# Symptoms Associated With Attention Deficit/ Hyperactivity Disorder and Autism Spectrum Disorders in School-Aged Children Prenatally Exposed to Substances

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**ABSTRACT:** Prenatal exposure to substances may influence a child's neurodevelopment and impact on subsequent mental health. In a hospital-based population of school-aged children prenatally exposed to opiates and a number of illicit substances (n = 57), we evaluated mental health symptoms associated with attention deficit/hyperactivity disorder (ADHD) and autism spectrum disorders (ASD) using the Swanson, Nolan, and Pelham Questionnaire, revision IV (SNAP-IV) and the Autism Spectrum Screening Questionnaire (ASSQ) and compared the scores to a reference group which comprised children from the population-based Bergen Child Study (n = 171). Prenatally exposed children had significantly higher SNAP-IV scores associated with ADHD symptoms in both areas of inattention and hyperactivity/impulsivity and also reported a higher ASSQ score related to an increased number of symptoms associated with ASD, compared with the reference group. Of tested predictors of mental health outcomes in the exposed group, the intelligence quotient was a strong predictor of most mental health outcomes, and neonatal abstinence syndrome was a predictor of inattention. In conclusion, prenatally exposed children had more mental health symptoms associated with ADHD and ASD, compared with the reference group.

**KEYWORDS:** Mental health, development, drug effects, child development, prenatal substance exposure

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## Introduction

Prenatal exposure to opiates and illicit drugs may influence neurodevelopment in children,[1] including mental health.[2–6] Earlier studies of prenatal substance exposure have reported neurodevelopmental impairments in school-aged children and adolescents.[7–11] However, it may be difficult to distinguish between long-term outcomes of prenatal substance exposure and outcomes of other influencing factors on a child's development.[3,12,13] Previous research suggested that in addition to prenatal substance exposure, genetic and epigenetic factors,[14] gender,[15,16] cognitive functioning,[17,18] and environmental conditions, including the quality of caregiving environment in early childhood,[10,11,19–23] are all associated with mental health outcomes in children and adolescents. Parental substance abuse is associated with an increased risk for foster care, heightening the risk for placement in foster care for the group of prenatal substance-exposed children.[24,25] Furthermore, it has been suggested that optimization of caregiving environments, including placement in foster care, may improve developmental outcomes in children prenatally exposed to substances.[9,11,20] Regardless of the different factors affecting children's neurodevelopment, it is important to examine the mental health status and describe potential challenges for the group of prenatally substance-exposed children.[26]

It is difficult to obtain a true estimate of the prevalence of prenatal substance exposure in children, due to stigmatization and the illegal nature of illicit drug use.[2,27] However, it is clear that the incidence has increased over the past decade in the United States and Western European countries, with an increasing number of neonates diagnosed with withdrawal symptoms.[28] Children prenatally exposed to substances, in particular opiates, are at risk for withdrawal symptoms and neonatal abstinence syndrome (NAS).[28,29] Neonatal abstinence syndrome is a complex disorder affecting various organs, and clinical manifestations range from mild, such as irritability and mild tremors, to severe such as seizures, excessive weight loss, and fever.[28,29] Neonatal abstinence syndrome occurs in 55% to 94% of children prenatally exposed to

**Table 1.** Characteristics of a hospital-based population of school-aged children prenatally exposed to substances, compared with a reference group.

| | EXPOSED GROUP (N = 57) | REFERENCE GROUP (N = 171) |
|---|---|---|
| Mean age in years (SD) | 10.4 (2.2) | 10.3 (2.0) |
| Gender (boys), N (%) | 37 (65) | 111 (65) |
| Mean IQ (SD) | 93.5 (20.4) | |
| Neonatal abstinence symptoms, N (%) | 41 (72) | |
| NAS, N (%) | 18/41 (44) | |
| Out of biological home at age ≤1 year[a], N (%) | 22 (39) | |

Abbreviations: IQ, intelligence quotient; NAS, neonatal abstinence syndrome; SD, standard deviation.
[a]Adopted or in foster care (n = 56) at age ≤1 year.

opioids.[28–30] A follow-up study of children with NAS also found an increased risk for rehospitalization due to maltreatment, trauma, mental health problems, and behavioral disorders when compared with controls.[5]

Overall, substance-exposed children seem to be vulnerable, having several risk factors for developing mental health problems. Interestingly, some studies have suggested that cumulative risk factors, including prenatal substance exposure and the caregiving environment, may exert a greater impact on development than prenatal substance exposure itself.[31,32]

A recent review of alcohol-exposed children found the rate of attention deficit/hyperactivity disorder (ADHD) to be 15 times higher, and autism spectrum disorders (ASD) twice higher, compared with the general population.[33] Moreover, it is well established that children prenatally exposed to substances other than alcohol have an increased risk for hyperactivity.[2,3,8] A recent study, using the Strengths and Difficulties Questionnaire (SDQ), reported that children exposed to alcohol and other substances had a higher risk for mental health problems, compared with controls, including hyperactivity problems as well as other domains of mental health problems.[26] Based on the above, it is of interest to examine in more details specific mental health outcomes in children exposed to substances during pregnancy.

The aims of this study are as follows: (1) to evaluate symptoms of ADHD and ASD in children prenatally exposed to substances other than alcohol, compared with a reference group and (2) to determine relevant predictors of mental health outcomes in substance-exposed children. We hypothesized that children prenatally exposed to substances would display a higher number of symptoms of ADHD and ASD, compared with the reference group.

## Methods

### *Study participants*

This study included children aged 6 to 14 years, prenatally exposed to opiates and a number of illicit drugs, who were referred to the Pediatric Department at Haukeland University Hospital in Bergen, Norway, from January 1997 to December 2012. The study population is hospital-based, including children referred to the pediatric department at the hospital, and referral criteria included symptoms of developmental impairment in the presence of a medical history of prenatal exposure to drugs. Some of the children were hospitalized after birth due to abstinence symptoms; others were referred later in childhood when suspecting developmental impairments.

Referrals were by health care providers, social workers, and physicians in primary health care, as well as in pediatric units and child psychiatric units. Of a total number of 128 children referred, informed written concent was provided for 87% (n = 111). Children mainly exposed to alcohol (n = 50) were excluded from the study. Of 61 children exposed to substances other than alcohol, 57 (93%) completed relevant questionnaires assessing the mental health status and care situation (Table 1). The questionnaires were distributed when the child was included in the study, earliest at 6 years of age. The mean age of the child at completion of the questionnaires is given in Table 1, and the current caretakers were the informants.

### *The reference group*

This group consisted of children participating in the longitudinal population-based Bergen Child Study (BCS). All children attending grades 2 to 4 at 79 schools in a geographically restricted area during the academic years of 2002/2003 were invited to participate in the study (N = 9430); there were no exclusion criteria.[34] Parent questionnaires were completed for about two-thirds of the participating children (N = 6297).[34] Of the participating children in the BCS, about 2 out of 3 lived in a family categorized as with good or very good family economy, and about 50% of the mothers and fathers had higher education.[35] More details about the reference group are presented in the papers by Heiervang et al,[34] Bøe et al,[35] and Stormark et al.[36] This study included participants from the first two waves of the BCS. The first wave, conducted in autumn 2002, was composed of a target population of 9430 primary schoolchildren aged 7 to 9 years, and informed consent to

participate was obtained 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 included in this study, 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 added for each case to improve the quality of the analyses.[37] 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 therefore allowed 3 eligible controls from the BCS. As we would have to considerably expand the age-matching criterion (to about ±2 years) to achieve a 4:1 ratio between controls and cases, we considered a 3:1 ratio to best use the available data.

### *Exposure to substances*

Children with confirmed prenatal exposure to substances were included in the study. Substance exposure was defined as prenatal exposure to opiates and a number of illicit drugs and illicit use of prescribed drugs with psychoactive or sedative effects. In addition, children were included in the study if they were exposed to opioids as part of the national opioid maintenance treatment program (OMT) and/or they presented with neonatal withdrawal symptoms or NAS after birth. Prenatal exposure was confirmed by information obtained from mothers and obstetric or pediatric records, including details from referring units and reports of neonatal withdrawal symptoms.

In cases involving exposure to both alcohol and other substances, the mother's main substance of use was taken into account to determine a child's eligibility for inclusion in the study. In cases involving a greater number of single episodes of alcohol exposure, or if a child met the criteria of fetal alcohol spectrum disorders (FASD), the child was excluded from the study.

### *Withdrawal symptoms and NAS*

The presence of withdrawal symptoms in children was assessed for and recorded, and abstinence symptoms were scored using a modified version of the Finnegan abstinence score.[29] Abstinence scores of 8 or above were classified as NAS.

### *Care situation*

Based on the medical records and questionnaires completed by the children's respective caregivers, data on the current care situation were obtained, as well as age at first placement outside of the biological home (before or after 1 year of age). Early placement in an adopted home or foster care was defined as placement before 1 year of age.

### *Cognitive functioning*

Cognitive functioning in exposed children was evaluated using either the Wechsler Preschool and Primary Scale of Intelligence (WPPSI) test[38] or the Wechsler Intelligence Scale for Children–Revised (WISC-R).[39]

### *Mental health*

Mental health assessment was based on 2 different questionnaires—the Swanson, Nolan, and Pelham Questionnaire, revision IV (SNAP-IV) and the Autism Spectrum Screening Questionnaire (ASSQ), both comprising items scored on a 3-point scale (0-2). The questionnaires were completed by the current caregivers.

*The Swanson, Nolan, and Pelham Questionnaire, revision IV.* The SNAP-IV is a screening tool for ADHD.[40] It contains 9 items on inattention and 9 items on hyperactivity/impulsivity, which correspond to the *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition; DSM-IV) criteria for ADHD.[41] Scores ranged from 0 to 18 for each scale. The SNAP Combined variables consisted of the sum of all 18 items. Reliability of SNAP-IV as a screening tool has been reported as good.

*The Autism Spectrum Screening Questionnaire.* The ASSQ consists of 27 items covering symptoms of ASD, ie, social interaction and communication, motor clumsiness, tics, and restricted and repetitive behavior.[43–45] In this study, one of the items (item 9 related to involuntary sounds and words) was inadvertently omitted for the reference group and therefore not included.[44] Scores ranged from 0 to 52.

For further description of symptoms reported in ASSQ, the 26 items were computed into 3 subscales, as suggested in Ryland et al[46]: (1) social difficulties, including items related to difficulties with friendship, prosocial behavior, and social communication; (2) motor/tics/obsessive–compulsive disorder (OCD), including items related to repetitive, stereotype behavior, and autism-associated symptoms such as motor difficulties and tics; and (3) autistic style, including items related to characteristics often seen in high-functioning individuals with ASD. The specific items included in each subscale are as follows: (1) social difficulties: lives in own world, no social fit in language, lacks empathy, naive remarks, deviant style of gaze, fails to make friends, sociable on own terms only, lacks best friend, lacks common sense, poor at games and own rules, and bullied by other children; (2) motor/tics/OCD: different voice/speech, clumsy, involuntary movements, compulsory repetition, insists on no change, idiosyncratic attachment, unusual facial expression, and unusual posture; and (3) autistic style: old-fashioned or precocious, eccentric professor, accumulates facts, literal understanding, robot-like language, idiosyncratic words, and uneven abilities.[46]

### *Statistical analyses*

Descriptive analyses were used to describe the sample (mean, standard deviation, and frequency). Group differences were analyzed using the *t*-test. Levene's test was used to test homogeneity of variances. If variances were found to be statistically unequal, the *t*-test not assuming equal variances was used.[47] Effect sizes were estimated by Cohen's *d*. IBM SPSS version 24 was used for all analyses.[48]

Regarding the use of ASSQ, it has been recommended a cutoff score of 17 or more is optimal in screening for ASD.[45] We therefore used a cutoff value of ≥17 as high score in our analyses comparing child placement outside of the biological home before and after 1 year of age. Due to skewness in outcome variables in the reference group, the program Mplus version 7.4 was used with the maximum likelihood robust (MLR) estimator and corrected standard errors for sensitivity analyses.[49,50] This analysis strategy does not assume equal variances when comparing the groups. Spearman correlation was used when analyzing the relationship between SNAP-IV and ASSQ scores.

In the group of children prenatally exposed to substances, multiple regression analysis was used to predict the outcome variables SNAP Combined, SNAP Inattention, and SNAP Hyperactivity/impulsivity and ASSQ Total score, ASSQ Social difficulties, ASSQ Motor/tics/OCD, and ASSQ Autistic style. Predictors were age, gender, intelligence quotient (IQ), NAS, and child placement outside of the biological home before or after 1 year of age based on earlier studies of prenatal substance exposure and mental health in children.[5,10,11,14–18,20,23]

For 21 children in the exposed group, one or more responses on the ASSQ were missing. For missing data, the variables were replaced with imputed data based on the expectation–maximization method and ASSQ total scores computed.[51]

### *Ethics*

The study was approved by the Regional Committee for Medical Research Ethics in Norway (approval number 2010/3301). For children prenatally exposed to substances, informed written consent was obtained from all participating caregivers. These included biological parents if the child was living in the biological home, adoptive parents, or foster parents if relevant for the care situation. For children in foster care, the social welfare office legally responsible for the participating child also gave written consent. In addition to the caregivers and social welfare office, children 12 years and older gave their independent consent to participate in the study. For the reference group, the caregivers gave informed written consent.

## Results

### *Study participants*

The characteristics of the hospital-based population of children prenatally exposed to substances and the reference group are presented in Table 1. Almost 2 in 3 participants were boys, and the mean IQ was within the normal range for the entire study sample. In the exposed group, all, except 1 child, lived in foster care (n = 54) or with adopted parents (n = 2), and of the children adopted or in foster care (n = 56), more than 1 in 3 were placed outside of their biological home before the age of 1 year. The mean age at follow-up was approximately 10 years, with age normally distributed and approximately 95% of the sample in the age range of 6.3 to 14.4 years. However, a weak positive skewness may reflect more children being older than expected under the assumption of perfect normality. Symptoms compatible with neonatal abstinence were reported in 41 of the exposed children, of whom 18 were diagnosed with NAS. Five children were reported without abstinence symptoms, and for 11 children, there was no valid information regarding abstinence symptoms.

### *Mental health outcomes*

Mental health outcomes are presented in Table 2. For the exposed group, the caregivers reported significantly higher scores of ADHD symptoms combined ($P < .001$) and Cohen's *d* was large ($d = 2.08$). The SNAP-IV scores were high in areas of both inattention and hyperactivity/impulsivity. Caregivers also reported an increased number of symptoms associated with ASD, with the largest Cohen's *d* in the subscale "social difficulties." For the ASSQ, 21 of the 56 (37%) of the children had high scores (≥17) in the exposed group, compared with 5 of the 162 (3%) in the reference group (odds ratio [OR] = 17.44, 95% confidence interval [CI] = 6.1-49.6, $P < .05$). However, there was no significant difference in high ASSQ scores between the group of children placed into foster care before and those after 1 year of age ($P = .083$). The effect sizes for the outcome variables were in the range of 0.44 to 3.60. Effects for the mental health outcomes were above the threshold for large effects. Mplus sensitivity analyses correcting for standard errors due to skewness in some variables confirmed that all differences were statistically significant ($P < .001$).

### *Predictors of mental health outcomes*

Regression analyses were performed to evaluate possible predictors of mental health outcomes available in this study. Seven mental health measures were chosen as dependent variables, and predictors were age, gender, IQ, the presence or absence of NAS, and child placement outside of their biological home before or after the age of 1 year. The standardized regression coefficients for the independent variables are given in Table 3. IQ was a statistically significant factor in 5 of the 7 regression models, whereby higher IQ scores predicted lower levels of mental health problems. Furthermore, NAS was a significant predictor of the SNAP Inattention scale.

When analyzing the correlation between ASSQ Total score and SNAP, we found a moderate to strong correlation between high ASSQ scores and high SNAP scores, with the strongest

**Table 2.** Mental health outcomes in a hospital-based population of children prenatally exposed to substances, compared with a reference group.

| | EXPOSED GROUP (N = 57) | REFERENCE GROUP (N = 171) | *t* | *P* | *d*[a] |
|---|---|---|---|---|---|
| | MEAN (SD) | MEAN (SD) | | | |
| SNAP Combined | 19.65 (9.06) | 4.13 (5.37) | 12.22 | * | 2.08 |
| SNAP Inattention | 10.79 (4.63) | 2.72 (3.49) | 12.05 | * | 1.97 |
| SNAP Hyperactivity/impulsivity | 8.86 (5.26) | 1.42 (2.41) | 10.31 | * | 1.82 |
| ASSQ total | 14.00 (7.98) | 3.57 (4.51) | 9.36 | * | 1.61 |
| ASSQ Social difficulties | 7.74 (4.99) | 1.47 (2.61) | 9.07 | * | 1.57 |
| ASSQ Motor/tics/OCD | 2.37 (2.22) | 0.36 (1.06) | 6.59 | * | 1.16 |
| ASSQ Autistic style | 3.89 (2.65) | 1.83 (2.06) | 5.37 | * | 0.87 |

Abbreviations: ASSQ, Autism Spectrum Screening Questionnaire; OCD, obsessive–compulsive disorder; SD, standard deviation; SNAP, Swanson, Nolan, and Pelham Questionnaire, revision IV (SNAP-IV).
[a]*d*: Cohen's *d; t*-test is corrected when Levene's test shows unequal variances.
*$P < .001$.

**Table 3.** Mental health outcomes in a hospital-based population of children prenatally exposed to substances (n = 57) and possible predictors of mental health.

| | SNAP COMBINED | SNAP INATTENTION | SNAP HYPERACTIVITY/ IMPULSIVITY | ASSQ TOTAL | ASSQ SOCIAL DIFFICULTIES | ASSQ MOTOR/ TICS/OCD | ASSQ AUTISTIC STYLE |
|---|---|---|---|---|---|---|---|
| | β | β | β | β | β | β | β |
| Age | −0.03 | 0.05 | −0.09 | 0.01 | 0.01 | −0.17 | 0.14 |
| Gender | −0.22 | −0.12 | −0.26 | 0.02 | 0.06 | 0.06 | −0.12 |
| Early placement[a] | 0.20 | 0.22 | 0.16 | 0.10 | 0.10 | 0.11 | 0.02 |
| NAS | 0.22 | 0.29* | 0.12 | 0.09 | 0.09 | 0.22 | −0.08 |
| IQ | −0.38** | −0.48*** | −0.22 | −0.35* | −0.40** | −0.40** | 0.02 |
| $R^2$ (adjusted) | 0.23 (0.16) | 0.28 (0.21) | 0.17 (0.09) | 0.12 (0.03) | 0.15 (0.07) | 0.18 (0.10) | 0.04 (0.00) |

Abbreviations: ASSQ, Autism Spectrum Screening Questionnaire; IQ, intelligence quotient; NAS neonatal abstinence syndrome; SNAP, Swanson, Nolan, and Pelham Questionnaire, revision IV (SNAP-IV).
Results from multiple regression analysis for SNAP Combined, SNAP Inattention, and SNAP Hyperactivity/impulsivity, and ASSQ Total, ASSQ Social difficulties, ASSQ Motor/tics/OCD, and ASSQ Autistic style. Relations are given by beta-weights (β) and model fit by explained variance.
[a]Placement in adopted home or foster care before 1 year of age.
*$P < .05$; **$P < .01$; ***$P < .001$.

correlation between ASSQ Social difficulties and both SNAP Inattention ($r = .702$, $P \leq .01$) and SNAP Hyperactivity/impulsivity ($r = .714$, $P \leq .01$).

## Discussion

In our hospital-based population of children prenatally exposed to substances, we found that exposed children had more symptoms associated with ADHD and ASD, compared with the reference group. Using the standardized instrument SNAP-IV and ASSQ, high symptom scores were obtained in the areas of inattention and hyperactivity/impulsivity, and in addition, the exposed children presented with an increased number of symptoms in all 3 ASSQ subscales. Of the available predictors of mental health outcomes in the exposed group of children, only the IQ could explain variances in some of the mental health scales and NAS only for ADHD/inattention problems. Gender, age, or early placement in an adopted home or foster care was not found to be predictive of mental health outcomes in the group of exposed children.

In line with earlier research in children prenatally exposed to substances,[2,3] caregivers in this study reported an increased number of ADHD symptoms in the exposed group, with higher symptom scores for both hyperactivity/impulsivity and inattention, compared with the reference group. Attention deficit/hyperactivity disorder is a complex disorder and may result from processes involving both genetic and nongenetic factors.[52] A previous study found adults with substance use disorder to have a higher rate of ADHD symptoms and suggested ADHD

as an independent risk factor for substance abuse.[53] Therefore, it is possible that prenatally exposed children may be genetically predisposed to ADHD, which could explain the increased number of ADHD symptoms in this group of children.

Mean level of symptoms associated with ASD was increased in the exposed group of children, compared with the reference group, with more than 1 in 3 exposed children having high ASSQ scores, mainly on the "social difficulties" subscale. In children with prenatal alcohol exposure, an increased risk for both ADHD and ASD has been described.[33] Autism spectrum disorder is characterized by symptoms of social impairment, as are other mental health disorders such as reactive attachment disorder (RAD), and therefore, diagnostic assessment is necessary to distinguish between these disorders.[41,54,55] Reactive attachment disorder may result from inadequate caregiving and can develop when a child's caregiving environment fails to address the child's care needs.[41,54–56] This study did not demonstrate any association between early placement in an adopted home or foster care and symptoms of ASSQ. We suggest future studies to evaluate possible associations between quality of the caregiving environment, as well as the timing, duration, and number of placements in foster care, and the development of mental health problems in prenatally exposed children.

In this study, IQ and NAS were the only predictors of mental health outcomes. The protective effect of a higher IQ against mental health problems is in line with findings from previous studies investigating other risk factors such as prematurity[57] and chronic illness.[58] In this study, the presence of NAS was a predictor of later inattention problems, suggesting a potential vulnerability for neurodevelopmental disorders in children with NAS; however, more research is needed to investigate this further.[5] Furthermore, children with overlapping symptoms of ADHD and ASD were found in the exposed group, which lends support to the suggested neurodevelopmental vulnerability in exposed children.

In summary, our study found that children prenatally exposed to substances presented with symptoms in more than one area of mental health problems. Although exposed children may not necessarily fulfill the diagnostic criteria of a specific psychiatric disorder, they may present with a range of symptoms associated with ADHD and ASD. The extent of these symptoms strongly suggests a functional impact on daily living for many of these exposed children, and this calls for more attention focused on follow-up programs.

This study has limitations. We were unable to confirm the accuracy of the types of substances to which the fetus was exposed, based on information reported by the biological mothers. It is possible this resulted in an underestimation of the actual prenatal exposure to specific substances, e.g., alcohol. Previous studies reported some concurrent illicit polydrug use by mothers while undergoing OMT, emphasizing the complexity of accurately measuring actual exposure.[59,60] In this study, it was not possible to ascertain whether the mothers had consumed alcohol, in addition to other substances during pregnancy, and we relied on obstetric and pediatric records, as well as reports from mothers. If there was confirmation or evidence of a greater number of single episodes of alcohol exposure, the children were excluded from this study, based on the known teratogenic effects of alcohol. Another limitation is that although nicotine exposure is a risk factor known to affect a child's neurodevelopment,[2,3] data on tobacco and nicotine use by mothers during pregnancy were not available in our study. Furthermore, the study design likely produced selection bias, as a hospital-based population tends to include the most severely affected children, which therefore has a major impact on the generalizability of the study findings. Also, it would have been useful to include mental health data collected from different settings, such as from teachers' reports, but due to ethical considerations, it was not possible to invite teachers to participate in the study. Another limitation of this study was that we did not have information about IQ and foster care for the children in the reference group. As the reference group was drawn from a population with parents reporting having relatively good family economy, and about 50% reported having higher education, this could lead the reference group to consist of more well-adjusted children than the general population. This should be taken into account when interpreting the findings from this study.

Important strengths of this study are the relatively large population of children prenatally exposed to substances and the use of standardized, validated screening tools to assess mental health symptoms. Also, the reference group consisted of children mainly from the same geographical area as the exposed group, which could contribute to the robustness of result comparability between the 2 groups, although there was no information on prenatal substance exposure for the reference group.

## Conclusions

Findings from our hospital-based study show that children prenatally exposed to substances presented with an increased number of symptoms associated with ADHD and ASD, compared with the reference group. In light of increased mental health symptoms in children prenatally exposed to substances and referred to the hospital, early mental health assessment is suggested for this population. Moreover, caregivers should be educated on the range of symptoms associated with mental health problems for which exposed children are at risk. There is a need for increased awareness of, and further research on, the impact of prenatal substance exposure on mental health outcomes and functioning of exposed children within the family, at school, and in the wider society.

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## Author Contributions

LBS, IBE, and SAN conceived and designed the experiments. LBS, SKEF, and RG analyzed the data. LBS, SKEF, and IBE wrote the first draft of the manuscript. LBS, SKEF, SAN, TB, RG, and IBE contributed to the writing of the manuscript.

LBS, SKEF, SAN, TB, RG, SH, and IBE agree with the manuscript results and conclusions. LBS, TB, SH, and IBE jointly developed the structure and arguments for the paper. LBS, SKEF, SAN, TB, RG, SH, and IBE made critical revisions and approved final version. All authors reviewed and approved the final manuscript.

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