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Review Article

Risk Factors of Low Birth Weight Baby: A Review

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Abstract:

Low birth weight (LBW) is one of the main predictors of infant mortality. The global incidence of LBW is around 17%, although estimates vary from 19% in the developing countries like Bangladesh to 5-7% in the developed countries. About one third of delivery is low birth weight. LBW is generally associated with situations in which uterine malnutrition is produced due to alterations in placental circulation. There are many known risk factors, the most important of which are socio-economic factors, medical risks before or during gestation and maternal lifestyles. However, although interventions exist to prevent many of these factors before and during pregnancy, the incidence of LBW has not decreased.

Key words: Low Birth Weight; Risk Factors; Epidemiology; Reproductive Health.

Introduction:

Low birth weight is one of the main risk factors for infant morbidity and mortality in Bangladesh. When considering a fetus that is small for its gestational age, it is important to differentiate whether this is due to intra-uterine growth restriction (IUGR), prematurity or other constitutional factors. Although prematurity has historically been defined (American Academy of Pediatrics, 1935) as the birth of a live infant weighing 2500g or less, experience in clinical practice showed that many of these infants were not actually premature, but rather full-term fetuses from a pregnancy in which growth had been limited due to different factors. In 1967 the World Health Organization (WHO) recognized this fact, designating infants weighing 2500 g or less as low birth weight[1].

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Three categories can be distinguished:

a) Premature or preterm LBW babies (born before 37 complete weeks of gestation or with fewer than 259 days of gestation). b) Term LBW that is, born between 37 and 42 complete weeks of gestation, or between 259 and 293 days of gestation. c) Post term LBW, born after 42 weeks or 294 days of gestation. LBW infants can be further classified as "very low birth weight" (1000-1499 g) and "extremely low birth weight" (500-999g). Small-for-gestational-age (SGA):- This term is based on a statistical definition, which refers to infants whose weight is less than the lower limit of the confidence interval of the normal curve for weight by weeks of gestation[2].

2. Incidence and consequences of LBW

The study of LBW is very important, since sub-optimal birth weight may have consequences in the perinatal period, during infancy, and even in adulthood. In the first place, perinatal morbidity and mortality are more frequent in LBW infants than in normal infants; LBW has become the second cause of death in this period, after premature birth. Furthermore, term infants weighing between 1500 and 2500 g at birth have a perinatal mortality rate 5-30 times greater than infants with birth weights between the 10th and 50th percentile, while infants born almost at term weighing less than 1500 g have 70-100 times higher mortality rates[3]. It has recently been reported that the intellectual quotient (IQ) of infants with IUGR, at 5 years of age, averages 3.3 points lower than that of normal infants; if

they were also premature, the IQ averages 6.7 points lower on intelligence tests. Hack et al[4] found that children with a small head circumference at birth who do not regain normal growth have a higher risk of having impaired neurological functions. However, infants with intra-uterine growth restriction but with a normal head circumference at birth, or those in whom normal head circumference is rapidly attained, are not likely to suffer subsequent neurological sequelae. They may, however, be slower to develop language abilities and may have problems in school. Finally, several epidemiological studies have suggested that infants born with IUGR, especially those who had a large placenta, have a higher risk of developing hypertension in adulthood[5]. For all these reasons, it is important to know the incidence of LBW babies.

3. Etiology of LBW: risk factors

A variety of factors influence fetal growth, although they can be grouped into several general categories: factors originating from the fetus itself, maternal factors, placental factors and finally, factors produced from the interaction of these factors. It should also be pointed out that LBW is usually associated with situations in which there is interference with placental circulation due to alteration of the mother-placenta-fetus interchange and, therefore, with intra-uterine malnutrition.

3.1. Socio-demographic risk factors

3.1.1. Constitutional factors

There are clear genetic and constitutional influences that act on fetal growth; it is estimated that 40% of birth weight is due to heredity and the remaining 60% to environmental factors. Thus, small mothers, especially those weighing less than 45 kg, are more likely to have small babies. Certain chromosomal factors also have an influence on birth weight. The Y chromosome is a special case: term male infants weigh between 150 and 200 g more than females. There are other chromosomal anomalies that result in fetal growth retardation, among them, trisomy 21, trisomy 18 and Turner's syndrome. Infants with trisomy 13 or 18 frequently have IUGR, with a mean birth weight of 2600 and 2240 g, respectively. Turner's syndrome is also associated with mild growth retardation, with mean birth weight equal to about 85% of normal birth weight.

3.1.2. Maternal age

A large number of epidemiological studies have noted that the incidence of low birth weight increases in the extremes of women's reproductive life; that is, between 15 and 19 years[6] and between 35 and 40 years of age[7]. In fact, it is seen that most adolescent mothers are single, with low incomes, inadequate prenatal care and lower antenatal maternal weight. At the other extreme, it is widely accepted that women older than 35 years have a higher incidence of pregnancy complications, including LBW.

3.1.3. Ethnicity

It is well known that black women have a higher incidence of LBW than white women, although it is difficult to find studies that are strictly comparable, with stratification by social class and socio-economic level[8].

3.1.4. Marital status

Another important risk factor for LBW is marital status, which is interrelated with other factors such as socio-economic level, age, culture and race. Thus, it has already been seen that LBW babies are frequently children of single mothers[8], which is directly related with younger maternal age, often adolescence, or of couples in which the father is absent during the pregnancy. Holt et al carried out a study and found that women who were married during the first pregnancy had a lower incidence of LBW than single mothers did, but if they were separated during the second pregnancy, the relative risk (RR) of low birth weight increased (RR ¼ 1:4) in comparison to those who remained married. Conversely, among women whose marital status changed from single to married between pregnancies, the risk of LBW decreased (RR ¼ 0:8).

3.1.5. Educational level

Some studies suggest the possibility of an important relation between maternal educational level and fetal birth weight[9], with an increased risk of prematurity and LBW associated with decreasing educational level of the mother.

3.1.6. Socio-economic level

Socio-economic level is one of the factors most closely related with the health status of populations. With regard to the problem that is the subject of this study, it is a proven fact that unfavorable socio-economic conditions increase the incidence of LBW. When analyzing this association, it is important to highlight the strong relation that exists with other factors such as maternal malnutrition, low educational level, smoking, alcohol consumption, drug abuse and stress[10].

3.2. Medical risks before pregnancy

3.2.1. Chronic hypertension

Chronic hypertension refers to any hypertensive disease before pregnancy, either by documentation of previous high blood pressure levels, or by diagnosis of the

process before the 20th week of pregnancy. Chronic hypertension, as well as some maternal diseases, may provoke alterations in fetal growth, perhaps as a consequence of reduced uteroplacental fluid. These vascular diseases, also including gestational hypertension, are clearly associated with reduced fetal growth. There is an activation of coagulation, with increased platelet aggregation, thrombopenia, and general and local vasoconstriction, which leads to reduced systemic perfusion and, finally, to a decrease in the uteroplacental fluid which results in increased IUGR[11].

3.2.2. Renal diseases

Chronic nephropathies, the same as other maternal systemic diseases, have a vascular pathology that reduces uteroplacental perfusion. Among the renal processes most closely associated with IUGR are chronic pyelonephritis, glomerulosclerosis, chronic glomerular disease and lupus glomerulonephritis[12]. In all these cases, the retardation of fetal growth is also related with the important loss of protein associated with these processes. Botet et al[13], in a study showing that one of every 50 women who received a kidney transplant subsequently became pregnant, carried out a follow-up of these women and found that 52.9% of their infants were premature, and that the incidence of LBW among them was 47.1%.

3.2.3. Glucose metabolism disorders

An important factor that influences adequate fetal growth is the triangle formed by glucose, insulin and placental lactogen or chorionic somatotropin. Maternal postprandial hyperinsulinism has often been shown due to excessive secretion, to low tissue resistance to this hormone, or to insufficient placental destruction of insulin (low levels of placental lactogen). This excess of maternal insulin accelerates anabolism and impedes the passage of carbohydrates to the fetus, giving rise to a situation opposite to that of the diabetic mother[14].

3.2.4. Genitourinary anomalies

Uterine malformations may cause fetal loss and prematurity, as in the case of Mu¨llerian anomalies or extrinsic masses such as myoma. The most important among them are uterine duplications, which have been associated with higher rates of miscarriage (four times more) and up to 10 times greater risk of prematurity (birth before 34 weeks of gestation).

3.2.5. Autoimmune diseases and inherited or acquired thrombophilia

Both systemic lupus erythematosus and antiphospholipid syndromes have been related with poor fetal growth. The common factor in all these cases is, again, the underlying vascular pathology that reduces uteroplacental perfusion that causes LBW[15].

3.2.6. Obstetrical history

Primiparity seems to be associated with a larger number of growth-retarded infants, preterm births and LBW infants. It is well known that second and third children weigh more than the first. A previous miscarriage may indicate a high-risk of adverse effects in subsequent pregnancies. A study of women with three or more previous miscarriages showed a higher risk of prematurity (RR ¼ 1:5), placenta previa (RR ¼ 1:8) and malformations (RR ¼ 1:8). In this regard, a study carried out by Mandelson et al[16] did not find evidence of harmful effects on birth weight after one, two or even more induced abortions.

3.3. Risks of the current pregnancy

3.3.1. Gestational hypertension

Hypertension induced by pregnancy is defined as the development of blood pressure values higher than 140/90 mm of Hg after the 20th week of pregnancy, in at least two independent measurements, in the absence of proteinuria (<300 mg/dl in 24 h) or previous changes in blood pressure values. Hypertension associated with symptoms of proteinuria, edema, or both would indicate the presence of preeclampsia[17]. As previously seen, hypertension in pregnancy is associated with reduced uteroplacental flow, which leads to an increased risk of preterm birt hand of LBW.

3.3.2. Gestational diabetes

Glucose is the main source of energy for the fetus and the substance most used by the fetal brain. Glucose crosses the placenta and is captured by the fetus in proportion to the levels of maternal glucose and the mother-fetus concentration gradient, so that glucose levels in the newborn are 70-80% of those in the mother's blood. It is well known that glucose availability plays a fundamental role in fetal growth. Fetuses with growth retardation have reduced concentrations of glucose in the intra-uterine blood and in cord blood. Conversely, it is also well known that increased levels of glucose and insulin in the mother's blood are related with increased fetal size. Diabetic mothers also have an increased risk of preterm birth and other complications. Finally, Plante[18] confirmed that female infants with low birth weight have a greater risk of developing diabetes later during pregnancy, and this would in turn imply a greater probability of having LBW children.

3.3.3. Weight gain

To provide the fetus with an adequate amount and diversity of substances, a normal woman should gain an average of 12-16 kg during pregnancy. Maternal weight gain during the first and second trimesters in pregnancy is mostly due to maternal components (blood, extra cellular liquid, tissues and fat reserves)

and to the placenta, while weight gain during the third trimester is due to fetal tissue. Thus, weight gain is a factor that predicts fetal size. Caufield et al[19] observed that, with regard to BMI, whereas there was no difference by race in women with low BMI, the higher risk for black women was maintained in women with medium and high BMI which increases risk of LBW.

3.3.4. Maternal nutrition

It has long been known that maternal malnutrition is an important cause of IUGR, although its effect is moderate. This additional intake is 300 kcal per day more than the normal needs of a non-pregnant woman, that is, a minimum intake of 2500 kcal per day. The amount of protein should be reinforced (60 g per day), although excessive intake should be avoided because it increases the risk of premature birth. Vitamin intake should also be increased by 10-50%, and the amount of calcium and iron by 50-100%.

3.3.5. Birth intervals

Short intervals between births constitute one of the main risk factors for prematurity and low birth weight, although information in this regard is contradictory. Ochoa found a strong association between short birth intervals and other covariates of obstetrical interest, such as a history of prematurity and LBW, and adolescent maternity[20].

3.3.6. Multiple pregnancies

Multiple pregnancies may produce IUGR. Although the growth rate of twins is similar to that of single fetus during the first two trimesters of pregnancy, mean growth is 220-240 g per week by week 34 for single fetus, and 160-170 g per week by week 30 in twins. Race and maternal age also influence the adverse results of these pregnancies, with poorer outcomes observed in black women and younger women (<22 years of age)[21].

3.3.7. Placental causes

Alterations in the placenta and the umbilical cord, such as chronic abruptio placentae, placental infarcts, placental hemangiomas and vascular anomalies are associated with IUGR. In all these cases, there is a decrease in blood transfer, which is especially important in the infarcted areas, changes in the villosities and if there is abnormal cord insertion. Premature displacement of a normally inserted placenta (abruptio placentae) may occur before expulsion or even before the beginning of labor. Another placental anomaly, placenta previa, is also associated with rupture of the placental decidua, which may lead to impaired fetal oxygenation and a compensatory increase of hemoglobin in the blood. The most important symptom of placenta previa is periodic hemorrhage in the last months of gestation. Other authors[22] comment that the association between LBW and placenta previa is mainly due to the higher frequency of prematurity and, to a lesser extent, to IUGR.

3.3.8. Bleeding

Vaginal bleeding is an important predictor of adverse effects in pregnancy. About 50% of women who bleed in the last half of pregnancy have placenta previa or abruption placentae. When the bleeding occurs at the beginning of pregnancy, however, the cause is often unknown. Some studies associate bleeding in the first weeks with increased preterm births (RR ¼ 4:3) and LBW (RR ¼ 2:1).

3.3.9. Increased α-fetoprotein

α-Fetoprotein is a glycoprotein synthesized by the fetus, which normally is produced only during fetal life and can be measured in the maternal blood. Unexplained elevations in a-fetoprotein during the second and third trimester are associated with 20-38% of adverse obstetrical outcomes such as pre-eclampsia, LBW, preterm birth, IUGR, abruptio placentae and fetal death[23].

3.3.10. Anemia

In a normal pregnancy, maternal concentrations of hemoglobin decrease in the first 20 weeks, remain constant up to week 30, and then increase slightly. Some authors have observed that hemoglobin of less than 9 g/dl during pregnancy is associated with an increased risk of LBW and prematurity[24].

3.3.11. Infections

Numerous microorganisms can cross the placenta and cause infection in the fetus. If the infection occurs at a critical moment in fetal development, some organisms can affect the fetal cells and cause IUGR. Many agents are associated with fetal growth disorders, including toxoplasma, rubella, cytomegalovirus and herpes simplex. In addition, different studies conclude that there is an association between LBW and such maternal infections as Chlamydia, β-hemolytic Streptococcus, Ureaplasma urealyticum, Mycoplasma, Trichomonas, Staphylococcus aureus and other vaginal infections, as well as untreated gonorrhea and syphilis[25]. A study by Dasanayake[26] concludes that periodontal disease during pregnancy is a potential risk factor for LBW. Similar studies support this conclusion[27], observing in

addition that up to 18.2% of LBW could be attributed to the existence of periodontal infection. Women with HIV infection have twice the risk of having a LBW infant as compared to non-infected women of the same socio-economic level, even after adjusting for gestational age[28].

3.3.12. Fetal congenital anomalies

Several chromosomal influences on neonatal weight are known. Fetuses with trisomy 21 are smaller at birth, with a mean weight at term of 2900 g, that is, a standard deviation smaller than average. Syndromes causing multiple malformations, such as Roberts' syndrome, often lead to IUGR. Single congenital malformations such as anencephaly are also usually associated with IUGR. Fetal heart diseases, especially those associated with septal defects, may be associated with IUGR. For all of these reasons, it is important to consider cytogenetic analysis in infants with dysmorphic features and low birth weight[29].

3.4. Prenatal Health Care

Many studies have established a link between these factors and LBW[30], a relation that is stronger if the first visit is delayed or if the number of visits is smaller than normal (<80%). Prenatal care begins later in rural areas[31], although this fact is not independently associated with increased LBW. On the other hand, excessive testing during pregnancy can create anxiety and may lead to an increase of unfavorable outcomes such as LBW[32].

3.5. Environmental and behavior risks

3.5.1. Maternal work and psychosocial stress

Moderate exercise may be beneficial for pregnancy outcome, but that intense exercise undoubtedly increases the risk of LBW[33]. Finally, a special problem that may cause stress in pregnancy is abuse: physical, sexual and emotional abuse during pregnancy is related with LBW.

3.5.2. Smoking:

Of all the drugs consumed by the mother that can affect the fetus, tobacco is undoubtedly the most common. Smoking during pregnancy leads to birth weights of 200 g less than the mean birth weight of children of non-smokers, with a range of 150-250 g less. The association between smoking and other undesirable effects is also well known, such as the higher incidence of miscarriage and prematurity.

3.5.3. Alcohol consumption

Fetal alcohol syndrome (FAS) is characterized by three main findings: abnormal facies, central nervous system (CNS) alterations and IUGR[36]. The development of FAS depends on the dose and time of consumption, with a greater risk when exposure is during the first trimester[37]. A multi-center study[38] of the relation between alcohol and LBW detected a synergistic effect with tobacco, when alcohol consumption was higher than 20 g/dl, the risk increased in both groups, smokers and non-smokers[39,40].

3.5.4. Caffeine consumption

The methylxantines, especially caffeine and teofiline, are contained in many food products, frequently consumed beverages (coffee, tea, cola and chocolate drinks), and drugs (against allergies, diuretics, stimulants)[41]. The methylxantines consumed by the mother cross the placenta and can enter the fetal blood, where they act as CNS and heart muscle stimulants, and smooth muscle relaxants. The adverse effects of caffeine during pregnancy are well known, such as congenital malformations, IUGR, prematurity and miscarriage[42].

3.5.5. Drug consumption

The consumption of illicit drugs has been associated with a lower birth weight, due not only to the increase in prematurity, but also to the increased risk of IUGR. The consumption of cocaine, especially crack cocaine, may produce IUGR, mainly as a consequence of vasoconstriction of the uterine vessels, which impedes the passage of nutrients to the fetus. A recent study identified cocaine as the drug with the strongest association with preterm birth and LBW. The consumption of crystal meta-amphetamine is also associated with IUGR. Narcotics such as heroin may produce IUGR seven times more frequently than in the general population, although it is not clear if opiates are an independent risk factor for IUGR. The consumption of methadone, marijuana or hallucinogenic drugs, alone, does not appear to be associated with IUGR. Finally, some drug prescriptions for the treatment of specific maternal diseases have been associated with increased IUGR, such as the phenytoin[43,44].

3.5.6. Exposure to toxic substances

A pioneering study in Sweden between 1976 and 1986 found an increased incidence of LBW and prematurity in a cohort of women workers in the chemical industry. It was also observed that when occupational improvements aimed at palliating the risks were introduced, the adverse effects on pregnancy slowly decreased[45]. Since that time, many substances have been associated with LBW, among them, exposure to organochlorine compounds[45] and sulfur dioxide.

3.5.7. Environmental exposures

Agricultural contamination of ground water may represent a health risk through the drinking water.

Among these risks, anecologic study highlighted exposure to drinking water contaminated with nitrates and its relation to IUGR and prematurity[46]. The results confirm a positive association with a clear dose-response association. Finally, there is no doubt that exposure to ionizing radiation during pregnancy can give rise to serious IUGR, together with the appearance of CNS lesions. The vulnerability of the fetus depends both on the dose of radiation received and on the moment in pregnancy when it is produced. Early exposures, in the first trimester, may cause general growth retardation, sometimes associated with microcephaly and other CNS anomalies.

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