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Positive Screening for Autism in Ex-preterm Infants: Prevalence and Risk Factors

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Abstract

OBJECTIVE—The survival of very low birth weight infants has increased markedly in recent years. Unfortunately, the prevalence of significant and lifelong motor, cognitive, and behavioral dysfunction has remained a major problem confronting these children. The objective of this study was to perform screening tests for early autistic features in children with a history of very low birth weight and to identify risk factors associated with a positive screening result.

METHODS—We studied 91 ex-preterm infants ≤ 1500 g at birth. Infants underwent conventional MRI studies at preterm and/or term-adjusted age. We collected pertinent demographic, prenatal, intrapartum, acute postnatal, and short-term outcome data for all infants. Follow-up assessments were performed at a mean age of 21.9 ± 4.7 months, using the Modified Checklist for Autism in Toddlers, the Vineland Adaptive Behavior Scale, and the Child Behavior Checklist.

RESULTS—Twenty-six percent of ex-preterm infants had a positive result on the autism screening tool. Abnormal scores correlated highly with internalizing behavioral problems on the Child Behavior Checklist and socialization and communication deficits on the Vineland Scales. Lower birth weight, gestational age, male gender, chorioamnionitis, acute intrapartum hemorrhage, illness severity on admission, and abnormal MRI studies were significantly associated with an abnormal autism screening score.

CONCLUSIONS—Early autistic behaviors seem to be an underrecognized feature of very low birth weight infants. The results from this study suggest that early screening for signs of autism may be

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warranted in this high-risk population followed by definitive autism testing in those with positive screening results.

Keywords

autism; prematurity; MRI; risk factors; outcome

Advances in neonatal intensive care have dramatically increased survival in preterm infants, most strikingly among the sickest and most preterm.[1] Unfortunately, this decrease in mortality has not been matched by a comparable decrease in long-term neurodevelopmental morbidity.[1,2] These trends underlie the increasing population of very low birth weight (VLBW) children with significant and costly disabilities.[3,4] Recently, a growing body of data has pointed to an astonishing prevalence of higher order neurodevelopmental impairment by the time these children reach school age. In some studies, up to 50% of ex-preterm infants experience difficulties in executive functioning, as well as in the areas of attention and behavior, often requiring special academic support.[5–13]

Despite recent progress, our understanding of the behavioral and psychosocial health of ex-preterm infants remains limited. Low birth weight and gestational age have been identified in several studies as important perinatal risk factors for disturbances in social interaction, communication, and behavior[14,15] as well as later psychoaffective disorders in adulthood.[16–18] During childhood and adolescence, VLBW children are reported to exhibit greater internalizing and externalizing behavior problems than their peers, as well as attentional difficulties and hyperactivity.[19–23] Difficulties with social integration including excessive shyness, withdrawn behavior, and poor social skills are also described.[24–26] Despite these reports of atypical psychosocial development in VLBW children, the prevalence of autism spectrum disorders has not been systematically explored in this population. Our anecdotal experience in the clinical follow-up of ex-preterm infants has suggested that a subgroup of these infants exhibit distinctly atypical behavioral features, many of which are similar to those typically seen in children with autism spectrum disorders.

Autism spectrum disorders are increasingly recognized as a public health problem of major importance.[27,28] According to a recent report from the Centers for Disease Control and Prevention, the prevalence of autism spectrum disorders is now 1 in 150.[27] The contribution from increasing survivors of extreme prematurity to this growing population of children with autism spectrum disorders is not well studied. Recently, major advances have been made in the field of early detection of signs of autism in infants, and validated screening tools now exist to facilitate the early and accurate screening of infants so as to prompt appropriate referrals for specialized autism diagnostic testing.[29,30] To begin addressing these questions, we decided to screen for early autistic features in a cohort of children with a history of VLBW. In addition, we sought to identify clinical predictors of positive autism screening results.

METHODS

The cohort of infants undergoing autism screening tests in this study were part of a previously reported prospective study of cerebrovascular function in a consecutive series of preterm infants <1500 g.[31,32] We excluded infants with known or suspected cerebral dysgenesis, obvious dysmorphic syndromes, or a known chromosomal disorder. We obtained written informed consent for these tests in all cases. The institutional review boards of the Brigham and Women's Hospital and Children's Hospital of Boston approved the study. We enrolled 103 children who met our inclusion criteria; 8 of these died in the early postnatal period, and 4 families could not be reached as part of our follow-up testing. The remaining 91 (96%) infants were successfully scheduled for follow-up.

Follow-up Studies

We performed standardized developmental outcome testing in 91 ex-preterm infants between the ages of 18 and 24 months adjusted for prematurity. Testers were blinded to past medical history and to the MRI findings.

The Modified Checklist for Autism in Toddlers (M-CHAT) is a 23-item (yes/no) parent-report checklist developed to screen children aged 16 to 30 months for early signs of autistic features.[33] The M-CHAT assesses sensory responsiveness (eg, overreaction to sound or touch), early language and communication (eg, responds when his or her name is called), social relatedness (eg, whether the child imitates the parents), and early joint attention (eg, whether the child follows a point to an object across the room). Psychometric data from the M-CHAT demonstrate high sensitivity and specificity.[33,34] A child fails the checklist when ≥ 2 critical items or any 3 items are failed. The critical items were identified by discriminant factor analysis of children with and without a disorder on the autism spectrum[33] and include items concerning joint attention (eg, pro-declarative pointing, bringing to show, following a point), interest in other children, responding to name, and imitation.

The Child Behavior Checklist (CBCL) for ages 1.5 to 5 years is a well-validated caregiver questionnaire[35,36] that includes 100 items on the frequency of behavioral and emotional problems in young children. Externalizing and internalizing problem behavior scores are derived. Internalizing behaviors include withdrawn, somatic complaints, anxious and depressed, and emotionally reactive syndromes scales. Externalizing behaviors include attention problems and aggressive behavior syndrome scales.[36] The abnormal range is defined at T scores ≥ 64, the borderline range as T scores from 60 to 63, and the normal range as T scores <60. For purposes of analysis, we dichotomized our outcomes into normal (T scores <60) and abnormal (T scores ≥ 60).

The Vineland Adaptive Behavior Scale (VABS) is a discriminative norm-referenced measure of functional status in a wide range of adaptive skills, including communication (receptive, expressive, and written), daily living (personal, domestic, and community), socialization (interpersonal relationships, play and leisure time, and coping skills), and motor (gross and fine) skills in children 0 to 18 years of age. Standard scores were generated using a mean of 100 and an SD of 15. A score <2 SDs of the normative mean was defined as abnormal.[37] Finally, we determined whether the children had received a diagnosis of a significant visual or hearing impairment.

Clinical Data Collection

To characterize our cohort, we performed medical chart reviews and collected demographic, prenatal, intrapartum, acute postnatal, and short-term outcome data on all infants. Demographic data included gestational age at birth, birth weight, and gender. Maternal data included maternal age, single versus multiple gestation, pregnancy-induced hypertension, prenatal infection (ie, intrapartum maternal temperature >100.4°F), intra- or antepartum hemorrhage, previous preterm labor during this pregnancy, and use of antenatal steroids. Intrapartum factors included fetal heart rate abnormalities (sustained fetal bradycardia with <100 beats per minute, decreased variability, and late decelerations), vaginal versus cesarean birth, Apgar score at 5 minutes, and need for respiratory and cardiovascular resuscitation (with or without medications). We also completed the Score of Neonatal Acute Physiology II (SNAP-II)[38] on admission and collected data from placental pathology reports for the presence of chorioamnionitis, placental abruption, or infarction.

Early postnatal data were collected in the first 5 days of life and included blood gases (pH, P_{CO_2}, P_{O_2}); need for cardiopulmonary support (volume expanders and/or pressor-inotropic

agents); and presence of a patent ductus arteriosus, pulmonary hemorrhage, and infection (confirmed by positive bacterial cultures or sufficient clinical suspicion to result in a full course of antibiotic treatment). Short-term outcome data included duration of mechanical ventilation and supplemental oxygen requirement, presence of necrotizing enterocolitis, and radiologic evidence of bronchopulmonary dysplasia.

MRI Studies

Infants underwent conventional, spin-echo T1-weighted and fast spin-echo T2-weighted MRI studies in the neonatal period once medically stable before discharge from the NICU. The MRI findings were categorized by a single experienced neuroradiologist who was blinded to the infants' perinatal history and outcome. Supratentorial parenchymal lesions included cystic or diffuse noncystic periventricular leukomalacia (PVL; the latter defined as diffuse, excessive, high signal intensity in the periventricular white matter on T2-weighted scans), periventricular hemorrhagic infarction (PVHI; defined as unilateral or asymmetric lesions of increased T2 signal in the periventricular white matter associated with ipsilateral germinal matrix-intraventricular hemorrhage), and ventriculomegaly. Parenchymal lesions of the cerebellum or brainstem were categorized as infratentorial. Combined lesions were diagnosed when both supratentorial and infratentorial parenchymal injury were present.

Predictor Variables

The following maternal, intrapartum, and postnatal factors[39–42] were identified a priori and analyzed as possible predictor variables for a positive autism screen: maternal age, maternal temperature, acute intrapartum or antepartum hemorrhage, preterm labor, placental infection, gestational age, birth weight, gender, SNAP-II score, length of oxygen requirement, and abnormal MRI study.

Statistical Analysis

Descriptive statistics were calculated on all measures to determine the characteristics of the sample, check normality assumptions, and ensure adequate variability. Univariate logistic regression analyses were performed to show unadjusted effects of all a priori identified risk factors. Multiple logistic regression analysis procedures were then applied to identify the final predictive model. Thus, in the initial multivariable model, all a priori identified risk factors were included. All factors that were not statistically significant at the .05 level were removed, whereas importance of the variables that remained in the model was assessed and confirmed by likelihood ratio test. In addition, Akaike information criterion and max-rescaled R^2 were used to compare goodness of fit of different models.

RESULTS

Clinical Characteristics

The gestational age at birth in the 91 study subjects ranged from 23 to 30 weeks, and birth weight ranged from 460 to 1490 g. Table 1 summarizes the pregnancy, labor, delivery, and placental findings characteristic of this cohort. Previous preterm labor (in 69%) and the use of antenatal steroids (in 87%) were common in our infants. Sixty-five percent were delivered by cesarean section, and 88% required ventilatory resuscitation at birth. Placental pathology studies showed evidence of chorioamnionitis in 31% of the infants. The severity of illness in this population is reflected in the mean SNAP-II score at admission of 23.7 ± 11.9. Table 2 summarizes the postnatal acute and subacute characteristics of our cohort.

Social, Behavioral, and Functional Outcomes

Follow-up autism screening tests were performed at a mean age corrected for prematurity of 21.9 ± 4.7 months. Of the 91 children in the study, 23 (25%) had positive results on the M-CHAT screening test (ie, 2 critical items or any 3). Of those who had positive M-CHAT scores, 16 (70%) reached positivity on the basis of critical items (ie, items concerning joint attention, interest in other children, responding to name, and imitation). Although the M-CHAT is not designed to test motor abilities, it is interesting that only 1 child (18 months of age at testing) who was not climbing on objects or stairs (question 3 on the M-CHAT) or walking (question 16) scored positive on the M-CHAT.

Functional performance on the VABS identified 26 (29%) infants with functional delays in motor abilities and 17 (19%) with delayed daily living skills. In addition, 21 (23%) had communication deficits and 26 (29%) experienced socialization difficulties. Behavioral outcomes measured by the CBCL demonstrated that 26 (29%) children experienced internalizing behavioral problems and 12 (13%) experienced externalizing behavioral problems (Table 3). Two of the 3 children with significant visual impairments had abnormal scores on the M-CHAT and CBCL. None of the cohort had significant hearing impairments.

Three (13%) infants with functional motor disabilities and delayed daily living skills on the VABS also had an abnormal M-CHAT score. Six (26%) infants with communication difficulties and 7 (30%) with socialization problems on the VABS also reached positivity on the M-CHAT. Internalizing behavioral problems on the CBCL were also present in 6 infants with abnormal M-CHAT scores.

Abnormal M-CHAT scores correlated highly with internalizing behavioral problems on the CBCL ($P < .01$), particularly in the withdrawn and emotionally reactive subscales. Conversely, M-CHAT scores were not associated with externalizing behavioral difficulties. Difficulties in socialization ($P < .01$) and communication abilities ($P = .03$) on the VABS were significantly associated with a positive M-CHAT screen; however, delays in daily living skills and functional mobility showed no significant association with performance on the M-CHAT. When communication problems on the VABS and age at follow-up testing were controlled, M-CHAT abnormalities remained significant.

MRI Abnormalities

MRI studies were performed at a mean age of 39.2 ± 3.9 weeks in 85 (93%) of the 91 infants who underwent follow-up neurodevelopmental testing. Among the 85 infants who underwent MRI studies, 57 (67%) had normal results and 28 (33%) had abnormal results. MRI abnormalities included diffuse PVL (13), PVHI (5), cerebellar hemorrhagic injury (5), and ventriculomegaly (2). In addition, 3 had combined diffuse PVL and cerebellar hemorrhagic injury, and 1 infant had combined PVHI and cerebellar hemorrhagic injury.

Risk Factors for a Positive M-CHAT Screen

We examined a number of clinical (maternal, pregnancy, intrapartum, and postnatal), neuroimaging, and developmental risk factors associated with a positive M-CHAT screen. The distribution of clinical risk factors with normal/abnormal M-CHAT is summarized in Table 4. On univariate analysis, lower birth weight and gestational age, male gender, greater acuity of illness on admission (higher SNAP-II score), chorioamnionitis, and acute intrapartum hemorrhage were associated with a positive M-CHAT screen. Furthermore, long-term complications, including prolonged supplemental oxygen requirements, and abnormal MRI findings were significantly associated with abnormal M-CHAT scores (Table 5). It is interesting that when we examined the association between type of MRI abnormalities and M-CHAT scores, ex-preterm infants with cerebellar hemorrhagic injury and combined

supratentorial and infratentorial parenchymal lesions were significantly more likely to have a positive M-CHAT screen compared with those with isolated supratentorial injury (ie, PVL or PVHI; $P < .001$). Multivariate analyses demonstrated that gestational age, birth weight, chorioamnionitis, gender, and acuity of illness severity on admission (SNAP-II) were independent predictors of abnormal M-CHAT scores (Table 6).

DISCUSSION

In this study, we describe a high prevalence of autism spectrum features among survivors of extremely preterm birth as detected by a positive score on a widely used screening instrument, the M-CHAT. In addition, we describe a strong correlation between positive M-CHAT scores in this population and the detection of internalizing behavioral problems and socialization and communication deficits using other widely used instruments, the CBCL and the VABS, respectively. Together, these findings provide evidence for a high prevalence of positive initial screenings for autism spectrum behaviors in survivors of extreme prematurity. To our knowledge, this is the first description of this phenomenon in expreterm infants. In addition, we have identified several factors that seem to increase the risk for positive M-CHAT scores in these children, including lower birth weight and gestational age, male gender, prenatal infection, greater illness acuity based on SNAP-II scores, and abnormal MRI studies.

No previous reports of autism screening testing in ex-preterm infants are available for comparison with our findings. Recent population-based studies identified pre-maturity or low birth weight,[29,43,44] as well as a history of neonatal intensive care,[39,40,45,46] as important perinatal risk factors for subsequent autism spectrum disorders. Badawi et al[40] found a sixfold increased risk for autism spectrum disorders among children with a history of moderate to severe neonatal encephalopathy. Others described the association between autism and severe medical conditions such as epilepsy, cerebral palsy, fragile X syndrome, tuberous sclerosis, Down syndrome, congenital rubella, and significant hearing and visual impairments.[41] As an explanation for these associations, it has been speculated that pregnancy, delivery, and/or neonatal complications act through independent etiologic pathways to increase the risk for autism or interact with a genetic predisposition by interfering in the developmental process at critical times.[39,42]

In this population, we identified several independent risk factors that were associated with a greater likelihood for abnormal M-CHAT scores. These included lower birth weight and gestational age, male gender, chorioamnionitis, and significantly greater illness severity (by the SNAP-II scores). Our finding of a high rate of chorioamnionitis by placental pathology in infants with positive M-CHAT scores is consistent with previous reports of recurrent maternal infections during pregnancy in children with autism.[44] The presence of a higher acuity of illness suggests that exposure to factors that are associated with preterm birth and the hazards of prematurity itself are associated with a greater risk for a positive autism screening. Finally, our finding of a higher prevalence of positive autism screenings among boys corroborates previous studies that reported a significant association between autism spectrum disorders and male gender.[38,43,44]

The children in our study were tested at a mean age of 21 months' adjusted age. To date, no studies have addressed the presence of neuroimaging abnormalities in children with autism spectrum disorders at such a young age, because autism is not typically recognized before 2 years of age[47]; however, a broad spectrum of neuroanatomic abnormalities have been reported in children with autism.[47–52] Recent studies suggest a role for disturbed connectivity between specific brain regions in autism spectrum disorders.[53,54] Cerebellar lesions, particularly in the vermis, have been a common finding in autopsy and neuroimaging studies of children with autism.[47,55–58] In our study, the presence of neonatal MRI abnormalities was a significant

univariate predictor of positive scores on the M-CHAT test at follow-up. Although the number of infants with cerebellar hemorrhage (either isolated or combined with supratentorial parenchymal injury) was relatively small, this subgroup was significantly more likely to have positive M-CHAT scores than infants without cerebellar injury on MRI. These findings corroborate our results from a previous study[59] in which more than one third of ex-preterm infants with isolated cerebellar hemorrhagic injury had positive autism screening tests at follow-up; however, in the current study, this specific relationship could not be tested in a multivariate model given the small size of the subgroup with cerebellar injury. Consequently, cerebellar injury was incorporated into an overall abnormal MRI category, which failed to reach statistical significance in its relationship with positive M-CHAT scores. Larger studies will be needed to address the potential importance of this relationship. Furthermore, it is important to note that in this study, a subset of ex-preterm infants with normal conventional MRI studies had positive screening scores for autism spectrum disorders. It is possible that these children have brain injury below the resolution of current conventional MRI techniques, and more sophisticated quantitative MRI techniques may be needed to address this issue. Using such techniques, we previously showed a significant impairment of cerebellar growth in preterm infants as early as term corrected age, even in the absence of obvious cerebellar injury by conventional MRI studies.[60]

Children with global developmental delay or specific language impairments and those with autism spectrum disorders may share a number of common features, particularly at a young age.[61–63] Although we have not yet tested our population with diagnostic instruments for autism, when controlling for the potential confounding effect of language delays and age at testing, we found no significant effect of these factors on positive M-CHAT scores. Furthermore, there was no significant association between functional motor delays on the VABS and an abnormal M-CHAT. Although we acknowledge that the presence of developmental delay in our cohort may have contributed to the high prevalence of positive M-CHAT scores, our findings suggest that any such contribution was modest at best.

We acknowledge several important limitations to our study. First, it is important to recognize that the M-CHAT is specifically designed as a screening instrument to identify toddlers at risk and is by no means diagnostic for autism spectrum disorders. More comprehensive and standardized diagnostic tests for autism (eg, Autism Diagnostic Interview,[64] Autism Diagnostic Observation Schedule[65]) are available and are specifically designed to be applied to children who have positive results on screening tests such as the M-CHAT. Because the M-CHAT is designed to screen toddlers at approximately 18 months of age, it is possible that the sociobehavioral deficits identified in this study are transient or, conversely, may emerge or increase over time. Furthermore, although we correlated autism with behavioral and adaptive measures, we did not use standardized cognitive assessment. For these reasons, we are performing standardized diagnostic tests for autism and cognitive testing in this study population. Another limitation of our study is the lack of socioeconomic data on our cohort, which may have influenced both child development and maternal reporting. Finally, our study cohort represents a selected high-risk population of preterm infants[31] and therefore may not be generalizable to healthier preterm populations.

CONCLUSIONS

We have described a high prevalence of positive screening tests for autism in a cohort of ex-preterm infants. These findings require corroboration in larger prospective studies and validation by more sensitive diagnostic testing; however, these data suggest that the unusual social and behavioral profile observed by many clinicians in the clinical follow-up of high-risk preterm infants may represent the early signs of an autism spectrum disorder. Current screening for early intervention services in this high-risk population tends to focus largely on neuromotor

and cognitive modalities. Our data support comprehensive screening for social and behavioral dysfunction in ex-preterm infants throughout the period of risk for autism spectrum disorders,[66] with diagnostic testing and close follow-up of children with positive screening tests. Such an approach is further supported by recent studies demonstrating the benefit of earlier, more intensive interventions in high-risk populations.[67,68]

What's Known on This Subject

Previous reports identified prematurity or low birth weight, history of neonatal intensive care, and history of moderate to severe neonatal encephalopathy as important perinatal risk factors for subsequent autism spectrum disorders. Others described the association between autism and severe medical conditions such as epilepsy, cerebral palsy, fragile X syndrome, tuberous sclerosis, Down syndrome, congenital rubella, and significant hearing and visual deficits.

What This Study Adds

We describe for the first time a high prevalence of a positive initial screening for autism spectrum behaviors in survivors of extreme prematurity. We identify several factors that increase the risk for a positive screening, including lower birth weight and gestational age, male gender, prenatal infection, greater illness acuity, and abnormal MRI studies.

Abbreviations

VLBW, very low birth weight; M-CHAT, Modified-Checklist for Autism in Toddlers; CBCL, Child Behavior Checklist; VABS, Vineland Adaptive Behavior Scale; SNAP-II, Score of Neonatal Acute Physiology II; PVL, periventricular leukomalacia; PVHI, periventricular hemorrhagic infarction.

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TABLE 1

Clinical Characteristics of Pregnancy, Labor, Delivery, and Placental Findings in the Preterm Cohort (*n* = 91)

Clinical Characteristic	Value
Pregnancy, *n* (%)	
Maternal age >35 y	24 (26)
Pregnancy-induced hypertension	12 (13)
Acute intrapartum or antepartum hemorrhage	19 (21)
Previous preterm labor	63 (69)
Antenatal steroids	79 (87)
Maternal fever (>100.4°F)	17 (18)
Labor and delivery	
Gestational age, median (range), wk	26 (23–30)
Birth weight, median (range), g	890 (460–1490)
Male gender, *n* (%)	55 (60)
Singleton, *n* (%)	62 (68)
Abnormal fetal heart rate, *n*=88, *n* (%)	34 (37)
Cesarean delivery, *n* (%)	59 (65)
Apgar score at 5 min, median (range)	7 (0–9)
Respiratory resuscitation in delivery room, *n* (%)	84 (88)
Circulatory resuscitation in delivery room, *n* (%)	6 (6)
SNAP-II, mean ± SD	23.7±11.9
Placental findings, *n*=80, *n* (%)	
Chorioamnionitis	25 (31)
Abruption	18 (23)
Placental infarction	7 (9)

TABLE 2

Acute and Subacute Postnatal Clinical Characteristics (n = 91)

Parameter	Value
Acute factors (day of life 1–5)	
Minimum pH, mean (range)	7.2 (6.8–7.4)
Minimum PCO_2, mean (range), mmHg	31.9 (17.2–47.9)
Maximum PCO_2, mean (range), mmHg	61.6 (36.5–169.5)
Minimum PO_2, mean (range), mmHg	42.6 (23.3–63.5)
Cardiopulmonary support, *n* (%)	71 (78)
Patent ductus arteriosus, *n* (%)	17 (19)
Pulmonary hemorrhage, *n* (%)	9 (10)
Clinical sepsis, *n* (%)	24 (26)
Subacute factors	
Length of ventilation, mean ± SD, d	29.1 ±30.4
Length of supplemental O_2, mean ± SD, d	58.5 ± 34.4
Necrotizing enterocolitis, *n* (%)	12 (13)
Bronchopulmonary dysplasia, *n* (%)	36 (40)

TABLE 3

Scores on the M-CHAT, the VABS, and the CBCL (*n* = 91)

Scale	Score, Median (Range) or Mean ± SD	Abnormal, *n* (%)
M-CHAT	2 (0–9)	23 (25)
VABS		
Communication	83.5 ± 11.2	21 (23)
Daily living	89.1±5.6	17 (19)
Socialization	81.2 ± 10.2	26 (29)
Motor	80.9 ± 8.3	26 (29)
CBCL		
Internalizing	58.4 ± 4.1	26 (29)
Externalizing	48.3 ± 3.2	12 (13)

TABLE 4

Distribution of Clinical Risk Factors With Normal/Abnormal M-CHAT Score

Variable	Normal (*n* = 68)	Abnormal (*n* = 23)
MRI, *n* (%)		
Normal	50 (79)	7 (32)
Abnormal	13 (19)	15 (68)
Gender, *n* (%)		
Male	37 (54)	18 (78)
Female	31 (46)	5 (22)
Chorioamnionitis, *n* (%)		
Yes	13 (22)	16 (76)
No	46 (78)	5 (24)
Maternal temperature ≤100.4°F, *n* (%)		
Yes	10 (15)	7 (30)
No	58 (85)	16 (70)
Acute intrapartum or antepartum hemorrhage, *n* (%)		
Yes	10 (15)	9 (39)
No	58 (85)	14 (61)
Preterm labor, *n* (%)		
Yes	45 (66)	18 (78)
No	23 (34)	5 (22)
Gestational age, mean ± SD	27.1 ± 1.6	26.2 ± 2.0
Birth weight, mean ± SD	959.6 ± 235.9	789.1 ± 192.0
SNAP-II, mean ± SD	18.1 ± 7.5	31.0 ± 6.6
Maternal age, mean ± SD	30.7 ± 6.8	31.5 ± 6.4
Length of oxygen requirement, mean ± SD	53.2 ± 34.3	73.4 ± 30.3

TABLE 5

Univariate Predictors of Abnormal M-CHAT Screening Scores (*n* = 91)

Variable	OR	95% CI	*P*
MRI	0.133	0.047–0.382	.0002
Gender	3.016	1.004–9.059	.0491
Chorioamnionitis	9.669	3.302–28.310	<.0001
Maternal temperature ≤100.4°F	2.538	0.834–7.724	.1011
Acute intrapartum or antepartum hemorrhage	3.729	1.275–10.904	.0162
Preterm labor	1.840	0.606–5.588	.2820
Gestational age	0.731	0.541–0.987	.0406
Birth weight	0.996	0.994–0.999	.0044
SNAP-II	1.276	1.145–1.422	<.0001
Maternal age	1.017	0.947–1.093	.6356
Length of oxygen requirement	1.018	1.003–1.033	.0174

OR indicates odds ratio; CI, confidence interval.

TABLE 6

Independent Risk Factors of Abnormal M-CHAT Scores

Covariates	Adjusted OR	95% CI	*P*
Gender	6.040	1.097–33.250	.039
Chorioamnionitis	16.240	2.798–94.270	.002
Gestational age	2.053	1.083–3.891	.027
Birth weight	0.993	0.987–0.998	.011
SNAP-II	1.287	1.121–1.478	.000