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CORRELATION OF MICRONUCLEUS SCORE AND OBSTETRIC COMPLICATIONS IN PERINATAL ASPHYXIA.

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ABSRACT

The present case control study was conducted to assess the correlation between Micronucleus Score and Obstetric complications in Perinatal Asphyxia. There were 80 term asphyxiated babies recruited as cases in which 69 (86.2%) had obstetric complications and 60 term babies were healthy. The Micronucleus Index was significantly different between obstetric complicated babies and controls ($p<0.001$). Lipid peroxidation was significantly more in obstetric complicated babies than controls ($p<0.001$). Apgar score was inversely proportional to Obstetric complications but Sarnat and Sarnat score was significant positive correlation. Serum Malodealdehyde was significant correlation with Obstetric complications ($p<0.001$).

KEYWORDS: Micronucleus Score, Obstetric complications, Lipid peroxidation, MDA.

INTRODUCTION

The prevalence of Obstetric complications like Pregnancy induced hypertension, Premature rupture of membranes cephalopelvic disproportion, Cord prolapse, maternal illness, meconium stained amniotic fluid, Intrauterine growth retardation, Breach presentation, Cesarian section and Oligohydramnios results Perinatal Asphyxia. The aforementioned incidence hamper the blood circulation of the foetus which leads to insufficient oxygen to the vital organs leads to multiorgan dysfunction in birth asphyxia. This dangerous situation causes disturbances in the integrity of nucleic acids resulting alteration in gene expression which negatively affects the Protein synthesis. Perinatal asphyxia due to obstetrical complications (OC) leads to significant DNA damage compared to controls with positive correlation to MDA.[1] Inorder to evaluate status of DNA damage whether the severe alteration in nucleic acid leads to Double strand break (DSB), we aimed to use Micronucleus assay.

MATERIALS AND METHODS

This study was carried out at the division of Cytogenetics of Department of Anatomy in collaboration with Department of Biochemistry and division of Neonetology of Department of Paediatrics of JIPMER, Pondicherry during 2008 to 2010. The study was approved by Institutional Research council and Ethical committee. Inclusion criteria of cases were term appropriate gestational age babies with Perinatal asphyxia without congenital anomalies and controls babies were similar demography without asphyxia. Perinatal Asphyxia was diagnosed by the following criterion, Apgar score less than 6 at 5 minutes, meconium stained liquor, change in fetal heart rate, clinical evidence of hypoxic ischemic encephalopathy, evidence of multiorgan dysfunction. Gestational age (LGA) and (SGA) and Preterm and Post term babies were excluded. Samples were taken from peripheral veins and stored in heparinised test tubes. The lymphocytes and plasma were separated from the whole blood by treating with Histopaque for which Micronucleus assay and Estimation of Malondealdehyde (MDA) were underwent respectively. Miconucleus Index of each samples were analysed by counting 1000 binucleated cells based on the guidelines of Bonanssi S et al[2] and methods of Manoj et al.[3] Estimation of MDA was done as per the methodology of Satoh et al[4] and Manoj et al.[5]

STATISTICAL ANALYSIS

Comparison between the cases and controls were done by t-test. Carl Pearson Correlation Coefficient was used for the association between the groups. All data were analysed by Microsoft Excel sheet-2007.

RESULT

In the present study we observed that the Micronucleus Index (MNi) of Obstetric complications in Perinatal

Asphyxia was significantly more than the control babies (p <0.001) (Table 1). The level of Serum Malondealdehyde was significantly more in obstetric complications than controls (p <0.001) (Table 1). The obstetric complications like Premature rupture of membranes (PRM), Prolonged labour(PL), Pregnancy Induced hypertension (PIH), Cord Prolapse(CP), Cephalopelvic disproportion (CPD) and Estimation of MDA were also significantly higher than the controls. Inorder to assess the correlation between Obstetric complication and the different variables of this study were also significantly different (Table 2). The R value of Apgar score, Hypoxic Ishemic Encephalopathy, Micronucleus Index, Serum MDA level were significantly associated with each other (P value 0.001) (Table 3) (Fig. 1).

Table 1: Showing Comparison of Micronucleus Score and Serum MDA in Obstetric complications of Perinatal asphyxia and controls (p <0.001).

Parameters	Obstetric complications	Controls	Significance
Micronucleus Score	3.678± • 15.116	1.60±1.12	p <0.001
Serum MDA	6.180 ±0.66	3.412± 0.536	p <0.001

Table 2: Exhibiting Micronucleus Score and Serum MDA in different types of Obstetric complications in Perinatal Asphyxia (p <0.001)

Obstetric complications(OC)	MNi	Serum MDA level
Premature Rupture of membrane (42%)	3.113±121	6.432±0.532
Prolonged labour(43%)	3.141±164	7.344±0.456
Pregnancy Induced Hypertension(07.2%)	3.510±131	7.112±0.142
Cord prolapsed(02.89%)	3.424±151	7.181±0.141
Cephalopelvic disproportion (05.79%)	3.111± 131	6.842±0.212

Table 3: Depicting Correlation coefficient between different Parameters between obstetric complicationsin Perinatal Asphyxia (p <0.001).

Parameters	Variables			
	HIE	Obstetric Complication	MNi	Serum MDA
Apgar Score	-0.6121	-0.6890	-0.7234	-0.8117
HIE		0.8089	-0.8211	0.8344
Obstetric complications			-0.7298	0.7568
MNi				0.8326

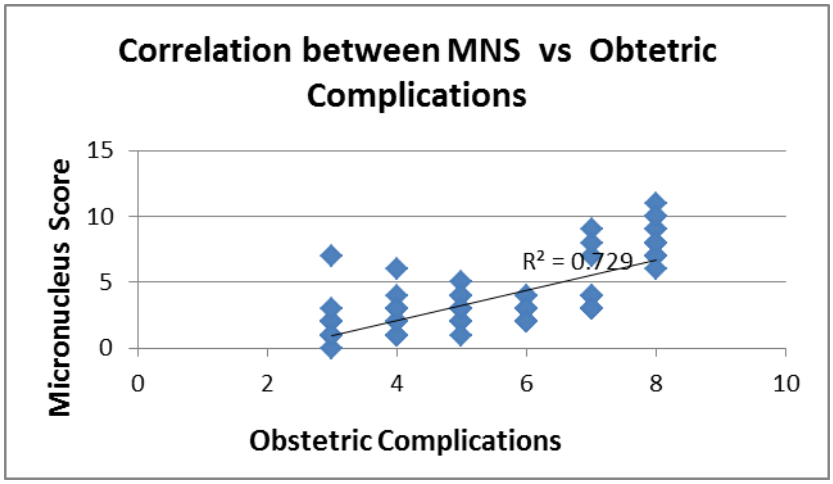

Figure 1: Depicting Coeffient Correlation between Obstetric complications and Micronucleus Score (MNS) in Perinatal asphyxia(R value 0.729) (P value<0.001).

DISCUSSION

The current study aimed to assess the Miconucleus score and serum MDA level in Obstetric complications of Perinatal Asphyxia compared to the controls. Micronucleus formation was due to double strand breaks of the DNA. We documented the Correlation between the different parameters such as clinical variables Apgar score, HIE and the MNS and MDA level to substantiate

the significant associations with Obstetric complications. WH Khreisat et al conducted Prospective study were 97 newborn infants participated which marked by higher percentage of deliveries were emergency caesarean section, intrauterine growth retardation, anepartum haemorrhage and maternal toxaemia had associated with high incidence of Asphyxia with low Apgar score and seizure.[6] The current study agrees the previous report that there was high incidence of obstetric complications leads to birth asphyxia and Hypoxic Ischemic encephalopathy in term babies with low Apgar and seizure. Apgar score was significant correlated with Micronucleus score. AL Chishty et al carried out the clinical spectrum of birth asphyxia and risk factors for adverse outcome in two hundred and ninety five cases fulfilling the inclusion criteria with multisystem involvement and higher mortality.[7] In the present study we found in 89% of babies born with obstetric complications and they had multiorgan dysfunction due to the deprivation of blood supply to vital organ which alters the structural and functional integrity of nucleic acids leads to oxidative DNA damage for which Obstetric complications were significantly associated with Micronucleus score.

Afsal MF reported that HIE is a common cause of neonatal mortality and long term squeal by finding out the frequency of risk factors in Asphyxiated newborns and out come of these newborn in relation to stages of HIE in hospital settings. Among of the 449 total admission in study period, 227 (51%) babies were asphyxiated. 165(73%) babies had cephalic presentation. Maternal hypertension was found in 53(23%), gestational diabetes in 9(4%), Pelvic abnormality in 30(13%) and antepartum hamorrage in 14(6%), 8(4%) babies had cord around the neck during delivery. Among the factors studied gestational age, weight, mode of delivery etc were found to be significant with p value (<0.05). They concluded that HIE is caused by the risk factors that may be antepartum, intrapartum or post partum, monitoring for the non risk factors of Asphyxia neonatal resuscitation services can minimize the incidence of HIE.[8] HIE was significantly associated with Double strand breaks in DNA. McDonald et al reported that Asphyxia occurred in 62.3%of infants <27 gestation and decreased to 0.4% in infants >38weeks gestation. Presence of asphyxia was associated with significant increase in neonatal mortality of infants >27 weeks gestation. The impact of asphyxia on mortality was most pronounced in more mature infants ie mortality was increase two fold for infants of 27 to 28 weeks gestation and greater than a hundred for infants > 36 weeks gestation.[9] In our study all babies were term and gestational age above 38+ weeks in which 69(86.2%) had obstetric complications, 20 (28.9%) infants were expired. When the gestational age increases in asphyxiated babies with obstetric complications the mortality rate also increases. Therefore earlier workers reports had agrees the current study. Hannah ME etal did a randomized trial to compare the policy planned of caesarean section with a policy of planned vaginal birth for selected breech presentation pregnancies. Among data of 2083women 1041 assigned planned caesarean section, 941 (90.4%) were delivered by caesarean section. Of the 1042 women assigned for planned vaginal birth 591(56.7%) delivered vaginally. Perinatal mortality, neonatal mortality and serious neonatal morbidity was significantly lower for planned caesarean section group than for planned vaginal birth group(1.6% vs 5.0%). The interpretation is planned caesarean section is better than planned vaginal birth for term fetus in breech presentation, serious maternal complications.[10] In our study the DNA damage was significantly more in Perinatal asphyxia with obstetric complications, but we could not assess the difference in caesarian section delivery and planned vaginal delivery of babies with Perinatal asphyxia. Bryce RL et al reported that the five perinatal findings felt to be indicators of asphyxia (meconium staining of amniotic fluid, abnormal foetal heart rate patterns, acidotic fetal scalp blood gases, low Apgar scores and acidotic cord blood gases). The strength of associations was found to vary inversely with the prevalence of outcome.[11] Infact the present study, the prevalence of perinatal asphyxia is due to the stress of the baby by obstetric complications, hence the observations of previous report had been strengthened that antepartum and intrapartum stress to the babies leads to significant double strand breaks in DNA.

CONCLUSION

DNA damage in Perinatal asphyxia correlates Obstetric complications which attributes not only single strand breaks of DNA but double strand breakage evidencing by significant Micronucleus score.

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