CHAPTER

8

Post-resuscitation Management of Asphyxiated Neonates

Perinatal asphyxia (PA) is a major cause of neonatal and under-5 mortality, particularly in developing countries. As per the latest estimates, PA accounts for 9.4% (i.e. 0.72 millions) of total under-5 child mortality worldwide. Along with prematurity and systemic infections, PA is one of the three most common causes of neonatal deaths.[1] It is also an important cause of stillbirths—of the total 2.7 million stillbirths that occur globally, about 1.2 million occur during the intrapartum period, largely due to asphyxia.[2] The National Neonatal Perinatal Database (NNPD; 2002–2003) reported PA to be the most common cause of stillbirths, accounting for 45.1% of all such cases.[4] Almost all (98.2%) asphyxia related deaths occur in first week of life, with 73% of asphyxia related deaths occurring within 24 hours of birth.[3] Therefore, providing adequate post-resuscitation care is essential to reduce neonatal and child mortality.

INCIDENCE

As per the NNPD (2002–2003), the incidence of PA—defined as Apgar score of <7 at 1 minute of life—was 8.4% of all live births.[5] Oxygen was the most commonly used resuscitative measure in 9.5%, bag and mask ventilation in 6.3%, chest compressions in 0.8%, and use of medications in 0.5%. PA was responsible for 28.8% of all neonatal deaths. Manifestations of hypoxic–ischemic encephalopathy (HIE) were seen in approximately 1.4% of live births. Asphyxia is also responsible for lifelong neuromotor disability in a large number of children.

DEFINITIONS

The terms used to evaluate a newborn with brain damage are as follows:

1. **Perinatal hypoxia, ischemia, and asphyxia:** Hypoxia refers to lower oxygen levels, ischemia to decreased blood flow, and asphyxia to decreased gas exchange in the fetus or newborn.

Table 8.1: Definitions of perinatal asphyxia	
	Definition
World Health Oragnization[6]	Failure to initiate and sustain breathing.
NNPD Network[5]	• **Moderate PA:** Slow/gasping breathing or an Apgar score of 4–6 at 1 minute of age. • **Severe PA:** No breathing or an Apgar score of 0–3 at 1 minute of age.
American Academy of Pediatrics and American College of Obstetrics and Gynecology[7]	Presence of all of following criteria: • Profound metabolic or mixed acidemia (pH <7.0) in umbilical cord blood. • Persistence of low Apgar scores less than 3 for more than 5 minutes. • Signs of neonatal neurologic dysfunction (e.g. seizures, encephalopathy, tone abnormalities). • Evidence of multiple organ involvement (such as that of kidneys, lungs, liver, heart and intestine).

2. **Perinatal/neonatal depression:** This term refers to the physical state of a newborn within the first hour of life following birth and is unrelated to the newborn's prenatal and postnatal conditions. It describes the clinical state of newborns, such as hypotonia, poor mental status, and/or cardiovascular and respiratory disturbances.
3. **Neonatal encephalopathy:** It is the clinical term for abnormal mental state, level of consciousness, brain stem damage, and motor dysfunction. It need not always be irreversible; it could also result from reversible causes such as maternal medicines, hypoglycemia, or medications given during cesarean section under general anesthesia.
4. **Hypoxic–ischemic encephalopathy (HIE):** This term refers to the objective proof that hypoxia and ischemia are causing the clinical characteristics of encephalopathy that were previously defined.

There is no single, well-accepted definition of PA (Table 8.1). The definition is context specific and can be sensitive (e.g. those given by WHO and NNPD for the purpose of deciding immediate care of newborn) or specific (such as the one given by AAP for the purpose of giving a label or predicting the long-term outcome).

Consequences of Asphyxia

PA is a multi-organ-system disorder affecting virtually every organ-system in the body including brain, heart, lungs, kidneys and

intestine. Care of asphyxiated infant therefore should be oriented towards determining the severity of dysfunction of critical organ systems and provide appropriate support to allow recovery to happen. Many of these complications are potentially fatal. In term infants with asphyxia, renal, CNS, cardiac and lung dysfunction occur in 50%, 28%, 25% and 25% cases, respectively.[8] The extent of organ system dysfunction determines the early outcome of an asphyxiated neonate (Table 8.2).

Hypoxic ischemic encephalopathy (HIE) is often the prime concern while managing asphyxiated neonates because it is not only associated with high risk of mortality but also carries a significant risk of serious long-term neuromotor sequelae among survivors.

A detailed classification of HIE in term neonates was proposed by Sarnat and Sarnat.[9] A simpler and practical classification of HIE by severity of manifestations provided by Levene is recommended for routine use (Table 8.3).[10] Recent addition to this list is the Thompson score, which is based on features of HIE and has a maximum (worst) score of 22. A score of 15 or more has shown a positive predictive

Table 8.2: Organ system dysfunction in perinatal asphyxia

CNS	Hypoxic–ischemic encephalopathy, intracranial hemorrhage, seizures, long-term neurological sequelae
Cardiac	Myocardial dysfunction, valvular dysfunction, rhythm abnormalities, congestive cardiac failure
Renal	Hematuria, acute tubular necrosis, renal vein thrombosis
Pulmonary	Delayed adaptation, respiratory failure, meconium aspiration, surfactant depletion, primary pulmonary hypertension
GI tract	Necrotizing enterocolitis, hepatic dysfunction
Hematological	Thrombocytopenia, coagulation abnormalities
Metabolic	Acidosis, hypoglycemia, hypocalcemia, hyponatremia

Table 8.3: Classification of HIE (Levene)

Features	*Mild*	*Moderate*	*Severe*
Consciousness	Irritable	Lethargy	Comatose
Tone	Hypotonia	Marked hypotonia	Severe hypotonia
Seizures	No	Yes	Prolonged
Sucking/ respiration	Poor suck	Unable to suck	Unable to sustain spontaneous respiration

value of 92%, negative predictive value of 82%, sensitivity of 71% and specificity of 96% for abnormal outcome at 12 months of age.[11]

Evolution of HIE Changes

HIE evolves gradually beginning from the time of insult to hours and days later (Table 8.4). The initial hypoxic–ischemic event results in infarction of the brain tissue (primary energy failure). The subsequent injury–secondary injury–is mediated by reperfusion and free radicals in an area surrounding the necrotic area (penumbra). The penumbra undergoes a programmed neuronal death (apoptosis) even after the hypoxic insult is over. The time gap between these two phases could be 6–24 hours and provides a window to institute specific therapeutic intervention.

MANAGEMENT OF A NEONATE WITH PERINATAL ASPHYXIA

Management of asphyxiated neonates is mainly supportive and involves maintaining optimum oxygenation, ventilation, perfusion, metabolic milieu and control of seizures.

Table 8.4: Clinical features of severe HIE and the timeframe

Time frame	*Clinical features*
Birth to 12 hours	• Decreased alertness and tone • Convulsions • Periodic breathing or respiratory failure • Intact pupillary and oculomotor responses
12–24 hours	• Change in alertness level • Apneic spells • Increase in convulsions • Jitteriness • Weakness in proximal limbs • In term neonates, upper limbs more involved than lower limbs; in preterm, lower limbs more involved
24–72 hours	• Further decrease in alertness • Pupillary and oculomotor disturbances • Respiratory arrest • In preterm neonates, intraventricular hemorrhage and periventricular hemorrhagic infarction
After 72 hours	• Persistent and diminishing stupor • Abnormal sucking, swallowing, gag and tongue movements • Hypotonia more common than hypertonia • Weakness in proximal limbs

Delivery Room Care

- For neonates born at term and near term (35 weeks) gestation, resuscitation should start with 21% oxygen.
- For preterm neonates born at less than 35 weeks of gestation, resuscitation should start with 21–30% oxygen; further oxygen concentration should be titrated to achieve target saturations.[12]
- For non-vigorous neonates born through meconium-stained amniotic fluid, the 2015 Neonatal Resuscitation Program (NRP) does not recommend routine intubation for suctioning of meconium, citing more harm due to intubation along with delay in providing adequate ventilation.[12]
- Obtain arterial cord blood for analysis: After cutting the cord, apply additional clamp on umbilical cord on placental side keeping a cord segment of 10–15 cm between two clamps.
- Take a heparinized syringe and puncture the cord (clamped segment, once placenta is out and resuscitation is over) to take blood sample from umbilical artery.

Presence of metabolic acidosis (pH <7.00 and base deficit greater than 16 mmol/L) indicates relatively long-standing asphyxia (many minutes to hours), while presence of respiratory acidosis in absence of metabolic acidosis indicates presence of acute asphyxia (minutes) as in cord prolapse, acute abruption of placenta, etc.

Cord blood gas in asphyxia: what is the evidence?

A recent meta-analysis has shown a good association of cord ABG abnormalities (pH<7.0 and base deficit ≥16 mmol/l) with short-term (mortality, HIE, IVH or PVL) and long-term adverse outcomes (cerebral palsy).[13]

NICU Care

Transfer the Neonate to NICU, If

- Apgar score at 1 minute is <3.
- Required prolonged bag and mask ventilation (60 seconds or more).
- Required chest compressions.

Even neonates transferred to mother should be monitored frequently in the first 48–72 hours for development of features suggestive of HIE.

Care in NICU

1. **Maintain normal temperature**
   - After drying, place the baby under the radiant warmer.

- Maintain normal body temperature.
- Avoid hyperthermia.[14]

2. **Maintain normal oxygenation and ventilation**
   - Assess the infant for adequacy of oxygenation and ventilation and provide support as needed.
   - Keep under oxygen hood if needed; maintain saturations between 90 and 95%; avoid any hypoxia or hyperoxia
   - Assisted ventilation is required if there is apnea, or spontaneous respiration is inadequate or there is continuing hypoxia or hypercarbia.
   - Measure arterial blood gas, if any respiratory or perfusion abnormalities are present (maintain pO_2 between 60 and 90 mm Hg and pCO_2 at 35–45 mm Hg). Avoid both hypocarbia (reduces cerebral perfusion) and hypercarbia (increases cerebral perfusion and intracranial pressure and predisposes to intracranial bleed).

3. **Maintain normal tissue perfusion**
   - Ensure normal perfusion i.e. capillary refill time of less than 3 seconds, absence of tachycardia and metabolic acidosis, normal blood pressure, and adequate urine output.
   - Start intravenous fluids in all neonates with Apgar scores <4 at 1 minute or <7 at 5 minutes of age or if the neonate is sick (respiratory distress, encephalopathy or abnormal tone).
   - In sick neonates, place arterial line for guiding management of blood pressure. BP should be tightly maintained in upper normal range according to gestation and postnatal age specific BP charts avoiding wider fluctuation.[15]
   - If tissue perfusion is inadequate, infuse normal saline or Ringer's lactate at 10 mL/kg over 5–10 min.
   - Administer dobutamine (preferred) or dopamine to maintain adequate cardiac output, as required.
   - Do not restrict fluid routinely because it may predispose to hypoperfusion; restrict fluids only if there is hyponatremia (sodium <120 mEq/L) secondary to syndrome of inappropriate secretion of ADH (SIADH) or if there is renal failure.
   - Do echocardiography in infants needing ionotropic support to assess decreased contractibility due to asphyxia related cardiogenic shock. This helps to guide appropriate management strategy.[16]

4. **Maintain normal hematocrit and metabolic milieu**
   - Check blood glucose levels and maintain blood glucose levels between 75 mg/dl and 100 mg/dl.
   - Check hematocrit; correct anemia and maintain hematocrit between 45 and 55%. If the venous hematocrit is above 65%, bring it down to 55% by partial exchange transfusion using normal saline.
   - Check blood gases to detect metabolic acidosis; maintain pH above 7.30.
   - In case of severe asphyxia (see AAP criteria in Table 8.1), provide calcium in a maintenance dose of 4 mL/kg/day of 10% calcium gluconate for 1–2 days as a continuous infusion or as 1:1 diluted boluses, slowly under cardiac monitoring; maintain serum calcium concentration in the normal range.
5. **Treat seizures**
   - Refer to protocol on 'Neonatal seizures'.
6. **Nutrition**
   - Start oral feeding once the neonate is hemodynamically stable, is off vasopressor support, and has normal abdominal examination findings (no distension and normal bowel sounds).

Role of Special Investigations

The role of special investigations is to provide information on long-term prognosis.

Electroencephalography (EEG)

EEG is not indicated routinely in all asphyxiated neonates, but it helps in diagnosis and management of seizures and prognosticating for long-term outcomes. The prognosis is likely to be poor, if the EEG shows any one of the following:

1. Long periods of inactivity (>10 seconds).
2. Brief period of bursts (<6 seconds) with small amplitude bursts.
3. Interhemispheric asymmetry and asynchrony.
4. Isoelectric and low voltage (<5 microvolts).[17]

Amplitude-integrated electroencephalography (aEEG) is a simple, reliable, non-invasive technique which can be applied at the bedside in NICU for monitoring EEG continuously. Following abnormalities in aEEG would indicate poor prognosis:

- Wide fluctuations in the amplitude with the baseline voltages dropping to near zero.
- Peak amplitudes under 5 mV.
- Seizure spikes.

While a normal aEEG may not necessarily mean that the brain is normal, a severe or moderately severe aEEG abnormality may indicate brain injury and poor outcome. The time of onset of sleep wake cycling (SWC) also has a prognostic value. If SWC returns before 36 hours of age, the prognosis is likely to be good.[18]

Cranial Ultrasound (US)

Cranial US is not good for detecting changes of HIE in term neonates. However, hypoechoic areas can be seen in very severe cases (having large areas of infarction).

In preterm neonates, US can detect periventricular leukomalacia and intraventricular–periventricular hemorrhage during the first week of life. US is more useful than CT in providing adjunct prognostic information in preterm neonates.

Computed Tomography (CT)

CT has a role in initial evaluation, if MRI is not readily accessible. In acute stage of HIE, CT in term babies show generalized low attenuation of brain parenchyma. However, several weeks after asphyxial insult CT readily picks up diffuse cortical neuronal injury, injury to basal ganglia and thalamus, focal and multifocal ischemic brain injury as well as periventricular leukomalacia. CT has a limited role in identification of parasagittal cerebral injury.

Magnetic Resonance Imaging (MRI)

MRI is the best imaging modality for determining prognosis in term neonates. Diffusion weighted MRI can detect abnormalities within 24–48 hours after birth (optimal time is 2–3 days), whereas conventional MRI can show abnormalities in the first 3–4 days (though optimal time is later during the first week of life). An altered signal at the level of posterior limb of the internal capsule and abnormalities of thalami and basal ganglia in term neonates and that of white and grey matter at term equivalent age in preterm neonates are strong predictors of subsequent risk of poor neurodevelopmental outcome.[19] Another common pattern of injury is injury to the watershed regions.

Prognostic test in neonates with asphyxia: what is the evidence?

In a recent meta-analysis of 29 studies describing 13 prognostic tests in 1306 term neonates with hypoxic-ischemic encephalopathy, aEEG in the first 6 hours showed maximum sensitivity and specificity (93% and 90% respectively).[20]

SPECIFIC MANAGEMENT

1. Therapeutic Hypothermia (TH)

Institution of moderate therapeutic hypothermia (TH; 33–34°C) in infants of at least 35 weeks' gestation with moderate to severe encephalopathy initiated within 4–6 hours and continued for 72 hours of age in ICU settings has been shown to reduce mortality and neuromorbidity by 18 months of age.[21] TH can be instituted by selectively cooling the head or the whole body. It is a safe modality in settings where intensive care facilities to manage sickest neonates are available.

TH has now become the standard of care in developed countries. However, this is not the case in low to middle income countries (LMIC), where the patient profile is different (concomitant IUGR, infection and nutritional deficiencies), there is a paucity of intensive care, and many births occur out of hospital. Indeed, a few studies have shown increased mortality following TH in these settings.[22,23]

Therapeutic hypothermia: What is the evidence?

The Cochrane review (8 RCTs; 638 term neonates with moderate/ severe encephalopathy and evidence of intrapartum asphyxia) showed that TH reduced combined outcome of mortality or major neurodevelopmental disability by 24% at 18 months of age.[24]

Evidence for Therapeutic Hypothermia from LMIC (Helix Trial)[31]

Evidence from Hypothermia for moderate or severe neonatal encephalopathy in low-income and middle-income countries (HELIX)Trial.

Countries Involved: India, Sri Lanka, Bangladesh.

Study Participants: Late preterm neonates (≥36 weeks) and term neonates with moderate to severe encephalopathy.

Enrolled participants (n): 408.

Intervention: Therapeutic hypothermia for 72 hours.

Primary outcome: Death or moderate to severe disability at 18–22 months.

Major results:

a. No effect on death or moderate to severe disability [50% vs 47% (RR:1.06; 95% CI 0·87–1·30; p=0·55)].
b. Increased risk of death before discharge in the intervention group [36% vs 24%; RR: 1·50; 95% CI: 1·10–2·04)].

Mechanism of Action of TH

TH has been shown to be protective at critical cellular and vascular sites of cerebral injury following asphyxia. It acts by the following mechanisms to reduce the extent of brain injury:[25]

1. Decreased cerebral metabolism and blood flow: Decrease in energy requirement and cerebral edema.
2. Decreased brain lactic acid, glutamate, and nitric oxide concentrations: Less excitotoxic and oxidative injury.
3. Inhibits protease activation, mitochondrial failure, free radical damage, lipid peroxidation: Less apoptosis and necrosis.

Selection of Neonates for TH (Table 8.5)

Table 8.5: Selection criteria of neonates for therapeutic hypothermia (NNF India 2021[32])

Whom to treat?	Neonates with the following characteristics: • Gestational age: ≥36 weeks • Age: <6 hours • Admission temperature: 36–37.4°C And following features: • Evidence of perinatal asphyxia as shown by any one of the following: A. pH <7 or Base excess >–16 in cord blood gas or arterial blood gas within 1 hour of birth. B. Apgar score <5 at 10 minutes of age. C. Positive pressure ventilation for at least 10 minutes. D. History of acute peripartum event like cord prolapse, uterine rupture. • Evidence of moderate to severe encephalopathy.
Whom not to treat?	Neonates with the following conditions: • Major congenital malformation. • Severe IUGR. • Severe coagulopathy. • Severe Intracranial bleed.
Where TH should be administered?	Level 3 NICU having a multidisciplinary team and following facilities can offer TH: • Bedside EEG, Cranial ultrasonography. • Access to MRI imaging, CT scan. • 24 hour monitoring of vital parameters like heart rate, respiration, blood pressure, temperature and saturation. • Desirable Nurse to patient ratio 1:2 or 1:1. • Long term follow up for at least 18 months.

(*Contd.*)

Table 8.5: Selection criteria of neonates for therapeutic hypothermia (NNF India 2021[32]) (*Contd.*)	
Which device should be used for TH?	Only servo-controlled devices should be used for providing hypothermia.
What should be the appropriate duration?	72 hours

Cooling Devices Used for TH

1. Whole body cooling devices
   a. High technology devices: Examples–Tecotherm™, Blanketrol™, Meditherm™
   b. Low technology devices: Example–Miracradle™
2. Selective head cooling device: Examples–Olympic cool cap system™

High Technology Devices

These devices usually have a circulating water/coolant system. The water/coolant flows over and around the heating/cooling element located in the circulating reservoir. The heated or cooled water/coolant then flows out of the reservoir to the circulating pump, through connecting hoses over a water temperature sensor to the blanket. The water circulates through the blanket(s) and returns to the unit.

Low Technology Devices

These devices use the phase change material (PCM) technology to induce therapeutic hypothermia. PCMs are special thermal energy storage materials that store and release heat at a particular temperature. The thermal energy transfer occurs when the material changes phase from solid to liquid or liquid to solid.

In our unit, we use 'Blanketrol III Hyper-hypothermia' temperature management system which is a servo-controlled whole-body hypothermia device.

How to Initiate Whole Body Hypothermia

1. Counsel the parents about indications, benefits and risks of therapy.
2. Prepare the cooling system for operation.
3. Set the cooling blanket temperature of 33.5°C.
4. Monitor and document the infant's pre-cooling vital signs.

5. Place the infant on the warmer in the supine position with the entire head and body resting on the cooling blanket.
6. Place and secure central and arterial lines before starting hypothermia.
7. Gently insert the patient rectal probe 2 cm into the infant's rectum, and secure to the infant's leg with tape.
8. The infant must lie directly on the cooling blanket, wearing a diaper only.

Monitoring after Initiating TH

The frequency of monitoring and investigations after initiating TH is shown in Table 8.6:

Rewarming

1. Increase the infant's core temperature by 0.5°C every hour until 36.5°C has been reached.

Table 8.6: Monitoring (frequency)

Parameter	*Day 1*	*Day 2*	*Day 3*
Vitals monitoring including invasive blood pressure monitoring	Q 1 hour	Q 1 hour	Q 1 hour
Neurological monitoring	Q 12 hours	Q 12 hours	Q 12 hours
Urine output	Q 6 hours	Q 6 hours	Q 6 hours
ECG	Continuously	Continuously	Continuously
aEEG	Continuously	Continuously	Continuously
Skin integrity	Q 6 hours	Q 6 hours	Q 6 hours
Investigations			
Glucose	Q 6 hours	Q 6 hours	Q 6 hours
Blood gas	Q 6 hours or as indicated by condition of baby	Q 12 hours or as indicated	Q 12 hours or as indicated
Renal function test	Once	Once	Once
Electrolytes	Once	Once	Once
Complete hemogram	Only if required	Only if required	Only if required
Neurosonogram	If abnormal	If abnormal	If abnormal

2. When the infant's core temperature is 36.5°C, remove the patient from the cooling blanket/device.
3. Re-activate the radiant warmer, monitor and document the infant's temperature with the skin probe.
4. Problems while rewarming: seizures and hypotension.

Supportive Therapy during TH

Sedative/analgesics	Morphine (preferred) or fentanyl should be given by infusion during therapeutic hypothermia.
Enteral feeds	Start MEN, if hemodynamically stable.
Antibiotics	Prophylactic antibiotics should not be given.
Anticonvulsants	Anticonvulsants should be given in the presence of seizures; electric seizures in absence of clinical correlates should be treated.
Platelet concentrate	If platelet count is less than 100,000/cmm.
Fresh frozen plasma	Only if there is active bleeding.

Adverse Effects of TH[24]

The common adverse effects include sinus bradycardia (heart rate <80/min) and thrombocytopenia (platelet count $<150 \times 10^9$/L).

2. Prophylactic Phenobarbitone

Some interest has been generated in the protective role of prophylactic phenobarbitone in newborns with perinatal asphyxia. A dose of 40 mg/kg administered prophylactically was associated with a better neurodevelopmental outcome at 3 years of age.[26] However, the Cochrane review that included 5 RCTs reported no difference in the risk of death, neurodisability.[26] Another study using 40 mg/kg within 1st hour showed a significant reduction in HIE with no difference in complications.[26] Recommendation for use of prophylactic phenobarbitone still awaits further studies.

Prophylactic phenobarbitone in HIE: What is the evidence?

The systematic review by Evans DJ showed no significant difference in the risk of the combined outcome of death or severe neurodevelopmental disability (typical RR 0.78, 95% CI 0.49, 1.23).[26]

3. Drugs under Investigation

A large number of drugs are under investigation for neuroprotection in HIE. They need to be used in the early period of

hypoxic–ischemic injury along with therapeutic hypothermia. They act by causing blockade of free radical generation (allopurinol, oxypurinol, melatonin), scavenging of oxidants (superoxide dismutase, glutathione, N-acetyl cysteine), calcium channel blockade (flunarizine, nimodipine), blockage of NMDA receptors (magnesium, Xenon, dextromethorphan) and blockage of inflammatory mediators (phospholipase A2, indomethacin, erythropoietin).[27] A recent multicenter 'Total body hypothermia plus Xenon' (TOBY-XE) trial reported no effect of this intervention on reduced thalamic lactate to N-acetyl aspartate ratio, a surrogate marker of good neurodevelopmental outcome.[28]

Follow-up

It is essential to follow all the neonates with the moderate and severe asphyxia, especially those with stage II and III HIE staging. They should have a complete neurological assessment and early intervention, if needed during the follow-up. A formal psychometric assessment at 18 months should be performed in them.

Long-term Outcome

Among the neonates who survive severe HIE, the sequelae include mental retardation, epilepsy, and cerebral palsy of varying degrees. The latter can be in the form of hemiplegia, paraplegia, or quadriplegia. Such infants need careful evaluation and support. They may need to be referred to specialized clinics capable of providing coordinated comprehensive follow-up care.

Predictors of mortality and neurological morbidity after perinatal hypoxic ischemic insult:

1. Extended very low APGAR scores (at 20 minutes or more).
2. Time to establish spontaneous respiration (for 30 or more minutes).
3. Neonatal neurological examination (severe HIE).
4. Brain imaging (USG, MRI).
5. Other investigations (EEG, aEEG, evoked potentials like BERA).

The incidence of long-term complications depends on the severity of HIE. Up to 80% of neonates with stage III HIE die whereas rest 20% have neurological sequelae. Up to 80% of infants who survive severe HIE develop serious complications, 10–20% develop moderately serious disabilities, and up to 10% are normal. The incidence of death is up to 5% and that of neurological sequelae is up to 24% after moderate birth asphyxia. Among the infants who

survive moderately severe HIE, 30–50% may suffer from serious long-term complications, and 10–20% with minor neurological morbidities. Infants with mild HIE tend to be free from death or any neurological sequelae.[29, 30]

A recent study on long-term outcomes of whole body hypothermia for HIE revealed the rate of combined end point of death or an IQ score of less than 70 at 6–7 years of age to be lower among neonates undergoing whole body hypothermia (47%) than those undergoing usual care (62%).[25]

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