A study to determine association of the interval between seizure and delivery with the APGAR scores and perinatal asphyxia of the neonates of eclamptic mothers of a rural tertiary care hospital in Eastern India

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ABSTRACT

Background: Eclamptic seizure not only affects maternal health but may predispose low APGAR scores and development of perinatal asphyxia and thereby influence perinatal mortality too. This study was carried out to evaluate the correlation of the interval between the onset of seizure and delivery with the APGAR scores (at 1 minute and 5 minutes) and perinatal asphyxia of the neonates of the eclamptic mothers.

Methods: A prospective, cross-sectional, observational, epidemiological study was conducted from April, 2012 to March, 2013 at a tertiary-care Government teaching hospital catering rural population of Eastern India. The participants comprised of 100 consecutive admitted eclamptic mothers and neonates born to them.

Results: Majority of mothers were unbooked, primigravidae (86%), aged below 20 years (66%). Significant inverse correlation was observed between seizure to delivery interval and Apgar scores (1 min and 5 minutes), while seizure to delivery interval >12 hours was found to be a significant risk factor for perinatal asphyxia (OR =16.824, 95% CI = 5.107-55.424, p <0.001).

Conclusions: Measures to minimise the interval between the onset of seizures and delivery will decrease the incidence of perinatal asphyxia and perinatal mortality of neonates of eclamptic mothers in rural areas.

Keywords: Apgar scores, Eclampsia, Perinatal asphyxia, Seizure to delivery interval

INTRODUCTION

Eclampsia (a Greek word e’klampsis literally meaning violent onset, sudden development) is currently defined in the obstetrical literature as the occurrence of unexplained seizure during pregnancy in a woman with preeclampsia.1 In India the incidences of eclampsia (about 1.5%) and perinatal mortality due to eclampsia (24.5-45%) have shown no reduction over the last few decades.2

The process of placentation is disordered in preeclampsia as the invasion of maternal spiral arteries in the decidua of myometrium by fetal cytotrophoblast is defective, resulting in development of small calibre vessel with high resistance flow that leads to decreased uteroplaentntal blood flow and hypoxia.3,4 Such ischemic and hypoxic placentia in preeclampsia releases several cytokines like Interleukins (6, 1 alpha, 2 beta) and TNF-alpha along with anti-angiogenic proteins like sFlt1, and s-Eng due to hypoxia induced over-expression and up-regulation.5,7,8 These substances cause systemic vascular endothelial dysfunction resulting into hypertension and proteinuria of preeclampsia.5,9 Eclampsia is hypothetically the result of cerebral hypoxia due to cerebral vasospasm by over-auto regulation in acute and severe hypertension.5,10 It may also be due to cerebral edema caused by capillary leakage.
due to endothelial dysfunction coupled with cerebral hyper-perfusion due to loss of cerebrovascular auto regulation (hypertensive encephalopathy) in the event of systemic hypertension (mean arterial pressure at or above 160 mmHg).\textsuperscript{5,11} Moreover placental ischemia causes the release of certain neuro-excitatory molecules like neurokinin-B (NKB) \textit{inflammatory cytokines, endothelins, and tissue plasminogen activator which may have a role in the development of seizures in eclampsia independent of cerebral vasculopathy.}\textsuperscript{12} During seizures placental ischemia and fetal hypoxia aggravate further resulting into fetal distress and fetal bradycardia.\textsuperscript{13,14} Thus the constellation of the above observations clearly suggests that the variables related to eclamptic seizures should have correlations with those of placental ischemia and hypoxia which is the fundamental mechanism in preeclampsia-eclampsia syndrome.

Since perinatal asphyxia is imperative in case of placental hypoxia, the present study was conducted in this background to evaluate the correlation of the interval between the onset of seizure and delivery (a variable related to eclamptic seizure) with the APGAR scores (at 1 minute and 5 minutes) and perinatal asphyxia of the neonates of the eclamptic mothers.

**METHODS**

This prospective, cross-sectional, observational, epidemiological study was conducted in the departments of paediatrics and obstetrics of a tertiary care rural teaching hospital in Eastern India from April, 2012 to March, 2013.

**Inclusion criteria**

- The study comprised of 100 consecutive mothers, booked or unbooked, who were admitted with eclampsia or with pre-eclampsia but subsequently developing eclampsia in the hospital.

**Exclusion criteria**

- Mothers less than 28 weeks of gestation or suffering from essential hypertension, chronic illness, epilepsy, taking any drug with teratogenicity or giving birth to twins or babies with gross congenital malformation were excluded from this study.

All eclamptic mothers included in this study were evaluated through detailed history with clinical examination (including time and place of onset of first seizure) and observation till delivery of the babies. Modified Kuppaswamy scale, 2007 was used for classification of socio-economic status (SES) of mothers.\textsuperscript{15} They were all treated according to institutional protocol with MgSO\textsubscript{4} routinely with loading doses of 2.5 mg deep im in each buttock and 3 g iv over 15 minutes along with a maintenance dose (2.5 mg every 4 hourly) and Labetelol if BP on admission was $>160/110$ mmHg (10 mg iv stat followed by a maintenance dose of 10 mg iv 8 hourly or 100 mg orally 8 hourly).

All the neonates were examined at birth at labor room or OT including time of birth and APGAR scoring at 1 minute and 5 minutes and evaluated for perinatal asphyxia according to WHO working definition (South East Asia Regional Neonatal Perinatal Database) and F-IMNCI guidelines, Ministry of Health, Government of India (2009) and managed accordingly.

**RESULTS**

In this study majority of eclamptic mothers were below 20 years of age (66%), nulliparous (86%), 40-44 kgs in weight as per antenatal cards (52%), 145-150cms in height (54%), attended at least 3 antenatal check-ups (52%) at the peripheral Government facilities and belonged to class-IV in Kuppaswamy socio-economic scale (92%) (Table 1). Majority of them were unbooked in this institution and referred from peripheral hospitals (80%).

**Table 1: Frequency distribution of maternal socio-demographic profile.**

| Variable | Groups | Percentage |
|----------|--------|------------|
| Age      | 17-19 years | 66%        |
|          | 20-21 years | 22%        |
|          | 22-24 years | 12%        |
| Parity   | 0      | 86%        |
|          | 1      | 14%        |
| ANC      | $\leq$ 2 visits | 12%        |
|          | $\geq$ 3 visits | 88%        |
| SES      | Class III | 8%         |
|          | Class IV | 92%        |
| Weight   | 30-34 kg | 10%        |
|          | 35-39 kg | 18%        |
|          | 40-44 kg | 52%        |
|          | 45-50 kg | 20%        |
| Height   | 132-143 cm | 16%        |
|          | 145-150 cm | 64%        |
|          | 152-168 cm | 20%        |

Majority (86%) had their first onset of seizures before admission to this tertiary care hospital and 66% of them experienced it at their home while the rest 20% at the local health centre or sub-division hospital (first Referral Unit). The Bar diagram shows the frequency distribution of intervals between the onset of seizures and delivery of babies of eclamptic mothers (Figure 1).

The Bar diagram describes the comparison of frequencies between the APGAR scores of the new-born babies at 1 minute and at 5 minutes (Figure 2). The mean duration of this interval was 14.47 hours±SD=9.70, while the means of APGAR scores at 1 and at 5 minutes were 5.57±SD=2.80 and 6.64±SD=3.01 respectively.
A significant negative correlation was observed between maternal seizures to delivery interval and APGAR score at 1 minute (p<0.001), Apgar score at 5 minutes (p<0.001) of the new-born (Table 2, Figure 3 and Figure 4).

In this study 30 neonates (30%) suffered from perinatal asphyxia which caused 60% (3 out of 5) of early neonatal death. It was also observed that the interval between onset of seizures to delivery of baby >12 hours was significantly associated with perinatal asphyxia (OR =16.824, 95% CI = 5.107-55.424, p <0.001) of the new-borns (Table 3).

### DISCUSSION

In this study 30% of babies of eclamptic mothers had suffered from perinatal asphyxia which was again found to be the major cause of perinatal mortality (60% of early neonatal death). In this study APGAR scores at 1 minute and at 5 minutes were found significantly correlated and inversely proportional to interval between onset of seizures of eclamptic mothers and delivery of their babies. In other words this study showed that perinatal asphyxia being the clinical version of low APGAR scores (<7 at 1 minute) was significantly correlated with the interval between onset of seizure and delivery in eclampsia. It was further observed that the interval between onset of seizure and delivery being more
than 12 hours was a significant risk factor for perinatal asphyxia.

This study was in consonance with several similar studies. Shaheen B et al, had observed in their study at a tertiary care hospital at Peshawar that 37.5% of perinatal mortality in eclampsia was due to perinatal asphyxia. They also inferred from their study that early delivery would decrease the proportion of perinatal asphyxia in eclampsia.16 George IO et al observed perinatal asphyxia to be the commonest cause (33.3%) of perinatal mortality in their study at a Nigerian tertiary hospital.17 In a study carried out in Bangladesh by Shahabuddin AKM et al, had also found perinatal asphyxia to be the major cause of perinatal mortality in eclampsia.18 Alam IP et al, observed in their study at Dhaka Medical college in Bangladesh that convulsion-delivery interval >12 hours had significant correlation with perinatal mortality (53%, p<0.001).19 Yaliwal RG et al, had observed in BM Patil Medical College Hospital in Karnataka that 26% of babies had suffered from perinatal asphyxia in eclampsia. They also observed regarding the interval between convulsion and delivery in their study that perinatal mortality was 18.8% (lowest) when it was <6 hours but increased to 30% at 12-17 hours and 47.05% (highest) at >18 hours.20

**CONCLUSION**

Perinatal asphyxia still remains the major cause of perinatal mortality in eclampsia in rural sectors of eastern India. In order to decrease the chances of perinatal asphyxia baby should be delivered as early as possible since the onset of seizure in eclamptic mothers. As the majority of eclamptic seizures occur at home in the periphery, transport facilities should be prompt in rural areas. Preeclampsia should be diagnosed during regular antenatal check-ups and the family members should be counselled properly to take the mother to tertiary care hospital without delay at the very onset of eclamptic seizure. The ultimate aim in tertiary care facility again should be to stabilise the mother and deliver the baby either vaginally or through caesarian section at the earliest possible time which should be preferably within 12 hours since the onset of seizure.

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**Ethical approval:** The study was approved by the Institutional Ethics Committee

**REFERENCES**

1. Cipolla MJ, Kraig RP. Seizures in women with preeclampsia: mechanisms and management. Fetal Maternal Medi Rev. 2011 May;22(2):91-108.
2. Nobis PN, Hajong A. Eclampsia in India through the decades. J Obstetr Gynecol Ind. 2016 Oct 1;66(1):172-6.
3. Damsky CH, Fisher SJ. Trophoblast pseudovascularogenesis: faking it with endothelial adhesion receptors. Curr Opin Cell Biol. 1998;10:660-666
4. Zhou Y, Damsky CH, Fisher SJ. Preeclampsia is associated with failure of human cytotrophoblasts to mimic a vascular adhesion phenotype. One cause of defective endovascular invasion in this syndrome?. J Clin Investig. 1997 May 1;99(9):2152-64.
5. Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, eds. Williams Obstetrics. 24th ed. New York: McGraw-Hill Professional; 2014: 732-743.
6. Brosens IA, Robertson WB, Dixon HG. The role of the spiral arteries in the pathogenesis of preeclampsia. Obstet Gynecol Annu. 1972;1:177-91.
7. Benyo DF, Smarason A, Redman CW, Sims C, Conrad KP. Expression of inflammatory cytokines in placenta from women with preeclampsia. The J Clin Endocrinol Metab. 2001 Jun 1;86(6):2505-12.
8. Nagamatsu T, Fuji T, Kusumi M, Zou L, Yamashita T, Osuga Y, et al. Cytotrophoblasts up-regulate soluble fms-like tyrosine kinase-1 expression under reduced oxygen: an implication for the placental vascular development and the pathophysiology of preeclampsia. Endocrinology. 2004 Nov 1;145(11):4838-45.
9. Roberts JM, Taylor RN, Musci TJ, Rodgers GM, Hubel CA, McLaughlin MK. Preeclampsia: an endothelial cell disorder. Am J Obstet Gynecol. 1989; 161:1200-4.
10. Sibai BM. Diagnosis, prevention, and management of eclampsia. Obstet Gynecol. 2005 Feb 1;105(2):402-10.
11. Wasseff S. Mechanisms of convulsions in eclampsia. Medi Hypoth. 2009 Jan 1;72(1):49-51.
12. Warrington JP. Placental ischemia increases seizure susceptibility and cerebrospinal fluid cytokines. Physiolog Rep. 2015 Nov;3(11):e12634.
13. Fleisher MD, Lee A. Eclampsia. In: Roizen, Michael F. Roizen, Jeffrey D, eds. Essence of Anesthesia Practice. 4th ed. Philadelphia, Pa: Elsevier Inc; 2018: 153-154.
14. American College of Obstetricians and Gynecologists. Diagnosis and management of preeclampsia and eclampsia. Obstet Gynecol. 2002;99:159-67.
15. Kumar N, Shekhar C, Kumar P, Kundu AS. Kuppuswamy's socioeconomic status scale-updating for 2007. Ind J Pediatr. 2007 Dec;74(12):1131.
16. Shaheen B, Hassan L, Obaid M. Eclampsia, a major cause of maternal and perinatal mortality: a prospective analysis at a tertiary care hospital of Peshawar. J Pak Medi Assoc. 2003 Aug;53(8):346-9.
17. George IO, Jeremiah I. Perinatal outcome of babies delivered to eclamptic mothers: a prospective study from a Nigerian tertiary hospital. Int J Biomed Sci: IJBS. 2009 Dec;5(4):390-4.
18. Shahabuddin AK, Hasnat M, Hamid T, Rahman AK. Perinatal outcome in eclampsia. Banglad J Child Health. 1996;20:8-14.
19. Alam IP, Akhter S. Perinatal Outcome of Eclampsia in Dhaka Medical College Hospital. Banglad J Obstet Gynaecol. 2008;23(1):20-4.
20. Yaliwal RG, Jaju PB, Vanishree M. Eclampsia and perinatal outcome: a retrospective study in a teaching hospital. J of Clin and Diagn Res. 2011;5(5):1056-9.