

A Retrospective Analysis of Perinatal and Early Childhood Risk Factors in a Chinese Autism Spectrum Disorder Cohort

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Abstract

Objective

Autism spectrum disorder (ASD) is a neurodevelopmental condition driven by complex gene–environment interactions, with specific environmental factors linked to elevated risk. In this study, we aimed to identify perinatal and early childhood risk factors associated with autism spectrum disorder (ASD) diagnosis and severity in a Chinese cohort.

Methods

We retrospectively analyzed clinical data from children with ASD (n = 708), children with language/social developmental delay (non-ASD, n = 164), and typically developing children (TD, n = 337). Data were collected via questionnaires and medical records. Binary logistic regression was used to examine factors associated with ASD diagnosis (full sample and excluding children aged < 2 years) and with ASD severity (mild-moderate vs severe, based on Childhood Autism Rating Scale scores).

Results

In the full-sample model (Nagelkerke $R^2=0.072$), language developmental regression (OR 1.94, 95% CI 1.12–3.34) and 2 to 4 hours/day screen time during the first postnatal year (OR 3.43, 95% CI 1.20–9.75) were associated with ASD diagnosis. After excluding children aged under 2 years (Nagelkerke $R^2=0.068$), language developmental regression (OR 1.88, 95% CI 1.05–3.36), second-year screen time of 2 to 4 hours/day (OR 2.71, 95% CI 1.26–5.81), and more than 4 hours/day (OR 6.33, 95% CI 1.45–27.68) were associated with ASD diagnosis. For ASD severity (Nagelkerke $R^2=0.041$), the presence of language developmental regression (OR 1.74, 95% CI 1.17–2.57) showed a positive association with greater symptom severity, whereas older paternal age was associated with milder symptoms (OR 0.96, 95% CI 0.93–0.99).

Conclusion

Our findings indicate that early childhood screen time and language developmental regression are associated with ASD diagnosis. Furthermore, language developmental regression also predicted greater symptom severity, whereas advanced paternal age predicted milder clinical presentations. However, causal inferences cannot be drawn from these observational data.

What is known

- ASD is a multifactorial neurodevelopmental condition with genetic and environmental contributions.

- Advanced parental age, perinatal complications, and maternal infection during pregnancy have been linked to ASD risk.
- Increased early-life screen time has been linked to ASD in several studies, but evidence is confounded by reverse causality and family environmental factors.

What is new

- In a Chinese cohort, screen time >2 h/day in the first two postnatal years and language regression were associated with ASD diagnosis.
- Language regression was also associated with greater symptom severity, whereas older paternal age was associated with milder symptoms.
- These readily ascertainable factors may serve as practical clinical clues for pediatricians to identify children warranting further developmental evaluation, although causal inference is precluded by the observational design.

1. INTRODUCTION

Autism spectrum disorder (ASD) is a heterogeneous neurodevelopmental condition characterized by impairments in social interaction, communication deficits, and restricted, repetitive patterns of behavior that typically emerge during early childhood [1, 2]. The rising prevalence of ASD [3, 4] underscores the need for research into its etiology. A strong genetic contribution to ASD pathogenesis is well established [5–8]. Nevertheless, specific genetic underpinnings remain unidentified in most cases.

The role of environmental factors in ASD has garnered increasing attention, based on the premise that early-life exposures modulate gene expression via epigenetic reprogramming [9–11]. Recent evidence further suggests potential gene–environment interactions operating during both the prenatal period and early childhood [12, 13]. Accordingly, identifying modifiable environmental factors associated with ASD has become a research priority.

Meta-analyses and systematic reviews have identified several ASD-associated factors: advanced parental age, pregnancy-related factors, maternal comorbidities, and nutritional status [12]. Prenatal and perinatal factors—including abnormal fetal presentation, umbilical cord complications, low birth weight, and hyperbilirubinemia—have shown small but significant associations [14, 15]. Birth asphyxia, preterm birth, and cesarean delivery have also been linked to ASD [16–18]. Maternal infection and prenatal stress during pregnancy may increase ASD risk through inflammatory and hormonal pathways, respectively [19–21].

Postnatal environmental factors—particularly increased screen time during the first three years of life—have been associated with elevated ASD likelihood [10, 11]. However, these factors are susceptible to confounding: parental educational attainment, socioeconomic status (SES), and parent–child interaction quality may influence children’s screen use patterns [22]. Excessive screen time in children under age 3

years exerts adverse effects on cognitive, language, and social–behavioral development [23–25]. Yet evidence confirming a causal relationship remains insufficient: it is unclear whether screen exposure predisposes children to social communication impairments or whether children with inherent socio-linguistic difficulties are more inclined toward screen-based activities [26–28].

The present study performed a retrospective analysis of clinical data from a Chinese cohort of children with ASD, compared with two control groups. Our objective was to identify perinatal and early childhood factors associated with ASD diagnosis and severity. Given the observational, cross-sectional design of this study, all reported associations should be interpreted with caution; causal inferences require confirmation through prospective research.

2. METHOD

2.1 Study population

We retrospectively enrolled participants who visited the rehabilitation clinic of the Children’s Hospital, Zhejiang University School of Medicine, between 2024 and 2025 with language and/or social developmental concerns as the primary complaint. No a priori sample size calculation was performed; the sample size was determined by clinic attendance during the study period. Participants comprised three groups:

ASD group. Diagnosed according to DSM-V criteria [29] by experienced pediatricians, with scores exceeding the threshold on the Childhood Autism Rating Scale (CARS) [30]. CARS scores of 30 to less than 36 indicate mild-to-moderate symptoms; scores of 36 or greater denote severe symptoms.

Non-ASD group. Children presenting with language and/or social developmental delay, with a developmental quotient below 70 in the Language and/or Personal–Social domain of the Griffiths Development Scales–Chinese edition [31], and in whom ASD was explicitly excluded.

TD group. Children with no developmental disorders, confirmed through clinical evaluation, recruited during routine physical examinations and age- and sex-matched with the ASD group.

2.2 Data collection

Data were collected through caregiver-completed questionnaires and medical record review, including: (1) demographic characteristics—sex, age, parental ages at delivery, parental educational level, family history of ASD or intellectual disability; (2) perinatal exposures—delivery mode (cesarean or vaginal), high-risk birth factors (prematurity, low birth weight, perinatal asphyxia, hyperbilirubinemia, multiple births, intracranial hemorrhage, nuchal cord), maternal status during pregnancy (folic acid supplementation, viral infection, emotional problems); (3) family environment—primary caregiver, daily screen-time exposure (hours/day watching television, smartphones, or tablets) during the first, second, and third postnatal years, categorized as none, < 1 hour, 1 to 2 hours, 2 to 4 hours, or ≥ 4 hours; (4) socioeconomic status—family living space (> 100 m² or not) and annual household income (> 500 000

RMB or not); (5) child health status—allergies, constipation, picky eating, language developmental regression, rehabilitation history.

The Ethics Committee of the Children's Hospital of Zhejiang University School of Medicine (2023-IRB-0307-P-01) approved all protocols in accordance with the Declaration of Helsinki. Parents or guardians provided written informed consent; children older than 8 years also provided assent.

2.3 Statistical analysis

Categorical variables across the three groups were compared using chi-square tests (significance threshold $p < 0.05$). Owing to the exploratory nature of this study, no correction for multiple comparisons was applied; results should therefore be interpreted with appropriate caution. Variables showing significant differences between the ASD and non-ASD groups were entered into binary logistic regression models.

The initial model included age group, daily screen time during the first postnatal year, and language developmental regression as covariates, with group (ASD vs non-ASD) as the dependent variable. A second regression was performed after excluding children aged under 2 years (ASD $n = 675$, non-ASD $n = 151$), examining age group and daily screen time during the second postnatal year. Within the ASD group, severity (mild-moderate vs severe) was analyzed using binary logistic regression with covariates selected at $p < 0.10$ in univariate screening (paternal age at delivery, screen time during the first postnatal year, paternal education, maternal education, and high-risk birth history). Model fit was assessed using the Hosmer–Lemeshow test; Nagelkerke R^2 is reported as a pseudo- R^2 measure. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated.

3. RESULTS

3.1 Clinical characteristics

The ASD group included 708 children (461 mild-moderate, 247 severe), with 164 in the non-ASD group and 337 in the TD group. Clinical characteristics are summarized in Table 1. Figure 1. and Fig. 2.

Table 1

Comparative analysis of clinical characteristics among children in the ASD, non-ASD, and TD groups.

Clinical characteristics	ASD(N = 708, %)	Non-ASD(N = 164, %)	TD(N = 337, %)	p-value (ASD vs. non-ASD)	p-value (ASD vs. TD)
Male sex, n (%)	573 (81)	130 (79)	259 (77)	0.661	0.139
Age (y), n (%)				0.004*	0.989
≤ 3 y	175 (25)	51 (31)	83 (24)		
3–6 y	347 (49)	57 (35)	164 (49)		
≥ 6 y	186 (26)	56 (34)	90 (27)		
Cesarean delivery, n (%)	351 (50)	75 (46)	136 (40)	0.387	0.005*
Paternal age at delivery ≥ 35 y, n (%)	232 (33)	41 (25)	55 (16)	0.061	0.000*
Maternal age at delivery ≥ 35 y, n (%)	141 (20)	28 (17)	39 (12)	0.444	0.001*
Father's education n (%)				0.196	0.000*
Master's degree and above	57 (8)	9 (5)	4 (1)		
College degree	393 (56)	84 (51)	153 (45)		
High school and below	258 (36)	71 (43)	180 (53)		
Mother's education n (%)				0.866	0.000*
Master's degree and above	48 (7)	10 (6)	2 (1)		
College degree	386 (54)	93 (57)	158 (47)		
High school and below	274 (39)	61 (37)	177 (52)		
High-risk birth history, n (%)	279 (39)	56 (34)	101 (30)	0.247	0.003*
Premature	65 (23)	9 (16)	29 (19)	0.161	0.761
Low birth weight	32 (11)	8 (14)	14 (14)	0.506	0.593
Perinatal asphyxia	39 (14)	8 (14)	3 (3)	0.850	0.000*
Hyperbilirubinemia	123 (44)	24 (43)	52 (52)	0.884	0.244
Multiple births	18 (6)	5 (9)	5 (5)	0.560	0.808
Intracranial hemorrhage	8 (3)	2 (4)	1 (1)	0.676	0.455
*, p < 0.05; CI, confidence interval; OR, odds ratio; SE, standard error; df, degrees of freedom.					

Clinical characteristics	ASD(N = 708, %)	Non-ASD(N = 164, %)	TD(N = 337, %)	p-value (ASD vs. non-ASD)	p-value (ASD vs. TD)
Nuchal cord	53 (19)	16 (29)	15 (15)	0.106	0.352
Allergy, n (%)	77 (11)	18 (11)	11 (3)	1.000	0.000*
Constipation and/or picky eating, n (%)	409 (58)	81 (49)	128 (38)	0.055	0.000*
Family history of ASD or ID, n (%)	18 (3)	2 (1)	1 (0.3)	0.398	0.011*
Primary caregiver other than mother, n (%)	260 (37)	66 (40)	95 (28)	0.08	0.005*
Folic acid supplements during pregnancy, n (%)	626 (88)	141 (86)	279 (83)	0.424	0.015*
Maternal history of prenatal viral infection, n (%)	54 (8)	18 (11)	5 (1)	0.159	0.000*
Maternal emotional disorders during pregnancy, n (%)	190 (27)	36 (22)	27 (8)	0.235	0.000*
Daily screen time during first year of life. n (%)				0.016*	0.000*
None	355 (50)	93 (56.7)	227 (67)		
<1 h	178 (25)	50 (30.5)	83 (25)		
1–2 h	90 (12.7)	14 (8.5)	17 (5)		
2–4 h	54 (7.6)	4 (2.4)	7 (2)		
> 4 h	31 (4.4)	3 (1.8)	3 (1)		
Daily screen time during second year of life, n (%)	675	151	328	0.008*	0.000*
None	135 (20)	40 (26.5)	105 (32)		
<1 h	268 (39.7)	67 (44.4)	151 (46)		
1–2 h	135 (20)	32 (21.2)	51 (16)		
2–4 h	92 (13.6)	10 (6.6)	15 (5)		
> 4 h	45 (6.7)	2 (1.3)	6 (2)		
*, p < 0.05; CI, confidence interval; OR, odds ratio; SE, standard error; df, degrees of freedom.					

Clinical characteristics	ASD(N = 708, %)	Non-ASD(N = 164, %)	TD(N = 337, %)	p-value (ASD vs. non-ASD)	p-value (ASD vs. TD)
Daily screen time during third year of life, n (%)	528	113	272	0.395	0.000*
None	30 (6)	8 (7)	39 (14)		
<1h	226 (43)	48 (42)	121 (44)		
1–2 h	158 (30)	35 (31)	90 (33)		
2–4 h	74 (14)	19 (17)	13 (5)		
> 4 h	40 (7)	3 (3)	9 (3)		
Family living space > 100 m ² , n (%)	386 (55)	80 (50)	158 (47)	0.193	0.024*
Annual household income > 500,000 RMB	75 (11)	17 (11)	7 (2)	1.000	0.000*
Rehabilitation, n (%)	411 (58)	59 (36)		0.000*	
Language developmental regression, n (%)	132 (19)	19 (12)		0.030*	
* ,p < 0.05;CI, confidence interval; OR, odds ratio; SE, standard error; df, degrees of freedom.					

Compared with the TD group, the ASD group showed significantly higher prevalence of cesarean delivery, advanced paternal and maternal age (≥ 35 years), high-risk birth history, allergic conditions, constipation/picky eating, family history of ASD or intellectual disability, primary caregiver other than the mother, maternal viral infection and emotional problems during pregnancy, and excessive screen-time exposure during each of the first three postnatal years (all $p < 0.05$).

Compared with the non-ASD group, the ASD group showed significant differences in age distribution (with diagnoses concentrated between 3 and 6 years), daily screen-time exposure during the first and second postnatal years, language developmental regression, and rehabilitation history (all $p < 0.05$).

3.2 Logistic regression: ASD vs non-ASD

The initial binary logistic regression model (Nagelkerke $R^2=0.072$) identified language developmental regression (OR 1.94, 95% CI 1.12–3.34, $p = 0.017$) and 2 to 4 hours/day screen time during the first postnatal year (OR 3.43, 95% CI 1.20–9.75, $p = 0.021$) as factors associated with ASD diagnosis. Age at diagnosis was concentrated in the 3 to 6 years group. After excluding children aged under 2 years, the refined model (Nagelkerke $R^2=0.068$) retained language developmental regression (OR 1.88, 95% CI 1.05–3.36, $p = 0.032$) and identified screen time during the second postnatal year: 2 to 4 hours/day (OR 2.71, 95% CI 1.26–5.81, $p = 0.010$) and more than 4 hours/day (OR 6.33, 95% CI 1.45–27.68, $p = 0.014$).

The low Nagelkerke R² values (0.068–0.072) indicate that the included variables explain only a small proportion of variance in ASD diagnosis—a finding consistent with the multifactorial etiology of ASD, in which unmeasured genetic and environmental factors account for the majority of variance [32].

3.3 ASD severity

In the severity model (Nagelkerke R²=0.041; Table 2), language developmental regression was associated with greater severity (OR 1.74, 95% CI 1.17–2.57, p = 0.006), whereas older paternal age was associated with milder symptoms (OR 0.96, 95% CI 0.93–0.99, p = 0.006). Perinatal high-risk factors showed no significant association (p = 0.066). For parental education, the confidence intervals for all comparisons included 1.0. For example, for paternal education (postgraduate vs high school or below), OR was 1.84 (95% CI 0.88–3.87), and for maternal education (postgraduate vs high school or below), OR was 0.48 (95% CI 0.21–1.08). These associations are not statistically significant; the observed trends require validation in larger studies.

Table 2
Multivariable logistic regression analysis of ASD symptom severity

Characteristics	B	SE	Wald	df	p	OR	95% CI	
							Lower	Upper
Language developmental regression	0.55	0.20	7.65	1	0.006	1.74	1.17	2.57
Paternal age at delivery	-0.04	0.02	7.44	1	0.006	0.96	0.93	0.99
High-risk	-0.30	0.17	3.38	1	0.066	0.74	0.53	1.02
Father's education (college degree vs. high school and below)	0.33	0.22	2.22	1	0.136	1.39	0.90	2.13
Father's education (master's degree and above vs. high school and below)	0.61	0.38	2.59	1	0.107	1.84	0.88	3.87
Mother's education (college degree vs. high school and below)	-0.24	0.22	1.22	1	0.268	0.79	0.51	1.21
Mother's education (master's degree and above vs. high school and below)	-0.73	0.42	3.12	1	0.078	0.48	0.21	1.08

4. DISCUSSION

In this study, we analyzed clinical characteristics of a Chinese ASD cohort and identified factors associated with ASD diagnosis and severity. Age at diagnosis was concentrated between 3 and 6 years, which is broadly consistent with patterns reported in U.S. surveillance data (median age 36–59 months) [3, 4].

Compared with typically developing controls, several factors were more prevalent in the ASD group—including cesarean delivery, advanced parental age, perinatal high-risk factors, maternal viral infection and emotional problems during pregnancy, family history of ASD or intellectual disability, and screen-time exposure exceeding 2 hours/day during the first three postnatal years. These findings are broadly consistent with previous literature [12, 14–16, 19, 20, 33], although the association with cesarean delivery remains debated [18].

Notably, screen-time exposure of more than 2 hours/day during the first two postnatal years, language developmental regression, maternal emotional disorders during pregnancy, and advanced paternal age appeared more specifically associated with ASD, as these factors distinguished the ASD group not only from TD children but also from those with non-ASD developmental delays.

The association between early-life screen exposure and ASD diagnosis has been reported in several studies [24, 25, 34–36]. The first two postnatal years represent a critical period of brain development; our finding that screen-time effects were evident during this window is consistent with this developmental sensitivity. However, the direction of this association cannot be determined from these cross-sectional data. Children with inherent social communication difficulties may preferentially engage with screens, and parents of children with emerging ASD features may be more likely to offer screen-based activities [22, 26, 37]. Moreover, the interpretation of screen-time effects is complicated by the potential displacement of parent–child interaction [38, 39]. While our findings align with pediatric guidelines recommending avoidance of screen exposure among infants under 2 years [40, 41], they cannot establish causation.

Language developmental regression was associated with ASD diagnosis, with a prevalence of 19% in our cohort—within the range reported in retrospective studies (approximately 20–30%) [42, 43]. This finding supports the clinical utility of regression history in distinguishing ASD from other developmental delays. We similarly observed that ASD children with language developmental regression presented with greater symptom severity at diagnosis compared to their non-regressive counterparts [42].

Advanced paternal age was associated with both ASD diagnosis and, within the ASD group, milder symptom severity. The association with diagnosis is consistent with epidemiological evidence [33, 44]. The observed association with severity (OR 0.958) is statistically significant but objectively small; inconsistent findings in prior research [45–47] may partly reflect differences in sample size and statistical power.

We observed that the parents of children with ASD in our cohort had higher educational attainment, better living conditions, and higher household incomes compared with those of TD children. This pattern

may reflect ascertainment bias: families with higher SES may have greater awareness of ASD signs and better access to diagnostic services, leading to higher rates of diagnosis and reporting [48, 49].

5. LIMITATIONS

Several limitations of this exploratory study must be acknowledged. First, the Nagelkerke R^2 values (0.041–0.072) indicate that the included variables explain only a very small fraction of the variance in ASD diagnosis and severity. Although low pseudo- R^2 values are common in epidemiological studies of multifactorial conditions [32], they underscore the weak predictive capability of the current models and the importance of unmeasured factors—including genetic predispositions and finer-grained environmental exposures. Second, this is a single-site, hospital-based study with a modest non-ASD sample ($n = 164$). The resulting wide confidence intervals for some estimates (e.g., OR 6.33, 95% CI 1.45–27.68 for > 4 hours/day screen time) reflect insufficient precision and limit the generalizability of findings. Third, our analytical approach involved univariate screening of multiple variables without correction for multiplicity, which increases the risk of type I error. Fourth, the cross-sectional, retrospective design limits causal inference: screen exposure was assessed via caregiver recall concurrently with diagnosis, precluding determination of temporal sequence. Fifth, the limited number of ASD-associated variables that could be examined in multivariable models—constrained by the sample size—means that several potentially relevant confounders could not be simultaneously adjusted for. Finally, the study is subject to recall and selection biases inherent to clinic-based sampling.

6. CONCLUSION

In this Chinese ASD cohort, we observed that screen-time exposure exceeding 2 hours/day during the first two postnatal years, language developmental regression, maternal emotional disorders during pregnancy, and advanced paternal age were associated with an ASD diagnosis. Furthermore, the presence of language developmental regression was associated with more severe clinical presentations, whereas older paternal age was linked to milder symptom severity among affected children. However, the observational design precludes causal inference; these associations require confirmation through prospective, longitudinal studies with adequate sample sizes and more comprehensive measurement of potential confounders.

Declarations

Fund

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Conflicts of Interest

The authors declare no conflicts of interest.

Ethics approval and consent to participate

The Ethics Committee of the Children's Hospital of Zhejiang University School of Medicine (2023-IRB-0307-P-01) approved all protocols. Parents or guardians provided written informed consent; children older than 8 years also provided assent.

Author Contribution

Author contributions: Hui Wang: Conceptualization, Data curation, Formal analysis, Investigation, Writing – original draft, Writing – review & editing. Hong-xia Zhao: Conceptualization, Data curation, Investigation, Methodology, Writing – review & editing. Yu Du: Data curation, Formal analysis, Writing – review & editing. Zheng-huan Mao: Data curation, Formal analysis, Writing – review & editing. Wei-jun Chen: Resources, Writing – review & editing. Li Ding: Data curation, Writing – review & editing. Ai-fen Zhao: Investigation, Resources, Writing – review & editing. Chuan-wen Wang: Methodology, Software, Writing – review & editing. Chao-chun Zou: Conceptualization, Methodology, Project administration, Supervision, Writing – review & editing. Hai-feng Li: Project administration, Supervision, Writing – review & editing. All authors have read and approved the final manuscript and agree to be accountable for all aspects of the work.

Data Availability Statement

The study team are available to collaborate with other research teams on receipt of a reasonable request to access study data. Expressions of interest to access study data will be considered and then group level or individual level deidentified data could be shared as appropriate.

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Figures

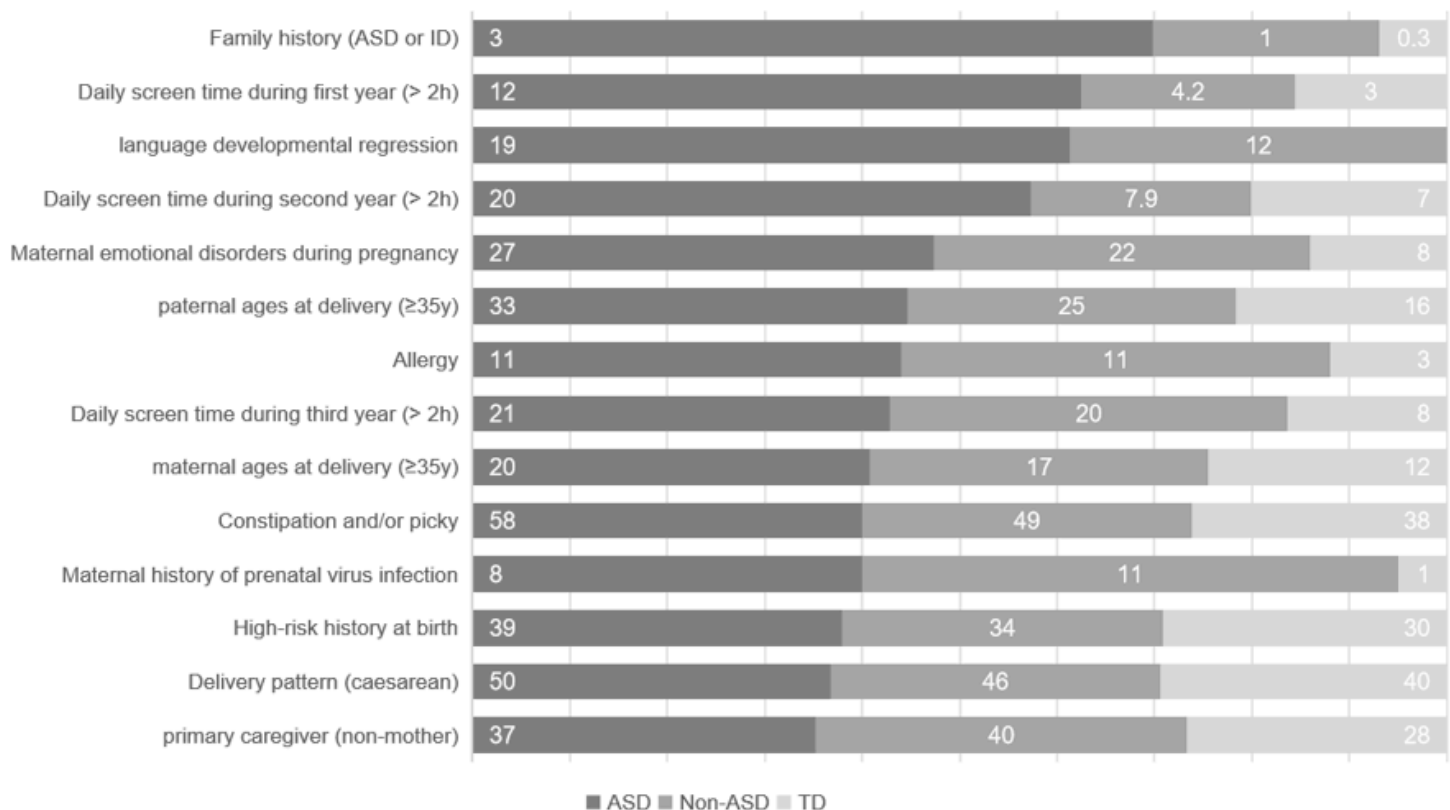


Figure 1

Percentage-stacked bar chart of high-risk factors for ASD. Numbers in percentage stacked bar charts represent percentage values.

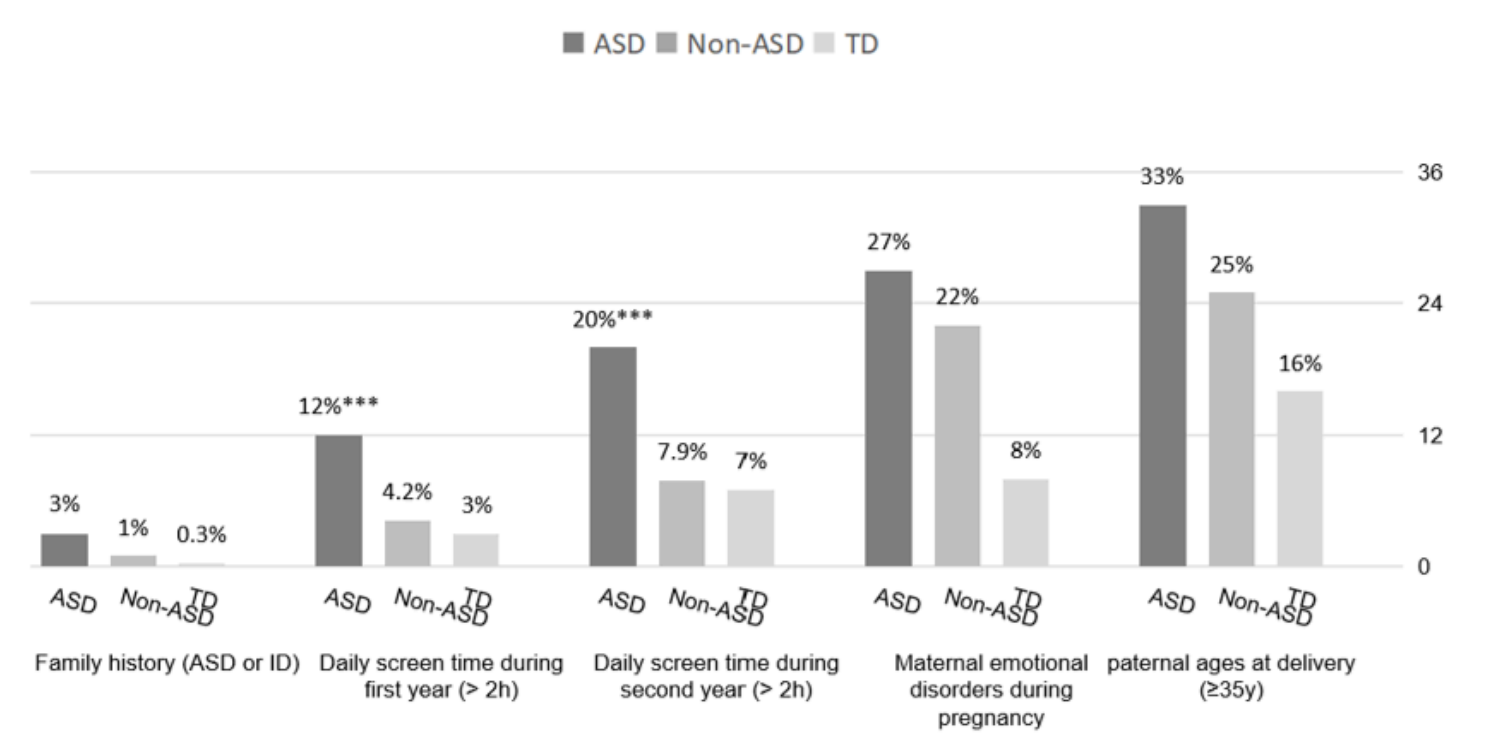


Figure 2

Representation of key risk factors via bar charts.