INTRODUCTION

The neonatal period, unquestionably is the most hazardous period of life, never again in life individual is confronted with more dramatic changes than in transition from dependent intrauterine existence to independent postnatal life. The new born brain responds in the form of convulsion even to minor insult, because of the immaturity of the nervous system. The presentation of a newborn with seizures represents a true emergency (Scher and Painter, 1989) and frequently indicates significant neurological dysfunction or damage to the immature nervous system (Holden and Freeman, 1975).

Seizures during the neonatal period are relatively common, occurring in approximately 1.8 to 3.5 per 1000 live births, with greater frequency in premature or low birth weight babies as compared to term babies (Mizrahi, 2001). The highest incidence of neonatal seizures occurs during the first 48 hours of life (Garg, 1972).

In the Neonatal Intensive Care Unit, the incidence goes as high as 10 to 25% out of which about 15% will die and 35 to 40% will have major neurological sequelae. (David et al., 2002)

The major causes of neonatal seizures are Hypoxic-Isschemic Encephalopathy (HIE), which represents about 50% of the causes of neonatal seizures. Metabolic abnormalities, infection, intracranial hemorrhage, developmental anomalies are the other important causes (Sabzehei et al., 2014; Marzoki, 2010). Inborn errors of metabolism are amongst the rare causes of neonatal seizures.
The causes of seizures in preterm neonates is different from that seen in term neonates, where the HIE is the most frequent cause in term neonates, followed by cerebral malformations and metabolic disturbances, while in preterm neonates intraventricular hemorrhage and infections are the most frequent causes. (Vasudevan and Levene, 2013)

Neonates can have subtle seizures or tonic, focal, multifocal and myoclonic types of convulsions.

There is increasing evidence that neonatal seizures have an adverse effect on neurodevelopment and may predispose to cognitive, behavioural or epileptic complication later in life. (Levene, 2002)

Therefore, the aim of the study was to determine the clinical profile of neonatal seizures.

MATERIALS AND METHODS

This was a prospective, observational study conducted over two years on the neonates with seizures admitted in NICU of a rural set up in central India.

Inclusion Criteria

All newborns of up to age </= 28 days brought to NICU during the study period with clinically identified seizures, defined as- sudden abnormal repetitive, rhythmic movement of any part of the body with or without deviation of angle of eyes and frothing from mouth which were not suppressed by physical pressure alone or subtle convulsion.

Exclusion Criteria

1. Neonates with known congenital malformation of the CNS.
2. Neonates with Hypoglycemia, Hypocalcemia, Hypomagnesemia, Dyselectrolytemia
3. Jitteriness in neonates.
4. Tetanic spasms in neonates.

Sample size

All babies fulfilling the inclusion criteria who were brought for hospitalization during the study period were consecutively recruited. There were thus neonates included in the study.

Study Method

Ethical clearance was obtained for this study from the Institutional Ethics Committee. Babies who were reported with clinical seizures identified on history or observation by the neonatal intensivist at the time of hospitalization were included after obtaining written consent from parents. At the time of recruitment, a detailed history was recorded. Their mothers’ previous obstetric history, family history, antenatal, natal and post natal risk factors which includes maternal drug addiction / withdrawal, maternal chronic disease, prolonged rupture of membranes, bleeding, pregnancy induced hypertension drugs taken during pregnancy, gestational age assessment by LMP, small for date, low birth weight baby, perinatal asphyxia, traumatic delivery, septicemia, meningitis, intracranial bleed and hyperbilirubinemia, The detailed history about age of occurrence of first seizure, duration of seizure, number of seizures, type of seizure. Clinical examination findings were noted including anthropometry. The course of illness was recorded and outcome noted. During hospitalization any relevant investigations done and treatment given as per protocol of NICU and was recorded in a prevalidated case record form.

Data Management and Statistical Analysis

Statistical analysis was performed using percentage. The analysis of Student’s t-test was used for comparisons. Categorical variables were compared using Chi square test and Fischer’s exact test. A p-value 0.05 was considered significant.

RESULTS

Out of total 82 newborns that were included in the study, 56 (68.29%) were admitted within first 3 days of life with clinical seizures, 12 (14.63%) in between day of life 4 & 7, while 14 (17.07%) were admitted after 7 days of life. The sex distribution showed that there was male preponderance in this study i.e., 49 out of 82 (59.75%). The overall mean for duration of stay was 14.34 (± 10.41) days and the interquartile range was 1-32 days. The majority of newborns admitted were outborn i.e., 51 out of 82 (62.19%) while only 31 were inborn (37.80%). 48 (58.53%) newborn were term. This shows that maximum newborns were term neonates. Only 2 (2.43%) newborn were very low birth weight (<1.5 Kg), 46 (56.09%) were between 2.5 Kg to 4 Kg, whereas 34(41.46%) were >2.5 Kg, whereas 50 (60.97%) had first episode of seizure within 3 days of life, while 20 (24.39%) had seizures between 4 to 7 days of life. Table 1

Out of the total 82 mothers, 11 (13.41%) mothers had pre-eclampsia or impending eclampsia while 65 (79.27%) mothers had no antenatal history of any disease. 5 of the 82 mothers had different illnesses like hypothyroidism (3), Valvular heart disease (1) and Multiple sclerosis (1) while one mother suffered from gestational diabetes mellitus.
Table 1: Maternal Diseases and neonatal seizures

| Maternal Diseases          | Total, n=82 (%) | p value |
|----------------------------|----------------|---------|
| Preeclampsia/Eclampsia     | 11(13.41%)     | 0.624   |
| Gestational Diabetes Mellitus | 1(1.21%)      |         |
| Others                     | 5(6.09%)       |         |
| None                       | 65(79.27%)     |         |

Majority of the neonates, 46(56.09%), were born via normal vaginal delivery.

A 34(41.46%) of the total neonates required resuscitation in the form of tactile stimulation/Bag & mask ventilation while 12(14.63%) required securing an alternate airway i.e., endotracheal intubation. It was inferred that a significant percentage, 56.09% (46/82) of the newborn who had seizures later on had received some form of resuscitation.

APGAR at 5 minutes of life, 15(18.29%) neonates had score <7 while 67(81.70%) neonates had score of 7 to 10. Out of the total 82 cases, 45 (54.87%) newborn were diagnosed as HIE, 36(43.90%) cases as CNS infection while only 1(1.2%) case had an ischaemic stroke.

If the frequency of seizures occurring was considered; 35(42.68%) neonates had only a single episode of seizures, while 47(57.31%) neonates had multiple episodes of seizures. For multiple seizures, 25 cases required use of ≥2 antiepileptic drug (AED).

The types of clinical seizures were seen in the study; 14(17.07%) neonates had subtle seizures, 57(69.51%) had multifocal, 9(10.98%) had focal, 2(2.44%) had GTCS while no neonate was observed to have myoclonic seizures. Thus, multifocal seizures were the most common type of seizures followed by subtle seizures.

A Neonatal sepsis was common co-morbidity in the study as 45 (54.87%) neonates had a positive blood culture report among all neonates. The overall mortality rate was 17.07% (14/82) while survival rate was 82.92% (68/82) in the present study.

In the present study many patterns of seizures were found with relation to patient characteristics, types of seizures, its causes and associations with the maternal and neonatal factors.

**DISCUSSION**

In the study carried out by Perveen et al. (2016), there were 41(68.33%) males with female: male ratio of 1:2.15. In another study conducted by Gowda et al. (2019) there was male preponderance as well with 56 (56%) male neonates and 44(44%) female neonates with female to male ratio of 1:1.27.

In yet another study by Rao et al. (2018), there was again male preponderance among neonates with seizures. In another study conducted in the NICU of a tertiary care hospital in Nasik (2019), out of the 127 neonates studied, 118 (92.91%) neonates were full term while 7 (5.51%) were preterm. Among the neonates studied by Gowda et al. (2019), the mean birth weight values were 2.56(±0.64) Kg.

Holden and Freeman (1975) found that the incidence of neonatal seizure were 63% in normal weight and 37% in less than 2.5 kg.

Shah and Singh (2008) in his study of neonatal seizures Clinico-biochemical profile of Neonatal Seizures studied 90 babies, found that the percentage of neonatal seizure was more in normal weight babies 66% than the babies whose weight was less than 2.5 kg. i.e. 33%. Similar results were found in our study.

In another study conducted by Patil et al. (2018), onset of seizures was found to be within first 3 days of life in 101(79.5%) neonates while after 3 days of life, only 26 (20.5%) neonates developed seizures. It was also concluded that, onset of seizures within first 3 days of life of had statistically significant correlation with birth asphyxia being the causative factor with p<0.001

In the study done by Amudhadevi and Kanchana (2018), the onset of seizures on the first two days of life was seen in 62 (59.6%) neonates,

In the study conducted by Arpino et al. (2001), there was a strong association between preeclampsia, chronic hypertension and PIH with neonatal seizures.

In the study undertaken for analysis of antenatal risk factors for seizures in term newborns by Glass et al. (2009) unadjusted analysis showed maternal hypertension was associated with seizures; however, in the adjusted analysis, which included all antenatal, intrapartum, and infant covariates, the
risk of maternal hypertension was no longer significant. Each of the variables was evaluated individually in a regression with hypertension and found that no single variable had a significant effect. Although the p value was not significant in this study for maternal diseases but a significant percentage of neonates had mothers with pre Eclampsia. This could be attributed to the fact that preeclampsia/eclampsia leads to decreased utero-placental perfusion.

Pathak et al. (2013), 78.89%(86/109) newborn had seizures attributable for perinatal insult while CNS infections was accountable for 16.51%(18/108) of cases. thus leading to adverse neonatal neurological outcome including seizures.

Brunquell et al. (2002), most common type of seizures were subtle (51%) followed by focal clonic (42%), multifocal clonic (30%) and generalized tonic (23%) In another study, evaluating the safety & efficacy of LEV in neonatal seizures, Ramantani et al. (2011) found subtle seizures to be the most common type (42.10%) Kher et al. (2017) having 18.35% (35/109) neonates who died, and our study had got near similar(17.07%) percentage of died neonates. that is 65(26%) can be due to the severity of the etiological factors in newborns with neonatal seizures. But when compared with the study done by Nunes et al. (2008) found that 24.7% of the cases died in the neonatal period; higher than the current study. Study in same setup by Kher et al. (2017) showed mortality of 26%. It can be due to the severity of the maternal risk factors in newborns with neonatal seizures. The study was not without limitations, first the neurodevelopmental outcome of neonates could not be done at later stages of life for assessment of long term effect of seizures on CNS development. Another shortcoming was EEG could not be done because of infrastructural limitations in the hospital. EEG monitoring is important to identify non-convulsive seizures and non obvious seizures in pre-disposed neonates.

CONCLUSION

The distribution of neonates in the study according to their gender, gestational age, birth weight, route of delivery, place of delivery, meconium stain of amniotic fluid, age of presentation, duration of stay, maternal factors and cause of seizure was found to be statistically insignificant. The most common cause of seizures and death was birth asphyxia. In the present study, multifocal seizures were most common type of neonatal seizures was observed.

Conflict of interest
The authors declare that they have no conflict of interest for this study.

Source of funding
The authors declare that they have no funding support for this study.

REFERENCES

Amudha Devi, S., Kanchana, P. 2018. A study on clinical profile of neonatal seizures in newborn babies born in Government Mohan Kumara Mangalam Medical College Hospital, India. International Journal of Contemporary Pediatrics, 5(6):2314–2314.

Arpino, C., Domizio, S., Carrieri, M. P., Brescianini, S., Sabatino, G., Curatolo, P. 2001. Prenatal and Perinatal Determinants of Neonatal Seizures Occurring in the First Week of Life. Journal of Child Neurology, 16(9):651–656.

Brunquell, P. J., Glennon, C. M., DiMario, F. J., Lerer, T., Eisenfeld, L. 2002. Prediction of outcome based on clinical seizure type in newborn infants. The Journal of Pediatrics, 140(6):707–712.

David, P., Vivo, D. D., Colin, D., Rudolph, A. D., Margaret, K., Hostetler 2002. The Nervous system. In: Rudolph text book of pediatric. McGraw Hills. 21st edition. New York: McGraw Hills. P.2267.

Garg, P. K. 1972. Neonatal seizures. The Indian Journal of Pediatrics, 39(6):208–213.

Glass, H. C., Pham, T. N., Danielsen, B., Towner, D., Glidden, D., Wu, Y. W. 2009. Antenatal and Intrapartum Risk Factors for Seizures in Term Newborns: A Population-Based Study, California 1998-2002. The Journal of Pediatrics, 154(1):24–28.

Gowda, V. K., Romana, A., Shivanna, N. H., Benakappa, N., Benakappa, A. 2019. Levetiracetam versus Phenobarbitone in Neonatal Seizures — A Randomized Controlled Trial. Indian Pediatrics, 56(8):643–646.

Holden, K. R., Freeman, J. M. 1975. Neonatal seizures and their treatment. Clin Perinatol, 2(3):2–13.

Kher, A., Thakur, N., Vagha, J. 2017. Clinico-Biochemical Profile of Neonatal Seizures. New Indian Journal of Pediatrics. Available, 7(1):15–22.

Levene, M. 2002. The clinical conundrum of neonatal seizures. Archives of Disease in Childhood - Fetal and Neonatal Edition, 86(2):75–77.

Marzoki, J. M. A. 2010. Clinico-Biochemical Profile of Neonatal Seizures. QMJ, 6(10):163–164.

 Mizrahi, E. M. 2001. Neonatal seizures and
neonatal epileptic syndromes. *Neurologic Clinics, 19*(2):427–463.

Nunes, M. L., Martins, M. P., Barea, B. M., Wainberg, R. C., da Costa, J. C. 2008. Neurological outcome of newborns with neonatal seizures: a cohort study in a tertiary university hospital. *Arquivos de Neuro-Psiquiatria, 66*(2a):168–174.

Pathak, G., Upadhyay, A., Pathak, U., Chawla, D., Goel, S. P. 2013. Phenobarbitone versus phenytoin for treatment of neonatal seizures: An open-label randomized controlled trial. *Indian Pediatrics, 50*(8):753–757.

Patil, S. V., Ahire, N. V., Reddy, K., Karne, T., Joshi, D. 2018. Onset and Clinical Manifestations of Neonatal Seizures. *MVP Journal of Medical Science, 5*(1):64–68.

Pervereen, S., Singh, A., Upadhyay, A., Singh, N., Chauhan, R. 2016. A randomized controlled trial on comparison of phenobarbitone and levetiracetam for the treatment of neonatal seizures: pilot study. *International Journal of Research in Medical Sciences, 4*(6):2073–2078.

Ramantani, G., Ikonomidou, C., Walter, B., Rating, D., Dinger, J. 2011. Levetiracetam: Safety and efficacy in neonatal seizures. *European Journal of Paediatric Neurology, 15*(1):1–7.

Rao, L. M., Hussain, S. A., Zaki, T., Cho, A., Chand, T., Garg, M., Sankar, R. 2018. A comparison of levetiracetam and phenobarbital for the treatment of neonatal seizures associated with hypoxic–ischemic encephalopathy. *Epilepsy & Behavior, 88*:212–217.

Sabzehei, M., Basiri, B., Bazmamoun, H. 2014. The Etiology, Clinical Type, and Short Outcome of Seizures in Newborns Hospitalized in BesatHospital/ Hamadan/ Iran. *Iran J Child Neural, 8*(2):24–28.

Scher, M. S., Painter, M. J. 1989. Controversies Concerning Neonatal Seizures. *Pediatric Clinics of North America, 36*(2):281–310.

Shah, G. S., Singh, B. 2008. Clinico-Biochemical profile of Neonatal seizures. *JNPS, 28*(1):7–9.

Vasudevan, C., Levene, M. 2013. Epidemiology and aetiology of neonatal seizures. *Seminars in Fetal and Neonatal Medicine, 18*(4):185–191.