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Pattern of neonatal seizures in Osogbo, south-western Nigeria

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Objectives. A study to determine the pattern and outcome of neonatal seizures.

Design. A prospective descriptive study.

Setting. Special Care Baby Unit, Ladoke Akintola University of Technology Teaching Hospital, Osogbo, Nigeria.

Subjects. All newborn infants with observed seizures admitted between January 2006 and December 2008.

Results. Of 866 neonates admitted, 59 (6.8%) had seizures; of these 43 (72.9%) had been born outside our health facility (outborn). Babies with seizures had a higher birth weight than babies without seizures (p=0.008), and the incidence of seizures had a linear relationship increasing with the weights of the babies and inverse to their ages. Of the 59 babies with seizures, 37 (62.7%) were considered to have had birth asphyxia. Meningitis, hypoglycaemia, and hypocalcaemia occurred in 7 (11.9%), 6 (10.2%) and 2 (3.4%) of cases, respectively, and 7 (11.9%) had undiagnosed causes. Forty-two (71.2%) of the 59 babies had both subtle and generalised seizures. Twenty-seven babies with seizures died (45.8%) compared with 131 of 807 babies without seizures (16.2%, p=0.0001). Babies with seizures and asphyxia or who had been outborn had the highest risk of death (59.5% and 48.8%, respectively).

Recommendations. The major causes of neonatal seizures and death are potentially preventable. Comprehensive and vigorous efforts are needed to achieve safe delivery, prevent birth asphyxia and improve care and transport of sick neonates at the primary care level. In view of the high prevalence of seizures among severely asphyxiated neonates and those with meningitis, anticonvulsant chemoprophylaxis is recommended in these groups.

Neonatal seizures are risk factors for long-term morbidity and neonatal mortality.[1] The presence of neonatal seizures is the best predictor of long-term physical and cognitive deficits.[1,2] Seizures are usually related to significant illnesses. There is increasing evidence that neonatal seizures have an adverse effect on neurodevelopmental outcome and predispose to cognitive, behavioural or epileptic complications in later life.[3] The precise mechanisms and pathways by which seizures in early life affect cognition later on remain elusive.[4] However, the outcome of neonates with seizures is largely dependent on the underlying cause of the convulsion and the extent of cerebral insult. Early-onset and asphyxia-induced seizures appear to have a worse prognosis.[5,6]

Recent advances in detection and management of neonatal seizures through the use of continuous electro-encephalographic (EEG) monitoring using compact digital systems with simultaneous video recording, automated seizure detection and neuro-imaging have made it possible to detect seizures with subtle manifestations. These facilities are not available in many developing countries, where such seizures can be missed or their management delayed.

This was a prospective study to determine the causation, pattern and outcome of neonatal seizures and their role in neonatal mortality among infants admitted to the Special Care Baby Unit (SCBU) of Ladoke Akintola University of Technology (LAUTECH) Teaching Hospital, Osogbo, south-western Nigeria, between January 2006 and December 2008.

Patients and methods

Newborn infants with seizures were prospectively studied. The diagnosis of a seizure was based clinically on the observation of abnormal movements, either localised or generalised, especially when these were repetitive, stereotyped, accompanied by abnormal eye deviation, and personally observed by an experienced nurse or doctor in the unit. Patients with mere jitteriness, startle reflex or tetanus were excluded. The collected data were entered into a research pro forma designed for the study.

Pregnancy, delivery and details of infant resuscitation were obtained from the mother, her relatives, or case notes and labour charts. The gestational age (GA) in weeks was determined using the mother's dates and Ballard's gestational assessment chart. Duration of labour, duration of drainage of liquor and its characteristics were all documented. The Apgar score at 1 and 5 minutes and time of initiation of respiration were noted. The length, head circumference and birth weight of each baby were recorded, and in the case of babies born outside our health facility (outborn) with no recorded birth weight, the weight at presentation was recorded as admission weight. At admission into the SCBU every neonate had a complete physical examination noting the degree of general physical and seizure activity, any congenital anomaly present, and stigmata of chromosomal disorders. Each baby was observed for presence of abnormal movements suggestive of seizures at presentation and subsequently during the course

of hospitalisation. Other abnormal signs such as respiratory distress, pallor or cyanosis were also noted.

Lumbar puncture, full blood count, measurement of electrolyte and urea, blood glucose and calcium levels, and blood, urine and cerebrospinal fluid cultures were done on all babies with seizures. We had no means of measuring blood pH, blood gases or blood and urine amino acids, or of doing viral studies. Cranial ultrasound was available, but there were no facilities in our centre for EEG monitoring or neuro-imaging such as magnetic resonance imaging and routine computed tomography scanning.

Patients were treated with intramuscular paraldehyde or intravenous diazepam to terminate seizures and were then given parenteral phenobarbitone and sometimes phenytoin sodium when phenobarbitone was unavailable. Intravenous diazepam or intramuscular paraldehyde was used for breakthrough seizures. Other definitive treatments were given as dictated by the primary cause of the seizure. These included antibiotics for bacterial infections and correction of metabolic abnormalities. Autopsies were not done on the majority of babies who died because of refusal of consent from the parents.

Hypoglycaemia was taken as a blood glucose level less than 2.20 mmol/l according to the definition then in use,[7] and hypocalcaemia as an ionised blood calcium level less than 1.75 mmol/l. Birth asphyxia was presumed in home deliveries when there was a history that the baby had failed to cry or breathe at birth, had gasped for a long time, had to be stimulated for a prolonged period of time, or was unable to suck in the first 24 hours. The Apgar score was used in all inborn infants; less than 4 in the first minutes and less than 6 at 5 minutes were regarded as significant asphyxia. Since many babies had multiple conditions or diagnoses, these were classified into main diagnoses and associated conditions or complications of the main diagnosis for easy computation of results. For example, a patient who suffered from asphyxia and hypoglycaemia was classified as having asphyxia as the main diagnosis.

Data obtained were analysed using SSPS for Windows version 11. Means and standard deviations (SD) were determined for continuous variables such as weight and were compared between the babies who had seizures and those who did not, using analysis of variance and Student's *t*-tests. Proportions and percentages were compared using the χ^2-test, $p<0.05$ being taken as statistically significant. Yates's correction was used where applicable. Multiple linear regression analysis was also used to determine the independent effects of each of the factors of mode of birth, place of birth, gender, anthropometric measurements, presence of asphyxia, hypoglycaemia and outcome on neonatal seizures.

Results

Eight hundred and sixty-six babies were admitted to the SCBU during the period of review. Of these, 59 had seizures. The incidence of seizures among neonatal admissions in our unit is therefore 6.8%. Table I shows the numbers of babies admitted from the LAUTECH Teaching Hospital ('inborn') and the various other referring centers ('outborn'). Forty-three (10.7%) of the 400 outborn babies had seizures, compared with 16 (3.4%) of the 466 inborn babies (df=1, χ^2=18.15, p=0.0001). Greater percentages of babies born at home, in mission houses, maternity clinics, mission hospitals and private hospitals and in taxis had seizures compared with babies delivered in the teaching hospital.

Babies born outside the teaching hospital had a higher mortality rate than inborn babies (108 of 400 outborn babies died, compared with 50 of 466 inborn babies (df=1, χ^2=38.2, p=0.0001)). On the other hand, there was no significant difference between inborn and outborn babies with seizures who died (df=1, χ^2=0.6, p=0.4).

The mean weight of the 59 babies with seizures was 3 810 (SD 54) g (95% CI 3 670 - 3 950) compared with 3 560 (SD 73) g (95% CI 3 510 - 3 610) for 807 babies without seizures (p=0.008). There was a linear relationship between baby weight and seizure incidence (regression coefficient -0.090; 95% CI 1.959 - 2.129) (Fig. 1).

Table II shows the diagnostic categories and the age of onset of seizures. Birth asphyxia was the main diagnosis in 37 (62.7%) of the 59 babies with seizures. All seizures in the first 24 hours of life were associated with asphyxia. Seizures following infection tended to occur at any age after 24 hours of life.

Forty-two (71.2%) of the 59 babies with seizures had both subtle and generalised seizures. Seizures were partial in 10 (16.9%) cases, and in 6 of these the left side was affected. Seven babies (11.9%) had unclassified seizures. Twenty-seven (45.8%) of the 59 babies with seizures died, compared with 131 (16.2%) of 807 babies without seizures (df=1, χ^2=32.1, p=0.0001).

Table III relates the frequency of deaths among babies with and without seizures to certain variables. The higher mortality rate among asphyxiated babies who had seizures compared with those without seizures is statistically significant ($p<0.0001$).

Discussion

The 6.8% frequency of neonatal seizures observed in the present study is higher than the 3% reported by Ment *et al.*[8] in 1982 and 4.1% by Asindi *et al.*[5] in 1990. However, subtle seizures have been reported to occur in more than 40% of neonates with seizures.[6] Connel *et al.*, who used continuous EEG monitoring, reported seizures in as many as 25% of high-risk admissions.[9] Our centre has no facility for EEG or continuous monitoring, and we are limited to assessing babies with seizures on clinical grounds alone. We are therefore probably missing some seizures.

It is critical to determine the underlying causation of neonatal seizures, as this determines prognosis and outcome and guides therapeutic strategies.[10] Birth asphyxia, infection and hypoglycaemia were the major aetiological factors for neonatal seizures in the present study, as was also found in Calabar.[5] Neonatal seizures often have multiple causes, which need to be investigated together.[7] In the present study, birth asphyxia was associated with 62.7% of seizures. This is in close agreement with the figures of 30 - 70% recorded by Volpe,[10,11] Omene *et al.*,[12,13] Finer *et al.*[14] and Mizrahi and Kellway.[15] More than 70% of the babies with seizures were outborn. Obstetric and early neonatal care facilities are inadequate in many of the outlying

The underlying causation of neonatal seizures determines prognosis and outcome and guides therapeutic strategies.

TABLE I. NUMBERS OF TOTAL AND SEIZURE ADMISSIONS FROM DIFFERENT SOURCES

	Total		Seizures		No Seizures	
	Admissions	Seizures (%)	Admissions	Deaths (%)	Admissions	Deaths (%)
Inborn						
LTH	466	16 (3.4)	16	6 (37.5)	450	44 (9.8)
Outborn	400	43 (10.7)	43	21 (48.8)	357	87 (24.4)
Government hospital	88	5			83	
Home/TBA	35	3			32	
Maternity clinics	53	6			47	
Mission hospital	61	8			53	
Mission house	21	2			19	
Private hospital	140	18			122	
In taxi	2	1			1	
Total	866	59 (6.8)	59	27 (45.8)	807	131 (16.2)

LTH = LAUTECH Teaching Hospital; TBA = traditional birth attendants.

TABLE II. AGE OF ONSET IN RELATION TO THE PRIMARY DIAGNOSIS OF NEONATAL SEIZURES

Age of onset (days)	Asphyxia	Hypoglycaemia	Sepsis/meningitis	Hypocalcaemia	Undiagnosed	Total
<1	22	0	0	0	0	22
1 - 3	9	3	2	1	1	16
3 - 7	6	2	2	1	3	14
>7	0	1	3	0	3	7
Total	37	6	7	2	7	59

TABLE III. OUTCOME IN RELATION TO SOME VARIABLES ACCORDING TO PRESENCE OR ABSENCE OF SEIZURES

	Babies with seizures		Babies without seizures			
Variable	Total admitted	No. of deaths (%)	Total admitted	No. of deaths (%)	χ^2	*p*-value
Male	38	17 (44.7)	492	68 (13.8)	25.0	0.0001
Female	21	10 (47.6)	315	63 (20.0)	8.8	0.003
Weight ≤2 490 g	11	7 (63.6)	273	76 (27.8)	4.9	0.03*
Weight ≥2 500 g	48	20 (41.7)	534	55 (10.3)	33.6	0.0001
Asphyxia	37	22 (59.5)	273	50 (18.3)	30.9	0.0001
Hypoglycaemia	6	2 (33.3)	36	4 (11.1)	0.6	0.45*
Meningitis	7	3 (42.9)	5	0 (0.0)	1.0	0.3*
Sepsis without meningitis	11	6 (54.5)	262	17 (6.5)	25.7	0.0001

*Yates' corrections applied. $p<0.05$ is significant.

health units in our area. Also, facilities for transferring sick babies are unsatisfactory. These shortcomings may predispose the babies to infections and hypoglycaemia and so worsen the severity of hypoxic ischaemic encephalopathy. With improved obstetric and neonatal care and management of birth asphyxia, the frequency of neonatal seizures should be reduced.

Hypocalcaemia accounted for 2 cases of neonatal seizures (3.4%). The cause of hypocalcaemia in the present study is not clear. Both these babies had mild birth asphyxia which was unlikely to have caused hypocalcaemia. They were full term, of appropriate weight for gestational age, and responded well to intravenous calcium gluconate. The lower percentage of seizures due to hypocalcaemia compared with Volpe's[11] study may be attributed to the high proportion of Nigerian mothers who breastfeed their babies.[5,12] The protective role of breastmilk compared with high phosphate load cow's milk, which was used in Volpe's[11] population, probably accounts for the differences.

Our finding that more than 60% of seizures presented in the first 72 hours of birth is in agreement with previous studies[5] and consistent with the recognised pattern of birth asphyxia, infection and hypoglycaemia as aetiological factors.[1]

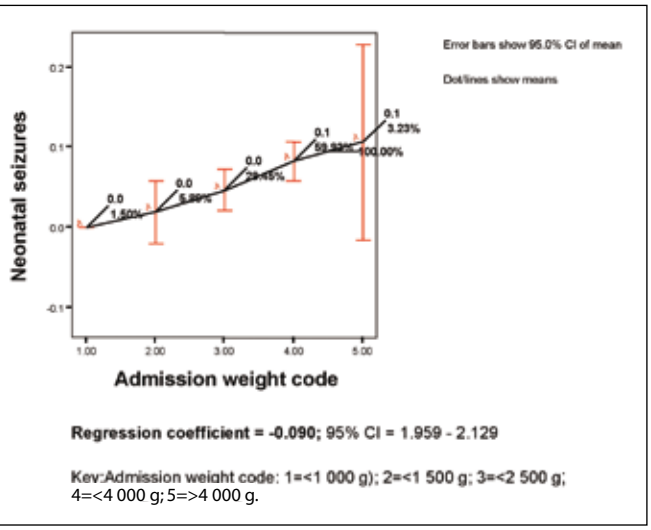

Fig. 1. Relationship between admission weight and occurrence of neonatal seizures.

The fact that seizures were not seen among the extremely low-birth-weight babies in our study, and were not commonly

encountered among the very low-birth-weight babies, may be because these babies were so ill that they did not survive to reach hospital.

More male than female babies were admitted to the SCBU. This may be because in our area male infants are more likely to be referred to hospital. The higher female case fatality rate for seizures and other conditions is in keeping with this observation.

More than 70% of the babies in our study had both subtle and generalised seizures. This is similar to the observation of Asindi *et al.*[5] and has been linked to mixed causes, which probably excite the brain cells more extensively and produce aggressive electrical discharges.[5]

Twenty-seven (45.8%) of the 59 babies with seizures died, of whom 21 had been born outside the teaching hospital. The significantly higher mortality among the outborn babies may suggest inadequate or late intervention. Our seizure-associated mortality is very high, similar to that in other Nigerian studies[5] and about four times as high as Eriksson and Zetterstrom's[16] figures. Our study also confirms that the outcome of conditions such as asphyxia, sepsis or hypoglycaemia is much worse once seizures develop. None of the babies with neonatal meningitis without seizures died. In our area many babies are still being delivered outside registered facilities, and our shortage of safe obstetric facilities and monitoring, intensive care and transport of very ill babies makes salvage difficult.

This study has a number of limitations. Firstly, our patient population may have been not representative because certain groups, such as very low-birth-weight or female babies, did not get to the hospital. Secondly, the definition of seizure relied entirely on clinical judgement. The fact that we made abnormal eye movements an important criterion for the diagnosis of seizure may have limited the number of cases of jitteriness, startle reflex or other non-seizure abnormal movements misdiagnosed as seizures, but we could well have missed a number of subtle convulsions. Thirdly, the definition of asphyxia in cases referred from outside relied on untrained observers and imprecise observations; however, the clinical picture and course were considered to be compatible. Finally, we were unable to apply more detailed diagnostic techniques such as neuro-imaging, EEG monitoring and extensive biochemical or virological testing, and were therefore restricted to limited diagnostic groups.

Our findings have, however, highlighted the major role of asphyxia in neonatal seizures and the poor outcome of neonatal conditions complicated by seizures.

To improve neonatal health and reduce the frequency of neonatal seizures, prevention of birth asphyxia and perinatal infections through the provision of effective and affordable antenatal care, safe delivery and neonatal care and facilities to transport sick babies are urgently needed. There may also be a role for anticonvulsant chemoprophylaxis among very ill babies, especially those who are severely asphyxiated or have meningitis or associated sepsis.

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