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CORRELATION OF DNA DAMAGE AND OBSTETRIC COMPLICATIONS IN PERINATAL ASPHYXIA

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ABSRACT

The current study was conducted to assess the correlation between DNA damage and Obstetric complications in Perinatal Asphyxia. Among eighty asphyxiated babies were examined and sixty healthy controls were participated in this case control study, 69 had obstetric complications (86.2%). The DNA damage was significantly different between asphyxiated babies with obstetric complication and control babies without obstetric complications ($p<0.001$). Serum Malondealdehyde (MDA) estimation was significantly more in obstetric complicated babies than control babies ($p <0.001$). Clinical parameters such as Apgar score and Sarnat and Sarnat score were significantly correlated with Obstetric complications ($p<0.001$). Comet tail length and Percentage of DNA in tail was significantly associated with Obstetric complications and Maternal Illness($p<0.001$).

KEYWORDS: DNA damage, Obstetric complications, MDA Estimation, Comet tail length, % DNA in tail of Comet.

INTRODUCTION

Perinatal asphyxia is a worldwide serious clinical problem which contributes greatly to neonatal morbidity and mortality.DNA is the genetic material of our life which controls all cellular activities, once development starts. Any disturbance in the oxygen carrying capacity of blood reflects in the functions of cells during Perinatal period there are chances impeding the blood supply to babies either due to maternal illness or obstetric complications, which are the risk factors.[1] Obstetrics complications such as Premature rupture of membranes (PROM) Prolonged labour(PL), Pregnancy Induced Hypertension(PIH), Cephalo Pelvic Disproportion (CPD), Cord prolapse (CP) and maternal complications (MC) ,hypertension (HP), meconium stained amniotic fluid(MSAF), Intrauterine growth retardation(IUGR), Breach presentation (BRP), Cesarian section(CS) and Oligohydramnios (OH) causes impairment in blood supply to growing baby which leads to oxdative stress results adducts in the DNA. Thus there are hindrances in the amino acid formation and protein synthesis which might alter the fundamental properties of living cell of the baby. Inorder to explore the Oxidative DNA damage in Perinatal asphyxia due the obstetric complications we choose Comet assay as a better parameter which is a sensitive test to assess genomic instability.[2]

SUBJECTS AND METHODS

The study was conducted at the cytogenetics division of Department of Anatomy JIPMER Pondicherry in collaboration with Neonetology division of Department of Paediatrics and department of Biochemistry from 2008 to 2011. The study was approved by the Institute Research council and Ethical committee. Inclusion criteria of cases and controls were term appropriate gestational age babies with perinatal asphyxia and babies without asphyxia respectively. Criteria for diagnosing Perinatal asphyxia were 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. Exclusion criteria included preterm and post term babies. Blood samples were collected peripheral vein into heparinised tubes. Whole blood was treated with Histopaque for separating leucocytes and plasma used for estimation of MDA. Single cell gel electrophoresis/ Comet assay was used for detection of DNA damage based on the protocol of Singh et al. Lipid peroxidation was observed by Estimation of MDA as per the guidelines of Satoh K et al.

Statistical Analysis

After validating the records in the database comparison between the groups were analysed by t-test. The correlation between the parameters were observed by

Carl Pearson correlation coefficient. All data were analysed by Microsoft Excel sheet-2007.

RESULTS

There was significant difference between parameters to assess the Oxidative stress induced DNA damages due to obstetric complication in perinatal asphyxia and healthy controls. Tail length of comet, % DNA in tail of comet and serum MDA level were significantly different with controls ($p < 0.001$), (Table:1). Obstetric complications such as Premature rupture of membrane (PROM), Prolonged Labour (PL), Pregnancy Induced Hypertension (PIH), Cord prolapsed (CP) and Cephalopelvic disproportion (CPD) shows extensive longer length of comet tail, high rate of % DNA damage in tail of comet and high level of serum MDA(Table:2). Correlation between Obstetric complications in Perinatal asphyxia and different parameters such as Apgar score, Hypoxic Ischemic Encephalopathy, Tail length of comet, %DNA in Tail and serum MDA level were significant (Table:3) (Fig:1).

Table 1: Showing Comparison Obstetric complications in Perinatal asphyxia and controls by different Parameters to assess Oxidative stress induced DNA damage($p < 0.001$).

Parameters	Obstetric complications	Controls	Significance
Tail length of comet	65.122± • 15.116	3.60±1.52	p <0.001
% DNA in tail of comet	51.551±13.885	7.23±1.58	p <0.001
Serum MDA	7.180 ±0.66	3.683± 0.536	p <0.001

Table 2: Exhibiting Tail length of comet, %DNA in Tail of comet and Serum MDA in different types of Obstetric complications in Perinatal Asphyxia.

Obstetric complications(OC)	Tail length of Comet	% of DNA in Comet tail	Serum MDA level
Premature Rupture of membrane (42%)	64.667±2.121	52.113±13.55	6.432±0.532
Prolonged labour(43%)	66.134±13.134	56.321±124	7.344±0.456
Pregnancy Induced Hypertension(07.2%)	65.432±14.112	55.421±151	7.112±0.142
Cord prolapsed(02.89%)	63.211±14.115	51.562±131	7.181±0.141
Cephalopelvic disproportion(05.79%)	60.117±142	52.161± 117	6.842±0.212

Table 3: Depicting Correlation coefficient between different Parameters between obstetric complications ($p<0.001$).

Parameters	Variables				
	HIE	Obstetric Complication	% of DNA in Tail of Comet	Length of Tail of comet	Serum MDA
Apgar Score	-0.6121	-0.6890	-0.6262	-0.6643-	-0.8117
HIE		0.8089	0.8654	0.8321	0.8344
Obstetric complications			0.725	0.789	0.7568
% of DNA in Tail of Comet				0.8298	0.8326
Length of Tail of comet					0.809

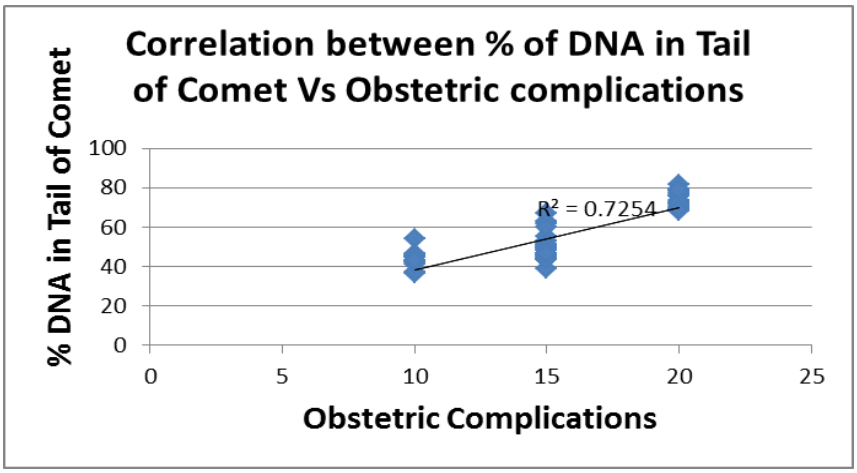

Figure 1: Exhibiting Coeffient Correlation between Obstetric complications and % DNA in Tail of Comet in Perinatal asphyxia.

DISCUSSION

An insult to the fetus or new born due to failure to breath which leads to decrease oxygen perfusion to the various organs which is due to risk factors including Obstetrics complications such as Premature rupture of membranes ,Prolonged labour, Pregnancy Induced Hypertension, Cephalo Pelvic Disproportion, Cord prolapse and maternal complications ,hypertension (HP), meconium stained amniotic fluid(MSAF), Intrauterine growth retardation, Breach presentation, Cesarian section, and Oligohydramnios. Mac Donald et al reported that the impact of asphyxia on mortality was most pronounced in more mature infants, mortality was increased in twofold for infants of 27 to 28 weeks gestation and greater than a hundred fold for infants >36 weeks gestation. In our study the mortality rate was due to the high risk factors in Perinatal asphyxia in which gestational age of cases were 39.42±1.490 in cases 28(35%) babies were expired. It had been observed that once the gestational age increases the mortality rate increases in cases with high risk factors like obstetrical complications associated with Perinatal asphyxia.[3] According Kothari SN, Obstetrical complications are important risk factors for asphyxia of new born. Among the important risk factors are those associated with prolonged labour and intrapartum accidents in which the incidence of risk for asphyxia broadly was 21.3% which is very close to the actual incidence of asphyxia of 22%. In the current study among the 140 infants participated 80 were cases and 60 were controls in which 69 (86.25%) babies were involved in obstetrical complications showing significant increase in the risk factors of birth asphyxia with 26.25%, 50.00% and 23.75% had mild moderate and severe stages of asphyxia. Both studies shows positive associations between risk factors and Perinatal asphyxia[4]. Milsom I et al reported that the influence of maternal, obstetric and fetal risk factors on the prevalence of birth asphyxia at term in a Swedish urban population were registered in 225 cases of birth asphyxia diagnosed in 42 203 live births shows that an association between neonatal asphyxia and cardiotocography parameters, intrauterine meconium release, operative delivery, breech delivery, single civil status, oxytocin augmentation, cord complication, external compression to assist delivery. In the present study foetal risk factors such as Premature rupture of membranes (PROM) Prolonged labour(PL), Pregnancy Induced Hypertension(PIH), Cephalo Pelvic Disproportion (CPD), Cord prolapse (CP) and maternal complications (MC) hypertension (HP), meconium stained amniotic fluid(MSAF), Intrauterine growth retardation (IUGR), Breach presentation(BRP), Cesarian section(CS) and Oligohydramnios (OH) were significantly associated with Perinatal asphyxia in which the DNA damage was positive correlation.[5] The data of Wubet Alebachew Bayih et al shows that the prevalence of birth asphyxia has remained a problem factors like antenatal obstetric complications parity, multiple births , gestational age < 37 or > 41 weeks, low birth weight , premature rupture of membranes, prolonged labor and fetal distress have already been identified to be among the risk factors of birth asphyxia.[6] Our study agreed the data of the previous report as obstetric complications and increased gestational age were risk factors of Perinatal asphyxia. Fifty-six cases and 168 controls were examined. Premature placental abruption (OR=41.09; 95% CI: 4.61-366.56), labor with a prolonged expulsive phase (OR=31.76; 95%CI: 8.33-121.19), lack of oxytocin use (OR=2.57; 95% CI: 1.08 - 6.13) and mothers without a partner (OR=2.56; 95% CI: 1.21-5.41) were risk factors for the development of perinatal asphyxia in the study population. Social difficulties were found in a greater proportion among the mothers of cases. Our study aimed to record the significant correlation between obstetrical complications in Perinatal asphyxia with Oxidative stress DNA damage which positively reflects in extension of Tail length of comet and increases in the amount of %DNA in Tail of comet. Risk of neonatal encephalopathy increased with increasing or decreasing maternal age.[7] Antepartum risk factors included non-attendance for antenatal care (64%). Multiple births increased risk in 4.8%. Intrapartum risk factors included non-cephalic presentation (20%), prolonged rupture of membranes (24%) and various other complications. Particulate meconium was associated with encephalopathy in 9.6%. 60% mothers were anaemic. Vaginal bleeding was strongly associated with birth asphyxia in 34.44% of neonates. 56% of mothers delivered at home, while 28% delivered at a private hospital or maternity home. Only 12% delivered at a tertiary care hospital. Lack of antenatal care, poor nutritional status, antepartum hemorrhage and maternal toxaemia were associated with higher incidence of asphyxia.[8] In the present study risk of hypoxic ischemic encephalopathy was increased due to obstetrical complications in which antepartum and intrapartum risk factors were hampered the circulation of blood to brain leads to severe hypoxia with consequential increase in oxidative DNA damage. Therefore HIE and Obstetric complications were significantly correlated and agreed with aforementioned two reports. Anne CC et al reported that 30% neonatal mortality accounted among the 9.7/1000 live birth in a cluster randomized, community based on cohort trial in southern Nepal, evaluating the impact of antepartum risk factors such as Maternal infections, multiple birth are important risk factors for birth asphyxia mortality in low resource, community based settings. Low socioeconomic status is highly associated with birth asphyxia, mechanism leading to mortality need to be elucidated.[9] In our study 28 (35%) babies were expired due to severe birth asphyxia.[10] It can be observed that antepartum risk factors leads to birth asphyxia which results in high mortality rate among our data and foreign data. The Apgar score was significant correlation with HIE, Oxidative DNA damage and Obstetric complications evidencing Maternal problems results high rate of DNA damage and increase level of serum MDA.

CONCLUSION

Obstetric complications leads significant correlation with Oxidative DNA damage in Perinatal Asphyxia.

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