

Prevalence of Neonatal Convulsion in Yemeni Children -A Hospital Based Study

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Abstract: Background: Seizure is a common neurological problem in small children, mainly seen at neonatal period. Neonatal seizures have always been a topic of interest because of their universal occurrence. It contributes significantly to neonates morbidity and mortality particularly in developing countries including Yemen. A varied number of conditions are capable of causing seizures in the neonatal period.

Objectives: study to determine the pattern, incidence and outcome of neonatal seizures.

Design: A prospective Descriptive study.

Setting: Pediatric unit, AL Salam Hospital (PUAH), Sadah, Yemen.

Subjects: All newborn infants with observed seizures admitted between July 2013 - Aug 2015.

Methods: A Hospital based prospective observational study was undertaken in the Pediatric unit AL Salam Hospital (PUAH) over two years period(July 2013 - Aug 2015) , All neonates < 28 days of life with observing of abnormal movements (seizures) were admitted in this unit. Detailed antenatal, natal and postnatal history was taken and examination of baby was done. Then, relevant investigations including biochemical parameters were done. Data were analyzed using SSPS for Windows version 10.

Results: Of 1732 admitted neonates 62.6% were males and 37.4% were females. The incidence of neonatal seizures in this pediatric unit was 68 per 1,000 admissions. Out Of 1732 neonates admitted, 118 (6.8%) had seizures; of these 86 (72.9%) had been born outside hospital (out-born). The incidence of neonatal seizures in Pediatric unit, AL Salam Hospital (PUAH) with seizures had a higher birth weight than babies without seizures ($p=0.008$), Of 118 babies with seizures, 74 (62.7%) were considered to have had birth asphyxia, 14(11.9%) Meningitis, 12(10.2%) hypoglycemia, 4(3.4%) hypocalcaemia and 14 (11.9%) had undiagnosed causes.

Eighty Four (71.2%) of the 118 babies had both subtle and generalized seizures. Fifty Four babies with seizures died (45.8%) compared with 262 of 1614 babies without seizures (16.2%, $p=0.0001$). Babies with seizures and asphyxia or who had been out born had the highest risk of death (59.5% and 48.8%, respectively).

Conclusion: Birth asphyxia was the main cause of 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. Major presentation of babies with seizures were both subtle and generalized seizures. The higher mortality rate among asphyxiated babies had seizures compared with those without seizures. Babies born outside this hospital had a higher mortality rate than those inborn babies.

Keywords: birth asphyxia, neonate, seizure, mortality.

Introduction

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 births and from 57.5-132 per 1,000 live births in premature infants (1). Additionally, seizures occur in 1-2% of newborns in the neonatal intensive care unit (1). A seizure is the most frequent sign of neurological dysfunction in the neonate (2,3). Due to immature developing brain in neonates, so neonatal seizures may adversely affect cerebral functions and may cause significantly damage to brain's neonates than in older children in high risk infant(4). Historically seizures were divided in following clinical categories viz. focal clonic, multifocal clonic, tonic, myoclonic, & subtle seizures.(5)Multiple medical conditions in the newborn can be associated with neonatal seizures, Hypoxia-ischemia is nonetheless traditionally considered the most common cause of neonatal seizures (5,6). The presence of seizures in sick neonates may be associated with increased risk of long-term neurologic sequelae and/or death.[7]

The nature and severity of the neurologic process causing neonatal seizures has been reported as a major determinant of outcome (8,9,10).Some babies with neonatal seizures seem to recover without overt sequelae while the others die or survive with neurologic deficit (10-12). Early-onset and asphyxia-induced seizures appear to have a worse prognosis(13,14).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(15). 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, incidence and outcome of neonatal seizures and their role in neonatal mortality among infants admitted to Pediatric unit AL Salam Hospital (PUAH), Sadah, Yemen, between July 2013 - Aug 2015.

Patients and methods

The usual diagnosis of a seizure was based clinically on the observation of abnormal movements, either localized or generalized, especially when these were repetitive, 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 designed study file. The Pregnancy, delivery and details of infant resuscitation were obtained from the mother, her relatives, or case notes and labor record files. The gestational age was determined using the mother's dates and intrauterine fetal ultrasound. Duration of labor, 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 head circumference and birth weight of each baby were recorded, and in the case of babies born outside our hospital (out-born) with no recorded birth weight, the weight at presentation was recorded as admission weight. At admission into the Pediatric unit AL Salam Hospital (PUAH), 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 hospitalization. Other abnormal signs such as respiratory distress, pallor or cyanosis were also noted. Investigations like Lumbar puncture, full blood count, measurements 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 urine amino acids, or of doing viral studies. Cranial ultrasound was available, but there were no facilities in our center for EEG monitoring or neuro-imaging such as magnetic resonance imaging and routine computed tomography scanning. The affected neonates with seizures were treated with intravenous diazepam, parenteral phenobarbitone and sometimes phenytoin sodium. Other definitive treatments were given as depend upon the primary cause of the seizure. These included antibiotics for bacterial infections and correction of metabolic abnormalities. Hypoglycemia was taken as a blood glucose level less than 40 mg.dl (2.20 mmol.l) according to the definition then in use (16) and hypocalcaemia as an ionized blood calcium level less than 7mg.dl (1.75mmol.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 hypoglycemia was classified as having asphyxia as the main diagnosis.

Our collected Data were analyzed using SPSS for Windows version 10. Means and standard deviations (SD) were determined for continuous variables such as weight and compared between the babies who had seizures and those who did not, using analysis of variance and Student's f-tests. Proportions and percentages were compared using the χ^2 -test, $p < 0.05$ being taken as statistically significant.

Results

One thousand seven hundred and thirty two babies were admitted to the (PUAH), during two years period of study. Of these 118 had seizures. The frequency of seizures among neonatal admissions in our unit is therefore 6.8%, and their incidence was 68.0 per 1000 neonates admission.

Table 1, shows the diagnostic categories and the age of onset of seizures. Birth asphyxia was the main diagnosis in 74 (62.7%) of the 118 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.

Eighty four (71.2%) of the 118 babies with seizures had both subtle and generalized seizures. Seizures were partial in 20 (16.9%) cases, and in 12 of these the left side was affected. Fourteen babies (11.9%) had unclassified seizures. Fifty four (45.8%) of the 118 babies with seizures died, compared with 262 (16.2%) of 1614 babies without seizures ($df=1, \chi^2=32.1, p=0.0001$).

Table 1: Time of seizures onset with main cause (Diagnosis) :

Age of onset (days)	<1	1-3	3-7	>7	Total
Asphyxia	44	18	12	0	74
Hypoglycemia	0	6	4	2	12
sepsis/meningitis	0	4	4	6	14
Hypocalcaemia	0	2	2	0	4
undiagnosed	0	2	6	6	14
Total	44	32	28	14	118

The higher mortality rate among asphyxiated babies who had seizures compared with those without seizures is statistically significant ($p<0.0001$).

The baseline characteristics of the neonates: sex distribution- 1732 neonates were admitted in two years out of which 62.58% were males and 37.42% were females (Table 4). The admission of inborn neonates (53.8%) was more than out born neonates (46.2%). This may indicate that, the people over there (pregnant females) prefer to deliver at hospital rather than home for neonatal proper health care.

Table (3) shows the total numbers of babies admitted in our hospital, ('inborn') and the various other referring centers ('outborn'). Eighty six (10.7%) of the 800 outborn babies had seizures, compared with 32 (3.4%) of the 932 inborn babies ($df=1 \chi^2=18.15, p=0.0001$). Greater percentages of babies born at home, with midwife/senior old lady houses, in maternity clinics, basic health unit, dispensaries and private hospitals and in taxis had seizures compared with babies delivered in our hospital.

Table 2: Relation of mortality to other factor (variables) based on Available/absent of seizures:

Factor (Variable)	Total admitted seizures	No. of seizure's death (%)	Total Admission with no seizures	No. of deaths without seizures(%)	X2	p-value
Male	76	34 (44.7)	984	136 (13.8)	25	0.0001
Female	42	20 (47.6)	630	126 (20.0)	8.8	0.003
Weight <2 490 g	22	14 (63.6)	546	152 (27.8)	4.9	0.03
Weight >2 500 g	96	40 (41.7)	1068	110 (10.3)	33.6	0.0001
Asphyxia	74	44 (59.5)	546	100 (18.3)	30.9	0.0001
Hypoglycemia	12	4 (33.3)	72	8 (11.1)	0.6	0.45
Meningitis	14	6 (42.9)	10	0 (0.0)	1	0.3
Sepsis without meningitis	22	12 (54.5)	524	34 (6.5)	25.7	0.0001

Babies born outside this hospital had a higher mortality rate than those inborn babies (216 of 800), compared with 100 of 932 inborn babies ($df=1, \chi^2=38.2, p=0.0001$). On the other hand, there was no significant difference between inborn and outborn babies with seizures who died ($df=1, \chi^2=0.6, p=0.4$). The mean weight of the 118 babies with seizures was 3 810 (SD 54) g (95% CI 3670 - 3 950) compared with 3 560 (SD 73) g (95% CI 3 510 - 3 610) for 1614 babies without seizures ($p=0.008$). From this, it was noted that there is a positive proportion of neonatal weight and the seizures.

Table 3: Relation of total convulsing neonates admission to their coming places :

Factor (Variable)	Total admission	Total Seizures (%)	no. of admitted seizures	no. of seizures with Deaths (%)	no. of Admissions with no seizures	no. of Deaths with no seizures (%)
Inborn at PUAH	932	32 (3.4)	32	12	900	88 (9.8)
Out-born	800	86 (10.7)	86	42 (48.8)	714	174 (24.4)
Government hospital	176	10			166	
Home(self/old lady)	70	6			64	
Maternity clinics	106	12			94	

Factor (Variable)	Total admission	Total Seizures (%)	no. of admitted seizures	no. of seizures with Deaths (%)	no. of Admissions with no seizures	no. of Deaths with no seizures (%)
Basic health unit	122	16			106	
Dispensary	42	4			38	
Private hospital	280	36			244	
In taxi	4	2			2	
Total	1732	118 (6.8)	118	54 (45.8)	1614	262 (16.2)

PUAH:: Pediatric unit, AL Salam Hospital

Table 4 : sex distribution of the admitted neonates:

Sex	In born n=932	(%)	Out born n=800	(%)	Total (%)
Male	550	59.1	534	66.84	1084 62.58
Female	382	40.9	266	33.16	648 37.41
Total	932	53.8	800	46.18	1732 100

Discussion:

The 6.8% frequency of neonatal seizures observed in this present study is higher than the 3.4% reported in Iraq, Ramadi city by Essam J AL Zawaini et al (17) in 2006 and 4.1% by Asindi et al(12).in 1990.

However, subtle seizures have been reported to occur in more than 40% of neonates with seizures(15,18) Connel et al., who used continuous EEG monitoring, reported seizures in as many as 25% of high-risk admissions(15,18). Our center 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. Moreover, the incidence of neonatal seizures in our study was 68.12 per 100 admitted neonates which is higher than that study at Ramadi city Iraq on 2006 which was 34 per 1000 admitted neonates(17), but still our incidence was lower than same study done at Nigeria on 2007 by Tinuade et al (18).It is critical to determine the underlying causation of neonatal seizures, as this determines prognosis and outcome and guides therapeutic strategies(2,19).birth asphyxia, infection and hypoglycemia were the major etiological factors for neonatal seizures in the present study, as was also found at Nigerian study in Calabar(6-8,12,14,18). Neonatal seizures often have multiple causes, which need to be investigated together(16). 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,(5,13) Omene et al (11,14) Finer et al(20).and Mizrahi and Kellway (19). More than 70% of the babies with seizures were outborn. Obstetric and early neonatal care facilities are inadequate in many of the Health units in our country, Also, facilities for transferring sick babies are unsatisfactory. These shortness/inadequate services may predispose the babies to infections and hypoglycemia and so worsen the severity of hypoxic ischemic encephalopathy. With improved obstetric and neonatal care and management of birth asphyxia, the frequency of neonatal seizures should be reduced. Hypocalcaemia accounted for 4 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 (5,13) study may be attributed to the high proportion of Yemeni mothers who breastfeed their babies. the protective role of breastmilk compared with high phosphate load cow's milk, which was used in Volpe's(5,13) population, probably accounts for the differences.

Our finding that more than 60% of seizures presented in the first 72 hours of birth as in agreement with previous studies (12) in Nigeria and consistent with the recognized pattern of birth asphyxia, infection and hypoglycemia as etiological factors(21).

The fact that seizures were not seen among the extremely low birth weight baby's in our study, and were not seen among the very low-birth-weight babies, may be because these babies were so ill that they did not survive to reach hospital.

More males than females babies were admitted to the PUAH. 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 generalized seizures. This is similar to the observation of Asindi et al (12),and has been linked to mixed causes, which probably excite the brain cells more extensively and produce aggressive electrical discharges (12).Fifty four (45.8%) of the 118 babies with seizures died, of whom 42 had been born outside the hospital. The significantly higher mortality among the outborn babies may be due to inadequate or late intervention. Our neonatal seizure-associated with mortality is very high, to compare to that study in Nigerian studies(12) and it's about four times as high as Eriksson and Zetterstrom's (22) figures.

Our study also confirms that the outcome of conditions such as asphyxia, sepsis or hypoglycemia is much worse with high mortality once seizures develop. In our area many babies are still being delivered outside hospital (registered health facilities), and our shortage of safe obstetric facilities and monitoring, intensive care and transport of very ill babies makes their life saving difficult. This study has limitations; Firstly, our patient of very low-birth-weight, may not be seen at this study .Secondly, the definition of seizure

relied 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 miss 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. Our findings have 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.

Author contributions: AK Sallam contributed to study design, literature search, data acquisition, data entry, statistical analysis, manuscript preparation and takes responsibility for the study as a whole.

AL Selwi AM Abdul Hakeem contributed to data collection, literature search, manuscript editing and critical appraisal of the manuscript.

AL Bahlooly AH Mohd contributed to, data collection, literature search and also helped in data entry and manuscript preparation. All authors have read and approved the final manuscript.

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معدل انتشار تشنجات حديثي الولادة في الأطفال اليمنيين - دراسة معتمدة على المستشفى.

المخلص: الخلفية: التشنج هو مشكلة عصبية مشتركة في الأطفال الصغار، ينظر أساساً في فترة حديثي الولادة. وكانت تشنجات حديثي الولادة دائماً موضوع اهتمام بسبب حدوثها العالمي. ويساهم بشكل كبير في اعتلال المواليد والوفيات وخاصة في البلدان النامية بما في ذلك اليمن. وهناك عدد متنوع من الظروف تكون قادرة على التسبب في النوبات في فترة الوليد.

الأهداف : دراسة لتحديد نمط، حدوث ونتائج التشنجات لحديثي الولادة.

التصميم : دراسة وصفية مستقبلية.

الإعداد : وحدة طب الأطفال، مستشفى السلام، صعدة، اليمن.

إطار الحالة: جميع الأطفال حديثي الولادة الملاحظ عليهم التشنجات أثناء رقدتهم في المستشفى بين يوليو 2013 - أغسطس 2015 .
الطريقة: أجريت دراسة مراقبة مستقبلية مستندة إلى المستشفى في وحدة طب الأطفال مستشفى السلام على مدى عامين (يوليو 2013 - أغسطس 2015)، تم قبول جميع الولدان أقل من 28 يوماً من العمر مع مراقبة الحركات الغير طبيعية (التشنجات) في هذه الوحدة. تم أخذ تاريخ مفصل لفترة ما قبل الولادة والولادة وبعد الولادة وفحص الطفل. ثم أجريت تحقيقات ذات صلة بما في ذلك الفحوصات الكيميائية الحيوية. تم تحليل البيانات باستخدام جهاز نظام الإحصاء لنظام التشغيل ويندوز الإصدار 10 .
النتائج: بينت النتائج أن من بين 1732 من الأطفال المرقيدين حديثي الولادة، كان 62.6 في المائة من الذكور و 37.4 في المائة من الإناث. وكانت نسبة معدل حدوث نوبات التشنج للولدان في هذه الوحدة 68 لكل 1000 حالة رقاد ومن أصل 1732 رقاد لحديثي الولادة، 118 (6.8%) كانت لديهم تشنجات. ومن بين هؤلاء 86 (72.9%) قد ولدوا خارج المستشفى. كان معدل إصابة الأطفال حديثي الولادة في وحدة طب الأطفال بمستشفى السلام بالتشنجات كان لديهم وزن أعلى مقارنة بالمواليد من غير تشنجات ، ومن أصل 118 مولود مع تشنجات كانت 74 (62.7%) اعتبر لديهم الاختناق الوليدي، 14 (11.9%) التهاب السحايا، 12 (10.2%) نقص السكر في الدم، 4 (3.4%) نقص عنصر الكالسيوم في الدم و 14 (11.9%) أسباب غير مشخصة.

وكان من بين 118 مولود 84 (71.2%) لديهم تشنجات دقيقة وعامة. وقد توفي 54 مولود مع تشنجات (45.8%) مقارنة مع 262 من 1614 طفل دون تشنجات (16.2%). وكان المواليد مع التشنجات والاختناق الوليدي أو من المواليد خارج المستشفى كانت لديهم مخاطر الموت أعلى (59.5% و 48.8%) على التوالي.

الاستنتاج: اختناق الولادة كان السبب الرئيسي للأطفال الذين يعانون من التشنجات. وجميع التشنجات في ال 24 ساعة الأولى من الحياة كانت مصاحبة للاختناق الوليدي. وكانت التشنجات المتبوعة للعدوى تميل إلى أن تحدث في أي عمر بعد 24 ساعة من الحياة. وبالعرض الرئيسي للأطفال مع التشنجات كانت تلك التشنجات دقيقة وعامة. وكانت نسبة ارتفاع معدل الوفيات بين الأطفال المواليد خارج المستشفى أعلى من المواليد بداخل المستشفى.

الكلمات المفتاحية: اختناق الولادة، الوليد، التشنجات، والوفيات