Outcomes of very low birth weight infants in a newborn tertiary center in Turkey, 1997-2000

Begüm Atasay, Ayla Günlemez, Sevim Ünal, Saadet Arsan

Division of Neonatology, Department of Pediatrics, Ankara University Faculty of Medicine, Ankara, Turkey

SUMMARY: Atasay B, Günlemez A, Ünal S, Arsan S. Outcomes of very low birth weight infants in a newborn tertiary center in Turkey, 1997-2000, Turk J Pediatr 2003; 45: 283-289.

Our purpose was to determine mortality and morbidity rates and selected outcome variables for infants weighing less than 1500 g, who were admitted to the neonatal intensive care unit of our hospital from 1997 to 2000. The ultimate goal of the study was to define a model for developing a regional database.

Information on all very low birth weight (VLBW) admissions to a tertiary level neonatal intensive care unit (NICU) in Ankara between January 1997 and December 2000 was prospectively collected by three neonatologists using a standard manual of operation and definitions. The data consisted of patient information including sociodemographic characteristics; antenatal history; mode of delivery; APGAR scores; need for resuscitation; admission illness severity (Clinical Risk Index for Babies-CRIB) and therapeutic intensity (Neonatal Therapeutic Intensity Scoring System-NTISS); selected NICU parameters and procedures such as respiratory support, surfactant therapy, and postnatal corticosteroid therapy; and selected patient outcomes such as intraventricular hemorrhage, septicemia, necrotizing enterecolitis, retinopathy of prematurity, and chronic lung disease.

The number of VLBW admissions to the NICU was 133, with 51 (28.6%) referrals from other maternity centers. The mean birth weight and gestational age of the infants were 1175±252 g and 30.3±2.9 weeks, respectively. One hundred and seventeen of 133 cases (88.7%) received at least one antenatal care visit. The median CRIB and NTISS scores were 4.5 and 31, respectively. Antenatal steroids had been given to 74 (55.6%) infants. Surfactant treatment and respiratory support were given to 33 (24.8%) and 73 (54.8%) infants, respectively. Among selected outcomes, chronic lung disease (CLD), threshold retinopathy of prematurity (ROP), severe intraventricular hemorrhage (IVH ≥ grade III), nosocomial infection and necrotizing enterocolitis (NEC) were encountered in 14 (12.6%), 9 (8.1%), 3 (2.2%), 34 (25.5%) and 35 (26.3%) of the infants, respectively. Overall survival rate was 83.5% (111/133); most of the deceased cases were under 750 g (12/22). It was prospectively shown that 111 (100%) of the surviving infants could be regularly followed in a newborn follow-up clinic to provide health maintenance, developmental assessment and support.

Compared with reports from other developing countries, VLBW infants at our center had higher survival rates. Compared to developed countries, survival rate was lower, especially for extremely very low birth weight infants. There is interaction between birth weight and survival rate. Among selected neonatal outcomes, chronic lung disease, threshold retinopathy, severe intraventricular hemorrhage (IVH ≥ grade III) and nosocomial infection rates at this center were comparable with some reports from developed nations.

Key words: very low birth weight, morbidity, mortality, prematurity, neonatal intensive care unit, outcomes.

Although outcomes of very low birth weight (VLBW) infants have been reported extensively from industrialized countries, less is known about the outcome of such infants in the developing world[1-6]. Medical outcomes of the VLBW infants from both the national and the individual neonatal intensive care units (NICU) have been reproduced in the United States, Canada and European countries[7,8].

Low birth weight (LBW) is an important determinant of neonatal mortality and morbidity. It is either the result of short gestation or intrauterine growth retardation, or both. Its prevalence is directly correlated with the developmental state of a country and it is associated with poverty. Turkey is a developing country and the prevalence of LBW is 8%[9]. Despite constituting a small portion of LBW newborns, VLBW infants have a large impact on both neonatal mortality and morbidity. They demand high technology health care delivery and consume a great amount of resources.

In Turkey, no highly regionalized system of neonatal-perinatal care exists. However, most of the distinct geographic regions have at least one tertiary NICU. Perinatal services are mostly provided at university teaching hospitals in major cities. Regional tertiary level institutions receive high risk pregnancies and high risk newborns from other cities or towns. The transport system is not very well coordinated. Only some of the newborns are socially secured through different governmental social security systems. The ones that are not socially secure cannot get free professional neonatal intensive health care.

In Turkey, no network of NICUs that maintains databases has been formed and the effectiveness and efficiency of NICUs has not yet been fully evaluated. Only the outcome statistics of individual tertiary level NICUs are presented[3-6]. Information gathered from individual units and a country-wide neonatal network can provide a basis for more useful application of available resources and will certainly increase the quality of care.

The use of intensive care facilities has been successful in decreasing the mortality rates of premature infants. However, with increasing survival, an increase in morbidities are encountered. Smaller infants with younger gestational ages are prone to invasive clinical interventions which result in higher incidence of nosocomial infections, necrotizing enterocolitis (NEC) and long-term sequelae such as threshold retinopathy of prematurity (ROP), chronic lung disease (CLD) and developmental disabilities. The long-term sequelae demand well-structured and coordinated country-wide medicosocial support systems. Most of the developing countries like Turkey lack these support systems in addition to regionalized neonatal-perinatal care systems. Running individual tertiary care units and modeling them according to the units in the industrialized countries is a common approach in most of the developing country settings. But this approach is neither sufficient nor appropriate without gathering information on the survivors and taking steps accordingly.

The purpose of the study was to report on the mortality and morbidity associated with VLBW infants cared for in a tertiary center in Ankara, Turkey. We hope that the documentation of such data related to intensive care and follow-up in a single center in a developing country will enable neonatologists in such countries to develop nationwide databases and reports.

Material and Methods

Neonatal Intensive Care Unit

The Ankara University Medical School, Department of Pediatrics, 25-bed nursery provides neonatal intensive care for 1700 inborn deliveries each year. Among 400 admissions, 35-40% are referrals, mostly from the central Anatolian region. There are 10 intensive care, 10 intermediate care and five rooming-in beds available in the unit. Rooming-in beds are designed to facilitate bonding between the intensive and intermediate care graudates with their mothers before discharge. Medical staffing consists of two full-time neonatologists two neonatology fellows, two pediatric residents, 10 neonatal nurses and a full-time pediatrician specialized in developmental pediatrics. Specialists in cardiac and general surgery, ophthalmology and radiology are readily available in the hospital. Regular follow-up care for most of the NICU graduates is provided by the same team.

Study Population

The data evaluated in this analysis comprised 135 admissions weighing between 501 and 1500 g, between 1 January 1997 and 31 December 2000. An admission is defined as stay in NICU for at least 24 hours. Readmission and

transfers were tracked as data from the same infant. After accounting for two infants who were readmitted, data from 133 infants are presented in this study.

Data Abstraction

The neonatologists abstracted patient information from the charts of the infants on a monthly prospective basis. Information was directly entered into the nursery computer using a database consisting of standard predefined variables. Patient information covering the NICU period was collected until death or discharge. Follow-up charts provide information afterwards. Data were double checked before the analysis.

Patient Information

Patient information included sociodemographic variables. Antenatal history, mode of delivery, APGAR scores, medical problems at birth, illness severity (Clinical Risk Index for Babies-CRIB), therapeutic intensity (Neonatal Therapeutic Scoring System-NTISS), selected NICU practices and procedures, and selected patient outcomes.

Definition of the Variables

Maternal and infant data were collected according to common definitions developed by the investigators of the international neonatal networks and described in the standard manual of operation[7,8]. Gestational age (completed weeks and days) was determined by the following obstetric and neonatal measures: last menstrual period, standard obstetric parameters, ultrasound and Dubowitz score[10]. An infant was defined as small for gestational age (SGA) if the birth weight was less than the 10th percentile for gestational age according to Lubchenco growth charts[11]. Prenatal care was defined as receipt of at least one obstetric examination performed by a physician during pregnancy. CRIB is an illness severity score calculated from seven initial items including gestational age, birth weight, presence of congenital anomalies, maximum and minimum fraction of inspired oxygen and base excess[12]. NTISS is a score of therapeutic intensity calculated from a list of 63 NICU therapies used in a 24-hour period[13]. CLD was defined as oxygen dependency (FiO2>0.21) at the 28th postnatal day[14]. Intraventricular hemorrhage (IVH) was defined according to criteria of Papile et al.[15] from head ultrasound performed at the end of first postnatal week NEC was defined according to criteria of Bell et al.[16] (Stage I-IV). The stage of ROP plus disease, and threshold ROP were defined according to International Classification of Retinopathy of Prematuriy[17]. Abnormally dilated veins and tortuous arterioles in the posterior pole were accepted as plus disease. Threshold ROP was defined as zone 1 or 2 ROP, stage 3 plus with five contiguous or eight cumulative sectors of fibrovascular proliferation. Nosocomial infection was diagnosed by using positive blood or cerebrospinal fluid cultures and/or a positive hematological sepsis score[18]. Diagnosis of patent ductus arteriosus (PDA) was based both on clinical and echocardiographic evidence.

Statistical Analysis

Data were analyzed with SPSS software. Mortality rates by birth weights and gestational ages were analysed by chi-square tests. Mortality rates by CRIB and NTISS scores were analyzed by Fisher's chi-square tests. $P<0.05$ was considered significant.

Results

Table I shows the perinatal risks and patient characteristics of the study population. Only 28.6% of the admissions were outborn. More than half received antenatal steroid. Delivery room resuscitation was needed in 48.8%. Multiple births accounted for 44.3% of the deliveries.

Birth Weight and Gestational Age Distribution

Figures 1a and 1b show the distribution of all infants admitted by birth weight (BW) and gestational age (GA) respectively. Twenty three percent of the infants were less than 1000 g and 27.8% were between 24-28 weeks gestation.

Admission Illness Severity

Admission day CRIB median was 4.5 CRIB scores were between 0-5 in 61% (81/133), 6-10 in 25.5% (34/133), 11-15 in 8.3% (11/133), and 16-20 in 5.2% (7/133) of the infants.

Survival to Discharge From NICU

Overall, 83.5% (111/133) of patients admitted to NICU survived until discharge. Mortality rates for VLBW infants cared for by birth weight and

gestational ages are show in Figures 2a and 2b. Mortality rates were highest among the infants who were less than 1000 g BW ($p<0.001$).

Increasing mortality with increasing CRIB and NTISS scores is shown in Figures 3a and 3b ($p<0.05$). A dramatic increase in mortality was noted for CRIB scores over 10 and for NTISS scores over 40.

Selected Neonatal Morbidities, Practices and Outcome Variables

Table II shows the selected morbidities, practices and outcome variables.

Chronic lung disease (CLD) was diagnosed in 10.5% (14/133) of the infants who received inhaled and/or parenteral steroid therapy. Five of the surviving 111 patients (4.5%) were discharged home on supplemental O_2 therapy.

Echocardiography was performed in all of the infants surviving beyond 72 hours. Twenty-two of 133 (16.5%) infants had PDA. Seventeen infants were administered indomethacin, and in three of them surgical ligation was performed.

At least one eye examination was performed in all of the infants surviving beyond four weeks. Nine out of 111 survivors (8.1%) had threshold ROP and cryotherapy was applied. Late sequelae of ROP developed in three patients (2.9%). Blindness developed in two eyes of a patient, one patient had refraction defect with strabismus and another suffered from strabismus.

All of the infants had at least one cranial ultrasound examination before seven days of life. Overall prevalence of IVH (any grade) was 9.7% (13/133). Severe IVH (Grade III or higher) occurred in 2.2% (3/133). Two patients required a surgical shunt.

Table I. Perinatal Information and Patient Profile

	%	Number of infants*
Outborn status	28.6	51/133
Infant characteristics		
Male	47.4	63/133
SGA**	24.8	33/133
Perinatal Risks		
No prenatal care	11.3	16/133
Antenatal steroids	55.6	74/133
Maternal age (<18, >35 years)	24	32/133
Maternal hypertension	33	44/133
Chorioamnionitis	21	28/133
Cesarean section	54.9	73/133
Multiple births (triplets: 7, twins: 19)	44.3	59/133
APGAR < 3 at 1 min	34.4	43/133
APGAR < 7 at 5 min	29.8	39/133
Delivery room resuscitation (≥ level II)	48.8	65/133

* Number of infants/total number of infants
** SGA: small for gestational age.

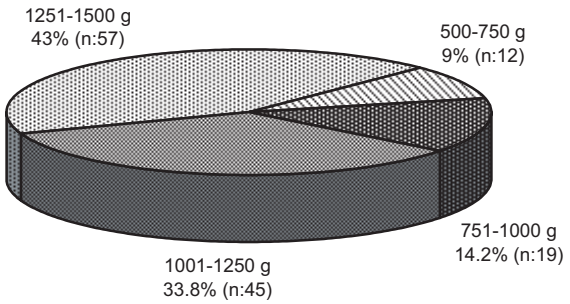


Fig. 1a. The distribution of all infants admitted by birth weight.

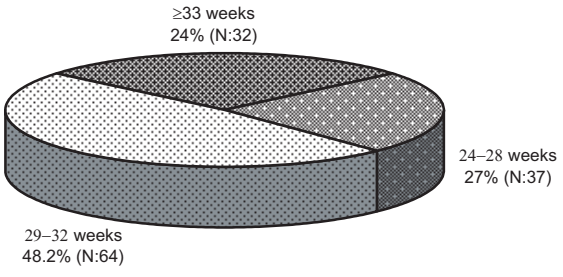


Fig. 1b. The distribution of all infants admitted by gestational age.

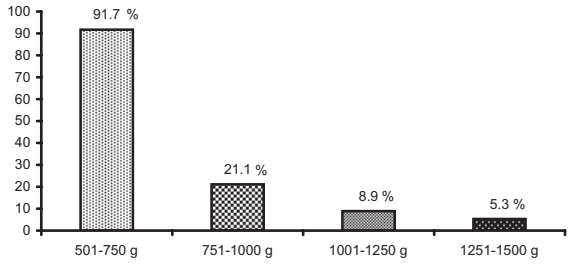


Fig. 2a. Mortality rates for very low birth weight infants by birth weight.

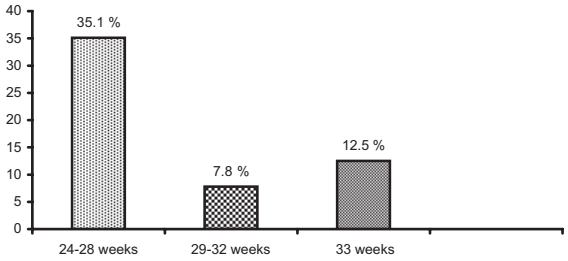
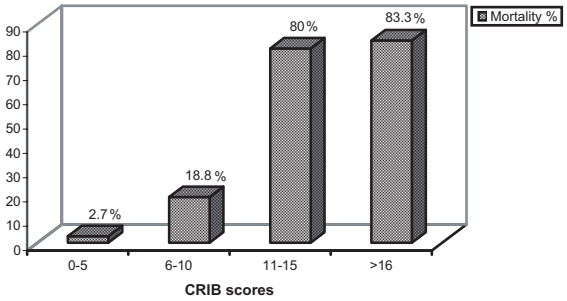
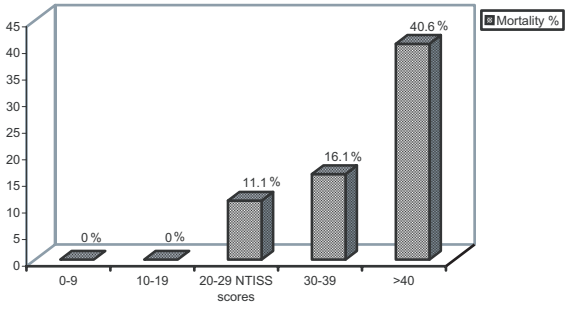


Fig. 2b. Mortality rates for very low birth weight (VLBW) infants by gestational ages.



CRIB: clinical risk index for babies.

Fig. 3a. Mortality rates for very low birth weight (VLBW) infants by CRIB scores.



NTISS: neonatal therapeutic intensity scoring system.

Fig. 3b. Mortality rates for very low birth weight (VLBW) infants by NTISS scores.

Table II. Interventions and Outcomes of VLBW Infants

	%	Number of Infants*
Respiratory support†	54.8	73/133
Surfactant therapy	24.8	33/133
Oxygen at 28 days-CLD‡	12.6	14/111
Postnatal corticosteroids‡	12.6	14/111
Intraventricular hemorrhage	9.7	13/133
IVH Grade ≥ III	2.2	3/133
PDA	16.5	22/133
NEC (any grade)	26.3	35/133
Early septicemia	31.5	42/133
Late septicemia	25.5	34/133
ROP ≥ grade 3‡	8.1	9/111

* Number of infants/total number of infants.

† Respiratory support including mechanical ventilation and continuous positive airway pressure.

‡ Of infants alive at 28 days.

CLD : chronic lung disease.
IVH : intraventricular hemorrhage.
PDA : patent ductus arteriosus.
NEC : necrotizing enterocolitis.
ROP : retinopathy of prematurity.
VLBW: very low birth weight.

Therapeutic Intensity

Fifty-four percent of the infants had NTISS score >40 and the median NTISS score was 31.

Maternal Characteristics

Three percent (3/100) of the mothers were illiterate, 35% (35/100) had completed primary school, 45% (45/100) high school, and 17% (17/100) university. Thirty-eight (38/100) of the mothers had regular work. Problem in infant-mother bonding was encountered in 18% (18/100) of the mothers. Individualized special psychological support was given to 30% (30/100) of the mothers.

Follow-up

It was prospectively shown that 111 (100%) of the surviving infants could be regularly followed in a newborn follow-up clinic to provide health maintenance, developmental assessment and support. Follow-up was monthly for the first year, four times in the second year, two times in the third year and annually thereafter until the age of seven years.

Discussion

This report presents the 1997-2000 status of mortality and morbidity among VLBW infants cared for at a tertiary center in Turkey. With respect to birth weight specific distribution of VLBW infants, our unit cares for less extremely low birth weights (ELBW) compared to the infants reported from the Canadian NICU Network and the National Institute of Child Health and Development (NICHD) Neonatal Network[7,8]. During the study period, 83.5% of VLBW infants survived to discharge, ranging from 9.3% of infants weighing 501 to 750 g at birth, to 79.9% of infants weighing 751-1000 g, to 91.1% of infants weighing 1001-1250 g, to 94.7% of infants weighing 1251-1500 g at birth. Compared with Canadian and North American statistics[7,8], overall survival is favorable, but survival rates for infants weighing less than 1000 g at birth was low, even though the percentage of infants <1000 g was low (Canada and NICHD vs our unit respectively, for <750 g BW: 62% and 54% vs 9.3%; for 751-1000 g BW 86% and 86% vs 79.9%). In the study group 23.3% of the infants were less than 1000 g BW and highest mortality was found in this group. More than 50% of the infants who died were below 750 g BW. Mortality rates increased as the gestational ages decreased. A strong effort and improvement of care must be made for these smallest infants. Fifty nine percent of the infants that died were below 28 weeks GA. Mortality among the infants who were over 33 weeks GA was higher compared to the mortality of the 28-32 weeks GA infants, perhaps the result of higher mortality risk in SGA preterms mostly crowded in this gestational age group. These overall differences are most likely the result of a certain degree of improvement in neonatal care but may also be attributable to differences in organization, staffing, training, and attitudes toward active treatment of ELBW infants. It is not clear whether and to what extent inter-country differences in health care systems, cultural factors and income disparities impact on NICU outcomes. Reports on VLBW outcomes from NICUs of the developing world between 1984-1994 also revealed higher mortality rates, especially for infants weighing <1000 g at birth[1-6].

Scoring for the assessment of severity of neonatal illness is increasingly utilized to compare population, and quality and cost of care at different NICUs as well as to predict morbidity and mortality. As in other studies, increasing mortality with increasing CRIB and NTISS scores was also encountered in our study[11,12].

Perinatal risk factors in our study (no prenatal care, maternal hypertension, chorioamnionitis, multiple births) were found to be high when compared with the reports of other international and national neonatal networks[7,8]. Multiple births comprised 44.3% of the study group. Compared to NICHD statistics (22%), multiple birth ratio was high because of increased application of artificial conception modalities in our center. Maternal age distribution, cesarean section rate and APGAR scores seemed to be similar[7,8]. Antenatal steroid administration was 55.6% in the study group and needs further improvement.

More than half of the infants received respiratory support; 24.8% were administered surfactant and approximately half of the surfactant-treated infants were on supplemental oxygen on the 28th postnatal day. These ratios are less than those reported by other neonatal network outcomes[7,8]. It may be due to smaller number of survivors in ELBW infants or due to strict national surfactant treatment strategies which limit prophylactic surfactant administration and favor early rescue with surfactant after at least a brief mean airway pressure application.

Among major morbidities, early septicemia was high, which might be a result of high maternal chorioamnionitis. This in turn may also be an important contributing factor for the occurrence of prematurity.

Percentages of severe IVH, threshold ROP and PDA were less compared to Canadian and NICHD outcomes[7,8]. In the current study, 23% of the infants enrolled were ELBW infants, whereas in the other reports ELBW infants accounted for around 45%. Thus, in the industrialized countries increased survival of ELBW infants with younger gestational ages may have a contribution to higher incidence of IVH and ROP. PDA occurrence is less due to strategies that favor more restricted fluid volumes given to the small prematures during the first days.

This study provides a view to assess the care and outcomes in our unit on an ongoing basis and can provide an insight for improving our clinical practices with the existing evidence. We also hope to provide a model for developing at least a regional database.

Acknowledgement

We would like to acknowledge Suat Fitöz, MD, the teaching staff of the Pediatric Cardiology Department and Associate Professor İlgi Ertem, MD, and Figen Batuoğlu, MD, for their assistance in cranial ultrasounds, echocardiographies, neurodevelopmental assessment and ROP examinations, respectively.

REFERENCES

1. Chye JK, Lim CT. Very low birth weight infants-mortality and predictive risk factors. Singapore Med J 1999; 40: 565-570.
2. Okoji GO, Oruamobo RS. Survival in very low birth weight infants at the University of Port Harcourt Teaching Hospital, Nigeria. West Afr J Med 1992;11: 1-6.
3. Erdem G, Tuncer M, Oran O. Premature infant mortality rates for five years at the Hacettepe University, 1978, 4-6 September Marseille-France XI Congress of the Union of Eastern and Mediterranean Pediatrics Societies Abstract Book, p. 112.
4. Erdem G, Tekinalp G, Yurdakök M. Mortality rates of premature infants in Turkey, 1992, 6-10 September Rio de Janerio-Brasil XX International Congress of Pediatrics Abstracts, p. 171.
5. Erdem G, Topçu M, Yiğit Ş, et al. Çok düşük doğum ağırlıklı çocukların nörolojik, elektrofizyolojik ve psikometrik yönden uzun süreli izlemi. Çocuk Sağlığı ve Hastalıkları Dergisi 1999; 42: 19-26.
6. Erdem G, Tekinalp G, Yurdakök M, Oran O, Tuncer M. Hacettepe Üniversitesi Çocuk Hastanesi premature mortalite istatistikleri. Çocuk Sağlığı ve Hastalıkları Dergisi 1994; 37: 361-371.
7. Stevenson DK, Wright LL, Lemons JA, et al. Very-low-birth-weight outcomes of the National Institute of Child Health and Human Development Neonatal Research Network, January 1993-December 1994. Am J Obstet Gynecol 1998; 179: 1632-1640.
8. Lee SK, McMillan DD, Ohlsson A, et al. Variation in practice and outcomes in the Canadian NICU Network. Pediatrics 2000; 106: 1070-1079.
9. State of the World's Newborns. A Report from Saving Newborn Lives/Save the Children, 2002, Dubowitz LMS, Dubowitz V, Goldberg C. Clinical assessment of gestational age in the newborn infant. J Pediatr 1970; 77: 1-10.
10. Dubowitz LMS, Dubowitz V, Goldberg C. Clinical assessment of gestational age in the newborn infant. J Pediatr 1970; 77: 1-10.
11. Lubchenco LO, Hansman C, Boyd E. Intrauterine growth in length and head circumference as estimated from live births at gestational ages from 26 to 42 weeks. Pediatrics 1966; 37: 403-408.
12. Tarnow-Mordi WO, Parry G, Moore J, et al. The CRIB (Clinical Risk Index for Babies) score: a tool for assessing initial neonatal risk and comparing performance of neonatal intensive care units. Lancet 1993; 342: 193-198.
13. Gray JE, Richardson DK, McCormick MC, Workman-Daniels K, Goldman DA. Neonatal therapeutic intervention scoring system (NTISS): a therapy-based severity of illness assessment tool. Pediatrics 1992; 90: 561-567.
14. Northway WH Jr, Rosan C, Porter DY. Pulmonary disease following respiratory therapy of hyaline membrane disease. N Engl J Med 1967; 76: 357.
15. Papile L, Burstein J, Burstein R, Koffler H. Incidence and evaluation of subependymal and intraventricular hemorrhage: a study of infants with birth weights less than 1500. J Pediatr 1978; 92: 529-534.
16. Bell MJ, Ternberg JL, Feigin RD, et al. Neonatal necrotizing enterocolitis, therapeutic decisions based on clinical staging. Ann Surg 1987; 187: 1-7.
17. American Academy of Pediatrics. Committee members: an international classification of retinopathy of prematurity. Pediatrics 1984; 74: 127-133.
18. Philip AG, Hewitt JR. Early diagnosis of neonatal sepsis, Pediatrics 1980; 65: 1036-1104.