

## **Maternal risk factors and consequences of low birth weight in Infants**

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**Abstract:** *Low birth weight is a multi-factorial problem with a wide spectrum of health related problems from its origin to later in life. It is one of the important causes of high infant's mortality and morbidity rate in developing countries. The rate of low birth weight continues to increase; putting more children at risk of health related consequences, because it has an independent effect on child health. It contributes to the costs to the family, society and the world as a whole in keeping Low birth weight infants alive and developing them. Neonatal hospital costs (antenatal cortico steroids, new modes of ventilation, exogenous surfactants) are high and it remains high after hospital discharge. as children grow older costs continues to be high and complications and their nature may change. Reduction in low birth weight mortality have greatly contribute to the reduction in overall mortality. According to W.H.O. concept "Health for all" neonatal and infants mortality rates have been decreased over the past few decades. Identification of risk factors of low birth weight is important in mediating the health consequences of LBW after birth and also in reducing the prevalence of LBW. In the recent decades, much progress has been made to improve the survival of LBW infants. Improvement in NICU services have greatly reduced the risk of LBW mortality. So efforts to reduce LBW mortality rate in developing countries requires greater attention on understanding and addressing the risk factors for low birth weight and, consequences of LBW. . The purpose of this paper is to provide a background and concept of related risk factors and consequences of LBW, as it relates to survival, growth and wellbeing of infants throughout the life.*

**Key words:** *Cortico steroid, ventilation, exogenous surfactants, low birth weight, antenatal, neonatal.*

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### **I. Introduction**

Low birth weight is a major public health problem, particularly prevalent in developing countries. It is as high as 30% in many developing countries. (Rizvi, S.A. et al., 2007). It contributes to neonatal, infant and child mortality, morbidity as well as inhibited growth and cognitive development and chronic health problems in later life. According to WHO, the 30 million low birth babies born annually (23.8% of all births), often face severe health problems.

**Global burden of illness**-The incidence of low birth weight is estimated to be 16 % worldwide, 19 % in least developed and developing countries and 7% in developed countries. The highest incidence is 31% in South Asia followed by middle and western Africa, Oceania and Latin America (5%) (Deonis, M. et al. 1998) Asia accounts for 75%, which is probably underestimates of global situation as in developing world a significant proportion of infants are born at home and are not registered as live birth. Preterm LBW are higher in United states, compared to other developed countries and are believed to contribute to higher infants mortality in U.S. compared to other industrialized nations despite of technological advances. (Paneth, N.S. 1995)

**Definition of Low birth weight** The W.H.O. has defined the term low birth weight as "the birth weight of a new born infants less than 2500 grams /8 ounces /5 pounds. According to the definition, babies with the birth weight of less than 2500 gms are classified as Low birth weight babies. There are some other categories also –

- 1) Very low birth weight infants- The baby whose birth weight is less than 1500 gms /3 pounds is termed very low birth weight infant.
- 2) Extremely low birth weight infants-Who has birth weight of less than 1000gms/2 pounds.

In India infants with birth weight of  $\geq$ 2500 gms constitutes about 33% of all live births. The average birth weight of an infant in India is approx 2,800 gms, while in affluent countries it is 3000 gms.

Low birth weight is either the result of;

- **Preterm birth** – That is a low gestational age at birth, commonly younger than 37 weeks of gestation. About 67% of all Low birth weight babies are premature (Martin, J.A. 2007). The earlier a baby is born, the less she is likely to weigh.

- **Fetal growth restriction-** These babies are called growth restricted or small for gestational age. These may be full term but they are under weight, may be small and have low birth weight because of slow growth in uterus.

**Risk factors for low birth weight:-**Women with these following factors are at increased risk of premature delivery and having low birth weight infant;

- Had a premature baby in a previous pregnancy.
- Are pregnant with twins /triplets or more.
- Have certain abnormalities of cervix and uterus.

There are multiple secondary factors triggering low birth weight, which are broadly classified in to following categories-

- Maternal factors-including previous history of preterm/LBW/IUGR, maternal age, birth interval, inadequate weight gain in pregnancy, infections and improper nutrition.
- Environmental factors-It includes stress, smoking and use of alcohol, pollution, violence and antenatal care.
- Social factors-life style, race/ethnicity, socio-economic status.
- Uterine factor.
- Fetal factors-sex and genetic factor.

Since the problem of preterm birth/low birth weight is multi factorial, the evaluation of various factors and their interaction in the causation of adverse pregnancy outcomes is not always easier, so it is necessary to describe these factors individually

#### **A. Maternal Factors-**

1- **Birth Interval-** Both short (<18 months) and long (>60 months) interval are associated with LBW and preterm birth.

- Short inter pregnancy interval may results in inadequate replenishment of maternal nutrient stores and reduced foetal growth.(Zhu,B.P.et.al.2001).
- Women with short inter pregnancy interval are more likely to have associated risk factors eg high parity, previous history of preterm birth/ LBW, improper education, minority race and use of tobacco.
- It can lead to stress and preterm birth /LBW.
- A mother's ability to facilitate growth to the foetus declines gradually over the year after the first pregnancy. This may lead to preterm birth/LBW in mothers with long inter pregnancy intervals.

2- **Parity-** There is a trend towards an increased risk of preterm birth/ IUGR/LBW for the first child compared to subsequent children in some studies. Henriksen et al in a prospective cohort study of singleton pregnancies reported a 4.3% incidence of preterm birth in primiparous working women and a 4.4 % incidence in multiparous women.

Kesmodel et al in a prospective cohort study assess the impact of alcohol on preterm delivery and observed that among nulliparous women the rate of preterm birth was 4.5%, in women who had one previous child the rate was 3.6% and among mothers of higher parity it was 4.2%. Thus there was a marginally lower risk of preterm birth for the second born child.

3- **History of previous preterm birth/LBW-** Preterm birth and LBW tend to repeat in families. The epidemiological evidence indicates an increased risk of preterm/LBW births in a subsequent pregnancy for women with a previous history of such outcomes. It is possible that the factors responsible for preterm/low birth weight births in the previous pregnancy may be operated. Mercer,B.M.et al1997in a prospective study of prediction of preterm births reported that mothers with a previous history of a spontaneous preterm birth had a 2.5 fold increased risk of a repeat spontaneous preterm birth compared to women with no previous history of preterm births.

Shiono et al1997 in a cohort study found that the mean birth weight was 3,117g for infants born to women with a history of a previous LBW birth while 3,429g for infants born to women with no history of a LBW birth .

4- **Race/Ethnicity-** The most commonly held hypothesis is that of stress. Corticotrophin releasing hormone ( CRH) is elevated in women who deliver preterm. Acute experiences of racism (defined as racial prejudice or discrimination) have been shown to be associated with increase in heart rate and blood pressure indicating release of stress hormones. Associated factors such as psychological disturbance, alcohol use, poor self esteem and abuse may aggravate the impact. Both chronic and acute stress may increase release of CRH and trigger the cascade resulting in preterm labor.(Copper,R.L.et.al.1996) Major factors associated with racial differences are nutritional deficiencies, unplanned pregnancies, pre-post natal health, socio economic status and unhealthy behaviours. Shiono et al1997 in a population based study of ethnic differences in birthweight found that maternal ethnic group was a strong correlate of birth weight.

5- **Maternal age-** Advanced maternal age deserves special attention. Epidemiological studies suggest that there is a change in developing countries to delay the age of first pregnancy but maternal age above 35 years for first pregnancies is associated with reduced intrauterine fetal growth. (Foix-L-Helias 2000)

The biological mechanism behind the increased risk of preterm/low birth weight births in adolescence is as follows-

- The blood supply to the cervix and uterus has not developed completely in some adolescence which leads to poor supply of nutrients to the fetus.
- Poor blood supply to the genital tract leads to an increased risk of infection which triggers the onset of preterm births. (Scholl, T.O. 1996)
- The levels of gonadal hormones are low in adolescents resulting in irregular menstrual cycle..
- There is a higher incidence of unplanned pregnancies among adolescents which is a risk factor of adverse outcomes. (Dickate et.al. 2004)

6- **Marital status-** There is an indication of increased risk of preterm/ IUGR births for unmarried women. The basis for protective effects of marriage may lie in social, psychological, emotional and financial support of partners.

Kramer et al 1998 in an analysis of births between 1978 – 1996 in Montreal, Canada reported an increased risk of preterm birth for unmarried women compared to married women (adjusted OR 1.51, 95% CI 1.36, 1.68).

Shiono et al 1995 in a population based study of ethnic differences in birth weight found a significant difference in the birth weight of offspring from married women compared to unmarried women (3403g vs. 3315g,  $p < 0.01$ )

B. **Nutritional Factors-** Inadequate nutrition is the most commonly implicated cause of impaired fetal growth.

The adequacy of fetal nutrition is dependent upon many factors and regulating mechanism. These include nutrient intake of mother, nutrition supply to the uterus and placenta, transport of nutrients across the placenta, fetal uptake and regulation of the nutrients. The nutritional need of a woman varies according to the stage of gestation. A malnourished woman gives birth to a growth restricted fetus that develops into a nutritionally deprived mother and gives birth to another child at similar disadvantage. Poor socio economic status aggravate the situation and inter intergenerational cycle at the time becomes difficult to break. Most importantly malnutrition may cause stress in the fetus which is an important risk factor for preterm birth. (Luke, B. 1994)

C. **Anthropometric Factors-** Anthropometric factors which are associated with LBW/ preterm births are maternal pre pregnancy weight, height and gestational weight gain. According to US Institute of Medicine recommended weight gain according to BMI prior to pregnancy are as follows-

For BMI below 19.8= 28-4lb

For BMI 19.8-26=25-35lb

For BMI 26.1-29=15-25lb

Above 29=15 lb. (Johnson, J.W. 1996)

- **Gestational Weight Gain-** It reflects increase in the uterine tissues, the fat stores placenta, plasma volume, the fetus and the breast tissue. It also reflects adequacy of calorie and micronutrients intake and poor weight gain reflects deficiency of these substrates, which are necessary for fetus growth. Nutritional deficiency can result in poor plasma volume expansion and undeveloped maternal tissues to support the fetus. Zinc deficiency is particularly related to improper weight gain as it suppresses appetite and also it impairs the synthesis of prostaglandins and collagen and affects uterine contraction. (Carmichael et al 1997)
- It is affected by genetic factors, environmental factors and nutritional status. It may be determinant of birth weight.
- **Pre-pregnancy weight-** Adequacy and inadequacy of nutrients is reflected in the mother's pre pregnancy weight which further determine the growth and weight of fetus. (Kirchengast et al 1998)

D- **Medical Factors-** Health of mother and her general medical conditions can affect the fetus in many ways. Supply of several nutrients and oxygen are the two key factors for the growth of fetus. Any alteration in this can result in alter fetal growth. Maternal infection transmitted through the placenta can also affect the growth. Beside this medical conditions affecting oxygen carrying capacity, utero placental blood flow and the size of uterus can also affect the gestational period and the growth of the fetus. Maternal diabetes causes long term changes in placenta and may cause fetal growth restriction. (Kliogman, R.M. 2001) (Bernstein, P.S. 1997)

Maternal hypertension can reduce fetal growth due to a reduction in blood flow or an increased risk of preeclampsia. (Haelterman et.al. 1997) Other chronic conditions which can affect fetal growth are cystic fibrosis, asthma, pancreatitis, malabsorption syndrome, starvation, short bowel, collagen vascular disorder, sickle cell anaemia.

**Pregnancy associated conditions-** Pregnancy induced hypertension is the most common disorder in which utero placental insufficiency is frequently seen in mothers. Gestational diabetes can also lead to growth restriction if the mother has previous glucose intolerance.

**Infections-** Maternal genital tract is infected with acidophilic lactobacilli, staphylococci and streptococci. Vaginal infection act as a starting point in the cascade of ascending infection, membrane rupture, infection of amniotic sac and subsequent pre term labor. (Lamont,R.F.1998)

Maternal infection with pneumonia, malaria and typhoid fever are associated with preterm labor, (Mcgregar,J.A.1986) Intrauterine infections also lead to preterm labor. Urinary tract infection is common during pregnancy. The incidence has been reported to be 17-20% in pregnant women. It leads to preterm labor and preterm rupture of membranes. HIV infections may be transmitted from mother to infant. (Brocklehurst,et.al.1998) in his prospective cohort study found that there was an increased risk of LBW/ preterm births and IUGR

**Periodontal infections-** It is caused by gram -ve anaerobic organism. Presence of these organisms, lipopolysaccharides and inflammatory mediators is proposed to react with the placenta fetal unit results in preterm/ LBW births. (Offenbacher,S. et al1996)

#### **E- Environmental Factors-**

- a. **Psychosocial Factors:** Stress and Socioeconomic status- Racial and social differences and their impact on pregnancy outcomes are the most extensively studied factors.. Neuro endocrine mechanism chronic stresses have been shown to increase the concentration of glucocorticoid and catecholamine in mother. The release of CRH from the placenta due to maternal stress increased production of prostanooids which are implicated in the onset of labor. It was observed that mothers with onset of preterm labor had high level of plasma CRH than mothers can not in preterm labor. Catecholamine released as a result of stress can reduce the placental blood flow and affect the growth of fetus. (Kramer,M.S. 2000)
- b. **Use of Tobacco:** Horta,B.L.et al1997 studied 5,166 mothers in Brazil by postnatal interviews. An increased risk of IUGR was found among smokers (adjusted OR 2.07, 95% CI1.69, 2.53). The risk of preterm birth was also increased for mothers who continued smoking throughout pregnancy (OR 1.54, 95% CI 1.24, 1.92). An etiological fraction of 17.7% for smoking in causing LBW was reported. A positive effect of interruption of smoking during pregnancy on birth weight was observed.
- c. **Alcohol use:** Alcohol is the second most common substance studied in relation to pregnancy. Fetal alcohol spectrum disorders include fetal alcohol syndrome, fetal alcohol effects (FAE) and alcohol related neuro developmental disorders.(Barr,H.M.et.al.2001).
- d. Caffeine blocks adenosine receptors, which leads to an imbalance between available oxygen and oxygen utilization. This imbalance increases the susceptibility of the cells to hypoxic insults and may cause LBW.(Rondo,P.H.et.al.1996)

## **II. Health consequences of low birth weight infants**

Every year many of medically fragile immature infants spend their first few days or weeks or months of life in NICU because of problems caused due to their incomplete growth and development in uterus. Researches has constantly documented the greater risk of developmental outcomes of these low birth weight infants, e.g. brain injury such as hypoxic ischemic encephalopathy ,periventricular leukomalacia, seizures and intra ventricular hemorrhage have been associated with neuro motor and cognitive abnormalities. Preterm and low birth weight infants who often suffer from one or more of these condition have also demonstrated disabilities in area of cognitive, academic, sensory motor, social, emotional and behavioral development.(Groen-Blokhuis et.al.2011)

Markestet et.al.(1997) compare the growth pattern and psychomotor development of LBW and normal infants and identified that LBW had showed partial catch in growth and they still had smaller weight, crown heal length and head circumference. They score lower on mental scale.

Avchen et.al.(2001) stated that while mortality rates declined for LBW, the consequences may be associated with adverse developmental outcomes.

Here are some complications, suffered by low birth weight infants-

1. **Thermoregulation-** Due to high body surface area to body weight ratio, decreased brown fat stores, non keratinized skin and decreased glycogen supply, infants with LBW are particularly susceptible to heat loss immediately after birth. Hypothermia may results in hypoglycaemia, apnea and metabolic acidosis.(Kaushal,M.et.al.2005)



2. **Hypoglycaemia**-Low birth weight infants have difficulty in maintaining glucose levels within reference range after birth. These infants are usually under increased stress and have insufficient level of glycogen stores. They are generally considered hypoglycaemic when Plasma glucose level is below 45 mg/dl.
3. **Fluid and electrolyte imbalance**- It may results due to patent ductus arteriasis (PDA), intra ventricular haemorrhage (IVH) and chronic lung disease. (bronco-pulmonary dysplasia).  
As compared to normal infants LBW infants have proportionally more extra cellular fluid then intra cellular fluid, so a larger portion of body weight is attributed to water. During 1<sup>st</sup> days after birth, diuresis results in 10-20% weight loss. These infants also have compromised filtration rates and decreased ability to reabsorb bi-carbonates.
4. **Nutrition**- Initiating and maintaining growth of these infants is a great challenge. The growth rate often lags because of complications eg. Pulmonary disease and sepsis. An additional contributing factor is inadequate caloric and protein intake. Concern that early feeding may be a risk factor for necrotizing enterocolitis often defers initiation of enteral feeding.(Blanco,C.L.et.al.2011)
5. **Hyper bilirubinemia** – Most infants develops hyper bilirubinemia (Jaundice) ,develops as a result of increased RBC turnover and destruction in the context of an immature liver that has physio-logically impaired conjugation and elimination of bilirubin. Most preterm infants have reduced bowel motility due to inadequate oral intake, which delays elimination of bilirubin. These complications of extreme prematurity in addition to typical complications cause jaundice.
6. **Chronic lung disease (respiratory distress syndrome)** – An early complication of extreme prematurity is respiratory distress syndrome caused by surfactant deficiency. Clinical signs includes tachypnea (>60 breath /minute), chest retractions and nasal flaring. Untreated RDS results in increasing difficulty in breathing and increased oxygen requirement. As a result of surfactant deficiency, the alveoli collapse, causing a worsening of atelectasis, oedema and decreased lung capacity. Surfactants decreased the surface tension of smaller airways so that the alveoli or the terminal air sacs do not collapse; result in less need of supplemental oxygen and ventilatory support.  
The incidence of RDS is inversely proportional to gestational age, with an incidence of 60% at 29 weeks gestation.
7. **Patent ductus arteriasis**- It is a heart problem that is common in premature babies. Before birth a large artery (ductus arteriasis) lets the blood by pass the body's non functioning lungs. The ductus normally closes after birth, so that blood can travel to the lungs and pickups oxygen. If the ductus does not closes properly it leads to heart failure.
8. **Infections**- Infections are the major contributing factor to the mortality and morbidity of infants with Low birth weight and can occurs at any point of clinical course. Early onset infection (occurs within 1<sup>st</sup> 72 hours of life) may present with immediate respiratory distress shortly after birth. Signs include temperature instability (hypo/hyper tension), Tachycardia, decreased activity, poor perfusion, apnea, Bradycardia, feeding intolerance, increased need of oxygen / higher ventilatory setting and metabolic acidosis. The most common cause of early sepsis are group B streptococci And E- coli. Fungi Candida albicans are frequently a cause of late onset sepsis.(Sarri,T.N.et.al.2003)
9. **Necrotizing Enterocolitis**- NEC is a disease of premature gastro intestinal tract that represent injury to the intestinal mucosa and vasculature and is the most common intestinal emergency in preterm infants. It is directly correlated with decreased gestational age, occurring in 1-8 % of infants ,admitted to NICU and in 1-3 infants /1000 birth. It accounts for approx 2600neonatal deaths annually, with a mortality rate of 10-50%. Symptoms are apnea, bradycardia, abdominal distension which quickly progress to symptoms of sepsis eg. Large gastric residual, metabolic acidosis and lethargy.(Clark,R.H.2007).
10. **Intra ventricular haemorrhage**-(bleeding in brain) –It occurs in some VLBW infants, usually in 1<sup>st</sup> 3 days . More severe bleeds can cause pressure on brain , which leads to brain damage. Both incidences and severity of IVH are inversely related to gestational age. Any event, results in disruption of vascular-auto regulation can cause IVH, including hypoxia, ischemia, rapid fluid change and pneumo thorax. Symptoms are apnea, hypertension or hypotension, sudden anemia, acidosis, changes in muscular tone and seizures.
11. **Apnea of prematurity**- It is cessation of respiratory activity of more than 20 seconds. The incidence is inversely correlated with gestational age and weight, occurring in 30 % of infants who weigh less than 1000 gm at birth. It is caused by decreased respiratory drive called central apnea, or by an obstruction in which no nasal airflow occurs despite initiation of respiration ( obstructive apnea) .It is also be induced by hypoxia, sepsis, hypoglycemia, neurologic lesions, seizures and temperature irregularities .
12. **Anaemia**- The physiologic anaemia occurs earlier in preterm infants. Reasons include physiologic responses to decreased oxygen consumption, blood secondary to phlebotomy for laboratory studies related to clinical management in first few weeks of life, an immature erythropoietic response to anaemia, decreased survival of RBCs in preterm infants and deficiency of folate, vitamin B-12 or vitamin E.  
**Retinopathy of prematurity**- It is a disease of the premature retina, that has not yet fully vascularized.

Changes in oxygen exposure results in abnormal growth of blood vessels which results in retinal detachment and blindness. Risk factors include prematurity and exposure to oxygen. Infants with ROP are at increased risk for sequelae eg myopia, strabismus and amblyopia.

**13 Hearing-** All ELBW infants are at increased risk of hearing impairment because of their LBW. Other risk factors include meningitis, asphyxia, exchange transfusion and administration of auto-toxin drugs eg. Gentamicin.

**14 Adult Health Problems-** Low birth weight babies may be at greater risk of certain chronic problems in adulthood including hypertension, type 2 diabetes and heart diseases. When these conditions occurs together, called metabolic syndrome. Growth restriction in uterus may cause lasting changes in insulin sensitive organs( liver, skeletal muscles and pancreas).(Valmiki,S.G.1992)

A number of studies found the links between LBW and problems in school performance, psychomotor development and emotional well being(Cheung 2002), problems in pulmonary functions, physical growth, neurological development, psycho-social development(Gissler et.al.1999)and respiratory problems, cognitive, neurological and psychological deficits.(Kelly et.al.2001)

### III. Conclusion

Low birth weight is one of the most serious challenges in maternal and child health and is the single most important factor that determines the changes of child survival. Nearly 50 % of neonatal deaths occur among LBW babies. LBW is a major determinant of mortality, morbidity and disability of infancy and childhood and also has a long term impact on health in adult life. The consequences have a negative impact on early development. The survivors among them are at increased risk of developing malnutrition, recurrent infections, neuro developmental handicaps and hearing impairments. These babies also may cause heavy emotional and economic burden for family and results in substantial cost to the health sector and impose significant burden on society as a whole.

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