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ORIGINAL ARTICLE

Effect of perinatal period and obstetric characteristics on neonatal mortality and morbidity in preterm SGA and AGA babies with a birth weight of 1000–2000 g

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ABSTRACT

Objective: Our study aimed to present obstetric follow-up data, neonatal mortality, short-term neonatal morbidity, and 2-year infant neuromotor development follow-up data in preterm, 1000–2000 g birth weight cases.

Material and Methods: The study was carried out with 148 cases. Two groups were formed with fetal birth weights below the 5th percentile and in the 5th–95th percentile range. Demographic and obstetric characteristics, fetal well-being tests, and antenatal and neonatal characteristics were evaluated. Neurological follow-up of babies continued at Metin Sabancı Spastic Children Foundation for 2 years.

Results: The study groups consisted of 63 small for gestational age (SGA) and 85 appropriate for gestational age (AGA) infants. Neuromotor development follow-up of 75 living infants continued for 2 years. There was no statistically significant difference between the two groups for the nonstress test, umbilical arterial blood gas pH and base deficit values, 1st and 5th minute Apgar scores, infant general condition. The 1st and 5th minute Apgar scores were statistically highly significant for deceased newborns in both groups (p=0.020 and p=0.012, respectively). Early neonatal morbidity and mortality rates and neuromotor development problems at 6–12 months in SGA and AGA groups were similar. At the end of two years, no pathological diagnosis was reported for motor and reflex development in 75 cases.

Conclusion: The gestational week of the SGA group is significantly ahead at birth, but the short- and long-term neonatal morbidities are similar for both groups. Our study reports the data of our clinic from 20 years ago. The infant mortality rate has shown a declining trend in recent years, but low birth weight infants are still at increased risk for mortality. Reinterpretation of morbidity and mortality data of preterm infants will be beneficial, together with innovations and improvements in neonatal care.

Keywords: Low birth weight, neonatal morbidity, neonatal mortality, preterm labor.

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INTRODUCTION

Preterm birth is a leading cause of neonatal mortality and morbidity.[1] Due to the difference created by geographical and demographic characteristics, the rate of preterm birth has been reported in the range of 6%–15%. Preterm babies account for 75% of neonatal deaths. Preterm birth is responsible for 50% of long-term morbidity.[2]

Fetal growth restriction (FGR) is defined as birth weight below the 10th percentile or the 5th percentile according to the week of gestation. Long- and short-term morbidity and mortality outcomes of babies with a low birth weight according to the gestational week at birth may be different. The condition leading to FGR may also lead to hypoxia and acidemia due to decreased uteroplacental perfusion.

Our study aimed to present obstetric follow-up data, neonatal mortality, short-term neonatal morbidity, and 2-year infant neuromotor development follow-up data in preterm, 1000–2000 g birth weight, small for gestational age (SGA), and appropriate for gestational age (AGA) cases.

Although our study was conducted with a small case group, the aim of this study is to present the data of our hospital. In the last 20 years, neonatal mortality and morbidity have undergone a transition with changes in the health system in our hospital and in Turkey. While the infant mortality rate was 13.9 per thousand in 2009, it was reported as 9.1 per thousand in 2019. These data of the year 2000 presented by our study will also form a comparison to show this change.

MATERIAL AND METHODS

The study was carried out with 148 cases delivered in Zeynep Kamil Women's and Children's Disease Training and Research Hospital, Istanbul, Turkey, between November 2000 and January 2001.

Cases diagnosed with maternal chronic disease, fetal chromosomal disease, and fetal anomaly were excluded from the study. Cases with birth weights above 1000 g and below 2000 g were included in the study. The gestational weeks were confirmed with the last menstrual period and first trimester ultrasonographic crown-rump length measurement. After birth, weeks of gestation were confirmed by the Dubowitz[3] scoring system.

Two groups were formed in the study. The first group was the cases with a birth weight between the 5th and the 95th percentile according to the week of gestation (AGA), and the second group was the cases with a birth weight below the 5th percentile (SGA) according to the week of gestation. The weight percentile table reported by Doubilet et al.[4] was used to determine the weight percentile according to the week of gestation.

Information about maternal age, parity, antenatal follow-up, consanguineous marriage, family history of disabled children, perinatal infant death, and preterm birth were questioned. Delivery type, birth weight, gender, 1st and 5th minute Apgar scores, and postpartum pediatrician's examination information about the infant's general condition were recorded. Information on the length of stay in the neonatal intensive care unit, neonatal complications, treatments, survival, and death was collected.

Cardiotocography follow-up was performed in cases where emergency termination of pregnancy was not decided during hospital follow-up. Umbilical artery blood flow could be evaluated by Doppler ultrasonography in cases followed up during weekday working hours.

In the prenatal period, maternal antibiotic therapy, maternal corticosteroid applications, and tocolytic treatment information were recorded.[5] If 24 h have passed since the last steroid dose, the dose was considered complete. Preeclampsia, eclampsia, HELLP syndrome, and premature rupture of membranes were diagnosed with clinical findings, follow-up, and laboratory data.

After delivery, 2 cc of blood was drawn from the umbilical artery into a heparinized syringe, and blood gas and electrolytes were studied. A pathological value of pH<7.2, base deficit<-10 was accepted.[6]

Neurological follow-ups of babies discharged from the neonatal intensive care unit continued at Metin Sabancı Spastic Children Foundation.

A physiotherapist and a specialist neurologist doctor within the foundation accepted the babies for follow-up. Babies were also evaluated by a psychologist. Parents were informed about the risks that may arise from preterm birth and their baby's low birth weight. Families were informed about the risks waiting for preterm and low birth weight babies. Babies were called for their first control at 4–6 months after birth. In these follow-ups, the motor and reflex developments of the babies were evaluated according to their corrected months.

Gross Motor Function Test for motor evaluation and Vojta tests for reflex evaluation were performed by a neurologist and a physiotherapist. A psychologist evaluated the babies using the Denver test.[7] With the cooperation of the families, the continuation of the physiotherapy of the babies both at the foundation and at home conditions was ensured. At the end of the second year, infant follow-up information was presented to the research team as a report.

SPSS (Statistical Package for Social Sciences) for Windows 10.1 program was used for statistical analysis. While evaluating the study data, Student's t-test was used to compare quantitative data as well as descriptive statistical methods (Mean, standard deviation). For qualitative data, the chi-squared test, Fisher's exact chi-squared test, and odds risk ratios were used. The results were evaluated at the 95% confidence interval and the significance level of $p<0.05$.

RESULTS

The study was carried out with 148 cases who were delivered in the Zeynep Kamil Women's and Children's Disease Training and Research Hospital, İstanbul, Turkey, in November 2000, December 2000, and January 2001.

The ages of the cases ranged from 17 to 39 years, and the mean age was calculated as 25.8±5.2 years. The study groups consisted of 63 SGA birth weight and 85 AGA birth weight infants. Nine babies from the group diagnosed with SGA and 22 babies from the group diagnosed with AGA were lost in the perinatal period. The number of babies who continue their neuromotor development follow-up was 75.

Table 1 shows maternal demographic and obstetric characteristics. Maternal age, inadequate antenatal follow-up, poor obstetric history, consanguineous marriage, cesarean section rates, HELLP syndrome, premature rupture of membranes, and incomplete maternal steroid dose were compared for SGA and AGA groups. There was no statistically significant difference between groups ($p>0.05$).

Table 1: Maternal demographic and obstetric characteristics

	SGA (n=63)		AGA (n=85)		p	OR (95% CI)
	n	%	n	%		
Maternal age, Mean±SD	25.2±5.0		26.3±5.4		>0.05	
Parity, Mean±SD	1.6±1.1		3.3±1.5		**<0.01***	
Bad obstetric history	6	9.5	16	18.8	>0.05	
Consanguineous marriage	4	6.3	5	5.9	>0.05	
Inadequate antenatal follow-up	32	50.8	43	50.6	>0.05	
Cesarean section	36	57.0	38	45	>0.05	
Preeclampsia	26	41.3	11	12.9	**0.001***	**4.72 (2.10–10.60)**
HELLP	5	7.9	2	2.4	>0.05	3.57 (0.67–19.07)
Preterm rupture of membranes	14	22.2	30	35.3	>0.05	
Incomplete betamethasone dose	38	60.3	48	56.4	>0.05	

*: p<0.01 was statistically highly significant; SGA: Small for gestational age; AGA: Appropriate for gestational age; CI: Confidence interval; OR: Odds ratio; HELLP: Hemolysis, elevated liver enzymes, low platelet; SD: Standard deviation.

Parity was calculated to be 1.6±1.1 in the SGA group and 3.2±1.5 in the AGA group. It showed a statistically significant difference (p<0.001). Twenty-six (41.3%) cases in the SGA group and 11 (12.9%) cases in the AGA group were diagnosed with preeclampsia. A highly significant difference was found between the two groups (p=0.001). It was found that being preeclamptic brought a 4.72-fold increased risk of being diagnosed with SGA (95% CI: 2.10–10.60) (Table 1).

The gestational week at birth was 35.0±1.4 weeks in the SGA group, while it was 32.7±1.9 weeks in the AGA group, and there was a statistically significant difference (p=0.0001). Both groups were similar in terms of parity and gender. Birth weights and birth weeks of babies who died in both SGA and AGA groups were found to be statistically significantly lower than those of surviving babies (p<0.001).

While five babies with meconium were delivered in the SGA group, no babies with meconium were delivered in the AGA group (p=0.013). Umbilical artery Doppler examination could be performed in 57 of the cases. The high umbilical artery S/D ratio was 30.8% in the SGA group and 6.5% in the AGA group (p<0.033). There was no statistically significant difference between the two groups for non-stress test, umbilical arterial blood gas pH and base deficit values, 1st and 5th minute Apgar scores, and infant general condition. Fifty percent of the infants with pH<7.2 in the AGA group and 25% of the infants with pH<7.2 in the SGA group died (Table 2).

In this study, the base gap value was found to be normal in all cases. Although there was no statistically significant difference, the rate of pH<7.2 cases in the SGA group was 42.1% higher than in the AGA group (23.1%). When surviving and deceased babies were compared, it was found that pH<7.2 increased the risk of neonatal death with an odds ratio (OR)=5.4 (95% CI: 1.1–25.8) (p=0.025). Neonatal death with a pH<7.2 for SGA and AGA babies was OR=3.33 (95% CI:0.246–45.10) and OR=9.0 (95% CI:1.031–78.57), respectively. The results were only statistically significant for the AGA group.

The 1st and 5th minute Apgar scores were 6.4±1.5 and 8.3±1.0 for surviving infants and 4.7±1.9 and 6.7±1.5 for deceased infants in the SGA group (p=0.020). Also 1st and 5th minute Apgar scores showed a statistically significant difference between living and deceased babies in the AGA group (p=0.012).

There was no statistically significant difference in infant mortality rates and length of stay in the neonatal intensive care unit in the SGA and AGA groups. Respiratory distress syndrome (RDS), intraventricular hemorrhage (IVH), necrotizing enterocolitis (NEC), and disseminated intravascular coagulopathy (DIC) rates were similar for the two groups. Of the 148 cases, 31 died in the neonatal period. Neuromotor development could be followed up to the end of the second year in 75 of the living babies. Both groups were similar in terms of neuromotor development problems at 6–12 months (for SGA, 10 babies, 33.3%; for AGA, 14 babies, 32.6%). At the end of 2 years, no pathological diagnosis was reported for motor and reflex development in 75 cases. Two cases from each group died in the late neonatal period (Table 3).

The response to contraction stress test, umbilical artery Doppler indices, arterial blood gas values, infant general condition, number of premature rupture of membrane cases, HELLP syndrome, preeclampsia, completion of steroid dose, and delivery type were compared for both groups separately in survived and not-survived cases, and they were found to be similar for both groups.

DISCUSSION

Fetal viability has been defined differently in many publications. At one end, the age at which the fetus can survive in the extrauterine environment, regardless of life expectancy and quality, was accepted as the limit, and at the other end, it was stated as the time when viability as well as the ability to grow and develop normally.[8,9]

Table 2: Fetal well-being tests and antenatal and neonatal characteristics for SGA and AGA groups

	SGA (n=63) n (%) or Mean±SD	p	AGA (n=85) n (%) or mean±SD	p
Gender (male)	29 (46.0%)		46 (54.1%)	>0.05
Gestational week	35.0±1.4	0.001	32.7±1.9	0.001
	Survived, not survived		Survived, not survived	
	35.2±1.2, 33.5±1.7		33.2±1.7, 31.3±1.8	
Birth weight (g)	1552±275		1638±258	>0.05
	Survived, not survived		Survived, not survived	
	1605±244, 1233±238	0.001	1698±228, 1466±265	0.001
Meconium staining	5 (7.9%)		0 (0%)	>0.05
Nonstress test (n=130)				
Category 2–3	40 (70.2%)		55 (75.4%)	
Category 1	16 (28.1%)		14 (19.2%)	
Umbilical arterial Doppler (n=57)				
Normal	16 (61.5%)		28 (90.3%)	
High S/D	8 (30.8%)		2 (6.5%)	
EDAF	2 (7.7%)		1 (3.2%)	
Umbilical arterial pH–base excess (n=45)				
N	11 (57.9%)		20 (76.9%)	
N-NA	8 (42.1%)		6 (23.1%)	
General condition of the baby				>0.05
	17 (27.0%)		20 (23.5%)	
	36 (57.1%)		52 (61.2%)	
	10 (15.9%)		13 (15.3%)	
	Survived, not survived		Survived, not survived	
Apgar 1	6.4±1.5, 4.7±1.9	0.004	6.3±1.4, 5.5±1.3	0.020
Apgar 5	8.3±1.0, 6.7±1.5	0.001	8.2±0.9, 7.6±1.0	0.012

EDAF: End diastolic absent flow; N: Normal values for pH and base excess; N-A:<7.2 pH and <–10 base excess; SGA: Small for gestational age; AGA: Appropriate for gestational age; SD: Standard deviation.

This study was not conducted with a group large enough to reflect preterm mortality and morbidity rates in the population. This study is based on data from a tertiary center 20 years ago. In Turkey, the number of studies with regular and sufficient data on long-term patient follow-up is limited. The data of our study may be valuable to compare the health transition and the development of health care in our hospital in the last 20 years. These advances can be a guide for further regulations.

In this study, neonatal morbidity and mortality data were reported separately for low birth weight SGA and AGA groups. The gestational week at birth was found to be statistically significantly lower in the AGA group (32.7±1.9 and 35.0±1.3, respectively, p<0.05). The fact that the study was limited to babies with a birth weight of 1000–2000 g and the birth weights of the two groups were close caused this difference between the weeks of gestation. In the literature, pregnancies of 2500 g or less are considered as low birth weight, those with a birth weight less than 1500 g are defined as very low birth weight, and those under 1000 g are defined as extremely low birth weight. The reason why the limit was determined as 2000 g in our study is that all babies with a birth weight below 2000 g are followed in the neonatal intensive care unit, even if there is no additional problem in the conditions of our hospital.

Pregnancy-related hypertensive diseases are seen in 7%–10% of all pregnancies. In our study, 41.3% of cases in the SGA group were diagnosed with preeclampsia. As reported before pregnancy-related hypertensive diseases are more common with 14.1% in primigravida.[10] In the first group, 52.9% of the patients were primigravid and 41.3% were diagnosed with preeclampsia. This can explain the low parity for the SGA group.

Table 3: Follow-up results of neonatal period and neuromotor development

	SGA (n=63)		AGA (n=85)		p
	n	%	n	%	
Neonatal death	9	14.3	22	25.9	>0.05
NICU days, Mean±SD	13.03±10.94		14.0±11.47		>0.05
Infection*	14	22.2	20	23.5	>0.05
RDS	9	14.2	13	15.2	>0.05
IVH	1	1.58	2	2.35	>0.05
NEC	1	1.58	2	2.35	>0.05
DIC	–	–	2	2.35	>0.05
6–12 month pathology in neuromotor development**	10	33.3	14	32.6	>0.05
2-year pathology in neuromotor development**	–	–	–	–	>0.05
Late death	2	3.2	2	2.4	>0.05

*: Newborn early and late sepsis, meningitis, and omphalitis; **: Number of patients with long-term follow-up (n=73); NICU: Newborn intensive care unit, RDS: Respiratory distress syndrome; IVH: Intraventricular hemorrhage; NEC: Necrotizing enterocolitis; DIC: Disseminated intravascular coagulopathy; SD: Standard deviation.

As stated above, 7%–10% of pregnancies are complicated by hypertensive disease and 5%–7% of all pregnancies are diagnosed with preeclampsia.[11] A close relationship has been shown between maternal hypertensive disease and restriction in fetal development resulting from uteroplacental circulatory defect developing at the base of vasculopathy.[12,13] Rasmussen and Irgens[14] reported that babies born to preterm preeclamptic mothers tended to have a birth weight below the 10th or 2.5th percentile, which increased 2–5 times compared to preterm babies who were not diagnosed with preeclampsia (OR=2.2–4.7). In our study, preeclampsia was found to be high in the first group at a high level of significance. The 4.72-fold increased risk of growth restriction in the presence of preeclampsia is consistent with the literature. HELLP syndrome is considered one of the complications of severe preeclampsia and eclampsia. In a study published by Sibai et al.[15] in 1993, it was reported that almost 20% of preeclampsia–eclampsia cases were diagnosed with HELLP syndrome. In our study, HELLP syndrome developed in 7 (18.9%) of 37 preterm preeclamptic pregnant women. In the group with intrauterine growth retardation, HELLP was found at a rate of 7.9%, compared with 2.4% in the other group. Although not evaluated as significant, being diagnosed with HELLP syndrome for developmental disability poses a 3.57-fold risk.

For the first time, J. Whitridge Williams[16] observed in 1903 that the appearance of meconium was an indicator for asphyxia. In a study conducted by Ramin et al.,[17] in 8000 births with meconium, it was reported that meconium aspiration syndrome was significantly associated with asphyxia at birth. Asphyxia and meconium in amniotic fluid are more common in cases with restricted fetal growth. In our study, out of 148 cases, meconium was detected only in 5 pregnancies from the SGA group. One of these babies was lost.

Doppler sonographic examination is the appropriate method for imaging chronic fetal hypoxia secondary to uteroplacental perfusion disorder. Umbilical artery systole/diastole blood flow value and pulsatility index are indicative of negative outcomes in the intrauterine and neonatal period, especially in infants with impaired intrauterine development.[18] Baschat et al.[19] reported that adverse fetal arterial and venous changes occur before abnormal biophysical profile findings, but the time between the two is around 24 h. In our study, high Doppler values within the SGA group constituted a significant difference with 30.8% and end-diastolic flow loss was observed in 2 (7.7%) cases. Doppler flow values of 90.3% of the cases in the AGA group were within normal limits. Today, all cases diagnosed with FGR in our clinic can be evaluated with Doppler USG 24/7. In this regard, we can say that during 20 years, the technical equipment of our clinic, medical residency training, and the skills of the experts in the field have shown improvement and progress.

Lin et al.[20] studied fetal blood gas and blood lactate levels in their study with 37 FGR and 108 normally developing infants and reported that infants with reduced development had less endurance for labor. In our study, the base gap value was found to be normal in all cases. Although there was no significant difference between the pH values of the SGA and AGA groups, the infants who died in both groups had significantly lower umbilical artery pH values than the surviving infants. Secondary analyses of a prospective cohort have shown that mild acidemia is associated with neonatal morbidity in term infants and the risk of morbidity increases as umbilical artery pH decreases.[21] It has also been reported that metabolic acidemia increases all neonatal risks in deliveries before 34 weeks.[22] The results of our study are consistent with these data.

Preterm rupture of membranes (PROM) is the cause of 25%–40% of preterm labor.[23] Of the 148 cases, 29.7% were PROM cases. In our study, the leading cause of preterm labor in the SGA group was preeclampsia. In the AGA group, 35.3% of the cases were diagnosed with PROM, and it is the most common cause of preterm birth in the AGA group, which is consistent with the literature.

In this study, neonatal death was determined as 14.3% in the SGA group and 25.9% in the AGA group. Studies conducted in the early 1990s advocated the idea that stress due to FGR accelerates lung maturation and that preterm labor poses less risk in these pregnancies.[24] In our study, the week of gestation was significantly higher for the SGA group. Of the lost cases in the AGA group, 57% were born at 28–31 weeks of gestation. This may explain the high neonatal mortality in the AGA group. In the study, the gestational week averages of the groups were different, and birth weight averages were similar. Chard et al.[25] investigated the relationship between RDS and neonatal infant death and infant birth weights and reported that both were associated with gestational week rather than birth weight.

Many studies reported different opinions on the effects of mode of delivery on neonatal mortality and short- and long-term morbidity in preterm pregnancies.[26] There was no difference between SGA and AGA groups in terms of delivery types. An abdominal delivery rate of 50% is high, but the study was conducted with low and very low birth weight cases and the accompanying obstetric problems may explain this.

In a comparative study, it was reported that hyaline membrane disease is more common in AGA infants but more severe in SGA infants, and therefore neonatal deaths due to respiratory causes are higher in SGA infants.[27] Sung et al.[28] could not find a difference in neuromotor development follow-ups between SGA and AGA babies at the end of 3 years, but they reported suspicious neurological findings for AGA babies in the birth weight comparison evaluation.

It has been reported that SGA babies need a ventilator more frequently and for a long time due to RDS.[29] A cross-sectional study of 7-year-old children in China reported that there was a 1.9-fold increased risk of cerebral palsy for preterm SGA infants and 4.2-fold increased risk for term SGA infants, and intrauterine growth restriction was an independent risk for cerebral palsy. It is stated in the literature that babies born in the preterm period due to preeclampsia are a high-risk group for neuromotor development problems.[30] When Simchen et al.[31] evaluated preterm SGA and AGA babies, they showed higher mortality and neonatal infection frequency for SGA babies, and they explained this with suppression of neutrophil production due to impaired oxygenation as a result of placental insufficiency in babies with developmental disabilities. Contrary to the previously advocated view of accelerated lung maturation for SGA infants, they found no difference in RDS between the two groups. It was reported that there was no difference between the two groups for IVH and NEC. In our study, no difference was found between the two groups for RDS, IVH, and NEC. Considering the causes of death, there is no significant difference between the rates of RDS, IVH, NEC, and DIC. Sixth to twelfth month neuromotor test results were similar for both groups. Considering the 2-year neuromotor follow-up, there was no infant diagnosed with cerebral palsy.

Eventually, the gestational week of the SGA group is significantly ahead at birth, it is noteworthy that short- and long-term neonatal morbidity in the 1000–2000 g weight range is similar for both groups.

For developed societies, keeping low and very low birth weight babies alive has led to an increase in long-term morbidity. In these babies, the struggle is given for problems such as motor development retardation and school-period learning difficulties. For developing societies, it should be essential to determine the statistics, prevent preterm labor, and provide maternal and fetal services as much as possible with early hospital admission. It will be possible for the team that will take responsibility for this to be aware of the real numbers through studies conducted with a large number of cases. In this way, prediction of fetal mortality and morbidity can be achieved at the stage of medical decision.

Our study reports the data of our clinic 20 years ago. The neonatal mortality rate in babies with a birth weight of 1000–2000 g in the year 2000 was found to be 20.9%. In 20 years, conditions have changed and life rates have improved. The infant mortality rate has shown a declining trend in recent years, but low birth weight infants are still at increased risk for mortality.[32] The increase in the viability of preterm and low birth weight babies brings an increase in the number of individuals living with neurological and developmental problems. The fact that no sequelae were detected for both groups in the 2-year neuromotor development follow-ups in our study can be explained by the possibility that the cases that will survive with the sequela died in the neonatal period. It will be instructive to study current neonatal morbidity, mortality, and long-term neurological development data with a similar group of patients.

Statement

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – AK; Design – AK, HAT; Supervision – HAT; Resource – AK, ED; Materials – ED, PK; Data Collection and/or Processing – HAT, NUT, NUK; Analysis and/or Interpretation – HAT, NUK; Literature Search – NUT, HAT; Writing – HAT; Critical Reviews – HAT.

Conflict of Interest: The authors have no conflict of interest to declare.

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