Retarded Fetal Growth Patterns and Early Neonatal Mortality in a Mexico City Population[1]

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The study reported here classified 9,660 newborn infants delivered at a maternal and child health center in Mexico City by length of gestation, presence or absence of growth retardation, and (in the case of growth-retarded infants) proportionate or disproportionate growth retardation in terms of the infants' weight and length. It was found that preterm infants (delivered before 38 weeks of gestation) had nine times the early neonatal mortality of term infants, irrespective of growth retardation patterns. Also, the type of fetal growth retardation involved (proportionate or disproportionate) in those cases where such retardation was present was found to have an impact on early neonatal mortality. That is, preterm and term infants classified as having proportionate growth retardation respectively exhibited 1.5 and 9.5 times the early neonatal mortality of preterm and term infants with disproportionate growth retardation. Among other things, these findings suggest a need for assessing types of growth retardation as well as etiologic factors when evaluating mortality risk in newborns.

The significance of low birthweight—in terms of poor prognosis for the neonatal period and subsequent growth and development—is well recognized (*1*). However, low birthweight infants constitute a very heterogeneous group including at least two major subgroups: premature infants and infants small for their gestational age whose intrauterine growth has been retarded. This fact has aroused public health interest in better defining the differential prognosis and etiology of low birthweight (*2, 3*). One of the approaches taken thus far has been to relate the different types of low birthweight to outcomes such as perinatal and neonatal mortality (*4–9*).

When analyzing the relative contributions of prematurity and intrauterine growth retardation (IUGR) to low birthweight and neonatal mortality, a distinction should be made between circumstances prevailing in developed and developing countries. The reason is that prematurity typically makes a relatively greater contribution to low birthweight in developed countries, while in developing countries IUGR or small-for-gestational-age (SGA) infants account for a larger share of those with low birthweight (*2*).

In evaluating the relationship between low birthweight and mortality, an additional distinction should be drawn between different types of low birthweight, because SGA infants are themselves a

[1]The work reported here was supported in part by funds from the Scott Paper Company and Cornell University's Division of Nutritional Sciences and Center for International Studies, through the university's Latin American Studies Program. This article will also be published in Spanish in the *Boletín de la Oficina Sanitaria Panamericana*, vol. 110.

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very heterogeneous group whose subgroups could have different prognoses during the neonatal period. To help assess this matter, birthweight, crown-to-heel length, and gestational age information has been used to subdivide SGA infants into separate risk categories based on the type of IUGR involved (3).

Among the most common distinctions made is one between SGA infants with "proportionate" versus "disproportionate" growth retardation (proportionately SGA infants have experienced comparable intrauterine growth retardation in both weight and length while disproportionately SGA infants have experienced greater retardation in weight relative to length—3). This distinction has proved useful for understanding the causes of SGA and also for understanding the timing of the insult to the fetus during pregnancy (3). Its significance points up the fact that the implications of these two types of IUGR for neonatal mortality risk need to be evaluated—especially in developing countries, where IUGR is the single major contributor to low birthweight.

Specifically, investigations that evaluate mortality among SGA infants with proportionate and disproportionate growth retardation are needed in order to learn more about health implications of the different types of low birthweight through population-based studies. Working along those lines, this article provides an analysis of various retarded fetal growth patterns relative to early neonatal mortality in a Mexico City population.

MATERIALS AND METHODS

The information analyzed was collected retrospectively at the "Maximino Avila Camacho" Maternal and Child Health Center in Mexico City. All infants born at the center during 1981, 1982, and 1983 were included in the study.

The information studied was obtained through a record-keeping system developed by the health center's statistics department. The system required that information reported daily regarding the outcomes of all deliveries be systematically recorded by members of the statistical department's staff. Double-checking was done periodically to ensure the system's reliability.

During subsequent evaluation, special emphasis was placed on information about certain specific variables—notably birthweight, gestational age, crown-to-heel length, and early neonatal mortality. Early neonatal mortality was defined as mortality occurring during the first three days of postnatal life. Birthweight was measured by registered nurses at the center immediately after delivery, using an infant weighing scale that was periodically checked and calibrated. Each infant was weighed to the nearest 10 grams. Gestational age was calculated from the mother's menstrual history by the attending physician. Crown-to-heel length was determined with the child in the supine position using a cloth tape measure, the measurement being recorded to the nearest centimeter.

The ratio of weight to crown-heel length was calculated for descriptive purposes according to Rohrer's ponderal index (weight $\times$ 100/length^3). This index estimates an infant's weight relative to its length and can be compared to reference data giving ponderal index values for different gestational ages (*10*). As can be seen, lower index values apply to infants that are light for their lengths, while higher values apply to those relatively heavy for their lengths.

Multiple deliveries were excluded from the study, as were deliveries for which the data were incomplete. The total number of live births included in the analysis was 9,660.

The scheme employed in this study for

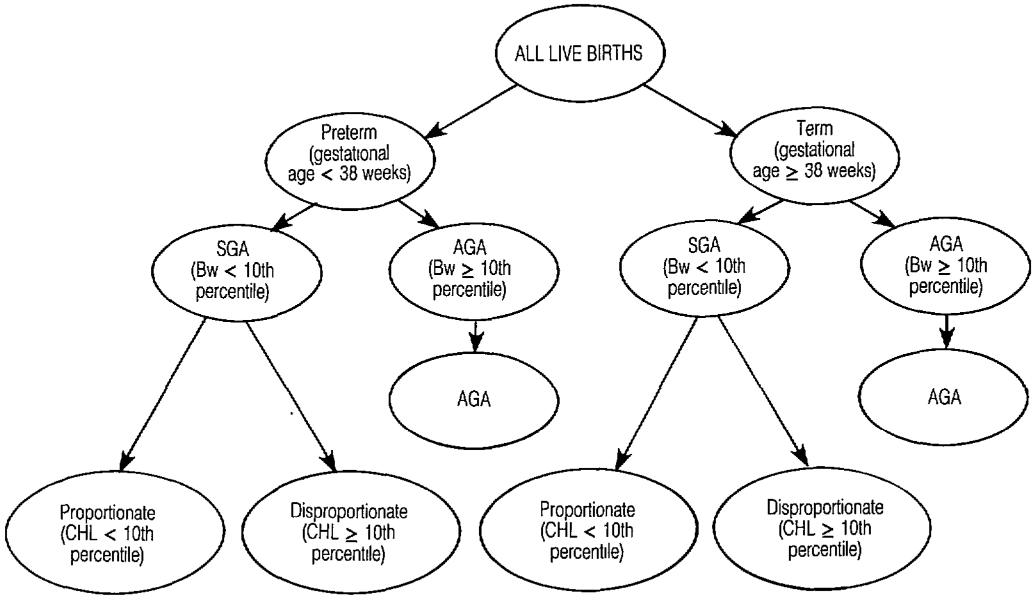

Figure 1. The scheme used for classifying newborns in the study sample. SGA = small for gestational age; AGA = adequate for gestational age; Bw = birthweight; CHL = crown-heel length.

classifying newborn infants is shown in Figure 1. Using gestational age data, all the deliveries were first classified as preterm or term. Following hospital procedures, deliveries occurring before 38 weeks of gestation were considered preterm, all others being considered term.

SGA infants, both preterm and term, were defined as those below the tenth percentile by weight with respect to Lubchenco's reference data (from a U.S. reference population) (*11*). These SGA infants (both preterm and term) were also classified as proportionately or disproportionately growth retarded, depending on whether or not their crown-heel length was below the tenth percentile shown in the same reference data.

Preterm and term infants whose weights were adequate for their gestational ages (AGA infants) were defined as those at or above the tenth percentile by weight with respect to the reference data (*11*).

Chi-square analysis was used to assess the significance of differences in the early neonatal mortality of different groups. Specifically, early neonatal risk ratios and their 95% confidence intervals were calculated for each of the various aforementioned subgroups within the newborn study population (*12*) (see Table 4 and Figure 1).

RESULTS

The observed distribution of newborns according to gestational age and type of fetal growth retardation is shown in Table 1. Using the hospital criterion of prematurity, 11.7% of the newborns were classified as preterm infants and 88.3% as term infants.

Based on the growth retardation classification scheme described above, 9.8% (approximately 10%) of the total infant study population was classified as SGA. Of the SGA infants, 12.6% were classified as proportionately growth retarded and 87.4% as disproportionately growth retarded.

Descriptive statistics regarding se-

Table 1. Distribution of newborn infants according to gestational age and type of fetal growth retardation.

Newborn classification	No.	%
Preterm (gestational age < 38 weeks)	1,134	11.7
Term (gestational age ≥ 38 weeks)	8,526	88.3
Small for gestational age (birthweight < 10th percentile)[a]	952	9.8
Proportionate (crown-heel length < 10th percentile)[a]	*120*	*1.2*
Disproportionate (crown-heel length ≥ 10th percentile)[a]	*832*	*8.6*
Adequate for gestational age (birthweight ≥ 10th percentile)[a]	8,708	90.2
Total sample	9,660	100.0

[a]Cutoff value for Lubchenco's reference growth data (*11*).

lected fetal growth indicators for term and preterm SGA and AGA neonates are shown in Table 2. This table presents the mean and standard deviation values for birthweight, crown-heel length, ponderal index, and gestational age in each of these four groups. The values shown are in the direction expected; that is, the mean values are higher for the AGA infants than for the SGA ones, and are also higher for the term infants than for the preterm ones.

The same descriptive information is presented in Table 3 for proportionately and disproportionately SGA infants. These data are consistent with the nature of the growth retardation categories involved. (Relative to disproportionately growth-retarded newborns, it was expected that the proportionately growth-retarded newborns in both term and preterm groups would have shorter average crown-heel lengths and higher ponderal indexes.)

Table 4 shows early neonatal mortality among different subgroups of the study population. The overall early neonatal mortality for the whole population was 7.9 deaths per thousand live births. Disregarding birthweight, the preterm infants had higher mortality (37.0 per thousand), while the term infants' mortality was substantially lower (4.1 per thousand).

Early neonatal mortality for the infants classified as SGA was 25.2 deaths per thousand live births, as compared to 6.0 per thousand for the infants classified as AGA. An even sharper contrast was found between mortality among preterm

Table 2. Selected growth indicators (mean and 1 standard deviation) found for the study population of term and preterm SGA and AGA infants.

	Preterm infants		Term infants	
	SGA (N = 68)	AGA (N = 1,066)	SGA (N = 884)	AGA (N = 7,642)
Crown-heel length (cm):				
Mean	44.5	48.6	47.8	50.6
1 SD	3.5	3.1	2.2	1.8
Ponderal index ($w \times 100/l^3$):				
Mean	2.08	2.36	2.18	2.45
1 SD	0.31	0.28	0.25	0.24
Gestational age (weeks):				
Mean	36.0	35.4	39.6	39.5
1 SD	1.9	2.1	1.3	1.3
Birthweight (g):				
Mean	1,851	2,747	2,377	3,182
1 SD	360	549	244	373

Table 3. Selected growth indicators (mean and 1 standard deviation) found for SGA infants in the study population with proportionate (prop.) and disproportionate (disprop.) growth.

	Preterm SGA infants		Term SGA infants	
	Prop. (N = 24)	Disprop. (N = 44)	Prop. (N = 96)	Disprop. (N = 788)
Crown-heel length (cm):				
Mean	41.6	46.0	43.4	48.3
1 SD	2.0	3.2	2.3	1.5
Ponderal index ($w \times 100/l^3$):				
Mean	2.34	1.94	2.48	2.14
1 SD	0.29	0.22	0.38	0.20
Gestational age (weeks):				
Mean	36.0	36.1	39.2	39.7
1 SD	1.4	2.1	1.1	1.3
Birthweight (g):				
Mean	1,707	1,930	2,051	2,416
1 SD	320	360	390	184

SGA infants and other groups, the preterm SGA mortality being 161.7 deaths per thousand live births, as compared to 14.7 for the term SGA infants, 29.0 for the preterm AGA infants, and 2.8 for the term AGA infants. These differences are statistically significant ($p < 0.05$).

In terms of the risk ratios shown in Table 4, it can be seen that the preterm and term SGA infants, respectively, experienced 58 and 5 times the relative risk of early neonatal death that was experienced by the term AGA infants. The fact that the lower limit of the 95% confidence interval for each group was greater than one, especially in the case of the preterm SGA infants, indicates statistically greater mortality for these two groups than for the term AGA infants. Similarly, the fact that the 95% confidence intervals

Table 4. Early neonatal mortality (deaths during the first three days per 1,000 live births) among infants in different groups of the study population.

Newborn classification	No. of newborns	Early neonatal mortality	Risk ratio[a]	Confidence interval[b]
Preterm AGA infants	1,066	29.0	10.3	6.6–16.0
Preterm SGA infants	68	161.7	57.7	38.7–85.9
Proportionate	*24*	*208.3*	*74.3*	*45.1–122.2*
Disproportionate	*44*	*136.3*	*48.6*	*28.9–81.7*
Term AGA infants	7,642	2.8	1	
Term SGA infants	884	14.7	5.2	2.7–9.6
Proportionate	*96*	*72.9*	*26.0*	*14.6–46.1*
Disproportionate	*788*	*7.6*	*2.7*	*1.1–6.5*
Total mortality		7.9		
Total live births	9,660			

[a]Risk ratio = mortality of a specific newborn classification group relative to mortality of the term AGA group (2.8 early neonatal deaths per thousand live births).

[b]Upper and lower limits of the risk ratios' 95% confidence intervals.

of the risk ratios for the preterm and term SGA infants did not overlap indicates statistically greater mortality among the preterm SGA infants than among their term SGA counterparts.

Regarding proportionate versus disproportionate growth retardation as previously defined, early neonatal mortality for the disproportionately SGA infants (irrespective of gestational age at birth) was 14.4 deaths per thousand live births, while that for proportionately SGA infants was 100.0 per thousand. When gestational age is considered (see Table 4), it may be seen that term proportionately SGA infants experienced significantly higher early neonatal mortality than their term disproportionately SGA counterparts (72.9 versus 7.6 deaths per thousand live births, respectively), and that this mortality was also higher among the preterm proportionately SGA infants than among the preterm disproportionately SGA infants, though this difference was not statistically significant. Overall, early neonatal mortality among the preterm proportionately SGA infants was higher (208.3 deaths per thousand live births) than among any other study group examined.

On the other hand, disproportionately SGA term infants experienced the lowest mortality (7.6 deaths per thousand live births) of all the infant groups with intrauterine growth retardation (the SGA groups). In terms of risk ratios, the 2.7 figure shown for this group in Table 4 compares favorably with the risk ratios for proportionately SGA term infants (26.0), disproportionately SGA preterm infants (48.6), and proportionately SGA preterm infants (74.3).

In examining the risk ratio 95% confidence intervals shown in Table 4, one finds some overlap between those for proportionately and disproportionately SGA preterm infants; but there is no overlap in those for proportionately and disproportionately SGA term infants, again demonstrating significantly lower risk for the disproportionately SGA term group. Overall, it is worth noting that the risk ratios' 95% confidence intervals are lower for disproportionately SGA infants than for proportionately SGA infants in both the term and preterm categories. It should also be observed that all lower values of the 95% confidence intervals for the four SGA groups are greater than one, indicating statistically greater mortality among these groups than among the term AGA infants.

DISCUSSION

In interpreting these results, several characteristics of the study should be considered, notably: (1) use of the criterion of early neonatal mortality (death in the first three days of life); (2) the definition used for prematurity (delivery at 37 weeks or less of gestational age); and (3) adoption of Lubchenco's growth reference data for purposes of classifying infants as small for gestational age (using the tenth birthweight percentile of Lubchenco's data) and as proportionately or disproportionately growth-retarded (using the tenth crown-heel length percentile of Lubchenco's data).

Early neonatal mortality (defined as mortality in the first three days of postnatal life) involved a three-day time period that coincided conveniently with the shortest time any of the living newborns stayed at the center before being sent home. Obviously, this mortality applies only to the first three days rather than to the entire neonatal period (the first 28 days). Adoption of this criterion is very practical, because mortality data on infant deaths occurring outside of hospitals in developing countries are seldom recorded. Nevertheless, it is possible that some infants may have been kept alive through the first three days by medical intervention and then died later; thus, in this sense the group's risk of early death could have been understated.

The definition of prematurity used in this study was delivery at less than 38 weeks of gestation, the same definition used at the Maximino Avila Camacho Health Center. This classification included more newborns in the preterm group than did the conventional definition of delivery at less than 37 weeks. Overall, 1,134 newborns were placed in the preterm group using the health center criterion, while only 692 would have been included if the conventional (37 week) definition had been used.

One result of this was to lower apparent mortality within the premature group—from 56.3 deaths per 1,000 live births if the conventional criterion had been applied to 37.0 using the hospital criterion actually employed. The reason is that although 442 "extra" newborns were added to the preterm group, only three of them died within three days of delivery. However, the relatively low early neonatal mortality within this group of 442 (6.8 deaths per 1,000 live births) was quite similar to the early neonatal mortality experienced by the 8,526 infants delivered at term according to the health center (38 week) definition, and so it had negligible apparent impact upon mortality within this latter group. (Classification of the study infants as SGA or AGA was unaffected by the definition of prematurity employed.)

The study used a two-stage classification scheme to classify infants first as AGA or SGA, and then to classify the latter as proportionately or disproportionately SGA. Among other things, this approach depended upon information being available on each study infant's gestational age at birth.

Using the definition of SGA employed in the study, the results demonstrated lower early neonatal mortality among the term SGA infants (14.7 deaths per thousand live births) than among all the preterm infants (37.0 deaths per thousand live births). This finding is consistent with results of the few studies done on this subject in developed countries (*5, 6, 13–15*).

More striking, early neonatal mortality among the SGA infants classified as proportionately growth-retarded was found to be seven times higher than mortality among the disproportionately SGA infants. This difference may well be associated with the severity of the growth retardation found in proportionately SGA infants. In turn, the more severe growth retardation of the proportionately SGA infants is probably ascribable to different causes that also compromise survival. This severity is reflected in the substantially lower weights and shorter crown-heel lengths observed in the proportionately SGA group relative to the disproportionately SGA group. (The data in Table 3 show that the proportionately SGA infants had lower mean birthweights and lower crown-heel lengths in both preterm and term categories than did their disproportionately SGA counterparts.)

Table 3 indicates that the differences in birthweight and crown-heel length within these preterm and term SGA groups do not merely reflect differences in gestational age. However, it is possible that the marked difference in mortality observed between proportionately and disproportionately SGA infants is confounded by the difference in birthweight observed in the two groups. Consequently, the results presented should be interpreted with caution.

Even though it would seem that the two-stage classification scheme of growth retardation used in this study was effective for the population to which it was applied, additional research is needed on the independent effects of birthweight and growth patterns on neonatal mortality in developing countries. Furthermore, the fetal growth classification schemes used in this study, especially with regard to the role of disproportionate versus proportionate growth retardation in explaining different rates of neonatal mortality, require further investigation. For example, a study conducted by Haas et al. (*16*), which was done in the same Mexican population as the present study,[4] found differences in the prevalence of proportionately versus disproportionately SGA infants and in the early neonatal mortality experienced by these groups. These differences appear at first sight to contradict the results of the present study.

However, the study by Haas et al. used different criteria for determining prematurity, growth retardation, and proportionate versus disproportionate growth retardation. Infants were classified as preterm if their gestational age was less than 37 weeks at delivery; and they were classified as SGA using a cutoff birthweight of 2,900 grams, which is equivalent to the tenth percentile at 40 weeks of gestation for a composite of several U.S. and European reference populations. The tenth percentile of Rohrer's ponderal index, according to the reference population of Lubchenco et al. (*10*), was used as the secondary indicator to distinguish between disproportionate and proportionate growth retardation.

The differences observed between these studies regarding early neonatal mortality and the percentages of infants in the term, preterm, AGA, SGA, and proportionately versus disproportionately SGA groups probably reflect differences in the classification schemes employed, combined with differences in the errors incurred in applying these schemes. Among other things, this suggests that more studies are needed to evaluate the effect of measurement errors upon results obtained with both of these schemes. In addition, it is important to do research directed at determining what fetal growth standards are most appropriate to use and what cutoff values should be employed in defining patterns of intrauterine growth retardation.

CONCLUSIONS

The results of the work reported here help to underscore a need existing in virtually all developing countries—the need to more thoroughly assess use of combined information on gestational age, birthweight, and crown-heel length at birth in order to better define patterns of intrauterine growth retardation. In addition, when seeking to apply classification schemes such as ours, attempts should be made to include maternal, demographic, medical, and social risk factors in order to identify the etiology of the growth retardation problems observed. In this same vein, when defining the etiology of growth retardation problems, efforts should be made to document the causes of death of all the infant fatalities involved and the type of growth retardation affecting each infant classified as SGA. This sort of analysis of causes of death among these different groups, besides indicating the etiologic factors associated with the different types of growth retardation, can shed new light on the kinds of interventions needed to reduce the risk of early death among growth-retarded newborns.

Acknowledgments. We wish to thank Dr. Calderón and the statistical department of the "Maximino Avila Camacho" Maternal and Child Health Center in

[4]The same study population of newborns delivered at the "Maximino Avila Camacho" Maternal and Child Health Center.

Mexico City for their valuable assistance in data collection.

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