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FREQUENCY, ETIOLOGICAL PROFILE AND MORTALITY OF NEONATAL SEIZURE DISORDERS

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ABSTRACT:

Objective: To determine the frequency, etiological profile and mortality in neonates with seizure disorders.

Study Design and setting : prospective study at National Institute of Child Health (NICH) Karachi from January 15th 2011 to 16th September 2011.

Material and Method: A total of 115 neonates (1 -28 days) with various types of seizures were enrolled after explaining purpose and procedure of the study, consent was taken from parents. Their detailed history, physical examination and appropriate investigations were recorded on a predesigned proforma. Data was analyzed using descriptive statistics.

Results: Out of a total 3240 admissions, 115 neonates (3.54%) presented with seizures. Birth asphyxia was the leading cause and found in 45(39.13%) of neonatal seizure disorders (NSDs). Hypoglycemia and hypocalcaemia was found in 35(30.43%) of the cases while 18 (15.65%) had infections like meningitis and sepsis. The common type of seizures observed were subtle (44.35%) followed by focal (27.83%), clonic (20.87%) and myoclonic types (6.95%).The overall mortality was 26 %. Brain malformations, Intracranial hemorrhage, kernicterus, birth asphyxia and infections were responsible for the mortality in 66.67%, 42.85%, 40%, 37.77% and 27.77% of cases respectively. There was no death attributed to metabolic causes.

Conclusion: In this study frequency of neonatal seizure disorders observed was 3.54%. Birth asphyxia, metabolic causes and infections has been observed to be the common cause of seizures in neonates. Brain malformation, intracranial hemorrhage, kernicterus, birth asphyxia and infections were significant contributors to mortality. Metabolic group had a favourable outcome.

KEY WORDS: Seizures. Birth asphyxia.

INTRODUCTION

Neonatal seizure disorders (NSDs) remain a diagnostic and therapeutic challenge to the clinician and are a known cause of morbidity and mortality. The most important factor that predicts the outcome is the underlying etiology. Common causes of neonatal seizure are birth asphyxia, metabolic disorders, infections and intracranial bleeding.

Seizure is defined clinically as a paroxysmal alteration in neurological function that is motor, behavior and/or autonomic function. These convulsive phenomena are the most frequent of the overt manifestations of neonatal neurological disorders. [1]

Neonatal seizures have an adverse effect on the neurodevelopment outcome and predispose to cognitive, behavioral or epileptic complications in later life. [2] Seizures during the neonatal period are relatively common, occurring in approximately 1.1 – 8.6/ per 1000 live birth.[3] In the newborn, seizures are most often due to an underlying cerebral or

biochemical abnormality.[4.] Immature brain of neonates is more epileptogenic than mature brain and seizure induced injury to developing brain may lead to serious consequences. [5.]

The commonest cause of neonatal seizures is birth asphyxia followed by hypoglycemia and intra ventricular hemorrhage (IVH). [6] Intraventricular hemorrhage occurs more frequently in preterm infants as compared to term infants. Fits among them are usually tonic or subtle in nature. [1, 7] Subarachnoid hemorrhages are more common in term infants.[7] Metabolic disorders like hypoglycemia, hypocalcaemia and hypomagnesemia may also contribute to NSDs. Taking into account the importance of neonatal seizures and its high mortality and morbidity, we designed this study with the aim to determine the frequency, probable etiology and mortality of neonatal seizures in the neonatal intensive care unit of National Institute of Child Health (NICH) Karachi.

With the help of this study our young doctors and other healthcare providers will diagnose the various type of seizures. They will treat them accordingly and thus, we can decrease the morbidity and mortality in NSDs.

MATERIAL AND METHOD

This prospective study was conducted in Neonatal Intensive Care Unit (NICU) of National Institute of Child Health (NICH) Karachi (the largest neonatal unit in the country), from January 2011 to September 2011. Patients were admitted in neonatal unit through emergency and well baby clinic. All neonates of either sex having seizures at presentation or during the stay in the neonatal unit were enrolled in the study. Procedure was explained to the parents/caregiver and implied consent was taken. All neonates with tetanus neonatorum, syndromic babies and babies with other complex malformation were excluded from the study.

A detailed history including antenatal, natal and postnatal were recorded on the predesigned proforma. Age of onset of seizures, frequency, duration and type of seizures were noted. Seizures were classified as subtle, focal, clonic and myoclonic type. A head to toe examination was done and pertinent investigations according to clinical suspicion were carried out like complete blood count (CBC), blood culture and sensitivity (C/S), cerebrospinal fluid (CSF) D/R and C/S, urine D/R and C/S. Metabolic work up like blood sugar, calcium, magnesium, electrolytes and blood urea were carried out in order to determine the etiology of seizures. Radio imaging studies, Ultrasound brain, CT Scan / MRI brain were done for congenital brain defects, cytoarchetectural problems, intracranial hemorrhage, and infarction. After exclusion of common causes screening tests including reducing substances in urine, serum ammonia, serum lactate and pyruvate, urinary ketones, urine amino acid chromatography and arterial blood gases (ABGs) were performed to exclude inborn error of metabolism (IEM). The data was recorded on proforma and analyzed using descriptive statistics.

RESULTS

One hundred and fifteen (115) neonates were included in the study. Sixty nine (60%) were males and 46(40%) females with male to female ratio of 1.5:1. Fifty eight (50.43%) of newborns were delivered at home while 57 (49.56%) were delivered at hospital. Eighty five (73.91%) cases were full term while 30(26%) were preterm (Table-1). The table 2 shows that birth asphyxia was the most common etiological factor for neonatal seizures in 45 (39.13%) followed by transient metabolic factors in 35(30.43%) and infections in 18(15.65%) cases. Other important etiological factors were intracranial hemorrhage 7(6.08%), kernicterus 5(4.34%) and brain malformations 3(2.6%). Regarding the transient metabolic cases, hypoglycemia was the commonest cause accounting for seizures in 22 (62.85%) cases. Hypocalcaemia was found in 13(37.14%) cases.

Thirty seven (32.17%) neonates had seizures in the first 72 hours of life, their mean age + SD at presentation was 1.62 + 0.792 days. Sixty two (53.91%) presented between 72 hrs to 7th day of life, with mean age + SD of 5.38 + 1.077 days while 16(13.91%) had seizure after 7th day of life with mean age + SD of 11.93 + 4.469 days (Table-3). The common type of seizures observed were subtle (44.35%) followed by focal (27.83%), clonic (20.87%) and myoclonic (6.95%) types (figure 1).

Among the 18 patients with neonatal infections, bacterial meningitis and septicemia was found in 6(33.33%) and 12(66.66%) cases respectively. Frequency of etiological factors and mortality of patients admitted in Neonatal Intensive Care Unit (NICU) with

TABLE-1:
DEMOGRAPHIC CHARACTERISTICS OF NEONATES WITH SEIZURE DISORDERS

Gender	No. of Patient	Percentage	P. Value
Male	69	60	
Female	46	40	0.002
Place of Delivery			
Home	58	50.43	0.895
Hospital	57	49.56	
Gestational Age			
Full term	85	73.91	
Pre term	30	26.08	0.001
Birth weight			
Normal Birth Weight	89	77.30	
Low Birth Weight	26	22.60	0.001

TABLE 2:
FREQUENCY OF ETIOLOGICAL FACTORS, AND MORTALITY IN NEONATAL SEIZURES

ETIOLOGY	Frequency	Died	Percentage
Birth Asphyxia	45(39.13%)	17	37.77
Metabolic causes	35(30.43)	0	0
Hypoglycemia	22	-	-
Hypocalcaemia	13	-	-
Infections	18(15.65)	5	27.77
Meningitis	6	2	33.3
Septicemia	12	3	25
Kernicterus	5(4.34%)	2	40
Intracranial hemorrhage	7(6.08)	3	42.85
Brain Malformation	3(2.6%)	2	66.67
Holoprosancephaly	1	1	33.33
Dandy Walker Cyst	1	1	33.33
Hydrocephalus	1	0	33.33
Idiopathic	2(1.73%)	1	50
Total	115	30	26.08%

TABLE -3:
TIME OF ONSET OF SEIZURE ACCORDING TO AGE.

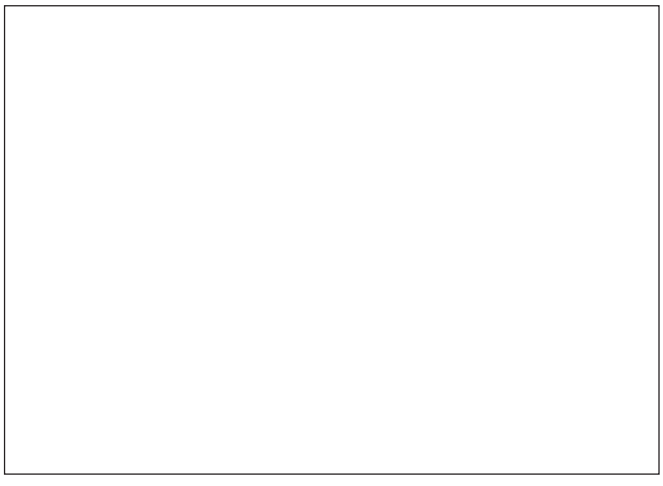
Age at Onset	No. of Patient (n = 115)	%age	Mean + S.D
< 72 Hours	37	32.17	1.62 + 0.794
72 Hours to 07 Days	62	53.91	5.38 + 1.077
> 7 Days	16	13.91	11.93 + 4.40

seizure disorder is shown in table 2. An overall mortality of 30(26.08%) was observed in our study. Seventy five (75) patient were discharged and 15 patient went LAMA (left against medical advice). Brain malformation, intracranial bleed, kernicterus, birth asphyxia, and infections had mortality of 66.67%, 42.85%, 40%, 37.77%, and 27.77% respectively. No mortality was seen in metabolic cases like hypoglycemia and hypcalcaemia in our study.

DISCUSSION

Neonatal seizure is an important neurological emergency causing mortality and morbidity in neonatal period. The frequency of neonatal seizure in our study was 3.54%. In Faiz et al study, the frequency of seizures in neonates was 18.6% and commonest type of seizure were tonic and clonic.[8] Considering the etiological factors, birth asphyxia was found to be the common cause of neonatal seizures, this is consistent with a study done by Faiz et al [8] which also reported birth asphyxia as the most common etiology of seizures 35(%). In our study subtle seizure was the commonest type (44.35%) in both term and preterm babies. This most common seizure is called 'subtle' because clinical manifestations are often mild and easily missed. There is usually mild paroxysmal alteration in motor, behavior and autonomic function.[9] Upadhyay A et al [10] mention that subtle seizure comprise 50% of NSDs which is comparable to our study. Taksande et al[11] and Soni et al[12] in their studies also showed subtle seizures as the commonest type of seizure occurring in 50% and 37.5% respectively.

FIGURE 1.
TYPES OF SEIZURE DISORDERS IN 115 NEONATES



Sood A et al[13] and Kumar A et al[14] reported birth asphyxia as the common etiology of neonatal seizures 71% and 48.27% respectively which is comparable to our results. Similarly Bushra A et al[15] and Sattar SA et al [16] reported birth asphyxia as the commonest cause of seizure occurring in 35% and 44.3% of the

cases respectively. Various authors gave different values for causes of unknown etiology (idiopathic) like 10% by Cloherty [9] and 5% by Volpe, [1] whereas our study shows 1.73%.

In our study hypoglycemia and hypocalcaemia were noted in 22(62.85%) and 13 (37.14%) of the neonates respectively. Kumar A et al[14] study showed (62.8%) biochemical abnormalities which is comparable to our study. Bushra A et al[13] reported that 12.5% of the neonates had metabolic abnormalities. Sood et al showed that 49.1% had biochemical abnormalities and the most common metabolic derangements were hypocalcaemia and hypoglycemia. . The study conducted by Kumar A et al [14] and Sood A et al [13] showed that biochemical abnormalities were seen in cases of birth asphyxia, intracranial bleeding, infections and metabolic disorder.. Moreover, Sood A, et al also demonstrated that hypocalcaemia and hypoglycemia were most common metabolic abnormality.

In our study neonatal infection was present in 15.65% of cases. In Faiz et al.[8] study infection as cause of seizure was present in 28.7% of cases. Taksande A et al [11] showed that infections were present in 28.2% of the neonates having seizure. A study conducted by Ronen GM et al[17] reported that 20% of cases of infections lead to seizure. Other causes of neonatal seizure were intracranial hemorrhage (ICH) and brain malformation. ICH was seen in 6.08% of the cases in our study. Bushra A et al[15] reported that intracranial bleed was seen in 9.5% of the cases which is comparable to our study. In the study by Faiz et al [8] intraventricular hemorrhage (IVH) was present in 13.8%, out of which 11% were preterm and 3% were full term neonates. The incidence of IVH was higher in preterm than full term neonates. Upadhhyay et al[10] also reported higher incidence of IVH in preterms.

CONCLUSION

The frequency of seizure observed in this study was 3.54%. Birth asphyxia (39.13%), metabolic causes (30.43%) and infections (15.65%) were the common etiological factor of NSDs.

Hypoglycemia (19.13%) and hypocalcaemia (11.30%) were two important metabolic causes whereas meningitis and septicemia were found to be the infective causes. Subtle seizures (44.35%) were the commonest type of seizure observed in term and preterm neonates

The overall mortality observed was (26.08%). A significant mortality was observed in brain malformations, intracranial bleed, kernicterus, birth asphyxia and infections (66.67%), (42.85%), (40%), (37.77%) and (27.77%) respectively. There was no mortality seen in patients with metabolic causes.

RECOMMENDATION.

Recognition of seizure is the key to management of seizure in newborn taking into account the brief and subtle nature of seizure in this age group.

Prompt diagnosis and treatment of NSDs are vital as delay in recognition of a treatable cause can have serious impact on the child's neurodevelopment outcome.

Parents and health care workers need to be made aware of neonatal seizure and the importance and appropriate treatment to decrease any further complication.

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