

Pune Low Birth Weight Study – Birth to Adulthood – Cognitive Development

SUDHA CHAUDHARI, MADHUMATI OTIV, BHARATI KHAIRNAR, ANAND PANDIT, MAHENDRA HOGE AND MEHMOOD SAYYAD

From Department of Pediatrics, KEM Hospital, Pune, Maharashtra, India.

Correspondence to: Dr Sudha Chaudhari, Consultant, Division of Neonatology, Department of Pediatrics, KEM Hospital Research Centre, Pune 411 011, Maharashtra, India. kemhrc@vsnl.net

Received: November 05, 2012; Initial review: November 29, 2012; Accepted: March 12, 2013.

Objective: To assess the cognitive development of non-handicapped low birth weight (LBW) infants at 18 years.

Design: Prospective cohort study.

Setting: Infants born between 1987 - 1989 with birth weight less than 2000g and discharged from a neonatal special care unit were followed up till the age of 18 years.

Methods: The intelligence quotient (IQ) was determined by Raven's progressive matrices. Assessment of adjustment and aptitude was done.

Results: The cohort of 161 LBW infants was divided into three groups according to their gestation - preterm SGA ($n=61$), full term SGA ($n=30$) and preterm AGA ($n=70$). 71 full term AGA infants served as controls. The IQ of the study group (Percentile 39.3) was significantly lower than that of controls (Percentile 54.9)

($P=0.002$). Preterm SGA subjects had the lowest IQ (Percentile 35.5), though just within normal limits. Males from the study group had significantly lower IQ than male controls ($P=0.03$). The IQ of PTSGA subjects of college educated mothers ($P=0.004$) and belonging to higher socio-economic class ($P=0.04$) was significantly higher. On the differential aptitude test, PTSGA subjects were poor in speed and mechanical reasoning. The 18 year IQ could be best predicted by IQ at 6 and 12 years.

Conclusion: Preterm SGA children have the lowest IQ at 18 years, males have lower IQ. Maternal education and socio-economic status have great impact on cognitive development. Good prediction of the 18 year IQ can be done by the 6 and 12 year IQ.

Keywords: Adulthood, Intelligence quotient, Low birth weight.

Advances in neonatal care have resulted in survival of lower and lower birth weight babies. Hence all the recent follow up studies have concentrated on very low birth weight (VLBW) or extremely low birth weight (ELBW) infants [1,2]. Very little attention has been paid to the outcome of moderately low birth weight (LBW) infants. Though a small percentage of these children develop cerebral palsy or mental retardation, long term follow up studies have shown mild problems in cognition, adjustment and behavior [3] in early adolescence. These problems continue into adulthood. Adverse socio-demographic factors affect the outcome and appear to have far greater impact on cognition, than biological factors [1].

In a recent paper on growth of LBW infants at 18 years, we have described this cohort, which was born in the late eighties [4]. We have previously reported [5,6] on cognitive development of these infants at school entry (6 years) and at early adolescence (12 years). This communication describes the intelligence of these "apparently normal" LBW infants at 18 years, their

educational achievement, and social integration. We have tried to find out the impact of socio-demographic and environmental factors on their intelligence quotient. We have also tried to find out if prediction of the final IQ could be done at an earlier age.

Accompanying Editorial: Pages 830-31

METHODS

The cohort consisted of infants weighing less than 2000g discharged from a Neonatal Special Care Unit during a 18 month period between October 1987 to April 1989. They were followed up prospectively till the age of 18 years. The LBW infants were classified into appropriate for gestational age (AGA) and small for gestational age (SGA) using standard criteria [7]. Full term neonates with birth weight of ≥ 2500 g with no antenatal, natal and postnatal risk factors born during the same period were enrolled as controls.

All neonatal risk factors were recorded. A detailed socio-demographic background of each child was

obtained by the social worker by making a home visit. Children with major neurologic sequelae like cerebral palsy and mental retardation were omitted from this study at the end of the three year follow-up, as they could not do the complicated tests of cognition. So the cohort now consisted of “apparently” normal children.

Assessment of Cognition was done by Raven’s Progressive Matrices [8]. It is a performance test of intelligence. It evaluates the subject’s ability to apprehend relationships, geometric figures and designs and to perceive the structure of the design in order to select the appropriate part. It is a test of innate educational ability with a small contribution of spatial perception factor. The result is expressed in percentiles and 25th to 75th percentile is considered as normal.

Assessment of Adjustment was done by Adjustment Inventory [9]. This test taps five areas of adjustment: (i) home/family adjustment; (ii) social adjustment; (iii) personal and emotional adjustment; (iv) educational adjustment; and (v) health adjustment.

Assessment of Aptitude was done by Differential Aptitude Test [10]. The Indian adaptation of the original American Version was used. It is a timed test and tests (i) numerical ability; (ii) abstract reasoning (iii) space relations (iv) mechanical reasoning; (v) clerical speed and accuracy; and (vi) language usage and verbal reasoning.

Interest Inventory Test was standardized in our own Child Guidance Clinic. It explores interest in medical, engineering, fine arts, commerce and arts. Socio economic status was assessed by the Kuppuswamy Scale.

Statistical analysis: Analysis was performed using statistical package for Social Sciences (SPSS) for windows (Version 11.5). The linear association between the normally distributed variables was assessed by Pearson’s correlation coefficients, otherwise Spearman’s correlation coefficients were used. The partial correlation analysis was also used to test the independent associations between several variables of interest.

The LBW and control groups were first compared using analysis of variance (ANOVA) procedure with Bonferroni’s method of correction. The non-parametric test (Mann Whitney U test) was also used when the variables were non-normally distributed. Chi-square or Fisher’s exact test was used to explore differences between proportions. For finding predictors of different variables, the multiple linear regression technique was used. For determining the predictors of binary outcome variables, the multiple logistic regression technique was used.

RESULTS

We have already described the cognitive development of 180 Low birth weight and 90 control children at 12 years [7]. This is a continuation of the same study and no new children were added. Five LBW children and 17 controls were lost to follow up and 14 LBW children refused to come for the assessment. So our final sample consisted of 161 LBW and 73 normal birth weight children. The children who dropped out of the study were similar to those who continued in the study and showed no statistically significant difference. Thus, out of the 201 LBW infants from the original cohort, 161 (80%) were available for the final 18 year follow up.

The birth weight of the study group ranged from 866 to 1999 g (mean 1545.5 ± 243.9 g). The mean (SD) birth weight of the control group was 2835.3 (305.8)g. The gestation of the study group ranged from 28-40 weeks with a mean of 34.7 ± 2.7 weeks. There were 91 males and 70 females in the study group and 43 males and 30 females in the controls. There were 131 preterms and 30 full terms in the LBW group. Out of the 131 preterms, 61 were small for gestational age (SGA) and 60 were appropriate for gestational age. Out of 91 AGA infants 61 (67%) were preterm and 30 (33%) were full term. The maternal demographics and Neonatal data are shown in **Table I**. There was no significant difference in the socio-demographic data of the subjects and controls.

Assessment of Cognition: **Fig. 1** shows the IQ of the three groups of LBW subjects according to weight for gestation at birth. The IQ of the study group (39.3) was significantly lower than the IQ of controls ($P=0.002$). There were 17 subjects out of the 61 PTSGA group, who had IQ below average (28.3%), compared to 12.7% below average in controls ($P<0.05$). The distribution of IQ in the study group and controls is shown in **Fig. 2**.

Fig. 3 shows the association between maternal education and IQ. As seen in this figure, the PTSGA children of college educated mothers had far better IQs compared to those with lesser education ($P=0.004$). A similar impact of socio-economic class was seen in the PTSGA subjects.

We could assess the IQ of 84 mothers to see if there was any correlation between mother’s IQ and the child’s IQ, but we found no such correlation. IQ was possible in only 35 fathers, and there was no correlation between father’s IQ and the child’s IQ. There were only 3 single mothers in the study group.

There were 41 children who had failed at least in one standard in school in the study group and only 4 children who had failed in the control group ($P<0.05$). Failures

TABLE I NEONATAL DATA AND SOCIO-DEMOGRAPHIC DATA OF PARENTS

	Cases (N=161)		Controls (N=73)	
	Male (N=91)	Female (N=70)	Male (N=43)	Female (N=30)
<i>Neonatal Data</i>				
Birthweight (g) [‡]	1568.9 (223.3)	1515.1 (267.0)	2898.8 (337.0)	2744.3 (230.4)
Gestation age (wks) [‡]	34.8 (2.6)	34.9 (2.9)	39.9 (0.54)	39.9 (0.51)
SGA	49 (53.8)	42 (60.0)	0	0
AGA	42 (46.2)	28 (40.0)	43 (100.0)	30 (100.0)
<i>Parental Data</i>				
<i>Socio-economic status</i>				
Higher	14 (15.7)	16 (23.5)	5 (12.2)	4 (14.3)
Upper middle	23 (25.8)	18 (26.5)	7 (17.1)	8 (28.6)
Lower middle	36 (40.4)	22 (32.4)	16 (39.0)	13 (46.4)
Lower	16 (18.0)	12 (17.6)	13 (31.7)	3 (10.7)
<i>Educational status of Mother</i>				
<10 th Standard	42 (47.2)	23 (33.8)	19 (46.3)	11 (39.3)
<i>Educational status of Father</i>				
<10 th Standard	25 (28.1)	12 (17.7)	10 (25.0)	4 (14.3)

[‡]Values are Mean (SD). The rest of the values are n (%); SGA: Small for gestational age; AGA: Appropriate for gestational age.

were more common in boys than in girls. There were 16 dropouts from the school in the study group (5 girls, 11 boys) and mostly around 10th standard. There were 4 drop outs amongst controls.

A multiple linear analysis was done to find out the determinants of IQ. The final model is shown in **Web Table I**. Birth weight and mother's education were found to be significant determinants of IQ. A regression analysis was done to find out the independent determinants of educational status at 18 years. IQ and

gender independently determined the educational status. Sepsis, as a risk factor at birth, was found to independently determine educational status. Lower IQ was associated with lower educational status ($P=0.0004$). It was seen that children with lower IQ failed more frequently compared to children with better IQs (Odd's ratio 14.1). School failure was more common in boys than girls. When independent determinants of failure were determined by a logistic regression, IQ ($P=0.003$) and male gender ($P=0.001$) were found to be significant.

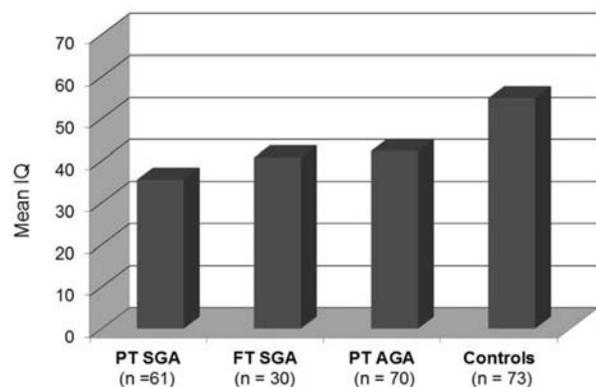


FIG.1 Mean IQ according to weight for gestation. Preterm SGA subjects had the lowest IQ, although it was within normal limits.

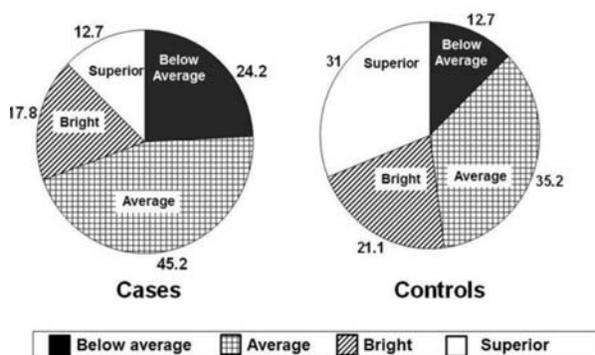


FIG.2 Distribution of IQ at 18 years (%). Incidence of below average IQ was high in preterm SGA subjects superior IQ was significantly higher in controls compared to cases ($P<0.05$).

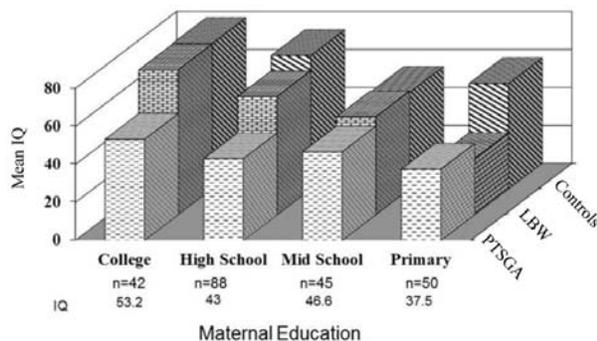


FIG.3 Maternal education and IQ at 18 years. Preterm SGA children of college educated mothers had far better IQs compared to those with lower education ($P=0.004$).

In order to see at what age we could predict the IQ at 18 years, we did a correlation with the mental quotient (MDI) at 1 year, the IQ at 6 and 12 years. All correlated with IQ at 18 years. However, six and twelve year IQ showed the highest correlation ($P=0.001$).

Assessment of Adjustment: We found no significant difference between the subjects and controls. Similarly there was no difference in the adjustment between boys and girls.

Assessment of Aptitude: All low birth weight subjects were poor in speed compared to controls. Preterm SGA subjects had significantly low scores ($P=0.024$) in mechanical reasoning, as compared to controls. They also showed poor speed in their tasks ($P=0.002$). Full term SGA subjects showed significantly less scores in space relations and speed (0.011). The PTAGA were poor in speed.

Interest Inventory: Those with aptitude for space relations opted for fine arts. Those who were poor in speed opted for arts colleges. Those who had poor abstract thinking and mechanical reasoning opted for commerce.

Out of 161 LBW subjects, 15% had chronic medical problems. Six subjects had visual problems, four had hearing problems, and two had speech problems. Two subjects were on medication for seizures. One subject had a hearing aid and wore glasses. Two subjects were on medication for hypertension and Two were operated for tendoachiles contractures. Five girls had menstrual problems.

DISCUSSION

This is the final phase of the "Pune Low Birth Weight Study", in which infants weighing less than 2kg have been assessed at 18 years. We could follow up 80% of

the original cohort of LBW infants. The LBW cohort and NBW controls were similar in their socio-demographic characteristics.

We had already assessed the verbal and performance IQ separately at 12 years by Weschler's Intelligence Scale [5]. Hence at 18 years, we used the Raven's Progressive Matrices, which is a performance test. The LBW children had lower IQs compared to controls. Similar findings are reported in a meta-analysis of cognitive outcome in VLBW infants [11]. The lowest IQ in our study was seen in the preterm SGA children, who had a double biologic jeopardy of prematurity and intrauterine growth restriction. Males from the study group had lower IQ compared to male controls. Similar findings were noted by Hack, *et al.* [1] in their study of VLBW children at 20 years. They also reported more failures in school in boys than girls and this was also seen in our study.

As the LBW children grow older, the biologic risk factors recede in the background, and environmental factors become important determinants of intelligence [12]. We found a significant association between maternal education and the intelligence, even amongst Preterm SGA subjects. Similar findings are reported in other studies [13]. Socio-economic status also had a great impact on the intelligence, as previously reported by Gorman, *et al.* [14]. The only biologic risk factor which had some contribution to the IQ was birth weight and this has also been reported previously [1,15].

Studies from the Western World [3] have described single mothers as a significant risk factor for low IQ. We had only three single mothers in our study group. A lot of stress is laid on chronic health problems in VLBW [16] and ELBW [17] children at adulthood. Fortunately, our LBW subjects did not have many chronic health problems.

Many adjustment problems are described in VLBW children [18]. However, our LBW cohort was well adjusted with themselves, their peers and their surrounding. This may be due to the strong family structure in India. In order to get a complete insight into the cognitive development of LBW subjects, only IQ was not enough. So we looked at their aptitude. We found that all LBW subjects were poor in speed. The PTSGA infants were not only poor in speed, but also addressed poor in mechanical reasoning. This aspect of cognition has not been in other follow studies.

Since this was a longitudinal study, we had a mental development quotient at 1 year, IQ at 6 and 12 years. We used these assessments of mental development to see if

WHAT IS ALREADY KNOWN?

- Low birth weight children have a low IQ

WHAT THIS STUDY ADDS?

- Preterm SGA children have the lowest IQ; 6 and 12 years IQ best predicts 18 year IQ.
- Maternal education and socio-economic status have a greater impact on IQ than the biologic risk factors as the children reach adulthood.

prediction of the final IQ could be done and found excellent correlation with the 6 and 12 year IQ. This kind of prediction has not been done in any other study.

The major strength of this study was the high participation rate over a span of 18 years. Another major strength was the complete parental information. Since the study started in the pre-ventilation era in India, a weakness was the small number of ELBW babies in the cohort. This study may not be relevant today for tertiary care units, which are saving extremely low birth weight and very premature babies. However, there are many level II care units in India, especially in smaller towns and this data will be very relevant for them. Adults who were moderately premature and moderately low birth weight are included in this study, a group that is rarely considered in follow up studies.

Contributors: SC: conceived the study, supervised it, wrote the manuscript and is the guarantor of the paper. MO: Supervised data collection and analyzed data. BK: collected data. AP: supervised the project. MH: Made home visits, ensured appointments, MGS: .did statistical analysis.

Funding: ICMR, New Delhi; *Competing interests:* None stated.

REFERENCES

1. Hack M, Flannery D, Schuller M Carter L, Borowski E, Klein N. Outcomes in young adulthood for very low birth weight infants. *N Engl J Med.* 2002;346-57.
2. Saigal H, Hault A, Streiner DJ. School difficulties at adolescence in a regional cohort of children who were extremely low birth weight. *Pediatrics.* 2000;105:325-31.
3. Hack N, Klein N, Taylor GH. Long term development outcomes of low birth weight infants. *The Future Children.* 1995;5:176-96.
4. Chaudhari S, Otiv M, Khairnar B, Pandit A, Hoge M, Sayyad M. Pune low birth weight study – growth from birth to adulthood. *Indian Pediatr.* 2012;49:727-32.
5. Chaudhari S, Kulkarni S, Pandit A, Deshmukh S. Mortality and morbidity in high risk infants during a six year follow up. *Indian Pediatr.* 2000;37:1314-20.
6. Chaudhari S, Otiv M, Chitale A, Pandit A, Hoge M. Pune low birth weight study – cognitive abilities and educational performance at twelve years. *Indian Pediatr.* 2004;41:121-8.
7. Singh M. Care of the Newborn. 4thedn. New Delhi: Sagar Publications; 1979.
8. Desphande CG, Oza JM. Raven's Progressive matrices – Standard progressive matrices – Indian adaptation. New Delhi; Manasayan, 2000.
9. Palsane MN. Adjustment Inventory, Pune: Anand Agencies, 1977.
10. Nemeta GK, Seashore HG, Wesman AG. Differential aptitude test. Psychological Corp. New York. Indian Edition by Manasayan, New Delhi.
11. Aarnoudse-Moeris CS, Weiglas KN, van Goudoever JB, Oosterlan J. Meta analysis of neuro behavioural outcomes in very low birth weight children. *Pediatr.* 2009;124:717-28.
12. Chaudhari S, Otiv M, Chitale A, Hoge M, Pandit A, Mote A. Biology versus environment in low birth weight children. *Indian Pediatr.* 2005;42:763-70..
13. Breslau N, Paneth NS, Lucia VC. The lingering academic deficits of low birth weight children. *Pediatr.* 2004;114:1035-40.
14. Gorman BK. Birth weight and cognitive development in adolescence: causal relationship or social selection ? *Social Biology.* 2003;49:13-33.
15. Conley D, Bennet NG. Is biology destiny! Birth weight and life chances. *Am Socio Rev.* 2000;65:458-67.
16. Hack M, Young adult outcomes of very low birth weight children. *Semi Foet Neonat. Medicine* 2000;11:127-37.
17. Saigal S, Stoskopf B, Boyle M, Paneth N, Pinelli J, Streiner D, *et al.* Comparison of current health, functional limitations, and health care use of young adults who were born with extremely low birth weight and normal birth weight. *Pediatr* 2007;119: e562-73.
18. Aylward GP. Cognitive and neuropsychologic outcomes. More than IQ scores. *Dev Disabil. Rev.* 2002;8:234-40.