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Birth-Associated Neonatal Encephalopathy: Postresuscitation Care in West African Newborns

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Education Gaps

1. Clinicians caring for newborns in low-resource settings need to recognize that several local and complex dynamics influence the burden of perinatal asphyxia in West Africa.
2. Appropriate use of clinical scores/tools may improve diagnostic accuracy of birth-associated neonatal encephalopathy.
3. Therapeutic hypothermia without an effective package of intensive monitoring and care may not be safe.
4. Prevention, early diagnosis, and management of secondary causes of brain injury are critical for improving health outcomes.

Abstract

The West African subregion has the highest burden of neonatal mortality globally and the neonatal mortality rate is decreasing very slowly. A high proportion of newborn deaths are preventable and improved quality of care can reduce long-term morbidity in survivors. Perinatal asphyxia is the major cause of death and disability in term infants in the subregion. Neonatal resuscitation training programs have reduced stillbirths and early neonatal mortality but the overall effect on survival to discharge, population-based perinatal mortality, and long-term impairment is uncertain. Gaps in the health system and quality of postresuscitation care for affected newborns may defeat gains from global efforts to improve care around the time of birth. The aim of this review is to discuss the current situation of postresuscitation care of term infants with presumed birth-associated neonatal encephalopathy in West Africa. Limitations in diagnosing and treating affected infants and feasible interventions to improve acute and postdischarge care are discussed.

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ABBREVIATIONS

HBB	Helping Babies Breathe
NE	neonatal encephalopathy
NRT	neonatal resuscitation training
PA	perinatal asphyxia

Objectives

After completing this article, readers should be able to:

1. Describe the burden and causes of birth-associated neonatal encephalopathy in West Africa.
2. Recognize limitations in diagnosis and appropriate management of neonatal encephalopathy in West Africa.
3. Review feasible community and facility-based interventions to reduce death and disability of newborns with encephalopathy in West Africa.

INTRODUCTION

The West African subregion is composed of 17 low- and low-middle income countries with an estimated 350 million people of great diversity in culture, language, religion, and colonial legacy (Fig). It has the highest burden of neonatal mortality globally. (1)(2) Available data on major causes of neonatal deaths and disability are estimates because about half of all births still occur at home without

skilled providers, vital registration systems are relatively weak, and health systems face many challenges. (1)(3)(4) Efforts by countries to improve maternal-newborn health outcomes have resulted in a significant increase in facility-based antenatal and delivery services. (4) However, there are still major gaps in the quality of services provided around the time of birth, and preventable birth complications, especially perinatal asphyxia (PA), remain a major cause of death and disability. (5)(6)



Figure. United Nations subregions of Africa and West Africa. Printed with permission from the United Nations: West Africa, Map No. 4533, October 2014, United Nations (<http://www.un.org/Depts/Cartographic/map/profile/westafrica.pdf>).

PA occurs when there is interruption of blood flow and gas exchange to the fetus around the time of birth. Significant interruption results in hypoxic brain injury and neonatal encephalopathy (NE). The “golden minute”—the first minute after birth—provides a crucial window of opportunity for skilled essential care to reduce death and disability. (7) Standardized neonatal resuscitation training (NRT) programs such as Helping Babies Breathe (HBB) have significantly improved resuscitation skills of frontline providers and reduced deaths on the first day after birth. (8)(9)(10) Although HBB may reduce intrapartum-related neonatal mortality by 30% in low-resource settings, the overall effect of NRT on survival to discharge, population-based perinatal mortality, and long-term impairment is uncertain. (7)(11)(12) Improving the quality of care beyond the time around birth may save more lives and reduce severe disability.

In West Africa, many births still occur at the community and primary health facility level, often without a skilled provider or 1 skilled provider attending to both the mother and newborn. (4) Newborns who require assistance with breathing or have a weak or no cry at birth may not receive effective resuscitative care. However, with government investments in community-based health services, the HBB program is making inroads into intrapartum care at all levels of health service delivery. (13) Consequently, an increasing number of successfully resuscitated newborns are being referred to higher-level facilities for postresuscitation care. This review describes the situation in West Africa and suggests options that may reduce the burden of birth-associated NE and improve hospital-based postresuscitation care for affected term newborns.

THE BURDEN OF PA

The burden of PA reflects the quality of maternal-newborn health services; underlying factors for inadequate services in the subregion have been described. (3) In Africa, the West Africa subregion has the poorest indices for facility-based maternal care; about 50% of births still occur at home with 20% occurring with no person present and only 35% attended by a physician or nurse/midwife. (14) Inequalities in access to health care and wealth contribute significantly to giving birth with no one present, and Nigeria accounts for a significant proportion of the global burden. (15)

Facility-based skilled delivery is inversely correlated to early neonatal deaths and varies widely between and within countries, from 7.2% in rural Burkina Faso to 78% in Senegal. (16) Overall, limited resources and inadequate

linkages and standards in the health system undermine maternal-newborn services; transportation is a major constraint to emergency obstetric care in rural communities. (17)(18) Ambulance services, where they exist, are not equipped for transportation of sick newborns. Infants who require postresuscitation care may not receive effective respiratory support during transportation to referral centers and this increases the risk of secondary brain injury.

Published country data on the burden of PA in the subregion are mostly estimates based on inadequate health information systems. In 2010, modeled estimates of population-level data on rates of adverse outcome related to intrapartum events showed an estimated 198,000 intrapartum stillbirths, 129,000 intrapartum-related neonatal deaths, and 173,000 incident cases of NE (Table 1). (6) Unpublished 2017 data from 16 neonatal referral centers in the Republic of Benin, Ghana, and Nigeria show that PA accounted for 30% (range, 14%–58%) of term newborn admissions and 20% (range, 11%–36%) of all neonatal admissions. According to World Health Statistics 2015 from the World Health Organization, intrapartum-related complications among live-born infants caused 8% to 13% of deaths in children younger than 5 years in West African countries. (19)

Survivors of PA in high-income countries have a high risk of impaired neurodevelopmental outcome. (20) Little is known about long-term morbidity among survivors of PA in low-resource settings. (21) Low quality of postresuscitation care has been described in this region and this may increase the risk of severe neurodevelopmental impairment in survivors. (22)

DIAGNOSIS OF BIRTH-ASSOCIATED NE

NE has been described as a clinical syndrome of impaired neurologic function often accompanied by difficulty with initiating and sustaining respiration around the time of birth. (23) Although maternal, placental, and fetal risk factors predispose newborns to NE, intrapartum-related acute hypoxic ischemia is the underlying cause in 50% to 80% of cases in high-income countries and this proportion may be higher in low-resource settings. (24) Antenatal inflammation including chorioamnionitis is common in low-resource settings; this inflammation may potentiate the effects of hypoxia on brain injury and significantly increase the risk for term encephalopathy. (25)

The criteria for attributing a birth-associated hypoxic-ischemic event as the underlying cause of NE have evolved since 1996 but the cornerstone criterion remains the

TABLE 1. IR Outcomes of NE in West Africa: Estimates for the Year 2010

COUNTRY	INCOME	BIRTHS	NMR	IR NEONATAL DEATHS	NE CASES	NE NEONATAL DEATHS	NE SURVIVORS (POSTNEONATAL)	NE SURVIVORS MODERATE-SEVERE IMPAIRMENT	NE SURVIVORS MILD IMPAIRMENT
Benin	LIC	350,300	31.8	3,126	3,967	1,051	2,915	840	708
Burkina Faso	LIC	713,200	37.9	7,280	9,322	2,470	6,852	1,973	1,665
Cameroon	LMC	709,900	33.5	6,666	8,404	2,227	6,177	1,779	1,501
Cape Verde	LMC	10,300	14.4	24	61	8	53	15	13
Cote d'Ivoire	LMC	673,100	40.5		9,301	2,465	6,836	1,969	1,661
Gambia	LIC	65,900	31.3	596	737	195	542	156	132
Ghana	LMC	769,700	28	6,054	7,867	2,085	5,782	1,665	1,405
Guinea	LIC	389,900	37.9	4,079	5,102	1,352	3,750	1,080	911
Guinea-Bissau	LIC	58,200	40.1	640	796	211	585	169	142
Liberia	LIC	153,700	34.1	1,478	1,843	488	1,354	390	329
Mali	LIC	714,100	47.7	8,485	11,260	2,984	8,276	2,383	2,011
Mauritania	LMC	116,800	39	1,202	1,565	415	1,150	331	280
Niger	LIC	754,900	32.4	6,500	8,691	2,303	6,388	1,840	1,552
Nigeria	LMC	6,300,000	40	69,240	86,636	22,959	63,678	18,339	15,474
Senegal	LMC	465,400	27.2	3,674	4,650	1,232	3,417	984	830
Sierra Leone	LIC	226,400	45.5	2,708	3,437	911	2,526	728	614
Togo	LIC	193,400	32.4	1,731	2,225	590	1,636	471	397

IR=intrapartum-related; LIC=low income country; LMC=low middle income country; NE=neonatal encephalopathy; NMR=neonatal mortality rate. Source: Lee et al.(6)

presence of severe metabolic acidosis (pH <7.0 and base deficit ≥12 mmol/L) with early signs of moderate or severe encephalopathy. Other minor criteria include a sentinel obstetric hypoxic-ischemic event, abnormal fetal heart rate patterns, low Apgar score, abnormal findings on neuroimaging, and multisystem organ complications. NE is an evolving disorder and no single test or clinical tool is diagnostic. (26)

Acid-base measurements and neuroimaging are not usually available at the point of care in West Africa. Currently, birth-associated NE is diagnosed when a newborn who required resuscitative care at birth presents with abnormal neurologic findings (especially a clinical seizure). Perinatal or birth asphyxia is still the most commonly used terminology. Almost all cases are presumed to be intrapartum-related and other causes of encephalopathy that present around the time of birth are largely underdiagnosed.

Several factors undermine accurate diagnosis of birth-associated NE in the subregion. The skilled workforce and

commodities for effective intrapartum monitoring are limited; available tools, particularly the partograph and Apgar scoring, are often not used appropriately or interpreted accurately; and clinical encephalopathy scoring is infrequently used. (27)(28) Integrated perinatal care is not standard practice and newborns referred for postresuscitation care arrive with inadequate information about perinatal events.

The Thompson score, first described in a South African population, is a sensitive early clinical scoring system that has been shown to be sensitive at predicting either abnormal amplitude-integrated electroencephalographic findings or moderate-severe encephalopathy. (29)(30) In Senegal, the modified Sarnat and Sarnat score has been used to diagnose cases of intrapartum-related NE among newborns referred with PA. (31) These approaches suggest that it is feasible to diagnose NE without expensive technology. The scoring tools are easy to use and can be applied as early effective screening tools for birth-associated NE

in low-resource settings. Accurate diagnosis of intrapartum-related NE is essential before application of specific therapies because routine application of therapeutic hypothermia may not be safe in the prevailing circumstances in West Africa. Training and supervision of front-line clinicians about the appropriate use of the partograph (or electronic monitoring where available), Apgar score, encephalopathy scoring tools, and checklists (Table 2) to capture intrapartum events and other clinical data may improve the diagnostic accuracy of birth-associated NE.

MANAGEMENT OF BIRTH-ASSOCIATED NE: CURRENT PRACTICE

There is no specific treatment for birth-associated NE, but therapeutic hypothermia reduces death and disability when included as part of a package of neonatal intensive care. (32) However, the safety and efficacy of therapeutic hypothermia in low-resource settings is uncertain. (33) In the West African subregion, the neonatal intensive care package is limited to tertiary centers and a few nontertiary hospitals. In addition to basic newborn care the package includes oxygen therapy, intravenous drugs and infusions including blood products, phototherapy, gavage feeding, and noninvasive respiratory support. Very few centers provide mechanical ventilation. Human resources are severely limited and certified neonatal nurses are rare. Laboratory and radiologic services may not be accessible at the point of care and basic monitoring devices such as pulse oximeters are very limited.

Effective care of newborns with NE requires a well-organized system that provides timely and appropriate supportive care. In rural settings, affected infants may not receive skilled postresuscitation assessment before discharge; it is not uncommon for cases to be referred on the second or third day of age because of poor feeding or seizures. None of the countries in West Africa have specific national guidelines for referral of infants for postresuscitation care. In the few countries with national guidelines for clinical care, the information is scanty and not updated, and some institutional guidelines are not evidence-based. (34)

In West Africa, clinicians would generally not provide extra warmth to affected infants during the first 3 days after birth; this practice is described as passive cooling in some countries. For infants with seizures, phenobarbital is the first-line anticonvulsant and phenytoin, where available, is the second-line agent. Some tertiary centers use midazolam infusion for intractable seizures. Concerns about respiratory depression from anticonvulsants limit

TABLE 2. Checklist for Perinatal Risk Factors for Birth-Associated Neonatal Encephalopathy and Related Events

Maternal factors
Chorioamnionitis
Maternal fever >100.4°F (38°C)
Prolonged rupture of membranes >18 hours
<ul style="list-style-type: none"> • Antibiotics given • Antibiotics not given
Prolonged hypoxia
Prolonged low blood pressure
Cardiovascular collapse
Obstetric complications
Umbilical cord prolapse
Rupture of the uterus
Severe antepartum hemorrhage
<ul style="list-style-type: none"> • Placental abruption • Placenta previa
Placental insufficiency
<ul style="list-style-type: none"> • Postdates • Scanty liquor
Fetal factors
Abnormal fetal heart rate pattern
<ul style="list-style-type: none"> • Persistent fetal tachycardia >160 beats/min >10 min • Persistent fetal bradycardia <110 beats/min >10 min • Absent baseline variability • Recurrent late deceleration • Recurrent variable deceleration
Infant status at birth
Inadequate or weak spontaneous respiratory effort
Weak or absent cry
Resuscitation provided
<ul style="list-style-type: none"> • Stimulation or simple oxygen therapy • Bag and mask resuscitation • Endotracheal intubation

appropriate treatment of clinically diagnosed seizures. All centers that provide an intensive care package provide postdischarge follow-up care for about 6 to 24 months but the content and quality of the service is variable because

there are no national standards. It is not uncommon for families to seek rehabilitation care from spiritual and traditional healers after discharge and only return for hospital care when there is severe disability.

Evidence-based guidelines and clinical pathways may reduce variability in practice and improve quality of services during the acute and rehabilitation stages of care. (35) (36) Limited capacity to continuously monitor body temperature and oxygen therapy is a major constraint. Infants undergoing facilitated endogenous cooling, so-called passive cooling, are at risk for severe hypothermia, hypoxia, or hyperoxia, which may worsen brain injury. Clinical observation, the only method available for diagnosing seizures, is known to be highly inaccurate with low sensitivity; underdiagnosis of seizures increases the risk for brain damage while overdiagnosis may lead to unnecessary and toxic treatments. (37)

RECOMMENDATIONS TO IMPROVE HEALTH OUTCOMES

Reductions in stillbirths and early neonatal deaths from improved intrapartum care and neonatal resuscitation programs may lead to an increase in the population of children and adults with severe disabilities and this has socioeconomic implications for society. (21)(38) Effective implementation of low-cost approaches could prevent some cases of NE, improve the quality of resuscitative and postresuscitation care, and enhance postdischarge rehabilitation services. (27)(39) This section provides general recommendations that can be adapted to local circumstances.

Community Engagement

Of the 3 major causes of neonatal death, PA is the least understood by communities in West Africa. Cultural beliefs and myths about pregnancy and birth-associated injuries affect health-seeking behavior for facility-based delivery and postdischarge rehabilitative care. Improving the health literacy of mothers and families about the risk and socioeconomic consequences of PA and benefits of acute and rehabilitative care is critical to reducing the burden of disease. (27)(39) An increasing number of women in the subregion are receiving antenatal care services in health facilities; this offers an opportunity for providers to improve the health literacy of mothers and communities on birth-associated injuries.

Effective community engagement has the potential to significantly reduce demand-side barriers to facility-based care. (40) Engaging traditional, political, and religious leaders, as well as social groups of women and men in

rural communities, as advocates for reducing PA and severe disability will reduce cultural barriers to care seeking. The tradition of restricting pregnancy-related information to only women needs to change. Community health services should create opportunities to educate men about PA; the “School for Husbands” in Niger is a program worth emulating. (41) Where limited access or cultural resistance to facility-based care is a constraint, integrating traditional birth attendants into the health system should be considered because this approach has improved maternal-newborn outcome in Sierra Leone and other African countries. (42)

Improve Referral Systems and Integrate Care

No single referral system can meet the needs of all communities; lessons can be learned from diverse approaches to improve referral systems for emergency maternal-newborn care. (43) Rural community efforts and social media platforms are bridging some gaps in maternal services. These approaches can be extended to newborns when intrauterine transfer is not possible. Adequate oxygen therapy and respiratory support should be provided throughout the journey from the labor room to the neonatal unit. Every birthing place should have a newborn

TABLE 3. **Content of Newborn Transport Kit**

Bag and mask equipment (appropriate sizes)
Portable suction device and accessories
Oxygen: Small oxygen cylinder with blender, oxygen delivery tube with face mask or nasal prongs
Pulse oximeter
Thermometer
Glucometer
Stethoscope
Intravenous cannula sizes 24G, 26G
Syringes and needles: 2 mL, 5 mL
Intravenous infusion set
Nasogastric tube sizes 5–8F
Intravenous infusions: D10W, normal saline
Thermal care: Cot sheets, blankets, cap
Medications: Epinephrine, phenobarbital, naloxone, calcium gluconate 10%
Hygiene supplies: Gloves, alcohol wipes, diapers, cotton wool
Other advanced equipment and supplies depending on available expertise

transport kit (Table 3) containing appropriate sizes of bag and mask and other supplies. If an ambulance or other forms of vehicular transport service exist, efforts should be made to equip them to meet basic needs, especially respiratory care, of sick newborns.

Formal communication between obstetric and pediatric services should extend beyond monthly or quarterly perinatal mortality meetings, and providers of neonatal care need to engage with rehabilitation service providers. Effective communication and collaboration between departments is essential. An integrated approach to perinatal care may improve diagnostic capacity and management for affected infants. (36)(44) Hospitals that offer comprehensive obstetric care should have a pediatric team responsible for the newborn around the time of birth. Limited human resources pose a major handicap at district hospitals where most births occur; many facilities may have 1 medical officer or pediatrician responsible for all neonatal and pediatric cases. However, a pediatric team of skilled nurses/midwives equipped with guidelines and checklist (Table 2) could provide this service under the supervision of a single physician.

Good-Quality Clinical Care

Many facility-based birth attendants in the subregion have not received NRT, and basic resuscitation equipment is not available at the point of care. (45) With central government support, national pediatric/neonatal societies have the pivotal role of formulating national guidelines, training birth attendants, and possibly instituting a national NRT program. Advocacy for essential equipment and supplies for newborn services is vital. Other approaches to improving essential care and resuscitation around the time of birth have been described. (46)

Infants with birth-associated NE are at high risk of having a secondary brain injury from secondary hypoxia and hyperoxia, hypocapnia and hypercapnia, untreated and prolonged seizures, sepsis, hyperthermia, and excessive (<91.4°F [33°C]) and prolonged cooling (>72 hours). Lessons can be learned from high-income countries over the last decade, with neonatal neurocritical care emerging as a culture change toward a “brain-focused” approach to mitigate secondary brain injury, rapid recognition of complications and seizures, consistent use of protocols, and use of experienced teams. There is an urgent need for a culture change in the practice of neonatology in West Africa, including a culture of teamwork and continuous quality improvement in the organization and practice of neonatal care.

A culture change in West African neonatal care will require basic training in measures to prevent secondary

brain injury and use of affordable and durable diagnostics, including simple amplitude-integrated electroencephalography devices to improve the diagnosis of seizures, especially in tertiary centers. Affordable and durable pulse oximeters and acid-base measurement equipment may improve the quality of care and health outcomes. Other options for anticonvulsant therapy for NE need to be considered because phenobarbital and phenytoin may not effectively treat neonatal seizures. (47)

Facilitated endogenous cooling (ie, passive cooling) is currently standard practice in most West African countries. Central cooling, the endogenous physiologic response to asphyxia, was observed in infants in 1958 by Burnard and Cross and recently in a pilot randomized trial in Uganda. (48)(49) The cooling response may be exaggerated and prolonged in infants with severe NE. It is unclear whether this endogenous cooling response is as neuroprotective as therapeutic hypothermia; also, the effect of antenatal inflammation on endogenous cooling is unknown. Concerted efforts should focus on reducing secondary brain injury until local randomized trials provide evidence for other therapies.

FUTURE INTERVENTIONS AND RESEARCH

Countries need to adopt continuous quality improvement initiatives and use available resources more efficiently. Tertiary institutions or countries should consider joining established neonatal networks. Collaborative networks provide opportunities for improving standards, learning, research collaborations, data-driven quality improvement, and more. Ethiopia has recently joined the Vermont Oxford Network and other countries can learn from Ethiopia’s experience. The West African Health Organization should recognize and prioritize the burden of birth-associated NE, advocate for improved neonatal services, and possibly facilitate a regional collaborative neonatal network.

TABLE 4. **Future Needs and Direction for Improving Care**

- National center of excellence that provides an intensive care package including neurocritical care to scale up national training
- Affordable effective technologies and drugs for accurate diagnosis and management of neonatal seizures
- Improved capacity for effective rehabilitative care especially at district level

Parenteral levetiracetam, commonly used for neonatal seizures in high-income countries is expensive and not available in the subregion. Safer, effective, and affordable drugs for neonatal seizures will reduce morbidity. Feasibility of conducting randomized clinical trials using newer anticonvulsants for newborns in the subregion should be explored.

Accurate diagnosis of antenatal inflammation in the subregion is a challenge. Research on rapid diagnostic tests is needed. The effect of endogenous physiologic cooling should be investigated in a randomized controlled trial in a setting with a high burden of disease. Future needs and direction for improving quality of care and outcome for birth-associated NE in West Africa are summarized in Table 4.

SUMMARY

- There are major gaps in the health system of West African countries that inevitably result in high burden of neonatal deaths and disability from perinatal asphyxia.
- Expensive technologies are not required to reduce the high burden of death and disability; engaging communities and improving timely access to quality maternal-newborn services is essential.
- New technologies and therapies will improve the diagnosis and management of newborns with birth-associated neonatal encephalopathy but the primary goal should focus on prevention.
- Quality improvement interventions should address the organization and culture of clinical care.
- More research on safer anticonvulsants and endogenous and therapeutic cooling is needed.

American Board of Pediatrics Neonatal-Perinatal Content Specifications

- Know the clinical features, diagnosis, and management of perinatal hypoxic ischemic encephalopathy.
- Know the issues in the organization of perinatal care (e.g., regionalization, transport, practice guidelines, benchmarking data, quality improvement).

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