

Postnatal genetic and neurodevelopmental assessment in severely small-for-gestational-age infants

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Objective

To assess the frequency of genetic syndromes and childhood neurodevelopmental impairment in non-malformed term infants with severely low birthweight and no evidence of placental insufficiency.

Methods

This case series was constructed of infants delivered at term between 2013 and 2018 with severely low birthweight defined as below -2.5 SD, with normal maternal and fetal Doppler studies (umbilical artery, fetal middle cerebral artery, cerebroplacental ratio, and uterine artery) and no hypertensive disorders during pregnancy or structural anomalies at prenatal ultrasound examination. Clinical exome sequencing and copy number variation (CNV) analysis were performed in DNA extracted from the children's saliva. Cognitive and psychomotor development was evaluated via The Bayley Scales of Infant and Toddler Development-Third Edition (BSID-III) or the Wechsler Intelligence Scale for Children-Fifth Edition (WISC-V) tests according to the child's age at testing.

Results

Among the 36,405 infants born within the study period, 274 had a birthweight below -2.5 SD (0.75%), of which 98 met the inclusion criteria. Median gestational age at delivery was 38.0 weeks (IQR, 37.3–38.5), and median birthweight was 2020 g (IQR, 1907.5–2247.5). Among the 63 families contacted, seven (11%) reported a postnatal diagnosis of a genetic syndrome and a further 18 consented to participate in the study. All 18 children showed a normal result upon clinical exome sequencing and CNV analysis, but six (33%) of them showed low scores at neurodevelopmental testing.

Conclusion

Non-malformed severely small term infants with no clinical or Doppler signs of placental insufficiency present an exceedingly high rate of genetic syndromes (11%) and neurodevelopmental impairment (33%) during childhood.