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Journal Title: Newborn and Infant Nursing Reviews
Volume: Volume 16, Number 4
Publisher: WB Saunders | 2016-12, Pages 340-347
Type of Work: Article | Post-print: After Peer Review
Publisher DOI: 10.1053/j.nainr.2016.09.033
Permanent URL: https://pid.emory.edu/ark:/25593/s5d3s

Final published version: http://dx.doi.org/10.1053/j.nainr.2016.09.033

Published in final edited form as:

Newborn Infant Nurs Rev. 2016 December ; 16(4): 340–347. doi:10.1053/j.nainr.2016.09.033.

Maternal and Neonatal Birth Factors Affecting the Age of ASD Diagnosis☆

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Abstract

Early diagnosis of autism spectrum disorders (ASD) enables early intervention that improves long term functioning of children with ASD but is often delayed until age of school entry. Few studies have identified factors that affect timely diagnosis. This study addressed how maternal education, race, age, marital status as well as neonatal birth factors affect the age at which a child is diagnosed with ASD. This study involved a retrospective analysis of 664 records of children treated at one of the largest autism treatment centers in the United States from March 1, 2009 to December 30, 2010. Logistic regression and Cox proportional hazards regression were used to identify maternal and neonatal factors associated with age of diagnosis. Infant gender, maternal race, marital status, and maternal age were identified as significant factors for predicting the age of ASD diagnosis. In the Cox proportional hazards regression model, only maternal race and marital status were included. Median survival age till diagnosis of children born to married mothers was 53.4 months compared to 57.8 months and 63.7 months of children born to single and divorced or widowed mothers respectively. Median survival age till diagnosis for children of African American mothers was 53.8 months compared to 57.2 months for children of Caucasian mothers. No statistically significant difference of timing of ASD diagnosis was found for children of varying gestational age. Children born to older or married mothers and mothers of minority races were more likely to have an earlier ASD diagnosis. No statistically significant differences in timing of ASD diagnosis were found for children born at varying gestational ages. Identification of these factors has the potential to inform public health outreach aimed at promoting timely ASD diagnosis. This work could enhance clinical practice for timelier diagnoses of ASD by supporting parents and clinicians around the world in identifying risk factors beyond gender and SES and developing strategies to recognize earlier signs of ASD and contribute to improved development outcomes in children with ASD.

☆Funding information: Children's Healthcare of Atlanta Dudley Moore Research Fund.

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Keywords

Autism; Diagnosis; Birth factors; Maternal factors

Autism spectrum disorder (ASD) is a complex developmental syndrome of the central nervous system characterized by deficits in communication and social interactions in combination with stereotyped or restricted behaviors or interests. Prevalence of ASD has risen dramatically over the past two decades, and ASD now represents the most common neurodevelopmental disability among children.[1] According to the Center for Disease Control Autism Network Surveillance, ASD affects one in 68 children in the United States.[1] Early interventions, tailored educational planning and family support are critical for later behavioral, language, and cognitive outcomes in children with ASD. Early interventions are more effective in younger children and reduce the long term family and societal costs related to ASD.[2] In addition, early interventions may prevent further manifestations of ASD by capitalizing on early brain plasticity, particularly in the social brain circuitry.[3] However, ensuring timely access to interventions is contingent upon early detection and diagnosis. Therefore, children whose diagnosis is delayed may miss the opportunity to receive intervention services necessary to optimize their developmental outcomes.

Diagnosing a young child with ASD can be a challenge for a variety of reasons. A growing body of literature has identified signs of autism in the first two years of life. The patterns of communication and social behavior of infants who later develop ASD are distinct from those of infants who have a typical developmental trajectory.[4,5] Early warning signs that present during infancy include delays in imitation, abnormal or blunted response to stimuli, and atypical patterns of visual attention.[6,7] Many parents express concerns about the development of their child between 12 and 18 months, yet their child is often not diagnosed until much later. Furthermore, repetitive behaviors may not present themselves until age 3–4, so younger children may not demonstrate diagnostic criteria.[8] In addition, there is a wide normal range for speech acquisition and communication.

Although diagnosis of ASD at a young age presents challenges, major advances have occurred in the field of early ASD detection. Knowledge regarding early warning signs and stability of diagnoses made in infancy and toddlerhood coupled with development of effective toddler screening and diagnostic instruments prompted the American Academy of Pediatrics to recommend that all children be screened at 18 and 24 months[9–13]; Sunita and Bilszta, 2013.[36] However, early diagnosis is not simply a function of developing better measures and better clinical skills. While a growing number of children (18%) are being diagnosed by age three, the average age of diagnosis of ASD nationwide continues to be after the age of 4.[1] Although the spread of knowledge about ASD to parents, physicians, nurse practitioners, and teachers has led to early treatment with better outcomes, the age of diagnosis has not declined uniformly for all children, and previous research suggests that factors such as gender, race, access to healthcare, and severity of symptoms are associated with age of diagnosis.[2,14,15] Recognition of disparities in early diagnosis is a priority for the American Academy of Pediatrics and the United States Department of Health and Human Services Defense and Education.[16] Identifying factors related to age of diagnosis may

inform public awareness campaigns and healthcare provider education. Understanding these factors may help identify barriers to early diagnosis and identify populations that should be targeted to reduce disparities in ASD diagnosis.

A recent review of studies examining child and family factors associated with age at ASD diagnosis found that more symptoms, language impairments, and having a family member with ASD are associated with an earlier diagnosis and that having a co-morbid intellectual disability or neurologic disorder is associated with a later diagnosis.[17] However, it is less clear how other child and family characteristics influence age of diagnosis. Findings from these studies were inconsistent with respect to how younger maternal age, lower maternal education, race, and gender affect age at diagnosis.[17] In addition, there was only one study that examined the association between any neonatal birth characteristics and ASD diagnosis.[17,18]

Given that ASD is presumably present in the first year of life, focusing on how maternal social factors and neonatal birth characteristics affect age of ASD diagnosis is appropriate. This study investigated the effect of gestational age, gender, and length of hospital stay, as well as maternal age, education, race, and marital status on the age of ASD diagnosis. We hypothesized that maternal and neonatal birth factors would account for variability in age of diagnosis among children with ASD.

Methods

Data Sources

This study involved a retrospective analysis of data from a cohort of children treated at a neurodevelopmental pediatric interdisciplinary clinic at a large autism center in the southeastern United States (center). The center is a nationally recognized center of comprehensive services for children with ASD. The center served more than 4500 children during 2010, 28% of whom were African-American, and 70% of whom rely on Medicaid.

This study analyzed data from the medical records of every child screened at the PNC from March 1, 2009 to December 31, 2010; data included ASD diagnosis, gestational age, and age of ASD diagnosis. The medical records contain in-depth clinical data regarding the basis for diagnoses.

ASD Diagnostic Evaluation and Setting

The PNC conducted multidisciplinary assessments for children referred from both internal and external sources. All assessments were conducted by a developmental pediatrician or pediatric nurse practitioner and a pediatric psychologist. In addition to a review of records, thorough medical and family history, and a physical exam, each child received a battery of psychological tests. The specific battery of tests was chosen by the psychologist based on the individual child's presenting concerns, age, and level of skill. Most assessments included a structured diagnostic play session (most commonly the Autism Diagnostic Observation Schedule-Generic), a standardized cognitive measure (e.g. Bayley Scales of Infant Development, Mullen Scales of Early Learning, Stanford Binet, Differential Ability Scales-II), an adaptive measure (e.g. Vineland Adaptive Measures Scales-Second Edition, Adaptive

Behavior Assessment System-II), and standardized parent/teacher report measures of social, emotional, and behavioral functioning (e.g. Social Responsiveness Scale-2, Social Communication Questionnaire, Childhood Autism Rating Scale, Autism Spectrum Rating Scale, Child Behavior Checklist, Caregiver-Teacher Report Form).

The final diagnosis was made using the criteria outlined in the American Psychiatric Association's Diagnostic and Statistical Manual (DSM-IV TR). All sources of information were considered when making a formal diagnosis. The DSM-IV-TR describes five categories of disorders that include autism, childhood disintegrative disorder, Rett's syndrome, Asperger's disorder and pervasive developmental disorder not otherwise specified (PDD-NOS).[19] While there are slight differences in the configuration of symptoms in each of these categories, all children diagnosed with one of these disorders qualitatively differ from typically developing children in three main areas: social interaction, communication, and restricted, repetitive and stereotyped patterns of behavior, interests and activities.

Statistical Analysis

Data records (n = 664) were reviewed for completeness and errors prior to analysis. All data were nearly complete; paternal age was the most common missing value, with 3.3% (22/664) unavailable. This small amount of missing data did not differ significantly between children with an ASD diagnosis versus those with no ASD ($p = .807$). The remaining variables had less than 1.5% missing data collectively.

Descriptive statistics were calculated for all variables considered, and the distributions were evaluated for significant deviations from normality (Table 1). Only length of hospital stay following delivery was significantly skewed (as expected); median length of stay was 3 days but ranged from 1 to 308 days. A median split was performed for this variable to compare those with a length of stay less than 3 days versus those with a length of stay greater than three days. Associations among the variables were assessed using correlation, analysis of variance, and chi-square tests as appropriate.

For all variables, comparisons were made between children diagnosed with ASD and those not diagnosed with ASD using independent group t-tests (for continuous normally distributed variables), Mann–Whitney non-parametric tests for independent groups (for continuous skewed variables), and chi-square tests (for categorical and ordinal variables). For considering potentially significant predictors of an ASD diagnosis, all variables with a $p \leq 0.10$ were considered for inclusion in a logistic regression model (Table 1). The final predictive logistic regression model included key variables (child's chronological age, maternal age at delivery, paternal age at delivery, gestational age (weeks), child's gender, maternal marital status, maternal race, length of hospital stay (days)) in a forward stepwise likelihood ratio variable selection ($p < 0.05$ for variable inclusion and $p > 0.10$ for variable removal) to create the best ASD predictive model (Table 2).

Additionally, to evaluate the predictors associated with the time (age) until ASD diagnosis, Kaplan–Meier analysis and Cox proportional hazards regression were used given that subjects who were not found to have an ASD diagnosis were "right censored" (i.e. ASD diagnosis was not observed up to the time (age) of the medical record available – it is

possible these children did go on to develop ASD at a later unobserved time).[20] Initial screening of all variables looked at each variable individually as a potential covariate for predicting the age of ASD diagnosis (Table 3). Based on initial screening results, covariates with $p < 0.10$ (maternal age, paternal age, child's gender, maternal race, maternal marital status) were considered for inclusion in a final predictive model. The final predictive Cox proportional hazards regression model selected final predictors using forward stepwise likelihood ratio variable selection ($p < 0.05$ for variable inclusion and $p > 0.10$ for variable removal) to create the most parsimonious model.

Results

Records were obtained for all children (n = 664) screened for ASD at the center from March 1, 2009 through December 30, 2010. In addition to the age at evaluation and diagnosis of ASD, infant birth weight, gender, gestational age at birth, and length of hospital stay (after delivery) were obtained. Maternal information included age at infant delivery, education at the time of the evaluation, race, and marital status. Paternal age was also reported.

The mean birth weight of children in this cohort was 3172 grams (SD 766) and mean gestational age was 38.1 (SD 3.3) weeks with 7.1% early preterm (EPT <33 weeks gestation) and 13.9% late preterm (LPT 34–36 weeks gestation) (Table 1). Median length of stay in the hospital after delivery was three days, with a range of one to 308 days. Males represented 79% of this cohort. Mean maternal and paternal ages were 28 years (SD 6.2) and 31 years (SD 7.4), respectively. On average, mothers completed 13.6 (SD 2.3) years of education. Forty-six percent were Caucasian and 34% were African American. Of note, the data did not specify ethnicity, thus Hispanic and non-Hispanic white were not differentiated in this data set. Most were married (64.5%) or single (23.3%) with 7.6% divorced or widowed and 4.6% cohabiting. Some significant associations among these variables were noted. As expected, maternal and paternal age were highly correlated ($r = 0.728$, $p < 0.001$), and the age of both the mothers (ANOVA $F_{(3, 653)} = 15.694$, $p < 0.001$) and fathers (ANOVA $F_{(3, 636)} = 7.459$, $p < 0.001$) varied with marital status with married parents older than single mothers. Additionally, marital status varied significantly by race. African Americans represented 41.4% of single mothers whereas Caucasians comprised 11.7% of single mothers. The majority of Caucasians were married (76.8%) compared to 66.9% mothers of other race and only 46.4% of African American mothers ($\chi^2_{(6)} = 81.499$, $p < .001$).

Sixty-one percent (406/664) of the children seen at the PNC were diagnosed with ASD. Characteristics of children with and without ASD can be found in Table 1. The median age of all 664 children was 47 months ranging from 9 to 188 months with the 406 ASD diagnosed children slightly younger with a median age of 46 months compared to 49 months for the 258 children without an ASD diagnosis ($p = .052$). Of the 406 children with ASD, 6.7% were EPT and 10.6% were LPT (Table 1). In addition to the child's age, significant differences ($p < 0.05$) between children diagnosed with ASD and those without ASD were noted for maternal and paternal age, gestational age, infant gender, and maternal marital status. Although length of hospital stay and maternal race did not reach statistical significance (with ≈ 0.10), they were considered for inclusion in the model. These eight

variables were evaluated for inclusion in a logistic regression model for predicting an ASD diagnosis. The final set of variables was selected using forward likelihood methods. As summarized in Table 2, marital status entered the model first as a significant predictor (Table 2, step 1 $p < 0.001$) classifying 62.1% of the ASD diagnoses correctly with married mothers 1.8 times more likely to have a child with an ASD diagnosis compared to divorced or widowed mothers. However, differences in ASD diagnosis between children of single mothers and divorced or widowed mothers did not reach statistical significance. Next, the infant's gender entered the model (Table 2, step 2 $p = 0.003$) with male infants 1.8 times more likely to have an ASD diagnosis compared to females. Finally, maternal race entered the model (Table 2, step 3 $p = .010$) with children of African American and other race mothers 1.7 times more likely to have children diagnosed with ASD. The final model classified 65.3% of the ASD diagnoses correctly. Child's chronological age, gestational age, length of stay in the hospital, maternal and paternal age were not statistically significant predictors of an ASD diagnosis.

When assessing variables as potentially significant covariates for predicting the age of ASD diagnosis (using Cox proportional hazards regression), maternal and paternal age, infant gender, maternal race and marital status were all considered as candidates in a final model with p-values <0.10 (Table 3). Female gender, Caucasian race, and divorced or widowed mothers were reference categories for infant gender, maternal race, and marital status, respectively. As shown in Table 3, older maternal and paternal age, African American and other race, and male gender were associated with a higher probability (hazards ratio (Exp (B)) > 1) of having a child diagnosed with ASD at a younger age. Children of married or cohabiting mothers were more likely to be diagnosed with ASD early compared to divorced or widowed mothers. Single mothers had a slightly increased likelihood of earlier diagnosis compared to divorced or widowed mothers (Table 3).

Considering these five potential covariates using forward likelihood ratio variable selection, only maternal race ($p = 0.008$) and marital status ($p = 0.022$) were retained in a final Cox proportional hazards regression model (Table 4). The overall hazard ratio of earlier ASD diagnosis for children of African American mothers and mothers of other minority races compared to children of Caucasian mothers was 1.35 and 1.46 respectively [95%CI: 1.061–1.717, 1.114–1.903]. African American and other minority race mothers had children with median survival age until ASD diagnosis of 53 and 52 months respectively compared to 57 months for Caucasian mothers (Fig. 1). Regarding maternal marital status, the only significant difference was between children of married mothers and children of divorced or widowed mothers. There were no significant differences between any other paired maternal marital status comparisons. The overall hazard ratio of earlier ASD diagnosis for children of married mothers compared to children of divorced or widowed mothers was 1.76 [95% CI: 1.164–2.659]. The median survival age until ASD diagnosis was the longest for divorced or widowed mothers at 63 months compared to 57 months for single mothers, 55 months for co-habitating mothers and 53 for married mothers (Fig. 1).

Discussion

The present study examined how maternal education, race, age, and clinical risk factors (e.g. birth characteristics) affect the likelihood of receiving an ASD diagnosis and the age at which a child is diagnosed. This was undertaken within the context of children treated at the center.

Children born to African American mothers or mother of other minority races were more likely to have their child diagnosed with ASD, and sooner than children of Caucasian mothers. This finding differs from previous research although studies report contradictory results regarding the role of race in ASD diagnosis. Some studies suggest that race does not influence age of diagnosis or that minority groups are diagnosed later whereas other studies suggest age at diagnosis is comparable across racial groups after controlling for socioeconomic status and maternal education.[14,15,17,21] However, the results of this study suggest that children born to Caucasian women are at a disadvantage for early identification. It is possible that these findings may have been observed because of the large African American and minority population that the center serves.

In addition, this study demonstrates that children are more likely be diagnosed at an earlier age if they are male or if their parents are older or married. While previous studies generally suggest that there is no association between gender and early diagnosis, there have been a few studies that have found an association between the male gender and an earlier diagnosis.[14,17,18,22] Although studies have found no association between maternal age and an earlier diagnosis, one study suggested that for every one year increase in maternal age at delivery, age of diagnosis decreased by 0.06.[17,18] However, our results may support the findings of this study since parental age for our cohort was associated (confounded) with martial status. To date, only one study has examined marital status a timeliness of ASD diagnosis, but no effect was identified.[18] However, we found that children whose mother identified herself as married were 1.8 times more likely to be diagnosed earlier than children whose mother is identified herself as widowed, single, or divorced. Marital status may mediate instead the association between maternal age and age of ASD diagnosis since maternal age and marital status were both found to be correlated at a level of statistical significance. Indeed, older mothers were more likely to be married, and children of married mothers were also more likely to be diagnosed earlier. Future larger studies are needed, however, to distinguish marital status as a separate risk factor independently from parental age or whether simply having another person in the home enables acknowledgement of early warning signs.

Previous studies have hypothesized that the association between maternal age and timeliness of ASD diagnosis is mediated by maternal education[18]; however, maternal education was not found to affect the age of diagnosis in this study. In addition, older maternal age is an established risk factor for ASD. In a recent study, the odds of children of mothers >35 years old having autism were 1.68 times greater than the odds of children of mothers <35 years.[23] Variability in age of diagnosis based on maternal age may reflect public awareness of ASD risk factors given the lay literature on maternal and paternal age as risk factors for ASD.

Similarly, differences in diagnosis between infant genders may also be a construct of public education about ASD. Prevalence of ASD in boys is approximately five times higher than in girls; thus, males are more likely to have referrals for ASD when developmental delays are observed.[1] Another possibility for this difference may be due to cultural expectations surrounding gender norms and greater social acceptance of shyness in girls. As a result, parental and provider concern may be delayed in females.[14] If awareness of risk factors for ASD does explain why gender and older maternal age are associated with the child's age at diagnosis, it would seem logical that the presence of other risk factors for ASD, specifically preterm birth, would also decrease age at diagnosis. However, gestational age was not associated with age at diagnosis.

Although cross-cultural comparisons are difficult, culture may play a large role in timing of diagnosis. Differences in individual behaviors that constitute abnormality are embedded in social contexts.[24] Therefore, what's perfectly normal in some cultures may signal pathology in others, generating differences in the timing of care seeking, diagnosis and treatment. Bernier, Mao and Yen[25] argue that macrocultural expectations, in addition to social and family norms, impact when ASD-related behaviors are suspected as pathological by parents. For example, work by Daley[26] suggests that appraising ASD-related social behaviors as positive or normal in young children contribute to delays in recognition of symptoms and treatment seeking in Indian families. In this investigation, quietness and aloofness suggested that a child is "good" and "trouble free" and it was regarded as normal for Indian boys to develop language later than girls,[26] whereas language delay is often the first red flag that prompts Western parents to seek assessment.[27] Other cultural social norms, such as avoidance of eye contact that is interpreted as respect in some Asian cultures[25] and shyness in females in many cultures[14] could impact whether or when families suspect behaviors to be abnormal. Also, stigma surrounding developmental disorders and beliefs in culpability of poor parenting are still widely felt in some Asian cultures and could discourage and delay parents in seeking assessment and treatment for their children.[28]

While these findings add to our understanding of factors contributing to early ASD diagnosis, this study has several limitations. Severity of ASD symptomology was not examined, which has been implicated as a predictor of diagnosis in previous studies and may mediate the relationship between age of diagnosis and other factors in our study.[2,14,15] Diagnosis of the children in the cohort was determined using the DSM-IV. In addition, screening for ASD at the center where this data were collected requires a referral due to an observed developmental delay. Males and early preterm infants have a referral bias within the center since these factors are known risks. Accordingly, this bias could produce an overestimate of relative percentages of preterm infants and males in our sample compared to the general population. Furthermore, the generalizability of these results may be limited as factors related to ASD diagnosis may depend upon availability and access to an autism center. The center where this data were collected provides community outreach and education campaigns so health care providers and families in a large, southern, metropolitan city and may be more educated about risk factors and symptoms of ASD as well as the importance of early identification of ASD compared to other areas that do not have a nationally recognized autism center.

The implication here is that when comparing data from different studies, local sociodemographic characteristics must be taken into account. There are elements in this metro area that will lead to specific results we may not obtain in other locations in the US or elsewhere. In fact, racial/ethnic and socioeconomic disparities in the US, with minorities and lower socioeconomic groups showing a lower prevalence of ASD, are not replicated in other countries with socialized medicine and nearly universal access to healthcare like Sweden.[29]

Despite these limitations, there are important implications of this study. Currently, there are conflicting findings regarding the role of race, maternal age, and gender on the age of ASD diagnosis. Additionally, other perinatal and neonatal markers should be considered when studying timing of ASD diagnosis. This is the first study to examine the association between length of hospital stay, a marker of neonatal illness, and early ASD diagnosis, and only one other study has investigated whether gestational age or marital status affect age of ASD diagnosis.

Our results add to the body of literature that has identified child and maternal factors associated with an early ASD diagnosis. Gestational age and length of hospital stay were not found to be predictors of the age of ASD diagnosis. Of particular interest is the finding that gestational age did not predict age of ASD diagnosis. While there is a paucity of evidence regarding the relationship between age of ASD diagnosis and neonatal birth characteristics, there is increasing evidence that gestational age is inversely related to the risk for ASD.[30] Given that 11% of all babies in the United States are born preterm, it is imperative that we improve our understanding of any relationship that may exist between gestational age and the age of ASD diagnosis.[31]

This study underscores the importance of including the contributions of sociodemographic status in our understanding of the complexity of autism. Even though it is a neurodevelopmental disorder, with a strong genetic component, there is a wide range of social and cultural variables that have an impact on comorbid symptoms and associated features. For example, although no significant differences have been reported in the social symptoms of ASD when comparing individuals from different countries, differences in verbal and nonverbal communication, some repetitive behaviors, and comorbid symptoms (e.g. avoidance, feeding, tantrums) do exist.[32,33]

This research could inform best practices for timely diagnosis of ASD and may contribute to the development of strategies to increase the ability of healthcare providers and parents to recognize warning signs of ASD during infancy. Further research is warranted to understand factors related to delay in diagnosis. Future studies should investigate the relationship between timely diagnosis and maternal age, maternal race, marital status, or infant gender and consider the effect of ASD education in the community. In addition, studies focusing on how to ensure timely diagnosis of ASD for preterm infants is imperative to minimize poor neurological outcomes of this vulnerable population.[34–39]

The benefits of early ASD detection are widely recognized, yet the vast majority of children are not diagnosed until after the age of 4. The gap in when children can be diagnosed and

when they are actually diagnosed highlights the importance of identifying factors related to this disparity. Identifying these factors may inform efforts to facilitate early ASD detection.

Acknowledgments

Thank you to Dr. Ken Hepburn for your help with editing this manuscript.

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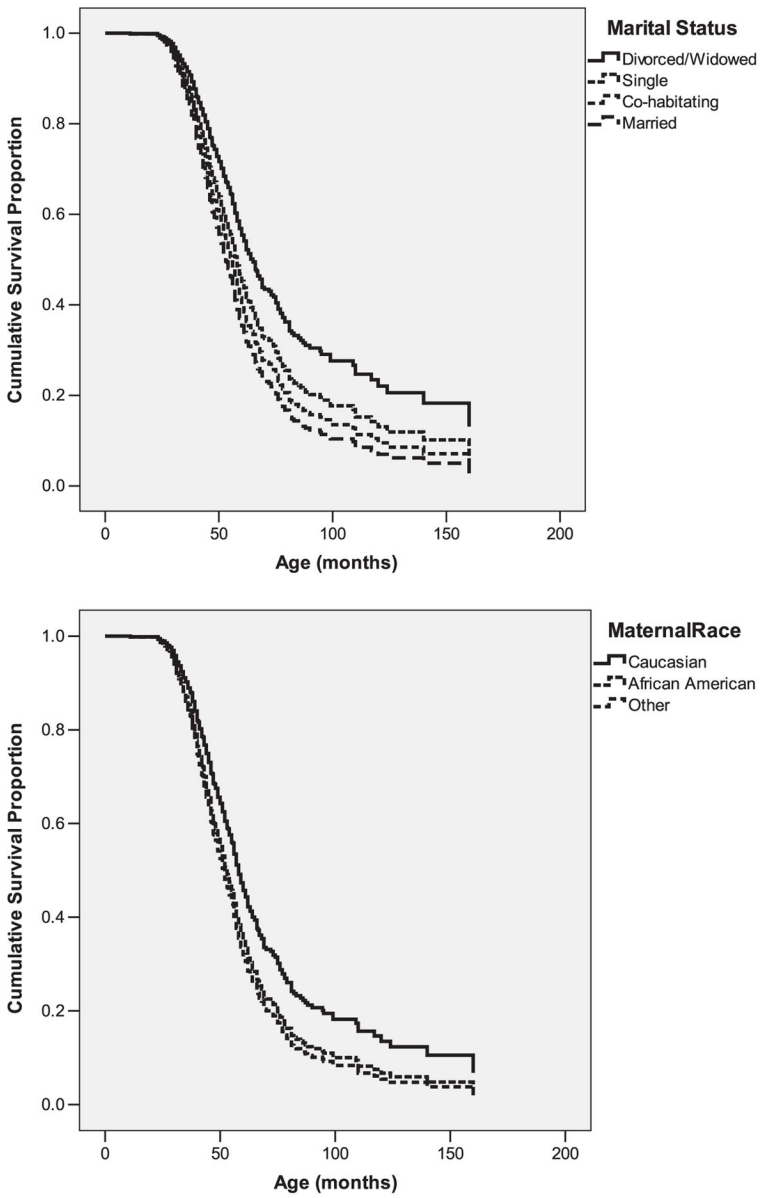

Fig. 1.

Cumulative proportion plot for survival age until ASD diagnosis for maternal marital status and race.

Table 1

Descriptive statistics: overall and by ASD diagnosis.

Variable N Mean (SD) Median (range)	Overall	No ASD	ASD	Difference tests t(df) or MWZ *p*-value
Chronological age (months)	664	258	406	t(412.3) = 1.952
(at admission/diagnosis)	51.3 (21.8)	53.6 (26.3)	49.9 (18.2)	$p = .052$
	47 (9, 188)	49 (9, 188)	46 (11, 160)	
Birth weight (grams)	658	255	403	t(656) = −1.069
	3171.6 (765.8)	3131 (762.4)	3197 (767.9)	$p = .285$
	3289 (400, 5160)	3232 (624, 5160)	3317 (400, 4904)	
Maternal age at delivery	661	256	405	t(659) = −2.416
	28.19 (6.23)	27.5 (6.4)	28.7 (6.1)	$p = .016$
	28 (14, 45)	27 (14, 45)	28 (15, 43)	
Paternal age at delivery	642	250	392	t(640) = −2.460
	31.21 (7.36)	30.3 (7.2)	31.8 (7.4)	$p = .014$
	31 (15, 61)	30 [15, 61]	31 [17, 56]	
Length of hospital stay (days)	661	258	403	MW Z = −1.615
	8.98 (28.07)	9.5 (29.9)	8.6 (26.9)	$p = .106$
	3 (1, 308)	3 (1, 308)	2 (1, 270)	
Gestational age (weeks)	664	258	406	t(662) = −2.072
	38.1 (3.25)	37.7 (3.3)	38.3 (3.2)	$p = .039$
	39 (22, 43)	38 (2, 43)	39 (23, 43)	
Maternal education (years)	654	254	400	t(652) = −1.031
	13.6 (2.3)	13.5 (2.3)	13.7 (2.3)	$p = .303$
	13 (5, 23)	13 (5, 22)	13 (8, 23)	
	n/total (%)	n/total (%)	n/total (%)	Chi-square test
Gender (% male)	524/664 (78.9%)	186/258 (72.1%)	338/406 (83.3%)	$\chi^{21} = 11.804$
				$p = .001$
ASD (% yes)	406/664 (61.1%)	0/258 (0%)	406/406 (100%)	N/A
Maternal race				
Caucasian	303/657 (46.1%)	130/255 (50.1%)	173/402 (43.0%)	$\chi^{22} = 4.396$
African American	224/657 (34.1%)	82/255 (32.2%)	142/402 (35.3%)	$p = .111$
Other	130/657 (19.8%)	43/255 (16.9%)	87/402 (21.6%)	
Maternal marital status				
Divorced or widowed	50/656 (7.6%)	24/255 (9.4%)	26/401 (6.5%)	$\chi^{23} = 18.925$
Single	153/656 (23.3%)	79/255 (31.0%)	74/401 (18.5%)	$p < .001$
Co-habitating	30/656 (4.6%)	13/255 (5.1%)	17/401 (4.2%)	
Married	423/656 (64.5%)	139/255 (54.5%)	284/401 (70.8%)	

Variable				
N				Difference tests
Mean (SD)				t(df) or MWZ
Median (range)	Overall	No ASD	ASD	*p*-value
Length of hospital stay (% 3 days or longer)	338/661 (51.1%)	140/258 (54.3%)	198/403 (49.1%)	$\chi^{21} = 1.658$ $p = .198$
Gestational category				
Early preterm ≤33 6/7 weeks	47/664 (7.1%)	20/258 (7.8%)	27/406 (6.7%)	$\chi^{23} = 10.594$ $p = .014$
Late preterm 34 0/7–36 6/7 weeks	92/664 (13.9%)	49/258 (19.0%)	43/406 (10.6%)	
Term 37 0/7–41 6/7 weeks	498/664 (75.0%)	181/258 (70.2%)	317/406 (78.1%)	
Post term ≥42 0/7 weeks	27/664 (4.1%)	8/258 (3.1%)	19/406 (4.7%)	

df: degrees of freedom, MWZ: Mann Whitney non-parametric test for independent groups Z test statistic, t(df): independent t-test, χ^{21}:Chi-square test.

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Table 2

Final logistic regression model – predictors of ASD diagnosis.

Variables in the equation[a]		B	SE_B	Wald	df	*p*-value	Exp(B)	95% C.I. for Exp(B)		Step	Model		Nagelkerke R2
								LB	UB	χ^2 (df), p	χ^2 (df), p	−2LL	% correctly classified
Step 1[b]	Marital status			17.750	3	.000				$\chi^{23} = 17.858$	$\chi^{23} = 17.858$	822.162	.038
	Single–D/W	−.184	.335	.302	1	.583	.832	.431	1.604	$p < .001$	$p < .001$		62.1%
	Co-habitating–D/W	.265	.475	.311	1	.577	1.303	.514	3.307				
	Married–D/W	.613	.307	3.985	1	.046	1.847	1.011	3.372				
	Constant	.257	.129	3.979	1	.046	1.293						
Step 2[c]	Gender (Male–Female)	.602	.201	8.999	1	.003	1.825	1.232	2.705	$\chi^{21} = 8.975$	$\chi^{24} = 26.832$	813.187	.057
	Marital Status			17.217	3	.001				$p = .003$	$p < .001$		63.7%
	Single–D/W	-.186	.338	.305	1	.581	.830	.428	1.609				
	Co-habitating–D/W	.255	.479	.285	1	.594	1.291	.505	3.299				
	Married–D/W	.606	.310	3.824	1	.051	1.832	.999	3.362				
	Constant	.089	.141	.393	1	.531	1.093						
Step 3[d]	Gender (Male–Female)	.620	.203	9.341	1	.002	1.860	1.249	2.768	$\chi^{22} = 9.264$	$\chi^{23} = 36.096$	803.923	.076
	Marital status			21.934	3	.000				$p = .010$	$p < .001$		65.3%
	Single–D/W	−.382	.349	1.197	1	.274	.683	.344	1.353				
	Co-habitating–D/W	.035	.487	.005	1	.943	1.035	.398	2.691				
	Married–D/W	.597	.313	3.627	1	.057	1.816	.983	3.356				
	Maternal race			9.096	2	.011							
	AA–Caucasian	.549	.206	7.111	1	.008	1.732	1.157	2.593				
	Other–Caucasian	.530	.232	5.228	1	.022	1.698	1.079	2.674				
	Constant	.113	.144	.609	1	.435	1.119						

AA: African American, B: logistic regression coefficient, CI: confidence interval, df: degrees of freedom, D/W: divorced or widowed, Exp(B): odds ratio, LB: lower bound confidence interval, SE_B: standard error of B, UB: upper bound confidence interval, χ^2(df): chi-statistic, degrees of freedom, − 2LL: −2* log likelihood.

[a]Variables included for consideration: child's chronological age, maternal age at delivery, paternal age at delivery, gestational age (weeks), child's gender, maternal marital status, maternal race, length of hospital stay (days).

[b]Variable(s) entered on step 1: marital status.

[c]Variable(s) entered on step 2: gender (female = 0, male = 1).

[d] Variable(s) entered on step 3: maternal race.

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Table 3

Covariate screening for Cox proportional hazards regression for age at ASD diagnosis.

Variable	B	SE_B	Wald	df	*p*-value	Hazard ratio	95% CI	
						Exp(B)	LB	UB
Birth weight (grams)	.000	.000	1.210	1	.271	1.000	1.000	1.000
Maternal age at delivery	.015	.008	3.478	1	.062	1.015	.999	1.031
Paternal age at delivery	.014	.007	4.334	1	.037	1.014	1.001	1.028
Length of hospital stay (= >3 days)	−.041	.100	.165	1	.684	.960	.789	1.168
Gestational age (weeks)	.013	.016	.709	1	.400	1.013	.982	1.045
Maternal education (years)	.002	.021	.010	1	.920	1.002	.961	1.045
Gender (Male)	.247	.133	3.450	1	.063	1.280	.986	1.662
Maternal race (overall)			8.401	2	.015			
Caucasian (reference)								
African American	.220	.114	3.738	1	.053	1.246	.997	1.557
Other	.366	.133	7.551	1	.006	1.441	1.111	1.871
Maternal marital status (overall)			8.728	3	.033			
Divorced or widowed (reference)								
Single	.412	.230	3.215	1	.073	1.510	.962	2.369
Co-habitating	.582	.314	3.434	1	.064	1.789	.967	3.311
Married	.576	.206	7.814	1	.005	1.779	1.188	2.665

B: Cox regression coefficient, CI: confidence interval, df: degrees of freedom, Exp(B): hazard ratio, LB: lower bound confidence interval, SE_B: standard error of B, UB: upper bound confidence interval.

Table 4

Final survival analysis model: Cox proportional hazards regression for age at ASD diagnosis.

	Change from previous step								95% CI	
	χ^2 (df) *p*-value	Variable(s) in model[a]	B	SE_B	Wald	df	*p*-value	Exp(B)	LB	UB
Step 1[b]	8.784 (2) *p* = .012	Maternal race (overall)			8.839	2	.012			
		AA–Caucasian	.234	.117	3.998	1	.046	1.264	1.005	1.589
		Other–Caucasian	.378	.134	7.906	1	.005	1.459	1.121	1.899
Step 2[c]	10.548 (3) *p* = .014	Maternal race (overall)			9.701	2	.008			
		AA–Caucasian	.300	.123	5.951	1	.015	1.350	1.061	1.717
		Other–Caucasian	.376	.137	7.571	1	.006	1.456	1.114	1.903
		Marital status (overall)			9.583	3	.022			
		Single–D/W	.297	.239	1.537	1	.215	1.346	.842	2.151
		Co-habitating–D/W	.442	.321	1.897	1	.168	1.555	.830	2.917
		Married–D/W	.565	.211	7.177	1	.007	1.759	1.164	2.659

AA: African American, B: Cox regression coefficient, CI: confidence interval, df: degrees of freedom, D/W: divorced or widowed, Exp(B): odds ratio, LB: lower bound confidence interval, SE_B: standard error of B, UB: upper bound confidence interval.

[a]Variables included for consideration: maternal age, paternal age, child's gender, maternal race, and maternal marital status.

[b]Variable(s) entered on step 1: maternal race.

[c]Variable(s) entered on step 2: maternal marital status.