

# Risk of developing adulthood obesity among females born with low birth weight: Results from a non-concurrent study from rural Southern India

Arup Chakraborty, P. S. Rakesh, V. Kumaran, Jasmin Prasad, Anu M. Alexander, Kuryan George

Department of Community Health, Christian Medical College, Vellore, Tamil Nadu, India

### ABSTRACT

**Objective:** To determine the relationship between birth weight and the evolution of obesity in adult life in women from a rural developmental block in southern India. **Design:** Non-concurrent cohort **Setting:** General community- a rural developmental block in southern India. **Participants:** Two hundred and seventy one young healthy females were recruited from a birth cohort. The study subjects were 98 women in the age group of 19-23 years who had been born with low birth weight (LBW) and 173 women in the same age group who had been born with normal birth weight (NBW). **Materials and Methods:** Data collection involved interview using a structured questionnaire and anthropometric measurements. **Analysis:** Chi-square test to assess significance of association, independent sample *t* test to assess the difference between means, odds ratios for measuring magnitude of association, stratified analysis to identify various interactions and confounders, and multiple logistic regression models to identify the relationship between birth weight and young adult obesity (BMI > 25). **Results:** A crude odds ratio of 0.564 (95% CI 0.262 - 1.214) was obtained for the association between LBW and development of obesity later in life. In the final logistic regression model, it was found that a young adult female with low birth weight who belonged to a higher socio-economic group had a higher risk of developing obesity (Adjusted odds for the interaction term between LBW and high SES 6.251; 95% CI 1.236 - 31.611). **Conclusion:** The study could not find any significant association between LBW and development of obesity later in life, but it found a higher probability of developing obesity later in life among low birth weight female children born in high socio-economic status families.

**Key words:** Barker's hypothesis, low birth weight, obesity

## BACKGROUND

Obesity and overweight are on the rise around the globe at an alarming rate. Around 65% of the world's population lives in countries where overweight and obesity are a larger cause of death than undernutrition. Worldwide, obesity has more than doubled since 1980 with an estimate of around 1.5 billion overweight adults. At least 2.8 million adults die each year as a result of being overweight or obese.<sup>[1]</sup> The

obesity has reached epidemic proportions in India and is steadily increasing over the years.<sup>[2]</sup>

The concept of fetal origins of adult disease was popularized by David Barker. According to Barker's hypothesis, various events during early development have a profound impact on one's risk for development of future adult disease. Many studies showed the association with poor early growth and adult obesity.<sup>[3-6]</sup> Low birth weight (LBW), being a surrogate marker of poor fetal growth and nutrition, is linked to coronary artery disease, hypertension, obesity, and insulin resistance.

Almost 30 million children worldwide are born every year with a birth-weight of less than 2,500 grams. Although the global prevalence of LBW births appears to be waning, the burden of LBW births in the developing countries still continues to be a cause for major concern. South Asia alone

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**Corresponding Author:** Dr. Rakesh P. S., Department of Community Health, Christian Medical College, Vellore - 632 004, Tamil Nadu, India.  
E-mail: rakeshrenjini@gmail.com

accounts for more than 50% of all LBW births worldwide, with 30% of all babies born LBW.<sup>[7]</sup> Estimates based on available data from institutional deliveries and smaller field-based studies suggest that one-third of all Indian babies are born with moderate to severe malnutrition and have less than optimal birth weight.<sup>[8-10]</sup>

Given the high prevalence of LBW and increasing trends of obesity in India, a better understanding of the relationship between LBW and obesity is essential and may help the policymakers and health professionals for planning prevention strategies. Previous work from Vellore with anthropometric studies and dynamic studies has shown that males born LBW were shorter and lighter than their counterparts born with normal birth weight (NBW).<sup>[11]</sup> The current study had followed up a birth cohort of females born between 1987-1992 in a rural developmental block in Tamil Nadu to find out the relationship between birth weight and the development of obesity in adult life.

## MATERIALS AND METHODS

The Community Health and Development (CHAD) program of the Community Health Department of a medical college has been providing primary health care to a population of over 120,000, spread out in the 82 villages of Kaniyambadi block of Vellore district in Tamil Nadu. The CHAD surveillance system has been described in detail elsewhere.<sup>[12]</sup> Reporting of marriages, eligible couples, pregnancies, deliveries, births, immunization, deaths, and morbidity in the village is done by trained health workers, who collect information through home visits. Reporting of the births includes date, gender, mode and outcome of delivery, and birth weight. The information is verified and maintained as an electronic database in the Health Information System of the department. The information is subjected to periodic checks and external validation.

This study looked at female births between Jan 1<sup>st</sup> 1987 and 31<sup>st</sup> December 1992. Female singleton births with birth weight less than 2.5 kg and born after 35 weeks of gestation were the primary focus (LBW group). Female singleton births with birth weight more than or equal to 2.5 kg and who were born after 35 weeks of gestation, during the same period were selected as the comparison group (NBW group). Those who permanently moved out of the area and those who were currently pregnant were excluded. Participants were selected by simple random sampling technique from the list.

The sample size was calculated presuming an  $\alpha$  error of 5%,  $\beta$  error of 20%, anticipated odds ratio of 2.5, the proportion of the unexposed group (normal birth weights)

with obesity (BMI >25) as 14%, and exposed to unexposed ratio of 1:2, the sample size was calculated to be 102 in LBW group.

A structured questionnaire including details regarding the socio-demographic characters, co-morbidities, supplementary nutrition during childhood, and physical activity was administered to all the participants. Physical activity questionnaire was adopted from the WHO-STEPS Global Physical Activity (GPAQ) questionnaire.<sup>[13]</sup> Dietary assessment was performed using a 24 hours diet recall method. The height was measured utilizing a portable stadiometer to the nearest 0.1 cm. The weight was measured with an electronic weighing machine to the nearest 0.1 kg. Socio-economic status (SES) was assessed using the previously validated CHAD SES scale, which included education, land ownership, monthly income, cast, and type of house.<sup>[14]</sup> The low and middle SES were clubbed to lower SES group. The Body Mass Index (BMI) above 25 is considered as obese. The study had got necessary ethical clearance from the Institution Review Board.

The data was entered using the software Epi Info 2001 version 3.2.2, and analysis was done using Statistical Package for Social Sciences (SPSS) version 12 for Microsoft windows. Descriptive statistics of various socio-demographic characters, Chi-square test to assess significance of association, independent sample *t* test to assess the difference between means, and odds ratios for measuring magnitude of association were used. Stratified analysis was done, and stratum specific and Mantel-Haenszel (MH) odds ratios were calculated to identify various interactions and confounders. Multiple logistic regression models were generated to identify the relationship between birth weight and adult obesity.

## RESULTS

There were 155 births satisfying the study criteria in LBW group and 760 in NBW group. We looked at all 155 women in the LBW group to get 98 subjects and 310 randomly selected women in the NBW group to get 173. Information was collected from 98 women in the age group of 19-23 years with LBW and 173 women in the same age group with normal birth weight. Others were not available at their homes for the interview.

The mean age in LBW group was 21.39 (SD 2.06) and in the NBW group was 21.34 (SD 1.98) (*P* 0.42). The proportions of those born at 35-37 weeks of gestation in LBW and NBW groups were 9.2% and 8.1%, respectively. The details regarding socio-demographic characteristics are shown in Table 1.

In the LBW group, the mean Body Mass Index (BMI) was 20.09 kg/m<sup>2</sup> (SD 4.02, range 14.46-35.03) while in the NBW group, it was 21.05 kg/m<sup>2</sup> (SD 4.46, range 14.48 -42.11) (*P* 0.468). The LBW group had a lower mean height [151.55 cm (SD 4.90)] as compared to the NBW group [154.02 cm (SD 6.32 cm)] (*P* 0.014). The differences between the mean weight and mean waist circumference among the LBW and the NBW groups were not statistically significant. The results are shown in Table 2.

Physical activity was categorized as less active, moderately active, and highly active according to the results of GPAQ questionnaire. Among the LBW subjects, 52%, 31.6%, and 16.3% subjects were in the less active, moderately active, and highly active groups, respectively, whereas in the NBW group, the figures were 50.9%, 36.4%, and 12.7%, respectively (*P* 0.53). The mean daily calorie intakes among the LBW and NBW group were 1772.21 Kcal (SD 304.2)

**Table 1: Socio-demographic characteristics of the study subjects**

Name of the variables	Description of variables	Low birth weight group N=98	Normal birth weight group N=173	P value*
Age	Mean	21.39	21.34	0.422
	SD	2.06	1.98	
	Range	19-25	19-25	
Education	Mean	11.91	12	0.221
	SD	2.89	3.21	
	Range	3-18	3-19	
Current employment	Employed	35 (35.7%)	43 (24.9%)	0.001
	Unemployed	63 (64.3%)	130 (75.1%)	
Marital status	Married	11 (11.2%)	14 (8.1%)	0.091
	Unmarried	87 (88.8%)	159 (91.9%)	
SES	Low	6 (6.2%)	13 (7.6%)	0.002
	Middle	57 (58.8%)	83 (48.3%)	
	High	34 (35.1%)	76 (44.2%)	

\*Students' *t* test for continuous variables and Chi-square test for categorical variables. SES: Socio economic status, SD: Standard deviation

**Table 2: Details of the anthropometric measurements among the study participants**

Anthropometric measurements	Low birth weight group N=98	Normal birth weight group N=173	P value*
BMI category	47 (48%)	55 (31.8%)	
Underweight (< 18.5)	34 (34.7%)	75 (43.4%)	
Normal (18.5-22.9)	7 (7.1%)	14 (8.1%)	
Overweight (23-24.9)	10 (10.2%)	29 (16.8%)	
Obesity (>25)			
Mean BMI (SD)	20.09 (4.02)	21.05 (4.46)	0.468
Mean weight (SD)	46.22kg (SD 9.84)	50.07kg (SD 11.6)	0.223
Mean height (SD)	151.55cm (4.90)	154.62cm (6.32)	0.014
Mean waist circumference (SD)	74.05cm (10.32)	76.55cm (11.29)	0.521

\* Students' *t* test for continuous variables. SD: Standard deviation, BMI: Body mass index

and 1768.21 Kcal (SD 348.5), respectively, (*P* 0.924) while mean daily protein intake was 36.9 g (SD 7.9) and 37.9 g (SD 8.5), respectively (*P* 0.382).

Among the study participants, 10.2% (10/98) in the LBW group and 16.8% (29/173) in the NBW group developed obesity (BMI >25) in the current study. A crude odds ratio of 0.564 (95% CI 0.262 - 1.214) was obtained for the association between LBW and development of obesity later in life. A stratified analysis was done, and stratum specific odds ratios were calculated for the association between LBW and obesity for different risk factor groups based on age, employment, marital status, and socio-economic status. Mantel Haenszel (MH) adjusted odds ratios were also calculated adjusting for each of these risk factors individually.

A considerable difference in the stratum specific odds ratio was noticed between those belonging to low SES [stratum specific odds ratio 0.258 (95% CI 0.08 - 0.79)] and those with higher SES [stratum specific OR 1.821; (95% CI 0.57 - 5.73)]. Among the high SES group, 17.6% (6/34) in the LBW group and 10.5% (8/76) in the NBW group developed obesity later in life. In the low SES group, 6.3% (24/159) with LBW and 20.8% (20/96) with NBW developed obesity later in life.

The stratified analysis showed that SES and age at marriage could be possible confounders in the association between birth weight and obesity. However, as the number of married subjects was less (25/271), age at marriage was not considered for further analysis.

A logistic regression analysis was done with obesity as dependent variable and birth weight (low), SES (high) and employment status as independent variable. None of the factors showed any statistically significant association. An additional interaction term between LBW and high SES was included in the next model along with birth weight, SES, and employment status. The model is shown in Table 3. It was found that a young adult female with low birth weight who belonged to a higher socio-economic group had a higher risk of developing obesity as compared to others (adjusted odds for the interaction term between LBW and high SES 6.251; 95% CI 1.236-31.611).

## DISCUSSION

Although the cause of the association between LBW and obesity in later life is unknown, several theories have been proposed. Barker's hypothesis proposes that the association is due to the result of changes in metabolism in response to adverse environment inside the uterus that result in

**Table 3: Logistic regression model showing association between low birth weight and adult obesity**

Risk factors	Adjusted OR	95% CI for adjusted OR	P value
Low birth weight	0.25	0.08-1.17	0.117
Currently employed	1.70	0.81-3.58	0.157
High SES	0.50	0.20-1.23	0.132
LBW and High SES*	6.25	1.23-31.61	0.027

\*interaction term . SES: Socio economic status, LBW: low birth weight, CI: Confidence interval, OR: Odds ratio

increased risk for metabolic disease in adulthood.<sup>[15-17]</sup> The increased risk of adult metabolic diseases in those who have LBW will be amplified by an accelerated pattern of growth during infancy and childhood. The thrifty phenotype hypothesis explains that the conserving adaptations of the fetus due to intrauterine malnutrition is overwhelmed by abundance of nutrients after birth and will manifest in adult metabolic diseases.<sup>[17]</sup> Singhal and Lucas propose that it is not LBW as such, but the rapid postnatal growth that is responsible for the increased risk for disease.<sup>[18]</sup> The fetal insulin hypothesis suggests the presence of common genes that affect birth weight and predisposition to adult diseases.<sup>[19]</sup> Several studies confirmed the presence of a high risk allele for obesity among LBW babies.<sup>[20]</sup>

The current study could not find a significant association between LBW and obesity. Rather, it pointed to a direction against the hypothesis. This finding is consistent with the findings from a British study, which showed a positive association between birth weight and adult BMI.<sup>[21]</sup> Another prospective study from Jerusalem also suggests that higher birth weights correlate strongly with being overweight in late adolescence independently of other factors considered.<sup>[22]</sup> In a study among men from Vellore, it was found that, men with LBW were shorter, lighter, and had a reduced lean body mass compared with NBW controls.<sup>[11]</sup>

These findings contradict many studies attempting to establish an association between LBW and an increased risk of the metabolic syndrome.<sup>[3-6]</sup> A similar study from Kerala showed high triglyceride values and overweight were significantly more in LBW adolescents when compared to NBW adolescents.<sup>[23]</sup> The reasons for not getting an association between LBW and obesity in the current study could be many. BMI incorporates both lean mass and body fat. Many different studies have appreciated the limitation of BMI in measuring adiposity.<sup>[24]</sup> BMI may not be an appropriate indicator in epidemiological research investigating the possible programming of body composition and obesity. BMI also fails to elucidate the body shape and the fat distribution.<sup>[5]</sup> Hence, it is possible that some important associations may not be detected. Also, the study looked at only young adult females in the

age group 19-23 years, and this age may be too early for the manifestation of many chronic diseases including obesity (BMI > 25). Whether other factors such as urbanization and ageing may unmask risk of obesity may require a long-term follow-up.

Similarly, birth weight may not be a perfect indication of fetal nutrition. Although there is evidence that adipose tissue distribution may be programmed during fetal life, the effects may function independently of birth weight. A recent study has shown that birth weight is reduced following intrauterine growth retardation during the third trimester of pregnancy, but is not reduced if growth retardation occurs during the first trimester of pregnancy.<sup>[25]</sup> Thus, the ability of birth weight to indicate fetal growth experience is crude.

The study found a higher probability of developing obesity later in life among LBW children born in high SES families. It would be bold to conclude so based on a retrospective survey; however, it can be a basis for hypothesis for further long-term prospective longitudinal study of LBW children. A study from Kerala showed high triglyceride values and overweight were significantly more in LBW adolescents when compared to NBW adolescents while in a study among men from Vellore, it was found that men with LBW were shorter, lighter, and had a reduced lean body mass compared with NBW controls.<sup>[11,23]</sup> Kerala is the state where socio-economic development and urbanization started very early. These findings when corroborated with the findings from our study warrants to further study the role of socio-economic status in development of obesity and metabolic syndrome among LBW babies.

Recent research suggests that the combination of LBW and high BMI has particularly detrimental effects on chronic disease in adult life, notably increased blood pressure, coronary heart disease, and impaired glucose tolerance.<sup>[26,27]</sup> A person from a higher socio-economic background had possibly more access to high energy foods, and probably indulged in a lower level of physical activity, making them vulnerable to increase weight gain in later life. Many studies suggest an interaction between the genetic determinants of birth weight, childhood growth, and risk of adult metabolic diseases with both the intra- and extra-uterine environments.<sup>[20]</sup> Thus, the genetic risks of obesity in the LBW individuals would have been manifested when exposed to a suitable environment as found in a family with high SES. Increased feeding might have happened in those LBW babies born in high SES families including use of high energy foods, probably due to a relatively higher purchasing power, better educational status, and better health-seeking behavior, which would have led to weight gain later in life.

Strengths of the study include its design, being done in a general community, data from a robust health information system, and the systematic way of analysis of the data. However, there was no information available of those who had not participated in the study and those who had moved out of the study area. There is a high chance of selection bias as the study excluded all those who moved out of the area. Residual confounding may remain. The fetal origins hypothesis has traditionally considered full-term, and we included those who were above 35 weeks of gestational age with an assumption to exclude only true preterm births. The proportion of births in the late preterm period was small and comparable in both the groups. Other markers of obesity or adiposity were not studied.

The study could not find any significant association between LBW and development of obesity later in life, but it found a higher probability of developing obesity later in life among low birth weight children born in high socio-economic status families. The findings could be the basis for hypothesis for further long-term prospective longitudinal assessment of both obesity and adiposity among LBW babies.

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