LOW BIRTH WEIGHT IN SOUTH ASIA

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ABSTRACT

Intrauterine growth and development is one of the most vulnerable process in the human life cycle and it's aberrations can result in profound and lasting influence in later life. In the context of developing countries, intrauterine growth has been invariably assessed by birth weight. Although it may be reasonable to infer that fetuses who have experienced growth restriction in utero will be lighter and smaller, it must be understood that size at birth does not completely reflect growth. The suitability of utilizing only birth weight as an indicator of fetal growth has been debated and criticized. However, it is sometimes the only measure available, especially in developing countries.

The World Health Organization (WHO), on the basis of world wide data, had recommended that newborns with birth weight less than 2500 g may be considered to fall in the low birth weight (LBW) category - carrying relatively greater risks of perinatal and neonatal morbidity and mortality, and substandard growth and development in later life. The validity of this definition and the "cut off point" of 2500 g has been occasionally challenged; but has by and large now gained general acceptance. The latest WHO recommendation has retained this "cut off point" of 2500 g to define LBW and recommended an additional demarcation of 1500 g, to define very low birth weight (VLBW) babies.

LBW infants encompass a heterogeneous population of newborns. Broadly, the birth weights may be low because the baby is born small for gestational age (SGA), as a result of intrauterine growth retardation (synonym intrauterine malnutrition) (IUGR) or because birth is preterm. In the developed countries, the overwhelming majority of LBW infants are preterms, whereasin the developing nations, including South Asia, the reverse is the case. The great majority of newborns with LBW are full term infants who are SGA. Attempts have also been made to further classify IUGR as disproportionate or proportionate on the basis of Ponderal index (weight/length^3). Disproportionate IUGR infants have a low ponderal index whereas proportionate IUGR babies have a normal ponderal index (all body dimensions proportionately small).

On the basis of available evidence, the ensuing sections will examine the nature, consequences and causes of LBW in the South Asian sub-continent and evaluate the various options for action to address this major public health problem in the region.

Key words: Low birth weight : IUGR : SGA : South Asia

NATURE OF THE PROBLEM

Magnitude of the Problem

In South Asia (excluding Sri Lanka), even today, a majority of the deliveries are conducted in the community. Logistic difficulties in recording birth weight at home preclude accurate national estimates of the magnitude and trends of LBW. However, a large volume of data on birth weight is available from individual studies, most of which are hospital based. Table 1 compares the LBW prevalence estimates from different countries in South Asia with that in other selected regions. The oft cited national estimates for South Asia should only be construed as broad indicators as these have not been derived on the basis of sound epidemiological methodology. South Asia has the highest prevalence of LBW and the disparity in comparison to developed countries and some developing regions (Africa) is obvious. In fact, the latest projections indicate that more than half of the world's LBW babies are born in South Asia (1).

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Table 1 : LBW Prevalence (%) in South Asia and Other Regions*

Region	Usual range in studies	Oft cited estimate	Major sources
SOUTH ASIA			
Bangladesh	23 - 60	50	UNDP1996(2),UNICEF 1996 & 1997 (1,3), Nahar 1997 (11), Roy 1997 (12)
Bhutan	35 - 44		UNICEF 1996 (1)
India	24 – 40	33	Srikantia1989 (22), UNDP 1996 (2), NNF 1997 (3), Sachdev 1997 (21), UNICEF 1997(4)
Maldives		25	UNICEF 1996 (1)
Nepal	25 - 50		UNICEF 1996 (1), Manandhar 1997 (18)
Pakistan	18 - 34	25	Arif 1985(5), UNDP 1996 (1), UNICEF 1996 & 1997 (1,3), Bhutta 1997 (29), Zaman 1997 (6)
Sri Lanka		25	UNDP 1996 (1), UNICEF 1996 & 1997 (1,3)
OTHERS			
Asia		21	WHO 1992 (7)
Africa		15	WHO 1992 (7)
Latin America		11	WHO 1992 (7)
North America		7	WHO 1992 (7)
Europe		6	WHO 1992 (7)
Oceania *		20	WHO 1992 (7)
USSR		7	WHO 1992 (7)
Developing countries		19	WHO 1992 (7)
Developed countries		7	WHO 1992 (7)
GLOBAL		17	WHO 1992 (7)

* Excluding Japan, Australia, New Zealand.

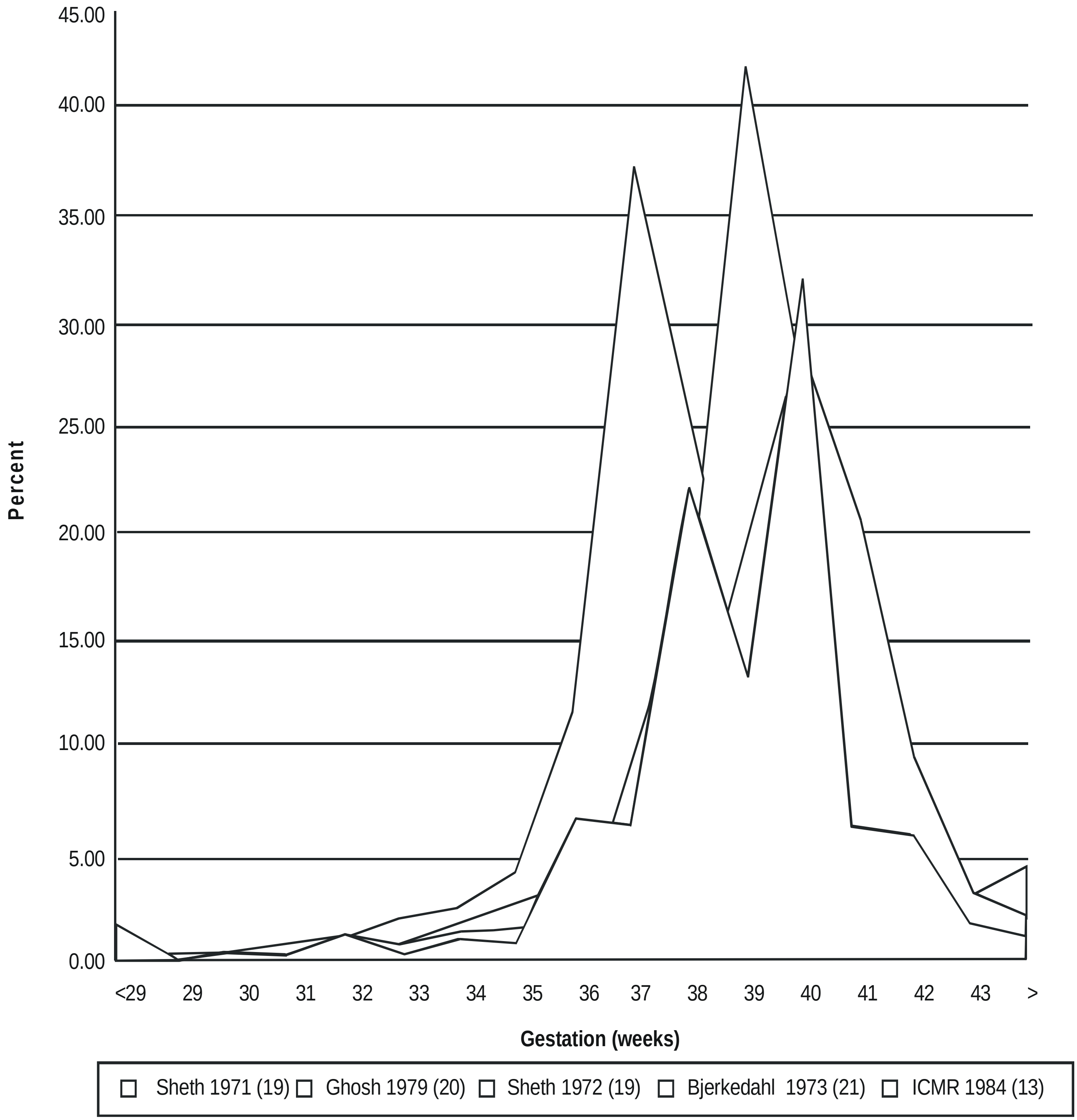
In India, recently efforts have been made to collect nationally representative estimates of birth weights from institutional (3) and community (8) deliveries. The reliable institution based National Neonatology Forum (3) data for the year 1995 on 37082 live births (nearly 0.1% births in the country) from 15 participating centers (Ahmedabad, Bangalore (3 centers), Baroda, Calcutta, Chandigarh, Delhi (2 centers), Indore, Ludhiana, Madras, Mumbai, Pondicherry and Shimla) yielded a LBW prevalence of 32.8%. Only 33% of the LBW infants were preterm. The Child Survival Safe Motherhood (CSSM) Programme linked District based data (Center based delivery in 14 Districts in 10 States - Assam, Gujarat, Madhya Pradesh, Karnataka, Maharashtra, Orissa, Punjab, Rajasthan, Tamil Nadu and West Bengal) on 27069 births estimated the LBW prevalence to be much lower at 18.4% (8). Wide regional variations were apparent with values ranging from a low of 2.7% (Madhya Pradesh) and 5.1% (Assam) to a high of 24.7% (Tamil Nadu) and 40% (Orissa). The strikingly low figures in comparison to earlier published literature, especially for the poor performing states (Madhya Pradesh and Rajasthan- 12.8%) in other nutritional parameters including protein energy malnutrition, however, questions the reliability of this integrated data. Reliable recording of birth weight in a community requires meticulous training and an accurate and sensitive instrument.

Variation in LBW Prevalence

Apart from manifest inter-country variations in South Asia (Table 1), there is a considerable variation in the prevalence of LBW within a country. Wide inter-regional, socio-economic and urban versus rural differences in the prevalence of LBW have been recorded (9-12). In India, the disparity has ranged from a prevalence of 10% (for the privileged high socio-economic class) to 56% (for the poor urban slum community) (10-13). Rural and urban slum deprived populations have consistently recorded the highest prevalence of LBW. Interestingly, even in the same region, the underprivileged population has a significantly higher proportion of LBW (14).

Low Birth Weight - Relation to Gestation and Intrauterine Growth

The general consensus is that in developing countries, particularly in South Asia, an overwhelming majority of LBW infants have adequate gestation (are term) but are growth retarded (IUGR) (15, 16). It would be of interest to examine some pertinent data from the region in this context. The recent multicentric data from India (3) on over 37,000 live births reveals that one-third (32.8%) of LBW babies are born preterm; a proportion which certainly can not be totally ignored. An earlier analysis of hospital and community births in Delhi (India) had revealed that in the birth weight group of 1501-2000 g, 30-45% were preterm, while the corresponding figure was 13-15% in the 2001-2500 g category (17). In the NNF study the prevalence of babies with birth weight <2000 g was 10.2%, <1500 g was 3.3% and <1000g was 0.7% (3). On the basis of this data, it would be justifiable to analyze the gestational distribution and intrauterine growth in the region in greater detail.



Gestation

Accurate assessment of gestational age is difficult, particularly in the context of community births. Table 2 , from the available data, compares the distribution of singleton live births according to different gestational ages from the various regions of India with similar studies from the developed countries. The depicted ICMR data refers to the multicentric studies of the Indian Council of Medical Research in rural areas and urban slums (13). Some of the important features are also highlighted in Figure 1.

In contrast to the developed countries, the process of labor appears to be initiated at an earlier period of gestation in a larger proportion of pregnant Indian women. The incidence of premature birth (<37 weeks gestation) ranges from 7.1% to 22.3%, in comparison to about 5% in the developed countries. The latest NNF data from India provides a national estimate of 12.3% (3) and a recent study from Kathmandu suggests a figure of at least 15% (18). Only 2% of births occur at 36 weeks in western countries, while 3-12% of infants are born at this gestational age in India.

Table 2 : Comparison of gestation distribution of live births (in per cent).

Author	Sheth 1972 (19)	Bhatia 1981 (22)	Ghosh 1971 (23)	Ghosh 1979(20)	Mittal 1976 (24)	Singh 1974 (25)	Sheth 1972 (19)	Babson 1970 (26)	Bjerkedahl 1973 (21)	ICMR 1984(13)	ICMR 1984(13)
Place	Bombay	Varanasi	Delhi	Delhi	Punjab	Delhi	Bombay	USA	Norway	India	India
Data Base	Hospital Low SE	Hospital	Hospital	Urban comm.	Hospital High SE	Hospital High SE	Hospital High SE	Hospital	Institution comm	Rural	Urban slum
Sample size	5336	5321	5031	6023	3163	3550	1242	40000	125485	3630	2534
Gestation (wk)											
<29	0.22	1.28	0.58	0.12	0.38		0.48	0.19		1.50	0.50
29	0.16	0.58	0.16	0.02	0.35		0.24	0.10		0.10	0.10
30	0.34	0.92	0.60	0.08	0.44		0.32	0.20		0.40	0.20
31	0.64	0.94	0.36	0.10	0.73		0.32	0.17	0.55	0.20	0.40
32	1.09	1.33	0.89	0.32	0.70	0.59	0.32	0.26	0.31	1.20	1.50
33	1.89	1.64	1.29	0.86	0.76		0.64	0.32	0.42	0.40	0.70
34	2.34	2.84	1.63	1.78	1.17	1.04	1.21	0.57	0.65	1.20	1.60
35	4.05	3.68	2.50	2.62	1.68	1.24	1.37	0.79	1.19	0.90	2.50
36	11.60	6.18	5.11	4.10	4.11	1.18	2.42	2.10	1.91	6.80	6.90
37	37.01	12.31	8.45	7.90	8.98	3.32	8.37	3.75	3.61	6.50	5.60
38	26.26	18.14	17.37	15.11	19.46	5.18	16.59	9.40	8.54	21.70	11.00
39	9.48	22.40	22.72	22.55	22.59	14.37	41.87	16.52	19.70	13.90	12.40
40	4.87	18.23	22.06	21.07	24.30	18.08	25.76	39.23	28.27	31.10	34.80
41	0.00	6.24	10.00	11.26	10.91	38.56	0.00	15.12	20.72	6.30	8.30
42	0.00	2.03	4.53	5.08	2.69	10.20	0.00	7.86	9.50	5.90	6.90
43	0.00	0.70	1.21	2.82	0.76	4.37	0.00	2.20	2.75	1.80	2.30
>43	0.00	0.32	0.48	4.22	0.00	1.46	0.00	0.57	1.88	1.10	4.30
37-41	77.67	77.56	80.66	77.88	86.23	86.80	92.90	84.02	80.84	78.50	72.10
<37	22.33	19.39	13.12	10.00	10.32	7.37	7.10	5.35	5.03	12.70	14.40
>41	0.00	3.05	6.22	12.12	3.45	5.83	0.00	10.63	14.13	8.80	13.50

In the Indian setting, the maximum number of births occur at 39-40 weeks gestation, whereas in the West the corresponding figure is 40-41 weeks (Table 2.). Apart from inter-regional difference, there is a marked variation in the gestational distribution in privileged versus under privileged segments of population in the same area. The contrast from the developed countries is very striking in the low socio-economic population, but the difference is considerably narrowed and even disappears in the privileged class. The gestational distribution in the region is therefore shifted to the left (about 1-2 weeks), more so in the underprivileged segments of the population.

From the foregoing, it would be logical to conclude that prematurity (especially borderline preterm births at around 36 weeks of gestation) too is a significant problem in the region and that it's contribution to LBW can not be totally ignored.

Intrauterine Fetal Growth

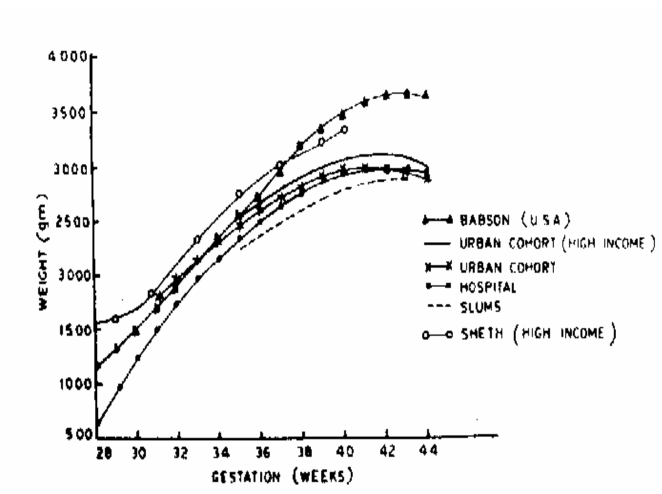
A comparison of fetal growth based on distance curves, reveals disparity from the developed countries and between regions and socio-economic classes. The socio-economically privileged population has higher mean birth weights at different gestations, the difference becoming pronounced after 34 weeks (Figure 2). The limited information on ultrasonography also reveals that the mean biparietal diameters values are lower than those from the developed nations in the third trimester and more so near term (27). It is evident that the magnitude of intrauterine growth retardation is maximal in the third trimester of pregnancy.

Table 3. Recent trends in prevalence of LBW in India.

Source	Area	Setting	Comparison period (Mean gap in years)	Change in birth weight	Change in gestation	Change in IUG
Satpathy 1990 (28)	Rourkela (Orissa)	Industrial hospital	1963 & 1986 (23)	MBW + 74g LBW -34 vs 25%	NA	NA
Man Mohan 1990 (29)	Delhi	Hospital (poor)	1969 & 1989 (20)	NA	Term *	0
Singhal 1991 (30)	Delhi	Hospital (better off)	1973-4 & 1985-7 (13)	NA	NA	+
CMC 1995 (31)	North Arcot (Tamil Nadu)	Rural	1969-73 & 1989-93 (20)	MBW + 78g LBW -27 vs 16%	M+0.7W PT -21 vs 16%	+ p
		Urban	1969-73 & 1989-93 (20)	MBW + 52g LBW -19 vs 11%	M +0.8W PT -20 vs 15%	+ p
Mathai 1995 (32)	Vellore	Hospital	1969 & 1994 (25)	MBW + 126g LBW -27 vs 15%	Me + 0.3W PT -14 vs 10%	NA
Fernandez 1996 (33)	Mumbai	Hospital (poor)	1988 & 1995 (8)	LBW -60 vs 38%	0	NA
Ramji 1996 (38)	Delhi	Hospital (poor)	1986 & 1996 (10)	0	0	NA

+: significant increase; +p: significant at some gestations; -: significant decline; 0: no significant change; IUG: intrauterine growth; M: mean; Me: median; MBW: mean birth weight; NA: not available; W; gestation in weeks; *: calculated in comparison with earlier study values cited by Bhargava et al. (9).

Figure 2. Comparison of intrauterine growth curves.



Recent Trends

An evaluation of the recent trends in the prevalence of LBW in the region may aid in the formulation of feasible strategies to tackle this public health problem. In recent years, an improvement in LBW prevalence has been reported from Sri Lanka (34). An up-to-date analysis of this nature from India has yielded interesting information (35).

It is felt that there have been no differences in the reported mean birth weights and the proportion of newborns with LBW in the three decades between late 1960s and late1980s (36, 37). These inferences were based on comparison of data from disparate settings at various time points. Given the expected marginal magnitude of change in birth weight in two to three decades in a nation commencing epidemiological transition, these inferences from such a research design are not surprising. It would however, be more valid to analyze data from the same area at different time points.

On analysis of this nature (Table 3), a positive time trend for birth weight is evident in most of hospital based data and the solitary community study. The mean magnitude of improvement is marginal (52 to 126g). However, this has resulted in a greater reduction of LBW prevalence (by 8 to 12% usually and 22% in one report). These calculated mean improvements in birth weight are probably underestimates (32) since concomitant changes in other important associates have been ignored. With time, the mean birth order has also decreased and correction for this factor alone (32) enhanced the magnitude of change in the community study (rural and urban areas combined) from 70g to 100g (the first born newborns have lower weights than later births). The absent time trend in the two Delhi hospitals may be related to the relatively short gap in one report (38) and the fact that these institutions primarily care to the underprivileged population in whom the transition is expected to commence last of all. In one of these studies (29), the higher percentage of term births could be regarded as the beginning, since term newborns have the best intrauterine growth as a group.

The slender improvement in birth weight is probably contributed to by increases in both gestation and birth weight at different gestations (intrauterine growth). The mean improvement in gestation was again marginal (0.3 to 0.8 weeks) and was not uniformly observed. However, these marginal changes in mean gestations resulted in greater improvement in prematurity rates (by 4 to 5%).

These improvements in the prevalence of LBW in the absence of any specifically targeted effective functional program have important managerial implications: (a) betterment in the LBW prevalence is possible even with the prevailing development scenario of the region; (b) both intrauterine growth and gestation are significant for enhancing birth weight; and (c) an all-round, integrated approach is likely to yield dividends rather than a narrow (food supplementation based) strategy.

CONSEQUENCES OF LBW

LBW newborns represent a heterogeneous group of term and preterm infants with varying risks in subsequent life. The adverse consequences of LBW, including the different types, have been extensively documented in the literature. This section is restricted to a brief delineation of those consequences of important public health significance in the context of developing countries, particularly South Asia to highlight the need for institution of remedial measures. In this context, the distinction between growth retarded and preterm infants has usually not been resorted to in the relevant literature.

Survival

In consonance with reports from the developed world, the early neonatal mortality in large birth weight cum gestational age blocks has a curvilinear appearance, increasing in all directions from a low central range (40). The striking inverse relationship between birth weight and infant morbidity and mortality has been documented by several studies from the region (9, 34, 41-43)). The recent NNF multicentric data on over 30,000 births confirms this even in a secondary and tertiary level care setting (3). In Delhi, a community based longitudinal study of infants with birth weights of 2000g or less, revealed that over a six year period two-thirds of them had died, mortality being especially high in the neonatal period and decreasing progressively till 3 years of age (44).

Growth

LBW survivors demonstrate significant growth retardation, as reflected by lower body weights, heights and head circumferences, in comparison to normal weight peers (14, 45-49). Although there is some tendency for catch up growth, the deficits persist even up till 14 years of age (47). The catch up is more for the preterm births in contrast to the growth retarded subjects. There is evidence of delayed skeletal growth and maturation in children aged between 6 to 10 years (50). While delayed puberty has been reported in LBW children (51, 52), an earlier onset of menarche (preterms - 6 mo and growth retarded - 1 year) was documented in a longitudinal follow up study (47). A similar observation has been made from the developed world setting also (53). This raises the possibility of an additional handicap for the continuing growth retardation in LBW infants - an earlier fusion of epiphyses resulting in a greater adult height handicap.

The above observations pertain to Indian LBW infants who were largely drawn from relatively poor Indian communities and continued to grow and develop during their childhood in the same sub-optimal socio-economic conditions. It may, therefore, be argued that these children continued to labor under the same conditions of relative deprivation that were operative at the time of their birth, and which in the first instance were responsible for their LBW. These studies do not, therefore, provide an adequate answer to the question as to whether the effects of the initial handicap of LBW in relatively poor communities can be reversed by and overcome in a vastly improved (postnatal) physical environment totally free from socio-economic and nutritional constraints on growth and development (54).

To seek an answer to this question, we need to look at growth performance of LBW children under optimal conditions. In a study of this nature (55), the effects of adoption soon after birth of poor Indian infants (81% LBW) into wealthy Swedish families were evaluated. While marked catch up growth was seen in childhood (mean stunting prevalence reduced from 62% to 20% after 2 years), inter-individual height and weight differences that existed at birth persisted in these children. The mean attained adult height (154 cm) of the adopted Indian girls was just 1cm higher than the mean height of poor adult women living in India and significantly lower than that for more affluent women in India (159 cm). Girls who were stunted at infancy when they were adopted were also significantly shorter in adulthood than their non stunted peers. The improved early childhood growth in these adopted girls had hastened the onset of menarche and thus cut short the period of rapid pre-menarcheal growth. Similar inference emerge from review of four other studies (56) in which undernourished children from poor families were adopted by age five into middle class families; the adoptees did catch up to some extent, but not all the height deficit suffered was made up.

From the foregoing, it would be reasonable to conclude that LBW suffer growth retardation in later life which persists till adulthood and that effects of IUGR cannot be entirely reversed by even ideal environment and nutritional inputs in postnatal life. These growth retarded adult women (stunted and underweight) are likely to give birth to LBW babies thereby perpetuating a vicious cycle through generations.

Development

Longitudinal studies reveal that LBW infants demonstrate retardation in motor, adaptive, personal, social and language development in the first five years of life (44, 57). A report suggests that uncomplicated preterms as a group can demonstrate catch up with normal peers in the motor and mental scales by 18-24 months age (58). Some of the developmental retardation can be argued to be a result of the continued socio-environmental deprivation.

Adult Diseases

Recent studies have brought to fore even more sinister possible late effects of LBW which may become manifest only in late adult life. These observations, briefly outlined below, lend an ominous new dimension to the traditionally accepted consequences of LBW.

Coronary heart disease (CHD) is common in the Indian sub-continent and the rates are rising (59, 60). These high rates, which rise further in migrants (61), are not explained by known risk factors including obesity, hypertension, smoking and raised cholestrol. Recent evidence indicates that CHD in the Indian sub-continent is associated with a particular metabolic profile, the insulin resistance syndrome, which includes impaired glucose tolerance or non insulin dependent diabetes, insulin resistance, raised serum triglyceride and low HDL cholestrol concentrations, abnormal plasma clotting factors and central obesity (62).

Following Barker's initial report from Hertfordshire, England (63), several subsequent studies have confirmed the association between LBW, especially SFD (64), and CHD (60, 65). The trends in cardiovascular disease with birthweight parallel similar trends in cerebral stroke (66) other major risk factors for CHD, including non insulin dependent diabetes mellitus, hypertension (meta-analysis of 32 studies by Law 1996) (67), and disordered lipid metabolism and blood coagulation (68). The "fetal origins hypothesis" has been proposed as an explanation for these associations, namely, that undernutrition in utero leads to fetal adaptations that permanently alter the physiology and metabolism of the body that lead to cardiovascular disease in adult life.

It is tempting to postulate this "fetal origins hypothesis" as the alternative explanation for the epidemic of CHD and non insulin dependent diabetes in India. Concrete evidence of a similar association between CHD and LBW has recently been reported from South India (69). A report from Pune suggests that components of the insulin resistance syndrome may be apparent in early childhood (70). Among 201 four-year old children, those with lower birthweight had higher plasma glucose and insulin concentrations after an oral glucose load, independently of their current size.

The "fetal origins hypothesis" is based on epidemiological evidence of associations and a cause and effect relationship can not be automatically implied. The hypothesis has been criticized on this and other epidemiological reasoning. Nevertheless, the suggestive evidence linking LBW and adult disease adds a new dismal dimension to the possible consequences of LBW.

ETIOLOGY OF LBW

From the preceding sections, it is obvious that LBW is a major public health problem in South Asia which needs to be addressed on an urgent basis. In order to plan and institute meaningful interventions, it is pertinent to review the various factors which have been reported to be a cause of LBW. The literature is replete with various studies which have attempted to answer this question and several exhaustive reviews on the topic have also been published including from the region (13, 15, 16, 54, 71-76). Before drawing any valid conclusions from such literature, it would be useful to briefly consider the pertinent methodological issues.

Methodological Considerations

The important methodological issues involved in inferring a cause and effect relationship for LBW on the basis of available studies have been elegantly summarized by Kramer (71). It is generally recognized that the etiology of LBW is multifactorial since many factors can influence the length of gestation or the rate of intrauterine growth. Nevertheless there is considerable confusion and controversy about the factors that have independent effects on LBW as well as the quantitative importance of these effects. The various reasons for this include: (i) Failure to distinguish between IUGR and prematurity as different causes of LBW; (ii) A given factor might affect the middle or upper range of the birth weight or gestational age distribution but not those infants identified by the conventional cut-off points as SFD or prematures; (iii) "Failure to distinguish markers or associated factors from true causal determinants. Many of the potential determinants are highly associated and their effects are thus mutually confounded. Failure to control for the confounding variables can lead to erroneous associations between a factor and IUGR or prematurity. For example, anemia is highly associated with under nutrition, and if insufficient caloric intake is a true cause of IUGR, failure to control for such intake will produce an association between anemia and IUGR. Anemia, however, may merely be a marker of poor maternal nutrition, and not a true causal determinant of IUGR. Thus if anemia has no independent effect on intrauterine growth, routine use of iron supplementation during pregnancy will have no impact on the rate of IUGR" (71); (iv) Failure to perform a "path analysis" on the identified factors resulting in lumping together of underlying or indirect determinants (for example, literacy or age at marriage) with direct or immediate determinants (for example, maternal anthropometry or food intake); (v) The large number of factors that could theoretically influence birth weight indicates that each one of them may have a rather small individual impact. Unequivocal demonstration of statistical significance for small effects requires the use of large sample sizes as well as control for confounding and other non-random sources of variation.

Majority of the research in relation to causation of LBW has relied on observational methods. It is only recently that well designed experimental methods have been utilized to unambiguously demonstrate a cause and effect relationship. These randomized clinical trials have enabled the impact of the factors that are amenable to experimental intervention to be also quantified for their effect. However, not all possible factors can be subjected to an experimental design (for example, race/ethnicity, socio-economic status or age of child bearing).

Intervention Based Causes of LBW

It is generally believed that the solution to LBW in the region lies in improvement of intrauterine growth. Consequently, majority of relevant research and suggested interventions have focussed on this aspect only. However, from the preceding sections it is apparent that for maximum benefit, efforts should also be directed at gestational duration because: (i) Nearly one third of LBW newborns are born preterm; (ii) The gestational distribution reveals a shift to the left in comparison to developed nations; and (iii) Positive time trends in prevalence of LBW in India have been associated with improvements in both intrauterine growth and gestation. In this context, improvement should be envisaged as a shift of the gestational distribution to the right (say by one week) even among term newborns (37 to 41 weeks gestation), rather than a classical decline in preterm births. It is conceivable that the factors affecting intrauterine growth and gestation are different and should, therefore be searched for separately.

LBW is multifactorial in etiology - nearly 50 individual factors have been evaluated for their role in causing prematurity and IUGR with statistically significant associations having been documented for several of them. In order to formulate a meaningful public health intervention policy, it would be useful to group the factors (71) by the: (i) strength of available evidence; (ii) potential for public health impact, which depends on both the magnitude of the effect, e.g., the number of grams of birth weight attributable to it or the relative risk of IUGR, and its prevalence in the population; and (iii) modifiability. An analysis of this nature (71) is summarized in Table 4. This analysis represents a synthesis of the currently available evidence, which is largely based on exhaustive meta-analyses or overviews including unpublished electronic database

Table 4: Intervention based assessment of factors evaluated for their effects on gestation duration and intrauterine growth in developing countries.

Intervention based assessment	Intrauterine growth	Gestation duration
Causal effect ruled out with a high probability	• Protein status/intake	• Infant sex • Paternal height and weight • Parity • Protein status/intake
Causal effect unlikely, but evidence insufficient to rule out totally	• Marital status • Maternal psychological factors • Sexual activity • Prior spontaneous abortions • Prior induced abortion • Prior still birth or neonatal death • Prior infertility • In utero exposure to diethylstilbestrol • Vitamin B12 • Zinc and copper • Calcium, phosphorous and Vitamin D • Vitamin B6 • Urinary tract infection • Genital tract infection • Caffeine and coffee consumption • Use of marijuana	• Racial/ethnic origin • Maternal height • Maternal hemodynamics • Marital status • Sexual activity • Prior still birth or neonatal death • Prior infertility • Gestational weight gain • Vitamin B12 • Zinc and copper • Calcium, phosphorous and Vitamin D • Other vitamins and trace elements • Urinary tract infection • Alcohol consumption • Caffeine and coffee consumption • Use of marijuana • Narcotic addiction
Causal effect uncertain, but importance unlikely, owing to small effect magnitude or low prevalence	• Birth or pregnancy interval • Heavy alcohol consumption • Narcotic addiction	• In utero exposure to diethylstilbestrol • Birth or pregnancy interval • Prior induced abortion • Vitamin B6
Causal effect established, but importance unlikely owing to small effect magnitude or low prevalence	• Antiplatelet agents (Aspirin)	• Antiplatelet agents (Aspirin)
Causal effect established and important, but unmodifiable	• Infant sex • Parity	
Causal effect established and important, but modifiable over long term	• Maternal height • Socio-economic conditions* • General morbidity, episodic illness	• Socio-economic conditions*

Table 4 - continued

Intervention based assessment	Intrauterine growth	Gestation duration
Causal effect established, important, and modifiable over short or intermediate term	• Pre-pregnancy weight • Very young maternal age* • Maternal education* • Gestational weight gain • Caloric intake • Malaria! • Tobacco chewing	• Pre-pregnancy weight • Very young maternal age* • Maternal education*
Causal effect uncertain, but potentially important and modifiable	• Maternal hemodynamics • Strenuous maternal work • Folic acid • Iron and anemia • Other vitamins and trace elements • Magnesium • Cigarette smoking and indoor smoke • First antenatal care visit • Number of antenatal care visits • Quality of antenatal care	• Stress and anxiety • Maternal work • Caloric intake • Other vitamins and trace elements • Iron and anemia • Folic acid • General morbidity, episodic illness • Malaria! • Genital tract infection • Cigarette smoking and indoor smoke • Tobacco chewing, environmental toxins • First antenatal care visit • Number of antenatal care visits • Quality of antenatal care

* These factors have indirect causal influences, i.e., they affect direct determinants but have no independent causal impacts of their own. Socio-economic status has been subdivided into maternal education and socio-economic conditions because of the temporal differences required for their modification.
For endemic areas.

Information on randomized controlled trials (RCTs) from the Cochrane Library (71, 73-75, 77, 78). The analysis is restricted to factors of importance in the developing countries, particularly this region, and also excludes those factors related to medical complications during pregnancy or evaluated in selected groups of suspected fetal growth retardation. In case of conflicting conclusions arising from observational or experimental study designs, the latter inference was selected. It should be borne in mind that no matter how convincing the evidence that a given factor is how convincing the evidence that a given factor is causally related to intrauterine growth or gestational duration, there is no guarantee that its elimination or reduction will lead to lower infant mortality or childhood morbidity (71) since there is hardly any data exploring this possibility.

Pertinent aspects of some of the important factors are briefly outlined below:

Adolescent Pregnancy

Maternal age does not appear to be an important independent determinant of intrauterine growth or gestational duration (71). However, a very young age exerts indirect effects by influencing maternal height, weight and nutrition. In a recent report on 242 adolescent pregnancies (10-18 years) from Gorakhpur in Uttar Pradesh, India (79), the LBW and prematurity rates were 67% and 33%, respectively. The corresponding figures for mothers below 17 years of age were 83% and 33%, respectively. The indirect causal effects of a very young maternal age are important, because interventions aimed at delaying pregnancy in young adolescents might be more effective or more practicable than attempting to influence their height, weight or gestational nutrition (15, 71). Although the average female age of first marriage in the region has steadily increased in the past few decades (1), there is still considerable scope for improvement as illustrated in Table 5.

Table 5. Average age (years) of first marriage in females.

Country	Average age (yrs)	Source
Bangladesh	<15	UNICEF 1996 (1)
Bhutan	>20	UNICEF 1996 (1)
India	15-17.5 (most states)	UNICEF 1996 (1)
	19.6 (20.3% < 18)*	SRS 1993 (81)
Maldives	17.5-20	UNICEF 1996 (1)
Nepal	15-17.5	UNICEF 1996 (1)
	16.4	Pradhan 1997 (82)
Pakistan	17.5-20	UNICEF 1996 (1)
Sri Lanka	>20	UNICEF 1996 (1)

* Refers to female age at "effective marriage".

Nutrient Supplementation

The "true" potential of this intervention, which can be modified over a relatively short term, needs a critical analysis. Meta-analyses (73, 75, 80) of randomized trials of balanced energy/protein supplementation (<25% protein/ daily consumption) reveal "only a modest increase in maternal weight gain and fetal growth, even in undernourished women, and no long term benefits to the child in terms of growth or neurocognitive development". The weighted mean benefit in birth weight was calculated as 30g (95% CI 1g to 58g) with, at best, a "clinically trivial effect on mean gestational age", which though statistically non-significant, resulted in a highly consistent reduced risk of prematurity (73). Another optimistic estimate of the "modest" increase in birth weight is about 100g (75). Three recently completed but unpublished trials from rural areas of India are nearer the former (73) lower benefit estimate. Surprisingly, there was no evidence of a larger effect in undernourished women; indeed the effect was actually smaller (weighted mean 24g vs 45g) (73). The "modest" benefits of such supplementation have been explained by the rather "modest" net increases in energy intake achieved. The average documented net increases were 200-250 kcal/day and in the trials recording relevant data, non compliance was substantial (73). The magnitude of non-compliance reported from research settings is likely to be magnified in the true operational setting of large scale programs. In a recent study in 174 pregnant beneficiaries of food supplementation (500 kcal/day protocol) in the Integrated Child Development Services (ICDS) Program, only 24% of those registered actually collected or received supplementary nutrition. Of those who collected, only 11% consumed 75-100%, and 36% less than 50% of the supplementary nutrition. All of them shared the supplementary nutrition; about 42% of them shared more than 75% of the food with their family members (83).

Neither balanced isoenergetic protein supplementation nor high protein supplementation have proved beneficial to either mother or infant and there is a suggestion that these may even impair fetal growth (73, 75, 80). Similarly, isolated micronutrient supplementation with either zinc, vitamin D, pyridoxine or iron has not resulted in clinically important or statistically significant positive effects on birth weight. Routine magnesium supplementation seems to have decreased the incidence of term LBW but the trials included in this systematic review have either a high number of exclusions or weaknesses in randomization procedures which makes the results inconclusive. Although, routine iron supplementation increased serum ferritin and hemoglobin levels, there were no differences on clinical outcomes of the fetus. The systematic review on routine folate supplementation shows a reduction in the incidence of term LBW. However, most of the trials defined their populations poorly and did not give details of the randomization procedures (all of these trials were performed in populations where iron supplementation was routine). Unfortunately, there is inadequate data from populations where these micronutrient deficiencies are more common; and relevant research in this context has been recommended for zinc, iron, folate and magnesium (73, 80).

In a systematic review of relevant studies (80), nutritional advice, either on one-to-one basis or to groups of women, proved effective in increasing the pregnant women's energy and protein intakes but the increases were lower than those reported in trials of actual protein/energy supplementation. It was felt that the implications for the fetal, infant or maternal health cannot be judged from the available trials. A recent study from Canada reported an average benefit of 55g in birth weight in adolescent pregnancy with nutrition intervention individualized as a function of diagnosed risk (84). Imparting relevant nutrition advice assumes significance in the context of developing countries since dietary intake in pregnancy is strongly influenced by cultural beliefs and practices. Data from 18 different cultures documents that food restriction is practiced during pregnancy, in order to facilitate an easier labor and delivery, by lowering birth weights (85). Quantitative data from rural South India demonstrates reduced intake in pregnancy, particularly between 5-7 months and months 8/9; the average caloric intake being 1700 kcal (86).

From the foregoing, it is evident that routine nutrient supplementation instituted through large scale programs will, at best, result in marginal benefits in birth weight. Considering the various aspects of food supplementation programs, particularly the financial perspective in the region, it may be pragmatic to resort to sound nutritional advice as an alternative economic intervention.

Energy Expenditure, Work and Physical Activity

Cross sectional data from Ethiopia indicates that among poor women subsisting on a calorie intake of less than 70% of the recommended intake, birth weights of offspring and weight gains in pregnancy of women who were actively engaged in heavy labor were significantly lower than the corresponding values for women who were not so engaged [mean (SD) birth weights 3068g (355) vs 3270g (368)] (87). However, the effect of energy expenditure, work and physical activity on intrauterine growth is uncertain from a systematic review of the available data in developing countries (71). Nevertheless, such an effect would be consistent with biological principles, at least for work involving high energy expenditure. Increased effects, if confirmed, would identify a factor of major importance in developing countries, where women often continue strenuous physical work through pregnancy (15, 71).

Maternal Anthropometry

Various maternal anthropometric criteria (pre-pregnancy weight, height, weight gain during pregnancy, attained weight at mid pregnancy and body mass index) have been significantly associated with intrauterine growth or prematurity. These parameters should be viewed as "predictors" of LBW to be used for risk detection and intervention targeting, rather than as representing direct factors amenable to intervention.

In the WHO multicentric study (74), pre-pregnancy weight (OR 2.55, 95% CI 2.3-2.7), attained weight at 20 weeks (OR 2.77, 95% CI 2.3 - 3.2) and attained weight at 36 weeks (OR 3.09, 95% CI 2.7-3.4) were the best predictors for delivering SGA babies while pre-pregnancy weight (OR 1.42, 95% CI 1.3-1.5) and pre-pregnancy body mass index (OR 1.33, 95% CI 1.1-1.4) were the best predictors for a preterm delivery. Obviously, attained weight at 36 weeks of pregnancy does not represent a useful indicator for preventing LBW as it would be too late to implement effective intervention.

Maternal Infections

Amongst the various researched maternal infections in pregnancy, systematic reviews indicate a beneficial effect with malaria chemoprophylaxis in endemic areas (75, 80). Overall, malaria chemoprophylaxis was associated with higher maternal hemoglobin levels and birth weights. These effects were also more prominent in primigravidae, who are known to be more susceptible, showing an increase in mean birth weight of 112g (95% CI 41-183g) (75). The current incidence of malaria is high in Chittagong Division of Bangladesh, Southern Bhutan and regions of Sri Lanka (1).

Other Factors

The comprehensive meta-analysis by Kramer (71) suggests that maternal socio-economic status (including maternal education) have no independent effect on intrauterine growth. "It is nevertheless, likely that low socioeconomic status may well be a social "cause" of other nutritional, toxic, anthropometric, or infectious factors that may themselves be causal determinants. As with maternal age, indirect causal effects may be important for intervention. The most easily modifiable aspect of socio-economic status is maternal education, although, in the long term, family income could also be influenced" (71).

There is scarce well controlled data from the developing world evaluating the impact of antenatal care on LBW (71). Nevertheless, organizing access to quality antenatal care should be viewed as potentially important since it also offers opportunities for counseling and risk detection apart from its necessity for maternal health.

Data from developed countries indicates that strategies to reduce smoking during pregnancy are associated with increased birth weight and lower rate of term

LBW (OR 0.80, 95% CI 0.65-0.98) (75). Smoking and tobacco chewing during pregnancy does occur in the region; the precise magnitude, however, is uncertain.

POSSIBLE PUBLIC HEALTH INTERVENTIONS TO REDUCE LBW

It is obvious that the suggested public health interventions to reduce LBW should be specific for the targeted population and directed at the quantitatively important modifiable determinants of intrauterine growth and gestation. The quantitative importance of a factor is dependent on its individual effect magnitude and prevalence; however, issues such as cost-effectiveness, cultural acceptability, and political feasibility are also important determinants of any intervention program (71). On the basis of the focused review in the preceding sections, the suggested public health interventions are summarized in Table 6. Some interventions (for example, nutrient supplementation) could be preferentially targeted towards "at risk" women identified by anthropometry. Over the long term, general improvements in nutrition, living conditions, water supply and sanitation should increase maternal height and reduce communicable diseases during pregnancy. It should also be borne in mind that no matter how convincing the evidence that a given factor is causally related to intrauterine growth or gestational duration, there is no guarantee that its elimination or reduction will lead to amelioration of all adverse consequences of LBW including lower infant mortality and childhood morbidity (71).

Table 6. Suggested public health interventions to reduce LBW.

Interventions
• Delaying child bearing in adolescents • Efforts to improve nutrition of women, particularly in pregnancy Options for pregnant women: • Nutrition advice • Food supplementation • Access to antenatal care • Advice on adequate rest in pregnancy, especially in undernourished women • Malaria prophylaxis or treatment in endemic areas • Efforts to stop smoking and reduce tobacco chewing (places where common practice) • Improve female education, especially maternal • General improvements in nutrition • General improvements in socio-economic conditions • Improve sanitation and water supplies

The expected benefit with each solitary intervention is small. Further, multiple pathologies coexist in the region which often adversely interact with each other making their combined effect greater than the simple additive effect of each condition. It has been appropriately questioned whether a single intervention is likely to reduce, in a population, the overall rate of a multicausal outcome like LBW which is so dependent on socio-economic disparities accumulated over generations (75). The maximum benefit is, therefore likely to accrue from institution of a combination of interventions.

Table 7. Changes in birth weight in developed countries.

Source	Place/Country	Period	Improvements in Birth weight	LBW prevalence
Lee 1980 (88)	USA National	1950 to 1975		No change
Kessel 1984 (89)	USA National (States with both weight & gestation data)	1970 to 1980	Median 60g	7.39% to 6.31% (14% reduction)
Johar 1988 (90)	Omaha (USA)	1935 to 1985	No change (term newborns)	No change (term newborns)
Evans 1989 (91)	ICE Countries*	1970 to 1984	40 - 100g (in most; derived from graph)	
Chike-Obi 1996 (92)	Illinois (USA)	1950 to 1990	33g (Black male) to 74g (White female)	~7% to 6% (White) ~13 to 14% (Black) (Derived from graph)

* The International Collaborative Effort (ICE) countries are USA, England and Wales, Denmark, Bavaria and North Rhine Westphalia of the Federal Republic of Germany, Israel, Japan, Norway, Scotland and Sweden.

Wherever possible, the suggested interventions should be amalgamated with the beneficial customs. For example, it is a common practice in India to deliver the child, particularly the firstborn at the parental home which offers benefits in term of adequate rest and nutritional intake in the pregnancy.

FUTURE PERSPECTIVES

Are The Targets Realistic?

The World Summit for Children had set a goal of reduction of the LBW prevalence to less than 10% (93). This translates into a prevalence reduction of 15% to 40% (or by 60% to 80% of the current estimates in Table 1) till 2000 A.D. In order to ascertain if these targets are achievable by even 2010 A.D. It would be useful to look at the changes in developed countries (Table 7).

In this context, it would be pertinent to examine the birth weight changes in the developed countries for the preceding few decades to account for the developmental gap between the industrialized and developing countries. Even in the developed nations, a few decades earlier, there was no consistent increase in birth weight or reduction in LBW prevalence (Table 7). In certain regions, no changes could be demonstrated over 25 or 50 years. Wherever evident, the increases in average birth weight were modest, ranging from 33 to 100g in 10 to 40 years, with a corresponding decrease in LBW prevalence of about 1% (nearly 14% reduction from the original value). In the USA, the decade of 1970s was a period of rapid growth of the number and scope of federal state and local health programs emphasizing maternal and child health including nutrition programs (Special Supplemental Food for Women, Infants and Children [WIC Program] and the Department of Health and Human Services sponsored programs providing such services as prenatal care, family planning, care of high risk pregnant women and newborns, regional perinatal care, health supervision and care of infants and children, care of pregnant adolescents, and genetic diagnostic and counseling services; yet, the median increase in birth weight was only 60g with a resultant decline in LBW prevalence of 1% (90). Another noteworthy aspect is the difference in level between the median birth weights for different countries or states or even amongst races in the same region (blacks and whites), and the way the relative positions tend to remain steady over the years (91, 92).

The secular changes in birth weight from India (Table 3) compare favorably with those from the developed nations (Table 7). However, almost similar improvements in average birth weights resulted in vastly different changes in LBW prevalence (8 to 12% vs 1%); indicating the importance of efforts to achieve even modest changes in the region. This difference is a reflection of the comparative birth weight distribution below the cut-off point of 2500g in these settings.

Considering the earlier time trends from the developed countries and India, it is evident that it would be virtually impossible to achieve the stated targets by even 2010 A.D. An "optimistic" target in this period would be an average increase in birth weight of about 100g with a corresponding reduction in LBW prevalence of 10-12%.

Public Health Interventions

Although there is no specifically instituted program for control of LBW in India, Bangladesh and Pakistan, majority of the suggested public health interventions (Table 6) are being addressed through the ongoing programs for population control, maternal and child health, nutrition and literacy. In India, the important relevant programs include the Reproductive and Child Health Program (Child Survival and Safe Motherhood Program) focussing on providing access to antenatal care and family planning including delaying pregnancy in adolescents; the Integrated Child Development Services Program where apart from new initiatives focussed on adolescent girls, pregnant mothers are given a nutritional supplement of 500 kcal; and Literacy Mission. In Bangladesh also, the nation wide Maternal Child Health Program has provision for antenatal care and family planning whereas the recently instituted Bangladesh Integrated Nutrition Project (BINP) focuses on family planning advice to newly wed couples and nutrition education and supplementary nutrition (600 kcal) to pregnant women. The BINP, a World Bank assisted project, currently covers only 6 thanas (sub districts) and will be extended to 40 thanas (out of 460) by the end of 1998 and the entire country by 2000 AD. In addition, NGOs like Bangladesh Rural Advancement Committee also provide supplementation and counseling to pregnant women in their operational areas (12, 94). Similarly, in Pakistan the maternal care programs, population planning initiatives and nutritional supplementation in pregnancy (part of safe motherhood initiative) have components addressing the problem of LBW (95). In addition, in thesecountries the ongoing initiatives for general improvements in socio-economic development, nutrition, literacy and water supply and sanitation are expected to have a beneficial effect on birth weight in the long term.

It is apparent that in a multi-dimension problem like LBW, no specific vertical program can be formulated to address the issue on a war footing. The ongoing initiatives in these countries are in the right direction but may need operational strengthening and convergence to yield the maximum benefit. An examination of the specific components of nutrition and other advice in pregnancy may lead to improvements like specific dietary advice, adequate rest and stopping smoking and tobacco chewing (in areas where these habits are prevalent). Initiatives to provide maternity leave for women in unorganized sector are worth considering. Provision of malaria chemoprophylaxis and treatment for pregnant women in hyperendemic areas deserves exploration. The relative cost effectiveness of providing nutritional supplementation to all pregnant women in preference to nutritional advice in pregnancy must be scientifically explored in a true program setting and the results should determine the need for investing a large proportion of the available health budget for the former option on a routine basis.

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