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DOES ONE SIZE FIT ALL?
Should India Adopt the New INTERGROWTH-21st "Prescriptive" Standard for Fetal Growth?

Michael S. Kramer

Introduction

The World Health Organization (WHO) defines low birth weight (LBW) as weight at birth below 2500 grams. It is well known that birth weight is determined by two separate, if not entirely independent, processes: (1) the duration of gestation and (2) the rate of fetal growth.[1] Thus, LBW can arise through one or both of two mechanisms. An infant can be born too soon, usually referred to as preterm birth (PTB) and defined as a gestational age at birth <37 completed weeks.[2] The second mechanism is an infant born too small for his or her age. Small-for-gestational-age (SGA) birth is usually defined as a birth weight below the 10th percentile for gestational age and sex, based on an appropriate population reference.[3]

Figure 1 is a venn diagram that illustrates the relationships among LBW, PTB, and SGA birth. As can be seen by the diagram, all LBW infants are SGA, preterm, or both. But the diagram also shows that a large fraction of SGA infants do not have LBW, i.e., their birth weight is ⩾ 2500 grams. The 10th percentile for gestational age in Canada is about 3000 grams (3079 grams for boys, 2955 grams for girls). Thus, most Canadian infants who are born at term weighing 2500-3000 grams meet the criteria for SGA birth and yet are not LBW.[4] For PTB, the median birth weight at 35 completed weeks is 2600 grams in boys and 2506 grams in girls. All late preterm infants (those born between 34 and 36 weeks ± 6 days of gestation) are defined as preterm, and a large fraction of those born in Canada have birth weights that exceed the 2500-gram cut-off for LBW.[4]

To further illustrate these distinctions, Figures 2 and 3 show three decades of national perinatal surveillance data for Canada.[5;6] In the early 1980s, Canadian rates of PTB and LBW were similar and declining slightly. From the early 1980s to 2004, however, PTB increased substantially and steadily; since 2004, the PTB rate has declined slightly. In contrast, LBW rates remained fairly steady from the mid-1980s until around 2000, with a slight rise over the most recent decade.

Figure 3 shows the contrasting rates for SGA and large-for-gestational-age (LGA) births, the latter defined as births ⩾ 90th percentile for gestational age and sex.[5;6] The 10th and 90th percentile cut-offs for the Canadian reference are based on births between 1994 and 1996. That is why (as seen in the Figure) the rates of both outcomes were near the expected 10% during those years. But over the 30-year period between 1981 and 2010, SGA births fell by almost 50% and have remained at about 8% since 2000. In contrast, LGA births increased by about 50% between 1981 and 2000, following which they have declined slightly.

The combined data in Figures 2 and 3 illustrate that between 1981 and 2000, Canadian newborns became larger (heavier). The probable major reasons for this trend were increases in maternal pre-pregnancy body mass index, gestational weight gain, and gestational diabetes, as well as reductions in maternal cigarette smoking.[7] That the trend did not continue over the most recent decade may be partly attributable to routine screening for gestational diabetes, as well as more aggressive treatment and earlier delivery of women who screen positive.

Although national data on all births from India are not available, LBW rates and SGA rates (based on an international standard) on the Indian subcontinent are among the highest in the world.[3,8,9] The question that I will address in the remainder of this article is whether any international standard should be applied to Indian newborns. Before taking on that specific question, however, I will first address the more general issue of physiological vs pathological differences in fetal growth.

Does One Size Fit All?

Birth weight for gestational age is a proxy for fetal "growth." Of course, true growth is defined as the increase in size between two ages or two time periods. Because the original zygote that results

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Figure 1. Venn diagram illustrating the relationships among low birth weight (LBW), preterm birth (PTB) and small for gestational age (SGA) birth

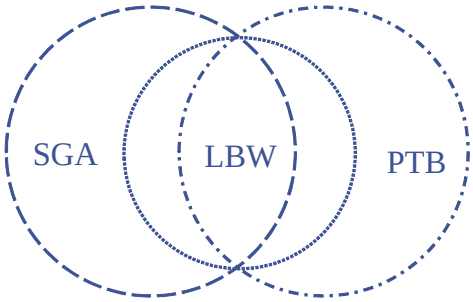
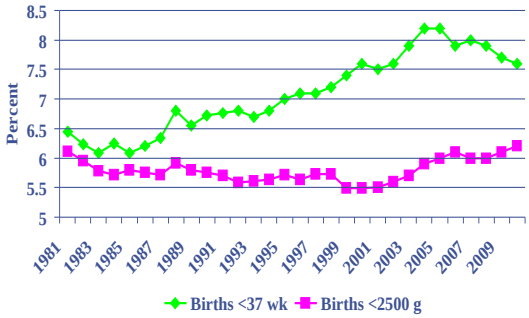


Figure 2. Temporal trends in preterm birth and low birth weight, Canada, 1981 - 2010



from fertilization is nearly mass-less, birth weight for gestational age reflects the fetus's total growth between the formation of the zygote and birth, and thus the overall adequacy of the in utero environment.

Girls have lower birth weights for their gestational age than boys, a difference that is evident as early as the first or early second trimester.[1] Yet at the same birth weight for gestational age, girls have lower mortality and serious morbidity rates, indicating that the smaller size of female fetuses is physiological, rather than pathological. Sex-specific birth weight-for-gestational-age standards are therefore widely accepted.[10]

Whether other differences in birth weight for gestational age are physiological or pathological, however, remains controversial. Primary among these differences are differences between high- and low-income countries.[3;8;9] Birth weights for gestational age are much lower among Indian, Pakistani, and Bangladeshi infants than among infants in other countries, even if the comparison is limited to low- and middle-income countries (LMICs). But many within-country differences are also robust, including those due to plurality (singletons vs twins vs higher-order multiples), ethnicity, parity, maternal height, and pre-pregnancy body mass index.[1]

Many clinicians and researchers have assumed that these robust differences are physiological, rather than pathological. In other words, they assume that one size does not fit all. It has recently become popular to "customize" fetal growth standards. Customization is based on comparing the observed birth weight for gestational age to the "expected" birth weight based on the maternal characteristics I mentioned earlier, using a regression model for maternal characteristics that are known to affect fetal size. The key feature of these standards is that the expectation is based on estimated fetal weight, not birth weight. The most commonly used customization approach has been popularized by Gardosi and colleagues[11] and is based on the Hadlock formula used to predict birth weight at 280 days (40 completed weeks).[12]

What is very clear is that birth weight references and estimated fetal weight references, although similar at term, are very different at preterm gestational ages. Figure 4 is taken from a 2008 paper by Hutcheon and Platt.[13] The dotted line represents the normally-distributed birth weight for male fetuses at 32 weeks of gestation, based on the Canadian birth weight for gestational age reference mentioned earlier. Superimposed on that normal distribution, however, is a histogram showing the distribution (also reasonably normal) of estimated fetal weights of males at 32 weeks, based on routine clinical ultrasound measurements (i.e., obtained routinely, rather than when pathology is suspected) at the Royal Victoria Hospital in Montreal.

It is clear from the figure that the estimated fetal weights are shifted to the right (i.e., to higher weights) vs the observed birth weights of babies born at 32 weeks. The medians of these distributions differ by 120 grams, but even more striking is the difference in cut-offs for SGA, defined by the 10th percentile. The cut-off according to the birth weight standard is about 1450 grams; the cut-off based on estimated fetal weight is more than 300 grams higher. This large difference in normal fetuses vs newborn infants characterized as SGA arises from the fact that it is abnormal to be born at 32 weeks. Infants born at 32 weeks represent an undergrown fraction of all fetuses who remain in utero at the same gestational age.

Figure 3. Temporal trends in small for gestational Age (SGA) and large for gestational age (LGA) birth, Canada, 1981- 2010

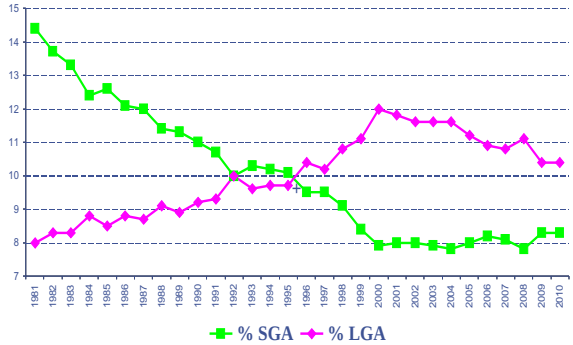


Figure 4. Comparison of distributions of birth weight in male infants (dotted line) and estimated weight of unborn male fetuses at 32 weeks, Royal Victoria Hospital, Montreal (taken from Hutcheon and Platt[13])

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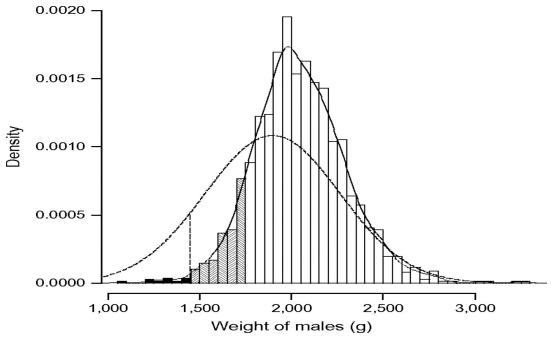

Figure 5. Gestational-age-specific perinatal mortality rate in four ethnic groups, British Columbia, 1981-2000 (taken from Kierans et al[16])

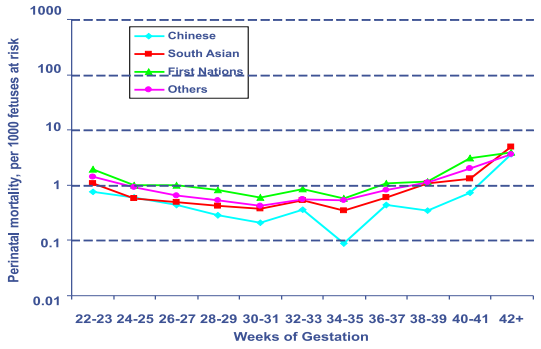

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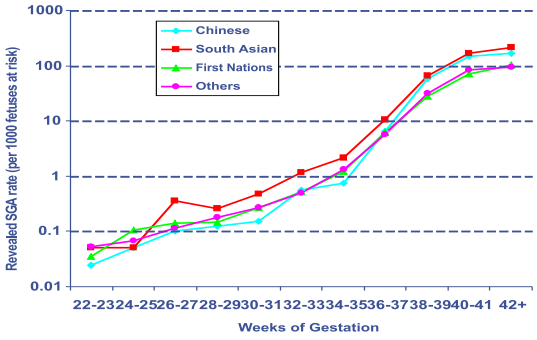
Figure 6. Revealed SGA birth rate based on an overall British Columbia standard in four ethnic groups, British Columbia, 1981-2000 (taken from Kierans et al[16])



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This contrast should not be surprising. An inadequate intrauterine environment is likely to compromise fetal growth but can also lead to early birth. My colleagues and I have shown that the use of estimated fetal weight instead of a population birth weight-based reference to define SGA leads to a tripling of SGA rates (from 9.9 to 33.6%) from 28 to 33 weeks, a 50% increase in SGA rates (from 9.9 to 15.5%) in those born at 34-36 weeks, but essentially no difference (9.9 vs 8.9%) in Swedish infants born at or after term ($\geqslant$ 37 weeks).[14] Additional (beyond estimated fetal weight) "customization" for maternal height, pre-pregnancy BMI, ethnicity, and parity resulted in virtually identical SGA rates among Swedish births as the use of estimated fetal weight alone. In other words, the additional maternal characteristics customized did not change the rate of SGA.

More importantly, as shown in the Table, the relative risks of SGA (vs AGA) birth for stillbirth and early neonatal death at preterm gestational ages were extremely high and very similar to one another using estimated fetal weight alone or fully customized fetal weight for gestational age.[14] But they were substantially higher than when SGA was defined based on population birth weight instead of estimated fetal weight. At term, however, the relative risks were similar for both stillbirth and neonatal death whether the population birth weight, estimated fetal weight alone, or fully customized fetal weight was used for defining SGA.[14]

Are Ethnic Differences in Birth Weight for Gestational Age Physiological or Pathological?

How can we decide whether ethnic differences in birth (or fetal) weight are physiological or pathological? Relative smallness or largeness is not sufficient by itself. The decision should depend on the consequences for the offspring's survival, health, or quality of life. I am aware of two approaches used to answer this question for South Asian or Indian infants.

The first approach makes use of an artificial entity, the "revealed" SGA birth rate developed by Joseph.[15] My colleagues and I had to resort to this measure, because no valid measure of growth restriction exists for all surviving fetuses, stratified by ethnicity, at each gestational age. For example, we do not have repeated longitudinal ultrasound measurements on fetuses of different ethnicities within the same population and environment, such as the 32-week ultrasounds shown in Figure 4 from the Royal Victoria Hospital in Montreal.

In the "revealed" SGA rate, the numerator is the number of SGA live births born to a given ethnic group, while the denominator is the number of fetuses still in utero at that gestational age for the same ethnic group. Using this measure, we carried out a study of over 800,000 live births and stillbirths in British Columbia between the years 1981 and 2000.[16] British Columbia has a large number of both Chinese and South Asian immigrants, and an even larger number of First Nations (American Indian) births.[16] The largest group, of course, is the "other" (primarily Caucasian) group.

Figure 5 shows the gestational age-specific perinatal mortality rates for the four ethnic groups we studied, expressed per 1000 fetuses at risk, i.e., per 1000 fetuses alive at the beginning of each week of gestation shown in the figure.[16] The Chinese ethnic group has the lowest perinatal mortality at all gestational ages. Perhaps somewhat surprisingly, the South Asian group has the next-to-lowest mortality of the four ethnic groups. As expected, the First Nations gestational

Figure 7. Revealed SGA birth rate based on ethnic-specific standards in four ethnic groups, British Columbia, 1981-2000 (taken from Kierans et al[16])

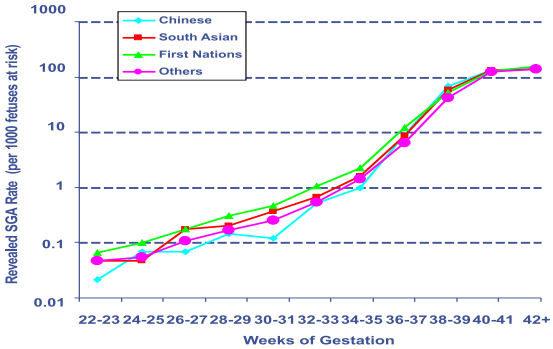

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Table Relative risks [RR (and 95% CI)] for stillbirth and early neonatal death (<7 days) in SGA vs AGA births based on birth weight (BW), estimated fetal weight (EFW) , or fully customized fetal weight standards (taken from Hutcheon et al [14])

Gestational Age	Stillbirth			Early Neonatal Death		
	BW	EFW	Customized	BW	EFW	Customized
28-33 weeks	2.8 (2.3-3.4)	12.2 (10.4-14.3)	11.4 (9.7-13.3)	2.2 (1.5-3.0)	8.3 (6.3-10.8)	8.3 (6.4-10.8)
34-36 weeks	4.5 (3.7-5.4)	7.9 (6.6-9.5)	7.9 (6.5-9.4)	4.2 (3.1-5.8)	6.5 (4.9-8.8)	7.0 (5.2-9.3)
=37 weeks	4.0 (3.6-4.5)	4.2 (3.7-4.7)	4.2 (3.7-4.7)	4.2 (3.4-5.2)	4.9 (4.0-6.1)	5.1 (4.1-6.2)

age-specific perinatal mortality is the highest of the four groups.

Figure 6 shows the revealed SGA rates of the four ethnic groups when SGA is defined as <10th percentile of the overall British Columbia standard.[16] Here, the highest SGA rates (based on the overall standard) at all gestational ages are seen in the South Asian ethnic group. The Chinese ethnic group has a low rate of revealed SGA at preterm gestational ages but rates nearly as high as South Asian infants at term and postterm gestational ages.

Finally, Figure 7 also shows a graph of revealed SGA, but this time using ethnic-specific standards for defining the 10th percentile cut-off for SGA.[16] Using these ethnic-specific standards, revealed SGA rates in First Nations infants are the highest of all four ethnic group at all gestational ages, but only slightly higher than those of the three other ethnic groups, which were quite similar to one another. At preterm gestational ages, Chinese infants had the lowest revealed SGA rates. Thus, this picture is quite similar (at least in terms of overall ranking) to that shown in Figure 5 for perinatal mortality. The gestational age-specific pattern for revealed SGA defined by ethnic-specific standards coheres better with the observed pattern for perinatal mortality than does the SGA pattern based on a single overall standard. In other words, these data suggest that the differences in fetal growth among the four ethnic groups are physiological, rather than pathological.

Of course, these data are affected by the well-known "healthy migrant" bias. Chinese and South Asian immigrants in British Columbia are wealthier and healthier than those of the same ethnic groups who remained in their country of origin. In fact, however, the neighborhood income distribution of these immigrants was lower than the average for British Columbia. But it is difficult to imagine any selection factor that could simultaneously explain the smaller size of fetuses of Chinese and South Asian immigrants and their lower perinatal mortality.

The second approach to answering the question posed in this section comes from a recent study in the province of Ontario, Canada's largest province.[17] Immigration records were linked to birth registrations. Similarly to the British Columbia example presented above, adverse outcomes among the Ontario births were compared between infants born to South Asian immigrant and Canadian-born mothers using two alternative fetal growth references: one based on births to Canadian-born mothers and the other based on those born to mothers from South Asia. Overall, South Asian infants had a similar neonatal mortality risk compared to nonimmigrants [adjusted OR (95% CI) = 1.13 (0.96-1.32)]. Based on the Canadian standards, South Asian infants defined as SGA had substantially lower neonatal mortality [0.57 (0.46-0.71)] than nonimmigrant infants, but not when SGA was based on the South Asia standard [0.95 (0.75-1.21)].

As in the British Columbia example, but here more directly than with the "revealed" SGA approach used in that example, ethnic-specific standards performed better at predicting perinatal mortality. The results are consistent with the first approach in suggesting that the lower birth weight distribution of South Asian infants is physiological, rather than pathological. As with the first approach, the "healthy migrant bias" may well explain lower neonatal mortality rates among South Asian immigrants than among those giving birth in South Asia. But the bias cannot simultaneously explain the lower mortality in SGA infants based on the Canadian standard but a similar mortality based on the South Asia standard.

In 2011, Mikolajczyk[18] et al published a fetal growth standard based on the WHO Global Survey on Maternal and Perinatal Health, which was carried out in 2004-2008.[19] Of note, the standard is based on the Hadlock formula,[12] so the SGA cut-offs at preterm gestational ages are appropriately based on estimated fetal weights, rather than on birth weights. The authors' Excel software program for calculating birth weight percentiles, which accompanies their article in a web appendix, permits customization by multiple maternal characteristics beyond country, sex, and ethnicity. Of note, however, those additional characteristics did not enhance prediction of a composite adverse fetal infant outcome.[18] The latter result thus parallels our results from Sweden (discussed above) concerning estimated fetal weight alone vs more extensive customization.[14]

A New "Prescriptive" Global Fetal Growth Standard

The INTERGROWTH-21st project is an ambitious, multi-centre study of true fetal growth.[20] It is based on well-standardized serial ultrasound measurements at pre-specified gestational ages. The project comprised eight country sites: Brazil, Italy, Oman, U.K., USA, China, India, and Kenya. At all eight sites, participants were restricted to healthy mothers between the ages of 18 and 35 years, all of whom were $\geqslant$ 153 cm in height, had pre-pregnancy BMI of 18.5-<30 kg/m^2, and began prenatal care in the first trimester. The INTERGROWTH-21st reference was intended to be a "prescriptive" fetal growth standard, i.e., to serve as a basis for recommending how healthy fetuses born to healthy mothers in healthy surroundings "should" grow, rather than a mere description how "typical" fetuses born in the same countries actually do grow.

To its credit, the INTERGROWTH-21st Project pre-specified that differences within half a standard deviation (SD) would be accepted as showing sufficient similarity to be considered "equivalent" in fetal growth among infants from all eight sites.[20] As it turned out, crown-rump length in the first trimester and fetal head circumference in the second and third trimesters were about half a SD lower among Indian infants than the overall mean, and those measured from Italy were about half a SD higher. In other words, the eight sites differed by as much as 1 SD from each other for these ultrasound measurements.

Although these differences were pre-specified as acceptable for showing similarity in infants born at the eight sites, they are very large. For birth weight, a 1-SD difference is about 500 grams. This is well within the range of differences reported between India and many European countries for mean birth weight at term and more than double the reduction in birth weight caused by maternal smoking, a widely accepted pathological factor causing fetal growth restriction.[1] Given what we know about the size of Indian mothers and their eating habits during pregnancy, it is not surprising that they are substantially smaller than those of other INTERGROWTH-21st project sites.

Which Fetal Growth Standard Should India Use?

Size at birth is highly variable. The "normal" range in birth weight at term ranges from 2500 to 4500 grams. As we have seen, the average birth weight at term varies widely across countries, and even within countries according to ethnic group and other maternal characteristics.[1;3;8;9] Some variations in birth weight for gestational age are clearly pathological, such as those due to maternal cigarette smoking or pre-eclampsia.[1] But we should not assume that factors such as short stature, ethnicity, and parity are physiological, just because they are well-known and "expected." Deciding about which characteristics leading to differences in birth weight for gestational age are pathological vs physiological must be made not on the basis of expectation, but on evidence that the resulting smallness (or largeness) has adverse consequences.

The adverse consequences I have discussed focus on perinatal and neonatal mortality, because in high-income countries, linked perinatal databases permit routine linkage of live births and infant deaths and also include stillbirths. Severe neonatal and maternal morbidity have also been reported in relation to SGA and LGA birth defined using alternative standards.[17;18] Longer-term consequences, including growth, cognitive ability, neurobehavioral function, and quality of life are much more difficult to carry out but would add to the evidence about the adverse consequences of small (or large) size.

In the meantime, the evidence I have presented here convinces me that Indian infants are indeed physiologically smaller than those from other world regions. Their relative smallness does not appear to have pathological consequences in and of itself.

Which standard should India use to define SGA birth? The recent global reference published by WHO[18] can be flexibly adjusted to the mean birth weight at 40 weeks in Indian boys and girls. To me, that seems a sensible, evidence-based approach for classifying the size of Indian newborns. Based on the data I have presented from British Columbia[16] and Ontario,[17] I am reasonably confident that clinical and public health decisions based on SGA defined using the WHO standard are more likely to be beneficial and less likely to do harm than those based on any single, "prescriptive" or otherwise, global standard.

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FOUNDATION NEWS

- We wish to place on record our deep sorrow at the passing away of Dr. Mrunalini Devi Puar on January 2, 2015. She was a valuable member of the Governing body of Nutrition Foundation of Iindia, and a generous supporter of the Foundation's activities from its very inception. We will miss her support and cheerful presence at our meetings and events.

- We wish to place on record our profound sorrow at the sudden demise of Dr. Kamala Ganesh, Chairperson, Institutional Ethics Committee of Nutrition Foundation of India, on 19.2.2015. She has earlier been a Consultant to NFI, and helped with carrying out important research. We will miss her clear and rational approach to ethical considerations in medical research.

- Three students of M.Sc. (Amity University) did their internshipsat NFI for three months between February and May 2015 and completed their MSc dissertations at NFI.

- In June 2015, nineteen students of M.Sc. Foods and Nutrition from Lady Irwin College, Institute of Home Economics, and Amity University did their internships at NFI.

NUTRITION NEWS

The 47th Annual Conference of the Nutrition Society of India will be held on 9th - 10th October, 2015, at National Institute of Nutrition, Hyderabad. The theme of the conference is 'Agriculture and Nutrition – the connect and the disconnect'. A pre-conference workshop will be held on 8th October 2015. Details of the conference can be accessed from the website: www.nutritionsocietyindia.org.

Health Consequences of Childhood Obesity

Kuldeep Singh

Obesity, defined as a condition characterised by 'excess body fat which creates increased risk for morbidity and/or premature mortality', is becoming one of the foremost public health challenges. "This insidious, creeping pandemic of obesity is now engulfing the entire world. It's as big a threat as global warming and bird flu. Initially, obesity was considered to be a problem of developed countries alone, but increasingly the developing world is also facing this public health challenge. Even as many low and middle income countries continue to face long-standing problems of undernutrition and communicable diseases, 'lifestyle disorders' related to rising trends of overweight and obesity are creating a "dual nutrition burden", adding to the overall disease burden[1]. The problem is compounded by the fact that obesity and overweight are seen increasingly even in children. In India too, obesity, including childhood obesity, has started raising concerns regarding the present and future health of the population.

Definitions of Childhood Obesity

According to the Centers for Disease Control (CDC), USA, overweight is defined as a BMI at or above the 85th percentile and lower than the 95th percentile for children of the same age and sex[2]. Obesity is defined as a BMI at or above the 95th percentile for children of the same age and sex[2]. The WHO, on the other hand, uses Standard Deviation (SD) instead of percentile for defining overweight and obesity[3,4]. Freedman et al. explored various cut-off levels of BMI for defining excess adiposity as risk factor for cardiovascular morbidity[5]. Overall, various definitions of childhood overweight are useful for tracking prevalence and trends, but these should not be confused with clinical diagnoses or functional definitions. This may be particularly true of the "at-risk-for-overweight" category, which was originally intended as a way to identify children who needed further clinical investigation. It was observed that children with childhood obesity also have an increased risk of impaired glucose tolerance, insulin resistance and type 2 Diabetes[6].

Assessment of Childhood Obesity

The prevalence of overweight / obesity is commonly assessed on the basis of body mass index (BMI), defined as the weight in kilograms divided by the square of the height in meters (kg/m^2). In a study carried out by Borruel et al, it was shown that waist circumference and BMI are not only the simplest to obtain, but are also the most accurate surrogate markers of visceral adiposity in young adults, and are good indicators of insulin resistance and powerful predictors of the presence of hepatic steatosis[7]. It has been recognized that, although BMI may not be a "perfect" marker for obesity, it is inexpensive and easy to use even by grass-root-level health workers, especially in children. Various studies have shown that for children with normal BMI, other tools such as dual-energy x-ray absorptiometry (DXA) and air-displacement plethysmography (ADP) can be used as secondary measures[8,9].

Magnitude of problem of childhood obesity

Globally, in 2013, the number of overweight children under the age of five years, was estimated to be over 42 millions. Close to 31 million of these were in developing countries[10]. Based on surveys from 144 countries, the World Health Organization (WHO) estimated that the prevalence of overnutrition (BMI more than 2 SD for age, equivalent to the 98th percentile) in children <5 years of age increased from 4.2% in 1990 to 6.7% in 2010 and is expected to reach 9.1% in 2020[11]. In the U.S., 8.5% of children below 5 years of age had a BMI above 98th percentile[12].

Etiological factors associated with childhood obesity

Obesity results from an imbalance between energy intake and energy expenditure. The trend towards reduction in physical activity, leading to sedentary life-styles, has been implicated as the major factor associated with increase in the prevalence of obesity across continents and across socioeconomic groups. The rise in the consumption of energy-dense foods with high fat and sugar content and of soft drinks with high sugar content have been cited as major factors responsible for the sustained rise in adiposity in some segments of the population in both developed and developing countries. Evidently, the overall obesogenic environment has been the major factor for global increase in the prevalence of obesity. Several research studies have focused on the genetic and epigenetic factors of obesity but these are not common causes of obesity.

The link between maternal nutrition and childhood obesity

Barker[13] proposed that the relationship between low birth weight and an increased susceptibility to non-communicable diseases in adult life is a result of fetal adaptations to maternal undernutrition during pregnancy. These adaptations were "predictive adaptive responses," i.e, the foetus which is exposed to poor nutrition anticipates a similarly harsh postnatal environment.

The link between childhood obesity and obesity in adulthood

There is accumulating evidence that childhood obesity leads to obesity in adulthood, together with related co-morbidities. Furthermore, in many obese children the severity of obesity increases with age[14,15]. Changes over the past 70 years in the distribution of body mass index (BMI) and development of overweight or obesity across childhood and adulthood were investigated by utilizing longitudinal data birth cohort studies in the United Kingdom[15].

Short-term Consequences of Childhood Obesity

Among the most acute problems associated with childhood obesity is sleep apnea which is reported in about 17 % of obese children[16]. Some of the other possible short-term obesity-related consequences in children and adolescents are given in Table 1[17-26].

Long-term Consequences of Childhood Obesity

Excellent reviews regarding all possible long-term effects of obesity are available (Must A, Strauss RS 1999)[27]. Long-term effects of obesity are given in Table2 [28-40].

Prevention

Despite 30 years of intensive research on childhood obesity, neither developed nor developing countries have been able to halt the "obesity epidemic", and there is currently no "one size fits all" solution. In a systematic review, 64 studies were examined including 54 studies on lifestyle treatments (with a focus on diet, physical activity or behaviour change) and 10 studies on drug treatment to

help overweight and obese children and their families with weight control. No surgical treatment studies were found to be suitable for inclusion in the review. The review showed that lifestyle programs can reduce the level of overweight, in child and adolescent obesity, 6 and 12 months after the beginning of the programme, respectively. In moderate to severely obese adolescents, a reduction in overweight was found when either the drug orlistat, or the drug sibutramine was given in addition to a lifestyle programme, although a range of adverse effects was also noted. The review concluded that information on the long-term outcome of obesity treatment in children and adolescents was limited and needs to be examined in some high quality studies[41].

Other systematic reviews on community-based prevention programmes in the US and other high-income countries showed moderate evidence that an intervention involving a combination of diet and physical activity, conducted in the community with a school component, is effective at preventing obesity and overweight[42]. More research studies are needed to understand the comparative effectiveness of childhood obesity prevention programmes in the community setting. An NHS UK review recommended adopting primary and secondary outcome measures and focusing on using existing measures rather than developing new tools[43]. Another recent review highlighted that physical activity programmes improve mathematical functioning ability in obese children and adolescents[44]. Some earlier studies were promising but have not yet been replicated[45]. Birch and Ventura suggested a multiphase method for accomplishing this, including screening intervention components, refining intervention designs and confirming component efficacy to build and evaluate potent, optimized interventions[46]. Obesity in childhood is often the forerunner of co-morbidities which can severely affect quality of life and impair social and psychological functioning. Urgent interventions are required to prevent development of childhood obesity, and this requires the collaborative efforts of all stakeholders involved with public health.

Management

The management / treatment of childhood obesity is as challenging as its diagnosis and detection. With the overall aim of restoring and maintaining normal weight, major intervention usually revolves around promotion of physical activity and healthy eating patterns, medical management of existing complications or co-morbidities, and promotion of psychosocial well being. Bariatric Surgery in children should be resorted to only when stringent criteria are met in morbidly obese children. However, there are some who advocate it as a measure to prevent intergenerational impact.

Table 1: Short term consequences of child hood obesity

Short term consequence	Study	Findings
Cardiovascular risks	Freedman DS *et al* (2007) [5]	Obese youth a re more likely to have risk factors for cardiovascular disease, such as high cholesterol or high blood pressure. In a population-based sample of 5 - to 17-year-olds, 70% of obese youth had at least one risk factor for cardiovascular disease.
Pre-diabetes	Li C *et al* (2007)[17] CDC factsheet 2011 [18]	Obese adolescents are more likely to have pre - diabetes, a condition in which blood glucose levels indicate a high risk for development of diabetes.
Bone and joint problems	Daniel *et al* (2005)[19] Taylor *et al* (2006)[20]	Slipped capital epiphysis and Blount's disease
Pulmonary	Daniels et al (2006) [21] Sutherland (2008)[22]	Asthma and obstructive sleep apnea
Psychological problems	Goodman & Whitaker (2002)[23] Lumeng *et al* (2003)[24]	Poor self esteem, depression which may lea d to persistence of obesity in adulthood. Clinically meaningful behavior problems in 8 - to 11-year-old children associated with obesity
Neuro-cognitive deficits	Rhodes *et al* (2005)[25]	14 morbid obesity children with obstructive sleep apnea had deficits in learning, memory, and vocabulary. Moreover, apnoeic/hypopneic events were inversely related to memory and learning performance.
Academic Consequences	Schwimmer *et al* (2003) [26]	Overweight and obese children were four times more likely to report having pr oblems at school than their normal weight peers.

Table 2: Long-term consequences of childhood obesity

Long-term effect	Study	Features /Findings
Likely to be obese as adult	Guo Chemle (1999)[28] Freedman *et al* (2005)[29]	Obese children and adolescents are more likely to be obese adults and consequently more predisposed to CVD, DM, arth ritis, stroke, cancer. Children who became obese as early as 2 years of age were more likely to be obese as adults.
Adult morbidity	Abraham *et al.* (1971)[03]	Of the individuals for whom school -based growth records were available for the years 1923-1928 in Washington County, Maryland, 42% were re -examined by county health department clinicians after 37 yrs. Concentrations of lipid, fasting blood sugar and BP, did not vary by childhood weight status. Morbidity from hypertensive vascular disease and cardiovascular renal disease was elevated in males who became overweight in adulthood, but not in relation to childhood weight status
Female reproductive health	Lake *et al.* (1997)[31]	British Birth Cohort of 1958, Prospective study. Obesity at the age of 7 yrs and a t the age of 23 yrs. was associated with menstrual problems and gestational hypertension by the age of 33 yrs.
Coronary heart disease mortality	Hoffman *et al.* 1988[32]	Elevated adolescent BMI (> 25 kg/m ^{2} compared to 19 kg/m ^{2}) recorded at military registra tion, was associated with a relative risk of 1.5 for all - cause and 2.5 for coronary heart disease mortality
Cardiometabolic mortality	Paffenbarger & Wing (1969) [33] Reilly and Kelly (2011) [34]	In Paffenbarger's studies using ponderal index to define obe sity (< 12.9), a relative risk of 1.3 was observed for coronary heart disease (CHD) mortality. The risk was further increased in the presence of elevated systolic BP and cigarette smoking. Based on their 2nd systematic review of evidence in the past 8 yea rs from 11 studies, authors concluded that overweight and obesity have adverse consequences on premature mortality and physical morbidity.
Risk of Cancer	Kushi *et al.* (2006)[35]	Overweight and obesity are associated with increased risk for many types of cancer, including cancer of the breast, colon, endometrium, esophagus, kidney, pancreas, gall bladder, thyroid, ovary, cervix, and prostate, as well as multiple myeloma and Hodgkin's lymphoma.
Polycystic ovarian disease (PCOD)	Anderson *et al.* (2014)[36]	Obesity is associated with increased risk of PCOS via insulin resistance and compensatory hyperinsulinemia; also enhanced androgen production /storage an expanded fat mass and potential effects of abnormal adipokine/cytokine levels. Adolescents are at higher risk for co-morbidities.
Non-alcoholic fatty liver disease (NAFLD)	Sanders *et al.* (2015)[37] Koot *et al.* (2015)[38] Castro Mendoza *et al.* (2014)[39](Spanish)	Based on systematic literature search from six databases (2004 -2014),overweight Australian children were found to be at higher risk for NAFLD Steatosis was found in 41 (53%) of subjects. Of these 41 children, 26(63%) had elevated ALT levels. Obesity and insulin resistance are risk factors for the development of fatty liver in children and adolescents.
Metabolic syndrome	Lloyd, Langley -Evans and McMullen (2012)[40]	Although there is no strong evidence to support the view that childhood obesity is an independent risk factor for adult blood lipid status, insulin levels, metabolic syndrome or type 2 Diab etes, if adjusted for adult BMI, the data showed a weak negative association between childhood BMI and metabolic variables; those at the lower end of the BMI range in childhood, but obese during adulthood were at higher risk of metabolic syndrome .

Conclusion

The health and social consequences of childhood obesity are substantial. The short-term risks are mostly confined to severely overweight children and adolescents. However, with the rise in

trends in obesity globally, we can anticipate some of the hitherto rare orthopaedic, endocrinal, gastroenterological, pulmonary and neurological consequences to become more common in future in obese children. Type II diabetes may become a widely prevalent chronic disease even in adolescents. The long-term consequences are also of significant public health importance. Thus, both prevention and treatment of obesity in childhood are essential. Clearly, in the face of increasing numbers of overweight children and mounting evidence of the substantial health consequences, both short and long-term, further research in design and implementation of strategies for successful prevention and treatment of childhood obesity is essential.

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