreted with caution due to some limitations. One limitation was our inability to verify the accuracy of the types of substances used and to which the fetus was exposed, as reported by the children's mothers. This underlines the potential risk of underestimating the actual prenatal exposure to specific substances. Previous studies have reported many mothers in OMT with an illicit polydrug use while on the opioid maintenance program, highlighting the complexity of accurately measuring actual drug exposure.[51,52] In this study, it was not possible to ascertain that mothers to children prenatally exposed to other substances had not consumed any alcohol, in addition to other substances, during their pregnancy. Thus, we relied on obstetric and pediatric records, as well as reports from mothers, and in cases showing any confirmation or evidence of a greater number of single episodes of alcohol exposure, the children were categorized in the FASD group. None of the children in the group of prenatal exposure to other substances met the criteria for FASD. Our initial hypothesis was that given the known teratogenic effects of alcohol, alcohol-exposed children had a higher risk of mental health problems, compared with children exposed to substances other than alcohol. However, we found this was not the case in this study and suggest that children with a positive medical record of prenatal substance exposure have an increased risk of mental health problems, irrespective of the mother's main substance of use.

Another limitation is that although nicotine exposure is also a known risk factor affecting a child's neurodevelopment,[1,6] data on maternal use of tobacco and nicotine were not available in our study. A further limitation is that the study has a hospital-based study design, which likely resulted in selection bias of participants meaning that our hospital-based study population represented mainly the most severely affected

children. This has a major impact on the generalizability of our study findings, and hence, the results should be interpreted with caution. Therefore, further studies on a wider and more general population, ie, not restricted to hospital-based settings, are warranted.

It is possible that the statistical models presented in this study could raise some methodological concerns using of IQ scores as a variable when exploring neurodevelopmental outcomes.[53] For our purpose, we found it appropriate to include the IQ scores when comparing the subgroups of exposed children because the scores are a measure of global cognitive function according to the diagnostic criteria of FASD.[10]

We consider the SDQ suitable for our study to identify the risk of mental health problems in prenatally exposed children, given that most of these children were taken into foster care. Indeed, a study examining the properties of the SDQ in children placed in foster care in Norway supports the use of the SDQ when screening children in foster care for mental health problems, compared with the diagnostic interview of Developmental and Well-Being Assessment.[36]

Conclusions

In this study of a hospital-based population of school-aged children prenatally exposed to alcohol or other substances, we found that these children were at increased risk of mental health problems affecting their daily life functioning, with no difference between whether the mother's main drug of use during pregnancy was alcohol or other substances.

Clinical implications

Given the increased risk of mental health problems, we recommend the performance of mental health assessment for this group of children when referring to healthcare providers. We believe this approach to be important in establishing an optimized healthcare plan, with minimal intervention delay, for this group of children, and more research to evaluate the treatment measures on mental health outcomes in this group is needed.

Author Contributions
LBS, IBE, MH, and SAN conceived and designed the experiments and contributed to the writing of the manuscript. LBS, IBE, and MR analyzed the data. LBS and MR wrote the first draft of the manuscript. LBS, IBE, MH, MR, and SAN agreed with manuscript results and conclusions. LBS, IBE, and MH jointly developed the structure and arguments for the paper. MH, IBE, and SAN made critical revisions and approved the final version. All authors reviewed and approved the final manuscript.

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