ETIOLOGICAL STUDY OF SEIZURES IN NEONATES

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ABSTRACT

Objective: To determine the incidence and etiology of seizures among neonates admitted to Nursery unit of Hayatabad Medical Complex, Peshawar.

Methodology: This descriptive study was conducted at Hayatabad Medical Complex, Peshawar, Pakistan from January to December 2011. During the study period, all admitted neonatal cases were examined and data on neonatal seizures was ascertained. Among admitted neonates, having seizures either at presentation or during their stay in the hospital were investigated for its cause. Cases with clinical diagnosis of neonatal tetanus were excluded from the study. In order to determine the etiology of seizures, metabolic profile including blood glucose, serum calcium and sodium levels and other necessary tests were done in all cases. A proforma was designed comprising detailed history, general physical examination, systemic examination and relevant investigations. Data was recorded for analysis.

Results: Seizures were observed in 159/1583 (9.95%) of neonatal admissions and 55.88% neonates had seizures during the first 72 hours of life. Commonest types of seizures observed in this study were subtle (39.6%) followed by tonic (31.4%), clonic (25.10%) and myoclonic (3.70%) seizures. Hypoxic ischemic encephalopathy was found to be the commonest cause (44%) of neonatal seizures, followed by hypoglycemia (18.8%) and hypocalcemia (12.5%). Cases of hypoxic ischemic encephalopathy were associated with higher mortality (42.85%) as compared to cases with metabolic seizures.

Conclusion: Neonatal seizures were found in about 10% of neonatal admissions and presented most commonly as subtle type. Birth asphyxia was the commonest etiology of neonatal seizures, followed by the metabolic causes.

Key words: Seizures, Etiology, Neonates, Birth Asphyxia, Hypoglycemia, Hypocalcemia.

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INTRODUCTION

The first month of life is one of the highest risk periods for seizures which constitute the most common manifestation of neurological conditions in the neonates. Neonatal seizures have been shown to be a major risk factor for in-patients mortality and subsequent neurological disability. Worldwide, 130 million children are born in a year and three quarters of them are in developing countries[1]. Out of 5.3 million children born every year in Pakistan, majority of deaths take place during early days of neonatal period[2].

Survival of a neonate always remains a matter of great concern in any society. As Pakistan's neonatal mortality rate is very high (49/1000 live births) accounting for 7% of global neonatal deaths[3], therefore, recognition of underlying factors and diseases leading to neonatal mortality becomes very important. Seizures in neonates are one of the most important neurologic events which contribute not only to increased mortality but also to long term sequelae.[4,5] In Pakistan, incidence of neonatal seizures has been reported as 4.8% in hospitalized neonates.[6]

Recognition of the contributory factors towards neonatal seizures would enable us to identify the quantum of a problem in our circumstances. Moreover this may also provide an opportunity to devise effective strategies for the reduction of morbidity and mortality caused by the neonatal seizures. In order to find out the incidence of seizures among admitted neonates and identify the common etiological factors, a prospective study was performed at the neonatal unit of Hayatabad Medical Complex, Peshwar, Pakistan.

METHODOLOGY

This hospital based descriptive study was conducted in the Neonatal unit of Hayatabad Medical Complex, Peshawar. All admitted neonates from 1st January 2011 to 31 December 2011, having seizures either at presentation or during their stay, were investigated especially for cause of seizures. Cases with clinical diagnosis of neonatal tetanus were excluded from the study.

A detailed history including gestational age, mode of delivery, birth events, Apgar scores and antenatal problems was recorded. Age of onset of seizures and frequency was also noted. Seizures were classified as subtle, clonic, tonic or myoclonic on the basis of detailed description[7]. Consent of the parents/ caregivers was taken and a thorough physical examination at the time of presentation or onset of seizures was carried out including neurological assessment to stage the level of asphyxia. The data was analyzed by SPSS version 10.

In order to determine the etiology of seizures, metabolic profile including blood glucose, serum calcium and sodium levels were done in all cases. Serum magnesium, arterial blood gas analysis and serum bilirubin levels were done in selected cases. In cases of suspected septicemia, full septic work-up including complete blood counts, blood cultures and CSF examination with culture was done. Cranial ultrasound and CT scan was done in cases where diagnosis of Intracranial hemorrhages (ICH) or post-asphyxial brain damage was considered. EEG was performed in very few cases of intractable seizures. For rare causes of inborn errors of metabolism, screening tests including serum ammonia level, urinary ketones and reducing substances were performed.

TABLE I: NEONATAL SEIZURES: AGE DISTRIBUTION (n=159)

Age	Frequency (n=159)	%age
< 1 day	48	30.18
1-3 days	41	25.7
4-7 days	30	18.8
> 7 days	40	25.15

TABLE II: TYPES OF NEONATAL SEIZURES (n=159)

Types of Seizures	Frequency (n=159)	%age
Subtle	63	39.60
Tonic	50	31.40
Clonic	40	25.10
Myoclonic	6	3.70

RESULTS

Out of 1583 neonates were admitted to the neonatal unit of the Hayatabad Medical Complex, Peshawar, 159/1583 (10%) neonates met the entry criteria.

Out of 159 cases, 90 (56.6%) were males and 69 (43.4%) were females. Forty-eight (30.18%) neonates had their first seizure within 24 hours of birth, 89 (55.97%) had seizures in the first 72 hours (Table I).

Commonest type of seizures observed in this study were subtle (39.6%) followed by tonic (31.4%), (Table II). Majority of patients (72.32%) had multiple episodes of seizures compared with those having single episode (27.68%).

Hypoxic ischemic encephalopathy (HIE) was the common etiological factor (44%) for neonatal seizures followed by metabolic causes (31.4%), infections (15.72%) and intracranial hemorrhage (3.14%). Among metabolic causes, hypoglycemia was the commonest factor accounting for seizure activity in 30 (18.8%) cases, 20 (12.5%) had hypocalcemia. Neonatal sepsis was diagnosed in 25 (15.72%) cases, with supportive evidence of sepsis, out of which 17 (10.69%) also had evidence of bacterial meningitis.

More than one etiological factor was diagnosed in several cases. Amongst the rare causes, 4 cases had kernicterus. Five cases (3.14%) remained undiagnosed, in spite of performing all available tests. Neonatal death occurred in 41 (25.8%) cases. The commonest cause of mortality was severe birth (73.17%), metabolic causes (12.2%) and Intracranial hemorrhage (7.3%) as shown in Table III.

DISCUSSION

Neonatal seizures have unique properties that have proved challenging for both clinicians and basic science researchers. Seizures represent the most distinctive signal of neurologic disease in the newborn period. After a dramatic occurrence, they are the most frequent cause of neonatal neurologic disorders.

Neonatal seizures are an important example of age-specific seizure syndrome. Compared with seizures in older ages, neonatal seizures differ in etiology[8],

TABLE III: NEONATAL SEIZURES: ETIOLOGICAL FACTORS IN RELATION TO OUTCOME (n=159)

Diagnosis		Total (n=159)		Died (n=41)		Survived (n=118)	
		Frequency	%	Frequency	%	Frequency	%
Hypoxic ischemic encephalopathy (n=70; 44.03 %)		70	44.03	30	73.17	40	33.9
Metabolic (n=50; 31.44%)	Hypoglycemia	30	18.87	0	0	30	25.42
	Hypocalcaemia	20	12.58	0	0	20	16.95
Infections (n=25; 15.72 %)	Pyomeningitis	17	10.69	3	7.31	14	11.86
	Septicemia	8	5.03	2	4.88	6	5.08
Miscellaneous (n=14; 8.81 %)	Intracranial hemorrhage	05	3.14	03	7.32	02	1.7
	Kernicterus	04	2.52	02	4.88	02	1.7
	Unidentified Group	05	3.14	01	2.44	04	3.39

clinical manifestations[9], electroencephalographic signature[10], management plan[11] and prognosis.[12] They are usually poorly organized and often focal. Generalized tonic clonic convulsions tend not to occur during the first month of life because of brain immaturity. A seizure discharge is usually not propagated throughout the neonatal brain to produce a generalized seizure.[13]

Neonatal seizures are unique and require special classifications. They can be classified in a number of ways e.g. clinical presentations of seizure i.e. tonic, clonic, myoclonic and subtle; presence of EEG findings or site of brain involvement or time of first appearance of seizures. In all these classifications, common identifiable causes include hypoxic ischemic encephalopathy, infections, metabolic derangements, developmental anomalies and intracranial hemorrhage (ICH)[14].

In the present study, 159 cases were found to have seizures. The incidence 9.95% is comparable with other studies[15,16] ranging from 1.5 to 14%. Incidence rate usually varies in population based and institution based studies, being lower in population based studies[16] (1.8%-4.4%) as compared to institution based studies[6]. In a study conducted in Lahore[6], it was estimated that only 35-40% of children in the community may have been admitted to hospital. It is also worth noting that up to two-thirds of deaths in children <5 years in the developing countries occur outside the hospital and this proportion may even be higher among neonates since the majority are born at home[15,17]. Thus, our data could have greatly underestimated the incidence of seizures in this community. Despite the above caveats, the study suggests that the incidence of neonatal seizures in this setting is much higher than that reported from developed nations[18] and this may reflect the high prevalence of risk factors for neonatal brain insult in this community.

Very few other centers in under developed countries have attempted to quantify the burden of neonatal seizures. In Kenya, the estimated incidence was 14%[19]. Similarly in Ethiopia, the incidence was found to be 13.6 %[20].

Among the etiological factors, hypoxic ischemic encephalopathy was found to be the commonest cause of seizures (Table-III); this tendency is noted all over the world.[4,18] In population based studies conducted in California[21] and Canada[16] over a period of five years, HIE was found to be the commonest cause of neonatal seizures. Another local study from Faisalabad[22] has also reported similar results.

The factors leading to birth asphyxia were multiple. They included maternal hypertension, uncontrolled diabetes mellitus, cord prolapse and compression, meconium aspiration and obstructed prolonged labour[23]. In majority of cases, no regular antenatal visits were found. Mothers usually presented an emergency with history of Dai handling, prolonged leaking per vaginum and bleeding, with evidence of fetal distress.

The second common group of metabolic causes included hypoglycemia and hypocalcemia. Prematurity and poor feeding in early neonatal age also caused hypoglycemia. It was frequently noted in mothers who had undergone cesarean section and babies without feeding in the initial few hours of life. Hypocalcemia alone was found more common in premature babies as a cause of true seizures. Next in frequency, infections were found as etiological diagnosis in neonates with seizures. Nearly 16% cases had evidence of neonatal infections. Among these 10.69% cases had meningitis and 5% cases had septicemia. Other studies show some difference with frequency ranging from 10-25%.[19,20] Prolonged rupture of membranes and maternal fever were the major risk factors for neonatal sepsis leading to seizures.

Other causes of seizures were intra-cranial hemorrhage and kernicterus. In 3% cases, despite all available investigations, no cause was detected ("unidentified" group). This proportion is even comparable with studies at centre having recent advanced diagnostic facilities.[25]

In the present study, neonatal seizures were found to be commoner in males than female babies (1.3:1). This finding is consistent with previous studies.[16] Similarly seizures were more common (56%) in first 3 days of life, compared to 19% cases in 3-7 days and 25% cases in age group > 7 days (Table-1). Gabriel et al[16] has reported in their study that 70% seizures occurred in the first 3 days and 83% in the first week of life.

Subtle seizures were found commonest in the present study (Table-II), consistent with other studies.[6,24] Better sensitization of resident and nursing staff can lead to higher detection rate from neonatal centers. Regarding the type of seizures, certain studies differ from our results like generalized tonic seizures were found being the commonest type in study by Azam et al[24] and multifocal clonic by Malik et al[22].

We have found a group fatality rate of 25.8%. This is within the range (18% to 63%) reported in clinical based studies of neonatal seizures.[19,20] The relatively high mortality rate is secondary from increased admission of critically ill, severely asphyxiated neonates in neonatal unit of tertiary care centers and included in this study.

Hypoxic ischemic encephalopathy was the commonest cause of neonatal seizures, followed closely by the metabolic causes and sepsis. Greater awareness regarding the health of the mother, importance of neonatal visits, hospital deliveries by trained staff, early breast feeding and detection of sick cases with early referral is required to minimize the incidence of birth asphyxia, infections and hypoglycemia. It is thought that morbidity and mortality from neonatal seizures can be prevented to a certain extent by taking these simple measures. Broad measures, such as ensuring safe deliveries, appropriate neonatal resuscitation, prevention

and early treatment of infections in the newborn period, early breast feeding and detection of sick cases with early referral is required to minimize the burden.

CONCLUSION

Neonatal seizure is not an uncommon neurological disorder and was found in about 10% of neonatal admissions and presented most commonly as subtle type. Birth asphyxia was the commonest etiology of neonatal seizures, followed by the metabolic causes. Mortality rate in neonatal seizures is quite high in our hospitalized patients.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

FUS: Conception and design, Acquisition of data; Analysis and interpretation of data, Drafting the manuscript, Final Approval of the manuscript

MJ & MAK: Acquisition of data; Critical revision, Final Approval of the manuscript

CONFLICT OF INTEREST

Author declares no conflict of interest

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