

The epidemiology of clinical neonatal seizures in Ramadi city

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A seizure is defined clinically as paroxysmal alternations in neurological function, namely, motor, behavioral, or autonomic function. Neonatal seizures tend to be brief, because immature neurons cannot sustain repetitive activity for a long time and tend to be focal or multifocal. Neonatal seizures are common: estimates of the incidence of clinical seizures in term infants range from 0.7-2.7 per 1,000 live birth and from 57.5-132 per 1,000 live birth in premature infants. Additionally, seizures occur in 1-2% of newborns in the neonatal intensive care unit.¹ Most neonatal seizures occur over only a few days and fewer than half of affected infants develop seizures later in life. Such neonatal seizures could be considered acute reactive (acute symptomatic) thus, the term (neonatal epilepsy) is not used to describe neonatal seizures. It is important to recognize the presence of seizure in the neonatal period, since they are often related to a significant underlying illness; in addition, seizures may be sustained for a considerable time, interfering with essential supportive care. Yet, the recognition of neonatal seizures is difficult as seizure activity may be subtle and because there may be marked difference of opinion on what clinical phenomena are considered to be epileptic seizures.² There are 5 major types of seizures in neonates: Focal, multifocal clonic, tonic, myoclonic, and subtle seizures. Common causes of neonatal seizure are asphyxic encephalopathy, intracranial hemorrhage, metabolic disturbance, and intracranial infection. The cause is unknown in 12%. The natural history of neonatal seizure has not been fully elucidated, although it has been observed that they are most severe during the first weeks of life and usually abate over time despite interventions.¹ The prognosis following neonatal seizures is vague. It is difficult to determine whether the neuronal injury that might follow neonatal seizures is a cause or effect. A mortality rate of 21-58% has been reported following neonatal seizure. Furthermore, neonatal seizures might have an adverse effect on neurodevelopmental progression and may predispose to cognitive, behavioral, or epileptic complications later in life.³ The present study was performed to evaluate the incidence, clinical type, and etiologic distribution of neonatal seizures in the neonatal care unit (NCU) of the Maternity and Children Hospital in Ramadi City, and to compare this with results of a previous study in Ramadi, and to see how it differs from the results of other studies.

This study was conducted in the Maternity and Children Hospital of Ramadi, the central city of Al-Anbar governorate, approximately 100 km west of Baghdad, Iraq. The NCU in this hospital is a 20-bed unit serving inpatient and outpatient delivered neonates. All neonates, including term and preterm babies, who were admitted to the NCU with seizures or who developed seizures while in the unit were included in this study. The study covers a 6-month period from the 1st of April to 1st of October 2005. Data were collected on gender, age of presentation, mode of delivery, site of delivery (inborn or outborn), preterm (<37 weeks) or term (38-42 weeks), and type of feeding. Weight and head circumference were recorded, and patients were examined for signs of sepsis and meningitis and full neurological examination was carried out. Clinical classifications of seizures were determined by the investigator. All cases were investigated for random blood sugar, serum calcium, and white blood cell count. Other neurometabolic disorders that can manifest with neonatal seizure were not investigated because tests were not available. Furthermore, neuroimaging such as CT scan and MRI were also not available. Blood culture and lumbar puncture were carried out when indicated clinically. The diagnosis of neonatal seizures was reached on a clinical basis, and EEG was not carried out as it was unavailable.

During the study period, there were 913 neonates attending the NCU. Thirty-one presented with seizures (18 boys, 13 girls). Thus, the incidence of neonatal seizures in the NCU was 34 per 1,000 admissions. Out of the 31 neonates, there were 12 (38.7%) preterm and 19 (61.3%) full term. Additionally, 15 (48.4%) delivered at home (3 preterm and 12 full term) and 16 neonates (51.6%) delivered at the hospital (9 preterm and 7 full term). The mean birth weight and head circumference for full term was 3.2 kg and 34.3 cm, and for preterm was 2.6 kg, and 32.8 cm. The mean gestational age of preterm was 32 weeks, ranging from 28-37 weeks. The total live births in our hospital during the corresponding period was 2,273 (2,134 full term and 139 preterm). Thus, the incidence of neonatal seizures was 3.3 per 1,000 live full term and 64.7 per 1,000 live preterm. Most patients presented after the first 2 days of life (61.3%). Hypocalcemia was the most common abnormal investigation (48.4%) followed by hypoglycemia (25.8%). Twenty-five neonates were investigated for blood culture and CSF examination. Positive blood culture was obtained in 6 (24%) and positive CSF results was 4 (16%). We found the subtle seizure to be the most common, occurring in 19 (61.2%) neonates followed by multifocal clonic in 4 (12.9%) neonates. Tonic occurred in 9.6%,

clonic in 9.6%, and myoclonic in 6.5%. Out of the 19 cases presenting with subtle seizures, 13 (68.4%) were full term and 6 (31.6%) were preterm. Sepsis with or without central nervous infection was the most common cause of neonatal seizures in our study (32.3%) followed by birth asphyxia (29%) (5 minute Apgar score below 7 was considered as diagnostic for asphyxia). No obvious cause could be detected in 6 patients (19.4%). Five of the neonates in this study died giving an over all mortality rate of 16.1%. Three were diagnosed to have sepsis (all of them premature), one birth asphyxia (full term), and in the fifth (preterm), the cause of death was not clear. The incidence of neonatal seizures in this study (3.3 per 1,000 live births in term neonates, and 64.7 per 1,000 live births in preterm neonates) is higher than the incidence reported from developed countries (2 per 1,000 live births in term neonates and 11.1 per 1,000 births in preterm neonates with an overall incidence of 1.8 per 1,000 live births).² The higher incidence in this study can be attributed to the higher incidence of septicemia and birth asphyxia in our hospital when compared with western hospitals. Furthermore, difficulties and personal differences in recognition of clinical neonatal seizures and lack of EEG confirmation of seizure, may contribute to this difference in the incidence, as some of the movement might not be epileptic. The study revealed a higher incidence of neonatal seizures in preterm than full term neonates (64.7 versus 3.3 per 1,000 live births). The higher incidence in preterm neonates had been documented by Ronen et al in 1999,² who found clinical neonatal seizures to be 6 times more often in preterm infants than in term infants. The higher incidence in preterm infants can be explained by increased susceptibility of premature infants to problems that might be associated with seizures, like hypoxic ischemic encephalopathy, sepsis, and metabolic derangement. Hypocalcemia was the most common abnormal finding on investigation in our study (48.4%). Neonatal seizures per se, are not a diagnosis, but are a presentation of an underlying pathology. Biochemical disturbances are one of the most important underlying pathologies. These biochemical disturbances could occur as an underlying cause or associated phenomena. This study reveals hypocalcemia to be an associated phenomenon in most cases, as its account for only 6.5% of the final diagnosis. The same is applicable for hypoglycemia. The higher incidence of hypocalcemia and hypoglycemia in this study can be attributed to the higher incidence of birth asphyxia and sepsis as a cause for neonatal seizures in our study. Sood et al,⁴ reported biochemical abnormalities in 38.8% of non-metabolic seizures in neonates. As in most studies, subtle seizures were the most common, occurring in

61.2% followed by multifocal clonic (12.9%). The results of our study agree with the general concept that subtle seizures are more common in full term than preterm infants. The reason is probably related to maturation of the brain. Some studies revealed that neonates with seizures might express 2 or more seizures types; this is not the case in our study as none of the neonates had more than one seizure type. The recognition of the clinical type of neonatal seizure is important for it has an influence on the out come of the seizure. The Collaborative Prenatal Project highlights this issue in their review of 181 survivors of neonatal seizures.⁵ Tonic and myoclonic seizures were the only types related to the outcome. Additionally, a multivariate analysis of 131 patients with neonatal seizures indicated that only tonic seizures are associated with adverse outcome. The authors cited the high occurrence of structural brain disease with this seizure type as the probable cause.⁶ The study identified septicemia with or without central nervous system infection as the most common cause for neonatal seizures in our hospital accounting for 32.3% of these cases. This result is in contrast to the experience from different parts of the world, which reports hypoxic ischemic encephalopathy as the most common cause.² Furthermore, the incidence is higher than reported previously from Ramadi city (25%),⁷ and from other countries (20-24%).² The higher incidence of infection as a cause of neonatal seizures in our hospital indicates that sepsis is still an important cause for morbidity in this vulnerable age group. The study showed small numbers of seizures were due to metabolic abnormalities, accounting for 19.4%. This agrees with a study by Ronen et al,² who reported 19%, and a study by Sood et al⁴ in India, who reported 16.9%. We could not investigate some rare metabolic causes for neonatal seizures, for example, hypomagnesemia and pyridoxine deficiency due to shortage of facilities. The cause of neonatal seizures in this study was undetermined in 6 patients (19.4%). Lack of essential investigations for diagnosing some causes of neonatal seizures is probably the cause. Eleven to twelve percent of neonatal seizures remain undiagnosed in western countries. The overall mortality rate of 16.1% in our study is lower than that reported in our hospital a few years ago by Al-Ezzi⁷ (29.3%), and in Baghdad (21.2%). An over all mortality rate of 21-58% has been reported following neonatal seizures. This difference may be related to the difference in sample size and competency of the health services.

The present study has several limitations including being hospital based, lack of complementary tests such as EEG, neuroimaging, and metabolic tests and investigations for neurometabolic and malformative disorders that might present in a similar way to sepsis

and asphyxia and could not be ruled out in this study. However, from the results of this study we can conclude that the incidence of clinical neonatal seizures in Ramadi is higher than that reported from other places and clinical neonatal seizure occurred 17 times more often in preterm than full term infants. Investigations for rare causes of neonatal seizures should be available soon. Control of infection in the NCU, with such measures as strict isolation and continuous surveillance of culture and sensitivity in the NCU environment is essential to reduce the incidence of neonatal seizures.

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