Length and ponderal index at birth: associations with mortality, hospitalizations, development and post-natal growth in Brazilian infants

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Background Low birthweight infants suffer greater mortality and neonatal morbidity, grow less well in infancy and show poorer psycho-motor development. However, this simple categorization may obscure important differences in aetiology and prognosis between infants born stunted, thin, or both.

Methods In 1993, all births in Pelotas, Brazil, were enrolled into a prospective study of health and development in infancy. Of 5249 live births, 5160 had length and weight measures at birth, and were classified into tertiles of length and ponderal index. All deaths and hospitalizations were monitored, and suspected developmental delay and attained growth at 12 months were assessed on a subsample of 1364 infants. Logistic regression was used to control for gestational age and socioeconomic status.

Results There was no association between birth length and ponderal index tertiles. After adjusting for gestational age, infants in the lower tertiles of both length and ponderal index presented a 3.8-times higher risk of mortality from day 8 to day 365, and a 2.5-times higher risk of hospitalization compared to infants with greater birth lengths and/or ponderal indices. Suspected developmental delay was associated with length and, less strongly, with ponderal index, but there was no synergism between the two. Infants in the middle and upper tertiles of ponderal index at birth became thinner.

Conclusions Birth length was strongly associated with development at 12 months, but only infants born both short and thin were at increased risk of mortality and hospitalizations. The combination of the two measures provides a useful classification of the anthropometric status of the newborn.

Keywords Anthropometry, body length, ponderal index, intrauterine growth retardation, infant mortality, hospitalization, child development, growth, Brazil

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The role of low birthweight as the single most important direct determinant of mortality in infancy in industrialized countries is well known. 1 Similar findings have been reported from Latin America and the Caribbean, 2-4 where rates of low birthweight are higher than in Europe or North America. Findings from a large, population-based cohort study in southern Brazil showed that in addition to dying more frequently, low birthweight infants suffered more hospitalizations in the first 12-20 months of life due to diarrhoea and pneumonia, 5 and had persistently lower weight-for-age and height-for-age for at least the first 2 years of life. 6 There is also evidence to suggest that low birthweight children tend to have lower IQs than normal birthweight children. 7
Newborn infants may be small because they have suffered retarded growth in utero and/or because they are born preterm; in addition, there are also individual differences in size among newborns who are neither growth-retarded nor preterm. Although the umbrella classification of low birthweight (<2500 g) is operationally convenient, it is increasingly clear that it may obscure functionally important differences of both aetiology and prognosis. In the case of infants with intrauterine growth retardation (IUGR), there has been a drive to further distinguish between those who are 'proportionately small' (generally defined on the basis of the ratios of different anthropometric measures) and others who are 'disproportionately small'.

More recently, Rosso has cautioned against undue emphasis on the proportionality of growth-retarded infants. He has suggested that skeletal growth, as reflected by body length and head circumference, may have considerable prognostic value for subsequent growth and development of the newborn, whereas soft tissue growth, measured by indices which reflect both body fat and muscle mass, may have better prognostic value for short-term complications. Recognizing that it is possible for a newborn infant to show compromised growth of either type, either in isolation or jointly, and each to a greater or lesser degree, we set out to investigate associations between these characteristics and each of mortality, hospitalizations, development and post-natal growth in a cohort of 5249 infants born in the south of Brazil in 1993.

Methods

The city of Pelotas, with approximately 300,000 inhabitants, is located in the extreme south of Brazil, a relatively wealthy part of the country. All 6410 hospital births occurring during the calendar year 1993 were monitored, with only 16 mothers untraceable or refusing to provide information. In all 5304/6410 infants were born to mothers living in the urban area of Pelotas, and of these, 5249 were born alive. All of these newborns were enrolled into a prospective study of mortality, morbidity, growth and psycho-motor development in infancy. The key features of this study, which is described in detail by Victora et al., are presented in the following paragraphs.

Each of the five maternity wards in the city was visited daily. Newborn infants were weighed using paediatric scales with a precision of 10 g (Filizola, São Paulo, Brazil), which were calibrated each week using standard weights. Supine length was measured using standard techniques and commercially available infantometers (AHRTAG, London, UK). Gestational age was assessed by the study team (paediatrician or senior medical students) using the method of Dubowitz. At the same time, mothers were questioned about their level of schooling and total family income.

Deaths were monitored by means of daily visits to the four main hospitals in the city and weekly visits to a small fifth hospital, supplemented by monthly visits to the public notaries, cemeteries and Regional Delegation of Health. All hospitalizations lasting 24 hours or longer were also monitored by means of hospital visits with similar frequencies.

A sub-sample of 1460 infants were selected for home visits at 12 months of age. In all, 1364 infants (93.4%) were successfully located. 97.5% of these during the infant's month of birth as intended. The procedure for selecting these infants was as follows: at the end of each month, all recorded live births were ordered by date and time of delivery, and a quota of 55 infants was selected systematically. To this sample were added all the remaining low birthweight infants and a further systematic sample of 32 adequate birthweight infants per month (incorporated because additional funds became available). Thus, the 12-month sample consisted of 416 low birthweight infants and 998 adequate birthweight infants selected systematically. The infants were weighed with portable scales with an accuracy of 100 g (CMS, London, UK), and had their supine length measured using standard infantometers (AHRTAG, London, UK). Their psycho-motor development was assessed using the Denver II Developmental Screening Test. Preterm infants had their nominal ages reduced by the difference between their gestational age and 37 full weeks for the purpose of calculating their Denver II scores. A random 5% of perinatal interviews were repeated by different paediatricians to assess data quality. The test-retest reliability of the Dubowitz score was excellent, with a kappa of 0.71 (dichotomous comparison, preterm versus term). A random 5% of the Denver II developmental screening tests were also repeated (test-retest reliability: kappa = 0.72).

Newborn infants were classified according to their length and ponderal index (weight/length^3), a measure of soft tissue growth. Because length was found to vary significantly by sex, measured values were converted to Z-scores using the National Center for Health Statistics reference. Ponderal index at birth did not vary by sex in this population. The tertiles of the length and ponderal index distributions were determined, and infants were classified as short, average or long, and of low, average or high ponderal index. This procedure was repeated for the 12-month sample, with the slight modification that because the low birthweight infants had been deliberately over-sampled at this age, they were proportionally down-weighted in the calculation of the tertile boundaries.

Suspected developmental delay was defined as stipulated by the makers of the Denver II test, as two or more items failed on the screening test. The impacts of length and ponderal index tertile of birth on mortality, hospitalizations (ever versus never) and suspected developmental delay were assessed using logistic regression. In analyses which controlled for gestational age, this variable was included as a continuous variable, using quadratic terms where necessary to allow for any non-linearity in the associations between gestational age and the various outcomes. The study had 80% power to detect an odds ratio (OR) of 3.0 for the mortality outcome (short and thin versus all other categories), 90% power to detect an OR of 1.5 for the hospitalization outcome, and 95% power to detect an OR of 2.0 for the development outcome.

The degree of concordance between tertile rankings of, e.g. length and ponderal index at birth was assessed using a weighted kappa statistic with weighting of 1, 0.5 and 0, so that an individual classified into the same tertile on each measure counted as an instance of perfect agreement, an individual classified into extreme tertiles on the two measures counted as an instance of perfect disagreement, and an individual classified into adjacent tertiles on the two measures counted as 50% agreement. All analyses were performed using SPSS/Windows version 6.0 (SPSS Inc., Chicago, Ill.).

The study was approved by the Scientific Committee of the Faculty of Medicine of the Federal University of Pelotas.
Table 1: Average (SD) birthweight (BW) and gestational age (GA) of infants classified into tertiles of ponderal index and length-for-age Z-score at birth. Pelotas, 1993

<table>
<thead>
<tr>
<th>Ponderal Index (PI)</th>
<th>Length-for-age Z-score</th>
<th>&lt; -1</th>
<th>≥ -1, &lt; 0</th>
<th>≥ 0</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 2.6</td>
<td>Low PI</td>
<td>n = 561</td>
<td>n = 689</td>
<td>n = 533</td>
<td>n = 1783</td>
</tr>
<tr>
<td></td>
<td>BW: 2342 (360)</td>
<td>BW: 2878 (199)</td>
<td>BW: 3342 (297)</td>
<td>BW: 2848 (486)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>GA: 38.1 (2.9)</td>
<td>GA: 39.5 (2.4)</td>
<td>GA: 39.8 (2.0)</td>
<td>GA: 39.2 (2.6)</td>
<td></td>
</tr>
<tr>
<td>2.6–2.8</td>
<td>Average PI</td>
<td>n = 406</td>
<td>n = 565</td>
<td>n = 528</td>
<td>n = 1499</td>
</tr>
<tr>
<td></td>
<td>BW: 2740 (231)</td>
<td>BW: 3186 (141)</td>
<td>BW: 3613 (235)</td>
<td>BW: 3216 (398)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>GA: 38.9 (2.5)</td>
<td>GA: 39.8 (2.1)</td>
<td>GA: 40.3 (1.9)</td>
<td>GA: 39.7 (2.2)</td>
<td></td>
</tr>
<tr>
<td>≥ 2.8</td>
<td>High PI</td>
<td>n = 709</td>
<td>n = 726</td>
<td>n = 443</td>
<td>n = 1878</td>
</tr>
<tr>
<td></td>
<td>BW: 3039 (338)</td>
<td>BW: 3519 (226)</td>
<td>BW: 3987 (335)</td>
<td>BW: 3448 (472)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>GA: 39.3 (2.2)</td>
<td>GA: 39.9 (1.8)</td>
<td>GA: 40.2 (2.0)</td>
<td>GA: 39.8 (2.0)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>n = 1676</td>
<td>n = 1980</td>
<td>n = 1504</td>
<td>n = 5160</td>
</tr>
<tr>
<td></td>
<td>BW: 2733 (442)</td>
<td>BW: 3201 (334)</td>
<td>BW: 3627 (388)</td>
<td>BW: 3173 (523)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>GA: 38.8 (2.6)</td>
<td>GA: 39.8 (2.1)</td>
<td>GA: 40.1 (2.0)</td>
<td>GA: 39.5 (2.3)</td>
<td></td>
</tr>
</tbody>
</table>

Mothers were fully informed of the aims of the study, and their consent was sought before each interview was conducted.

Results

Of the 5249 liveborn infants recruited into the Pelotas cohort, birthweight was recorded for 5232 infants (99.7%) and length at birth for 5162 (98.3%). The present analysis is based on 5160 infants who had both weight and length measured at birth. As described above, infants were divided into approximate tertiles of length-for-age Z-score and ponderal index, forming a matrix with nine possible outcomes. Table 1 shows that in this population there was no association between length and ponderal index tertiles at birth (weighted kappa = -0.05, indicating no more than chance agreement between the two classifications).

As expected, birthweight increased markedly with each of gestational age, birth length and ponderal index. Thus, long infants with high ponderal index weighed >1600 g more on average than infants in the short, low ponderal index group. Shorter infants, and to a lesser extent those with lower ponderal index, tended to have relatively low gestational ages. 29% of infants with low ponderal index and small stature were preterm (<37 weeks gestation), as opposed to only 6% of high ponderal index, large stature infants.

There were 111 infant deaths in this cohort, 62 in the early neonatal period and 49 in the late neonatal or post-neonatal periods. We were unable to analyse the impact of birth length on early neonatal deaths since 38 out of the 62 infants who died in this period did not have their birth lengths measured. Of the 49 infants who died aged one week or older, 43 (87.8%) had valid birth length data. One-third (14/43) of the infants who died in this period were born short and thin, with the result that the mortality rate for days 8–365 was 3–7 times higher in short, thin infants than in infants of the other eight groups, which had two to five deaths each (Figure 1). The 14 short, thin infants who died in the late-neonatal/post-neonatal period had a mean birthweight of 2251 g (SD 469 g) and a mean gestational age of 36.1 weeks (SD 3.1).

Figure 2 shows that hospitalizations were also markedly more frequent among short, low ponderal index infants. This group experienced a rate of hospitalization 2–3 times higher than other infants. We wished to quantify the excess of mortality and...
Table 2 Estimated impact of low ponderal index combined with small stature at birth on late/post-neonatal mortality and hospitalizations, before and after adjusting for gestational age. Pelotas, 1993

<table>
<thead>
<tr>
<th></th>
<th>Unadjusted odds ratio (95% CI)</th>
<th>Adjusted odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All individuals</td>
<td>Individuals with known gestational age</td>
</tr>
<tr>
<td><strong>Late-neonatal/post-neonatal mortality</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n = 5136</td>
<td>n = 4596</td>
<td>n = 4596</td>
</tr>
<tr>
<td>4.13 (2.17–7.86)</td>
<td>4.89 (2.40–9.94)</td>
<td>4.09 (1.92–8.72)</td>
</tr>
<tr>
<td>( P &lt; 0.001 )</td>
<td>( P &lt; 0.001 )</td>
<td>( P &lt; 0.001 )</td>
</tr>
<tr>
<td><strong>Hospitalizations</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n = 5160</td>
<td>n = 4610</td>
<td>n = 4610</td>
</tr>
<tr>
<td>3.34 (2.77–4.04)</td>
<td>3.18 (2.58–3.91)</td>
<td>2.65 (2.13–3.29)</td>
</tr>
<tr>
<td>( P &lt; 0.001 )</td>
<td>( P &lt; 0.001 )</td>
<td>( P &lt; 0.001 )</td>
</tr>
</tbody>
</table>

Infants born both short and thin presented a 4.1-fold greater risk of mortality in the late/post-neonatal period, and a 3.3-fold higher risk of hospitalization. Excluding from the analysis those infants whose gestational ages could not be ascertained slightly increased the estimated OR for mortality to 4.9 (Table 2, column 2). Excluding infants with unknown gestational age did not change the estimated impact of small stature and low ponderal index on hospitalizations. Controlling for gestational age reduced the estimated impact of low stature and low ponderal index for both outcomes, and controlling for maternal education and family income resulted in further small reductions. Nevertheless, even after these adjustments, infants born with short stature and low ponderal index experienced a 4-fold greater risk of mortality in the late/post-neonatal period and a 2.5-fold greater risk of hospitalization.

Figure 3 shows that suspected developmental delay at 12 months was associated both with shorter stature at birth and, to a lesser degree, with lower ponderal index. In contrast to the other outcomes, there was no apparent interaction between length and ponderal index. This observation was confirmed using logistic regression (\( P = 0.41 \)). In spite of the fact that the Denver scores were already corrected for prematurity (see Methods), the odds of suspected developmental delay was found to decrease as a linear function of gestational age. Controlling for gestational age reduced the OR for the lowest length tertile compared to the highest from 3.51 to 2.96. All other coefficients remained essentially unchanged (Length II versus III: OR_{adjusted} = 2.23; Ponderal Index I versus III: OR_{adjusted} = 1.46; Ponderal Index II versus III: OR_{adjusted} = 1.19). Further controlling for maternal education and family income had only a minimal impact on the estimated OR for length and ponderal index at birth, but adding head circumference at birth to the model resulted in a significant attenuation of the coefficients of the other anthropometric variables (Length I versus III: OR = 2.25, II versus III: OR = 2.00; Ponderal Index I versus III: OR = 1.23, II versus III: OR = 1.11).

Figure 4 shows mean change in ponderal index from birth to 12 months of age for the 1336 infants for whom this information was recorded. On average, the infants in the cohort became...
Discussion

These results show that in a cohort of over 5000 Brazilian infants, both mortality and severe morbidity in infancy were heavily concentrated in those born in the lower tertiles of the distributions of both length and ponderal index. These 561 infants (11% of the total) accounted for 14/43 (33%) deaths in the late-neonatal or post-neonatal periods for which valid birth length measurements could be obtained, and 23% of hospitalizations in infancy (208/8897). Interestingly, infants born short but not thin, or thin but not short, did not appear to be at significantly raised risk of either mortality or hospitalization.

We were able to show that part, but by no means all, of the apparent effect of the combination of low stature with low ponderal index at birth on both mortality and hospitalizations could be attributed to the high prevalence of preterm births in this group. Our study had a relatively reliable measure of gestational age, and we were thus able to account for some of the confounding effects of this variable in the adjusted analyses. However, overestimation of the gestational age of the most immature infants, a feature of the Dubowitz method, could have resulted in some residual confounding by gestational age in these analyses. Gestational age was not known for 11% of the infants included in the unadjusted analysis and exclusion of these infants appears to have biased upwards our estimate of the effect on late/post-neonatal infant mortality of low stature combined with low ponderal index at birth.

The ability to adjust for the potential confounding effects of the infants’ socioeconomic environments is an important feature of our study. However, controlling for maternal education and family income did not appreciably alter the estimated impacts of low stature plus low ponderal index on mortality or hospitalizations. It therefore appears that inadequate skeletal growth in utero, when (and only when) combined with inadequate soft tissue growth, is a major risk factor for death and morbidity in infancy, and not simply a marker for gestational immaturity or poor socioeconomic conditions. Previous studies have shown that particularly small infants have a greater risk of severe diarrhoea, and also have narrower airways and thus a greater risk of acute lower respiratory infections and pneumonia.

By dividing our study population into tertiles of length and ponderal index at birth we were able to obtain large numbers in each cell and to describe effects which have major public health impacts in populations comparable to that which we studied. In this population, few infants (7.8%) had birth lengths more than 2 standard deviations below the NCHS median, so that most of the infants in the ‘short’ categories had length-for-age Z-scores between -1 and -2. Thus, the associations reported may be less marked than in studies using a cutoff of -2 Z-scores. However, to our knowledge, no other studies have adequately separated skeletal from soft tissue growth in a large, representative sample of newborn infants using measures uncorrelated at the level of the individual infant. Indeed, there are altogether few studies of the effects of body proportions at birth on medium- and long-term prognosis. In a study of 2609 small-for-gestational age infants in Italy, those who had small head circumferences in addition to low birthweight for their gestational age were found to have markedly higher rates of neonatal mortality than infants with larger heads. There was also some tendency in this study for neonatal morbidity to be higher in the infants with small heads. Various other authors have found that neonatal morbidity tends to be higher in small-for-gestational age infants with low ponderal indices than in similar infants with adequate ponderal indices.

We found that the effect of birth anthropometry on suspected developmental delay at one year was quite different from the effect on mortality and hospitalizations. There was a clear reduction in the risk of developmental delay with both increasing length at birth and (to a lesser degree) increasing ponderal index, but no interaction between the two. As has previously been suggested in relation to intrauterine growth retardation, skeletal growth was shown to be a more important determinant of developmental delay than was soft tissue growth. Indeed, the weak association between ponderal index at birth and suspected developmental delay at 12 months disappeared completely when head circumference at birth was controlled for in our analyses. It should be borne in mind that the Denver II test is a screening test which has been found to have high sensitivity (83%) but limited specificity (43%). The same results would not necessarily have been obtained if a more specific diagnostic test had been used, although it is important to note that at the population level, non-differential misclassification would have the effect of diluting the true association with birth size.

Infants with low length measures at birth showed no clear tendency to catch up in linear growth, whereas those with low ponderal indices were protected from the decrease in ponderal index over infancy experienced by infants with average or high ponderal indices at birth. These findings are consistent with an earlier study of 205 term Guatemalan infants, which showed that infants with birthweight and ponderal index below the 10th centile for gestational age rapidly caught up in weight with infants with birthweights above the 10th centile. On the other hand, infants with low birthweight but adequate ponderal index (who were 2.3 cm shorter at birth than the normal birthweight infants, and 2.8 cm shorter than the low ponderal index infants) never caught up in length. In this same study, there was a marked gradient in cognitive composite score at 3 years of age: the normal birthweight infants had the highest scores, followed by the low birthweight, low ponderal index infants, and then the low birthweight, normal ponderal index infants.

In conclusion, we found a strong, direct association between birth length on the one hand and psycho-motor development and attained length at 12 months on the other. However, only
those infants who were born both short and with low ponderal index were at increased risk of mortality and severe morbidity in infancy. Other authors have shown that both the size and shape of the newborn infant may be related to measurable characteristics of the mother and gestation.\textsuperscript{14,33} We believe that the combination of length and ponderal index at birth may well provide a functionally relevant means of classifying the newborn infant's anthropometric status, since the two measures are relatively independent of each other at the level of the individual, and appear to bear upon different aspects of the infant's subsequent health and development.

Acknowledgements

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References