

CORRELATION OF CHROMOSOMAL ABERRATIONS WITH MULTIORGAN DYSFUNCTION IN PERINATAL ASPHYXIAA. Manoj^{1*}, B. Vishnu Bhat², C. Venkatesh², Z. Bobby³¹Departments of Anatomy, Jawaharlal Institute of Post Graduate Medical Education and Research (An Institution of National Importance -Govt. of India Ministry of Health and Family Welfare) Pondicherry, India.²Paediatrics Jawaharlal Institute of Post Graduate Medical Education and Research (An Institution of National Importance -Govt. of India Ministry of Health and Family Welfare) Pondicherry, India.³Biochemistry Jawaharlal Institute of Post Graduate Medical Education and Research (An Institution of National Importance -Govt. of India Ministry of Health and Family Welfare) Pondicherry, India.***Corresponding Author: A. Manoj**

Department of Anatomy Govt. medical College-Thrissur, Kerala-680596, India.

Article Received on 05/04/2018

Article Revised on 26/04/2018

Article Accepted on 16/05/2018

ABSTRACT

The current study evaluated oxidative stress induced DNA damage and chromosomal aberrations on multiorgan dysfunction in perinatal asphyxia. Eighty term asphyxiated babies were recruited in this study and all of them had organ dysfunction. Conventional Cytogenetic screening test was used for identification of chromosomal aberrations. Oxidative stress was assessed by estimation of serum MDA level. Chromatid breakage, dicentric chromosomes, inter chromatid connections, ring chromosomes and acentric chromosomes were recorded. The chromosomal aberrations in two, three, four and five systems were 2.75 ± 0.942072 , 3.052632 ± 0.998614 , 3.25 ± 1.409787 and 4.85 ± 0.726292 respectively. Chromosomal aberrations increased with severity of asphyxia and it was well associated with oxidative stress ($p < 0.05$). Involvement of Organ systems in perinatal asphyxia positively correlated with Chromosomal damage ($p < 0.05$).

KEYWORDS: Perinatal asphyxia (PA), Multiorgan dysfunction (MOD), Chromosomal aberrations (CA), Serum malonaldehyde (MDA).

INTRODUCTION

Multiorgan dysfunction is one among the criteria for diagnose Perinatal Asphyxia.^[1] Vital organ damage occurs inspite of diving reflex causing diversion of blood from less important organs to vital organs.^[4] Insufficient blood circulation leads to release of catalytic copper ions within the cell and generation of hydroxyl radicals which cause strand breakage and base modification of DNA culminating in chromosomal aberration.^[8] The Conventional Karyotyping with Automation software system is a gold standard method to determine chromosomal aberrations.^[2] Oxidative stress can be assessed by estimation of MDA levels. The present study was conducted to correlate the organ damage with chromosomal aberrations and oxidative stress.

PATIENTS AND METHODS

The study was conducted in the Cytogenetic unit of Department of Anatomy in collaboration with Department of Neonatology and Biochemistry of JIPMER from February 2008 to July 2010. The study was approved by Institute Research and Human Ethical committee. Inclusion criteria for selection of babies were

Apgar score less than 6 at five minutes, meconium stained liquor, changes in foetal heart rate, evidence of Hypoxic ischemic encephalopathy and evidence of organ dysfunction. Babies who were pre-term or post term birth, large or small gestational age, babies whose mothers had significant illness and those with congenital malformations were excluded. Cytogenetic investigation was conducted as per the recommendations of International System of Human Cytogenetic Nomenclature (ISCN) and analysis was done using metasytem IKROS software, Germany.^[2] Among the eighty asphyxiated babies forty with metaphase good quality spreads were included in this study. Oxidative stress was assessed by estimation of serum MDA level.^[3,9]

Statistical Analysis

Comparison of different groups was carried out using one way ANOVA. Correlation between different variable was assessed by Carl Perarson co-efficient Correlation. Data was analysed by Graph Pad (InStat, San Diego, USA) and P value < 0.05 was taken as significant.

RESULTS

Among the eighty asphyxiated babies 20 (25%) each had five ie; CNS (central nervous system), RS (Respiratory system), CVS (Cardiovascular system), DS (Digestive system), US (Urinary system) and four system involvement (CNS, RS, CVS, DS), 19 had three system involvement and 21 had two system affected The

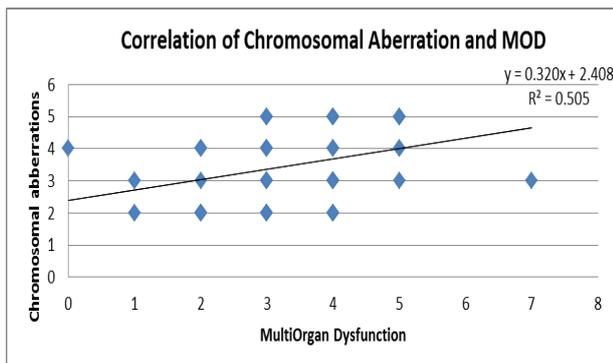
Chromosomal aberrations found in this study were chromatid breakage, Interchromatid connection, Dicentric chromosome, Ring chromosomes and Acentric chromosome. Serum MDA level was significantly increased with involvement of more organ system. Chromosomal aberration was significantly associated with increased organ dysfunction ($P < 0.05$).

Table 1: Chromosomal aberration score, Serum MDA level with Multiorgan Dysfunction.

No. System Involved	Chromosomal Aberrations	Serum MDA level
Two	2.75± 0.942072	4.703476±0.894624
Three	3.052632±0.998614	5.543737±1.257756
Four	3.25±1.409787	7.1174±0.502454
Five	4.85±0.726292	8.4883± 0.576468

Table 2: Delineating Correlation Co-efficient (r) between Parameters.

Parameter	Variables			
	HIE	MOD	CA	MDA
APGAR	-0.7315**	-0.6301**	0.592**	-0.5045**
HIE		0.9235*	0.531*	0.8070*
MOD			0.528*	0.9341*



Depicting Correlation Coefficient (Pearson) Chromosomal Aberration and MOD ($p < 0.01$ and $r = 0.505$).

DISCUSSION

The occurrence of organ dysfunction in perinatal asphyxia affects the outcome adversely.^[5] In our study all neonates had involvement of nervous system and respiratory systems indicating severity of cases. Martin et al reported that 82% of asphyxiated infants had involvement of one or more organs; CNS being most frequently affected (72%) followed Renal (42%), Cardiac (29%), Gastrointestinal (29%) and Pulmonary (26%).^[5] Martin et al suggested that Apgar score at 5 minutes is the perinatal marker that may best identify infants at risk of organ dysfunction. Our study revealed that Apgar score had negative correlation with Chromosomal aberrations.

Unrepaired adduct can interfere in the formation of RNA polymerase and block the production of vital genes leading to cell death.^[8] In fact oxidative stress induced DNA damage was significantly associated with severity of asphyxia.^[10] In our study oxidative stress and

chromosomal aberrations were significantly associated with each other. DNA was severely damaged in HIE stage-3 with eventual adverse outcome. In our study there was 35% mortality.^[6] However study by Shah et al concluded that MOD had no correlation with outcome.^[4]

In our study we found the occurrence of Chromatid breakage, dicentric chromosomes, Interchromatid connections, Ring chromosomes and Acentric chromosomes. Neilson et al reported 4.2% babies having chromosomal aberration in neonatal asphyxia. Our study showed that five and four organ dysfunction babies had chromosomal aberration of 4.85% and 3.25% respectively.^[7] The percentage of Chromosomal aberrations had positive correlation with MOD and MDA level. There was positive correlation between HIE severity and chromosomal aberrations.

CONCLUSION

Hypoxic ischemic encephalopathy had positive correlation with multiorgan dysfunction and high mortality Serum MDA level significantly increased with chromosomal aberration and organ dysfunction.

ACKNOWLEDGEMENTS

My gratitude to Dr. Ramachandra Rao (Late) former Senior Professor and Head of Department of Anatomy, JIPMER Pondicherry who was the Guide and my mentor of my doctoral Research studies.

REFERENCE

1. Lisa M, Adcock, Lu-Ann papile Perinatal Asphyxia , Chapter 27 c Manuel of Neonatal CareSixth Edition Lippincott Williams & Wilkins, a Wolters Kaluwer India Pvt. Ltd, New Delhi, 2008; 518.
2. Rooney DE, Czepulkowski BH, Gosden GM, Davidson C, Robertson M. Human Cytogenetics. Constitutional analysis. A practical approach. Lymphocyte culture, Oxford University Press, Walton street USA, 1992; 1: 31-37.
3. Satoh K. Serum lipid peroxide in cerebrovascular disorder determined by anew calorimetric method. Clin Chem Acta, 1978; 90: 37-43.
4. Shah P, Riphagen S, Beyene J, Perlman M. Multiorgan dysfunction in infants with post-asphyxial hypoxic ischemic encephalopathy. Arch Dis Child Fetal Neonatal Ed, 2004; 89: F152-F155.
5. Martin-Ancel A, Garcia-Alix A, Gaya F, Cabanas F, Burgueros M, Quero J. Multiple organ involvement in perinatal asphyxia. J Pediatr, 1995; 127: 786-793.
6. Manoj A, Rao RK, Bhat VB, Venkatesh C, Bobby Z. Chromosomal aberrations in Perinatal asphyxia. Curr Ped Res Curr Pediatr Res., 2012; 16(1): 65-68.
7. Neilson J, Hansen KB, Sillesen I, Vedobech P. Chromosome abnormalities in newborn children Hum Genet, 1981; 59: 194-200.
8. Kaufmann WK, Richard S, Paules. DNA damage and cell cycle and checkpoints. FASEB journal USA, 1996; 283: 238-247.
9. Singh SK, Dua T , Tandon A, Kumari S, Ray G , Batra S. Status of lipid peroxidation and antioxidant enzymes in hypoxic ischemic encephalopathy. Indian Pediatr, 1999; 2: 659-668.
10. Manoj A, Rao RK, Bhat VB, Venkatesh C, Bobby Z. Oxidative stress induced DNA damage in Perinatal asphyxia. Curr Ped Res., 2011; 15(1): 19-23.