Morbidity in early adulthood among low-risk very low birth weight children in Turkey: a preliminary study

Gülay Can[1], Leyla Bilgin[2], Burak Tatlı[3], Reyhan Saydam[4], Asuman Çoban[1], Zeynep İnce[1]

Divisions of [1]Neonatology, and [3]Pediatric Neurology, Department of Pediatrics and [4]Department of Child Psychiatry, İstanbul University İstanbul Faculty of Medicine, İstanbul, and [2]Division of Neonatology, Ankara Children's Hematology and Oncology Research Hospital, Ankara, Turkey. E-mail: leylakaradeniz@yahoo.com

SUMMARY: Can G, Bilgin L, Tatlı B, Saydam R, Çoban A, İnce Z. Morbidity in early adulthood among low-risk very low birth weight children in Turkey: a preliminary study. Turk J Pediatr 2012; 54: 458-464.

The objective of this study was to assess low-risk very low birth weight (VLBW) children, before the era of modern neonatal intensive care in Turkey, during adolescence. Forty-one VLBW adolescents were compared with 40 adolescents who had normal birth weight. The physical and neuromotor development, educational achievement and psychosocial status were assessed at a mean age of 17±1.6 years. VLBW adolescents were shorter than normal birth weight adolescents (p=0.01). A major neurological abnormality (cerebral palsy) was seen in 12% and a minor neurological abnormality (tremor, coordination, behavioral and speech disorders) in 17%. VLBW adolescents had higher rates of visual problems (56% vs 5%). School failure was present in 27%. There were no differences in behavioral problems or quality of life between the two groups, but VLBW adolescents did have a lower self-esteem score. Neurodevelopment and growth sequelae were a significant problem in VLBW adolescents. As early intervention might help to prevent or ameliorate potential problems, long-term follow-up is essential.

Key words: very low birth weight, neurological impairment, educational achievement, behavioral problems.

The studies on the evaluation of very low birth weight (VLBW) children during adolescence have revealed that neurodevelopment and growth sequelae persist into adolescence. In those adolescents without severe neurological impairment, lower educational achievement, lower intelligence quotient (IQ), learning difficulties, and a higher incidence of chronic illness have been identified in comparison with term-born young adults[1-6]. Some reports indicate that deficits in cognitive and academic achievement persist over time[7]. Other studies have found greater impairments with increasing age[8-10]. Although behavioral problems and depression are more frequently reported, quality of life and adaptation to social life have been reported to be normal[11-15]. These data have been reported from the United States and European countries.

There is no information on the outcome of VLBW children in adolescence in Turkey. In this retrospective study, we assessed a group of low-risk VLBW infants born between 1985 and 1990 in our hospital, before the era of modern neonatal intensive care, in their adolescent ages. Their physical and neurological development, level of educational achievement and psychosocial status during adolescence were compared with normal birth weight (NBW) controls.

Material and Methods

Between 1985 and 1990, 256 VLBW infants (≤1500 g) were discharged from the Neonatology Unit of İstanbul Medical Faculty. For logistical reasons, VLBW-born adolescents who were living in İstanbul or near İstanbul were contacted and invited for assessment. The study was approved by the Medical Ethics Committee, and all parents gave their informed consent.

The study group included 41 VLBW participants (20 boys, 21 girls). The perinatal characteristics of the patients including gestational age, BW and clinical features were extracted from the hospital records. The mean age at the time of assessment was 17.0±1.6 years (range:

14-20 years). The control group included 40 NBW children (25 boys, 15 girls) who were selected by means of a population-sampling procedure. Their mean age was 16.4±0.5 years (range: 16-17 years). Maternal and paternal education, occupation and socioeconomic status were classified according to the Hollingshead classification[16].

Assessments were performed by a neonatologist, pediatric neurologist and clinical psychologist. The neurologist and psychologist had no information about the perinatal histories of the patients. The neonatologist interviewed VLBW-born adolescents and performed a detailed physical examination. Current height and weight were noted. All subjects were personally interviewed and were requested to complete a written questionnaire for the psychological assessment. Interviews were also conducted with the mothers on separate occasions. Information concerning educational attainment, current enrollment in an educational program and other activities was obtained by means of interviews. Health status was ascertained by means of questions concerning chronic medical, neurologic or psychiatric conditions, as well as detailed questions on alcohol and tobacco use and contact with the police. The assessment by the pediatric neurologist consisted of a standardized neurological examination. Psychological assessment included Youth Self-Report (YSR) 11-18, Rosenberg Self-Esteem Scale and Quality of Life Score.

The YSR 11-18 assesses internalizing (anxiety, depression, and overcontrolled), externalizing (aggressive, hyperactivity, noncompliant, and undercontrolled) and total problem behavior scores. It consists of 112 problem items concerning the last six-month time period. These 112 questions are scored on a 3-step scale ranging from 0 to 2, where 0= not true, 1= somewhat or sometimes true, and 2= very often or often true. It is recommended for use only with children 11 to 18 years of age[17].

The Rosenberg Self-Esteem Scale is a 10-item self-report measure of global self-esteem. It consists of 10 statements related to overall feelings of self-worth or self-acceptance. The items are answered on a four-point scale, ranging from strongly agree to strongly disagree. Five of the scale items have positively and five have negatively worded statements. The scale ranges from 0-30, with 30 being the highest score. Higher scores indicate a higher level of self-esteem[18].

Quality of life is an all-inclusive concept generally defined as total well-being, encompassing physical, psychological and social determinants. In order to assess this dimension, the subjects are interviewed and instructed to make a global assessment on a 100-grade Visual Analogue Scale (VAS-scale), where "1" represents the least desirable quality of life and "100" the most desirable[19].

Statistical Analysis

All statistical analyses were performed with the Statistical Package for the Social Sciences (SPSS) ver. 13 for Windows. Differences between the groups were determined with the use of Student's t-test for continuous variables and with the Pearson chi-square test or Fisher's exact test for discrete variables. P values of <0.05 were considered significant.

Results

The mean gestational age and BW of the study group were 31±2.7 weeks ($25^{5/7}$–36) and 1252±217 g (700-1500), respectively, whereas the mean gestational age and BW of the control group were 39±1 weeks (38-40) and 3549±615 g (2600-5250), respectively. Five VLBW infants (12%) had a BW of <1000 g. There were no major congenital malformations or congenital infections. Assisted ventilation had been provided to none of the infants. The perinatal characteristics of the study group are presented in Table I. The control group consisted of completely healthy newborns with uneventful perinatal histories.

The follow-up time range of VLBW-born adolescents was between 2 months and 7 years (median: 18 months), with 19 cases (46%) having a follow-up period of <1 year.

In the study group, 29 (71%) of the mothers and 17 (41%) of the fathers had only primary school education as compared to 18 (45%) of the mothers and 12 (30%) of the fathers in the control group. The level of maternal and paternal education was lower in the study group, but the distribution of socioeconomic class was similar in both groups[16] (study group: class 1: n= 3, class 2: n=15, class 3:

Table I. Perinatal Characteristics of the Study Group

	n
Small for gestational age	17
Sepsis	13
Apnea	7
Perinatal asphyxia	6
Respiratory distress syndrome	6
Hyperbilirubinemia requiring exchange transfusion	5
Hypoglycemia	4
Seizure	3
Patent ductus arteriosus	2
Polycythemia requiring partial exchange transfusion	2

n= 21, class 4: n=2; **control group:** class 1: n=2, class 2: n=17, class 3: n=20, class 4: n=1) ($p>0.05$).

Physical development

A comparison between the current height and weight of the study and control groups showed that VLBW-born adolescents were significantly shorter than NBW adolescents (164±10 cm vs 172±8 cm, $p=0.01$), but there was no significant difference between the groups in current weight: 58±13 kg in the study group as compared to 61±12 kg in the control group ($p=0.51$). There were no differences with respect to gender.

Neuromotor development

The neurological problems diagnosed at the time of assessment in the study group are presented in Table II. The percentages of major (cerebral palsy) (5/41) and minor (tremor, coordination, behavioral and speech disorders) (7/41) neurological abnormalities were 12% and 17%, respectively. Table III shows the perinatal features of the cases with cerebral

Table II. Neurological and Visual Problems of the Study Group

Diagnoses (n)	Total, n (%)
Major neurological problems	5 (12%)
Spastic diparesis (3)	
Spastic tetraparesis (1)	
Spastic hemiparesis (1)	
Minor neurological problems	7 (17%)
Coordination disorder (1)	
Tremor (1)	
Behavioral disorder (1)	
Speech disorder (4)	
Visual problems	23 (56%)
Myopia (14)	
Strabismus (4)	
Astigmatism (2)	
Diplopia (1)	
Ptosis (1)	
Blindness (1)	

Table III. Perinatal Characteristics of the Cases with Cerebral Palsy

Case no	I	II	III	IV	V
Gender	G	B	B	G	B
Gestational week	$30^{3/7}$	35	$29^{2/7}$	30	33
Birth weight (g)	1310	1370	1330	1500	1160
Neonatal problems	RDS PDA Apnea	SGA Sepsis Apnea	RDS	Sepsis	SGA
Follow-up time	3 months	4 years	2 months	4 years	2 months
Age at assessment	16 years	17 years	18 years	20 years	18 years
Current diagnosis	Spastic diparesis	Spastic diparesis	Spastic tetraparesis	Spastic diparesis	Spastic hemiparesis
Education	High School	Secondary School	Illiterate	Primary School	Illiterate

G: Girl. B: Boy. SGA: Small for gestational age. RDS: Respiratory distress syndrome. PDA: Patent ductus arteriosus.

Table IV. Educational Status of VLBW Adolescents

	Cerebral palsy (+) (n=5)	Cerebral palsy (-) (n=36)	Total n (%)
Illiterate	2	1	3 (7%)
Primary school	1	1	2 (5%)
Secondary school	1	5	6 (15%)
High school	1	22	23 (56%)
College	0	7	7 (17%)

palsy. No neurological problems were detected in the control group.

Very low birth weight (VLBW)-born adolescents had poorer visual outcomes compared with their NBW peers (56% vs 5%; $p<0.01$). The visual problems encountered were myopia, strabismus, astigmatism, diplopia, ptosis, and blindness (Table II). Five VLBW-born adolescents out of 41 cases had hearing problems.

Educational attainment

Table IV shows the level of educational attainment of the study group. More than half of the cases (56%) were either attending (n=16) or graduated from (n=7) high school, and an additional 7 cases were attending college. Out of 11 adolescents (27%) who had not completed their education, four were the ones with cerebral palsy, and their mothers' education was at the elementary school level.

Psychosocial status

Seven attendants in the VLBW group (3 boys, 4 girls) could not take the YSR, Rosenberg Self-Esteem and Quality of Life Scales because of their disability. In addition, 5 children (3 boys, 2 girls) in the NBW group did not answer the self-rating questionnaires accurately and were excluded from the statistical analysis.

Youth Self-Report (YSR) 11-18: The age of 10 children in the VLBW group was >18 and they were not given the YSR questionnaire. There were no significant differences in the internalizing, externalizing, or total problem behavior scales between the groups (Table V). However, the VLBW group had higher

Table V. Mean Values of Youth Self-Report

	VLBW (n=24) Mean (SD)	Control (n=35) Mean (SD)	t value	p
Total problems	51.13 (9.37)	51.20 (10.14)	.03	.98
Internalizing	55.33 (10.79)	52.89 (11.77)	.81	.42
Externalizing	45.46 (8.75)	49.14 (10.77)	1.39	.17
Withdrawn	48.33 (12.74)	42.83 (10.19)	1.84	.07
Somatic complaints	43.46 (8.87)	43.77 (7.29)	.15	.88
Anxious/depressed	46.08 (8.27)	45.86 (8.46)	.10	.91
Social problems	43.50 (6.26)	43.43 (7.77)	.25	.81
Thought problems	41.88 (4.97)	43.29 (6.91)	.86	.39
Attention problems	43.00 (9.73)	40.51 (13.02)	.79	.43
Delinquent behavior	38.13 (6.55)	41.43 (7.67)	1.51	.14
Aggressive behavior	38.00 (7.16)	40.83 (9.86)	1.20	.23

internalizing problem scores (which includes anxiety/depression, withdrawn behaviors and attention problems), while the NBW group had higher externalizing problem scores (which includes aggressive behaviors, delinquent behavior and thought problems).

Rosenberg Self-Esteem Scale: There were significant differences between the groups on self-esteem scores (Pearson chi-square=6.65, $p<0.01$). There were no low self-esteem scores in the two groups. Sixteen cases (37%) in the VLBW group and 27 cases (63%) in the NBW group had high-level self-esteem scores. Meanwhile, 8 cases (31%) in the NBW group and 18 cases (69%) in the VLBW group had moderate-level self-esteem scores. In conclusion, the VLBW group had moderate-level self-esteem scores, while the NBW group had a high level of self-esteem.

Quality of life scores: Self-rated quality of life scores did not differ between the groups (Pearson chi-square=3.80, $p>0.05$). Twenty cases (45%) in the VLBW group and 24 cases (55%) in the NBW group rated their quality of life under "good and very good" condition.

There were no significant differences between the two groups in the rates of smoking, alcohol use, and general health status. There was also no illicit drug use or contact with the police.

Discussion

Most preterm infants may survive without major disabilities; however, some of them have major problems such as cerebral palsy, mental retardation, blindness, and deafness[20]. Before the use of surfactant, multiple studies reported elevated rates of adverse neurologic outcomes including cerebral palsy and visual impairment in VLBW infants. In an Australian cohort of children with a birthweight <1000 g who were evaluated at 14 years of age, 6% had bilateral blindness, 5% had deafness requiring hearing aids, and 10% were severely disabled[21,22]. Hille et al.[4] documented that 12.6% of very preterm and/or VLBW infants experienced moderate or severe problems in cognitive or neurosensory functioning at 19 years of age. In our study, cerebral palsy was present in 12% and minor neurological impairment in 17% in VLBW adolescents, and they had poorer visual outcomes compared with their NBW peers.

Very low birth weight (VLBW) may influence adult growth attainment. Weiler et al.[23] showed that young adults born preterm were significantly shorter than those born at term. They concluded that premature birth resulted in a lower height achievement by young adult age. Hack et al.[2] examined the growth of VLBW infants to the age of 20 years. They reported that VLBW females catch-up growth by the time they are 20 years of age, whereas VLBW males remain significantly shorter and lighter than controls. In our group, VLBW-born adolescents were shorter than their NBW-born peers, but there was no difference in their current weights. There were also no differences with respect to gender.

Studies on very preterm and VLBW children

reported lower academic skills in young adulthood as compared with control subjects or the general population[1,4,13,24]. Among the articles on VLBW survivors as young adults, the most notable is the study by Hack et al.[1], which describes a large cohort. They reported that fewer VLBW young adults than NBW young adults had graduated from high school (74% vs 83%, p=0.04). Subanalyses of those participants with the lowest education (<high school) revealed a higher proportion of male participants in this category than female participants, and fewer VLBW male participants compared with female participants. However, according to Saigal[25], the proportion of extremely (E)LBW young adults who graduated from high school was similar to their NBW peers (82% vs 87%, p=0.21). In our study, school failure was present in 27% in VLBW adolescents (11/41). As all the subjects in the control group were high school students, no comparison could be made.

During childhood and adolescence, VLBW children are reported to have more overall behavioral problems in comparison with NBW control subjects. The most common problems are attention weakness, hyperactivity, withdrawn behavior, anxiety, and depression[12,26,27]. Hack et al.[11] showed significantly more psychopathology among VLBW young adults than control subjects, including internalizing symptoms in women and possible thought problems in both men and women. In our study, there were no significant differences in the internalizing, externalizing, or total problem behavior scales between VLBW and NBW adolescents.

As a complement to somatic and mental health measures, the assessment of long-term outcome has increasingly included subjective ratings of self-esteem and quality of life in order to incorporate the patients' own perspective. According to some studies, preterms did not differ from full-terms in measures of self-esteem[24,28], but in our study, VLBW adolescents had a lower self-esteem score than their NBW peers. Most of the earlier studies found a normal perceived quality of life in early adulthood[12,24,29], similar to our study. In a systematic review, Zwicker and Harris[14] reported that in young adulthood, differences in physical functioning persisted, but subjective quality of life was similar to that of their NBW peers. Similarly, Johnson et al.[30] found that extremely low gestational age teenagers at 16 years of age had an optimistic view of the future, despite academic and health difficulties.

Although Bjerager et al.[19] noted similar rates of alcohol and drug use in VLBW young adults and controls, Hack et al.[1] reported lower rates of alcohol and drug use among VLBW subjects. They postulated that it might result from increased parental monitoring of VLBW children. In our study, there were no significant differences between VLBW and NBW adolescents in the rates of smoking and alcohol use.

In our group, the follow-up time was significantly lower. Previous studies of VLBW infants had greater loss to follow-up among children whose mothers had lower levels of education and were of a lower social class[1,31]. Similarly, in our study, 71% of mothers had only primary school education.

This study has a number of limitations. One of the principal limitations is the loss of 84% of the eligible patients. All efforts to trace the cohort by post were made, but many had moved in the preceding 10 years. Therefore, the data presented here underestimates the problems faced by the total surviving population of VLBW teens. Despite its limitations, this study shows that even low-risk VLBW adolescents carry a high risk of morbidities in the long-term: they are shorter, have higher rates of neurological impairment, poorer visual outcomes, and lower self-esteem score compared with their NBW peers.

In conclusion, long-term monitoring of VLBW infants extending into adolescence and adulthood is important in terms of morbidity. We are of the opinion that babies should be followed closely and home visits should be done, if necessary, to determine these problems. Early diagnosis and support programs should be developed considering the education of the parents in relation to the adolescent's academic success, in addition to physical, neurologic, psychopathologic, and late visual morbidities.

REFERENCES

1. Hack M, Flannery DJ, Schlucher M, Cartar L, Borawski E, Klein N. Outcomes in young adulthood for very-low-birth-weight infants. N Engl J Med 2002; 346: 149-157.

2. Hack M, Schluchter M, Cartar L, Rahman M, Cuttler L, Borawski E. Growth of very low birth weight infants to age 20 years. Pediatrics 2003; 112: 30-38.
3. Hack M. Young adult outcomes of very-low-birth-weight children. Semin Fetal Neonatal Med 2006; 11: 127-137.
4. Hille ET, Weisglas-Kuperus N, van Goudoever JB, et al. Functional outcomes and participation in young adulthood for very preterm and very low birth weight infants: the Dutch Project on Preterm and Small for Gestational Age Infants at 19 years of age. Pediatrics 2007; 120: 587-595.
5. Gäddlin PO, Finnström O, Samuelsson S, Wadsby M, Wang C, Leijon I. Academic achievement, behavioural outcomes and MRI findings at 15 years of age in very low birthweight children. Acta Paediatr 2008; 97: 1426-1432.
6. Aarnoudse-Moens CS, Weisglas-Kuperus N, van Goudoever JB, Oosterlaan J. Meta-analysis of neurobehavioral outcomes in very preterm and/or very low birth weight children. Pediatrics 2009; 124: 717-728.
7. Breslau N, Paneth NS, Lucia VC. The lingering academic deficits of low birth weight children. Pediatrics 2004; 114: 1035-1040.
8. Botting N, Powls A, Cooke RW, Marlow N. Cognitive and educational outcome of very-low-birthweight children in early adolescence. Dev Med Child Neurol 1998; 40: 652-660.
9. Taylor HG, Klein N, Minich NM, Hack M. Middle-school-age outcomes in children with very low birthweight. Child Dev 2000; 71: 1495-1511.
10. O'Brien F, Roth S, Stewart A, Rifkin L, Rushe T, Wyatt J. The neurodevelopmental progress of less than 33 weeks into adolescence. Arch Dis Child 2004; 89: 207-211.
11. Hack M, Youngstrom EA, Cartar L, et al. Behavioral outcomes and evidence of psychopathology among very low birth weight infants at age 20 years. Pediatrics 2004; 114: 932-940.
12. Hayes B, Sharif F. Behavioural and emotional outcome of very low birth weight infants-literature review. J Matern Fetal Neonatal Med 2009; 22: 849-856.
13. Cooke RW. Health, lifestyle, and quality of life for young adults born very preterm. Arch Dis Child 2004; 89: 201-206.
14. Zwicker JG, Harris SR. Quality of life of formerly preterm and very low birth weight infants from preschool age to adulthood: a systematic review. Pediatrics 2008; 121: 366-376.
15. Hack M, Cartar L, Schluchter M, Klein N, Forrest CB. Self-perceived health, functioning and well-being of very low birth weight infants at age 20 years. Pediatr 2007; 151: 635-641.
16. Hollingshead AB. Four Factor Index of Social Status (unpublished working paper). New Haven, Conn: Department of Sociology, Yale University; 1975.
17. Achenbach TM. Manual for the Youth Self-Report and 1991 Profile. Burlington, VT: University of Vermont, Department of Psychiatry; 1991.
18. Rosenberg M. Society and the Adolescent Self-Image. Princeton, NJ: Princeton University Press; 1965.
19. Bjerager M, Steensberg J, Greisen G. Quality of life among young adults born with very low birthweight. Acta Paediatr 1995; 84: 1339-1343.
20. Escobar GJ, Littenberg B, Petitti DB. Outcome among surviving very low birthweight infants: a meta-analysis. Arch Dis Child 1991; 66: 204-211.
21. Halsey CL, Collin MF, Anderson CL. Extremely low-birth-weight children and their peers. A comparison of school-age outcomes. Arch Pediatr Adolesc Med 1996; 150: 790-794.
22. Doyle LW, Casalaz D. Outcome at 14 years of extremely low birthweight infants: a regional study. Arch Dis Child Fetal Neonatal Ed 2001; 85: 159-164.
23. Weiler HA, Yuen CK, Seshia MM. Growth and bone mineralization of young adults weighing less than 1500g at birth. Early Hum Dev 2002; 67: 101-112.
24. Tideman E, Ley D, Bjerre I, Forslund M. Longitudinal follow-up of children born preterm: somatic and mental health, self-esteem and quality of life at age 19. Early Hum Dev 2001; 61: 97-110.
25. Saigal S, Stoskopf B, Streiner D, et al. Transition of extremely low-birth-weight infants from adolescence to young adulthood: comparison with normal birth-weight controls. JAMA 2006; 295: 667-675.
26. Botting N, Powls A, Cooke RW, Marlow N. Attention deficit hyperactivity disorders and other psychiatric outcomes in very low birthweight children at 12 years. J Child Psychol Psychiatry 1997; 38: 931-941.
27. Saigal S, Pinelli J, Hoult L, Kim MM, Boyle M. Psychopathology and social competencies of adolescents who were extremely low birth weight. Pediatrics 2003; 111: 969-975.
28. Wintgens A, Lepine S, Lefebvre F, Glorieux J, Gauthier Y, Robaey P. Attachment, self-esteem, and psychomotor development in extremely premature children at preschool age. Infant Ment Health J 1998; 19: 394-408.
29. Dinesen SJ, Greisen G. Quality of life in young adults with very low birth weight. Arch Dis Child Fetal Neonatal Ed 2001; 85: 165-169.
30. Johnson A, Bowler U, Yudkin P, et al. Health and school performance of teenagers born before 29 weeks gestation. Arch Dis Child Fetal Neonatal Ed 2003; 88: 190–198.
31. Wolke D, Sohne B, Ohrt B, Riegel K. Follow-up of preterm children: important to document dropouts. Lancet 1995; 345: 447.