Original Research Paper

Volume : 5 | Issue : 11 | November 2016 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 69.48

ROLE OF INFECTIONS AND GENETIC INSTABILITIES AMONG LOW BIRTH WEIGHT BABIES

Microbiology

KEYWORDS: Low birth weight, Chromosomal abnormalities, Cytokinesis-Block Micronuclei (CBMN) Assay

Swapna C Senan	Research Scholar, Meenakshi University, West KK Nagar, Chennai- 600 078. TN, India.
Sarala Gopalakrishnan	Department of Medical Microbiology, St Pius X College, Kasargod -671532, India.
Sadiya Ahammed	Genetika, Centre for Advanced Genetic Studies, Pettah P O, Thiruvananthapuram-695 024, India.
Dinesh Roy D	Genetika, Centre for Advanced Genetic Studies, Pettah P O, Thiruvananthapuram-695 024, India.

ABSTRACT

Birth weight is one of the most sensitive and reliable predictors of health of any community. Low birth weight (LBW) is an important factor for high prenatal and infant morbidity and mortality. The health of the mother is of prime importance in the outcome of pregnancy and health of the baby. Prenatal diagnosis enables early diagnosis of congenital anomalies and genetic disorders in utero. The proper diagnosis of chromosomal abnormalities can lead to the prevention of future birth of similarly affected children. The aim of the present study was to determine the role of infection and genetic instabilities among low birth weight babies. The study was carried out in 42 study subjects and 18 subjects without any chronic illness were also selected as control for this study. Cytokinesis-Block Micronuclei (CBMN) Assay was performed on each sample by using cytochalasin B for quantitating the extent of somatic DNA damages. The present study demonstrated that micronuclei frequency was significantly elevated in the study subjects than control subjects. The mean CBMN frequency of the subjects was statistically higher than that of the healthy control subjects. This study clearly demonstrated that the mean CBMN frequency of study subjects increases with respect to demographic and clinical risk factors such as maternal and paternal age, duration of married life, history of maternal infection, maternal illness and drug intake. LBW babies usually need extra hospital care, and there is a constant concern and uncertainty over future health outcomes. However, little attention is paid to birth weight improvement as a means of reducing child mortality. An affordable health care service, the preconception counseling and care for young women is strongly needed for a healthy future outcome.

INTRODUCTION

Low Birth Weight (LBW) baby is defined as baby having weight less than 2.5 kg within 24 hours of birth[1]. LBW is an important public health problem in developing world[2]. The proportion of LBW reported from India is 21.5%[3]. Birth weight of a child is an important indicator of its vulnerability for childhood illness and chances of survival[4].

In developing countries, LBW is a major determinant of perinatal mortality and morbidity[5]. According to Neonatal mortality, LBW babies are 20 times more likely as compared to babies heavier than 2.5kg[6]. The incidence of LBW was significantly higher in the group of teenage mothers[7]. A high incidence of LBW babies among women living in rural areas with low coverage of safe water supply. This could be because of increased episodes of gastro intestinal infections impairing normal fetal development[8]. Significantly higher incidence of LBW babies among anemic as compare to non anemic mothers[9].

There are certain risk factors which are strongly associated with LBW babies[5]. Young maternal age was a significant risk factor for LBW[10]. A baby's birth weight is related to birth weight of both parents and more strongly through the line. Women born with LBW have a higher risk of having LBW babies. Cigarette smoking, tobacco and chewing is also a risk factor for LBW[11]. Prenatal growth retardation, premature birth and congenital malformations appear the most important factors that determine low birth weight[12].

During gestation, many microorganisms can infect the foetus, causing severe birth defects and the resulting clinical syndrome have been categorized as TORCH infection[13]. Genital tract infection during pregnancy can cross into the amniotic fluid and result in prelabour rupture of the membranes and preterm labour. Globally, at least 7.6 million children are born annually with severe genetic or congenital malformation, 90% of these infants are born in mild and low income countries. Congenital anomalies are associated with premature labour. In fact, many of these foetus are spontaneously aborted very early in pregnancy[14].

Low birth weight constitutes about 17% of all live births globally. Children of low birth weight are at an increased risk from neurosensory, developmental, physical and physiological problems. Chromosomal abnormalities and various other syndromes are one of the most common causes of low birth weight. Maternal infections also cause major birth defects in new born babies. These infections are most serious during pregnancy and when transmitted in utero, can cause congenital malformation in neonates. A detailed evaluation for the etiology of these low birth weight babies is necessary and has good clinical implications. No serious attempts were made earlier to correlate between the role of infection and genetic instabilities among low birth weight babies. Hence the present study was undertaken to evaluate the role of infection and genetic aspects of children born with low birth weight.

MATERIALS AND METHODS

Forty two subjects suffering with low birth weight were selected for this study. The samples were referred from various maternity centres of kerala for genetic testing to Genetika, Centre for Advanced Genetic Studies, Trivandrum, Kerala. Eighteen subjects without any chronic illness were also selected as control for this study. Detailed demographic, clinical and lifestyle characteristics were recorded using proforma. In this study, Cytokinesis Block Micronuclei (CBMN) assay was carried out in each subject. CBMN assay was performed by using Cytochalasin B for quantitating the extent of somatic DNA damages.

The fresh blood collected by venepuncture was transferred to vacuutainer containing sodium heparin as anticoagulant. Added 5 to 6 drops of whole blood samples to a vial containing 10 mL RPMI 1640

supplemented with 100 units/mL penicillin, 100µg/mL streptomycin, 15% fetal bovine serum and 100µg/mL phytohemagglutinin. Cytochalasin B was added to the cultures at a final concentration of 4.5µg/mL (Sigma) after 44th hours of initiation of cells with phytohaemagglutinin. Cells were harvested after 72 hr incubation, and they were treated with a hypotonic solution (0.075M KCl) for 1 min and fixed in fresh fixative solution (methanol: acetic acid, 3:1). The cells were dropped onto slides and the slides were air dried and stained with 10% Giemsa. Micronucleated cells were analyzed under light microscopy at 100X magnification. The number of micronuclei is not less than 1000 binucleated cells were scored and the distribution of micronuclei among binucleated cells was recorded.

Table 1- Distribution of mean CBMN frequency according to various demographic characteristics of the study subjects

Category	Variables	Total	Percentage (%)	Mean CBMN Frequency
Age (Years)	<1	22	52.3	14.25
	1 to 15	12	28.5	14.26
	16 to 30	2	4.7	13.94
	New born	6	14.2	14.28
Sex	Female	20	47.5	14.28
	Male	22	52.3	14.19
Birth weight (Kg)	<2	14	33.3	14.28
	≥2	28	66.6	14.26
Paternal age (Years)	20 to 40	31	73.80	14.25
	41 to 60	11	26.19	14.33
Maternal age (Years)	20 to 40	40	95.23	13.94
	41 to 60	2	4.76	14.29
Duration of married life of parents(Years)	<1	2	4.76	13.94
	1 to 15	38	90.47	14.28
	16 to 30	2	4.76	14.59

Distribution of mean CBMN frequency according to various demographic characteristics of the study subjects were showed in Table 1. The subjects were grouped on their demographic characteristics such as age, sex, birth weight, paternal age, maternal age and duration of married life of parents. Among the 42 study subjects, 22 subjects (52.3%) were belonged to <1 years of age and showed a mean CBMN frequency of 14.25. 12 subjects (28.5%) with age between 1 to 15 years and showed a mean CBMN frequency of 14.26. 2 subjects (4.7%) were belonged to age between 16 to 30 years and showed a mean CBMN frequency of 13.94. New born babies showed highest mean CBMN frequency of 14.28. 20 female subjects showed mean CBMN frequency of 14.28 and 22 male subjects showed mean CBMN frequency of 14.19. Birth weight of the subjects were divided in to <2 kg and ≥2 kg. Subjects with <2 kg of birth weight showed highest mean CBMN frequency of 14.28. Paternal age and maternal age between 41 to 60 years were showed highest mean CBMN frequencies (14.33 and 14.29). Parents having 16 to 30 years duration of married life showed mean CBMN frequency 14.59.

Table 2- Distribution of mean CBMN frequency according to the various clinical characteristics of the study subjects

Category	Variables	Total	Percentage (%)	Mean CBMN
Clinical conditions	Congenital abnormalities	9	21.4	14.42
	Cleft palate	2	4.7	13.87
	Developmental delay	8	19.04	14.39
	Dysmorphism	19	45.2	14.07
	Multiple anomalies	4	9.5	14.87
H/o maternal infection	Yes	16	38.09	14.3
	No	26	61.90	14.26
H/o illness	Yes	14	33.33	14.31
	No	28	66.66	14.26
H/o drug intake	Yes	16	38.09	14.35
	No	26	61.90	14.23
CMV IgG antibody	Positive	6	14.28	14.36
	Negative	36	85.71	14.26
Rubella IgG antibody	Positive	6	14.28	14.28
	Negative	36	85.71	14.25
USS finding	Normal	20	47.61	14.25
	Abnormal	22	52.38	14.3

Distribution of mean CBMN frequency according to the various clinical characteristics of the study subjects were showed in Table 2. The subjects were grouped on their clinical characteristics such as clinical conditions, H/o of maternal infection, H/o of illness, H/o drug intake, CMV IgG antibody, Rubella IgG antibody and USS finding. According to their clinical conditions, 19 subjects (45.2%) had dysmorphism, 9 subjects (21.4%) had congenital abnormalities, 8 subjects (19.04%) had developmental delay, 4 subjects (9.5%) had multiple anomalies and remaining 2 subjects (4.7%) had cleft palate. The highest mean CBMN frequency (14.42) was showed by subjects with congenital abnormalities. 16 subjects have history of maternal infection and they showed the mean CBMN frequency of 14.3. 14 subjects have history of illness showed a mean CBMN frequency of 14.31. History of drug intake was showed by 16 subjects and they showed mean CBMN frequency of 14.35. Subject with CMV IgG antibody was positive and showed a mean CBMN frequency of 14.28. Subject with Rubella IgG antibody was positive and showed a mean CBMN frequency of 14.28. Normal USS finding subjects showed mean CBMN frequency of 14.25 and abnormal USS finding subjects showed mean CBMN frequency of 14.3.

DISCUSSION

Low birth weight infants fail to achieve their ultimate growth potential as a result of intrauterine and postnatal growth failure. In 2012, an estimated 15 million babies (11.3 % of live births) worldwide were born preterm, about 13 million of these infants survived beyond the first month of life[15]. In the present study, newborn babies had high risk of low birth weight compared with other ages and they showed highest mean CBMN frequency.

Birth weight is a technically simple parameter to monitor prenatal health in a population. Prenatal growth retardation, premature birth, and congenital malformations appear the most important factors that determine low birth weight[12]. In the present study, 33.3% of the study subjects have birth weight less than 2 kg. Babies with birth weight less than 2kg showed highest mean CBMN frequency of 14.28.

In the cross sectional study conducted by Rizvi et al.,[16], the newborns were assess for congenital anomaly (CA). In the present study, it was analyzed that majority of the subjects (n=19) have dysmorphism. Among these clinical conditions, the highest mean CBMN frequency showed by subjects had multiple anomalies (14.87).

Rizvi et al.,[16] reported increased risk of LBW with increasing maternal age. A study from India failed to find any association between LBW and increasing maternal age as significant risk factors[17]. According to Dinesh Roy et al.,[18] the incidence of chromosome anomalies was significantly increased after 30 years. The observation found in the present study was the mean CBMN frequency increases with increasing maternal age.

In some maternal conditions, the risk lies with the drugs used for treatment, rather than the illness itself. Some drug may induce teratogenic effects that are clinically evident until many years after birth[19]. In the present study, it was observed that the distribution of mean CBMN frequency was higher in those subjects with the history of drug exposure and the history of illness.

Presence of IgM antibodies is associated with acute infection. IgG avidity test may have a higher specificity in the detection of acute infection; however, it still cannot identify a neonatal infection[20]. Rahav et al.,[21] demonstrated a vertical transmission of CMV in about 30% of mothers infected by CMV during pregnancy. However,

Volume : 5 | Issue : 11 | November 2016 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 69.48

abortion rate is relatively high in pregnancies complicated by CMV infection. In the present study showed that 14.28% subjects were CMV IgG antibody positive with a mean CBMN frequency of 14.36 and 85.71% showed CMV IgG antibody negative.

Risk for congenital rubella syndrome happens when infection occurs in early stages of pregnancy. Specifically, the percentage of infants with congenital rubella syndrome exceeds 50% in cases of infection during the first trimester of pregnancy while the relative percentage is significantly reduced after the 20th gestational week[22]. In the present study, subjects with Rubella IgG antibody positive showed increased mean CBMN frequency than the subjects with Rubella IgG antibody negative.

CONCLUSION

In short, the present study involves the role of infection and genetic instabilities among low birth weight babies. The distribution of mean CBMN frequency according to demographic and clinical factors of the study subjects was observed. Age, sex, birth weight, paternal age, maternal age etc. showed increased level of CBMN frequency. The level of mean CBMN frequency was higher among those who have the history of maternal infection and history of illness. CMV IgG antibody and Rubella IgG antibody were also found to be significantly elevated in study subjects. These findings suggest that the Low birth weight have a high incidence of infection and genetic instability but these are the major contributors to infant mortality. Efforts towards preventing early marriage would contribute significantly in reducing the prevalence of low birth weight. Public education and awareness are on how to carry a healthy pregnancy. Likewise; women should be linked to the appropriate maternal health services including antenatal care and nutritional counseling services.

REFERENCE

1. Yilgwan CS, Abok II, Yinnang WD, Vajime BA. Prevalence and risk factors of low birth Jos. Jos J Med. 2009; 4(1):13–15.
2. Jitendar Nagpal, Ajay kumar and Siddarth Ramji Anterior Lens Capsule Vascularity in Evaluating Gestation in Small for Gestation Neonates. Indian Pediatrics.(2004) 817-821.
3. Mumbare SS, Maindarkar G, Darade R, Yenge S, Tolani MK, Patole K. Maternal risk factors associated with term low birth weight neonates: a matched-pair case control study. Indian Pediatr. 2012;49(1):25–28.
4. Sudesh Raj Sharma, Smith, Giri, Utsav Timalsina, Sanjiv Sudarshan Bhandari, Bikash Basyal, Kusum Wagle, and Laxman Shrestha. Low Birth Weight at Term and Its Determinants in a Tertiary Hospital of Nepal: A Case-Control Study PLoS One. 2015; 10(4): e0123962.
5. Ayesha Khan, Farah Deeba Nasrullah, and Riffat Jaleel. Frequency and risk factors of low birth weight in term pregnancy Pak J Med Sci. 2016; 32(1): 138–142.
6. UNICEF and WHO. Low Birth weight: Country, Regional and Global Estimates. NY: UNICEF Editorial and publication center; 2004. division of communication.
7. Banerjee B, Pandey GK, Dut D, Sengupta B, Mondal M. Teenage Pregnancy: A Socially Inflicted Health Hazard. Indian J Community Med. 2009; 34(3):227–231.
8. Kayode GA, Amoakoh-Coleman M, Agepong IA, Anash AE, Grobbee DE, Klipstien-Grobusch K. Contexual risk factors for LBW;A multilevel analysis. PLoS ONE. 2014; 9(10):e109333.
9. Badshsh S, Mason L, Mckelvie K, Payne R, Lisboa PJG. Risk factors for Low Birth Weight in the Public Hospitals at Peshawar, NWFP-Pakistan. BMC Public Health. 2008; 8: 197–206.
10. Viengsakhone L, Yoshida Y, Harun-or-Rashid M, Sakamoto J. Factors affecting low birth weight at four central hospitals in Vientiane. Lao PDR Nagoya J Med Sci. 2010; 72:51–58.
11. Gupta PC, Sreevidya S. Smokeless tobacco use, birth weight, and gestational age: population based cohort study of 1217 women in Mumbai, India. BMJ. 2007;328(7455):1538.
12. Paliwa ASV, Mohan I, Choudhary RM, Sharma BN. Risk factros associated with low birth weight in newborns: a tertiary care hospital based study. Int J Cur Res Rev. 2013;05(11):42–8.
13. Franca CM and Mugayar LR. Interauterine infection: a literature review.(2004) 24(5):250-253.
14. Creasy RK and Resnik R. Maternal-Fetal Medicine: Principles and Practice. 5th ed. Philadelphia PA:WB ,Saunders 2004.
15. Lawn JE, Blencowe H, Oza S, You D, Lee AC, Waiswa P, et al. Lancet every newborn study group: every newborn: progress, priorities, and potential beyond survival. Lancet. 2014; 384(9938):189–205.
16. Rizvi SA, Hatcher J, Jehan I, Qureshi R. Maternal risk factors associated with low birth weight in Karachi: a case control study. Eastern Mediterranean Health J. 2007; 3(6):1343–1352.
17. Mumbare SS, Maindarkar G, Darade R, Yenge S, Tolani MK, Patole K. Maternal risk factors associated with term low birth weight neonates: a matched-pair case control study. Indian Pediatr. 2012; 49(1):25–28.
18. Roy D. Dinesh, K. Pavithran, P. Y. Henry, K. E. Elizabeth, P. Sindhu, T. Vijayakumar. Correlation of Age and Birth Order of Parents with Chromosomal Anomalies in Children. 2003, Volume 39, Issue 6, pp 695–699.
19. Hansen N, Stoll BJ, Fanaroff AA. etal. Changes in pathogens causing early-onset sepsis in very-low-birth-weight infants. N Engl J Med. 2002; 347:240-247.
20. Yamada H, Nishikawa A, Yamamoto T, Mizue Y, Yamada T, Morizane M, et al. Prospective study of congenital toxoplasmosis screening with use of IgG avidity and multiplex nested PCR methods. J Clin Microbiol. 2011; 49:2552–6.
21. Rahav G, Gabbay R, Ornoy A, Shechtman S, Arnon J, Diav-Citrin O. Primary versus nonprimary cytomegalovirus infection during pregnancy, Israel. Emerg Infect Dis. 2007; 13:1791–3.
22. Namaei MH, Ziaee M, Naseh N. Congenital rubella syndrome in infants of women vaccinated during or just before pregnancy with measles-rubella vaccine. Indian J Med Res. 2008; 127:551–4.