

Maternal Risk Factor for Seizures in Term Neonate: A Hospital –Based Case Control Study.

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Received: July 2016

Accepted: July 2016

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ABSTRACT

Background: Assessing the maternal risk factors for seizure in first 72 hours of life in term neonate. Design: Case control study. Setting: Department of Paediatrics, Neonatology unit and Maternity ward tertiary care centre Govt. Medical College, Nagpur. **Methods:** A 210 cases [Term neonate with seizure within first 72 hours of life] and 210 controls [Term neonate without seizure in first 72 hours of life] were randomly selected as study subject over a period of two year. Primary exposure variables in mothers including age, parity, diabetes mellitus, hypertension, anemia, intrapartum fever, mode of delivery and prolonged second stage of labor were considered in study population. Neonates were carefully examined and observed for seizures and manage accordingly. **Results:** Maternal diabetes mellitus and anemia were potentially significant in their association with term neonatal seizure while maternal hypertension, intrapartum fever and prolonged second stage of labor were not significantly associated with seizure. Neonates born to diabetic mother, young maternal age, anemic mother and cesarean delivered neonate had 1.97, 0.95, 1.83 and 2.18 time more risk to developed seizure respectively. **Conclusion:** Early identification and timely intervention of maternal risk factor may reduces the seizure in term neonate.

Keywords: Maternal risk factor, Neonatal seizure, term neonate.

INTRODUCTION

Seizures are the often the first sign of neurological dysfunction in neonate but their clinical expression at this age is quite variable, poorly organized and often subtle. Neonatal seizure are difficult to recognize consequently; determination of the etiology and initiation of therapy may be delayed, which result in poor neurological outcome.^[1] The estimated incidence of neonatal seizure is 1-3.5 per 1000 live birth and highest in the first 72 hours of life.^[2-4] Though hypoxic ischemic encephalopathy is the most common cause of seizure in term neonate other causes like respiratory distress, congenital anomalies, sepsis and multiorgan failure are also playing a very important role. Several maternal antepartum and intrapartum risk factor increased the risk of seizure, but information is limited.^[5, 6] So this hospital based case control study was carried out to assess the antepartum and intrapartum risk factors for neonatal seizure in 72 hours of birth in term neonates.

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MATERIALS AND METHODS

A hospital based case control study was carried out in the Government Medical College, tertiary care & referral hospital that provide care to underprivileged, socioeconomically deprived population of central India from September 2011 to August 2013. The study population comprised of 210 cases (Term neonate with seizures within first 72 hours of life) and 210 controls (Term neonate without seizure in first 72 hours of life) over a period of two years. Sample size was estimated assuming proportion of neonatal seizure in neonate born to mothers with cesarean section 29% and 14% in case and control group respectively with power of 90% and alpha error of 5% .The mothers in cases and control were match for age, parity, mode of delivery.

Selection criteria of cases include term neonate who develops seizure within 72 hours of life and controls were defined as normal term neonate without seizure in first 72 hours of life and born at same hospital.

After approval from institutional ethical committee a pretested, semi structural questionnaire was used comprising of detail information about primary exposure variable in mothers including maternal age, parity, diabetes mellitus, hypertension, anaemia, intrapartum fever, mode of delivery and prolonged second stage of labour. Preparatory educational

session was held for resident in order to standardize and to improve the quality of observation and identification of seizure. Neonates were carefully examined and observed for seizure and manage accordingly.

Statistical Analysis

Statistical software STATA version 10.0 was used for statistical analysis. Continuous variable were compared between cases and control by performing unpaired 't' test. Categorical variable were compared by performing chi square test. Significant risk factor for neonatal seizure was identified by univariate analysis on the basis of odd's ratio and 95%

confidence interval. A multiple logistic regression analysis was performed to evaluate the independent effect of risk factor on neonatal seizure. P<0.05 was considered as statistical significant.

RESULTS

Maternal diabetes, hypertension, anaemia, cesarean deliveries were significantly more common in cases than control otherwise demographic characteristics did not differ significantly between two groups. The demographic data of seizure cases and control are presented in [Table 1].

Table 1: Characteristic of cases & control (n, %).

Characteristic	Cases n=210	Control n=210	P value
Maternal			
Mothers age (yrs)	25.59±5.42	27.09±5.47	0.005
Age group			
18-22	80(38.1)	61(29.0)	0.03
23-27	56(26.7)	45(21.4)	
28-32	46(21.9)	73(34.8)	
33-37	28(13.3)	31(14.8)	
Parity			
Primiparous	141(67.1)	139(66.2)	0.939
Para 2	17(8.1)	19(9.0)	
Para>3	52(24.8)	52(24.8)	
Mode of delivery			
Cesarean	115(54.8)	71(33.8)	0.00001
Normal	95(45.2)	139(66.2)	
Neonatal			
Age in hours	23.90±15.28	23.57±15.18	0.824
<24	130(61.9)	126(60.0)	
24-48	63(30.0)	66(31.42)	
48-72	17(8.1)	18(8.58)	
Gender (n,% male)	118(56.2)	107(50.9)	1.277
Birth weight (gms)	2220±460	2450±430	0.0001
<1500	2(0.9)	0(0)	
1500-1999	56(26.7)	31(14.8)	
2000-2499	121(57.6)	145(69.0)	
2500-3499	25(11.9)	28(13.3)	
>3500	6(2.9)	6(2.9)	

In the univariate analysis, maternal diabetes mellitus and anaemia were potentially significant in their association with term neonatal seizure while maternal hypertension, intrapartum fever, and

prolonged second stage of labor were not significantly associated with term neonatal seizure [Table 2].

Table 2: Univariate analysis of maternal risk factor as predictors of neonatal seizure in term neonate.

Risk factor	Cases n, %	Control n, %	OR	95% CI	P value
Diabetes mellitus	84(39.0)	56(26.7)	1.83	1.19-2.85	0.0038
Hypertension	79(37.6)	62(29.5)	1.43	0.93-2.20	0.0790
Anaemia	115(54.8)	94(44.8)	1.49	1.01-2.24	0.0404
Intrapartum fever	6(2.9)	3(1.4)	2.02	0.42-12.68	0.3121
Prolonged second stage of labor	9(4.3)	4(1.9)	2.30	0.63-10.39	0.1589

Neonates born to diabetic mothers had 1.97 times more risk for seizures than neonates born to non-diabetic mothers while neonate delivered by anaemic mothers had 1.83 times more risk of seizure than neonates of non-anaemic mothers. Young maternal age had 0.95 times more risk for neonatal seizures (95% C I 0.92-0.99 P<0.03). Neonates of maternal

age between 18 to 22 years are at more risk neonatal seizure in term neonates. Neonates born to mothers with caesarean delivery had 2.18 times more risk of seizure than normal vaginally delivered [Table 3]. In the present study, 57.6% neonates had developed seizure between 48-72 hours of life followed by 26.7% in between 24-48 hours and 15.7% within 24

hours. Subtle type of seizure was observed in 73% cases followed by clonic (16%), tonic (10%) and myoclonic (1%).

Table 3: Predictors of neonatal seizure in term neonate(From Multiple Logistic Regression).

Predictor	OR	95% CI	P value
Maternal age	0.95	0.92-0.99	0.03
Diabetes mellitus	1.97	1.20-3.26	0.007
Anaemia	1.83	1.15-2.90	0.010
Cesarean Delivery	2.18	1.40-3.38	0.001

In study population, 15 (7.1%) neonates died in case group compared to 3 (1.4%) in the control group which was statistically highly significant (OR 3.98, 95% CI 1.23-16.7, P<0.0095). Neonates with seizure had 3.98 times more risk of mortality than controls.

DISCUSSION

Seizures in neonate frequently reflect significant underlying brain injury, such as hypoxic ischemic injury, stroke, intracranial infection and metabolic like hypoglycemia and hypocalcemia. [3] Neonates with seizures have a high incidence of mortality and adverse long term neurological outcome. By identifying and timely intervening maternal risk factor for neonatal seizure may improve mortality and neurological morbidity.[7]

Neonatal seizure can exert a range of adverse effect on brain development. The disruption of the process such as cell division, myelination and stabilization of synapse during seizure activity in the neonate interferes with normal brain maturation. An altered neuronal connectivity might account for the increased susceptibility of the developing brain to suffer a subsequent seizure induce injury during adolescence or early adulthood. The elucidation of modifiable maternal risk factor for neonatal seizure might facilitate early diagnosis, treatment and possible prevention of neonatal seizure and their long term adverse sequelae.[8]

In the present study, maternal age is found to be one of the significant risk factors for seizure. Neonates of maternal age between 18 to 22 years are at 0.95 times more risk for seizure. A 1.6 times of high risk of neonatal seizure in 18-24 years of age group mothers than the age of 25-29 years were reported by Rima M Saliba et al^[1]. A study done by Kirke AB revealed, neonates born to mother with age of 28.5 years had a 1.5% chance of neonatal seizure compared with average mothers in Western Australia^[9] while a study done by Hannah C Glass et al were found an increased risk of seizure during birth hospitalization among mothers >40 years of age compared to mothers of 25 to 29 years. Reason for increased seizure in this study is unknown and may be related to change in uterine function.^[6]

Maternal diabetes is an important risk factor for seizure. In the present study, it was found that 39%

neonates born to diabetic mothers had seizures. Neonates of diabetic mother had 1.83 times more risk for seizure (OR 1.83, 95% CI 1.19-2.83, P<0.0038). Biological plausible cause for seizures in neonate born to diabetic mother is hypoglycemia owing to hyperinsulinemia in neonate secondary to maternal hyperglycemia. An alternative mechanism for seizure in term neonate born to diabetic mothers with preexisting diabetic could be diabetic vasculopathy leading to placental insufficiency and inadequate oxygen delivery to neonatal brain tissue. A study done by Deborah et al suggested that the risk of maternal and fetal outcome is known to be increased for mother with diabetic compared to nondiabetic mother.^[10] Similarly, high perinatal mortality and morbidity were reported by Honko and Reece et al^[11], Hannah et al^[6], Joan L et al^[12] and Yang J et al.^[13]

In the present study, it was found that 54.8% neonates born to mother with antenatal anemia developed seizures. Risk of seizure is 1.49 times more in neonates born to anemic mother. Neonates of anemic mother developed seizure may be due to impaired maternal oxygenation, impaired placental oxygen transfer and fetal hypoperfusion. Similar types of 2.65 times more risk for seizures were reported by C. Anne Patterson et al.^[14]

In our study, the risk of neonatal seizure was found to be 2.37 times more with cesarean delivered neonate than normal vaginally delivered. Similar high risk of neonatal seizure with cesarean delivered neonates were reported by Deborah et al^[6], Rima M Saliba et al ,and Manoel RR Holanda et al.^[15] Our study did not identify common indications for cesarean section such as failure to progress in labor, previous cesarean section or fetal malpresentation & fetal distress because such factor could have been surrogate for perinatal hypoxia in the newborn. Therefore, it could not be stated that cesarean section per se places the neonate at risk for seizure. Additional studies stratifying cesarean section deliveries by indication might be needed to better understand the mechanism underlying the risk of neonatal seizure associated with cesarean section and to more carefully discern weather this risk is truly independent of fetal distress.

In our study, the majority (57.6%) neonates developed seizure between 48-72 hours. However study done by Rima Saliba et al reported 46% of seizures in term small for gestational age neonate within 48 hours of life and Mcintire et al^[16] & Min chom et al^[7] reported two fold increases the incidence of seizure in the first 24 hours of life in term small for gestational age neonates. Present study also reveals most of seizures developed in neonates with birth weight of 2000 to 2499 gms and <2000 gms with 95% CI between 0.12-0.38 with P value <0.0001. Similar observation of two times more risk of seizure were recorded by Rima saliba et al, Minchonnet al, Mary Jo Lanska et al^[4], Memon S

and Memon MM et al^[17], F. Eghbalian MD et al^[18], Seay and Brayfound et al^[19].

CONCLUSION

Our study concludes neonates of maternal age between 18-22 years had more risk of seizure than others. Neonates of mother having low maternal age had 0.95 times of more risk of seizure. Neonates born to anemic mother had 1.83 times more risk of seizure than non-anemic mother. It was also observed that neonates born to diabetic mother had 1.97 times more risk seizure than neonates born to non-diabetic mother. The study also concludes that mode of delivery is an important risk factor for seizure. Neonates born by cesarean delivery had 2.18 times more risk of seizure than neonates born by normal vaginal delivery. However, it could not be emphasized that cesarean section per se place neonates at risk for seizure rather the condition that makes the procedure necessary. So, early identification maternal risk factor and timely intervention may reduces the seizure in term neonate.

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How to cite this article: Meshram R, Merchant S, Rakhade CW. Maternal Risk Factor for Seizures in Term Neonate: A Hospital –Based Case Control Study. *Ann. Int. Med. Den. Res.* 2016; 2(5):PE05-PE08.

Source of Support: Nil, **Conflict of Interest:** None declared