
بسم الله الرحمن الرحيم
١٤٣٨

Asphyxia

Prenatal And Antenatal Risk Factors

Preconception Sociodemographic and Maternal Medical Conditions That Are Independent Risk Factors for Newborn Encephalopathy

Risk Factor	Factors for Newborn Encephalopathy		
	Reference Group	Unadjusted Odds Ratio	Adjusted* Odds Ratio (95% confidence interval)
Maternal age (years)	<20	1†	1†
	20–24	2.37	4.21 (1.10–17.50)
	25–29	1.85	5.91 (1.42–24.54)
	30–34	1.31	6.71 (1.53–29.44)
	≥35	1.46	6.01 (1.28–28.15)
Blume US (2007[4], 2008[5])	<20	1.2 (1–1.5)	
	20–24	1†	
Cowan UK (2003[6])		Significantly younger maternal age distribution (chi-square test)¶	
Maternal employment	Professional	1†	1†
	Unskilled manual	2.35	3.84 (1.43–10.28)
	Housewife	3.57	2.48 (1.14–5.39)
	Unemployed	4.47	3.60 (1.10–11.80)
Blume US (2007[4], 2008[5])		Not reported	
Cowan UK (2003[6])		Not reported	
Health Insurance	Private	1†	1†
	Public	2.2	3.46 (1.25–9.59)
Blume US (2007[4], 2008[5])		Not reported	1.4 (1.2–1.7)#
Cowan UK (2003[6])		Not reported	
Family history of seizures**	No	1†	1†
	Yes	3.10	2.55 (1.31–4.94)
Blume US (2007[4], 2008[5])		Not reported	
Cowan UK (2003[6])		Significantly higher frequency (Fisher's exact test)¶	
Family history of neurologic disorder††	No	1†	1†
	Yes	2.6	2.73 (1.16–6.41)
Blume US (2007[4], 2008[5])		Not reported	
Cowan UK (2003[6])		Significantly higher frequency (Fisher's exact test)¶	
Infertility treatment	No	1†	1†
	Yes	2.23	4.43 (1.12–17.60)
Blume US (2007[4], 2008[5])		Not reported	
Cowan UK (2003[6])		No significant difference in frequency (Fisher's exact test)¶	

Antepartum and Prenatal Maternal Medical and Obstetric and Fetal Characteristics That Are Independent Risk Factors for Newborn Encephalopath

Risk Factor	Reference Group	Unadjusted Odds Ratio	Adjusted* Odds Ratio (95% confidence interval)
Maternal thyroid disease	No	1†	1†
	Yes	5.9	9.70 (1.97–47.91)
Blume US (2007[a], 2008[b])		Not reported	
Cowan UK (2003[b])		No significant difference in frequency (9% missing data; Fisher's exact test)¶	
Preeclampsia	No	1†	1†
	Severe	3.93	6.30 (2.25–17.62)
Blume US (2007[a], 2008[b])		2.1 (1.6–2.5)	
Cowan UK (2003[b])		No significant difference in frequency of maternal hypertension (Fisher's exact test)¶	
Vaginal bleeding (moderate or severe)	No	1†	1†
	Yes	2.32	3.57 (1.30–9.85)
Blume US (2007[a], 2008[b])		Not reported	
Cowan UK (2003[b])		Lower frequency, but not significant (Fisher's exact test)¶	
Viral illness	No	1†	1†
	Yes	2.10	2.97 (1.52–5.80)
Blume US (2007[a], 2008[b])		Not reported	
Cowan UK (2003[b])		No significant difference in frequency of infection (chi-square test)¶	
Gestational age (weeks)	39	1†	1†
	37	1.44	2.35 (1.11–4.97)
	38	1.10¶	1.18 (0.90–1.56)
	40	0.57	1.41 (1.17–1.70)
	41	1.77	3.34 (2.09–5.35)
	42	3.97	13.2 (5.03–34.83)
Blume US (2007[a], 2008[b])		Agrees with J curve	
Cowan UK (2003[b])		Agrees with J curve	
Centile birth weight**	>90th	1†	1†
	3rd–9th	1.63	4.37(1.43–13.38)
	<3rd	13.2	38.23 (9.44–154.79)
Blume US (2007[a], 2008[b])		Not reported	
Cowan UK (2003[b])		Nonsignificant trend for higher frequency of lower centile birth weights (chi-square test)¶	
Appearance of placenta	Normal or missing	1†	1†
	Abnormal	3.21	2.07 (1.15–3.73)
Blume US (2007[a], 2008[b])		Not reported	
Cowan UK (2003[b])		Not reported	
Late or no antenatal care	No	1†	1†
	Yes	15.14	5.45 (0.47–62.98)
Blume US (2007[a], 2008[b])		1.3–1.6 (1–2.3)	
Cowan UK (2003[b])		Not reported	

Intrapartum Conditions That Are Independent Risk Factors for Newborn Encephalopathy

Risk Factor	Reference Group	Unadjusted Odds Ratio	Adjusted* Odds Ratio (95% confidence interval)
Occipitoposterior position	No	1†	1†
	Yes	2.97	4.29 (1.74–10.54)
Blume US (2007[a], 2008[b])		Not reported	
Cowan UK (2003[b])		Not reported	
Maternal pyrexia	No	1†	1†
	Yes	5.34	3.82 (1.44–10.12)
Blume US (2007[a], 2008[b])		Not reported	3.1 (2.3–4.3)‡
Cowan UK (2003[b])		Not reported	
Acute intrapartum event[a]	No	1†	1†
	Yes	6.80	4.44 (1.30–15.22) 29% intrapartum event and possible intrapartum hypoxia
Blume US (2007[a], 2008[b])		4.2 (3.6–4.9) 30% of study infants had acute complications	
Cowan UK (2003[b])		87% of study infants had acute timing of brain injury	
Mode of delivery	Spontaneous	1†	1†
	Instrumental, vaginal	2.23	2.34 (1.16–4.70)
	Emergency cesarean	2.94	2.17 (1.01–4.64)
	Elective cesarean	0.23	0.17 (0.05–0.56)
Blume US (2007[a], 2008[b])		Not reported	
Cowan UK (2003[b])		Not reported	
General anesthesia	No	1†	1†
	Yes	4.40**	3.08 (1.16–8.17)
Blume US (2007[a], 2008[b])		Not reported	
Cowan UK (2003[b])		Not reported	

Maternal Bleeding in Pregnancy

- Third-trimester placental bleeding is often associated with a chronic and long-standing underlying condition that may have resulted in fetal injury antedating clinical bleeding.
- Third-trimester bleeding is rarely associated with neonatal HIE.

Maternal Trauma During Pregnancy

- Fetal trauma during pregnancy appears to be quite rare and typically is due to severe and direct abdominal trauma.
- Ascribing causation of fetal trauma in pregnancy with subsequent adverse ex utero neurologic sequelae is most accurate if fetal brain imaging in close proximity to the trauma demonstrates findings consistent with fetal TBI.
- Because fetal TBI appears to be so rare, fetal brain imaging following the traumatic event is not routinely recommended.

Coagulation Abnormalities andAutoimmune Disorders

- Some studies have found that placental vascular lesions, including those likely to be thrombotic, are associated with inherited thrombophilias of the mother or fetus or neonate, but causality has not been established.
- Factor V Leiden and prothrombin mutations may be associated with a modest increase in risk of perinatal stroke. The relationship between maternal and fetal thrombophilias and cerebral Palsy remains unclear.

- Large, properly designed studies are required to determine if thrombophilias are significant and independent causes of cerebral palsy.
- Case reports suggest a possible relationship between antiphospholipid antibodies and fetal or neonatal stroke, although the occurrence seems infrequent.
- Some autoantibodies associated with systemic lupus erythematosus cross-react with neuronal membrane receptors. The implication of this for the fetus–neonate is uncertain at present.

Maternal Infection

- Antenatal intrauterine infection is a risk factor for neonatal encephalopathy and neurologic disability.
- The prevalence of bacterial, viral, And protozoan infections during pregnancy that can cross the placenta and have a neurotropic effect on the developing fetus may be underestimated.

Maternal Thyroid Disorder

- Maternal thyroid disease, clinical or subclinical, is common in pregnancy and in developed countries is chiefly autoimmune.
- Maternal thyroid disease is a risk factor for neona- tal encephalopathy and for lower cognitive perfor- mance in the child.
- The role of maternal thyroid status in cerebral palsy remains uncertain.
- Current guidelines do not recommend routine antenatal screening for hypothyroidism in preg- nancy.

Maternal Epilepsy

- It is unclear whether poor neurodevelopmental outcomes in the offspring of women with epilepsy are due to the underlying pathology of the disease, teratogenic effects of AED treatment, or a combi- nation of both.
- The mechanism behind the association between maternal epilepsy, the occurrence of maternal sei- zures, and neonatal encephalopathy in the offspring is unclear and could be due to shared genetic causes of anatomic or metabolic abnormalities.
- There are no data to support an association between maternal epilepsy or the use of AEDs in the mother with the development of cerebral palsy in the offspring.

Environmental Factors and Alcohol and Drug Exposure

- Moderate to heavy maternal alcohol use may result in neurologic dysfunction, behavioral abnormali- ties, and cognitive dysfunction.
- There is no known relationship between alcohol consumption and cerebral palsy.
- No definite relationship exists between cerebral palsy and cocaine unless associated with a coexis- tent obstetric problem (eg, abruptio placentae).
- Maternal cocaine use may affect fetal neurologic development.

Infertility Treatment

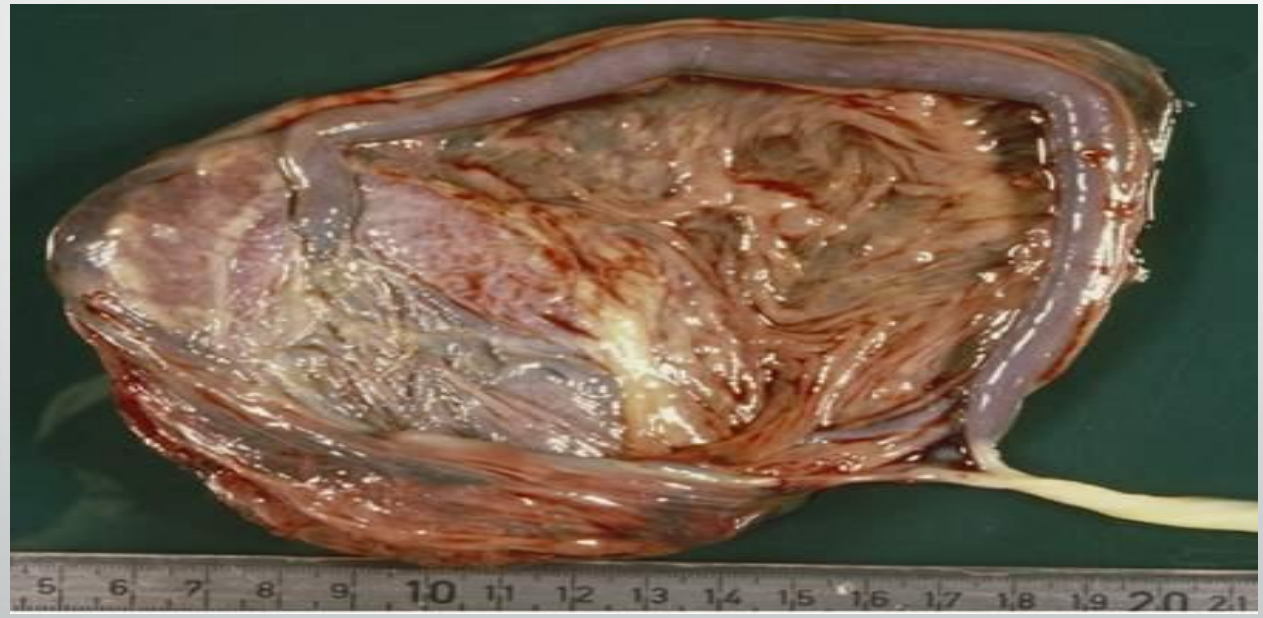
- Several large, population-based studies have docu- mented an association between infertility treat- ments and cerebral palsy. In most, the association was explained by preterm delivery, multiple birth, or both.

- In all of the studies examined, it was not possible to disentangle completely the infertility treatment from the underlying infertility disorder.

Maternal Age

It is controversial whether advancing maternal age and obesity are associated with increased risk of neonatal encephalopathy or cerebral palsy in term singleton pregnancies.

The Role of Placental Pathology in Neonatal Encephalopathy and Cerebral Palsy



Placental Histology and Neonatal Neurologic Outcome

- Placental Weight
- Decidual Vasculopathy
- Placental Infarction
- Intervillous Thrombi, Retroplacental Hematomas, and Abruptio Placentae
- Massive Perivillous Fibrin Deposition

- The few appropriate studies available do not establish that placental weight per se is related to neurologic outcome.

- Decidual vasculopathy is associated with the clinical syndromes of preeclampsia, maternal hypertension, maternal autoimmune disease or thrombophilias, and fetal growth restriction, the latter of which has been associated with neonatal encephalopathy and cerebral palsy.

- Although placental infarcts are identified in a substantial percentage of clinically uncomplicated pregnancies, the presence of infarcts in the placentas of cases of cerebral palsy appears to be increased.

- Retroplacental hematomas leading to significant abruptio placentae are associated with intrauter- ine fetal demise and neonatal encephalopathy.

- Clinically significant massive perivillous fibrin deposition is rare, occurring in approximately 1 in 10,000–20,000 pregnancies, but has a strong association with fetal death and fetal growth restriction.

- Cases with maternal floor infarction had lower developmental scores in all areas tested and more often had neurologic or developmental impairment.

Fetal Vascular Thrombosis

Among live births, fetal vascular thrombosis is associated with cerebral and visceral infarcts, liver dysfunction, neonatal seizures, neonatal hemorrhagic stroke, cerebral edema, "birth asphyxia," cerebral palsy and elevated circulating nucleated red blood cells, hypoglycemia, thrombocytopenia in the early postnatal period, or a combination of these.

The entire matrix of lesions, antecedent risk factors, and outcomes in placental–fetal vascular thrombosis has not been established in large, well-structured clinicopathologic series.

Inflammation and Infection

- Population-based studies demonstrate that the clinical diagnosis of chorioamnionitis is associated with elevated cerebral palsy risk.
- An enlarging literature links some placental lesions with neonatal encephalopathy, perinatal stroke, cerebral palsy, and with risk factors for those conditions. However, the magnitude of these associations has not been established.
- Few studies have investigated the association of villitis of unknown etiology with neonatal encephalopathy or cerebral palsy, and are predominantly derived from medicolegal cases.

Umbilical Cord Abnormalities

- Single Umbilical Artery
- Velamentous Cord Insertion
- Vasa Previa
- Umbilical Cord Knots
- Nuchal Umbilical Cord
- Umbilical Cord Length
- Abnormal Umbilical Cord Coiling
- Umbilical Cord Stricture
- Umbilical Cord Cysts
- Umbilical Cord Vein Varix

- Abnormally short or long umbilical cords are associated with abnormal amniotic fluid volume, abnormal fetal neuromuscular activity, and acute intrapartum events, such as abruptio placentae.
- Abnormal umbilical cord length is not associated with umbilical acidosis at birth.
- Short umbilical cord length may be associated with increased incidence of abnormal neurologic outcomes beyond 4 years of age if other factors, such as low Apgar score and low birth weight, also are present.
- Single umbilical artery has not been directly linked to postnatal neurologic abnormalities or cerebral palsy.

- Despite the significant evidence relating umbilical vein varix to increased rates of fetal and neonatal death, no studies to date have linked umbilical vein varix to neonatal encephalopathy or cerebral palsy.

- Umbilical cord stricture is a major contributor to intrauterine fetal death, but there is no established link with cerebral palsy.

- Hypocoiling of the umbilical cord may correlate with increased risk of preterm birth, but there is no present evidence of an association of abnormal umbilical cord coiling and perinatal neurologic injury.

- Fetal thrombotic vasculopathy associated with obstructive lesions of the umbilical cord, including cord hypercoiling and hypocoiling, velamentous cord insertion, true knot, nuchal cord, and umbilical cords with decreased Wharton's jelly is highly associated with neonatal encephalopathy and cerebral palsy.
- Nuchal cord is common, and the vast majority of term deliveries with nuchal cord have normal out- comes.
- A large population-based study found no association of true cord knot with cerebral palsy.
- If twin gestations and vasa previa are excluded, there are no convincing data linking velamentous cord insertion to neonatal encephalopathy or cerebral palsy.


Thank
you!